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FULL PAPER

Strategies for reducing ovarian dose in volumetric modulated arc therapy (VMAT) for postoperative uterine cervical cancer

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Objective: To reduce the ovarian dose with volumetric modulated arc therapy (VMAT), an original VMAT was designed with two types of arcs to restrict angles and fields (R-VMAT).

Methods: The subjects were 11 patients who underwent ovarian transposition with clips left by a surgeon. Three methods, intensity-modulated radiotherapy (IMRT), standard VMAT (S-VMAT) and R-VMAT, were optimized for assessment of the ovarian dose with the target coverage kept high.

Results: The homogeneity and conformity indexes for the planning target volume (PTV) were similar for the three methods. However, the average $\pm$ SD of the ovarian mean dose (OMD) was 5.0 ± 1.5 , 4.9 ± 1.9 and 3.5 ± 1.4 Gy, and the percentage of ovarian volume exceeding 5 Gy

(V5) was $41.5 \pm 34.1\%$, $34.1 \pm 38.05\%$ and $8.4 \pm 20.5\%$ for IMRT, S-VMAT and R-VMAT, respectively. The OMD and V5 were significantly smaller for R-VMAT than for the other plans ($p < 0.01$). Correlation values between the OMD and the lateral distance from the ovaries to the PTV surface were 0.86, 0.81 and 0.82 for IMRT, S-VMAT and R-VMAT, respectively.

Conclusion: These findings suggest that R-VMAT delivered the lowest dose to the ovaries. To reduce the OMD to less than 3 Gy, ovaries should be transposed laterally 6.1 cm away from the PTV surface when R-VMAT is used.

Advances in knowledge: When organs with high susceptibility to radiation, such as ovaries, are near the PTV, R-VMAT is superior to IMRT and S-VMAT.

INTRODUCTION

The ovaries are highly susceptible to radiation.¹ Studies have reported that the risk of premature menopause showed a steep increase at a dose of 3 Gy.^{2,3} In addition, Swerdlow et al⁴ found that the risk of premature menopause under the age of 40 years increased when irradiation to the ovaries exceeded 5 Gy. Taking these results into consideration, the dose delivered to the ovaries should be less than 3.0 or 5.0 Gy.

To reduce the ovarian dose, it is important to transpose the ovary to outside the radiation field. With radiation therapy, the box technique reduced the ovarian dose by 90–95% as a result of ovarian transposition, as reported by Husseinazadeh et al.³ Hwang et al⁵ found that, with the box technique, transposition of the ovaries to more than 1.5 cm above the iliac crest was the only independent factor that accounted for maintaining intact ovarian function.

Intensity-modulated radiotherapy (IMRT) is considered effective for reducing the incidence of acute and late gastrointestinal toxicities associated with whole pelvic radiotherapy.^{6,7} For irradiation of pelvic and para-aortic lymph nodes, extended field IMRT (EF-IMRT) has shown significant effectiveness in reducing acute gastrointestinal toxicities, compared with the available data for conventional radiotherapy.⁸ Zhang et al⁹ found that the ovarian functions of approximately 80% of patients with ovarian transposition could be maintained by controlling the ovarian dose with EF-IMRT to between 2.5 and 3.5 Gy. EF-IMRT made it possible to reduce the ovarian dose while reducing the gastrointestinal dose for patients who had undergone ovarian transposition.

The irradiation dose to healthy tissues and organs at risk (OAR) depends on the peripheral dose composed of scatter and leakage doses. Some studies have reported

that volumetric modulated arc therapy (VMAT) could reduce the peripheral doses more than IMRT. Qiu et al¹⁰ found that scatter doses from IMRT and VMAT were similar in magnitude, whereas Cozzi et al¹¹ reported that VMAT had a better profile than IMRT in terms of peripheral doses, because the relative difference in reduction of the peripheral dose between VMAT and IMRT was approximately 8% at 5 cm and approximately 30% at 15 cm from the planning target volume (PTV) surface. Jia et al¹² reported that VMAT showed a dosimetric advantage and resulted in a lower peripheral dose than IMRT. Therefore, it can be concluded that VMAT has a greater potential for reducing ovarian dose than IMRT.

Postoperative radiotherapy for uterine cervical cancer has been the subject of major discussions on the applicability of IMRT and VMAT.^{11,13,14} Most studies have claimed that VMAT is superior to IMRT in terms of the dose delivered to the OAR. However, few studies have examined the reduction of the ovarian dose using VMAT in postoperative radiotherapy for uterine cervical cancer. In this study, a novel VMAT technique to restrict angles and fields (R-VMAT) was designed with a view to reducing the ovarian dose. The aim of this study was to compare the performance of R-VMAT to that of IMRT and standard VMAT (S-VMAT) in reducing ovarian dose and to investigate the modulation for each VMAT and the deliverability of each plan. This study assessed the optimal distance for reducing the ovarian dose for IMRT, S-VMAT and R-VMAT.

METHODS AND MATERIALS

Subjects and CT simulation

The subjects in this study were 11 patients who underwent radical surgery for cervical cancer and had an ovarian transposition with clips left by the surgeon with the aim of maintaining ovarian function. They received postoperative VMAT or VMAT with concurrent chemotherapy between 2012 and 2015 at our institute. The study was approved by the Institutional Review Board.

Each patient was immobilized with a blue bag (Elekta AB, Stockholm, Sweden) for CT simulation and treatment. CT images were acquired using 2.5-mm-thick contiguous slices with a CT scanner (Lightspeed; General Electric Co., Waukesha, WI) and transferred to the treatment planning system Eclipse v. 11 (Varian Medical Systems, Palo Alto, CA).

Contouring

The clinical target volume covered all pelvic lymph node regions (common iliac, external iliac, internal iliac, obturator, presacral and parametrial). The lymph node region was defined as an area enclosed by a 7 mm margin around the relevant pelvic vessels, but not including the bones and muscles, as specified by Toita et al.¹⁵ The PTV was created by adding 5 mm margins for clinical target volume set-up variations. OARs (*i.e.* the spinal cord, small bowel, large bowel, rectum, bladder, bone marrow and ovaries) were contoured by radiation oncologists following the recommendations of the International Commission on Radiation Units Reports 50 and 62.^{16,17}

Designs for the three plans

Three plans were created with Eclipse using 6 MV photons from a Varian 23Ex linear accelerator equipped with a Millennium 120-leaf multileaf collimator (MLC) by two physicists with more than 10 years of experience. The MLC had two parameters in Eclipse: a dosimetric leaf gap of 0.1613 mm and transmission of 0.0160. Transmission represented the ratio of the dose with open field and that with field where MLC is closed.

The first was the IMRT with seven coplanar beams using the sliding window technique. The gantry angles of beams were 0°, 51°, 102°, 145°, 215°, 255° and 306°. The collimator angle of each beam was 0°. In this plan, restricted field techniques reported by Allen et al were used¹⁸ to reduce ovarian doses. The field setting of the beam on its eye view where the ovary hid part of the PTV is shown in [Figure 1a,b](#). The area where the ovary hid on the beam's eye view (BEV) was removed from the irradiation field with jaws.

The second plan was the S-VMAT plan using two 360° coplanar arcs. The field setting of S-VMAT is shown in [Figure 1c](#). One arc rotated clockwise from 181° to 179°, and the other rotated counter-clockwise from 179° to 181°. These arcs had collimator rotation of ±10° or ±15°.¹⁹

The third plan was R-VMAT using two types of arcs whose fields and angles were restricted to reduce ovarian dose. The field setting of the first type of arcs was the same as that of S-VMAT and is shown in [Figure 1c](#) and the second type is shown in [Figure 1d](#). The first type also had beam avoidance sectors where the regions of radiation beam stop during radiation delivery. The range of sectors is shown as arrows in [Figure 2a](#). Each BEV at each gantry angle is shown in [Figure 2b](#). The range of the sectors depended on the position of the PTV and ovaries. In BEVs on beam avoidance sectors, an ovary hid part of the PTV. For each of these arcs, two different arcs that rotated in opposite directions were prepared; one rotated clockwise from 181° to 179° and the other rotated counter-clockwise from 179° to 181°.

Dose-volume limitations

The optimization of dose for IMRT and VMAT was carried out by the optimizer of Dose Volume Optimizer v. 11 and Progressive Resolution Optimizer v. 11 of Eclipse. The three plans complied with the same dose-volume limitations, and the final dose of each plan was calculated using the analytical anisotropic algorithm v. 11 with a grid resolution of 2.5 mm. The PTV was prescribed with 50.4 Gy in 28 fractions to 95% of its volume.

For the PTV and OAR dose-volume limitations, we referenced the Radiation Therapy Oncology Group study #1203. A limitation was that a volume of at least 0.03 cm³ within any PTV should not receive > 110% of the prescribed dose. In addition, any contiguous volume of 0.03 cm³ or larger of the tissue outside the PTVs should not receive > 110% of the dose prescribed. OAR dose-volume limitations followed that V40 of the rectum was 80% or less, V45 of the bladder was 35% or less, V40 of the small bowel was 30% or less, V10 and V40 of bone marrow were 90% or less and 37% or less, respectively and V45 of the spinal cord was 0.1 cm³ or less. The aim was for the ovaries to receive

Figure 1. The field setting for IMRT, S-VMAT and R-VMAT. Dotted square indicates the jaw position in each image. (a, b) The field setting of the beam where the left ovary hides part of the PTV on the BEV in the IMRT. The two fields were created by separating one beam of gantry angle 51°. When the left ovary hides part of the PTV on BEV, the hidden area is excluded from the treatment fields by jaws. (c) The field setting for S-VMAT and the first type of the arcs for R-VMAT. The jaw width was 15 cm and jaw height was defined to cover whole PTV. (d) The field setting for the second type of the arcs for the R-VMAT. The jaw width was 15 cm. The superior jaw position was determined so that both the ovaries would not be exposed to the MLC leakage in the 360° arc. The inferior jaw position was determined to cover the lower part of PTV. BEV, beam's eye view; IMRT, intensity-modulated radiotherapy; MLC, multileaf collimator; PTV, planning target volume; S-VMAT, standard volumetric modulated arc therapy; R-VMAT, restricted field and arc volumetric modulated arc therapy.

a mean dose of 3 Gy or less. V45, V40 and V10 represent the OAR volume ratio that receives a dose exceeding 45, 40 and 10 Gy. D2 represents the dose in Gy to 2.0% of the volume. Dmean was the mean dose. Several dosimetric parameters were read from the dose-volume histograms of each plan. The conformity of each plan was evaluated with the conformity index (CI90), defined as the ratio between the volume of the patient who received at least 90% of the prescribed dose and the volume of the PTV. The homogeneity index of each plan was also calculated as the ratio of the maximum to the minimum dose of the PTV. In addition, by analysing the plan quality, the total number

of monitor units (MU) of each plan was also compared. Then, to investigate the influence of reducing ovarian dose on the characteristics of S-VMAT, the relationship between the ovarian mean dose (OMD) and the number of MU used in the range where the ovary hid the PTV on the BEV was measured.

MLC performance and deliverability for each plan

To evaluate the complexity of the modulation for S-VMAT and R-VMAT, a modified modulation complexity score for VMAT (MCSv) was calculated.^{20,21} The MCSv has values ranging from 0 to 1 and a small MCSv indicates that MLC motion of the plan is highly complex. Masi et al²¹ reported a MCSv applied to VMAT to predict the accuracy of the dose delivery in patient-specific quality assurance for complex VMAT plans. They found that MCSv had a significant correlation with gamma pass rate, resulting in that the lower value of MCSv was induced to larger dosimetric errors. The deliverability of each plan was investigated using a gamma analysis measured on a helical diode array dosimeter (ARCCHECK; Sun Nuclear Corp., Melbourne, FL). Low-dose thresholds of 1% were applied for the gamma analysis.

Statistical analysis

A Wilcoxon signed-rank test (SPSS 8.0; SPSS, Inc., Chicago, IL) was used to calculate and evaluate the differences in dosimetric parameters, MCSv and gamma score for each plan. A value of $p < 0.05$ was defined as significant.

RESULTS

The mean $\pm$ SD of the numbers of MU were 1418.5 ± 99.8 for IMRT, 516.9 ± 61.0 for S-VMAT and 748.6 ± 165.8 for R-VMAT. For arc-restricted angles in R-VMAT, the means of the angles ranged from 58° to 117° and from 249° to 311°, while the mean of range-restricted angles was 122° per arc. The mean $\pm$ SD of MCSv for S-VMAT was 0.33 ± 0.03 . In R-VMAT, the mean $\pm$ SD of MCSv for the first type was 0.34 ± 0.03 and for the second type, 0.26 ± 0.06 . In our previous study about MCSv,²² arcs with the value of MCSv ≥ 0.3 showed $\geq 95\%$ gamma pass rate with 3%/3 mm criteria. So, the dosimetric accuracy for the second type was lower than that for the first type and arcs for S-VMAT. The modulation in the second type arc for R-VMAT had more complexity than that for S-VMAT. The average and SD of gamma pass rate for each plan are shown in Table 1. There was no significant difference in deliverability between R-VMAT and S-VMAT.

Figure 3 shows the dose distributions on axial images at the levels of the ovaries (top) and the head of the femur (bottom) for (a) IMRT, (b) S-VMAT and (c) R-VMAT. The red lines show the PTV, the blue dose lines show the 90% isodose and the white dose lines show the 10% isodose. At the ovary level, the 10% isodose line shows that irradiation of the ovaries was avoided with R-VMAT, but not with IMRT and S-VMAT. At the head of the femur level, the 90% isodose line shows that every plan met the PTV specifications.

Table 2 summarizes certain dosimetric parameters for the PTV and the OAR. There were no significant differences for the CI90 and HI. For the V40 or V45 of OARs in the pelvis, rectum, bladder and large bowel, R-VMAT and IMRT delivered a slightly

Figure 2. Beam avoidance sectors for first type of the arcs for R-VMAT. (a) A circle on a CT image represents the trajectory of a gantry in VMAT. The dotted line marks the start angle for beam avoidance sectors and the dashed line marks the end angle for the beam avoidance sectors when the gantry rotated clockwise. Two straight arrows represent the beam avoidance sectors. (b) A BEV at each gantry angle is shown. The left or right ovary hides part of the PTV on BEV at the gantry angles in beam avoidance sectors. BEV, beam's eye view; PTV, planning target volume; R-VMAT, restricted field and arc volumetric modulated arc therapy.

lower dose compared with S-VMAT. V40 of the small bowel and D2 and Dmean of the spinal cord were significantly higher for R-VMAT than for S-VMAT and IMRT. These OARs were situated at the level above the iliac crest. The OMD was significantly

lower for R-VMAT than for S-VMAT and IMRT. The difference in OMD was slightly more than 1 Gy, and the difference in V5 was more than 20% for one or both ovaries.

Table 1. The mean $\pm$ SD of gamma pass rate of IMRT, S-VMAT and R-VMAT

Gamma pass limitation	IMRT	S-VMAT	R-VMAT	<i>p</i> -value; (R-VMAT vs IMRT, R-VMAT vs S-VMAT)
3%/3 mm	98.0 $\pm$ 1.7	99.5 $\pm$ 0.2	99.2 $\pm$ 0.9	(0.08, 0.31)
2%/2 mm	87.3 $\pm$ 5.0	95.6 $\pm$ 1.1	94.9 $\pm$ 2.7	(< 0.01, 0.42)
1%/1 mm	50.4 $\pm$ 6.8	70.9 $\pm$ 3.9	66.9 $\pm$ 7.0	(< 0.01, > 0.05)

IMRT, intensity-modulated radiotherapy; VMAT, volumetric modulated arc therapy; R-VMAT, restricted field and arc volumetric modulated arc therapy; S-VMAT, standard volumetric arc modulated therapy.

Figure 3. Comparison of the dose distribution for the three plans at the level of the ovaries (a) and of the upper edge of the femoral head (b). The red lines show the planning target volume, the blue lines show the isodose relative to 90% of each dose specification and the white isodose lines show a 10% dose.

Figure 4a indicates the relationship between the OMD and the lateral distance from the centre of the ovaries to the nearest point of the PTV surface (NPP) for each plan. The NPP was located inside the psoas major muscle. The median and range of the distance were 6.0 cm and 3.0–7.4 cm, respectively. Each plan showed a strong correlation: correlation values (R) were 0.86 for IMRT, 0.81 for S-VMAT and 0.82 for R-VMAT. In Figure 4a, dashed lines show the linear regression with the coefficient of determination, R^2 . The following are the regression formulas for predicting the OMD with the lateral distance.

$$\text{IMRT: OMD} = -1.23 \times d + 12.0$$

$$\text{S-VMAT: OMD} = -1.52 \times d + 13.6$$

$$\text{R-VMAT: OMD} = -1.11 \times d + 9.8$$

where d is the lateral distance from the centre of the ovaries to NPP. To reduce the OMD to 5 Gy or less, the ovaries had to be kept more than 5.7 and 5.6 cm from the NPP for IMRT and S-VMAT, respectively, and more than 4.3 cm for R-VMAT. To reduce the OMD to 3 Gy or less, the distance between the ovaries and the NPP should be more than 7.4 and 7.0 cm for IMRT and S-VMAT, respectively, and more than 6.1 cm for R-VMAT.

Figure 4b shows the relationship between the OMD and the craniocaudal distance from the centre of the ovaries to the iliac crest for each plan. The median and the range of the distance were 0.2 cm and from –4.0 to 5.2 cm, respectively. The negative value represents the below iliac crest. The distance also correlated strongly with the OMD: R was 0.75 for IMRT, 0.54 for S-VMAT and 0.59 for R-VMAT. IMRT showed the strongest correlation of the three plans. When the ovaries were transposed above the iliac crest, the mean OMD was 4.4 Gy for IMRT, 4.4 Gy for S-VMAT and 3.1 Gy for R-VMAT. When the ovaries were transposed

below the iliac crest, the mean OMD was 5.8 Gy for IMRT, 5.6 Gy for S-VMAT and 4.1 Gy for R-VMAT. A lower dose was thus delivered to the ovaries transposed above the iliac crest than to those transposed below it, but the difference was significant only for IMRT.

In S-VMAT, the relationship between OMD and the number of MU used in the range where the ovary hid a part of the PTV on the BEV is shown in Figure 5. A strong correlation ($R = 0.66$) was observed between the OMD and the number of MU used in the range. To reduce the ovarian dose, the delivered dose in the range was restricted for S-VMAT.

DISCUSSION

The performance of reducing ovarian dose was investigated in VMAT and IMRT. The R-VMAT delivered the lowest ovarian dose, OMD and V5 of the three plans. This study also indicated that the deliverability and intensity modulation for R-VMAT were almost the same compared with those for S-VMAT and IMRT.

Husseinzadeh et al³ and Hwang et al⁵ reported on transposition of ovaries using the box technique. There was no report that mentioned ovarian transposition for reducing ovarian dose in VMAT and IMRT. Although Zhang et al⁹ reported that ovaries were transposed as high or as laterally as possible, they did not clearly prove the relationship between ovarian transposition and ovarian dose in IMRT and VMAT. In this study, it was clear that transposition is important to reduce ovarian dose less than 3.0 Gy in IMRT and VMAT. Transpositions of the ovaries were typically performed by the surgeon.

According to Jia et al,¹² it is thought that the peripheral dose comprises the scattering and MLC leakage doses. Hardcastle et al²³ showed that the maximum leakage dose measured for a

Table 2. Dosimetric comparison of IMRT, S-VMAT and R-VMAT

Structures	Dosimetric parameters	IMRT	S-VMAT	R-VMAT	<i>p</i> -value; R-VMAT vs IMRT, R-VMAT vs S-VMAT
PTV	D2 (Gy)	54.7 ± 0.5	53.8 ± 0.7	53.7 ± 0.8	< 0.01, 0.37
	D98 (Gy)	49.8 ± 0.1	49.7 ± 0.2	49.8 ± 0.1	0.16, 0.82
	HI	1.3 ± 0.0	1.3 ± 0.0	1.3 ± 0.0	0.59, 0.29
	CI90%	1.7 ± 0.3	1.6 ± 0.2	1.6 ± 0.1	0.79, 0.53
Rectum	Dmean (Gy)	44.1 ± 1.9	44.3 ± 1.8	43.8 ± 2.0	0.18, 0.13
	D2 (Gy)	53.1 ± 0.9	52.4 ± 0.4	52.3 ± 0.6	< 0.01, 0.37
	V40 (%)	73.3 ± 9.7	75.2 ± 10.7	71.5 ± 10.7	0.42, 0.09
Bladder	Dmean (Gy)	38.3 ± 2.3	40.7 ± 2.5	39.9 ± 2.9	< 0.01, 0.03
	D2 (Gy)	53.1 ± 0.9	52.5 ± 0.6	52.4 ± 0.6	0.03, 0.48
	V45 (%)	31.4 ± 9.3	36.5 ± 11.3	32.9 ± 11.5	0.21, 0.02
Large bowel	Dmean (Gy)	31.5 ± 6.4	32.4 ± 6.0	30.7 ± 6.7	0.13, < 0.01
	D2 (Gy)	53.2 ± 0.5	52.7 ± 0.5	52.7 ± 0.7	0.08, 0.86
	V40 (%)	39.2 ± 15.1	41.9 ± 16.1	40.2 ± 16.3	0.29, 0.25
Small bowel	Dmean (Gy)	31.8 ± 3.0	32.6 ± 3.1	31.5 ± 3.2	0.48, < 0.01
	D2 (Gy)	52.8 ± 0.6	52.6 ± 0.7	52.4 ± 0.6	0.11, 0.21
	V40 (%)	33.5 ± 6.4	33.9 ± 8.2	35.4 ± 7.1	0.03, 0.29
Left ovary	Dmean (Gy)	5.1 ± 1.8	5.0 ± 2.2	3.6 ± 1.7	< 0.01, < 0.01
	D2 (Gy)	7.2 ± 2.6	6.8 ± 3.2	5.3 ± 3.2	< 0.01, < 0.01
	V5 (%)	35.6 ± 34.1	31.0 ± 35.5	10.8 ± 28.1	< 0.01, < 0.01
Right ovary	Dmean (Gy)	4.9 ± 1.3	4.8 ± 1.8	3.4 ± 0.9	< 0.01, < 0.01
	D2 (Gy)	7.0 ± 2.0	6.8 ± 3.8	5.8 ± 4.5	< 0.01, 0.01
	V5 (%)	47.5 ± 34.7	37.3 ± 41.9	6.1 ± 9.2	< 0.01, < 0.01
Both ovaries	Dmean (Gy)	5.0 ± 1.5	4.9 ± 1.9	3.5 ± 1.4	< 0.01, < 0.01
	D2 (Gy)	7.1 ± 2.3	6.8 ± 3.4	5.6 ± 3.8	< 0.01, < 0.01
	V5 (%)	41.5 ± 34.1	34.1 ± 38.0	8.4 ± 20.5	< 0.01, < 0.01
Bone marrow	Dmean (Gy)	30.4 ± 1.1	28.8 ± 1.1	28.2 ± 1.2	< 0.01, < 0.01
	D2 (Gy)	52.4 ± 0.5	52.5 ± 0.4	52.5 ± 0.4	0.53, 0.93
	V40 (%)	30.9 ± 3.8	25.5 ± 2.9	28.3 ± 4.8	< 0.01, < 0.01
	V10 (%)	86.4 ± 2.6	86.2 ± 2.5	82.3 ± 2.6	< 0.01, < 0.01
Spinal cord	Dmean (Gy)	27.1 ± 5.7	25.2 ± 3.9	29.3 ± 4.8	< 0.01, < 0.01
	D2 (Gy)	39.4 ± 2.6	37.8 ± 2.8	41.3 ± 1.9	0.03, < 0.01

CI90, the ratio of the volume receiving at least 90% of the prescribed dose to the PTV volume; D98 and D2, the dose in Gy to 98 and 2.0% of the volume. V45, V40, V10 and V5 the OAR volume ratio that receives a dose exceeding 45, 40, 10 and 5 Gy.

single field with a Millennium MLC was 0.39 cGy MU⁻¹ for a 0 mm gap and 0.51 cGy MU⁻¹ for a 0.6 mm gap. They concluded that an MLC leakage dose of 2–3 Gy was added during the treatment course. It is critical that this dosimetric contribution of MLC leakage be prevented to reduce the ovarian dose. To reduce the impact of MLC leakage on the ovaries with IMRT in the present study, the restricted field technique was used to block leakage with collimator jaws, as proposed by Allen et al¹⁶ S-VMAT involves the MLC leakage dose to the ovaries in the range where the ovary hides part of the PTV on the BEV.

To reduce the OMD to 3 Gy or less for S-VMAT, the number of MU used in the range must be reduced to 36 MU, based on the formula in Figure 4. Reducing the delivered dose at the range leads to a poor PTV conformity dose. For VMAT with large fields, effective irradiation does not permit restricting the angles because of the presence of organs such as the ovaries. To improve the limitation of S-VMAT, two types of the arc were used, thus effectively blocking MLC leakage for R-VMAT.

Figure 4. Relationships of the OMD and (a) the lateral distance from the nearest point of the PTV surface (NPP) and (b) the craniocaudal distance from the iliac crest. Dashed lines are the linear regressions with the coefficient of determination, R^2 . IMRT, intensity-modulated radiotherapy; NPP, nearest point of the PTV; OMD, ovarian mean dose; PTV, planning target volume; VMAT, volumetric modulated arc therapy; R-VMAT, restricted field and arc volumetric modulated arc therapy; S-VMAT, standard volumetric modulated therapy.

In the present study, each plan had a higher priority for ovarian dose compared with the doses for other organs. To reduce the ovarian dose, lateral beams should not be used for VMAT. The intensity of the beam fluence, therefore, led to a disproportionate emphasis on the anteroposterior direction for the protection of the ovaries. Consequently, PTV conformity was reduced so that comparatively higher doses were delivered to the OARs, the small bowel, and spinal cord. Portelance et al²⁴ reported that the V45 of the small bowel was 11% for IMRT, which was also less than for any plan in this study. The V40 of the small bowel was larger for R-VMAT than for S-VMAT and IMRT. Isohashi et al²⁵ reported

Figure 5. Relationship between the OMD and the number of MU used in the range where the ovaries hide a part of the PTV on the BEV in S-VMAT. The line is the linear regression with the coefficient of determination, R^2 . BEV, beam's eye view; MU, monitor units; OMD, ovarian mean dose; PTV, planning target volume; S-VMAT, standard volumetric-modulated arc therapy.

that the V40 for the small bowel was predictive of chronic gastrointestinal complications and set the threshold for V40 at 340 ml. In all cases, the V40 for the small bowel for R-VMAT was at most 295 ml and smaller than 340 ml. Taking their suggestion into consideration, the V40 in R-VMAT may be acceptable.

CONCLUSIONS

To reduced ovarian dose of transposed ovaries, R-VMAT was superior to IMRT and S-VMAT. In S-VMAT, it was difficult to keep the conformity high for the whole PTV, because the dose delivered with lateral beams was curtailed to reduce the ovarian dose. To eliminate the disadvantages of S-VMAT, R-VMAT has two types of arcs to restrict the angles and fields and delivered the lowest dose to the ovaries compared with IMRT and S-VMAT. The present findings suggest that the lateral distance between the PTV surface and the OMD was inversely proportional to the OMD, with a strong correlation. Moreover, to reduce the OMD to less than 3 Gy, ovaries should be transposed laterally 6.1 cm away from the PTV surface, when R-VMAT is used compared to when IMRT or S-VMAT is used, which requires over 7 cm.

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REFERENCES

1. Lushbaugh CC, Casarett GW. The effects of gonadal irradiation in clinical radiation therapy: a review. *Cancer* 1976; 37(2 Suppl): 1111–20. doi: [https://doi.org/10.1002/1097-0142\(197602\)37:2+<1111::AID-CNCR2820370821>3.0.CO;2-E](https://doi.org/10.1002/1097-0142(197602)37:2+<1111::AID-CNCR2820370821>3.0.CO;2-E)

2. Chambers SK, Chambers JT, Kier R, Peschel RE. Sequelae of lateral ovarian transposition in irradiated cervical cancer patients. *Int J Radiat Oncol Biol Phys* 1991; **20**: 1305–8. doi: [https://doi.org/10.1016/0360-3016\(91\)90242-V](https://doi.org/10.1016/0360-3016(91)90242-V)
3. Husseinazadeh N, van Aken ML, Aron B. Ovarian transposition in young patients with invasive cervical cancer receiving radiation therapy. *Int J Gynecol Cancer* 1994; **4**: 61–5. doi: <https://doi.org/10.1046/j.1525-1438.1994.04010061.x>
4. Swerdlow AJ, Cooke R, Bates A, Cunningham D, Falk SJ, Gilson D, et al. Risk of premature menopause after treatment for Hodgkin's lymphoma. *JNCI: Journal of the National Cancer Institute* 2014; **106**: 1–12. doi: <https://doi.org/10.1093/jnci/dju207>
5. Hwang JH, Yoo HJ, Park SH, Lim MC, Seo SS, Kang S, et al. Association between the location of transposed ovary and ovarian function in patients with uterine cervical cancer treated with (postoperative or primary) pelvic radiotherapy. *Fertil Steril* 2012; **97**: 1387–93. doi: <https://doi.org/10.1016/j.fertnstert.2012.02.052>
6. Mundt AJ, Roeske JC, Lujan AE, Yamada SD, Waggoner SE, Fleming G, et al. Initial clinical experience with intensity-modulated whole-pelvis radiation therapy in women with gynecologic malignancies. *Gynecol Oncol* 2001; **82**: 456–63. doi: <https://doi.org/10.1006/gyno.2001.6250>
7. Beriwal S, Heron DE, Kim H, King G, Shogan J, Bahri S, et al. Intensity-modulated radiotherapy for the treatment of vulvar carcinoma: a comparative dosimetric study with early clinical outcome. *Int J Radiat Oncol Biol Phys* 2006; **64**: 1395–400. doi: <https://doi.org/10.1016/j.ijrobp.2005.11.007>
8. Beriwal S, Gan GN, Heron DE, Selvaraj RN, Kim H, Lalonde R, et al. Early clinical outcome with concurrent chemotherapy and extended-field, intensity-modulated radiotherapy for cervical cancer. *Int J Radiat Oncol Biol Phys* 2007; **68**: 166–71. doi: <https://doi.org/10.1016/j.ijrobp.2006.12.023>
9. Zhang G, Fu C, Zhang Y, Wang J, Qiao N, Yang Q, et al. Extended-field intensity-modulated radiotherapy and concurrent cisplatin-based chemotherapy for postoperative cervical cancer with common iliac or para-aortic lymph node metastases: a retrospective review in a single institution. *Int J Gynecol Cancer* 2012; **22**: 1220–5. doi: <https://doi.org/10.1097/IGC.0b013e3182643b7c>
10. Qiu Y, Moiseenko V, Aquino-Parsons C, Duzenli C. Equivalent doses for gynecological patients undergoing IMRT or RapidArc with kilovoltage cone beam CT. *Radiation Oncol* 2012; **104**: 257–62. doi: <https://doi.org/10.1016/j.radonc.2012.07.007>
11. Cozzi L, Dinshaw KA, Shrivastava SK, Mahantshetty U, Engineer R, Deshpande DD. A treatment planning study comparing VMAT and IMRT for cervix uteri radiotherapy. *Radiation Oncol* 2008; **89**: 180–91.
12. Jia MX, Zhang X, Yin C, Feng G, Li N, Gao S, et al. Peripheral dose measurements in cervical cancer radiotherapy: a comparison of volumetric modulated arc therapy and step-and-shoot IMRT techniques. *Radiat Oncol* 2014; **9**: 61: doi: <https://doi.org/10.1186/1748-717X-9-61>
13. Palma D, Vollans E, James K, Nakano S, Moiseenko V, Shaffer R, et al. Volumetric modulated arc therapy for delivery of prostate radiotherapy: comparison with intensity-modulated radiotherapy and three-dimensional conformal radiotherapy. *Int J Radiat Oncol Biol Phys* 2008; **72**: 996–1001. doi: <https://doi.org/10.1016/j.ijrobp.2008.02.047>
14. Yang R, Wang J, Xu F, Li H, Zhang X. Feasibility study of volumetric modulated arc therapy with constant dose rate for endometrial cancer. *Med Dosim* 2013; **38**: 351–5. doi: <https://doi.org/10.1016/j.meddos.2013.04.001>
15. Toita T, Ohno T, Kaneyasu Y, Uno T, Yoshimura R, Kodaira T, et al. A consensus-based guideline defining the clinical target volume for pelvic lymph nodes in external beam radiotherapy for uterine cervical cancer. *Jpn J Clin Oncol* 2010; **40**: 456–63. doi: <https://doi.org/10.1093/jjco/hyp191>
16. International Commission on Radiation Units and Measurements. Prescribing, recording and reporting photon beam therapy Report No: ICRU Report 50. Bethesda, MD: ICRU; 1993.
17. International Commission on Radiation Units and Measurements. Prescribing, recording and reporting photon beam therapy (supplement to ICRU Report 50) Report No: ICRU Report 62. Bethesda, MD: ICRU; 1999.
18. Allen AM, Schofield D, Hacker F, Court LE, Czerminska M. Restricted field IMRT dramatically enhances IMRT planning for mesothelioma. *Int J Radiat Oncol Biol Phys* 2007; **69**: 1587–92. doi: <https://doi.org/10.1016/j.ijrobp.2007.06.075>
19. Huang B, Fang Z, Huang Y, Lin P, Chen Z. A dosimetric analysis of volumetric-modulated arc radiotherapy with jaw width restriction vs 7 field intensity-modulated radiotherapy for definitive treatment of cervical cancer. *Br J Radiol* 2014; **87**: 20140183. doi: <https://doi.org/10.1259/bjr.20140183>
20. McNiven AL, Sharpe MB, Purdie TG. A new metric for assessing IMRT modulation complexity and plan deliverability. *Med Phys* 2010; **37**: 505–15. doi: <https://doi.org/10.1118/1.3276775>
21. Masi L, Doro R, Favuzza V, Cipressi S, Livi L. Impact of plan parameters on the dosimetric accuracy of volumetric modulated arc therapy. *Med Phys* 2013; **40**: 071718. doi: <https://doi.org/10.1118/1.4810969>
22. Ohira S, Ueda Y, Isono M, Masaoka A, Hashimoto M, Miyazaki M, et al. Can clinically relevant dose errors in patient anatomy be detected by gamma passing rate or modulation complexity score in volumetric-modulated arc therapy for intracranial tumors? *J Radiat Res* 2017; **58**: 685–92. doi: <https://doi.org/10.1093/jrr/rrx006>
23. Hardcastle N, Metcalfe P, Ceylan A, Williams MJ. Multileaf collimator end leaf leakage: implications for wide-field IMRT. *Phys Med Biol* 2007; **52**: N493–N504. doi: <https://doi.org/10.1088/0031-9155/52/21/N01>
24. Portelance L, Chao KS, Grigsby PW, Bennet H, Low D. Intensity-modulated radiation therapy (IMRT) reduces small bowel, rectum, and bladder doses in patients with cervical cancer receiving pelvic and para-aortic irradiation. *Int J Radiat Oncol Biol Phys* 2001; **51**: 261–6. doi: [https://doi.org/10.1016/S0360-3016\(01\)01664-9](https://doi.org/10.1016/S0360-3016(01)01664-9)
25. Isohashi F, Yoshioka Y, Mabuchi S, Konishi K, Koizumi M, Takahashi Y, et al. Dose-volume histogram predictors of chronic gastrointestinal complications after radical hysterectomy and postoperative concurrent nedaplatin-based chemoradiation therapy for early-stage cervical cancer. *Int J Radiat Oncol Biol Phys* 2013; **85**: 728–34. doi: <https://doi.org/10.1016/j.ijrobp.2012.05.021>