Dosimetric Evaluation of Different Optimization Algorithms Used in Interstitial Brachytherapy of Cervical Carcinoma

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ABSTRACT

Background: Conventional optimization techniques are based on the planning approach in which positions and weights are varied to generate the desired dose distribution. Inverse planning simulated annealing (IPSA) is an advanced optimization method developed to automatically determine a suitable combination of positions to design an acceptable plan.

Objective: In this study, three optimization techniques namely IPSA, graphical optimization (GROPT), and geometrical optimization (GOPT) methods are compared in high-dose-rate interstitial brachytherapy of cervical carcinoma.

Material and Methods: In this retrospective study, twenty computed tomography (CT) data sets of 10 cervical cancer patients treated with Martinez Universal Perineal Interstitial Template-based interstitial brachytherapy were studied. The treatment plans generated were optimized using the IPSA, and GOPT methods. The prescribed dose was 24 Gy in 4 fractions. Plans produced using IPSA, GrOPT, and GOPT techniques were analyzed for comparison of dosimetric parameters, including target coverage, homogeneity, conformity, and organs at risk (OAR) doses.

Results: V100 values for IPSA, GrOPT and GOPT plans were 95.81±2.33%, 93.12±2.76% and 88.90±4.95%, respectively. The mean D90 values for the IPSA, GrOPT, and GOPT plans were 6.45±0.15 Gy, 6.12±0.21 Gy, and 5.85±0.57 Gy, respectively. Significantly lower doses of OAR were in the IPSA plans that were more homogeneous (HI=0.66). Conformity was comparatively higher in IPSA-based plans (CI=0.75).

Conclusion: IPSA plans were superior and resulted in better target coverage, homogeneity, conformity, and minimal OAR doses.

Keywords

Introduction

The standard model of definitive treatment in patients with locally advanced cervical carcinoma involves both components of radiotherapy: external beam radiotherapy (EBRT) and brachytherapy [1,2]. Intracavitary brachytherapy (ICBT) is an essential pillar of radiotherapy and plays a significant role in the management of cervical cancer. In cervical carcinoma cases where intracavitary technique is not feasible due to various factors such as involvement of the medial parametrium, bulky tumor (diameter>4 cm), and recurrent disease, interstitial brachytherapy is the preferred modality. Interstitial implants are

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performed using trans-perineal [3] or trans-vaginal templates [4]. The Martinez Universal Perineal Interstitial Template (MUPIT) is a template designed to deliver dose in interstitial brachytherapy [5].

The primary focus of interstitial brachy-therapy is to achieve a plan providing a desired dose distribution and reducing the dose to the critical structures surrounding it. Conventional methods such as graphical optimization (GrOPT) and geometrical optimization (GOPT) use a planning approach for selecting parameters first and then evaluating the desired dose distribution. Here, the user achieves the dose distribution by manually adjusting the dwell times or by graphical tools. However, to achieve an isodose distribution that just surrounds the implant and leads to better tumor coverage, conformity, homogeneity, and minimum dose to OARs, a more sophisticated method of planning known as inverse planning was developed. Initially, an inverse planning algorithm was introduced in brachytherapy for the prostate [6-8]. Here, constraints or parameters are adjusted according to the initially defined clinical objective.

Various optimization algorithms used in interstitial brachytherapy for gynecological malignancies have mostly reported findings in prostate cancer, and limited studies have been conducted on patients with cervical cancer. Moreover, they have compared three optimization methods, which are different from the present study. In this study, we have evaluated dosimetric parameters of different conventional optimization techniques and compared them with the anatomy-based optimization method known as inverse planning simulated annealing (IPSA) in patients with cervical cancer.

Material and Methods

A retrospective study was conducted on ten patients with cervical cancer (stage IIB-IIIA), treated with interstitial implants between February 2019 and December 2019 with a high dose rate (HDR) brachytherapy. Of the 10 cases, 6 were definitive and 4 were recurrent. All patients underwent EBRT at a dose of 50 Gy in 25 fractions using a box field technique followed by MUPIT interstitial implants. Two implants separated at an interval of one week were performed for each patient under general anesthesia. In the implant procedure, a Foley urinary catheter was first inserted into the bladder and filled with 7cc of contrast agent to inflate the bulb and ensure that the urinary catheter is snugly fit around the bladder neck. Interstitial needles were then inserted into the target area. The choice of the number of the needles used in implants is depended on the tumor size and topography. Patients underwent a computed tomography (CT) scan (BRIVO CT 385, GE) with a slice thickness of 3 mm after each implant. These images were then exported to Oncentra TPS version 4.5.2 (Elekta, Veenendaal, The Netherlands) for contouring and treatment planning.

HR-CTV (High-risk clinical target volume) and OARs, including the bladder, rectum, sigmoid, and bowel were contoured with the help of Magnetic Resonance Imaging (MRI) images acquired post-EBRT and CT images acquired after the completion of the implant procedure, using GYN GEC-ESTRO guidelines (European Group of Curietherapie and the European Society For Therapeutic Radiology and Oncology). To minimize the inter-observer bias, target volume and OARs were contoured by the same radiation oncologist, having vast experience in the field. For each fraction, plans already treated using graphical optimization, were re-optimized with the IPSA and GOPT techniques for comparison purposes. These optimization techniques are discussed below. The dose distributions obtained using these three optimization methods are shown in Figure 1. A dose of 24 Gy in 4 fractions was prescribed to all patients.

Geometrical Optimization (GOPT)

GOPT on volume was performed on the implants. In GOPT, based on the implant geom-

(a) IPSA

(b) GrOPT

(c) GOPT
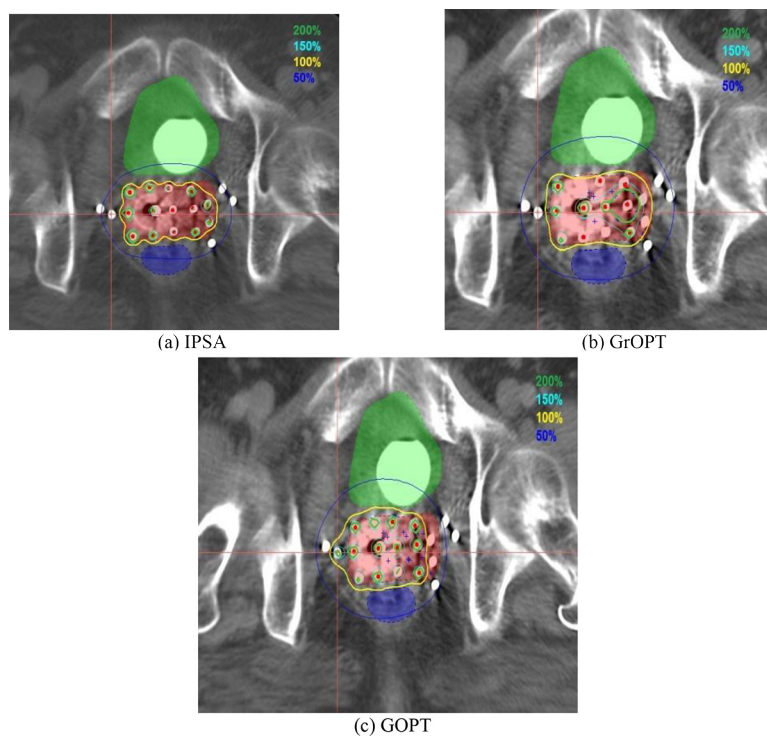
Figure 1: Isodose distribution in a patient with Martinez Universal Perineal Interstitial Template (MUPIT) implant, calculated using (a) the inverse planning simulated annealing (IPSA) (b) graphical optimization (GrOPT), (c) geometrical optimization (GOPT) algorithms

etry and distance between the catheters, dwell times are varied. Because this method is not based on anatomical information, dwell times are further adjusted manually to obtain the desired dose distribution and minimize the OAR dose. Therefore, this adjustment of dwell times becomes a time-consuming process.

Graphical Optimization (GrOPT)

In this method, isodose lines were manually adjusted to cover the target adequately while maintaining the minimum OAR doses. The act of isodose dragging changes the dwell weight and calculates the corresponding dwell times such that the required dose distribution is achieved. This is an iterative process and is repeated until the desired result is obtained. GrOPT is dependent on the skill of a planner and is also a time- consuming process. A planner with several years of experience can take around 20 to 25 min to generate an optimal

plan [9,10].

Inverse planning simulated annealing (IPSA)

The anatomy-based algorithm IPSA, utilizing anatomical information for the desired dose distribution, was used to achieve an acceptable plan. Here, clinical objectives are first defined and represented in the form of mathematical equations. Constraints are adjusted according to the given objective. The equations are processed iteratively to arrive at an optimal solution [10] by finding a suitable combination of dwell positions to achieve the desired goal considering for the dose constraints defined for CTV and OARs [11-13]. The dose objective parameters used in IPSA planning in this study are shown in Table 1.

Plan evaluation

Dose computation in all plans was per-

Table 1: Set of objectives- dose constraints and weight factors used in inverse planning simulated annealing (IPSA) plan.

ROI	Min surface dose weight	Min surface dose (Gy)	Max surface dose (Gy)	Max surface dose weight	Min Volume dose weight	Min Volume dose (Gy)	Max Volume dose (Gy)	Max Volume dose weight
HRCTV	170	6	7.5	25	170	6	7.5	25
Bladder	0	0	4.5	50	0	0	0	0
Rectum	0	0	4.5	40	0	0	0	0
Sigmoid	0	0	0	0	0	0	0	0
Bowel	0	0	0	0	0	0	0	0

ROI: Region of interest, HRCTV: High-risk clinical target volume

formed with a voxel size of 1 mm^3 and with uniform calculation settings. The maximum dose limit for target surface and target volume was set as 7.5 Gy, while for OARs, the maximum dose limit was set as 4.5 Gy. The activity of the Ir-192 source used for treatment planning of all patients was between 8 Ci to 3 Ci. Various dosimetric parameters were analyzed by Dose Volume Histogram (DVH) and compared for IPSA, GrOPT, and GOPT-based plans. The planning criteria were to cover at least 95% target volume with 100% of the prescribed dose while minimizing the doses to the bladder, rectum, sigmoid, and bowel. For HR-CTV, minimum doses to 90% (D90) and 100% (D100) volume of HR-CTV, percentage of treatment volume enclosed by 100% (V100), 150% (V150), and 200% (V200) of the prescribed dose were evaluated.

For OARs, the dose received by 2cc volume (D2cc) was evaluated. The indices for assessing conformity and homogeneity of implants, that is conformity index (CI) and homogeneity index (HI), were calculated using the following formulae [14,15].

$$HI = (V100 - V150)/V100 \qquad (1)$$

$$CI = \left(\frac{CTV_{ref}}{CTV}\right) / \left(\frac{CTV_{ref}}{V_{ref}}\right) \qquad (2)$$

CTV_{ref} =CTV enclosed by reference isodose curve

CTV = Volume of target

V_{ref} = Volume inside CTV as well as outside the CTV enclosed by reference isodose

For statistical analysis, SPSS software, version 20, was used in the study. The normality of the data set was assessed by using the Shapiro-Wilk Test and it was found that the data were normally distributed. Dosimetric parameters of the respective algorithms were statistically compared using a one-way analysis of variance (ANOVA) test at a 5% level of significance.

Results

In the analysis of IPSA, GrOPT, and GOPT-based plans, the mean V100 was found to be 95.81±2.33%, 93.12±2.76%, and 88.90±4.95% for the IPSA, GrOPT, and GOPT plans, respectively (Table 2). Significant differences were found in the target coverage among the three optimization methods (IPSA and GrOPT: p=0.023; IPSA and GOPT: p<0.05). As illustrated in the box and whiskers plot of Figure 2, IPSA resulted in improved target coverage compared to other methods.

The mean D90 values for the IPSA, GrOPT, and GOPT plans were 6.45±0.15 Gy 6.12±0.21 Gy, and 5.85±0.57 Gy, respectively, while D100 values for IPSA, GrOPT, and GOPT plans was 4.32±0.57 Gy, 4.37±0.79 Gy, and 3.75±0.74 Gy, respectively. D90 values

Table 2: Comparison of dose-volume parameters among inverse planning simulated annealing (IPSA), graphical optimization (GrOPT), and geometrical optimization (GOPT) plans.

| Parameters	IPSA	GrOPT	GOPT	p-value (IPSA vs. GrOPT)	p-value (IPSA vs. GOPT)
V100 (%)	95.81±2.33	93.12±2.76	88.90±4.95	0.023	p<0.001
V150 (cc)	31.84±7.17	33.14±10.55	34.04±10.59	0.669	0.471
V200 (cc)	12.74±3.40	13.23±5.88	14.48±4.84	0.754	0.260
D90 (Gy)	6.45±0.15	6.12±0.21	5.85±0.57	0.005	p<0.001
D100 (Gy)	4.32±0.57	4.37±0.79	3.75±0.74	0.636	0.008
HI	0.66±0.81	0.62±0.13	0.60±0.14	0.325	0.127
CI	0.75±0.06	0.55±0.17	0.52±0.17	p<0.001	p<0.001
Bladder D2cc (Gy)	4.16±0.15	4.51±0.33	4.62±0.30	p<0.001	p<0.001
Rectum D2cc (Gy)	4.12±0.43	4.51±0.20	4.39±0.36	0.001	0.017
Sigmoid D2cc (Gy)	1.06±0.25	1.39±0.35	1.80±0.52	0.009	p<0.001
Bowel D2cc (Gy)	1.28±0.40	1.54±0.33	2.13±0.68	0.093	p<0.001

IPSA: Inverse planning simulated annealing, GrOPT: Graphical optimization, GOPT: Geometrical optimization, HI: Homogeneity Index, CI: Conformity Index
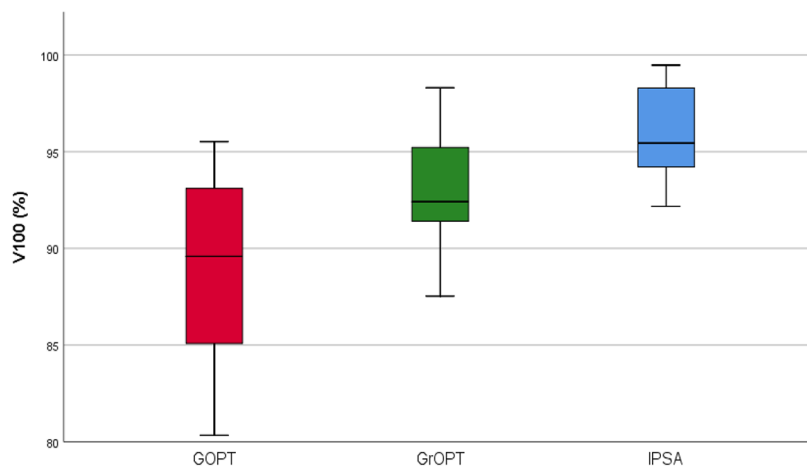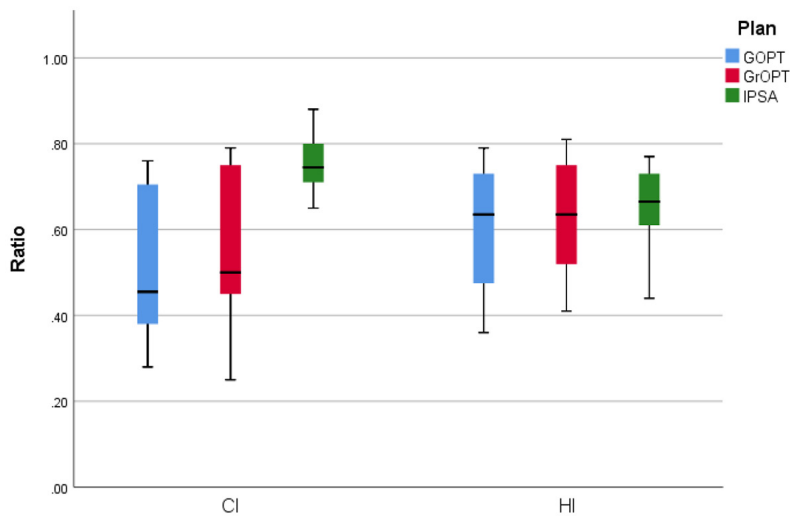

Figure 2: Comparison of V100 obtained with the inverse planning simulated annealing (IPSA), graphical optimization (GrOPT), and geometrical optimization (GOPT) methods.

were to be significantly different for IPSA and GrOPT plans (p=0.005), and IPSA and GOPT (p<0.001) plans, as seen in Figure 3, while the D100 value was not significant between IPSA and GrOPT (p=0.636), but significant between IPSA and GOPT plans (p=0.008).

IPSA plans were more homogeneous with an HI value of 0.66 compared to GrOPT (HI=0.62, p=0.325) and GOPT (HI=0.60, p=0.127) plans (Figure 4). Significant differences were not found among the HI values. Conformity index was significantly higher in
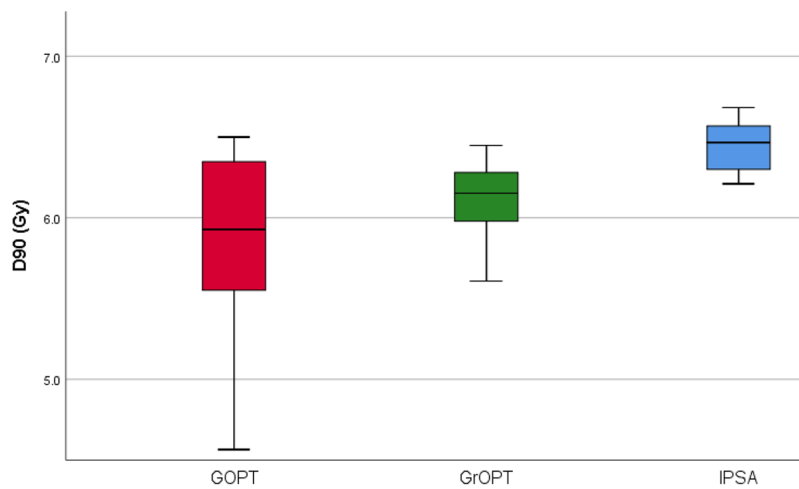
Figure 3: Comparison of the D90 parameter obtained with the inverse planning simulated annealing (IPSA), graphical optimization (GrOPT), and geometrical optimization (GOPT) methods

Figure 4: Comparison of Homogeneity Index and Conformity Index (IPSA), obtained with the inverse planning simulated annealing (IPSA), graphical optimization (GrOPT), and geometrical optimization (GOPT) methods.

the IPSA-based plans (CI = 0.74) than in the GrOPT plan (CI= 0.55, $p<0.05$) and GOPT (CI= 0.52, $p<0.05$) plans (Figure 4). Volumes receiving 150% and 200% of prescribed dose were greater in GOPT plans than in IPSA and GrOPT-based plan.

Lower doses to the bladder (D2cc=4.16±0.15 Gy), rectum (D2cc = 4.12±0.43 Gy), sigmoid (D2cc = 1.06±0.25 Gy), and bowel (1.28±0.40 Gy) were found in IPSA based plans than in GrOPT-based (doses to the bladder, rectum, sigmoid and bowel doses were 4.51±0.33 Gy, 4.51±0.20 Gy, 1.39±0.35 Gy, and 1.54±0.33 Gy, respectively) and GOPT (dose to the bladder, rectum, sigmoid, and bowel were 4.62±0.30 Gy, 4.39±0.36 Gy, 1.80±0.52 Gy,

2.13±0.68 Gy, respectively) plans. There existed a significant difference in the mean D2cc dose to the bladder, rectum, sigmoid and bowel (Figure 5) from all three optimization methods.

Discussion

In the present study, the dosimetric parameters of the anatomy-based IPSA plans were compared with those of GrOPT- and GOPT-based plans. IPSA resulted in improved target coverage and better sparing of OARs. It was easier to arrive at an optimal dose distribution within a few minutes using IPSA. Mean V100 and mean D90 were higher in the IPSA plans than in the GrOPT and GOPT plans. Moreover, a significant difference in target coverage was found among IPSA, GrOPT, and GOPT. Figures 2 and 3 show that the mean values of V100 and D90 were higher in IPSA plans compared to other methods. Other investigators [10,16] also demonstrated an improved target coverage with IPSA. However, they did not observe this difference significantly with graphically optimized plans. In addition, although an acceptable plan can be achieved using graphical optimization, it is a little time-consuming and is dependent on planner skills. The authors

[17], who performed a similar study in prostate showed that CTV coverage differed significantly using the IPSA and GOPT methods.

The mean D2cc doses of OARs in this study were found to be higher in the GrOPT- and GOPT-based plans. IPSA resulted in reduced doses to OARs and demonstrated a significant difference in OAR doses incomparison with the GrOPT- and GOPT-based plans as it offered the facility to vary the dose constraints and weights of the OARs till the desired goal was achieved. The dose constraints used in our study were different from those used by other investigators [17,18] where they had used IPSA in interstitial brachytherapy of prostate cancer, consisting of a different set of OARs. However, despite the difference in the site of treatment, it was found the bladder and rectum received lower doses with the IPSA method that was in agreement with our results. This is because IPSA uses anatomical information to optimize a plan. The dose constraints for the OARs are defined such that the optimization algorithm works to find the suitable combinations of dwell positions and dwell weights for achieving an acceptable plan. Therefore, we optimized the plan with IPSA, till the dose to the OARs met the desired criteria. In another
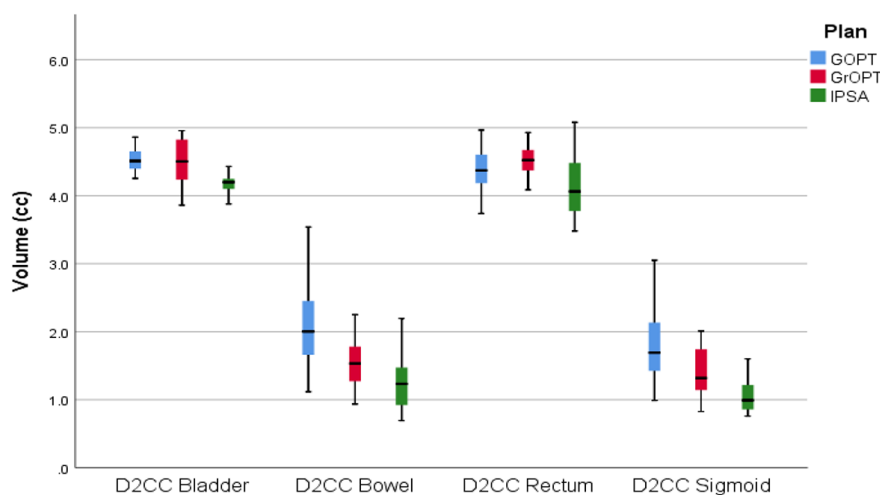
Figure 5: Comparison of doses delivered to 2cc volumes of the bladder, bowel, rectum, and sigmoid obtained with the inverse planning simulated annealing (IPSA), graphical optimization (GrOPT), and geometrical optimization (GOPT) methods.

study of interstitial brachytherapy in cervical carcinoma [10], it was concluded that IPSA improved the sparing of OARs while keeping the CTV coverage optimum. As seen in Figure 5, the median D2cc values of the bladder, rectum, bowel, and sigmoid were lower in IPSA plans which was in agreement with the findings of Matias et al. [19] who compared another inverse planning optimization method HIPO with a graphical optimization method in cervical cancer patients.

The homogeneity and conformity of the IPSA plans were better than those of the GrOPT and GOPT plans. HI was higher in IPSA, but did not differ significantly over the other two methods. Jamema et al. [10] and Yoshio et al. [16] also found no significant difference in the homogeneity of GrOPT and IPSA plans. As observed from the HI values shown in Table 2 and Figure 4, highly homogeneous plans were not obtained since we emphasized more on obtaining good target coverage with minimum OAR doses allowing a little flexibility in the homogeneity. The priority in target coverage thus came at the expense of decreased homogeneity. Vikram et al. [20] demonstrated that dose homogeneity was relatively less important with respect to normal tissue complications and that complication rates may not necessarily correlate with HDR interstitial brachytherapy. Therefore, one could relax the HI criteria on minimizing the dose to OARs. However, in a different site prostate, the HI values were found to be significantly different [9,17]. This may be attributed to the difference in CTV volume and implant geometry in the prostate as compared to the cervical implants. V150 and V200 were the lowest in the IPSA plans compared to the GrOPT and GOPT plans, implying that the hot spot volume in implants was greater in the latter methods.

Good conformity was achieved in the IPSA plans as compared to the GrOPT and GOPT methods. As illustrated in Figure 4, the median value of CI was higher in the IPSA plans. The geometrically optimized plans had the lowest CI and had inferior conformity around the implant. The possible reason could be achieving a CTV coverage with the desired objective and hence compromising the conformity. Moreover, it required too much time in planning to achieve the target coverage, and relaxing the criteria of conformity. We have observed that, dosimetrically, using IPSA certainly has advantages. However, there is a need to establish a clinical correlation with these dosimetric parameters and their relationship with the clinical outcome.

Conclusion

The IPSA optimization technique is better than the conventional optimization methods using a forward planning approach. In scenarios with multiple target volumes and OARs, the use of traditionally available methods such as changing manual dwell weights and pulling isodoses to obtain the required dose coverage is quite tedious and time-consuming. Techniques such as IPSA minimizes the planning time and offers the advantage of improved target coverage and sparing of critical structures while maintaining the homogeneity and conformity of the implant.

Authors' Contribution

This work is a combined effort of the authors of this article. The idea was conceived and written by Dr. Sh. Srivastava. The data collection and proofreading were done by Dr. N. Singh, while the statistical analysis was carried out by Dr. VK. Kashyap. All the authors had read, modified, and approved the final version of the manuscript.

Ethical Approval

This study was approved by the Institutional Ethics Committee (Reference no. 81st ECM II B-Ph.D./P3) of King George's Medical University, Lucknow, India.

Conflict of Interest

None

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