



# Advantages of IMRT optimization with MCO compared to IMRT optimization without MCO in reducing small bowel high dose index for cervical cancer patients – individualized treatment options

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**Background:** Traditional intensity-modulated radiation therapy (IMRT) planning for cervical cancer is time-consuming and require iterative repeated optimization. In this study, we focused on leveraging multi-criteria optimization (MCO) to reduce the impact of small bowel high-dose indices on other optimization targets, thereby providing a rapid approach to individualized IMRT for cervical cancer patients.

**Methods:** Our research involved a cohort of 25 cervical cancer patients who underwent IMRT radiotherapy. The patient inclusion criteria were as follows: (I) histopathological confirmation of cervical cancer, (II) underwent IMRT radiation therapy, and (III) a prescribed dose of 180 cGy/28 fractions for the patient. All plans were replanned by an experienced dosimetrist without the MCO (W-IMRT). On the basis of the W-IMRT plan, the individualized IMRT (I-IMRT) plan was generated under the priority trade-off of reducing the D2cc (D2cc is the minimal dose to the 2 cm<sup>3</sup> of the small bowel receiving the maximal dose) index of the small bowel using the MCO method, maintaining target coverage and protecting other organs at risk (OARs) as much as possible. Statistical analysis was performed using the Wilcoxon signature rank test.

**Results:** When the MCO method was applied to the IMRT plan, the high dose index decreased in the overlapping area between the small bowel and the planning treatment volume (PTV) ( $P < 0.001$ , respectively). The D2cc index of the small bowel decreased to below 5,200 cGy in all I-IMRT plans. On the other hand, in PTV, the I-IMRT plan achieved a better homogeneity index (HI) compared to the W-IMRT plan. Significant dose reductions were also observed in the bladder ( $D_{\text{mean}}$  144.8 cGy and  $V_{40}$  1.45%) ( $P < 0.001$ , respectively), rectum ( $D_{\text{mean}}$  43.9 cGy and  $V_{40}$  2.7%) ( $P < 0.001$ , respectively) and bilateral femur heads ( $D_{\text{mean}}$  150 cGy) ( $P < 0.001$ , respectively).

**Conclusions:** Dosimetric differences suggest that the I-IMRT plan using the MCO method provides better protection of other OARs and equivalently in PTV coverage, while lowering the high-dose index in the small bowel as much as possible for patients with cervical cancer, thus providing a rapid approach to achieving individualized IMRT for cervical cancer patients.

**Keywords:** Multi-criteria optimization (MCO); dosimetric comparisons; intensity-modulated radiation therapy (IMRT); cervical cancer; small bowel

Submitted Apr 28, 2023. Accepted for publication Nov 08, 2023. Published online Dec 27, 2023.

doi: 10.21037/tcr-22-2792

View this article at: <https://dx.doi.org/10.21037/tcr-22-2792>

## Introduction

Cervical cancer is one of the diseases with high incidence and mortality among malignant tumors of the female reproductive system (1). It has been reported that the global incidence of cervical cancer in women in 2018 was about 569,000 cases, and the number of deaths exceeded for 361,000 cases (2). Surgery, external irradiation, brachytherapy (radiotherapy), and chemotherapy are the main treatments used for cervical cancer. Of these, among which radiotherapy plays a crucial role in the treatment of cervical cancer (3,4).

In the field of radiation therapy, there have been advancements in radiation treatment techniques. Compared to the earlier 3D conformal radiation techniques (3D-CRT), techniques such as intensity-modulated radiation therapy (IMRT), volumetric-modulated arc therapy (VMAT), and image-guided radiation therapy (IGRT) achieve adequate dose coverage of the tumor while minimizing radiation to surrounding normal tissues (5-7). IMRT allows higher radiation doses to be delivered to the tumor while reducing

the toxicity to the surrounding normal tissue, ultimately improving the treatment efficacy. Due to these advantages, IMRT is widely used in clinical treatment protocols for cervical cancer (7).

The quality of the IMRT plan depends on how well it meets the clinical objectives during the planning phase. These objectives primarily include target area dose coverage and preservation of normal organs. These two conflicting parameters are weighed and optimized by the dosimetrist based on priorities. Ultimately, the clinical intent of the physician is translated into a truly executable treatment plan. However, multiple optimizations are often required to obtain an IMRT plan with better benefits, which can also be considered a trial-and-error process. Especially in cervical cancer radiotherapy, the small bowel of some patients is sensitive to radiation. This necessitates lowering the  $D_{2cc}$  ( $D_{2cc}$  is the minimal dose to the 2 cm<sup>3</sup> of the small bowel receiving the maximal dose) level below 5,200 cGy to reduce radiotherapy side effects, with a total dose of 5,040 cGy delivered to the patient (8). However, the  $D_{2cc}$  index is an unclear optimization target compared to the maximum dose, which would consume a significant amount of time and effort until an acceptable and optimal clinical delivery plan can be created. In addition, the quality of the plan can be influenced by the experience of the dosimetrist.

Multi-criteria optimization (MCO) is a new optimization method that operates using Pareto surfaces of optimal plans (9-11). Its efficiency has been demonstrated in terms of dose quality and planning time (12-16). In recent years, Varian has developed the MCO tool in Eclipse (commercial treatment planning system), which can be manipulated by visualized trade-off exploration. This advanced tool within Eclipse facilitates the creation of Pareto surfaces, which graphically represent the ideal dose distribution, providing physicians and dosimetrists with invaluable real-time dosimetry parameters. One of the pivotal factors significantly influencing the outcomes of optimization in MCO IMRT plans lies in the selection of optimization objectives and the associated weightings. Physicians and dosimetrists play a crucial role in achieving optimal planning for their intended treatment objectives by meticulously adjusting the balance of these specific optimization goals. Consequently, MCO streamlines the

### Highlight box

#### Key findings

- In this study, we found that the individualizing intensity-modulated radiation therapy (IMRT) plan using the multi-criteria optimization (MCO) method provides better protection of other organs at risk (OARs) and equivalently in planning treatment volume (PTV) coverage, while lowering the high-dose index in the small bowel as much as possible for patients with cervical cancer, thus providing a rapid approach to achieving individualized IMRT for cervical cancer patients.

#### What is known and what is new?

- Traditional IMRT plans are time-consuming and labor-intensive, while MCO helps reduce optimization time.
- Investigated the dosimetric changes in the treatment target volume and the OARs after reducing high-dose exposure to the small bowel through the application of the Eclipse MCO program.

#### What is the implication, and what should change now?

- IMRT optimization with MCO has advantages in reducing the small bowel high-dose index of cervical cancer patients, and can provide a rapid method for individualized treatment of cervical cancer patients.

process, bypassing time-consuming iterative calculations and assisting physicians and dosimetrists in achieving more favorable IMRT plans.

However, to the best of our knowledge, there is a notable gap in existing research when it comes to the utilization of the Eclipse MCO project within the context of participation in IMRT planning for cervical cancer radiation therapy. Specifically, there has been limited exploration of the dosimetric effects on adjacent normal tissues and organs when implementing MCO to mitigate high-dose exposure to the small bowel. Therefore, the primary objective of this study is to identify and analyze the dosimetric changes in the treatment target volume and the surrounding organs at risk (OARs) after reducing high-dose exposure to the small bowel through the application of the Eclipse MCO program. This research has the potential to enhance the efficiency of treatment planning and prognosis for cervical cancer radiation therapy, thereby contributing to the overall improvement in the quality of life for patients undergoing such treatment. This article is presented in accordance with the MDAR reporting checklist (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-2792/rc>).

## Methods

### *Patient cohort*

The present study compared the dose parameters of target areas and OARs in IMRT planning with and without MCO. The outcome measures included dose parameters of target areas and OARs, which belonged to a comparison of means between two sample groups. Based on previous research, comparative studies of planning typically require a minimum of 20 study subjects. The study recruited 25 patients with cervical cancer who had previously received radiotherapy using the IMRT technique between January 2021 and May 2022. The patient inclusion criteria were as follows: (I) histopathological confirmation of cervical cancer, (II) underwent IMRT radiation therapy, and (III) a prescribed dose of 180 cGy/28 fractions for the patient. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Shandong First Medical University Affiliated Cancer Hospital (approval ID: SDTHEC2020008005) and patient informed consent for this retrospective study was waived. During the simulated positioning, all patients underwent computed tomography

(CT) in the prone position (CT, Siemens Healthcare, Forchheim, Germany) with a pelvic holder for fixation. It should be noted that before the CT scan, the patient took 300 mL of water to fill the bladder volume.

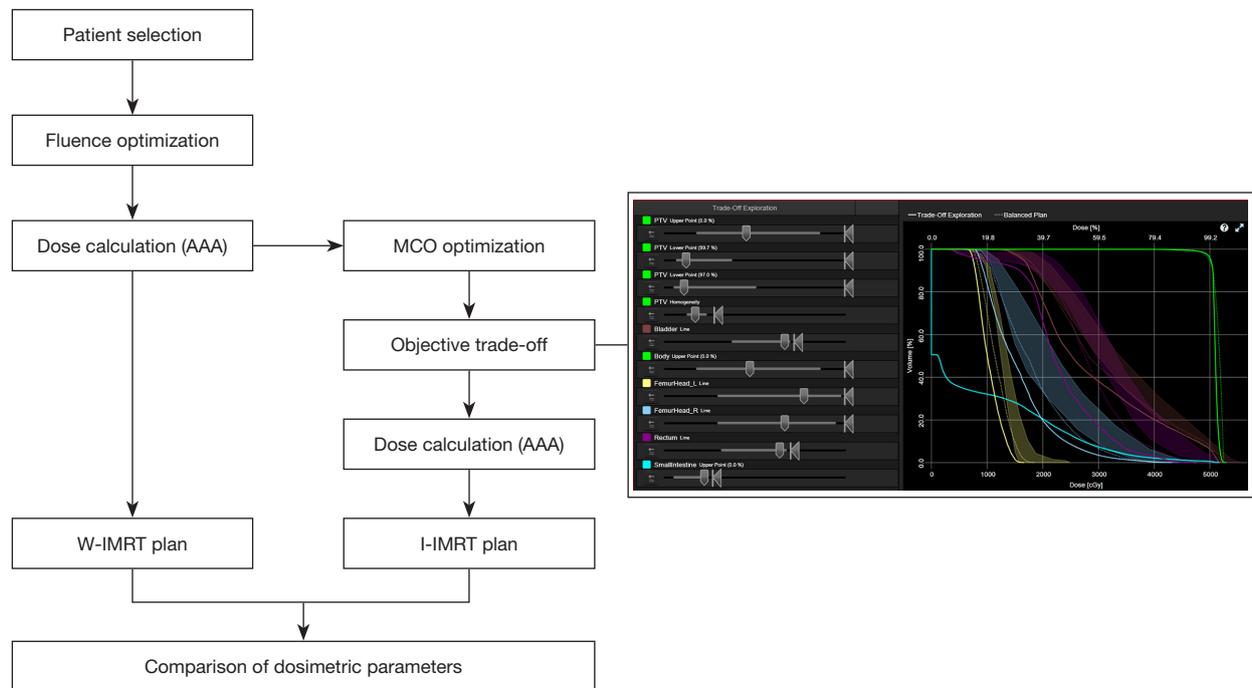
### *Target definitions*

Experienced physician delineated the clinical target volume (CTV) of cervical cancer based on CT images, which followed the radiation therapy oncology group (RTOG) outline guidelines (17-19). The CTV included the primary cervical tumor site as well as the metastatic lymph node area. The planning target volume (PTV) was created from the CTV and extended outward by 5 mm. To ensure accuracy and precision, a senior physician reviewed the delineation process. OARs including the rectum, bladder, femur-head, and small bowel were also depicted.

### *Treatment planning*

The steps of this study are shown in *Figure 1*. IMRT plans without MCO (W-IMRT) were generated using a commercial treatment planning system (Eclipse, version 15.6, Varian Medical System, Palo Alto, CA, USA). The beam fields were divided into 9 fields equally. All W-IMRT plans were calculated by anisotropic analytic algorithm (AAA). The prescribed dose of 50.4 Gy (180 cGy/28 fraction) was delivered to the PTV. All plans met that at least 95% of the PTV would receive the prescribed dose, while the maximum dose would not exceed 110% of the prescribed dose. The dose constraints for OARs were as follows: bladder and rectum, mean dose less than 4,000 cGy and  $V_{40} < 40\%$  (the volume of the bladder or rectum covered by 40 Gy was less than 40%), bilateral femur-head mean dose less than 2,500 cGy and  $V_{40} < 5\%$  (the volume of the femur-head covered by 40 Gy is less than 5%). All plans were completed by experienced dosimetrists and reviewed and approved by senior physicists.

The individualizing IMRT (I-IMRT) plans with MCO were generated in the MCO program of Eclipse version 15.6, which offers tools for real-time exploration and visual evaluation of the range of trade-offs in target coverage and healthy tissue sparing for IMRT plans. The I-IMRT plan was developed by experienced dosimetrist based on the MCO “trade-off” to achieve both optimal PTV coverage and sufficiently OAR dose sparing while reducing the small bowel  $D_{2cc}$  index to 5,200 cGy.



**Figure 1** Dosimetric comparison work flow in the study. AAA, anisotropic analytic algorithm; MCO, multi-criteria optimization; IMRT, intensity-modulated radiation therapy; W-IMRT, IMRT plans without MCO; I-IMRT, individualizing IMRT.

### Dosimetric evaluation

Dose differences between the W-IMRT plans and the I-IMRT were analyzed based on multiple dosimetry parameters. For PTV, maximum dose ( $D_{\max}$ ), minimum dose ( $D_{\min}$ ), mean dose ( $D_{\text{mean}}$ ), minimum dose in 2% of the PTV indicating the maximum dose ( $D_{2\%}$ ) and minimum dose in 98% of the PTV indicating the minimum dose ( $D_{98\%}$ ) were analyzed. Conformity index (CI) and homogeneity index (HI) were calculated for PTV according to the following equations (20):

$$HI = \frac{D_5}{D_{95}} \quad [1]$$

where  $D_5$ ,  $D_{95}$  were the doses to 5% & 95% volume of the PTV

$$CI = \frac{V_{TP}^2}{V_T \cdot V_P} \quad [2]$$

where  $V_T$  denoted the volume of the PTV,  $V_P$  represents the area covered by the prescribed dose, and  $V_{TP}$  denoted the PTV area covered by the prescribed dose.

In addition to the  $D2_{cc}$  index for the small bowel, the

indicators of  $V_{40}$  and  $D_{\text{mean}}$  were also analyzed for rectum, bladder and bilateral femur-head.

### Statistical analysis

Statistical analyses were performed on all data using Statistical Package for Social Sciences v20.0 software (SPSS Inc., Chicago, IL, USA). Differences in dose were analyzed using the Wilcoxon-signed rank tests for different plans. Differences were considered statistically significant when  $P < 0.05$  (2-tailed).

### Results

A total of 25 cervical cancer patients who received IMRT radiotherapy were included in this study. The average age of the patients in this cohort was 57 years (range, 27–68 years; *Table 1*). The median volume of the PTV, rectum, and bladder were  $901.5 \pm 180.27$ ,  $73.2 \pm 46.06$ , and  $278.7 \pm 181.75 \text{ cm}^3$ , respectively (*Table 1*). The dose distribution of the two plans for representative cases is shown in *Figure 2*, and the corresponding dose-volume histogram (DVH) is shown in *Figure 3*.

**Target**

The dosimetric parameters difference of PTV are summarized in Table 2. When compared to the W-IMRT plan, the I-IMRT plan resulted in significant improvement

**Table 1** Patient characteristics

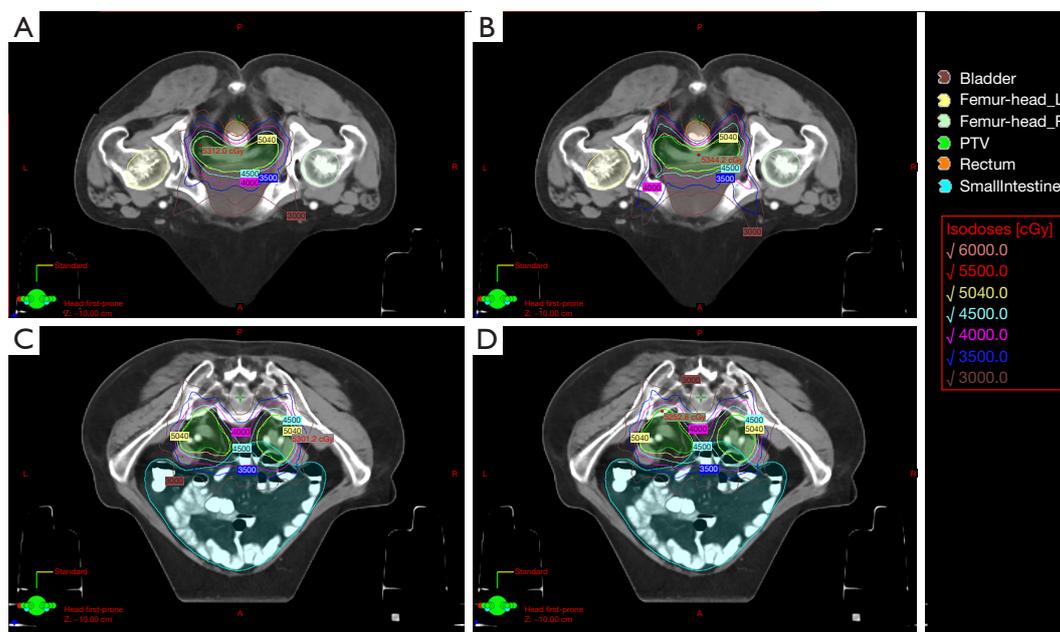
Variable	Value
Age, years	
Median	57
Range	27–68
PTV volume, cm <sup>3</sup>	
Mean ± SD	901.5±180.27
Range	501.3–1,098.5
Rectum volume, cm <sup>3</sup>	
Mean ± SD	73.2±46.06
Range	19.9–220.3
Bladder volume, cm <sup>3</sup>	
Mean ±SD	278.7±181.75
Range	210.4–857.7

PTV, planning target volume; SD, standard deviation.

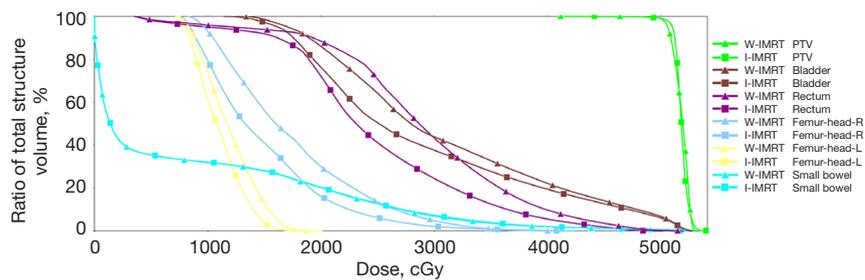
in the PTV. In the PTV, the I-IMRT plan generated a better HI from 1.05 to 1.03 in comparison to the W-IMRT plan, respectively. On the other hand, the CI for the I-IMRT plan was decreased from 0.91 to 0.87, which was slightly worse than the W-IMRT plan. With regard to the D<sub>max</sub>, the I-IMRT plan showed more increment than W-IMRT. The D<sub>max</sub> for I-IMRT plan increased from 5,398.5 to 5,470.0 cGy in comparison to the W-IMRT. Nevertheless, D<sub>max</sub> was less than 110% of the prescribed dose, which met the criteria for clinical treatment. The D<sub>mean</sub>, D<sub>min</sub>, D<sub>98%</sub> and D<sub>2%</sub> of the I-IMRT plan did not show a statistically significant difference when compared with the W-IMRT plan (P=0.635, P=0.599, P=0.233, P=0.554).

**OARs**

The dosimetry difference statistics for OARs are shown in Table 3. Figure 4 shows a violin plot of the average amount of these normal organs. In the dosimetry parameters of the bladder, compared with the W-IMRT plan, the D<sub>mean</sub> dose of the I-IMRT plan was significantly reduced by 144.8 cGy, from 2,997.3 to 2,852.5 cGy, and the V<sub>40</sub> was reduced by 1.45%, respectively (Table 3, Figure 4A). For the rectum doses, compared with the W-IMRT plan, the D<sub>mean</sub> dose of the I-IMRT plan was reduced by 43.9 cGy, from 2,938.1 to



**Figure 2** Axial isodose curve for a typical cervical cancer case in different plans. (A) and (C) for the W-IMRT plan, (B) and (D) for the I-IMRT plan. IMRT, intensity-modulated radiation therapy; W-IMRT, IMRT plans without MCO; I-IMRT, individualizing IMRT; MCO, multi-criteria optimization; PTV, planning target volume.



**Figure 3** Dose-volume histogram of plans with W-IMRT and I-IMRT. W-IMRT, IMRT plans without MCO; I-IMRT, individualizing IMRT; PTV, planning target volume; IMRT, intensity-modulated radiation therapy; MCO, multi-criteria optimization.

**Table 2** The dosimetry parameter results of PTV for 25 test patients

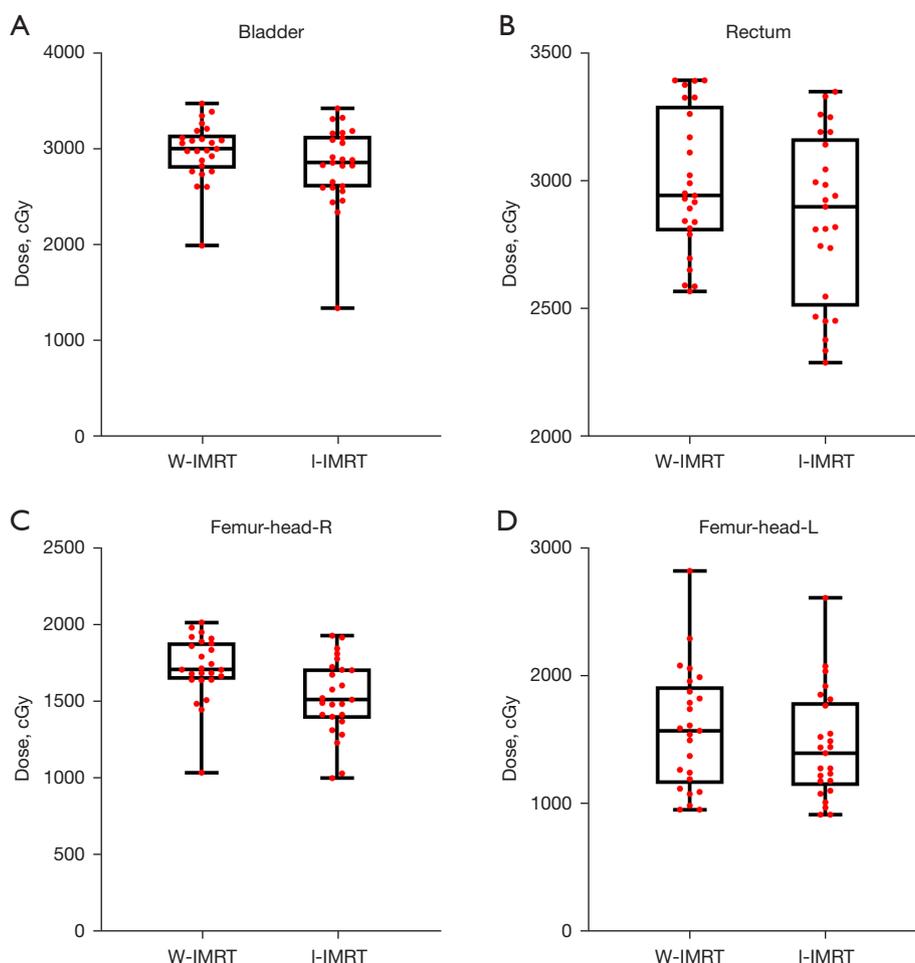
Dosimetry parameter	W-IMRT		I-IMRT		P value
	Mean	SD	Mean	SD	
$D_{max}$ (cGy)	5,398.5	48.75	5,470.0	54.64	<0.001
$D_{mean}$ (cGy)	5,206.6	44.79	5,213.2	41.38	0.635
$D_{min}$ (cGy)	4,074.4	133.82	4,110.5	246.27	0.599
$D_{98\%}$ (cGy)	5,047.9	44.42	5,068.0	40.86	0.233
$D_{2\%}$ (cGy)	5,325.5	48.07	5,332.1	43.03	0.554
HI	1.05	0.002	1.03	0.197	<0.001
CI	0.91	0.018	0.87	0.015	<0.001

PTV, planning target volume; W-IMRT, IMRT plans without MCO; I-IMRT, individualizing IMRT; IMRT, intensity-modulated radiation therapy; SD, standard deviation;  $D_{98\%}$ , minimum dose in 98% of the PTV indicating the minimum dose;  $D_{2\%}$ , minimum dose in 2% of the PTV indicating the maximum dose; HI, homogeneity index; CI, conformity index.

**Table 3** The dosimetry parameter results of OARs for 25 test patients

OARs	Dosimetry parameter	W-IMRT		I-IMRT		P value
		Mean	SD	Mean	SD	
Bladder	$D_{mean}$ (cGy)	2,997.3	305.11	2,852.5	428.07	<0.001
	$V_{40}$ (%)	19.36	8.096	17.91	7.871	<0.001
Rectum	$D_{mean}$ (cGy)	2,938.1	275.14	2,894.2	328.94	<0.001
	$V_{40}$ (%)	19.3	9.41	16.6	8.92	<0.001
Femur-head-L	$D_{mean}$ (cGy)	1,602.2	451.95	1,450.3	422.22	<0.001
	$V_{40}$ (%)	0.12	0.32	0.02	0.09	0.063
Femur-head-R	$D_{mean}$ (cGy)	1,722.5	208.79	1,530.2	248.08	<0.001
	$V_{40}$ (%)	0.11	0.31	0.08	0.23	0.542
Small bowel	$D_{2cc}$ (cGy)	5,282.3	33.17	5,186.7	18.58	<0.001

OARs, organs at risk; W-IMRT, IMRT plans without MCO; I-IMRT, individualizing IMRT; SD, standard deviation; IMRT, intensity-modulated radiation therapy;  $V_{40}$ , the volume of the femur-head covered by 40 Gy;  $D_{mean}$ , mean dose;  $D_{2cc}$ , the minimal dose to the 2 cm<sup>3</sup> of the small bowel receiving the maximal dose.



**Figure 4** Boxplots of  $D_{\text{mean}}$  for (A) bladder, (B) rectum, (C) femur-head-R and (D) femur-head-L. IMRT, intensity-modulated radiation therapy; W-IMRT, IMRT plans without MCO; I-IMRT, individualizing IMRT; MCO, multi-criteria optimization.

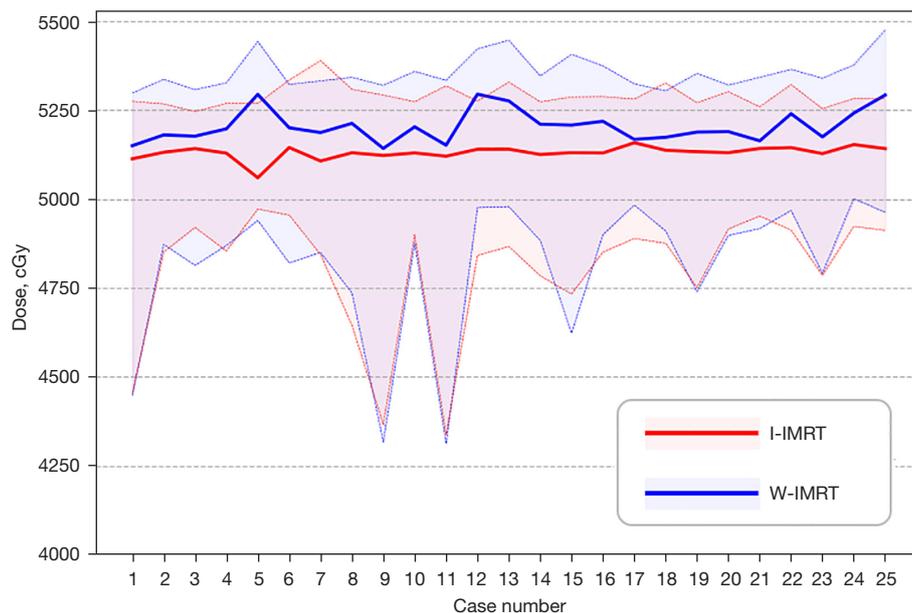
2,894.2 cGy, and the  $V_{40}$  was significantly reduced by 2.7% (Table 3, Figure 4B). In bilateral femur heads, the  $D_{\text{mean}}$  of the I-IMRT plan decreased by more than 150 cGy from the values of W-IMRT plan (L: 1,602.2 to 1,450.3; R: 1,722.5 to 1,530.2), respectively (Table 3, Figure 4C, 4D). On the other hand, The  $V_{40}$  of the I-IMRT plan did not show a statistically significant difference when compared with the W-IMRT plan ( $P=0.063$ ,  $P=0.542$ ).

For  $D2_{\text{cc}}$  of the small bowel, a high dose indicator that we focused on, the I-IMRT plan was significantly reduced by 95.6 cGy, from 5,282.3 to 5,186.7 cGy. In particular, the  $D2_{\text{cc}}$  for all I-IMRT plans had been reduced to 5,200 cGy. Furthermore, we analyzed the overlapping area of the small bowel and PTV (S&P, Figure 5). The  $D_{\text{mean}}$  of S&P decreased, from 5,205.6 to 5,130.7 cGy. Also, the  $D_{\text{mean}}$  of S&P for all I-IMRT plans had greater than 5,040 cGy,

respectively.

## Discussion

Our study investigated dosimetry parameters differences between W-IMRT plan and I-IMRT plan—for 25 patients with cervical cancer. To our knowledge, we are the first to use the Eclipse MCO program to participate in the IMRT program of cervical cancer radiotherapy. In particular, we investigated dose changes in other normal tissues and organs when using the MCO approach to lower the high-dose index of the small bowel. In the trade-off of I-IMRT plan, particular emphasis was placed on maximizing PTV coverage and sparing of other OARs while lowering the high dose parameters ( $D2_{\text{cc}}$  &  $D_{\text{mean}}$  of S&P) of the small bowel. The results showed a significant superiority of



**Figure 5** Strips of S&P in different plans. Blue represents the W-IMRT plan, red represents the I-IMRT plan, the shaded part is the range from the minimum dose to the maximum dose, and the solid line represents the  $D_{\text{mean}}$  of the plan. I-IMRT, individualizing IMRT; W-IMRT, IMRT plans without MCO; IMRT, intensity-modulated radiation therapy; S&P, the overlapping area of the small bowel and PTV; MCO, multi-criteria optimization.

I-IMRT in dosimetry. With the same dose constraints, I-IMRT plan provided better OAR sparing through a trade-off, both in the rectum, bladder and bilateral femur-head (Table 2; Figure 4), while the high dose parameter of small bowel achieved a sufficiently optimistic level. In PTV, the better HI indices improved despite an increase in  $D_{\text{max}}$  and a slight deterioration in the CI index.

In external radiation therapy for cervical cancer, the potential effects of radiation on the bladder, rectum, bilateral femoral heads and other OARs are routinely considered. It has been reported that radiotherapy-related urogenital toxicity, often manifested as dysuria, rectal pain, or bleeding, significantly reduces patients' quality of life (21-23). The incidence of acute genitourinary toxicity and late genitourinary toxicity was 31.9% and 28.0%, respectively. In recent years, research has gradually paid attention to the toxicity analysis of the small bowel. As reported in the National Comprehensive Cancer Network (NCCN) guidelines, the dose-volume effect relationship for predicting advanced small bowel morbidity suggests that the small bowel  $D_{2\text{cc}}$  threshold should be maintained at 5,200 cGy when delivering 5,040 cGy to patients (24). Under computer optimization, IMRT for cervical cancer can obtain a high dose conformity and a steeper dose

gradient, and its dose conformity can ensure that the tumor area receives a high dose of radiation, while the OARs receive less radiation dose, so it will reduce the incidence of acute and chronic radiation injury. Importantly, it is a critical step in determining the quality of an IMRT plan, in which seeking a balance between optimizing target coverage and preserving OARs. However, the  $D_{2\text{cc}}$  index is an unclear optimization target compared to the maximum dose, which would consume a significant amount of time and effort until an acceptable and optimal clinical delivery plan can be created.

MCO is a useful tool for obtaining a satisfactory IMRT plan (25-28). It helps the treatment planning process be more efficient by allowing plan designers to explore multiple dose-target trade-offs for a given patient, including between target coverage and OARs. In recent years, MCO has been extensively studied and has been integrated into radiation therapy planning systems, which simplifies the complexity of MCO methods and avoids the disadvantage of requiring additional computational resources. Currently, the MCO algorithm is mainly implemented in two commercial treatment planning systems, RayStation (RaySearch Laboratories AB, Stockholm, Sweden) and Eclipse (Varian Medical System, Palo Alto, CA, USA) (29).

Existing researches have mainly focused on the MCO program of the RayStation treatment planning system (TPS), which was developed earlier. Craft *et al.* first provided concrete evidence for the superiority of the MCO program (30). In their study, the RayStation MCO-based IMRT plan was superior to the conventional trial-and-error-based IMRT plan in planning efficiency and dose distribution quality in all cases. Subsequent studies have confirmed that RayStation-based MCO planning is a promising and effective radiotherapy planning optimization technique. In the study of McGarry *et al.*, the RayStation MCO-based plan showed equivalent or better target homogeneity with significantly lower rectal dose ( $490 \pm 280$  cGy) (31). Similar results were also demonstrated by Guerrero *et al.* using the latest version of RayStation (version 6) (32). However, another widely used treatment planning system, Eclipse, was relatively late to offer an MCO option, and to our knowledge there is only one study evaluating the effectiveness of using MCO in Eclipse treatment planning. In the study by Park *et al.* in prostate cancer patients, the MCO program achieved a steeper dose drop across overlapping regions, resulting in lower dose parameters. There were significant reductions in intravesical doses (241 *vs.* 254 cGy;  $P < 0.001$ ) and rectum (474 *vs.* 604 cGy,  $P < 0.001$ ) (29). Compared to the report in the Park *et al.* study, our results suggest that the sparing of the rectum and bladder is comparable. However, in our study, the mean dose to the bilateral femur heads was also reduced, not increased. This difference may be due not only to physician preferences weighing conflicting priorities, but also to the added indicator of small bowel  $D_{2cc}$  in our study.

In conclusion, comparing to the conventional single-objective optimization, the MCO method has the flexibility, which can help dosimetrists and radiologists to complete the plan design process more efficiently without constant trial and error. Moreover, the MCO plan can better retain OARs. Of course, the application of the MCO method in the design of radiotherapy plans for other types of tumors remains to be further studied. At the same time, the application of MCO in new radiotherapy technologies such as protons and heavy ions should also attract our attention.

In this study, an analysis of dose differences between I-IMRT and W-IMRT reveals that the application of the MCO method in I-IMRT planning offers superior protection to adjacent OARs. This improvement is achieved while maintaining comparable PTV coverage. Furthermore, the MCO method effectively reduces the high-dose exposure to the small intestine in patients with

cervical cancer. Notably, the MCO approach streamlines the planning process by eliminating time-consuming iterative calculations. Thus, it provides a swift and valuable tool for aiding physicians and dosimetrists in the creation of more advantageous IMRT treatment plans. However, this study also has some limitations. Firstly, the patient data for the study were collected retrospectively, with a lack of follow-up for overall survival. This implies a lack of clinical evidence for the association of lowering the small intestinal high dose index with translation into a significant reduction in toxicity in actual clinical practice. In the future, we will collect more case and prognostic information to obtain the correlation between dosimetric parameters and the toxicity of OARs. Secondly, as this is a retrospective study, planning efficiency metrics such as planning time were not evaluated in our study. In the future, we plan to collaborate more closely with clinicians to proactively gather parameters that capture planning efficiency and other relevant metrics. Finally, considering that the precision radiotherapy such as IMRT has inter-fraction and intra-fraction setup errors, respiratory motion, and uncertainties in bladder, rectal, and small bowel positions and filling degrees, the MCO method would be combined with adaptive radiotherapy to achieve more precise tumor treatment and minimize radiation damage to surrounding tissues in the future.

## Conclusions

Dosimetric differences suggest that the I-IMRT plan using the MCO method provides better protection of other OARs and equivalently in PTV coverage, while lowering the high-dose index in the small bowel as much as possible for patients with cervical cancer, although its clinical utility requires further prospective studies to demonstrate.

## Acknowledgments

*Funding:* This study was supported by the National Natural Science Foundation of China (grant No. 82072094), the Natural Science Foundation of Shandong Province (grant No. ZR2019LZL017), the Taishan Scholars Project of Shandong Province (grant No. ts201712098).

## Footnote

*Reporting Checklist:* The authors have completed the MDAR reporting checklist. Available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-2792/rc>

*Data Sharing Statement:* Available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-2792/dss>

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-2792/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was reviewed and approved by Ethics Committee of Shandong First Medical University Affiliated Cancer Hospital (approval ID: SDTHEC2020008005) and patient informed consent for this retrospective study was waived.

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**Cite this article as:** Jiang Z, Zhang G, Sun T, Zhang G, Zhang X, Kong X, Yin Y. Advantages of IMRT optimization with MCO compared to IMRT optimization without MCO in reducing small bowel high dose index for cervical cancer patients—individualized treatment options. *Transl Cancer Res* 2023;12(12):3255-3265. doi: 10.21037/tcr-22-2792