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A Fuzzy-Based Approach for Optimizing Dose Distribution in High-Dose-Rate Prostate Brachytherapy Using Multi-Objective Evolutionary Algorithms

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Prostate cancer is among the most prevalent malignancies in men, with high–dose-rate (HDR) brachytherapy recognized as an effective treatment modality. A primary challenge in HDR brachytherapy planning is balancing adequate tumor irradiation with protection of surrounding organs at risk (OARs). This study presents a fuzzy-based multi-objective optimization framework to enhance the accuracy, flexibility, and personalization of dose distribution. A fuzzy-constrained integer programming model was developed, incorporating patient-specific factors such as physical condition, age, and physician preferences to support individualized treatment planning.

The framework was evaluated using four state-of-the-art multi-objective evolutionary algorithms (MOEAs)—NSGA-II, SPEA-II, PESA-II, and MOPSO—applied to clinical datasets from 14 prostate cancer patients. All algorithms generated diverse Pareto-optimal solutions, enabling trade-off analyses between tumor coverage and OAR sparing. Among them, a modified MOPSO consistently achieved superior performance, demonstrating higher target coverage, lower variability, and improved solution diversity.

To address uncertainties in tumor volume, gray numbers were employed to represent tumor size. Results indicate that the proposed framework improves planning precision, reduces treatment duration, and provides a robust, clinically applicable methodology for personalized HDR brachytherapy, highlighting the value of integrating fuzzy logic with MOEAs to advance treatment efficacy and planning accuracy.

Keywords: *Prostate Cancer, Brachytherapy, Multi-objective Optimization, Evolutionary Algorithms, Fuzzy Logic.*

1. Non-dominated Sorting Genetic Algorithm
2. Pareto Envelope Based Selection Algorithm
3. Strength Pareto Evolutionary Algorithm
4. Multi-Objective Particle Swarm Optimization

1. Introduction

Prostate cancer is among the most prevalent malignancies affecting men worldwide. Conventional therapeutic strategies include surgical resection, chemotherapy, and radiation therapy, the latter of which may be delivered through external beam radiation (teletherapy) or internal radiation modalities, such as brachytherapy [2]. Brachytherapy involves placing radioactive sources in or near the tumor, allowing direct irradiation of malignant tissue. In contrast, external beam radiation therapy directs high-energy beams through the body. The

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primary advantage of brachytherapy lies in its ability to deliver radiation in close proximity to the target volume [10], enabling precise dose conformation to the tumor while minimizing exposure to surrounding healthy organs. High–dose-rate (HDR) brachytherapy further reduces the number of required treatment sessions compared to external beam approaches.

Despite its clinical efficacy, HDR brachytherapy planning presents significant challenges, particularly in balancing tumor coverage with sparing of organs at risk (OARs) and accounting for patient-specific variability. Existing optimization methods often rely on deterministic or single-objective models, limiting flexibility and personalization, while uncertainties in tumor volume further complicate treatment planning [9].

To address these limitations, this study proposes a fuzzy-based multi-objective optimization framework for HDR brachytherapy. A fuzzy-constrained integer programming model is formulated, incorporating key clinical parameters such as patient condition, age, and physician preferences to enhance individualized planning. The framework employs four state-of-the-art multi-objective evolutionary algorithms (MOEAs)—NSGA-II, SPEA-II, PESA-II, and MOPSO [5] to determine optimal dose rates and enable systematic trade-off analysis between tumor coverage and OAR protection.

By integrating fuzzy logic with evolutionary optimization, this research aims to improve dose distribution accuracy, reduce treatment time, and facilitate patient-centered HDR brachytherapy planning. The proposed methodology addresses critical gaps in current brachytherapy optimization, offering a robust and clinically applicable framework that advances personalized prostate cancer treatment.

1.1. Research Gap

Although multi-objective evolutionary algorithms (MOEAs) have been applied to brachytherapy optimization, several critical gaps remain. First, most existing methods do not adequately address uncertainties in tumor volume or other patient-specific variables. Second, conventional approaches often fail to integrate fuzzy logic, limiting their ability to model the inherent uncertainty and variability present in clinical settings. Third, comprehensive comparative evaluations of different MOEAs for HDR brachytherapy are sparse, leaving open questions about their relative performance in generating clinically relevant, patient-centered treatment plans.

1.2. Contribution and Novelty

This study addresses the identified gaps by proposing a fuzzy-based multi-objective optimization framework for HDR brachytherapy. Key contributions include:

- *Integration of Fuzzy Logic*: A fuzzy-constrained integer programming model is developed to incorporate patient condition, age, and physician preferences, enhancing dose personalization and adaptability.
- *Handling Uncertainty with Gray Numbers*: Tumor volume uncertainty is explicitly modeled using gray numbers, enabling robust and clinically realistic dose planning.
- *Comparative MOEA Evaluation*: Four state-of-the-art MOEAs—NSGA-II, SPEA-II, PESA-II, and MOPSO—are applied to clinical datasets from 14 prostate cancer patients, providing a systematic performance assessment.
- *Clinical Applicability*: The proposed framework improves dose distribution accuracy, reduces treatment time, and generates diverse Pareto-optimal solutions, supporting more precise and individualized HDR brachytherapy planning.

This approach demonstrates significant novelty by combining fuzzy logic, gray number modeling, and evolutionary optimization, offering a clinically viable, patient-centered methodology that advances the state-of-the-art in prostate cancer radiotherapy.

2. Methodology

A treatment plan is considered clinically acceptable if it adheres to established protocols that define the minimum practical dose limits for surrounding healthy tissues. However, it is important to recognize that plans deviating from these protocols may still be regarded as clinically viable [1]. The threshold for acceptable deviation depends on several practical factors, including the potential availability of more effective treatment designs. Typically, a standard brachytherapy (BT) protocol includes dose-volume (DV) indices, with corresponding criteria defined as follows [17]:

- The V_d^o criterion specifies the total volume of organ o that receives at least the radiation dose level d, which corresponds to the prescribed target dose in the treatment plan.
- The criterion D_v^o shows an organ's maximum accumulated volume and the appropriate level of radiation dose.

Table 1: Dosimetric criteria for high-dose brachytherapy treatment planning

Prostate	Bladder	Rectum	Urethra	*Vesicles*
$V_{100} > 95\%$	$D_{1cc} < 86\%$	$D_{1cc} < 78\%$	$D_{0.1cc} < 110\%$	$\mathbf{V_{80} > 95\%}$
$V_{150} < 50\%$	$D_{2cc} < 74\%$	$D_{2cc} < 74\%$		
$V_{200} < 20\%$				

To avoid necrosis (tissue death) in prostate cells due to excessive irradiation, $V_{200}^{prostate} < 20\%$ indicates that the cumulative volume of the prostate covered with at least 200% of the dose should be less than 20% of the prostate [12]. To avoid excessive radiation exposure of the rectum, $D_{1cc}^{rectum} < 78\%$ indicates that a maximum of 1 cubic cm of rectal volume should receive less than 78% of the radiation dose. A crucial step in evaluating a treatment plan involves computing the dose–volume (DV) index values and comparing them against the evaluation criteria presented in Table 1. Dose calculations follow the TG-43 protocol, which accounts for the strength and geometry of the radiation source as well as the distance between the dose calculation points and the dwell positions (DPs). The dosimetric indicators and their acceptable ranges, as outlined in Table 1, constitute the dosimetric criteria, which are based on the TG-43 formalism [13].

3. Operation Method

This study analyzed data from 14 patients, aged 46 to 68 years (mean age: 57), who underwent prostate cancer brachytherapy at the Academic Medical Center (AMC) in Amsterdam, the hospital participating in this research [13], [18]. These data were provided to enable the implementation and evaluation of various algorithms. None of the 14 patients had previously received treatments such as chemotherapy or radiation therapy. Patient selection was based on prostate volumes ranging from 35 to 98 cubic centimeters. To compare brachytherapy treatment plans involving high interstitial doses, the dose rate of Iridium-192 (^{192}Ir) radiation was calculated at 13 Gy/s in accordance with the standard TG-43 protocol.

Computed tomography (CT) or magnetic resonance imaging (MRI) scans of each patient's pelvic region were acquired and imported into the treatment planning software. Brachytherapy specialists—including radiation oncologists, therapists, and clinicians—used these images to identify access catheters, target volumes, and organs at risk (OARs). Depending on the target volume's size and location, between 14 and 20 catheters were inserted to access the designated areas. Each catheter contained multiple dwell positions, typically spaced 2.5 mm apart. As the

radiation source traveled through the catheters, it could be activated at any dwell position, remaining there for a specific dwell time before moving to the next position [13].

The longer the source remained at a given dwell position, the higher the dose delivered to the surrounding tissue. These data were then compiled and used as input for the optimization process. Once an acceptable treatment plan was developed and approved, the implanted catheters were connected to the afterloading (AL) device, which controls the source movement. The source traveled through the catheters, pausing at each dwell position for a set duration. Upon completion of treatment, the source was retracted back into the afterloading device [6].

3.1. Formulating the Fuzzy Multi-Objective Optimization Problem

This section presents a novel model that incorporates two antagonistic objective functions for optimizing high-dose-rate brachytherapy treatment planning. A detailed overview of the model's framework, including its parameters and variables, is provided in Table 2 [8].

Table 2: Definitions of high dose rate brachytherapy model terms.

Idiom	Description
S	Set of organs
I	Set of dose-points
J	Set of dwell positions
G_s	Set of dose values in the *S* organ
P_{si}	Three-dimensional coordinates of the dose-point in $\boldsymbol{G_s}$
N_s	Number of dose points in $\boldsymbol{G_s}$
T_j	Three-dimensional coordinates of position *J*
N_T	Number of dwell positions for the patient
D_{sij}	Transfer dose rate from $\boldsymbol{T_j}$ to $\boldsymbol{P_{si}}$
t_j	Dwell time in $\boldsymbol{T_j}$
D_{si}	Dose rate in $\boldsymbol{P_{si}}$
R_s	**Value of the tolerance threshold for $\boldsymbol{G_s}$**
M_s	Maximum dose for $\boldsymbol{G_s}$
X_{si}	Indicator variable for $\boldsymbol{P_{si}}$
V_S	Dosimetric index for $\boldsymbol{G_s}$
L_s	The low limit for $\boldsymbol{V_S}$
U_s	High limit for $\boldsymbol{V_S}$

Given the nature of this problem, two objectives are investigated. The first objective is to maximize target coverage, which is expressed as follows:

In this expression, O denotes the volume of the target.

$$f_o(t_j) = \sum_{j=1}^{N_T} D_{oij} t_j \gtrsim R_o + \delta \qquad \forall\, i \in G_o \qquad (1)$$

Where the inequality is fuzzy. The second objective is to minimize radiation exposure to organs at risk, which is incorporated into the model as the following constraint:

In this expression, S denotes the organs at risk.

$$f_s(t_j) = \sum_{j=1}^{N_T} D_{sij} t_j \lesssim M_s - \varepsilon \qquad \forall\, s,i \in G_s \qquad (2)$$

Again, the inequality in the above constraint is fuzzy. In both constraints, t_j is the optimal stop time for these variables. And we have

$0 \le t_j \le 3600 \quad Second \quad \forall j$

Using the appropriate membership functions, the aforementioned inequalities are first transformed from their fuzzy form into a crisp (non-fuzzy) representation [7], [11]. After this transformation, the corresponding mathematical model can be formulated. The membership function associated with relation (1) is defined as follows:

$$\mu_o(t_j) = \begin{cases} 1 & f_o(t_j) \ge R_o + \delta \\ \dfrac{f_o(t_j) - R_o}{\delta} & R_o \le f_o(t_j) \le R_o + \delta \\ 0 & f_o(t_j) \le R_o \end{cases}$$

Moreover, the membership function of relation (2) is as follows.

$$\mu_s(t_j) = \begin{cases} 1 & f_s(t_j) \le M_s - \varepsilon \\ 1 - \dfrac{f_s(t_j) - (M_s - \varepsilon)}{\varepsilon} & M_s - \varepsilon \le f_s(t_j) \le M_s \\ 0 & f_s(t_j) \ge M_s \end{cases}$$

We argue that the outcomes of such a formulation remain insufficient to fully satisfy all clinical requirements associated with the nine dose–volume (DV) indices outlined in Table 1 [10]. Furthermore, the results of the referenced study do not allow for straightforward analysis of Pareto fronts or interpretation of non-dominated solutions by treatment planners [14], [19]. To address these limitations, we categorized the DV indices specified in the clinical protocol into two distinct groups:

1. Target coverage: $V_{100}^{prostate}, V_{80}^{vesicles}$

2. Protection of organs: $V_{200}^{prostate}, V_{150}^{prostate}, D_{1cc}^{rectum}, D_{2cc}^{rectum}, D_{1cc}^{bladder}, D_{2cc}^{bladder}, D_{0.1cc}^{urethra}$

This article proposes a new formulation using DV indices in the clinical protocol.

For treatment design t, to maximize the target coverage group, the FMCI[1] is calculated as:

$FMCI(t) = \sum_{j=1}^{N_T} D_{oij} t_j - \delta \times \mu_o(t_j) - R_o$

One of the objectives of the problem is to maximize the FMCI value, which should be optimistically determined according to the threshold values of the DV indices within the target coverage group. Positive values indicate that both clinical protocol requirements of $V_{100}^{prostate} < 95\%$ and $V_{80}^{vesicles} < 95\%$ have been achieved. Negative values indicate that at least one of the target volumes received an underdose.

Also, for the treatment plan$t$, when we want the organs at risk to be less damaged, the FMSI[2] value is calculated as follows:

$FMSI(t) = \mu_s(t_j) \times \varepsilon + f_s(t_j) - M_s$

Another objective is to minimize the FMSI value. Negative values signify that none of the D_v^o indices have surpassed their respective thresholds, thereby satisfying all the D_v^o index criteria outlined in Table 1. Conversely, positive values indicate that at least one index has exceeded its threshold.

[1] Fuzzy Model Coverage Index
[2] Fuzzy Model Survival Index

Any treatment plan can be assessed based on these conflicting objectives (FMSI and FMCI). The proposed approach guarantees that the values of all DV indices within a given group adequately represent that group. A treatment plan is considered compliant with all clinical protocol criteria listed in Table 1 if it satisfies the conditions FMSI ≤ 0 and FMCI ≥ 0.

3.2. Multi-Objective Evolutionary Algorithms (MOEA)

Multi-objective optimization involves the simultaneous consideration of multiple, often conflicting objectives, where the aim is not to obtain a single optimal solution but rather a set of trade-off solutions, collectively referred to as the Pareto-optimal set. Within this set, no solution is strictly superior across all objectives; instead, each represents a compromise reflecting different trade-off scenarios. Evolutionary algorithms have demonstrated particular effectiveness in this domain, as they are inherently well-suited for exploring complex, high-dimensional, and multimodal search spaces. Compared with traditional optimization techniques, multi-objective evolutionary algorithms (MOEAs) generally achieve superior performance in terms of convergence, diversity preservation, and robustness [9].

In the context of radiotherapy, and specifically brachytherapy treatment planning, MOEAs have been widely applied to optimize dose distribution by balancing tumor coverage against the sparing of surrounding organs at risk [16]. In this study, we conduct a comparative evaluation of four well-established MOEAs: the Non-dominated Sorting Genetic Algorithm II (NSGA-II), Multi-Objective Particle Swarm Optimization (MOPSO), Strength Pareto Evolutionary Algorithm II (SPEA-II), and the Pareto Envelope-Based Selection Algorithm II (PESA-II). Their performance is assessed with respect to solution quality, diversity, and clinical applicability, providing insights into their relative strengths and limitations for brachytherapy optimization.

3.2.1. NSGA-II Evolutionary Algorithm

The Non-dominated Sorting Genetic Algorithm II (NSGA-II) is one of the most widely utilized multi-objective evolutionary algorithms (MOEAs), specifically developed to address optimization problems characterized by conflicting objectives. It was introduced to overcome the limitations of conventional genetic algorithms in multi-objective contexts, particularly with respect to computational complexity and preservation of solution diversity. The central mechanism of NSGA-II is non-dominated sorting, which ranks individuals according to the number of solutions that dominate them, with lower ranks corresponding to superior solutions.

The algorithm integrates two essential components: dominance sorting and crowding distance. Dominance sorting stratifies the population into hierarchical non-domination levels, while crowding distance provides a density estimation that preserves population diversity by favoring well-distributed solutions along the Pareto front. Based on these measures, selection is carried out through a binary tournament procedure, prioritizing individuals with superior ranks and larger crowding distances.

Offspring are generated via classical genetic operators, including crossover and mutation, and combined with the parent population to form a temporary pool. From this pool, the most promising solutions are retained to constitute the subsequent generation. This evolutionary process is repeated until a predefined stopping criterion, typically the maximum number of generations, is reached.

NSGA-II is widely recognized for its computational efficiency, ease of implementation, and ability to yield a diverse and high-quality approximation of the Pareto-optimal front. Owing to these advantages, it has been extensively applied across diverse domains such as engineering design, robotics, bioinformatics, and financial modeling to solve complex multi-objective optimization problems.

3.2.2. PESA-II Evolutionary Algorithm

The Pareto Envelope-Based Selection Algorithm II (PESA-II) is a population-based multi-objective evolutionary algorithm designed to generate diverse and high-quality solutions for complex optimization problems. The algorithm employs a Pareto envelope strategy, which partitions individuals into multiple "envelopes" according to their dominance levels within the population. In this framework, solutions are ranked based on the number of individuals dominating them, thereby enabling an efficient and structured hierarchy for selection.

A distinctive feature of PESA-II is its use of dual archives to preserve non-dominated solutions. The internal archive serves as the selection pool for generating offspring, while the external archive retains the best non-dominated solutions identified throughout the evolutionary process. During each iteration, non-dominated solutions from the internal archive are promoted to the external archive, thereby maintaining elitism and safeguarding solution quality across generations.

The algorithm further applies environmental selection by combining individuals from both archives and employing a crowding distance metric to maintain solution diversity. This balance between selection pressure and diversity preservation allows for effective exploration of the Pareto front while mitigating the risk of premature convergence to suboptimal regions.

Owing to these design features, PESA-II has demonstrated strong performance in large-scale optimization problems and in complex multi-objective landscapes, consistently achieving a favorable trade-off between solution quality and population diversity.

3.2.3. MOPSO Evolutionary Algorithm

Multi-Objective Particle Swarm Optimization (MOPSO) is an evolutionary algorithm inspired by the collective behavior observed in bird flocking and fish schooling, specifically designed to address multi-objective optimization problems. In MOPSO, the population consists of particles, each representing a candidate solution, which navigate the search space under the influence of their personal best positions and the global best positions identified by the swarm. These components guide particle velocities, steering the population toward promising regions of the solution space.

Within a multi-objective context, MOPSO maintains an approximation of the Pareto front by updating particles according to dominance relations. Each particle preserves a memory archive of non-dominated solutions to maintain diversity and direct the search toward the Pareto-optimal set. Particle updates incorporate both individual and social learning components, balancing exploration and exploitation.

To manage multiple objectives effectively, MOPSO employs metrics such as crowding distance to evaluate solutions and ensure a well-distributed Pareto front. This enables the algorithm to produce a diverse set of trade-off solutions rather than converging on a single optimal point.

MOPSO has demonstrated strong performance across a wide range of applications, including engineering design, economics, and scheduling. It is particularly effective at efficiently exploring complex, high-dimensional solution spaces while generating high-quality and diverse Pareto-optimal solution sets.

3.2.4. SPEA- II Evolutionary Algorithm

The Strength Pareto Evolutionary Algorithm II (SPEA-II) is an advanced multi-objective evolutionary algorithm that improves upon its predecessor, SPEA, by enhancing fitness assignment and diversity preservation. The algorithm operates with two populations: an external archive that stores the best non-dominated solutions, and the current population, which undergoes

standard evolutionary operations such as selection, crossover, and mutation. Solutions in the archive are assigned fitness values based on their strength, defined by the number of solutions they dominate, as well as the dominance relationships relative to other solutions.

To maintain diversity along the Pareto front, SPEA-II employs a density estimation technique, which favors solutions located in less crowded regions, thereby promoting an even distribution of solutions. Its fitness assignment strategy balances solution quality with diversity, ensuring that superior solutions are consistently prioritized. The algorithm also incorporates elitism to preserve high-quality solutions across successive generations.

Through this archive-based framework and refined fitness assignment, SPEA-II effectively addresses multi-objective optimization problems with conflicting objectives, generating a well-distributed and diverse set of Pareto-optimal solutions. The algorithm has been widely applied to complex multi-objective challenges across diverse domains, including engineering design, resource allocation, and scheduling, demonstrating robust performance and adaptability.

3.3. Gray System Theory

Gray System Theory (GST), introduced by Professor Deng Julong in the early 1980s, is a mathematical framework designed to analyze and model systems characterized by incomplete, uncertain, or partially known information. GST provides systematic methods for studying systems in which only limited or imprecise data are available, making it particularly valuable in applications across engineering, economics, social sciences, and management.

A gray system is described using constructs such as gray numbers, gray equations, and other related components. At the core of GST are gray numbers, which represent quantities whose precise values are unknown but are constrained within known intervals. These numbers serve as the foundational elements for modeling uncertainty in gray systems, enabling quantitative analysis when traditional probabilistic or deterministic approaches are not applicable. By incorporating gray numbers and their associated mathematical operations, GST offers a structured methodology for reasoning under uncertainty and extracting meaningful patterns from limited data. The gray number is defined as $\otimes \mathrm{A} = [\underline{A}.\overline{A}]$.

4. Results

To evaluate the performance of the proposed algorithms and identify the most effective approach, the high-dose-rate brachytherapy planning problem was addressed using four multi-objective evolutionary algorithms: NSGA-II, PESA-II, SPEA-II, and MOPSO. The evaluation utilized clinical data from 14 prostate cancer patients with a mean age of 57 years. These patients were selected to represent a wide range of prostate volumes, from 23 to 103 cubic centimeters.

In prostate cancer treatment, target volumes typically include the prostate and, in some cases, a portion of the seminal vesicles, while the organs at risk (OARs) comprise the bladder, rectum, and urethra. Depending on the size and anatomical location of the target volumes, between 14 and 20 catheters were inserted into each patient to ensure adequate coverage of the treatment area.

After catheter implantation, a pelvic computed tomography (CT) scan was acquired for each patient. The resulting images were processed using treatment planning software to extract the spatial coordinates of points within the target volume, which were then used as input for the evolutionary algorithms. The accuracy of the dose–volume (DV) indices improve with an increased number of dose calculation points, denoted by the set D. In this study, D comprises a total of 2,000 points—approximately 400 points per target volume—thereby enhancing the precision of dose distribution assessments compared with previous studies [18], [19].

Each of the four algorithms—NSGA-II, MOPSO, SPEA-II, and PESA-II—was implemented independently. The algorithms were run for 20 generations, and the optimal solution from each generation was identified and recorded. These solutions were then plotted as individual points on a graph, with each point representing the best solution obtained in a given generation by the corresponding algorithm. This graphical representation was subsequently used to analyze and compare the performance of the algorithms.

Since the brachytherapy model formulated in this study involves two conflicting objectives, Pareto fronts can be readily generated. These fronts allow treatment planners to evaluate trade-offs between the objectives and understand how improvement in one criterion may entail compromise in another. The primary purpose of the Pareto front, which consists of non-dominated solutions, is to support informed and balanced clinical decision-making.

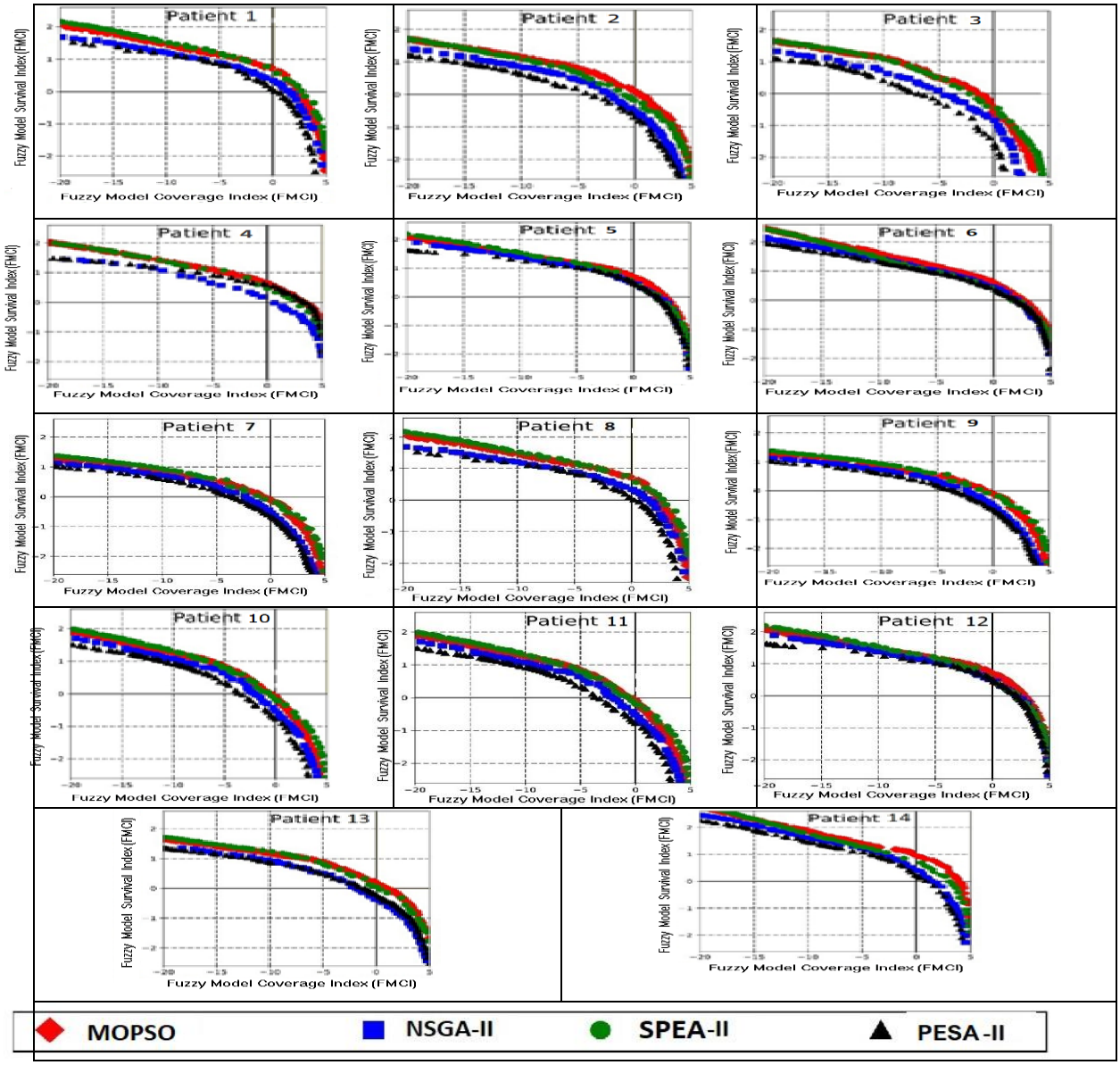

Figure 1: Assessment of Four Evolutionary Algorithms and Informed Decision-Making Using the Pareto Front

Figure 1 presents the Pareto fronts obtained from 20 independent executions of each multi-

objective evolutionary algorithm (MOEA). Examination of the results indicates that the modified

MOPSO algorithm generates higher-quality Pareto fronts more rapidly than the other three algorithms. As shown in Table 4, these results confirm that the modified MOPSO algorithm exhibits greater consistency compared with the others. In all cases, it produces a larger number of non-dominated solutions with higher concentrations than the other MOEAs.

Table 3: Target volume coverage under irradiation was assessed via four different optimization algorithms.

Patient ID	PESA-II	NSGA-II	SPEA-II	MOPS
1	0.945372	0.950003	0.948945	**0.959032**
2	0.950007	0.95704	0.950127	**0.958982**
3	0.950288	0.95701	0.948812	**0.959101**
4	0.955814	0.940000	0.946321	**0.958702**
5	0.953215	0.958008	0.950108	**0.955065**
6	0.956900	0.949879	0.958001	**0.959891**
7	0.947947	0.95001	0.95015	**0.959086**
8	0.95090	0.951009	0.949008	**0.959015**
9	0.949980	0.950320	0.950006	**0.956801**
10	0.953984	0.952718	0.952718	**0.957503**
11	0.950187	0.948250	0.950259	**0.958082**
12	0.950000	0.952548	0.942548	**0.956032**
13	0.940056	0.950007	0.950000	**0.959159**
14	0.950015	0.950108	0.950108	**0.957548**

Table 3 presents the target coverage during radiation, with optimal coverage defined as exceeding 95% of the tumor volume. Radiation duration, expressed in seconds and indicated in parentheses, was calculated using four algorithms: MOPSO, NSGA-II, SPEA-II, and PESA-II. The results show that the modified MOPSO algorithm consistently achieves target coverage above 95% for all 14 patients.

In contrast, the PESA-II algorithm resulted in coverage below 95% for four patients (numbers 1, 7, 9, and 13). Using NSGA-II, three patients (numbers 4, 6, and 11) had coverage below 95%, while SPEA-II yielded coverage below 95% for five patients (numbers 1, 3, 4, 8, and 12). The highest coverage, 0.959891, was achieved for patient number 6 using the modified MOPSO algorithm.

Table 5 presents the standard deviation of the results obtained from independent executions of the NSGA-II, MOPSO, SPEA-II, and PESA-II algorithms. The standard deviation quantifies the variability of the data, indicating the extent to which the results deviate from the mean. A low standard deviation signifies that the data points are closely clustered around the mean, whereas a high standard deviation reflects greater dispersion. Based on the data reported in Tables 3 and 4, it is evident that the modified MOPSO algorithm outperforms the other multi-objective evolutionary algorithms, with these differences being statistically significant.

Table 4: Standard deviations of the NSGA-II, MOPSO, SPEA-II, and PESA-II algorithms.

Patient ID	PESA-II	NSGA-II	SPEA-II	MOPS
1	0.001347	0.004253	0.003621	**0.000904***
2	0.001079	0.002715	0.004186	**0.000964***
3	0.001752	0.003482	0.001082	**0.000774***
4	0.001039	0.007595	0.003751	**0.000832***
5	0.000979	0.002229	0.002013	**0.000889***
6	0.002644	0.005344	0.002846	**0.000812***
7	0.001084	0.005960	0.003671	**0.000941***
8	0.001205	0.007621	0.001125	**0.000831***
9	0.000979	0.002329	0.001754	**0.000881***
10	0.001084	0.006428	0.001326	**0.000833***
11	0.002847	0.005569	0.003851	**0.000911***
12	0.001099	0.004065	0.001181	**0.000728***
13	0.001777	0.001462	0.001803	**0.000895***
14	0.001039	0.007391	0.001062	**0.000704***

5. Discussion and conclusion

In this study, each of the four algorithms was independently implemented and evaluated using clinical data from prostate cancer patients. Prior research has demonstrated the advantages of formulating brachytherapy planning as a bi-objective optimization problem. For instance, Akinlade et al. [1] and Dabic-Stankovic et al. [3] reported that adopting a two-objective framework resulted in improved treatment outcomes compared with single-objective formulations. Similarly, Shi et al. [13] demonstrated that the application of a multi-objective evolutionary algorithm (MOEA) for dose optimization produced clinically acceptable treatment plans, further supporting the use of multi-objective approaches in this context.

Various objectives have been employed in the literature to represent the brachytherapy problem. For example, Dehabal et al. [4] developed an optimization model incorporating two objectives: one focused on achieving adequate target dose coverage, while the other aimed at minimizing the proportion of tissue receiving doses exceeding ten percent above the prescribed level. These studies highlight the flexibility of multi-objective modeling in capturing clinically relevant trade-offs between tumor control and normal tissue protection, providing a strong rationale for its application in prostate brachytherapy optimization.

In this study, the modified MOPSO algorithm demonstrated superior performance compared with other multi-objective evolutionary algorithms, including PESA-II, MOPSO, and SPEA-II. Similar algorithms have been applied in earlier studies, such as those by Wang et al. [16] and Takasu et al. [15], to generate higher-quality brachytherapy (BT) treatment plans with improved efficiency and reduced computational time. However, in direct comparison, the modified MOPSO consistently achieved the most favorable outcomes in terms of solution quality, robustness, and clinical relevance.

Analysis of clinical data from 14 prostate cancer patients further confirmed that the modified MOPSO algorithm is a promising optimization approach for dose-rate brachytherapy treatment planning. Its ability to generate diverse and clinically acceptable Pareto-optimal solutions within shorter runtimes highlights its potential as a practical tool for clinical decision support. These findings not only demonstrate the clinical applicability of the modified MOPSO algorithm but also underscore the need for further validation and broader implementation in real-world brachytherapy planning.

6. Managerial and Clinical Insights

The findings of this study provide several important insights for clinical practice and treatment management in HDR brachytherapy. First, the proposed fuzzy-based multi-objective optimization framework allows clinicians to personalize treatment plans by considering patient-specific factors such as physical condition, age, and tumor volume uncertainty. Second, the comparative evaluation of four state-of-the-art MOEAs offers guidance on algorithm selection, highlighting that the modified MOPSO achieves superior target coverage, reduced variability, and enhanced solution diversity, which can improve treatment effectiveness and consistency. Third, by generating Pareto-optimal solutions that balance tumor coverage and organ-at-risk sparing, the framework enables evidence-based decision-making in scheduling and dose distribution, optimizing resource allocation in radiotherapy departments. Finally, the integration of fuzzy logic and gray numbers demonstrates a practical approach for handling clinical uncertainties, providing a robust and flexible tool that can be readily adopted in routine HDR brachytherapy planning. Collectively, these insights underscore the translational value of the proposed methodology and its potential to enhance patient outcomes and operational efficiency in prostate cancer radiotherapy.

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