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Dosimetric Impact of Bladder Volumetric Changes During Helical Radiotherapy for Rectal Cancer

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ABSTRACT

Introduction: This study aims to investigate the dosimetric impact of bladder volumetric changes during helical radiotherapy (RT) for rectal cancer (RC).

Material and Methods: A total of 42 RC patients' helical RT treatment plans were analyzed. The bladder volumes were divided into 3 groups (Group1: V<100ml, Group2 100ml≤V≤200ml, and Group3V>200ml). Planning target volume (PTV), PTV boost, bladder, bowel, right, and left femoral head dose values were analyzed and compared between groups. Statistical analysis was done with a one-way ANOVA test in SPSS18.0 program. A value of $p < 0.05$ was considered statistically significant.

Results: The median age of the patients was 59 (range:22-87) and bladder volume ranged from 41.44ml-620.82ml. In the dosimetric data comparison of the patient groups with different bladder volumes, the D50 dose values of PTV and PTV boost volume was highest in Group 3 ($p=0.039$). No statistical significance was found between PTV and PTV boost' doses of D98 and D2 and groups. The optimum PTV dose value was in Group2. Bowel doses were highest in Group 1. As the bladder volume increased, the Dmax, Dmean, V15%, and V30% values of the bowel doses decreased. There was a statistically significant relationship between bladder Dmax doses and groups ($p = 0.024$). Femoral heads doses increased in proportion to increasing bladder volume groups and these results were statistically significant for V5% and V30% ($p < 0.05$).

Conclusion: In our study, as the bladder volume increased, there was an inversely proportional decrease in the bowel doses and a directly proportional increase in the femoral head and bladder doses. Bladder volume values significantly affected values of the target and critical organs dose during helical RT for RC.

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Introduction

Rectal cancer (RC) is among the most common types of cancer. Radiotherapy (RT) has an increasing role in the treatment of RC. RT alone or with chemotherapy is the standard treatment of preoperative locally advanced RC [1,2]. The most important difficulty encountered during the RT planning of RC is to reduce the critical organ doses while ensuring a homogeneous dose of the planning target volume (PTV). Due to the shape and location of the rectum, it may cause an increase in acute and late toxicities related to RT. RT methods used with developing technology help reduce these problems. Intensity-modulated RT (IMRT) is the most frequently used planning method in RT [3]. RC's RT needs attention to reduce the critical organ (bladder, bowel, femoral heads, etc.) doses around the target [4]. Simultaneous integrated boost (SIB-IMRT) technique can provide clinical and dosimetric advantages by increasing the fraction size of the boost volume with a lower dose to the elective volume [5,6].

Recent studies have shown that IMRT shows significant benefit in terms of reduced toxicity or improved cancer outcomes. [1,5,7,8,9,10]. Besides, studies are stating that the IMRT method is beneficial for reduced toxicity and improved cancer outcomes for RC [1,5,10]. Helical Tomotherapy (HT) (Accuary Inc., Sunnyvale, CA) used Image Guide RT (IGRT) technologies include megavoltage computed tomography (MVCT). HT uses this method before each treatment fraction [11]. Although RC has a structurally complex area, HT can deliver a more uniform dose to the target [3,12].

Many studies have reported on the dosimetric effect of bladder volume changes during RT. These studies focused more on prostate and cervical cancer [13]. Ma et al. investigated the effect of bladder volume in cervical cancer radiotherapy both dosimetrically and clinically. As a result of the study, they found that bladder volume significantly affected the rectum, bladder, and target dose. [14]. Ye Lan and colleagues investigated the dosimetric effect of bladder volume status in the treatment of cervical

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cancer. As a result, they determined that bladder fullness can protect the small intestine during radical IMRT [15]. Dutta et al. showed that a full bladder is the main reason for saving dose in near-critical organ protection [16]. Nakamura et al. found that changes in bladder volumes caused changes in both bladder dose and location of adjacent organs for prostate cancer [17].

The number of studies investigating the effect of bladder volume values on other adjacent organ doses in RC irradiated helically with the SIB method is not many. In the study of Jhaveri et al. HT and 3D-CRTplans were compared in the treatment of RC and a significant advantage of HT was found in the bladder, small bowel, and femoral head doses [3]. Another RT of RC study showed that the use of SIB-IMRT techniques was associated with a 64% reduction in the percentage of bowel volume irradiated to 45 and 50 Gy compared to 3D-CRT [18].

The maximum bladder capacity of peaple is various. Also, each person has diverse bladder filling states. Changing the bladder volume affects both the bladder dose volumes and the position of neighboring organs (Bowel, prostate, seminal vesicles, and sigmoid colon) [19]. By filling the bladder, a part of the bladder can be removed from the target volume and bladder toxicity can be reduced during radiotherapy [19,20]. In addition, a full bladder helps to reduce the toxicity that may occur in these organs by removing the small and large intestines from the irradiation area [21,22].

Different volumes of the bladder can affect the target and other critical organ doses during RT of RC. In the literature, there are few studies revealing the dosimetric differences depending on the bladder volume of RC patients who are helically irradiated with the SIB technique. [23]. This study aims to investigate the dosimetric impact of bladder volume values to target and critical organs during helical RT with the SIB technique for RC. Our results may be beneficial when choosing an ideal bladder volume before RT of RC.

Materials and Methods

A total of seventy-eight RC patients who were treated with HT between January 2014-January 2020 were obtained retrospectively. Among these patients, forty-two pre-operative patients were selected. Patients treated with the SIB technique at doses of 45Gy (25 fractions) to the PTV area and 50.4Gy (25 fractions) to the PTV boost area were divided into 3 different bladder volume groups. The median age of the patients was 59.38 (22–87) SD: 16.61; 23 (55%) were women, 19 (45%) were men. Patient demographic and clinical characteristics are shown in Table 1.SD, standard deviation; V, volume; ECOG, Eastern Cooperative Oncology Group; GTV, gross tumor volume; Group 1. bladder volume values were less than 100 ml (V<100ml); Group 2. bladder volume values were between 100 ml and 200 ml (100ml≤V≤200ml); Group 3. bladder volume values were greater than 200ml (V>200ml).

According to our clinical protocol, patients are required to empty the bladder, drink 500 ml of water and wait 30-60 minutes for CT simulation [24]. Patients were asked to empty their rectum before CT. All patients were immobilized in a supine position on a Civco wing board (Civco Medical Solutions, Kalona, IA) and scanned with 3 mm slice thickness. The target and the organ at risk (OAR) volumes were outlined with a Focal (ElektaTM) workstation. PTV, PTV boost, and OARs volume (bladder, femoral heads, and bowel) contoured according to RTOG guidelines [25].

Table1. Demographic and clinical characteristics of patient groups with different bladder volumes

Characteristic	Group1 (N=16) (V<100ml)	Group2 (N=12) (100ml≤V≤200ml)	Group 3 (N=14) (V>200ml)
Age (years) Median ±SD (range)	62,67±14,14 (34-85)	61,83±19,62 (34-87)	53,31±15,45 (22-75)
Gender(%)			
Female	10 (62.5)	7 (58.33)	6 (42.9)
Male	6 (37.5)	5 (41.67)	8 (57.1)
T-stage(%)			
T3	11(68.75)	9 (75)	12 (85.7)
T4	5 (31.25)	3 (25)	2 (14.3)
N-stage(%)			
N0	4 (25)	1 (8.3)	2 (14.3)
N1	9 (56.25)	10 (83,3)	10 (71.4)
N2	3 (18.75)	1 (8.3)	2(14.3)
ECOG(%)			
0	6 (37.5)	5 (41.7)	9 (64.3)
1	6 (37.5)	3 (25)	4 (28.6)
2	3 (18,75)	3 (25)	1 (7.1)
3	1 (6.25)	1 (8.3)	-
GTV Location(%)			
Proximal	8 (50)	6 (50)	5 (35.7)
Middle	6 (37.5)	1 (8.3)	4 (28.6)
Distal	2 (12.5)	5 (41.7)	5 (35.71

The 3-dimensional images obtained were sent to the HT Treatment Planning (TPS) system and the treatment plans were created on the HT TPS (Accuray Inc., Madison, USA). For all patients, a field width of 2.5cm, a pitch of ranged from 0.287 to 0.314, a modulation factor of 2.0-2.5 was used during optimization. All plans made were normalized for 95% PTV to receive the prescribed dose. The treatment plans of the patients were created in 45Gy and 50.4Gy treatment doses were given in 25 fractions to PTV and PTV boost area simultaneously with the SIB technique.

Plan evaluation

Dose-volume histograms (DVHs) were used to compare and evaluate plans. Patients who had a treatment plan were divided into different groups according to their bladder volume values. In order to see the difference between small, medium and large bladder volumes, we divided the patients' bladder volumes into three groups. Bladder volume was a minimum of 41.44ml and a maximum of 620.82ml. PTV, PTV boost, bladder, and bowel volumetric differences were analyzed between groups. PTV, PTV boost; D98, D50, D2, bladder; Dmax, Dmean, V15%, V45%, bowel; Dmax, Dmean, V15%, V30%, V45%, right femur; Dmax, Dmean, V5%, V30% and V45% values and left femur; Dmax, Dmean, V5%, V30% and V45% dosimetric values were evaluated.

Statistical analysis

Descriptive statistical analysis (percentages and mean values) was used to evaluate the data of patients. Measurement data of groups with different bladder volume was evidenced as mean ± SD and analyzed with a one-way ANOVA test. All statistics were calculated by using SPSS 18.0 statistical software (SPSS Inc., Chicago, USA). A value of $p < 0.05$ was considered statistically significant.

Results

Volumetric changes between groups

A total of 42 patients were included in the study and each of them is divided into 3 different groups according to bladder volume. Mean PTV, PTV boost, bladder, and bowel volumes calculated from Accuray treatment planning system (TPS). Volumetric parameters were compared and presented in Table 2. PTV and PTV boost volume mean values are the highest in Group 3. There was no statistically significant difference in volumetric parameters (excluding bladder) among the three groups ($p > 0.05$). The change in bladder volume for different patients is highlighted in Fig. 1.

Changes in bladder volume and dosimetric variations of PTV and PTV boost

One-way ANOVA test analyzed D98, D50, and D2 values of PTV and PTV boost. There was a statistically significant difference in PTV D50 (p=0,039). The D50 of the PTV in Group 1 was the highest. There was no statistically significant difference in dosimetric parameters (excluding bladder) among the three groups ($p > 0.05$). Dosimetric parameters were compared and presented in Tables 2, 3, and 4.

Table 2. Comparison of volumetric data and patient groups with different bladder volumes

Volume Parameters	Group 1 (N=16) (V<100ml)	Group 2(N=12) (100ml≤V≤200ml)	Group 3(N=14) (V>200ml)	P value
PTV Mean (cc)	1256.47±452.84	1425.57±431.34	1526.80±313.84	0.452
PTV Boost Mean (cc)	602.08±389.14	677.94±345.35	941.24±499.56	0.227
Bladder Mean (cc)	76.54±15.97	156.66±36.90	396.02±188.07	0.000*
Bowel Mean (cc)	1416.71±523.63	1556.11±726.38	1281.08±522.06	0.282

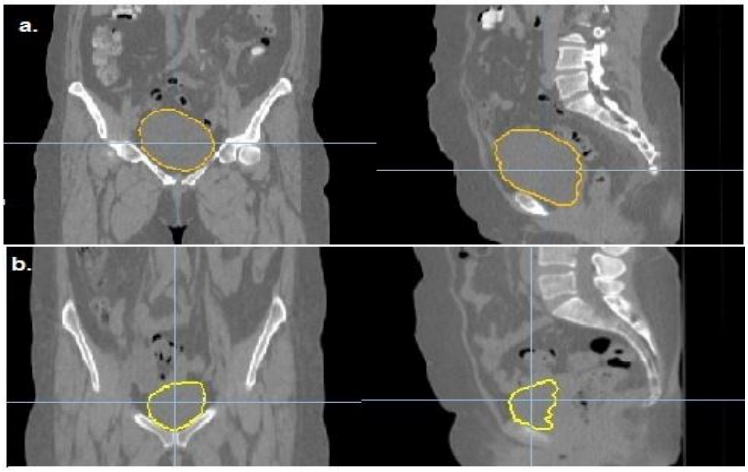

Figure 1. Sagittal and coronal views of two patients with different bladder volumes. a. Image of patient with bladder volume greater than 200 ml (V>200ml) b. Image of patient with bladder volume less than 100 ml (V<100ml)

Table 3. Comparison of dosimetric data and patient groups PTV an PTV boost dose with different bladder volumes

Parameters	Group 1 (N=16) (V<100ml)	Group2 (N=12) (100ml≤V≤200ml)	Group 3 (N=14) (V>200ml)	P-Value
PTV Dose (Gy)				
D98	52.87±0.64	52.25±1.02	52.52±0.26	0.071
D50	48.48±2.02	46.79±1.49	48.78±1.85	0.039
D2	39,64±7,39	36.66±3.66	38.24±4.17	0.405
PTV Boost Dose				
D98	51.57±4.69	52.64±0.74	52.87±0.67	0.469
D50	50.25±1.71	51.00±1.71	49.70±3.01	0.358
D2	52.87±0.67	51.01±0.70	49.70±3.25	0.489

Table 4. Comparison of dosimetric data and patient groups OAR's dose with different bladder volumes

Parameters	Group 1 (N=16) (V<100ml)	Group2 (N=12) (100ml≤V≤200ml)	Group 3 (N=14) (V>200ml)	P-Value
Bladder Dose (Gy) ±SD				
V15Gy	44.89±7.47	47.69±2.61	49.00±3.10	0.113
V45Gy	35.31±11.14	37.31±6.78	41.49±6.15	0.171
Dmax	51.24±1.88	51.82±0.95	52.69±0.69	0.024
Dmean	34.92±10.6	33.45±9.92	38.21±7.51	0.453
Bowel Dose (Gy) ±SD				
V15Gy	42.75±10.21	40.10±4.84	36.10±10.56	0.180
V30Gy	32.93±8.93	31.62±5.97	27.55±10.65	0.287
V45Gy	20.57±7.13	21.70±5.23	18.17±8.89	0.709
Dmax	51.24±1.42	50.53±3.22	49.61±4.10	0.385
Dmean	22.25±9.32	24.22±10.11	17.50±9.08	0.226
Femoral Head (Right) Dose (Gy) ±SD				
V5%Gy	29.43±6.85	36.74±5.91	37.21±7.27	0.005
V30%Gy	16.18±5.74	21.55±5.57	20.77±4.34	0.035
V45%Gy	11.18±5.75	14.47±5.01	13.94±3.32	0.172
Dmax	41.57±5.34	43.78±4.26	46.09±3.62	0.041
Femoral Head (Left) Dose (Gy) ±SD				
V5%Gy	29.37±7.63	36.47±6.46	36.56±7.28	0.120
V30%Gy	16.56±6.64	20.35±8.18	23.19±4.43	0.037
V45%Gy	11.87±6.20	14.56±3.94	14.47±3.82	0.312
Dmax	42.45±6.63	43.56±3.31	45.10±4.84	0.351

Changes in bladder volume and dosimetric variations of bladder

Bladder volumes were measured with TPS from CT planning images. The Dmax of the bladder in Group 3 was highest (p=0.024). Compared to other groups, the highest dose values are in group3, but there was no statistically significant between the bladder Dmean, V15%, and V45% doses (p >0.05).

Changes in bladder volume and dosimetric variations of bowel

Doses of bowel Dmax, V15%, and V30% were highest in Group1, while it decreases in Group 2 and Group 3. The bowel dose was the lowest in Group 3 with the highest bladder volume. There was no statistically significant between the bowel doses and the groups (p >0.05).

Changes in bladder volume and dosimetric variations of femoral heads

As a result of the analysis, there was a correlation between bladder volume and femoral head radiation dose. The lowest doses were in Group 1, while the highest doses were in Group 3. There was a statistically significant difference in the right femoral head V5% (p=0,005) and V30% (p=0,035) and left femoral head V30% (p=0.037).

Discussion

Bladder volume or fullness capacity varies from person to person. While the maximum bladder volume filling V> 200 ml in some patients, this rate may be V <100 ml in other patients. Anatomically, the small bladder capacity can reduce the effect of the bladder filling procedure. In this study, we looked at the impact of different bladder volume values on the dose of PTV

and OARs during RT of RC. While examining this, we divided the patients with different bladder capacities into three groups and compared the dosimetric results we obtained.

The rectum is located near many critical organs (bowel, bladder, femoral head, etc). Irradiation of the bladder and bowel from critical organs during the RT of RC can cause toxicity [26]. Treating RC patients with a full bladder is one of the important and practical solutions to reduce bowel toxicity [13]. Yaparpalvi et al. looked at the bowel doses in the full bladder and empty bladder states in the dose comparison and they found a statistically significant dose increase in the empty bladder [27]. Also, Hatanaka et al. found significant relationships between Dmax values and bladder volume variation in both the small and large intestines [28]. In our study, although it was not statistically significant, a decrease in bowel doses was detected with increasing bladder volume. Since our study examined the retrospective data, we were not able to present the bladder wall doses depending on the bladder volume variations. In the study of Hatanaka et al., no significant relationship was found between the doses of the bladder wall and the variation of bladder volume [28]. As the bladder volume increases, the bladder wall thickness will decrease [29], but we do not think that this will affect the results obtained in this study.

The increase in the fullness of the bladder caused the displacement of the bladder especially in the anterior and cranial directions. As the bladder volume increases, the bladder approaches the rectum in the LR direction [30]. The study conducted by Nakamura et al. investigated the relationship between bladder volume value for localized prostate cancer and treatment plan values, and as a result, it states that a full bladder the volume of more than 150 ml may not help meet planning dose constraints [17]. Ma et al. determined that the optimum bladder volume range for dose distribution and some side effects in cervical cancer is 100-150 ml [14]. In our study, the PTV D50 dose was the lowest in Group 2 (100ml≤V≤200ml) ($p = 0.039$). In addition, although the PTV D98 and D2 dose was not statistically significant, the lowest value was observed in Group 2. When we looked at our dosimetric values for this study, we could say that PTV values were better in Group 2.

In the study of Hatanaka et al. on prostate patients, it was stated that a decrease in bladder volume increased the bladder dose [30]. But in this study, as the bladder volume increases, the Dmax dose of the bladder increases. We speculate that this is because large bladder volume may increase the likelihood of near-target hotspot areas occurring in the bladder.

Today, many centers follow bladder filling protocol during pelvic region RT planning to treat easily [18,31]. Daily MVCT control in HT provides a method that allows the bladder volume to be taken at a certain standard [32]. Easy and accurate bladder volume control can be achieved with MVCT. Therefore, this study ignored both intra- and inter fractionally changes in bladder filling that could occur during the study period. In this study, we only focused on dose verification of the bladder volume for treated RC patients.

This study has some limitations. Firstly, the study was designed retrospectively and in a single-center without a large number of patients in the groups. Secondly, studies involving different bladder volumes dosimetric and clinical results should be conducted in the future.

Conclusion

In this study, we observed the significant effect of bladder volume values on PTV and critical organs. In patients with high bladder volume, there was a decrease in the intestinal doses and an increase in the femoral head and bladder doses. PTV dose value was better in Group 2 (100ml≤V≤200ml). We think that this study, in which we examine the dose change depending on the bladder volume values of rectum patients who underwent helical RT with the SIB technique, will guide new studies in the future.

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