Plan-Optimization Method for Central-shielding Pelvic Volumetric-modulated Arc Therapy for Cervical Cancer

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Abstract. *Aim: To establish a method of plan optimization in pelvic volumetric-modulated arc therapy (VMAT) for cervical cancer using the central-shielding (CS) principle. Patients and Methods: We created external beam VMAT plans for eight cases with non-bulky stage I-IIb using the CS principle based on the Japanese standard guideline. Clinical target volumes (CTVs) for whole-pelvis (WP) irradiation were created using published guidelines, and CTVs for CS irradiation were created by subtracting the uterus corpus and 4 cm-wide regions centered at the cervix and vagina from the CTVs for WP irradiation. For plan optimization of CS irradiation, a 4-cm diameter cylindrical volume centered in the cervix and vagina was created as the volume receiving a high dose in brachytherapy, and the volume overlapping with the rectum was defined as the Ant-Rectum. Dose-volume histogram (DVH) parameters of two CS VMAT plans with and without (VMAT_{OPT}/VMAT_{NO}) dose optimization to the Ant-Rectum were compared. Results: VMAT_{OPT} plans resulted in significantly lower DVH parameters of the Ant-Rectum and rectum compared to VMAT_{NO} plans. These were comparable to the DVH parameters of three-dimensional conformal radiotherapy (3DCRT) plans. Both VMAT plans resulted in significantly better coverage of planning target volumes than did the 3DCRT plans. Conclusion: In the implementation of IMRT/VMAT as the standard treatment for cervical cancer in Japan, our optimization method may be an essential step toward fully benefitting from the CS principle.*

The standard radiotherapy for uterine cervical cancer is a combination of external beam radiotherapy (EBRT) and intracavitary brachytherapy (ICBT). In Japan, standard EBRT consists of whole pelvic (WP)- and central shielding (CS)-EBRT (1). CS-EBRT is generally achieved by placing a rectangular midline block (3-4 cm width) or equivalent shielding with multileaf collimators in two opposing anterior-posterior fields, thereby reducing the radiation dose to organs at risk (OARs) such as the bladder and the rectum, while providing the necessary dose to the pelvic lymph nodes and parametria. This treatment strategy may be responsible for the relatively low incidence of late toxicities in the rectum and bladder of patients treated according to Japanese treatment protocols (2-4). Given that CS-EBRT is applied using the technique of two-dimensional or three-dimensional conformal radiotherapy (3DCRT), there are several drawbacks, including inadequate shielding of OARs outside the midline block, such as the small bowel, sigmoidal colon, and pelvic bones. In addition, the shielding does not always conform to the shape of the bladder and the rectum.

Compared to 3DCRT, intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT) have superior dose distributions that conform to the shape of the target volume, and as a result, yield lower acute and late radiation toxicities without compromising the treatment effects for various types of tumors. WP-IMRT/VMAT has been used increasingly to treat cervical cancer in countries which do not perform CS-EBRT and was shown to yield better dose distribution and clinical results for OARs (5-9). In order to improve standard radiotherapy for cervical cancer in Japan, we previously conducted a dose-planning study which applied IMRT/VMAT to radiotherapy for early-stage non-bulky cervical cancer cases. For CS-EBRT in that study, we re-examined the principle of CS and defined the specific clinical target volume (CTV) of CS-EBRT, a crucial step in the treatment planning of IMRT/VMAT (10). Nonetheless, the original purpose of CS-EBRT, which is to specifically shield the bladder and the rectum, must be maintained in CS-VMAT.

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Figure 1. Schematics of the definition of the clinical target volume with central-shielding external beam radiotherapy (CTV-CS) (A) and the Ant-Rectum (B). The cylindrical volume was positioned in the cervix and vaginal canal.

The principle of CS can easily be visualized and is conceptually clear in 3CDRT, given the presence of midline block/shielding. However, it may be unclear and easily overlooked in the planning of IMRT/VMAT because optimizing the doses simply for the planning target volume (PTV) and the overall volume of OARs may not be sufficient to achieve the original purpose. It is essential to identify specific regions with high risk of radiation toxicities, *i.e.* regions which receive high doses from ICBT (ICBT hotspot). In radiotherapy for cervical cancer, the anterior rectal wall is one of the most critical areas of OARs because it is in close proximity to the cervical tumor and susceptible to receiving a high radiation dose from the combination of EBRT and ICBT (11, 12). The reported dose constraint for the anterior rectal wall is lower than that for the posterior wall of the bladder (13, 14), and reducing the radiation dose to the anterior rectal wall is important in minimizing the risk of late rectal toxicities and overall toxicities (15, 16). In fact, the concept of optimizing the dose to ICBT hotspots in CS-VMAT planning is a unique concept for the following two reasons. Firstly, unlike other types of cancer, cervical cancer requires not only EBRT but a combination of EBRT and ICBT. Secondly, as opposed to CS-VMAT, the PTV of WP-VMAT may frequently include the anterior rectal wall and therefore provides no opportunity to lower the dose to the ICBT hotspot.

In the present study, we introduced a dose optimization method which entails identifying the ICBT hotspot in the anterior rectal wall. We analyzed dose distributions and dose-volume histograms (DVHs) of CS-VMAT and evaluated treatment plans which were optimized only for the overall OARs or additionally for the identified ICBT hotspot. Our results showed the effectiveness of the optimization method,

which minimize the dose to the ICBT hotspot in the anterior rectal wall, and highlights the importance of the method when implementing CS-VMAT.

Patients and Methods

Delineation of target volumes and OARs. This study was approved by the Institutional Review Board of our Institute. Computed tomographic image data of eight patients with cervical cancer who underwent definitive radiotherapy at our hospital from January 2015 to August 2015 were analyzed in the study. All patients had stage I-IIB disease with a maximum tumor size <4 cm. Definitions of the CTVs for non-bulky cervical cancer cases were defined and described in a previous report on the application of WP-VMAT and CS-VMAT (10). Briefly, the CTVs for primary disease of the uterine cervix (CTV-PD) and pelvic lymph nodes (CTV-LN) were delineated according to published guidelines (17, 18). CTV-WP was defined as the sum of the CTV-PD and CTV-LN. In order to create the CTV-CS, the uterus corpus and a 4-cm wide region centered at the cervical canal and the center of vagina, but not at the center of the pelvic bony structure, were subtracted from the CTV-WP (Figure 1A). The outer contours of the bladder, rectum, bowel bag (small and large intestines), and the bilateral femoral head were delineated as OARs. In addition, a 4-cm diameter cylindrical volume centered in the cervix and vaginal canal was created and represented the volume irradiated with a high dose in ICBT. The overlapping region between the rectum and the 4-cm diameter cylindrical volume was defined as the dummy structure, Ant-Rectum, which represented the high-risk region of radiation rectal toxicity caused by high dose irradiation (Figure 1B). The Ant-Rectum was created for the optimization process to minimize the anterior rectal dose in CS-VMAT.

Planning. In this planning study, we postulated that all patients were treated with 20 Gy/10 fractions of WP-EBRT and 30 Gy/15 fractions of CS-EBRT according to Japanese guidelines (2-4). For the treatment planning of CS-EBRT, a PTV margin of 5 mm was

Figure 2. Dose distributions of three-dimensional conformal radiotherapy (A), volumetric-modulated arc therapy (VMAT) without dose optimization for the Ant-Rectum (VMAT_{NO}) (B), and VMAT with dose optimization for the Ant-Rectum (VMAT_{OPT}) (C). The upper panel shows axial views and the lower shows sagittal views. Dose range of 50% or more of the prescribed dose is indicated by color wash.

added to the CTV-CS, and the following three treatment plans were evaluated: 3DCRT, VMAT with dose optimization only for the OARs (VMAT_{NO}), and VMAT with dose optimization for the Ant-Rectum in addition to the OARs (VMAT_{OPT}). For 3DCRT, the anterior and posterior parallel opposed portals were created, and a 3-cm wide CS was placed at the center of the bony pelvis. The height of the CS was adjusted such that it did not compromise the presacral lymph node region. A total dose of 30 Gy/15 fractions was delivered using 10 MV X-rays. For VMAT planning, a double-arc VMAT plan using 10 MV x-ray beams was created for the PTV-CS. The dose prescription was based on PTV-CS $D_{50\%}$ values with the planning aims as follows: PTV-CS $D_{95\%}>92\%$ and PTV-CS $D_{2\%}<110\%$. For VMAT_{NO}, planning aims for OARs were set as follows: for the rectum, volume receiving 24 Gy ($V_{24\text{ Gy}}$) $<85\%$, volume receiving 30 Gy ($V_{30\text{ Gy}}$) $<40\%$, the maximum dose (D_{max}) $<110\%$; for the bladder, $D_{\text{max}}<110\%$; for the bowel bag, $V_{24\text{ Gy}}<40\%$; for the femoral heads, $V_{18\text{ Gy}}<40\%$; and for the whole body, $D_{\text{max}}<115\%$. For VMAT_{OPT}, in addition to meeting the planning aims of VMAT_{NO}, the plans were optimized to reduce the dose to the Ant-Rectum to the maximum extent while maintaining the required coverage of the PTV-CS ($D_{95\%}>92\%$). All calculations were performed using the treatment planning system Eclipse version 11 with Analytical Anisotropic Algorithm (AAA, ver. 11.0.31; Varian Medical Systems, Inc., Palo Alto, CA, USA). To evaluate the treatment plans, $D_{95\%}$, $D_{98\%}$, and $D_{2\%}$ of the PTV-CS, $V_{60\%}$, $V_{80\%}$, D_{max} , and $D_2\text{ cm}^3$ of the rectum, bladder, and the bowel bag were analyzed for 3DCRT, VMAT_{NO}, and VMAT_{OPT} plans. In order to assess the dose to the anterior rectal wall, we also analyzed $V_{60\%}$, $V_{80\%}$, D_{max} , and $D_2\text{ cm}^3$ of the Ant-Rectum. Parameters for each plan were compared using the non-parametric Wilcoxon signed-rank test. p -Values less than 0.05 were considered statistically significant.

Results

The Ant-Rectum was contoured successfully in all studied cases, and the average volume $\pm$ SD of the Ant-Rectum was

6.5 $\pm$ 3.3 cm³. Overlap of the PTV-CS and the Ant-Rectum was minimal (0.2 $\pm$ 0.2 cm³).

Dose distributions of the 3DCRT, VMAT_{NO}, and VMAT_{OPT} plans of a case are shown in Figure 2, and representative DVHs of the PTV-CS, rectum, Ant-Rectum, bladder, and the bowel bag are shown in Figure 3. Table I summarizes the DVH parameters of the eight cases. Most of the Ant-Rectum was directly shielded by the midline block in 3DCRT plans. DVH curves revealed that the dose to the Ant-Rectum was lower in VMAT_{OPT} plans than that in VMAT_{NO} plans. When comparing DVH parameters of the Ant-Rectum, all parameters of VMAT_{OPT} plans were significantly lower than those of VMAT_{NO} plans. VMAT_{OPT} plans showed almost equivalent $V_{60\%}$, $V_{80\%}$, and D_{max} to 3DCRT plans. Regarding DVH parameters of the rectum, VMAT_{OPT} plans showed significantly lower $V_{60\%}$, $V_{80\%}$, and $D_2\text{ cm}^3$ than those of VMAT_{NO} plans. VMAT_{NO} and VMAT_{OPT} plans showed significantly lower $V_{80\%}$ than that of 3DCRT plans, although $V_{60\%}$, D_{max} , and $D_2\text{ cm}^3$ did not differ significantly between 3DCRT and VMAT_{NO}/OPT plans. For the bowel bag, VMAT_{NO} and VMAT_{OPT} plans showed comparable DVH parameters (D_{max} of the bowel bag was slightly (1%) higher in VMAT_{OPT} with a p -value of 0.0547). Compared to 3DCRT plans, both VMAT_{NO} and VMAT_{OPT} plans had lower $V_{60\%}$ and $V_{80\%}$ and higher D_{max} . For the bladder, VMAT_{NO} and VMAT_{OPT} plans had comparable DVH parameters ($V_{60\%}$ of the bladder was slightly (2.2%) higher in VMAT_{OPT} with a $p=0.0547$). Compared to 3DCRT plans, both VMAT_{NO} and VMAT_{OPT} plans had lower $V_{80\%}$ and higher $V_{60\%}$ and D_{max} .

In Figure 2A, the medial portion of the PTV-CS which had midline shielding did not receive a high dose in the

Figure 3. Representative dose-volume histograms (DVHs) of the planning target volume with central-shielding (PTV-CS) (A), rectum (B), Ant-Rectum (C), bladder (D), and bowel bag (E) comparing three-dimensional conformal radiotherapy (3DCRT) and volumetric-modulated arc therapy (VMAT) plans in clinical cases. Solid line: DVH curve of 3DCRT plan; dashed line: DVH curve of VMAT plan without dose optimization for the Ant-Rectum (VMAT_{NO}); dotted line: DVH curve of VMAT plan with dose optimization for the Ant-Rectum (VMAT_{OPT}).

3DCRT plan. In contrast, this portion was covered with a high dose in both VMAT_{NO} and VMAT_{OPT} plans (Figure 2B and C). DVH curves also revealed the higher dose coverage of the PTV-CS in both VMAT_{NO} and VMAT_{OPT} plans compared to that in the 3DCRT plan (Figure 3A). DVH parameters also showed improved coverage of the PTV-CS in both VMAT_{OPT} and VMAT_{NO} plans compared to the 3DCRT plan, as reflected in the significantly higher $D_{95\%}$

and $D_{98\%}$ of the PTV-CS. When comparing the two VMAT plans, the VMAT_{OPT} plan had lower $D_{95\%}$ and $D_{98\%}$ than those of the VMAT_{NO} plan.

Discussion

In radiotherapy for cervical cancer, late rectal toxicities, such as a radiation proctitis, rectal ulcer, and rectovaginal fistula,

Table I. Comparison of parameters of the planning target volume with central-shielding (PTV-CS) and the Ant-Rectum between three-dimensional conformal radiotherapy (3DCRT) and volumetric-modulated arc therapy (VMAT) plans.

Volume of interest (average $\pm$ SD)	Parameter	3DCRT	VMAT _{NO}	VMAT _{OPT}	p-Values		
					3DCRT vs. VMATNO	3DCRT vs. VMATOPT	VMATNO vs. VMATOPT
PTV-CS (760.7 $\pm$ 71.4 cm ³)	$D_{95\%}$	84.4 $\pm$ 9.8	93.4 $\pm$ 0.7	92.8 $\pm$ 0.8	0.0391	0.0547	0.0234
	$D_{98\%}$	45.5 $\pm$ 23.9	91.1 $\pm$ 1.0	90.1 $\pm$ 1.3	0.0078	0.0078	0.0234
	$D_{2\%}$	101.9 $\pm$ 0.8	106.3 $\pm$ 0.7	106.3 $\pm$ 0.5	0.0078	0.0078	0.8438
Rectum (58.4 $\pm$ 23.2 cm ³)	$V_{60\%}$	21.4 $\pm$ 8.8	16.7 $\pm$ 3.8	15.2 $\pm$ 4.6	0.1953	0.1484	0.0391
	$V_{80\%}$	15.8 $\pm$ 7.9	7.7 $\pm$ 3.3	6.5 $\pm$ 3.0	0.0156	0.0156	0.0234
	$D_{\max}$	99.1 $\pm$ 2.6	100.4 $\pm$ 3.1	99.2 $\pm$ 2.7	0.1953	0.9453	0.0781
Ant-Rectum (6.5 $\pm$ 3.3 cm ³)	D_2 cm ³	89.8 $\pm$ 18.3	87.3 $\pm$ 6.9	85.3 $\pm$ 6.9	0.1953	0.1953	0.0078
	$V_{60\%}$	1.5 $\pm$ 2.0	17.1 $\pm$ 8.3	0.9 $\pm$ 0.7	0.0078	>0.999	0.0078
	$V_{80\%}$	0.7 $\pm$ 1.2	3.6 $\pm$ 3.4	0.0 $\pm$ 0.0	0.0781	0.5000	0.0156
Bowel bag (1457.0 $\pm$ 559.4 cm ³)	$D_{\max}$	65.0 $\pm$ 26.8	91.1 $\pm$ 6.2	71.4 $\pm$ 6.3	0.0234	0.5469	0.0078
	D_2 cm ³	15.8 $\pm$ 5.1	46.2 $\pm$ 18.5	33.0 $\pm$ 9.5	0.0078	0.0078	0.0156
	$V_{60\%}$	58.7 $\pm$ 3.9	46.9 $\pm$ 6.0	47.9 $\pm$ 5.8	0.0078	0.0078	0.1484
Bladder (83.6 $\pm$ 44.1 cm ³)	$V_{80\%}$	55.6 $\pm$ 3.8	28.7 $\pm$ 4.1	29.0 $\pm$ 4.3	0.0078	0.0078	0.7109
	$D_{\max}$	103.8 $\pm$ 1.9	107.3 $\pm$ 1.4	108.3 $\pm$ 2.1	0.0156	0.0156	0.0547
	D_2 cm ³	103.4 $\pm$ 1.8	104.3 $\pm$ 1.2	104.6 $\pm$ 1.2	0.3828	0.1484	0.1406
	$V_{60\%}$	49.2 $\pm$ 9.4	68.2 $\pm$ 16.7	70.4 $\pm$ 14.6	0.0156	0.0078	0.0547
	$V_{80\%}$	42.8 $\pm$ 10.2	33.6 $\pm$ 9.5	34.4 $\pm$ 9.1	0.1953	0.1953	0.1953
	$D_{\max}$	100.8 $\pm$ 2.0	104.9 $\pm$ 2.1	105.0 $\pm$ 1.4	0.0078	0.0156	0.5469
	D_2 cm ³	99.5 $\pm$ 2.5	98.5 $\pm$ 2.8	98.3 $\pm$ 3.2	0.25	0.1953	0.6172

VMAT_{NO}: VMAT plan without dose optimization for the Ant-Rectum; VMAT_{OPT}: VMAT plan with dose optimization for the Ant-Rectum. Parameters are given in percentages (% for both volume and dose). Statistically significant *p*-values are shown in bold.

are some of the most common and critical radiation complications. The incidence and severity of rectal toxicity depend on the dose received by the rectum, and it is often recommended that the total rectal dose (D_2 cm³; minimum dose delivered to 2 cm³ of the most irradiated tissue volume) should be less than 70-75 Gy_{EQD2} (13, 14). Therefore, minimizing the dose to the rectum, particularly to the anterior rectal wall, is of great importance.

For cervical cancer, use of the IMRT/VMAT technique in WP-EBRT has been shown to reduce toxicities in OARs such as the bowel and bone marrow (5-9). However, the CTV-PD extends very close or adjacent to the rectum by definition (17), resulting in a PTV which includes the anterior rectal wall in most cases. Therefore, it is often theoretically impossible to significantly reduce the dose to the anterior rectal wall in WP-EBRT. Consequently, the combination of WP-IMRT/VMAT and ICBT may deliver an unacceptably high dose to the anterior rectal wall. If CS-EBRT is applied, a high dose to the anterior rectal wall can possibly be avoided. Defining the CTV-CS by excluding the central portion of the cervix (or cervical cancer) and the vagina from the CTV (10) leads to a PTV (PTV-CS) which does not overlap with ICBT hotspots. Our present study demonstrates this advantage of CS-EBRT, since the overlap between the PTV-CS and the Ant-Rectum was minimal.

In IMRT treatment planning, allocation of dummy structures is occasionally used to lower the radiation dose to OARs. Leicher *et al.* introduced a method to allocate a dummy structure in the anterior part of the abdomen to lower the dose to the small bowel in IMRT planning for rectal and anal cancer (19). Neil introduced a method to improve the target conformity and lower OAR doses by setting two kinds of dummy structures around the target in IMRT planning for prostate cancer (20). These methods are routinely utilized in the treatment planning of these cancers and are essential for producing optimal plans. The main objective of CS-EBRT is to minimize the dose to the anterior rectal wall, more precisely, to minimize the radiation dose to the area which is at a high risk of developing late complications. Therefore, it is logical to define this volume as a dummy structure to be used for plan optimization. In this study, we created the dummy structure, the Ant-Rectum, which corresponded to the volume of the rectum expected to receive a high dose in ICBT (ICBT hotspot), and optimized the dose to this volume. To the best of our knowledge, introduction of the concept of 'expected high-dose volume in brachytherapy' or 'high-risk volume' into EBRT plan optimization has not been reported previously.

The present study showed that identification of the Ant-Rectum as the dummy structure for IMRT/VMAT

optimization is an essential step in the treatment planning of CS-VMAT, and that optimization only for overall OAR volumes (*e.g.* the rectum) may not be sufficient. VMAT_{OPT} plans showed more favorable DVH parameters of the Ant-Rectum and the whole rectum than VMAT_{NO} plans, which were comparable to those of 3DCRT plans at least in the high dose range. As for the bowel bag and bladder, VMAT_{NO} and VMAT_{OPT} plans showed comparable DVH parameters. Based on these results, we considered the plan-optimization method to be an effective way to minimize the dose to the anterior rectal wall in CS-VMAT while maintaining a good dose distribution to other OARs.

Both VMAT plans had significantly higher $D_{98\%}$ and $D_{2\%}$ of the PTV-CS compared to 3DCRT plans. $D_{95\%}$ and $D_{98\%}$ of the PTV-CS were lower in VMAT_{OPT} plans than those in VMAT_{NO} plans. However, the magnitude of the decrease was approximately 1% (0.3 Gy), and thus its clinical impact was unlikely to be critical. In CS-VMAT plans, the 4-cm wide volume within the cervix and vagina is excluded from the CTV-PD, and the radiation dose to the whole CTV-PD is logically reduced by the proportion of the CS-VMAT in EBRT. However, this volume can be irradiated with very high doses in ICBT, which compensates for dose reduction in CS-EBRT (21, 22).

Macdonald *et al.* (23) and Kidd *et al.* (24) defined the target for conventional split-field 3DCRT irradiation using the step-wedge technique in order to delineate the primary disease of cervical cancer with reference to positron-emission tomography images with ^{18}F -fluorodeoxyglucose and excluded it from the target of WP-EBRT. This resulted in a transition to IMRT with the pseudo-step-wedge technique and a reduction of doses to and toxicities of OARs (23-25). Their treatment concept, pseudo-step-wedge intensity modulation (PSWIM), appears to be similar to VMAT_{NO}. Cheng *et al.* also reported that the simultaneous integrated boost technique using IMRT/VMAT to boost the parametrium dosimetrically produced better target coverage but resulted in slightly higher doses to OARs (26). In our study, however, it was possible to reduce the dose to the anterior rectal wall to the maximum extent while maintaining the dose coverage to the PTV by creating the Ant-Rectum and optimizing the dose to the anterior rectal wall. Thus, the dose to the anterior rectal wall in our VMAT_{OPT} plan might be lower than that reported by them. Nonetheless, our plan-optimization method might also be applicable to the PSWIM technique proposed by Macdonald *et al.* and Kidd *et al.*, the simultaneous integrated boost technique proposed by Cheng *et al.*, and other IMRT plans for cervical cancer.

Another major OAR in the radiotherapy for cervical cancer is the bladder. Specifically, the posterior wall of the bladder represents a potential OAR which may provide an opportunity for further plan optimization. However, the dose

constraint for the bladder is generally higher than that for the rectum, and we concentrated on use of the Ant-Rectum to improve our plans. Moreover, in a previous study that analyzed the composite dose distribution of WP and CS-EBRT and ICBT, the benefit of dose reduction from CS was greater in the rectum than in the bladder, and the bladder received a relatively large dose contribution from the high dose region at the outside of CS (21). Further studies aimed at improving plans by additionally optimizing for potential hotspots in the bladder may be warranted.

This study has several limitations. First, this was a radiotherapy dosimetric study which evaluated the feasibility of CS-VMAT with the plan-optimization method. Therefore, the sample size was small, and there may have been patient selection bias. All patients had tumors <4 cm, therefore a 4-cm diameter cylindrical volume centered in the cervix and vaginal canal was created to represent the volume irradiated with high dose in standard ICBT. This volume may need to be adjusted, particularly when the dose of ICBT is escalated in order to treat bulky cervical cancer. Further studies to confirm the effectiveness of the optimization method are needed using a large sample population with various stages of cervical cancer. Secondly, inter- and intra-fractional organ positional uncertainties are major issues in EBRT for cervical cancer, suggesting the need to further examine optimum internal target volume (ITV) margins and appropriate conditions for adaptive image-guided radiotherapy. Thirdly, the high dose region in ICBT was simplified to the 4-cm diameter cylindrical volume. However, the high-dose region in ICBT may change according to applicator position and treatment planning. Despite these limitations, we consider the present study to be important with regard to enabling optimal treatment planning, because CS-IMRT/VMAT without using this method may result in high-dose irradiation to the anterior rectal wall.

In summary, the plan-optimization method introduced in the present study resulted in significantly improved dose distributions of the CS-VMAT plan by identifying ICBT hotspots in the anterior rectal wall. This optimization method may be an essential step in the implementation of IMRT/VMAT which applies the principle of CS in radiotherapy for cervical cancer.

Conflicts of Interest

The Authors declare that there are no conflicts of interest.

Author's Contributions

All Authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by RH, TT, and MI. The first draft of the article was written by RH and all Authors commented on previous versions of the article. All Authors read and approved the final article.

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