

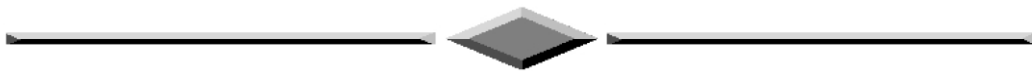
ISSN 2710 – 1681 (ONLINE)

ISSN 2710 – 1673 (PRINT)

National Academy of Sciences of Ukraine  
Institute of Artificial Intelligence Problems MES of Ukraine and NAS of Ukraine

# ARTIFICIAL INTELLIGENCE

2023 № 3 (97)



Національна академія наук України  
Інститут проблем штучного інтелекту МОН України і НАН України

# ШТУЧНИЙ ІНТЕЛЕКТ

2023 № 3 (97)



KYIV 2023

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## INTELLIGENT SYSTEM FOR RADIO-SURGICAL TREATMENT PLANNING USING SPHERES PLACEMENT OPTIMIZATION WITH OVERLAPS

**Annotation.** In this study, we introduce a novel approach employing sphere placement with controlled overlaps to strategically position radiation shots within a three-dimensional tumor characterized as a convex polyhedral set. Our primary goal is to ensure optimal radiation dosage by managing sphere overlaps. We present a method that guides a systematic sphere placement procedure, utilizing predetermined sizes, to achieve a heightened filling coefficient within the tumor volume. Through the dense arrangement of these spheres, we effectively minimize uncovered regions, contributing to improved radiation coverage. The iterative packing process concludes upon reaching the threshold where no additional spheres can be accommodated, accounting for permissible overlaps. The proposed methodology embodies principles of an intelligent system, orchestrating the placement sequence to enhance treatment efficacy. A practical illustration is included to demonstrate the application of our approach.

**Keywords:** sphere, polyhedron, radio-surgical treatment, non-linear programming.

### Introduction

Modern medical practice is constantly evolving, and radiosurgery, as an important area, does not stand aside. Radiosurgery is a unique method of treating tumors and other pathologies, allowing to achieve high efficiency without the need for surgical intervention. However, successful radiosurgery treatment requires not only medical knowledge, but also comprehensive planning to ensure accurate delivery of the radiation dose, minimize the risk of damage to surrounding healthy tissue, and ensure optimal treatment for the patient. In this context, the development of intelligent systems for radiosurgery treatment planning has become critical as they promise to significantly improve the planning process and treatment outcomes.

Intelligent systems in medicine have become reliable partners of doctors and specialists in the field of radiosurgery. They have the ability to analyze large volumes of medical data, including images, biometrics and patient data, allowing them to create accurate and personalized treatment plans.

A major aspect of intelligent systems in

radiosurgery is their ability to optimize treatment planning. This is achieved through the use of machine learning methods and optimization algorithms that take into account the unique anatomical features of the patient and the nature of the tumor. Such systems are able to predict the optimal distribution of radiation dose while minimizing the negative impact on surrounding healthy tissue.

In this context, the article represents an important contribution to the development of intelligent systems for radiosurgical treatment. The article explores an optimization method based on overlapped sphere placement, which can improve the accuracy and efficiency of radiosurgical treatment planning. This method promises to enrich the radiosurgery's toolkit by improving the process of determining radiation dose and reducing the time required to develop treatment plans.

The rest of the article will discuss the details of this method, its advantages and prospects for application in clinical practice, as well as possible challenges and future directions of research.

Gamma Knife radiosurgery is a minimally invasive medical procedure that employs radiation to eliminate tumors within the human body. The Gamma Knife system comprises multiple radiation sources, which emit gamma rays focused on a central point, generating a concentrated high-dose radiation sphere. The main geometric challenge in gamma knife treatment revolves around accurately positioning a series of spheres within a three-dimensional tumor of variable shape. Substantial sphere overlap can result in excessive dosages, whereas controlled, minor overlap is generally acceptable.

The Gamma Knife system generates uneven radiation spheres of varying radii. In practical terms, a commonly employed strategy entails initially identifying the placements for larger spheres and subsequently incorporating smaller spheres in the available space. The primary objective is to minimize radiation exposure to adjacent tissue while maximizing radiation dose to the targeted region. Reducing the overall number of spheres can lead to a decrease in the treatment duration.

### **Recent Research and Publications**

Wang's research, as discussed in [2], delves into an optimization challenge involving the arrangement of dissimilar spheres within a three-dimensional (3D) confined area, particularly in the context of planning for radiosurgical treatment.

The optimization of sphere placement plays a pivotal role in the treatment planning process for Gamma Knife radiosurgery. The research paper [1] delves into the mathematical facets of this optimization challenge. The authors explore diverse mathematical methodologies to determine the most optimal configuration of spheres within the tumor volume. One approach mentioned in the paper involves formulating the issue as an optimization model and utilizing mathematical algorithms to pinpoint the best sphere arrangement. The primary goal is to minimize both excessive radiation due to sphere overlap and insufficient radiation due to low packing density. The authors discuss the complexities tied to this optimization dilemma, including the irregular tumor shape

and the necessity for efficient algorithms capable of addressing extensive-scale problems. The study underscores the significance of striking an optimal balance between sphere overlap and packing density to guarantee accurate and efficient radiation delivery. By diminishing the total number of spheres while upholding satisfactory coverage, treatment duration can be shortened without compromising the quality of radiation therapy.

The study outlined in [3] centers around the utilization of reformulation strategies to tackle an intricate challenge related to sphere coverage in the design of a gamma ray machine for radiotherapy. The issue at hand pertains to determining the most favorable disposition of spheres in order to encompass a designated area, guaranteeing efficient dose administration while mitigating any excessive overlap. Due to its intricate nature, solving this problem can prove to be quite demanding.

The study documented in [6] introduces an approximate algorithm designed for packing spheres within irregularly shaped tumors. The primary goal is to encompass the greatest number of tumor pixels while simultaneously avoiding any interference with healthy tissues. This algorithm employs distance transformation iteratively to generate spheres and presents an innovative technique for the placement of multiple spheres. The research prioritizes the optimization of target coverage over conventional clinical design practices. The algorithm's outcomes exhibit promise, achieving a tumor coverage rate exceeding 90% within a reasonable computation period. A limitation of this algorithm arises when dealing with a small quantity of spheres, which often mirrors practical scenarios.

In [7], the research paper tackles the challenge of arranging spheres of varying sizes within a 3D polytope. The core objectives encompass preventing sphere overlap and maximizing the cumulative volume of spheres enclosed within the polytope. This issue is conceptualized as a non-convex optimization problem featuring quadratic constraints and a linear objective function. The authors propose multiple

algorithms, including a simplicial branch-and-bound algorithm, alongside heuristic strategies aimed at enhancing the optimization process's efficiency.

The study presented in [9] centers its attention on an intermediate quandary that falls between sphere packing and coverage. This particular scenario involves sphere centers positioned on a distinct set of lattices generated from the diagonally skewed integer grid.

In this paper, we tackle the challenge of placing spheres with controlled overlap, aiming to position radiation sources over a three-dimensional tumor represented as a convex polytope. Our methodology ensures an acceptable radiation dose by placing restrictions on sphere intersections. Concurrently, our objective is to attain maximum coverage of the tumor region, emphasizing the achievement of a high sphere distribution density with a specified level of overlap.

### Problem formulation

We consider a set of spheres

$$\mathbf{S} = \{S_1, S_2, \dots, S_N\}$$

with different radii

$$r_i, i \in I_N = \{1, 2, \dots, N\}$$

and a convex polytope

$$P = \{X = (x, y, z) \in \mathbf{R}^3 : A_j x + B_j y + C_j z + D_j \leq 0, \\ j \in J = \{1, 2, \dots, n_f\}\}$$

where  $A_j x + B_j y + C_j z + D_j = 0, j \in J$  are normal equations of the faces,  $n_f$  is the number of faces of  $P$ . We assume that radii of the spheres can take given values  $R_k$ ,

$$k \in I_K = \{1, 2, \dots, K\}, R_1 > R_2 > \dots > R_K.$$

We introduce several parameters that play a pivotal role in the selection of the treatment plan. It is imperative to thoroughly assess the radiation dose administered to various regions of the tumor to guarantee their receipt of sufficient treatment.

$$\text{If } r_i + r_j - \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2} > 0,$$

we define

$$o_{ij} = r_i + r_j - \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2}$$

as an overlap of  $S_i$  and  $S_j, i, j \in I_N, i \neq j$ .

To ascertain the maximum permissible overlap of spheres, it is possible to evaluate the radiation dosage levels at the centers of these spheres. This approach ensures that the combined radiation dosage within the overlapping regions stays within safe and acceptable thresholds during the radiosurgical treatment of tumors.

Additionally, if

$$r_i - (A_j x + B_j y + C_j z + D_j) \geq 0,$$

we define

$$O_{ij} = r_i - (A_j x + B_j y + C_j z + D_j)$$

as an overlap of  $S_i, i \in I_N$ , and

$$P_j = \{X \in \mathbf{R}^3 : A_j x + B_j y + C_j z + D_j \geq 0\}, j \in J.$$

The set defines the tumor's perimeter, while the overlap essentially represents an extension of the sphere beyond the treatment zone – commonly referred to as an 'overhang'. The magnitude of this overhang is directly linked to the acceptable radiation dosage for the healthy tissue encompassing the tumor. Establishing the highest acceptable extent of this overhang is crucial to ensure favorable outcomes in radiation therapy, all the while mitigating any potential negative repercussions on the adjacent healthy tissue.

*Problem.* Place spheres from the set  $\mathbf{S}$  in the polytope  $P$  keeping the maximum allowable overlaps  $o_{ij}, i, j \in I_N, i \neq j$ , the maximum allowable overhangs  $O_{ij} = O_i, i \in I_N, j \in n_f$ , and the maximum limitation for  $d_m = \hat{d}_m$  to maximize the volume of the occupied part of  $P$ .

### Mathematical modelling

Given the lack of foreknowledge regarding the potential quantity of spheres

that can be accommodated within the polyhedron, a more precise mathematical formulation of the packing dilemma can be established as a nonlinear programming problem featuring a step-based objective function:

$$\max \frac{4}{3} \pi \sum_{i=1}^N r_i^3 H_i(v_i, r_i) \quad (1)$$

$$\text{s.t. } X = (v, r) \in W \subset \mathbf{R}^{3N}$$

where

$$H_i(v_i, r_i) = \begin{cases} 1 & \text{if } \Phi_i(v_i, r_i) + O_i \geq 0, \\ 0 & \text{otherwise,} \end{cases} \quad (2)$$

$$W = X \in \mathbf{R}^{3N} : \{(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2 - (r_i + r_j - o_{ij})^2 \leq 0, i < j \in I_N\}. \quad (3)$$

$$\Phi_i(v_i, r_i) = \min \{A_j x_i + B_j y_i + C_j z_i + D_j - r_i, j \in J\}.$$

The inequality  $\Phi_i(v_i, r_i) + O_i \geq 0$  is equivalent to the following system of inequalities:

$$A_j x_i + B_j y_i + C_j z_i + D_j - r_i + O_i \geq 0, j \in J. \quad (4)$$

### Solution method

The issue posed by equations (1)-(4) is a complex one that cannot be readily solved. To address this challenge, we can adopt a decomposition strategy, sequentially positioning spheres of the largest feasible dimensions, while reorganizing the spheres already positioned at each phase. Furthermore, we employ the multi-start technique to enhance the pursuit of an optimal solution, as it explores various initial points for the optimization procedure.

The problem (1)-(4) is transformed into a sequence of problems, where each subsequent problem utilizes the outcomes obtained from solving the preceding ones.

Firstly, we randomly choose a position for the first sphere  $S_1$  with radius  $r_1 = R_1$  within the polytope  $P$  taking into account possible overlaps  $O_{1j}$ ,  $j \in J$ .

Then we try to place spheres  $S_2, S_3, \dots, S_N$  sequentially, solving the following problems:

$$\max \rho_l, \quad l = 2, 3, \dots, \quad (5)$$

$$\text{s.t. } X^l = (v^l, \rho_l) \in W^l \subset \mathbf{R}^{3l+1}$$

where

$$\begin{aligned} W^l = & \{X \in \mathbf{R}^{3l+1} : (x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2 \\ & - (r_i + r_j - o_{ij})^2 \leq 0, \\ & i, j = 1, \dots, l-1, i < j, \\ & (x_i - x_l)^2 + (y_i - y_l)^2 + (z_i - z_l)^2 \\ & - (r_i + \rho_l - o_{il})^2 \leq 0, i = 1, \dots, l-1, \\ & \Phi_i(v_i, r_i) + O_i \geq 0, i = 1, \dots, l-1, \\ & \Phi_l(v_l, \rho_l) + O_l \geq 0\} \end{aligned} \quad (6)$$

$\rho_l$  being a variable radius of  $S_l$ .

If  $(v^l, \rho_l^*)$  is a local maximum point of the problem (5), (6), we take  $r_l = \max_{k \in I_N, \rho_l^* \geq R_k} R_k$  and consider  $X^l = (v^l, r_l)$  as a starting point for next iterations.

### Computational results

We consider the cuboid with sizes. The base corner of the cuboid is located in the origin.

We obtain the placement of 15 spheres illustrate in Fig.1.

Coordinates of centers of spheres are given in Table 2.

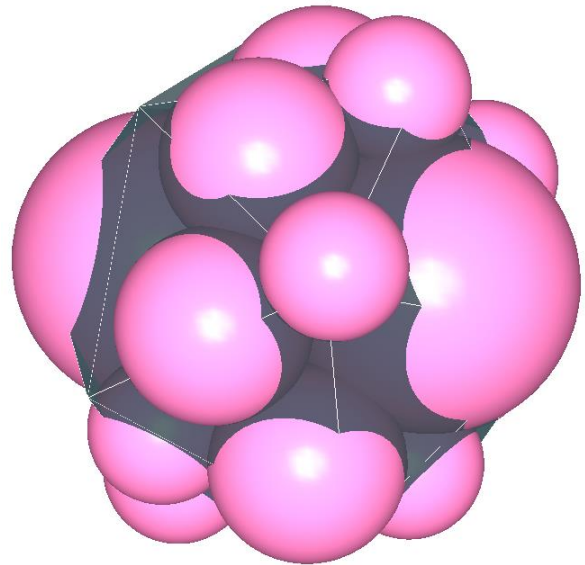


Fig. 1. Illustration of spheres placement

Table 1. Radii and coordinates of the placed spheres

	$r_i$	$x_i$	$y_i$	$z_i$
1	6	6.086204	9.449381	13.120516
2	6	14.455536	13.887612	6.510611
3	4	11.170378	3.240086	9.510000
4	4	15.476932	7.747643	12.780645
5	4	8.764285	18.068663	11.761179
6	4	5.856700	15.630738	5.831249
7	4	7.910047	8.965939	3.263578
8	4	13.324653	13.984235	15.237109
9	3	13.552971	6.742831	2.186175
10	3	1.855787	15.617167	10.515062
11	3	7.879322	15.843331	17.436595
12	3	15.930279	6.113909	6.858569
13	3	12.126251	7.739458	17.949636
14	3	2.372065	9.843667	6.049521
15	3	5.726137	4.523220	6.929419

### Conclusion

In this study, we present a strategy to tackle the challenge of sphere placement with controlled overlaps for positioning radiation sources within a three-dimensional tumor delineated as a convex polytope. Our approach involves a procedural solution for placing pre-defined-sized spheres, optimizing the packing density within the tumor volume. By densely arranging the spheres, we effectively minimize uncovered regions, thus contributing to enhanced treatment outcomes.

The proposed solution algorithm encompasses an approach, where spheres are placed sequentially, with subsequent rearrangements at each stage. To further enhance the search for optimal solutions, the multi-start method is employed, exploring diverse starting points for the optimization process.

One of the primary challenges involves formulating the problem as a nonlinear programming issue with a step-based objective. Our approach adeptly addresses this intricate problem, offering approximate solutions that can be subsequently refined.

The utilization of a random iterative process facilitates the identification of feasible starting points, thereby bolstering the

efficiency and effectiveness of the solution algorithm.

Our research showcases a promising avenue for enhancing automated radiosurgical treatment planning by optimizing the placement of spheres within three-dimensional tumors. This devised method introduces the potential for more precise and targeted radiation therapy, ultimately leading to improved patient outcomes.

Looking forward, future research could be directed towards refining the algorithm, exploring alternate optimization techniques, and undertaking comprehensive clinical validation to further amplify the applicability of our proposed approach in real-world medical scenarios.

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The article has been sent to the editors 08.10.23.

After processing 25.10.23.

Submitted for printing 30.11.23.

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