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ORIGINAL ARTICLE

Evaluation of the Dosimetric Effects of Bladder and Rectum Filling in Patients with Gynecologic Cancer Receiving Adjuvant Radiotherapy

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OBJECTIVE

To evaluate the effect of volumetric changes in the bladder and rectum on clinical target volume (CTV) and organs at risk doses during adjuvant radiotherapy in gynecologic cancers.

METHODS

The study included 19 patients with gynecologic cancer who received adjuvant radiotherapy. Nineteen planning computed tomography scans and 171 megavoltage computed tomography (MVCT) scans were evaluated retrospectively. All structures were re-contoured on MVCT images using MIM software. The isodoses obtained from the reference plan were loaded onto the contoured MVCT images, and dose-volume histogram-based analysis was performed.

RESULTS

Analyses showed that patients with a bladder volume of ≥300 cc at the time of planning had lower bladder volumes (p=0.03) and higher mean bladder doses (p=0.04) during treatment compared with planning. Bladder volume deviation was found to be significantly higher in patients with a bladder volume of ≥300 cc at the time of planning (p=0.002). The mean treatment CTV V95% values of patients with planning bladder volumes of <150 cc, 150–300 cc, and ≥300 cc were 97.2%, 98.7%, and 98.9%, respectively (p=0.005).

CONCLUSION

Bladder and rectum filling have a critical impact on patients receiving adjuvant radiotherapy for gynecologic cancer. For optimal results, the bladder volume should be planned between 150 and 300 cc.

Keywords: Adjuvant; bladder; filling; gynecologic cancer; radiotherapy; rectum.

INTRODUCTION

Cervical cancer is the fourth most common cancer, and uterine cancer is the sixth most common cancer among women.[1] In managing these two cancer types, surgery, radiotherapy, and chemotherapy are the three preferred modalities, used alone or in combination. Randomized clinical trials have shown that adding pelvic irradiation to the treatment of patients with cervical and endometrial cancer who underwent radical hysterectomy improves both local recurrence and progression-free survival (PFS).[2] Most clinics have switched from the conven-

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tional 4-field box technique to intensity-modulated radiotherapy (IMRT) to treat gynecologic malignancies, providing appropriate target volume coverage and excellent success in sparing surrounding tissues.[3] With its advantages, this advanced method requires creating a protocol to minimize inter-fractional dose variation by regulating internal organ placement and using image-guided radiotherapy (IGRT).[4] Bladder filling is usually the preferred method to spare organs at risk (OAR).[5] However, it is not clear how much can be filled by the patient and exactly how much should be filled. Moreover, rectal emptying is recommended to decrease anterior-posterior (AP) movement of the vaginal cuff.[6] Some patients are not able to adhere to the protocol, resulting in variations in bladder and rectal volume, which lead to alterations in target volume coverage and doses received by the OAR. In this study, we aimed to evaluate the effect of rectum and bladder filling patterns on clinical target volume (CTV) coverage and OAR doses during adjuvant radiotherapy in gynecologic cancers.

MATERIALS AND METHODS

Patient Selection

Our institutional review board approved the present study (Approval No: 774 and Date: 28.12.2022). We retrospectively analyzed 19 patients with gynecologic cancer who received adjuvant radiotherapy using a TomoTherapy HDA (Accuray, Madison, USA) treatment device between July 2020 and September 2022. In the analyzed cohort, 16 patients had endometrial cancer, and three had cervical cancer. The median age at diagnosis was 62 years (range, 41–76 years). Fourteen patients were prescribed a total dose of 45 Gy with a daily fraction of 1.8 Gy. Four patients received radiotherapy with a total dose of 50 Gy, and one received a total dose of 46 Gy delivered in daily fractions of 2 Gy.

Patient Preparation and Computed Tomography (CT) Simulation Scanning

CT images were obtained on a GE Discovery RT simulation device (GE Healthcare, USA). According to our clinic protocol, these patients were advised to empty their rectum and fill their bladder before CT imaging. Patient stabilization was achieved using a T-board and a knee and feet positioner. Patients were instructed to drink 1000 mL of water within 30 minutes after emptying their bladders, followed by CT simulation. If patients' bladders were not adequately filled, they were advised to drink an additional 500 mL of water and undergo simulation after 15 minutes. In cases where patients' bladders were excessively full, emptying the bladder and restarting the protocol were recommended.

There was no specific protocol for emptying the rectum; if patients had regular bowel movements in the morning, no additional treatment was recommended. However, if they were constipated or a properly empty rectum could not be obtained, laxative use was prescribed. Following this preparation, a CT scan with a slice thickness of 2.5 mm was performed with the patient positioned supine and the head in.

Contouring

The target volumes and OAR were delineated according to the Radiation Therapy Oncology Group (RTOG) consensus panel atlas.[2] A vaginal cuff CTV was created to include the proximal vagina and paravaginal-parametrial tissue that could be visualized on the planning CT. The anterior boundary of the vaginal CTV was the posterior aspect of the bladder wall. Posteriorly, the vaginal CTV extended toward the anterior rectal wall, including approximately one-third of the mesorectum.

The nodal CTV was created to include the obturator, internal-external iliac lymph nodes, and presacral lymph nodes, covered according to stage and histopathology. In the presence of metastases at the level of the common iliac or para-aortic lymph nodes, the para-aortic lymph nodes were included in the nodal CTV. The planning target volume (PTV) was created by giving a 7-mm margin to the nodal and vaginal cuff CTVs.

Planning

Treatment plans were created using the TomoTherapy HDA IDMS Precision Planning System software (version 2.0.1.1; Accuray, Madison, Wisconsin, USA). In the plans, the prescribed dose was intended to cover 95% of the PTV. For the jaw width, 2.5 and 5 cm were preferred in the dynamic mode, and the pitch factor was chosen as 0.436 and 0.433, respectively. For the modulation factor, values between 2–3 were used. In treatment plans, it was aimed that the 40 Gy dose (V40) received by the bladder was less than 40%, and the 50 Gy dose (V50) received by the rectum was less than 50%. Additionally, it was aimed that the volume of the intestines receiving 45 Gy should not exceed 195 cc.

Megavoltage CT (MVCT) Scanning

Preliminary preparation was made for patients in accordance with the treatment planning CT before the treatment. Before each treatment, 3D MVCT imaging was performed to check the patient's position, bladder, and rectum. Following the positioning of the patient, the

Table 1 Statistical comparisons of mean bladder diameters between planning and treatment based on paired t-test

All patients	Bladder AP diameter (cm)		Bladder transvers diameter (cm)		Bladder longitudinal diameter (cm)	
	Mean±SD	p	Mean±SD	p	Mean±SD	p
Planning	8.32±2.10	0.03	9.21±1.16	0.53	6.76±2.56	0.44
Treatment	7.81±1.71		9.12±1.22		6.47±2.14	

AP: Anteroposterior distance; SD: Standard deviation

radiation therapist evaluated the bladder and rectal filling. If the volumetric alterations in these organs did not result in the displacement of CTV beyond the PTV, the treatment proceeded. If the fullness of the bladder and the empty rectum was not acceptable, the patient's pretreatment preparation was redone as described in the CT simulation patient preparation section. The MVCT scan length was determined to include the PTV to shorten the scan time and reduce the dose the patient would receive from the scan. MVCT scanning parameters were chosen as coarse for pitch and 3 mm for the interval.

Recontouring on MVCT Images

A total of 190 CT images (including 19 planning CT and 171 MVCT images) were evaluated in the study. Nine MVCT images for each patient, obtained at 3-day intervals starting from the first day of the patient's treatment, were used. These images were transferred to MIM software running with Accuray TomoTherapy Precision TPS, and automatic deformable fusions were made on the planning CT image. The system automatically created CTV, bladder, and rectum in all images. Subsequently, radiation oncologists corrected these constructs in all MVCT images. The simulation CT plan is referred to as planning CT, and plans made using MVCT images in the MIM are named treatment CT.

Dosimetric Evaluation

Each patient's reference plan was recalculated using MIM software on all MVCT images where new contours were created. Dimensions and doses during treatment were considered the mean value of dimensions, and doses were obtained from 9 MVCT scans for each patient. In the study, besides CTV, dose changes in the bladder and rectum as OAR were evaluated. The dose covering 95% (V95%) was evaluated for CTV. Bladder mean dose and the percentage of bladder volume (%) that received a 40 Gy dose (V40) were examined. For the rectum, the volume (cc) covered by the 40 Gy dose (V40) and AP diameter were evaluated.

The cut-off point for the rectum AP diameter was chosen as 4.2 cm, which was the mean value for all patients, while the cut-off point for the bladder volume was set at 300 cc, based on previously published literature.[7]

Statistical Analysis

Descriptive statistics were performed to present baseline characteristics. The Kolmogorov-Smirnov and Shapiro-Wilk tests were employed to assess the normality of the data distribution. Parametric tests were applied as the data satisfied the assumption of normality based on the results of these tests. The planning and treatment parameters were compared using the paired t-test. Repeated measures ANOVA was used to analyze the difference between treatment fractions.

The difference in parameters between the groups formed according to bladder and rectum size was analyzed using an independent t-test and one-way analysis of variance (ANOVA). Furthermore, a post-hoc analysis was conducted using Tukey's test to determine whether significant differences existed in the treatment CTV V95% values among subgroups classified by planning bladder volume. The deviation of bladder volume from planning bladder volume was demonstrated using scatter plots. Pearson's correlation coefficient was used to assess correlations between the dimension and dose changes. P-values of <0.05 were considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics version 24.0 software (Armonk, NY: IBM Corp. 2016).

RESULTS

The most significant change was observed in the AP diameter, followed by the longitudinal diameter; the change in the transverse diameter was minimal. The mean ± standard deviation value for the bladder AP diameter at planning was 8.32± 2.10 cm, and during treatment was 7.81±1.71 cm (95% CI: [0.04–0.95]; p=0.03). Table 1 represents a comparative analysis of bladder diameters between planning and treatment scans.

Turk J Oncol 2025;40(1):11–19
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Table 2 Statistical comparisons of bladder volume, mean dose, and V40 values between planning and treatment based on paired t-test

Patient groups	Bladder volume (cc)		Bladder mean dose (Gy)		Bladder V40 (%)	
	Mean±SD	p	Mean±SD	p	Mean±SD	p
All patients						
Planning	323±232.94	0.39	30.46±3.35	0.53	28.83±6.23	0.50
Treatment	302±210.01		30.70±3.66		29.61±6.98	
Patients with bladder volumes <300 cc at planning						
Planning	145±53.66	0.11	30.03±3.08	0.37	29.07±5.47	0.62
Treatment	182±71.35		29.54±3.44		28.22±5.54	
Patients with bladder volumes ≥300 cc at planning						
Planning	520±188.72	0.03	30.93±3.76	0.04	28.57±7.31	0.09
Treatment	436±235.76		31.98±3.66		31.15±8.37	

SD: Standard deviation

Comparisons of bladder volume, mean dose, and V40 values between planning and treatment are given in Table 2. Initial analysis, including all patients, demonstrated no statistically significant difference between planning and treatment regarding bladder volume, mean dose, and V40 values. Patients with a mean planned bladder volume of less than 300 cc showed an increase in mean bladder volume during treatment, while patients with a mean planned bladder volume of more than 300 cc showed a decrease. Further analysis showed that patients with a bladder volume of ≥300 cc at planning had lower bladder volumes (95% CI: [7.35–162.01 cc]; p=0.03) and higher bladder mean doses (95% CI: [0.03–2.06 Gy]; p=0.04) during treatment compared with planning.

Assessment of the plans based on MVCT images revealed no statistically significant differences in bladder volume, mean dose, and V40 between treatment fractions (p=0.16, p=0.51, and p=0.79, respectively). The deviation of the bladder volume from planning to treatment for each evaluated fraction was obtained, and the mean deviation volume was calculated for each patient. Patients with planning bladder volumes of <300 cc and ≥300 cc were compared for bladder volume deviations. Notably, patients with a bladder volume of ≥300 cc during planning exhibited significantly higher bladder volume deviations (95% CI: [45.10–161.40 cc]; p=0.002) (Table 3). The deviations of bladder volume from planning bladder volume for patients with a planning bladder volume of <300 cc and ≥300 cc are illustrated in Figure 1a, b.

Table 4 outlines comparisons of rectum AP diameter and V40 values between planning and treatment.

Table 3 Statistical comparisons of bladder volume deviation between patients with bladder volume <300 cc and ≥300 cc at planning based on independent t-test

Bladder volume at planning	n	The deviation of bladder volume (Mean±SD)	p
<300 cc	10	77.77±35.24	0.002
≥300 cc	9	181.02±72.17	

n: Number of patients; SD: Standard deviation

When all patients were included in the analysis, no statistically significant difference was found between planning and treatment regarding rectum AP diameter and V40. Patients with a rectum AP diameter of <4.20 cm at planning had higher rectum AP diameters during treatment compared with planning (95% CI: [0.05–0.78 cm]; p=0.02). Patients with a rectum AP diameter of ≥4.20 cm at planning had lower rectum V40 values during treatment compared with planning (95% CI: [1.51–8.52 cc]; p=0.01).

Assessment of the plans based on MVCT images revealed no statistically significant difference in rectum AP diameter and V40 between treatment fractions (p=0.75 and p=0.24, respectively). The mean CTV V95% value for all patients at planning and treatment was 100% and 98.4%, respectively (95% CI: [1.02–2.07]; p=0.001). The mean treatment CTV V95% values of patients with planning bladder volumes of <150 cc, 150–300 cc, and ≥300 cc were 97.2%, 98.7%, and 98.9%, respectively (p=0.005).

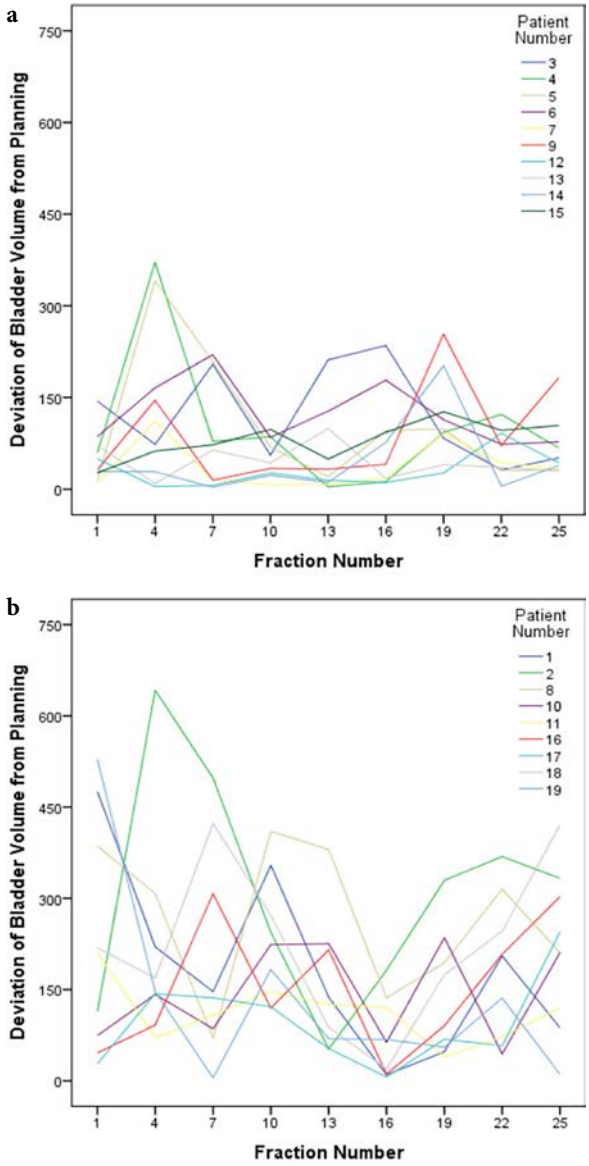

Fig. 1. (a) The deviations of bladder volume from planning bladder volume for patients with planning bladder volume <300 cc. (b) The deviations of bladder volume from planning bladder volume for patients with planning bladder volume ≥300 cc.

Post hoc analysis revealed lower treatment CTV V95% for a planning bladder volume of <150 cc compared with 150–300 cc and ≥300 cc (p=0.02 and p=0.004, respectively). However, no significant difference emerged between 150–300 cc and ≥300 cc regarding CTV V95% (p=0.89). In addition, planning bladder longitudinal diameter and planning bladder volume correlated with treatment CTV V95% (r=0.53, p=0.01 and r=0.48, p=0.03, respectively). The change in bladder volumes and CTV contours between two treatment fractions of a patient is shown in Figure 2.

On the other hand, when the treatment CTV V95% values of patients with planning rectum AP diameters of <4.2 cm and ≥4.2 cm were compared, no statistically significant difference was identified (p=0.66).

Correlation analysis was also performed by taking the differences between the treatment and planning data. Changes in bladder volume were negatively correlated with changes in bladder mean dose (r=-0.77, p<0.001), bladder V40 (r=-0.72, p=0.001), and CTV V95% (r=-0.53, p=0.01). Changes in rectum AP diameter were positively correlated with changes in rectum V40 (r=0.57, p=0.01). There was no significant correlation between changes in rectum AP diameter and changes in CTV V95%.

DISCUSSION

It has been demonstrated that planned and actual doses may differ depending on pelvic organ movements in the treatment of gynecologic cancers using definitive radiotherapy.[7,8] However, this issue has not yet been extensively investigated for patients receiving adjuvant radiotherapy. This study represents a pioneering investigation into the dosimetric impact of bladder and rectum filling on target volume and OAR in adjuvant radiotherapy for gynecologic cancers. The use of the MIM software program for dosimetric analyses in this study further contributes to its unique value.

Although the bladder filling protocol was implemented in our study, significant differences in bladder volume were observed among the patients. Chan et al.[9] demonstrated a systematic decline in bladder filling during treatment, and Ahmad et al.[10] reported a substantial 71% decrease in mean bladder volume between planning and week 6 of treatment for patients with cervical cancer. Despite showing alterations in bladder volume, no other studies established a clear pattern throughout treatment.[11,12] Similarly, our findings show no systematic decline in bladder volumes over the course of treatment.

We divided the sample into two groups based on planning bladder volume (cut-off 300 cc) and found that the group with greater bladder volumes at planning CT had lower reproducibility during treatment. In agreement with our findings, Eminowicz et al.[7] found that bladder volumes above 300 cc were associated with higher variations in bladder filling. Turner et al.[13] also noted that bladder size changes during

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Table 4 Statistical comparisons of rectum AP diameter and V40 values between planning and treatment based on paired t-test

Patient groups	Rectum AP diameter (cm)		Rectum V40 (cc)	
	Mean±SD	p	Mean±SD	p
All patients				
Planning	4.20±0.88	0.80	29.15±19.27	0.87
Treatment	4.24±0.69		29.51±18.04	
Patients with rectum AP diameter <4.2 cm at planning				
Planning	3.46±0.43	0.02	22.91±10.67	0.12
Treatment	3.88±0.68		29.24±12.51	
Patients with rectum AP diameter ≥4.2 cm at planning				
Planning	4.88±0.59	0.15	34.77±23.82	0.01
Treatment	4.57±0.55		29.75±22.62	

AP: Anteroposterior distance; SD: Standard deviation

treatment depended on initial bladder size, with larger bladders being more likely to experience random fluctuations than smaller bladders.

Our results showed that bladder volumes above 300 cc in the initial CT simulation led to higher mean doses and V40 of the bladder during treatment compared with planning. Greater bladder volumes in the simulation cause an increase in the doses received by the bladder as an OAR and can lead to alterations in target coverage by changing the position of the uterus or vaginal cuff. Okamoto et al.[14] revealed uncertainties in the position of the vaginal cuff in patients with cervical cancer after radical hysterectomy due to variations in bladder filling. Eminowicz et al.[7] showed improved target coverage in patients whose initial CT was obtained with a bladder volume closest to 300 cc but not exceeding it. Remarkably, we found that bladder volumes below 150 cc were associated

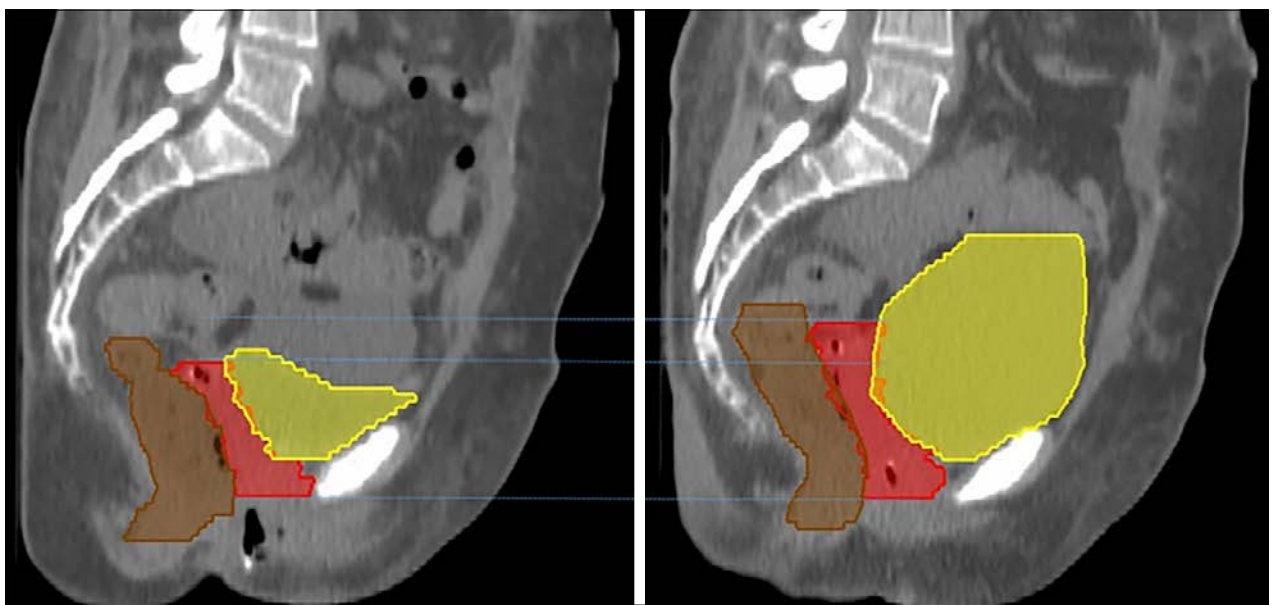

Fig. 2. Variation of bladder volume and CTV contour between two treatment fractions for a sample patient.
CTV: Clinical target volume.

with decreased treatment CTV V95% in adjuvant radiotherapy for gynecologic cancers.

Therefore, it is recommended to maintain planning bladder volumes within the range of 150–300 cc to minimize deviations during treatment and reduce radiation doses to nearby organs.

Shah et al.[15] analyzed bladder diameter changes during the radiotherapy of pelvic malignancies, and significant alterations were observed in AP, longitudinal, and transverse diameters (53%, 38%, and 23% of patients, respectively).[15] In our study, the AP diameter showed the most significant changes in bladder volume when planning and treatment images were compared. Similar results regarding bladder diameters have also been observed in other studies evaluating patients with bladder cancer.[16,17]

In addition, we showed that the planning bladder longitudinal diameter and bladder volume were correlated with treatment CTV V95%. Changes in bladder longitudinal diameter and volume affect the location of the bowel. In patients with short longitudinal diameters of the bladder, the bowel is displaced towards the lower parts of the pelvis, which results in shorter contouring of CTV. This smaller target delineation causes decreased CTV doses in treatment.

To monitor bladder volume, patients should be subjected to a standardized protocol; however, it has been observed that the same protocol can lead to different bladder volume fillings in different patients. Therefore, during the initial days of treatment, patients' adherence to protocols should be carefully monitored, and personalized protocols, such as shortening the waiting period or increasing fluid intake, should be established accordingly.

Regarding rectal filling, a systematic review including five studies comprising 103 patients undergoing definitive radiotherapy demonstrated that rectal filling had a more pronounced effect on the motion of the cervix and the upper part of the vagina compared with the uterus. Also, a significant correlation between the rectal volume and the AP shift of the CTV has been shown.[18] Several studies explored the impact of rectal volume on vaginal motion in postoperative patients with gynecologic cancer. Rash et al.[19] showed a significant correlation between the AP movement of the fiducial marker placed on the vaginal cuff and the rectum's AP diameter. Jhingran et al.[20] reported that the filling of the bladder and rectum significantly influenced the displacement of the vaginal cuff, particularly in the AP direction.

Agrawal et al.[6] showed that the volume of the rectum had a greater impact on the AP direction of vaginal movement than the bladder volume. Wang et al.[21] evaluated the effect of inter-fractional changes in the bladder and rectum on the vagina in postoperative cervix patients and interestingly found that vaginal movement correlated with bladder volume but not rectal volume.[21] We examined the correlation between the AP diameter of the rectum and coverage of CTV (V95%) and found no correlation, consistent with the findings of Wang et al.[21]

Even though we found no correlation, many studies have demonstrated a relation between rectal filling and CTV motion. Especially in clinics where IGRT is not used, patients should be instructed to empty their rectum before both simulation and treatment to reduce variations.

Daily IGRT ensured consistency between the actual CTV doses and the prescribed CTV dose in our study. As mentioned in the method, if the changes in the bladder and rectum before treatment are substantial enough to cause the target to exceed the pre-defined PTV, the patient's preparation is re-done. This clinical protocol leads to better compatibility of CTV coverage and OAR doses with planning.

Limitations

It should be noted that the treatment period in the study ranged from 25 to 28 days, but nine CT scans were selected for each patient to analyze. To enhance the strength of the study, it would be valuable to include evaluations based on data collected throughout the entire treatment course.

CONCLUSION

Bladder and rectum filling during adjuvant radiotherapy for patients with gynecologic cancer impacts CTV and OAR doses. Bladder volume should be planned between 150–300 cc for the best results. Although the effect of the rectum on CTV movement seems less important, an empty rectum should be preferred during planning and treatment.

IGRT is a strong tool to demonstrate the displacements of target volumes and OAR. Daily use of IGRT helps increase the compatibility of treatment doses with planned doses, and it will also help calculate the cumulative dose accurately for patients receiving adjuvant radiotherapy and brachytherapy. Dose calculations based on IGRT images can be helpful in deciding offline adaptive planning. Therefore, if possible, the implementation of daily IGRT should be put into practice.

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