Nuclear Engineering and Technology 54 (2022) 1414–1420

Contents lists available at ScienceDirect

Nuclear Engineering and Technology

journal homepage: www.elsevier.com/locate/net

Original Article

Variation of optimization techniques for high dose rate brachytherapy in cervical cancer treatment

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ARTICLE INFO

Article history:
Received 9 June 2021
Received in revised form
16 September 2021
Accepted 6 October 2021
Available online 8 October 2021

Keywords:
Brachytherapy
3-D
Treatment planning
Cervix cancer
Optimization techniques

ABSTRACT

High dose rate (HDR) brachytherapy treatment planning usually involves optimization methods to deliver uniform dose to the target volume and minimize dose to the healthy tissues. Four optimizations were used to evaluate the high-risk clinical target volume (HRCTV) coverage and organ at risk (OAR). Dose-volume histogram (DVH) and dosimetric parameters were analyzed and evaluated. Better coverage was achieved with PGO (mean CI = 0.95), but there were no significant mean CI differences than GrO ($p = 0.03322$). Mean EQD_2 doses to HRCTV (D_{90}) were also superior for PGO with no significant mean EQD_2 doses than GrO ($p = 0.9410$). The mean EQD_2 doses to bladder, rectum, and sigmoid were significantly higher for NO plan than PO, GrO, and PGO. PO significantly reduced the mean EQD_2 doses to bladder, rectum, and sigmoid but compromising the conformity index to HRCTV. PGO was superior in conformity index (CI) and mean EQD_2 doses to HRCTV compared with the GrO plan but not statistically significant. The mean EQD_2 doses to the rectum by PGO plan slightly exceeded the limit from ABS recommendation (mean EQD_2 dose = 78.08 Gy EQD_2). However, PGO can shorten the treatment planning process without compromising the CI and keeping the OARs dose below the tolerance limit.

1. Introduction

Brachytherapy is a treatment in which the radioactive source is located within or near the target volume. In cervical cancer treatment, using a 3D technique showed increased local control and improved overall survival with reduced toxicity compared to the conventional 2D brachytherapy technique [1]. With the aid of Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) scans and CT/MRI compatible High Dose Rate (HDR) applicators, 3D planning produces more conformal treatment plans with careful assessment of the dose cloud in the specific context of the high-risk clinical target volume (HRCTV) and organ at risk (OAR) and decreases inaccuracy and oversimplification of doses to HRCTV and OAR [2]. The objective of optimization in cervical cancer brachytherapy is to achieve a typical pear-shaped distribution with a distinct pattern of high dose regions that cover the target volume completely while minimizing dose to the OARs. This type of dose distribution would give high local control and minimal side effects [3]. HDR brachytherapy treatment planning is always related to optimization methods to calculate dwell times and dwell positions of the radioactive source and specified applicators [4]. This retrospective study was conducted to determine whether another optimization technique could deliver a higher dose to the HRCTV while delivering a lower dose to the OAR than the routine optimization (GrO) currently used in the clinical setting. Four optimization techniques were evaluated, and the optimal technique will be determined by prescribing a higher dose to HRCTV D_{90} and a lower dose to OARs D_{2cc}.

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https://doi.org/10.1016/j.net.2021.10.004

2. Materials and methods

2.1. Brachytherapy planning using Oncentra treatment planning system

For this retrospective study, the CT data of six patients with the International Federation of Gynecology and Obstetrics (FIGO) IIB to IVA cervical cancer treated at Advanced Medical and Dental Institute (AMDI) with HDR hybrid brachytherapy using the Vienna applicator were analyzed. The prescribed dose ranged from 6 to 9.5Gy. The medical doctor (oncologist) contoured the HRCTV and OAR (sigmoid, rectum, and bladder) according to GEC-ESTRO guidelines [5] and planned brachytherapy using the Oncentra Treatment Planning System (Nucletron). Then the treatment was planned using the methodology of graphical optimization (GrO) as regular optimization. DVH summarised the information of 3-D dose distribution and was used to evaluate the radiation doses to HRCTV and OARs.

2.2. Optimization techniques of Oncentra Treatment Planning System

Graphical Optimization (GrO) is an interactive optimization method where the user grabs an isodose line and drags it to a new position until an optimal solution is obtained. This method works as when the left mouse button is pressed down, the mouse position is stored as the begin position, and the dose D_{begin} at the begin position is calculated. Then, the isodose line is dragged while keeping the left mouse button pressed down. When the left mouse button is released, the mouse position is stored as the end position, and the dose D_{end} at the end position is calculated. This method allows the user to change the dwell weights manually or mouse drag the isodose lines such that the target coverage is adequate with maximal sparing of organ at risk (OAR). The active dwell weights were changed by adjusting the isodose line and mouse dragging it to the desired location to cover the HRCTV. The graphical optimization technique is a routine treatment planning currently used in our institute. Then, the plan was copied and modified by using different optimization techniques; no optimization (NO), point optimization (PO), and point graphical (PGO) optimization techniques.

No optimization (NO) technique is the primary treatment planning without considering the tumor control probability and risk to the organ at risk (OAR). The dwell position and dwell times are set to the same value, usually 1. This optimization technique is routinely used in 2D brachytherapy treatment planning.

Dose-point optimization is placed at a given distance along the active source may be utilized [6]. Point optimization (PO) is treatment planning by normalizing the tumor cell's surface points. At these points, a 100% dose is normalized and conformed to the surface of the tumor. Target contour points are located on the target contours obtained from the CT data sets. Normalization is usually performed on the mean dose around the target contour points [6]. First, the new point set was created, and the region of interest was set as a target point of HRCTV. Then, the points at the tumor surface were normalized.

Point Graphical optimization (PGO) is a combination of point and graphical optimization techniques. After the PO plan was conducted, DVH was checked to see whether the percentage of dose that covered the 90% of HRCTV volume at least achieved 100% or not. Usually, the PO would not receive 100% of the prescribed dose to 90% HRCTV volume. Thus, isodose reshaping through the GrO plan was conducted. The 95% and 100% reference isodose lines were dragged using the mouse to cover certain parts of HRCTV until at least 100% of the prescribed dose was achieved by 90% volume of HRCTV. Care was taken during the dragging process to avoid unnecessary doses to the OARs. Two isodose lines were generated with different spectrums to show 95% and 100% dose coverage to each CT data slice. Finally. The isodose lines were adjusted to cover the HRCTV better while sparing the OARs. Then, DVH was checked, and the percentage of dose that covered the 90% HRCTV volume must at least achieve 100% dose. Table 1 shows the summary of optimization techniques.

2.3. Evaluation of HRCTV and OAR doses in four different optimization techniques

The treatment plans were assessed for respective optimization techniques. The doses to HRCTV and OARs (bladder, rectum, and sigmoid) were evaluated using dose-volume histogram (DVH) parameters from the Oncentra software for every optimization technique according to GEC ESTRO recommendations. D_{90} and V_{100} were the parameters collected for the analysis of HRCTV coverage from the DVH of each treatment plan. Meanwhile, D_{2cc} was the parameter used to calculate the doses to the OARs (bladder, rectum and sigmoid). D_{90} is the minimum dose delivered to 90% target volume. V100 is the volume, which is enclosed by 100% of the prescribed dose. D_{2cc} is the minimum dose in the most irradiated 2 cm^3 of the volume. All this information was obtained from DVH analysis from each treatment plan for respective optimization techniques.

3. Data analysis

The doses to HRCTV and OARs were evaluated by calculating and comparing the mean values of Conformity Index (CI) and mean total effective dose (EQD_2) between routine technique, GrO, with another alternative technique (NO, PO and PGO).

A conformity index is a complementary tool that attributes a score to a treatment plan or compares several treatment plans for the same patient. CI describes how well the reference isodose encompasses the target volume and excludes non-target structures [15]. The CI value was calculated using equation (1): all of the formula's information was obtained from the DVH.

$$CI = \frac{CTV\ target}{V\ total} \tag{1}$$

where CTV target is the HRCTV volume that received the prescribed dose (D_{90}), and V total is the total volume that received the prescribed dose (V100). The ideal value of CI is equal to 1.

The linear-quadratic (LQ) model is most commonly used in radiotherapy units. It makes the evaluation for different fractionations of equivalent dose (EQD_2) easier [16]. This concept involves the α/β ratio, as shown in equation (2):

$$EQD2 = D\,\frac{d\ +\ (\alpha\ +\ \beta)}{2\ +(\alpha\ +\ \beta)} \tag{2}$$

where D is the total dose for a fraction size of d gray, and α/β is the ratio to measure the fractionation sensitivity of the cells: cells with a higher α/β, are less sensitive to the sparing effect of fractionation. In this research, the α/β that used is 10 for High-Risk Clinical Target Volume (HRCTV) [17].

EQD_2 is the dose obtained using a 2 Gy fraction dose, which is biologically equivalent to the total dose D given with a fraction dose of d gray. The values of EQD_2 may be added in separate parts in the treatment plan. This formula may be adapted to fraction doses other than 2 Gy. EQD_2 was calculated and evaluated to determine the total equivalent dose received by HRCTV and was compared to

Table 1
Summary of optimization techniques.

Optimization techniques	Details
Graphical optimization (GrO)	• The isodose line is manually dragged to improve dose coverage [7–10]
No optimization (NO)	• Treatment planning without considering the tumor control probability and dwell position and dwell times are set to the same value [11]
Point optimization	• Reference isodose line is optimized along with predefined dose points on the target's surface [12] [–] [14].
Point graphical optimization	• combination of point and graphical optimization techniques [9,14].

the American Brachytherapy Society consensus guideline for locally advanced carcinoma of the cervix [18].

A simple mean paired *t*-test was used to make a statistical comparison of different dosimetric quality indices of treatment plans optimized by different optimization algorithms [8]. The statistical comparisons were carried out between GrO with alternative techniques (No, PO and PGO). Statistical significance was accepted with a p-value of <0.05.

4. Results

4.1. Comparison of mean conformity index (CI) of HRCTV between graphical optimization (GrO), no optimization (NO), point optimization (PO), and point graphical optimization (PGO) techniques

Based on Fig. 1, the results showed that PGO delivered better HRCTV coverage (mean CI = 0.9543), followed by GrO (mean CI = 0.9389), NO (mean CI = 0.8994), and lastly, PO (mean = 0.7804). PO followed by isodose reshaping (GrO), known as the PGO technique, resulted in a better mean CI of HRCTV (D_{90}). It is seen that the PO plans were very inferior compared to GrO, NO and PGO techniques in terms of HRCTV coverage.

Based on Table 2, according to the *p*-value, the mean CI value for NO and PO techniques was statistically significant ($p < 0.05$) in comparison to GrO. Meanwhile, there was no significant difference in mean CI value ($p = 0.3322$) when comparing PO with the GrO technique.

4.2. Comparison of mean EQD_2 doses of HRCTV between graphical optimization (GrO), no optimization (NO), point optimization (PO), and point graphical optimization (PGO) techniques

The mean EQD_2 doses were tabulated, like in Fig. 2. The mean EQD_2 doses to HRCTV calculated were 91.52 Gy EQD_2, 87.22 Gy EQD_2, 80.07 Gy EQD_2, and 91.7 Gy EQD_2 for different optimization techniques GrO, NO, PO, and PGO, respectively. The above results show that the mean EQD_2 doses for all optimization techniques achieved the recommendation EQD_2 doses from ABS-like in Table 1. PGO demonstrated better EQD_2 doses to HRCTV among all optimization techniques, followed by GrO, NO, and PO.

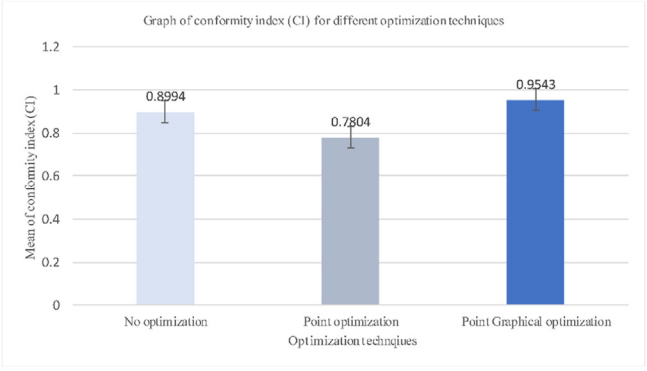

Fig. 1. Comparison mean conformity index (CI) of high-risk clinical target volume (HRCTV) (D_{90}) for different optimization techniques.

Table 3 presented a significant relationship of mean EQD_2 doses (p = 0.0316) between PO and GrO techniques. However, the p-values for NO (p = 0.0706) and PGO (p = 0.9410) were not statistically significant compared to GrO.

4.3. Comparison of mean EQD_2 doses of OARs between graphical optimization (GrO), no optimization (NO), point optimization (PO), and point graphical optimization (PGO) techniques

Fig. 3 shows that the PO had the lowest mean EQD_2 doses for bladder with a value of 78.75 Gy EQD_2 among all optimization techniques, indicating the PO technique was good in sparing the bladder region. Mean EQD2 doses bladder for NO technique exceeded the limit set by ABS with a value of 90.52 GyEQD2. The mean EQD2 doses bladder for NO and GrO were also below the ABS set limit with 88.18 Gy EQD2 and 83.85 GyEQD2, respectively.

Table 4 reveals a statistically significant relationship of mean EQD2 doses for bladder between PO (p = 0.0385) and PGO (p = 0.0217) compared with GrO. However, NO demonstrated no significant relationship (p = 0.6910) with the GrO technique.

Based on Fig. 4, GrO, NO, and PGO techniques exceeded the mean EQD_2 doses limit recommended by ABS (should be < 75 $GyEQD_2$) with a value of 76.85 $GyEQD_2$, 97.88 $GyEQD_2$, and 78.08 $GyEQD_2$, respectively. Also, mean EQD_2 doses rectum for PO techniques obeyed the recommendation from ABS with a value of 69.75 $GyEQD_2$.

Table 5 shows a statistically significant relationship between mean EQD_2 doses of D_{2cc} rectum ($p = 0.0395$) between PO and GrO techniques. However, there were no significant difference values of mean EQD_2 doses of D_{2cc} rectum between PGO ($p = 0.5523$) and NO ($p = 0.0661$) compared to GrO.

Fig. 5 documented the mean EQD_2 doses to sigmoid for four different optimization techniques. NO exceeded the limit recommended by ABS with a value of 81.5 $GyEQD_2$. Meanwhile, mean EQD_2 doses for GrO, PO, and PGO were below the dose limit with 74.46 $GyEQD_2$, 67.56 $GyEQD_2$, and 73.4 $GyEQD_2$, respectively.

Table 6 portrayed a statistically significant difference of mean EQD_2 of D_{2cc} sigmoid between GrO with PO technique (p = 0.0412). There was no significant difference in mean EQD2 doses of D_{2cc} sigmoid between NO (p = 0.1170) and PGO (p = 0.2474) compared to the GrO technique.

4.4. Comparison of percentage difference values of the HRCTV and OARs between graphical optimization (GrO), no optimization (NO), point optimization (PO), and point graphical optimization (PGO) techniques

From Table 7, the NO demonstrated −8.18%, 3.25%, 40.27%, and 22.19% percentage differences of dose to HRCTV (D_{90}), D_{2cc} bladder, D_{2cc} rectum, and D_{2cc} sigmoid in comparison to GrO.

According to Table 8, PO documented percentage difference

Table 2
Values of mean CI between the GrO and alternative techniques with significant difference.

Optimization technique	Mean CI	*p*-value	Significant Difference ($p < 0.05$)
No optimization	0.8994	0.0019	Yes
Point optimization	0.7804	0.0009	Yes
Point Graphical optimization	0.9543	0.3322	No

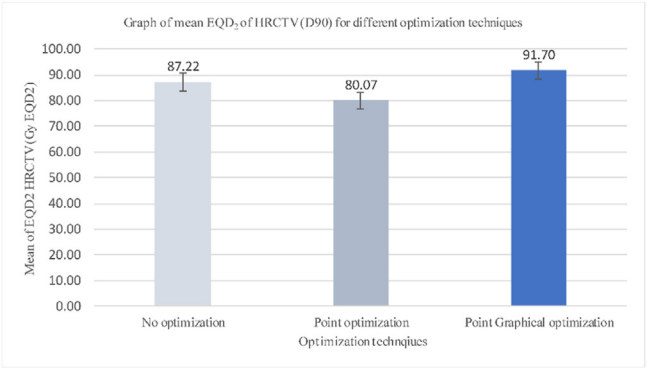

Fig. 2. Comparison mean EQD_2 of HRCTV (D_{90}) for different optimization techniques.

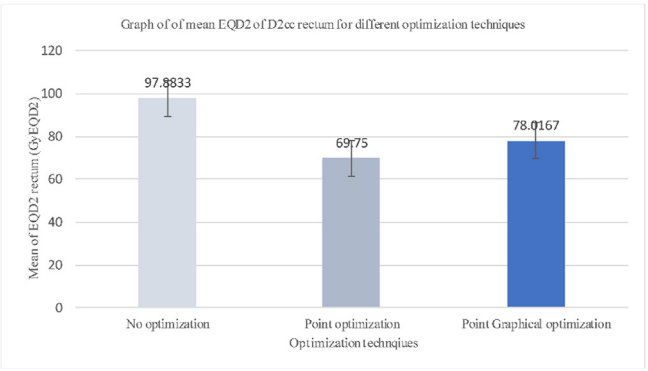

Fig. 4. Comparison of mean EQD_2 of D_{2cc} rectum for different optimization techniques.

Table 3
Values of mean EQD_2 doses HRCTV between values of mean CI between the GrO and alternative techniques with significant difference.

Optimization technique	Mean EQD_2doses HRCTV (Gy EQD_2)	*p*-value	Significant difference ($p < 0.05$)
No optimization	87.2167	0.0706	No
Point optimization	80.0667	0.0316	Yes
Point Graphical optimization	91.7000	0.9410	No

with values −22.35% for D_{90} HRCTV dose, −19.35% for D_{2cc} bladder dose, −20.99% for D_{2cc} rectum dose and - 18.95% for D_{2cc} sigmoid dose when comparing with GrO technique.

Table 9 proved that PGO resulted in the lowest percentage differences among all alternative optimization techniques compared to GrO with 0.46%, 7.12%, 2.10%, and 2.24% of doses for D_{90} HRCTV, D_{2cc} bladder, D_{2cc} rectum, and D_{2cc} sigmoid, respectively.

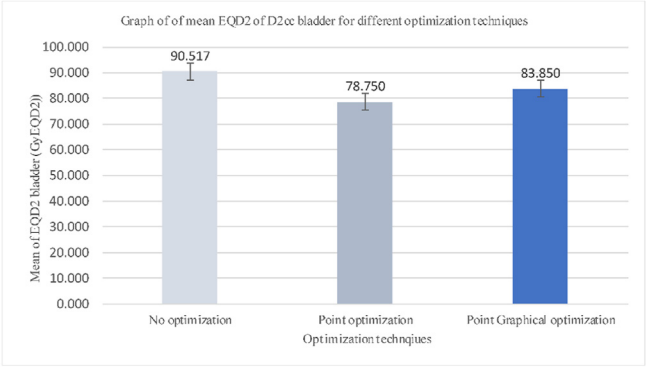

Fig. 3. Comparison of mean EQD_2 of D_{2cc} bladder for different optimization techniques.

5. Discussion

5.1. Mean of conformity index of HRCTV and EQD_2 doses between graphical optimization (GrO), no optimization (NO), point optimization (PO), and point graphical optimization (PGO) techniques

The conformity index (CI) or target coverage describes how well the isodose reference line conforms to the target volume and excludes the surrounding normal tissue. The ideal value for CI is 1, which indicates the full coverage of the isodose line to the volume of HRCTV. In this study, PGO delivered better HRCTV coverage (mean CI = 0.9543) followed by GrO (mean CI = 0.9389), NO (mean CI = 0.8994), and lastly, PO (mean = 0.7804). These findings are comparable with those found in the literature, where the conformity index value is between 0.6 and 0.8 for vaginal cancers [19]. A simple mean Paired *t*-test is applied for the interpretation of CI of GrO with other optimization techniques. There was no significant difference between NO (p = 0.0019) and PO (p = 0.0009). It was found that GrO produces good target coverage and improves the results in brachytherapy planning. These findings are consistent with those that suggest that dose restriction to OAR is possible using graphical optimization and offer better target coverage for implants with non-uniform geometry and target volume [11,13]. On the contrary, there was a significant difference between PGO (p = . 0.3322). The CI of PGO was significantly improved compared with GrO. Another author pursued similar work in which DPO + GrO

Table 4
Values of mean EQD2 doses of D_{2cc} bladder between the Gro and alternative techniques with significant difference.

Optimization technique	Mean EQD_2 doses bladder ($GyEQD_2$)	*p*-value	Significant difference ($p < 0.05$)
No optimization	90.5167	0.6109	No
Point optimization	78.7500	0.0385	Yes
Point Graphical optimization	83.8500	0.0217	Yes

Table 5
Values of mean EQD_2 doses of D_{2cc} rectum between the Gro and alternative techniques with significant difference.

Optimization technique	Mean EQD_2 doses rectum ($GyEQD_2$)	*p*-value	Significant difference ($p < 0.05$)
No optimization	97.8833	0.0661	No
Point optimization	69.7500	0.0395	Yes
Point Graphical optimization	78.0167	0.5523	No

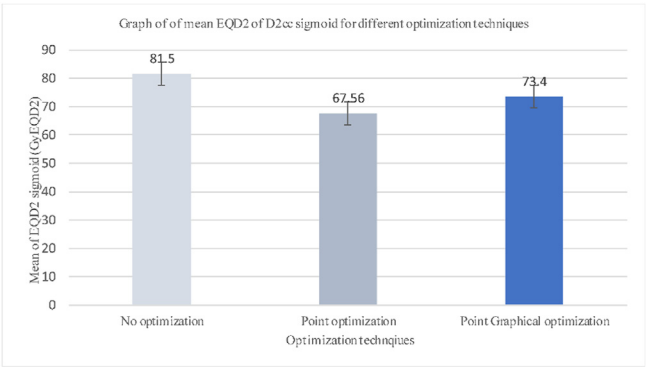

Fig. 5. Comparison of mean EQD_2 of D_{2cc} sigmoid for different optimization techniques.

showed better results in target coverage in multi-channel vaginal cylinders treatment [9].

American Brachytherapy Society (ABS) recommends EQD_2 doses of 80–90 Gy for HRCTV (D_{90}). The mean total EQD_2 doses to HRCTV calculated were 91.52 $GyEQD_2$, 87.22 $GyEQD_2$, 80.07 $GyEQD_2$, and 91.7 $GyEQD_2$ for different optimization techniques GrO, NO, PO, and PGO, respectively. PGO demonstrated superior mean EQD_2 doses to HRCTV among all optimization techniques. Meanwhile, the PO gave the lowest result. NO gave a better CI value and mean EQD_2 doses to HRCTV than PO, but slightly lower than GrO and PGO because no optimization process was made. If the dose distribution of an implant was not optimized, the parts of the target volume near the outer ends of the catheters often get a lower dose than required [20]. The percentage difference dose of D_{90} HRCTV was −8.18%. A study conducted by Chakrabarti et al. [11] found that the percent-

Table 6
Values of mean EQD_2 doses of D_{2cc} Sigmoid between the GrO and alternative techniques with significant difference.

Optimization technique	Mean EQD_2 doses sigmoid ($GyEQD_2$)	*p*-value	Significant difference ($p < 0.05$)
No optimization	81.50	0.1170	No
Point optimization	67.560	0.0412	Yes
Point Graphical optimization	73.40	0.2474	No

Table 7
Values of percentage difference of doses for D_{90} HRCTV, D_{2cc} bladder, D_{2cc} rectum, and D_{2cc} sigmoid between the graphical optimization and no optimization techniques.

	Mean doses of GrO (Gy)	Mean doses of No Opt (Gy)	Dose Difference (Gy)	Percentage Difference (%)
HRCTV (D_{90})	8.68	7.97	−0.71	−8.18
Bladder	6.46	6.67	0.21	3.25
Rectum	5.24	7.35	2.11	40.27
Sigmoid	4.01	4.90	0.89	22.19

Table 8
Values of percentage difference of doses for D_{90} HRCTV, D_{2cc} bladder, D_{2cc} rectum, and D_{2cc} sigmoid between the Graphical Optimization and Point Optimization techniques.

	Mean doses of GrO (Gy)	Mean doses of No Opt (Gy)	Dose Difference (Gy)	Percentage Difference (%)
HRCTV (D_{90})	8.68	6.74	−1.94	−22.35
Bladder	6.46	5.21	−1.25	−19.35
Rectum	5.24	4.14	−1.10	−20.99
Sigmoid	4.01	3.25	−0.76	−18.95

Table 9
Values of percentage difference of doses for D_{90} HRCTV, D_{2cc} Bladder, D_{2cc} rectum, and D_{2cc} sigmoid between the Graphical Optimization and Point Graphical Optimization techniques.

	Mean doses of GrO (Gy)	Mean doses of No Opt (Gy)	Dose Difference (Gy)	Percentage Difference (%)
HRCTV (D_{90})	8.68	8.72	0.04	0.46
Bladder	6.46	6.00	−0.46	−7.12
Rectum	5.24	5.35	0.11	2.10
Sigmoid	4.01	4.10	0.09	2.24

age average dose for contoured CTV using ring applicator was higher when GrO technique was used (median = 311%) compared with NO technique (median = 194%). PO demonstrated the lowest HRCTV coverage and mean EQD_2 doses among all the optimization techniques with a −22.35% percentage difference of dose compared to GrO.

In the PO plan, points were normalized at the surface or border of the contoured HRCTV. The F-factor influenced point dose normalization, the ratio between the normalization dose and the (mean) dose in the points used for normalization. Normalization is usually performed on the mean dose in target contoured points. This mean dose was used for normalization with F-factor less than 1.0 to cover the HRCTV with minimal peripheral dose [20]. As a result, PO received low mean EQD_2 doses of HRCTV (D_{90}) and CI. When a PO plan is used, the target coverage and dose to HRCTV are frequently reduced in order to meet critical structure constraints. According to the HDR interstitial cervix implants study by Shwetha et al. [15], volume optimization (VO) alone resulted in lower target coverage (mean CI = 0.69). The target coverage then was improved (mean CI = 0.75) by reshaping the isodose line through volume optimization followed by an isodose reshape (VO_IsoR) plan.

Priority was given to the target volume in order to achieve better conformity and a higher dose. The addition of PO followed by GrO optimizes the distribution in terms of conformity and dose delivered to HRCTV. Dose adjustment via the GrO technique is valuable for ensuring optimal target coverage while also limiting doses to the organ at risk [15].

By implementing the PGO plan, the graphical normalization mode, the old normalization dose value was assigned to that new position. In this study, isodose lines covering 95% and 100% of the HRCTV area were drawn following the PO plan until at least 100% of the prescribed dose was achieved by D_{90} HRCTV. This PGO plan did not influence dwelling weights, but the dwelling times changed accordingly. As a result, PGO has a higher mean of EQD_2 doses to HRCTV (D_{90}) and better HRCTV coverage, with a 0.46% difference than GrO doses, meeting one of our main objectives: delivering the maximum dose to the target volume. A study found that combining the GrO with anatomy-based inversed optimization (ABIO) and geometric optimization (GO) improved the mean target coverage for prostate treatment compared to ABIO and GO alone [21].

Varying the dwell times throughout the applicators make it possible to deliver more radiation to a particular area. Increasing the dose in tumor volume might also increase the dose in healthy tissues and critical organs, depending on the catheter positioning and patient geometry [22].

5.2. Mean of EQD_2 doses of OAR between graphical optimization (GrO), no optimization (NO), point optimization (PO), and $_{point}$ graphical optimization (PGO) techniques

The recommended EQD2 doses for D_{2cc} bladder are less than 90 GyEQD2, and ABS has reported less than 75 GyEQD2 for rectum and sigmoid. NO plan had produced the highest mean EQD_2 doses to the bladder (90.52 $GyEQD_2$), rectum (97.88 $GyEQD_2$), and sigmoid (78.08 $GyEQD_2$) with percentage differences of 3.25%, 40.27%, and 22.19%, respectively. The reason is that the dwell position and dwell times were all set to 1 during NO, which means no adjustment was made. The source was activated along with the dwell position of the applicator, exposing the high radiation to the normal tissues. Consequently, the organs at risk in this study (bladder, rectum, and sigmoid) received total mean EQD_2 doses, which exceeded the ABS recommendation. This finding is in line with most reports which show that the average doses to rectum, bladder, and sigmoid were the highest by using Fletcher style tandem without optimization compared to average doses of Fletcher style tandem integrated with graphical optimization [11].

The average EQD_2 doses for bladder, rectum, and sigmoid for PO plan were 78.75 $GyEQD_2$, 69.75 $GyEQD_2$, and 67.56 $GyEQD_2$, respectively, with percentage dose difference values of −19.35%, −20.99%, and −18.95% for bladder, rectum, and sigmoid. PO plan had produced the lowest mean EQD_2 doses to all OARs, which means very good in sparing the normal tissues, compromising the HRCTV coverage and doses to the low level compared to GrO, NO, and PGO techniques. Our main goals of optimization techniques were not only to minimize the dose to OARs but also to maximize the coverage and dose received by the HRCTV. The F-factor value was set to less than 1, which had an effect on the point dose normalization at the HRCTV border in terms of delivering the minimal amount of dose to the peripheral area of the HRCTV surface. So, it will deliver a lower dose to the organ at risk surrounding the HRCTV, resulting in the lowest mean EQD_2 doses of bladder, rectum, and sigmoid for the PO plan. The results exhibited a range of values compared with others stated that the CI for dose point optimization (DPO) resulted in the lowest conformity index of 0.68 compared with GrO with 0.72 conformity index [23]. PO then was combined with GrO, known as PGO, to give a better dose to HRCTV.

Consequently, PGO resulted in higher mean EQD_2 doses to the bladder (meanEQD_2 = 83.85 $GyEQD_2$) and sigmoid (mean EQD_2 = 73.4 $GyEQD_2$) compared to PO alone, but still below the limitation recommended by ABS, except for rectum (mean EQD_2 = 78.03 $GyEQD_2$). The percentage difference values were −7.12%, 2.10%, and 2.24% for bladder, rectum, and sigmoid, respectively. The most likely explanation is that when 95% isodose lines were dragged around the surface of HRCTV during GrO, it was possible for the 95% isodose line to be slightly included in the rectum area, resulting in the rectum receiving high doses. Optimal reduction of dose to the rectum by using GrO and PGO without compromising the target coverage can be replanned, and it depends on the clinician's decision and the physician's experience. This argument is consistent with other studies' findings that GrO is not reproducible and is primarily influenced by a physician's experience and that the geometric shape of the target varies between patients may be a factor in achieving desired dose coverage [8]. Isodose reshaping is a useful tool that allows the planner to manipulate and adjust as required. Care should be taken to ensure that the target coverage is maximized when manipulating the isodose line in a single CT slice while maintaining an acceptable dose to the bladder, rectum, and sigmoid.

6. Conclusion

In conclusion, the mean of CI for all different optimization techniques was clinically acceptable; however, PGO was much better than NO and PO techniques in comparison with GrO. Mean EQD_2 doses HRCTV for all optimization techniques were also clinically acceptable, while PGO documented the highest mean EQD_2 with no significant difference compared to GrO. Unfortunately, mean EQD_2 doses OARs for NO were not clinically acceptable because mean EQD_2 exceeded the tolerance mean EQD_2 dose limits recommended by ABS for all organs at risk (bladder, rectum, and sigmoid). PO was much superior in sparing critical structures but very poor in target coverage and dose to HRCTV. Generally, in our finding, PGO shows comparable optimization compared to routine optimizations (GrO) in treatment planning, while other optimizations are still clinically acceptable to be used PGO demonstrated exceptional mean CI performance, which is advantageous for treatment planning procedures such as dose coverage (CI) and OAR

sparing. Our study recommends PGO as an alternative optimization technique for GrO in brachytherapy planning whenever demanded. In the future, the performance of PGO, GrO, and Inverse Planning Simulated Annealing (IPSA) will be explored.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors wish to express their heartfelt appreciation to the Department of Higher Education (Malaysia) for funding this research through a RUI Grant (No. 1001304/CIPPT/8011001). Additionally, we appreciate the Advanced Medical and Dental Institute of Universiti Sains Malaysia and the staff of the Radiotherapy Department of the Hospital Universiti Sains Malaysia.

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