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ORIGINAL ARTICLE

The Comparison of Volumetric Optimization and Reference Line Optimization on Organs at Risk Doses in Three-dimensional Vaginal Vault Brachytherapy

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OBJECTIVE

To compare reference-line (RL) and “inverse” optimization (IO) on organs at risk (OAR) and clinical target volume (CTV) doses in patients receiving vaginal cuff (VC) brachytherapy (BT).

METHODS

CT images of 20 patients were used who received VC BT using “Stump” applicator after external-beam RT (EBRT). Reference-line optimization (RLO) was performed to the line composed of 8 symmetrical points at 0.5cm from the applicator’s surface. Dose was prescribed to CTV in IO with introduction of optimization goals (CTV: D98%≥85%, D90%≥100%, V100%≥92.5%, and OARD2ccEQD2 total doses: Bladder ≤9000 cGy, rectum, sigmoid, and bowel ≤7000 cGy). Using Wilcoxon Signed-Rank test, 2 different optimization techniques were compared with respect to their effects on CTV dose-volume parameters and OAR D2cc.

RESULTS

Significantly lower D2ccEQD2 doses could be obtained with IO compared to RLO (p<0.001, p=0.004, p=0.001, and p=0.001 for bladder, rectum, sigmoid, and bowel, respectively). Significantly higher doses could be obtained with RLO for CTV D90% and V100% (p<0.001, and p<0.001, respectively). D%50/D%90 is significantly lower in IO (p<0.001). It was detected that CTV criteria could be met in all cases where OAR criteria of ≤7000cGy was violated only for rectum in 1 case in IO and 3 cases in RLO.

CONCLUSION

In both types of optimizations, desired criteria are met for CTV while they may not be met constantly in all cases. The resultant significant difference in favor of IO regarding OARs supports the routine clinical use of IO in VC BT.

Keywords: Brachytherapy; clinical target volume; inverse optimization; organs at risk; reference line optimization; vaginal cuff.

INTRODUCTION

Intracavitary vaginal brachytherapy (BT) can be administered either alone or after external beam radiotherapy (EBRT) in the adjuvant treatment of patients who have undergone surgery for cervical and endometrial cancer.[1,2] In intracavitary vaginal BT applications, the organs at risk (OARs) affected by radiotherapy (RT) include

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the bladder, rectum, sigmoid colon, and small bowel. Reducing the potential side effects associated with BT is highly dependent not only on the quality of the application and the administered dose but also on the quality of the computerized treatment planning (TP) for BT. Computerized TP enables the delivery of an adequate dose to the clinical target volume (CTV) while restricting the doses to the OARs. Compared to single-point optimization, more optimal dose distributions can be achieved through various optimization strategies, including manual optimization, geometric optimization (normalized to a point or line), graphical optimization, and inverse planning volumetric optimization.[3–8]

In the literature, there exists only one study that compares inverse planning volumetric optimization with forward planning reference line (RL) optimization in vaginal cuff BT. In Bahadur et al.[7]s study, the coverage of the CTV and the doses received by OARs, specifically in terms of 2 cc volumes (D2cc) (maximum radiation dose delivered to the most exposed 2 cc of a specified organ or tissue in a RT treatment plan) were compared among forward planning techniques using 2 conventional optimization methods (optimization at a single point 0.5 cm proximal to the apex of the stump applicator and optimization at the RL drawn 0.5 cm away from the lateral aspect of the applicator) and the inverse planning technique utilizing volume optimization. However, in that study, the line in the RL optimization is a straight uncurved line and does not adequately represent the dose received by the vaginal vault. Given that the vaginal cuff is not solely represented by the vaginal side walls, an accurate comparison between RL optimization and volumetric optimization necessitates that RL covers both the curved apex and straight side walls of the vaginal cuff. Thus, our study aims to compare inverse planning using vaginal cuff CTV optimization with forward planning using RL optimization (RL created by combining 8 points at 0.5 cm from the apex and side walls of the vaginal cuff surface) in terms of CTV dose-volume parameters and OAR doses. As the first study comparing forward planning using an accurate RL optimization technique with inverse planning using volumetric optimization, our aim is to elucidate which optimization technique proves more relevant for routine clinical applications in vaginal cuff BT.

MATERIALS AND METHODS

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Non-interventional Research Ethics Committee (No: 2019/13-21, Date: 22/05/2019).

This retrospective study used CT scans of 20 patients with cervical and endometrial cancer who underwent adjuvant EBRT (4500 cGy) followed by 3D BT (3x600 cGy). Our study aimed to compare the doses obtained from volumetric optimization and RL optimization in vaginal cuff BT using the stump applicator. The Varian ARIA Oncology Information System for Radiation Oncology (OIS for RO) server and Varian BrachyVision v.11.0 Brachytherapy Treatment Planning System were utilized for data management and BT planning, respectively. GammaMedplus iX HDR Afterloader System housing ^{192}Iridium radioactive source was used for treatment delivery in BT.

In vaginal cuff BT, stump applicator with the largest diameter suitable for the patient's vaginal width had been inserted. In the CT slices obtained, vaginal length was measured in sagittal sections from the vaginal apex to the vaginal entrance. Vaginal cuff CTV's length was taken as one third of the measured vaginal length. Vaginal cuff CTV volume was delineated by adding a 0.5 cm margin to the cylindrical applicator contour in all directions and cropping the cylindrical applicator contour from the CTV contour. For RL length determination, the vaginal cuff CTV length was considered from the sagittal CT sections. The midline of the stump applicator in the coronal plane was selected as the section to draw RL, and the RL was drawn symmetrically on both sides of the applicator with a total of 8 points located 0.5 cm away from the applicator. Figure 1 illustrates the creation of the RL for each case.

In inverse planning using volumetric optimization, dose-volume parameter criteria for the CTV were determined as follows: D98%≥85%, D90%≥100%, V100%≥92.5% and D50%/D90%≤1.5 (DX%: minimum dose expressed in percentage received by a volume of a structure, V100%: percentage of CTV receiving 100% of the defined dose). In inverse planning using volumetric optimization, the biological equivalent dose in terms of 2 Gy per fraction (EQD2) according to α/β=3 that 2 cc volumes of OARs would receive were restricted ensuring they did not exceed recommended limits. In the light of GEC-ESTRO recommendations, OAR D2cc EQD2 cumulative doses for bladder, sigmoid, rectum and bowel were set as ≤9000 cGy, ≤7000 cGy, ≤7000 cGy and ≤7000 cGy, respectively.[9] In inverse planning, all criteria (CTV and OARs) were given equal priority, and no user intervention was made during volumetric optimization in any plan. Figure 2 illustrates 3D view of CTV and OARs contoured for inverse planning using volumetric optimization. RL optimization aims to ensure dose consistency along the RL without consideration

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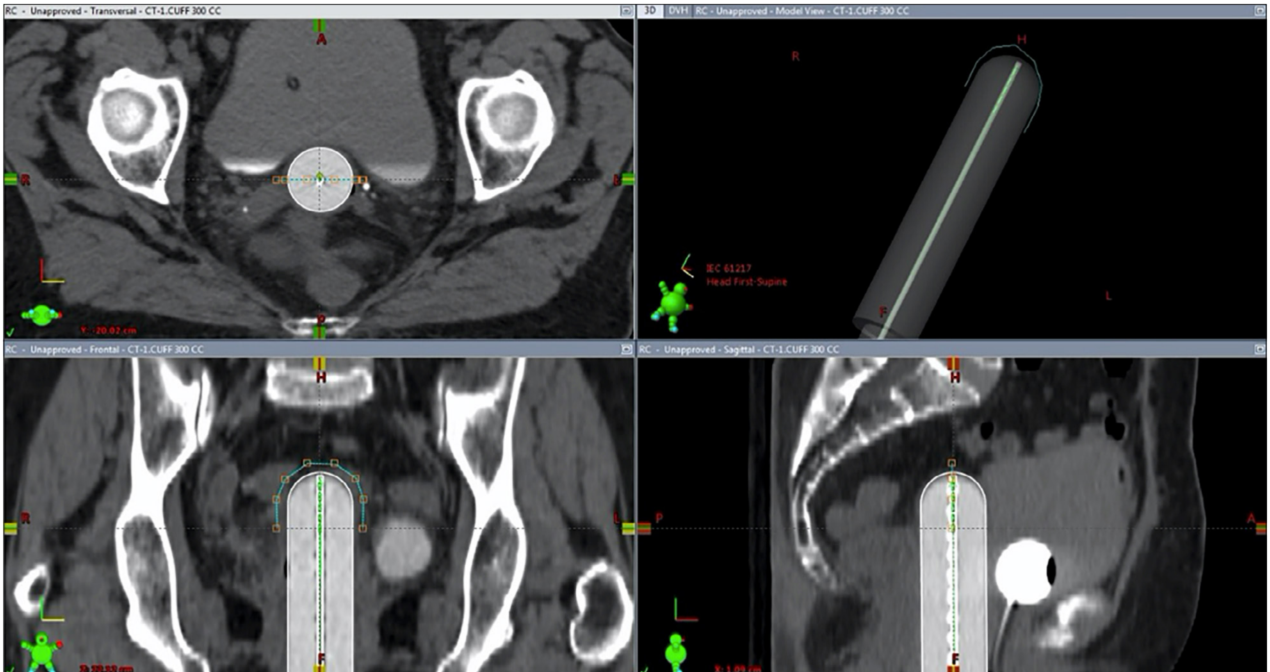

Fig. 1. Determining the reference line in the computed tomography sections.

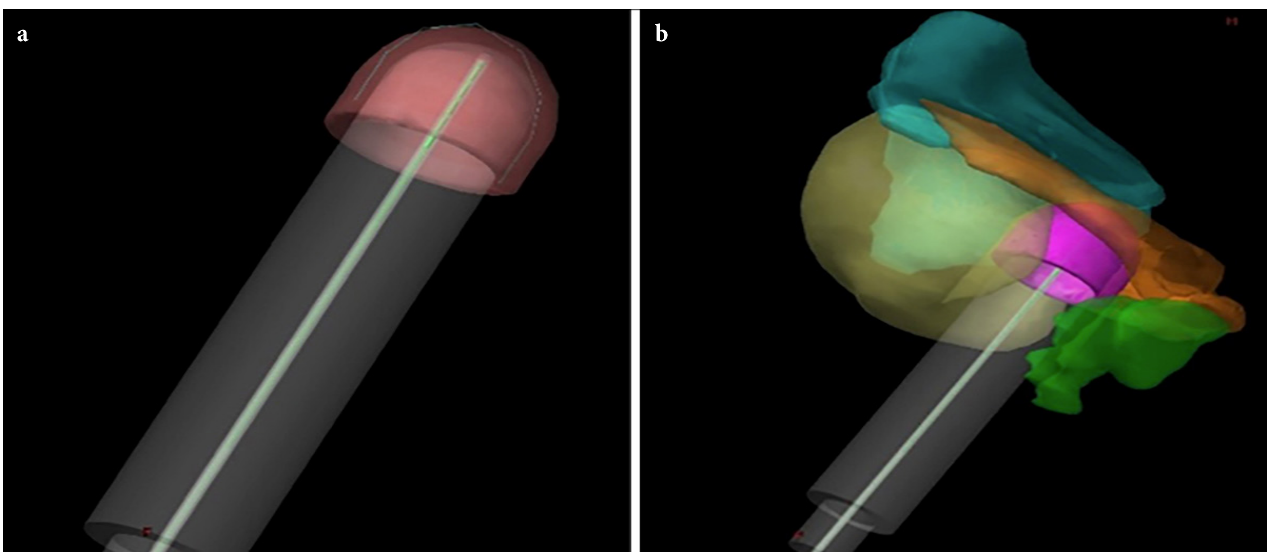

Fig. 2. (a) CTV contour in 3D, (b) CTV and OAR contours in 3D.
CTV: Clinical target volume; OAR: Organs at risk.

of dose to OARs during optimization. Inhomogeneity correction was not performed in BT planning. After dose calculation was made in RL, the dose-volume parameters of the vaginal cuff CTV and OARs were examined through Dose Volume Histogram (DVH).

Comparisons were made between the two optimization techniques (volumetric and RL optimization) in terms of OAR (bladder, rectum, sigmoid, and bowel) D2cc doses. In addition, two optimization techniques were compared in terms of CTV dose-volume parameters (D90%, D50%/D90% and V100%).

Given the number of cases included in the study was below 30, statistical analysis was performed using non-parametric tests (Wilcoxon Signed-Rank test comparing two paired samples) with SPSS software. The p value of <0.05 was considered statistically significant.

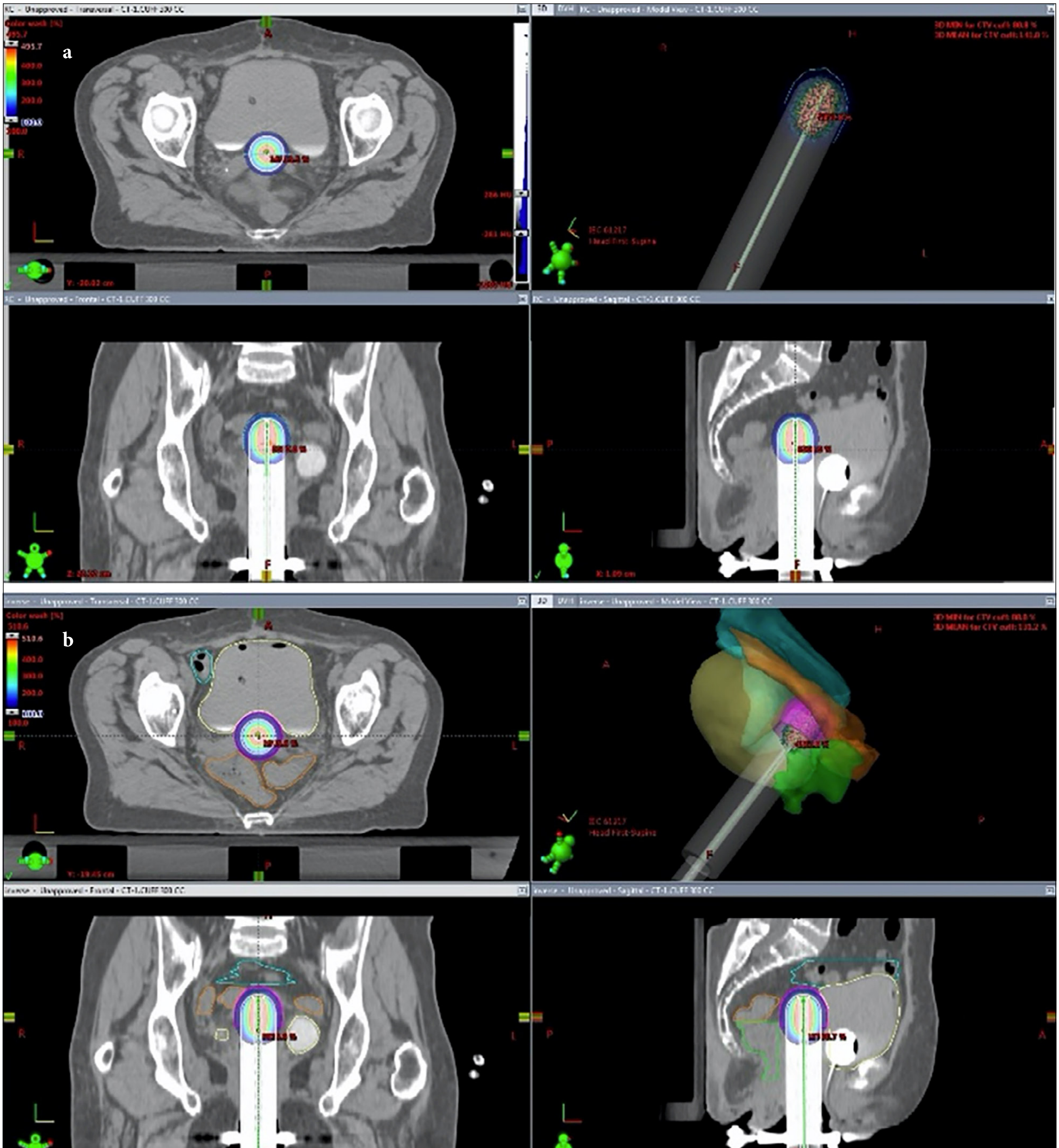

Fig. 3. (a) Cross-sectional images of the dose distribution obtained by reference line optimization, (b) cross-sectional images of the dose distribution obtained with volumetric optimization.

RESULTS

The stump applicator diameters used in our study were 3 and 3.5 cm. It was found that the craniocaudal length of CTV varied between 2.5 and 4 cm across cases.

Cross-sectional images illustrating the dose distributions of inverse planning volumetric optimization and forward planning RL optimization are presented in Figure 3.

Table 1 displays the statistical comparison of OAR EQD2 total (EBRT+BT) doses obtained through volu-

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Table 1 Statistical comparison of OAR EQD2 total (EBRT+BT) doses obtained through inverse planning volumetric optimization and forward planning RL optimization

	OARs		
	D2cc EQD2 total*	**Mean(cGy)±SD**	**p-value RL vs volumetric**
Bladder	RL	7077±562.2	<0.001
	Volumetric	6837.1±428.5	
Sigmoid	RL	5996.3±609.7	0.001
	Volumetric	5883.9±575.9	
Rectum	RL	6304.0±656.7	0.004
	Volumetric	6184.3±595.5	
Bowel	RL	5651.8±687.0	0.001
	Volumetric	5570.5±660.9	

*: Total: sum of external beam radiotherapy and brachytherapy doses. OAR: Organs at risk; EQD2: Biological equivalent dose in terms of 2 Gy per fraction according to α/β=3; RL: Reference line; D2cc: Maximum radiation dose delivered to the most exposed 2 cc of an organ; SD: Standard deviation

Table 2 Statistical comparison of CTV dose-volume parameters D90%, V100% and D50%/D90% obtained through inverse planning volumetric optimization and forward planning RL optimization

	CTV	
	Mean±SD	**p-value RL vs volumetric**
D90%* RL	106.9±3.2	<0.001
D90% volumetric	102.7±0.9	
V100%** RL	97.1±1.8	<0.001
V100% volumetric	94.3±1.2	
D50%*** /D90% RL	1.20±0.02	<0.001
D50%/D90% volumetric	1.19±0.02	

*: D90%: Percentage of minimum dose received by 90% of CTV; **: V100%: Percentage of CTV volume receiving 100% of the prescribed dose; ***: D50%: Percentage of minimum dose received by 50% of CTV. CTV: Clinical target volume; SD: Standard deviation; RL: Reference-line

metric and RL optimization across all cases (Table 1). In Table 1, it is seen in general that statistically significantly lower doses were obtained from volumetric optimization for all OARs compared to RL optimization.

Table 2 presents the statistical comparison of CTV dose-volume parameters, including D90%, V100%, and D50%/D90%, obtained through volumetric and RL optimization (Table 2). Across all cases, D90% and V100% parameters obtained from RL optimization are observed to be statistically significantly higher compared to volumetric optimization. Conversely, D50%/D90% parameter (recommended to be as low as possible below the 1.5 threshold value) obtained from volumetric optimization is statistically significantly lower compared to RL optimization.

Mean total reference air kerma (TRAK) was 3213±323 (2526–3573) cGy.cm^2 and 3071±306 (2246–3507) cGy.cm^2 for RL and volumetric optimization, respectively. Range of dwell times was 16–119.8 seconds, and 9.3–73.3 seconds for RL and volumetric optimization, respectively.

DISCUSSION

In vaginal cuff BT, geometrical line optimization, graphical, or inverse planning volumetric optimization have been shown to achieve more optimal dose distribution compared to geometrical single-point optimization.[3–8] However, a standardized approach has not yet been established in this regard.

In Bahadur et al.[7]s study, CTV and OAR dose-volume parameters were compared using three different optimization techniques in BT TP. In their series, 26 patients were administered three fractions of 400 cGy as BT after a total dose of 4500 cGy EBRT. The three techniques included normalization to a single reference point positioned 0.5 cm away from the vaginal vault towards cranial direction, optimization to the RL created 0.5 cm away from only the lateral wall of the vagina, and inverse planning volumetric optimization using dose-volume criteria for CTV and OARs.

In our study, we compared CTV and OAR dose-volume parameters using two different optimization techniques: Inverse planning volumetric optimization and forward planning RL optimization. In our series, 20 patients had been treated with three fractions of 600 cGy BT following a total dose of 4500 cGy EBRT.

Bahadur et al.[7] study compared inverse planning volumetric optimization with forward planning RL optimization; however, their RL was not curved in accordance with the shape of vaginal cuff and thus did not represent the apex of vaginal cuff. However, since the vaginal cuff is not solely represented by the vaginal side walls, an appropriate comparison necessitates RL covering both the vaginal apex and vaginal side walls completely. In our study, RL was created by combining 8 symmetrical points 0.5 cm away from the apex and side walls of the vaginal cuff surface. The superiority in our study is the formation of a curved RL similar to the shape of CTV. To our knowledge, our study is the first one to compare forward planning RL optimization and inverse planning volumetric optimization in vaginal cuff BT with an accurate methodology, and it aims to determine the more relevant optimization technique for clinical routine applications.

Although the optimization criteria for CTV and OARs in inverse planning volumetric optimization differed between the two studies, equal priority was given to all criteria in both studies. Bahadur et al.[7] found that among 3 different optimizations, inverse planning volumetric optimization provided the best CTV dose coverage. In our study, criteria including D98%≥85%, D90%≥100%, V100%≥92.5%, and D50%/D90%≤1.5 for CTV were provided for all cases in both volumetric and RL optimizations. Although RL was statistically significantly superior in D90% and V100% parameters of CTV, volumetric optimization was statistically significantly superior in D50%/D90%.

Since CTV dose-volume criteria were met in all cases in our study, the choice between optimization methods is unlikely to create a disadvantage in terms of disease control.

In Bahadur et al.[7]s study, RL optimization provided the lowest dose among 3 different optimizations for OARs. In our study, it was observed that the limit of D2cc EQD2≤7000 cGy was exceeded in only 1 case for the rectum in the volumetric optimization and in 3 cases in the RL optimization. It should be noted that 7500 cGy - which is the most recommended upper dose limit - was not exceeded in these 4 cases. Unlike Bahadur et al.[7]s study, our study showed that volumetric optimization could provide statistically significantly lower doses for OARs compared to RL optimization. This difference in the sparing of OARs between the two studies is attributed to differences in RL shape and location as well as OAR optimization criteria.

Recently, Rovirosa et al.[10] reported the results of a dosimetric study on HDR 3D planning in vaginal cuff BT. In that study, it is concluded that prescribing at 5 mm and the use of an applicator diameter of 3.5 cm is the most adequate for CTV coverage with a lower vaginal mucosa dose. In our study, we also preferred drawing the reference line at 5 mm distance from the vaginal surface for RL optimization, and we contoured the vaginal cuff CTV with a thickness of 5 mm for inverse planning volumetric optimization. In terms of applicator diameter, we also preferred using the largest stump applicator diameter suitable for the patient's vaginal width. Thus, the applicator diameter was 3.5 cm in relevant patients in our series.

When multichannel applicators are used instead of single channel applicators in vaginal BT, the choice of optimization method becomes even more important. In a study performed by Carrara et al.,[11] different treatment planning optimization methods were compared in vaginal HDR BT with multichannel applicators. IO methods were more effective in reducing hot spots to the vaginal mucosa compared to forward optimization methods.

It should be noted that when time required for different optimization methods is considered, geometric optimization (normalized to a point or line) and graphical optimization usually are more advantageous than IO methods. Especially in busy clinics with high workload, selection of optimization method may also be influenced by this time factor.

Limitations of the study

The limitation of the study is the number of patients included in the study being less than 30.

CONCLUSION

Consequently, while both volumetric and RL optimizations meet the determined criteria for CTV, this is not always the case for OARs. In RT, adherence to the "As Low As Reasonably Achievable" (ALARA) principle for OARs is essential, aiming to minimize OAR dose exposure. In this context, the resultant significant difference in favor of inverse planning volumetric optimization regarding OARs supports the use of this optimization technique for routine clinical applications in vaginal cuff BT with the stump applicator.

Ethics Committee Approval: The study was approved by the Dokuz Eylül University Non-interventional Research Ethics Committee (no: 2019/13-21, date: 22/05/2019).

Informed Consent: Informed consent was obtained from all participants.

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