Evaluation of Dose Distribution Due to Change in Bowel Position in Patients Treated with SBRT for a Target Lesion Neighboring the Intestine

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ABSTRACT

Stereotactic radiotherapy is becoming increasingly important in cancer treatment. Uncertainty due to internal organ movements causes confusion in bowel contouring and dose optimization. In this study, it was aimed to evaluate the dose changes due to bowel movements in patients who applied SBRT to the abdominopelvic area. A fusion was created between the cone beam Computed Tomography (CT) images obtained during the treatment and the planning CT. Thus, the dose to which the bowels were actually exposed during treatment was calculated. Bowel dose (Dmax, D2cc) calculated in the treatment plan was defined as 'Planning dose'. Bowel doses calculated according to the bowel position during treatment was defined as 'Administering dose'. The dosimetric results obtained from the patient's first plan data were compared with the bowels doses obtained by recalculating the dose received in the treatment separately for each fraction. There was no statistically significant difference in terms of bowel total maximum dose (p= 0.615), maximum dose per fraction (p= 0.798), and maximum dose of 2 cc bowel per fraction (p= 0.580). On the other hand, there is a statistically significant difference for the maximum dose of 2 cc in the bowel values between two calculations(p=0.016). According to our study, only bowel 2 cc dose values were found to differ significantly between planning and applied values, depending on bowel movements. Further studies are needed to understand the clinical significance of this difference.

Keywords: Stereotactic body irradiation, Toxicity, Bowel, Contouring

INTRODUCTION

Stereotactic body radiotherapy (SBRT) is an increasingly used radiotherapy technique in cancer treatment.[1] The primary purpose is to protect the surrounding tissues and obtain ablative treatment while applying a high dose of radiation to the target lesion with high accuracy. Although the benefits it provides and tumor control, if it is not used correctly, it can cause severe toxicities due to the high dose to which normal tissues will be exposed.[2-4]

Intestines are among the tissues at risk, which care is taken to protect in the radiotherapy of tumors located in the pelvis and abdomen. Exposure to radiation, especially at high doses, causes severe toxicities.[5] In addition to limiting the doses applied here, another important point is that the bowel position observed while obtaining the planning computed tomography can change considerably during the treatment. It is not known how accurate the intestinal doses we see in the planning data are. In this study, it was aimed to compare the bowel dose calculated in planning and actually taken due to bowel movements.

PATIENT and METHODS

In our study, 13 patients who underwent SBRT to the pelvic region for various diagnoses and indications in Ankara City Hospital and were found to have ≤ 1 cm target volume proximity to the bowel loop in planning tomography were evaluated prospectively. Only the below-knee apparatus was used in the patients. No additional procedures were performed on bladder filling in patients who underwent SBRT for bone metastases. Only patients who underwent SBRT for pelvic LN metastases were allowed to drink 500 cc of water before the simulation.

The adjacent bowel loops were recontoured on the patients' kvCTs taken in each fraction treatment. These created contours were transferred to the planning computed tomography. By combining the bowel contours created in each fraction, the organ at risk due to internal organ movement was created (Planning organ at risk volume= PRV intestine, in which the internal organ movement is taken into account for the intestine) (Figure 1. Creation of PRV_ bowel volume with bowel organ movement using kvCTs). The dose distribution in the applied treatment plan and the dose taken by the intestine in the treatment position were evaluated and recorded. The study aimed to assess whether there is a difference between the intestinal doses calculated in the target SBRT planning and the intestinal dose calculated in each fraction and, if there is a difference, whether this difference is significant or not. The doses in the approved radiotherapy plan are called "the planning doses". The doses received by the patient during treatment were calculated and defined as "the administering doses"

Ethics committee approval of the study was obtained from the ethics committee of Ankara City Hospital No: 1 (25/08/2021 E1-21-1955).

Statistical Analysis

The data were recorded in the SPSS version 23.0 (IBM Corporation, Armonk, NY, USA) statistical program and analyzed. Descriptive values for quantitative variables are specified as median, mean, standard deviation, and range. Categorical variables are defined as the number (n) and ratio (%). The suitability of the investigated variables to the normal distribution was evaluated by visual and analysis methods, and it was seen that they did not comply with the normal distribution. Non-parametric tests were used for analysis. The Wilcoxon rank-sum test was used for the dependent variable analysis. The statistical significance limit was accepted ≤ 0.05.

RESULTS

In the current study, 13 patients who underwent SBRT at a target volume of 1 cm or closer to the intestinal loop between March 2019 and July 2021, and a total of 59 SBRT fractions were evaluated retrospectively. The median age of patients was 58 (range 52-78). SBRT target areas are including; sacrum metastasis 1 (7.7%); pelvic bone metastasis (right) 2 (15.4%); paraaortic lymphadenopathy 2 (15.4%); pelvic lymphadenopathy 5 (38.5%); vertebral metastases 2 (15.4%); metastatic soft tissue 1 (7.7%). The target volume is median 7 (range 0.4-58,7) cc, and the highest target volume is 58,7 cc of pelvic bone irradiation (Figure 1). The closest distance between the intestine and PTV was measured in simulation CT, and the median result is 1 (range 0.01-1,02) cm. The SBRT fraction numbers are as follows; 5 fractions in 11 patients (84.6%); 3 fractions to 1 (7.7%) patient and 3 fractions to 1 (7.7%) patient. Fraction doses are 5 Gy in 2 (15.4%) patients; 6 Gy in 1 (7.7%) patient; 6.5 Gy in 1 (7.7%) patient; 8 Gy in 2 (15.4%) patients; 7 Gy in 7 (53.8%) patients. The median total dose is 35 Gy (8-35 Gy) (Table 1).

According the results of the study; the difference between the total planning maximum dose (mean 1863 cGy, range 791-2817 cGy, SD: 548.3) and the administering total bowel maximum dose (1911 cGy, range 710-2972 cGy, SD: 572.2) is not significant (p= 0.615). The difference between the planning total fraction bowel max dose (mean 434 cGy, range 258-791, SD 406.0 cGy) and the administering fraction total bowel maximum dose (440 cGy, range 325-710 cGy, SD: 406.6) is also not significant (p= 0.798). The difference between the planning fraction bowel 2 cc dose (mean 422 cGy, range 37-2960 cGy, SD: 191.4) and the administering fraction bowel 2cc dose (mean 321 cGy (range 206-518 cGy SD: 284.9) is not statistically significant (p= 0.0580) (Table 2).

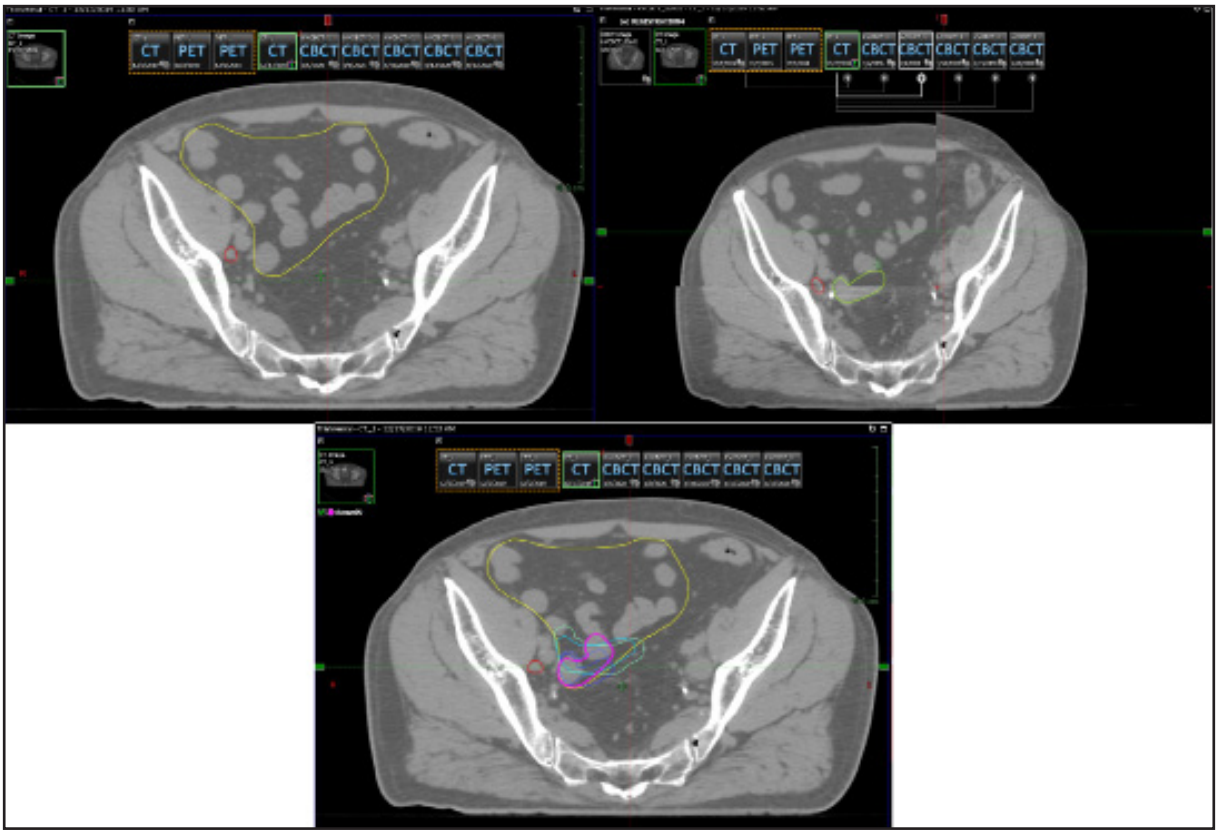

Figure 1. Creation of PRV_bowel volume with bowel organ movement using kvCTs

The difference between the planning total bowel 2cc dose (933 cGy, range 8.8-1940 cGy, SD: 504.1) and the administering total bowel 2cc dose (1412 cGy, range 518-2731 cGy, SD: 439.2) is significant (p= 0.016). Wilcoxon test details for this significant test are shown in Table 3. In 10 of 13 patients, the patient received a higher dose than planned, and three patients received lower doses than those that have been planned.

DISCUSSION

In the current study, the doses calculated in the bowel planning and administered to the patient during the treatment were analyzed in detail for SBRT. Only the total 2cc bowel doses were significantly different between the planned and administered doses among the evaluated parameters. In 10 of 13 patients, the total 2cc intestinal dose was higher than the planned value. SBRT is an increasingly used treatment technique, and the possible high intestinal doses should be considered, especially in abdominal irradiations.

Bowel are important dose-limiting organs in abdominopelvic region irradiation. Many factors affect bowel movements. The main ones are the patient's eating habits, motility regulator drugs used during the treatment, body mass index, and history of previous surgery.

There are different approaches to contouring the bowel as an organ at risk. While contouring guides take into account possible bowel movements by contouring the entire peritoneal area, there are also contouring guides based on drawing only the bowel loops again, which segments to include in the bowel definition differ between guidelines.[6-8]

SBRT is increasingly taking its place in the cancer treatment. The application of higher doses in a shorter treatment time than conventional therapies makes the dose taken by the intestines important, especially in abdominopelvic area irradiation, and dose change due to internal organ movements becomes even more critical.

Table 1. Patients and Radiotherapy Details

Gender	Female	2 (145.4%)
	Male	11 (84.6%)
SBRT Site	Sacrul Bone	1 (7.7%)
	Pelvic Bone (right)	2 (15.4%)
	Paraaortic LAP	2 (15.4%)
	Pelvic LAP	5 (38.5%)
	Vertebra	2 (15.4%)
	Metastatic Soft Tissue	1 (7.7%)
Target Volume (median)	7 cc	Range 0.4- 587 cc
Closest distance of Bowel- PTV (median) on Planning CT	1 cm	Range 0.01-1,02 cm
Number of Fractions	5 frc	11 (84.6%)
	3 frc	1 (7.7%)
	1 frc	1 (7.7%)
Fraction dose	5 Gy	2 (15.4%)
	6 Gy	1 (7.7%)
	8 Gy	2 (15.4%)
	7 Gy	7 (53.8 %)
Total dose (median)	35 Gy	Range 8-35

Abbreviations: SBRT=Stereotaktik body radiotherapy; LAP= Lymphadenopathy; CT= Computed Tomography; cc= cubic centimeter; cm= centimeter; PTV= planning target volume; Gy= Gray;Frc= Fractions

Based on this idea, it was desired to evaluate the doses taken due to bowel movements of patients who were administered SBRT due to the lesion located in the vicinity of the intestine. A statistically significant difference was found only in the total intestinal D2cc dose. However, new clinical studies should be planned to obtain information about the clinical significance of this difference. On the other hand, another issue is that bowel mobility may differ in different anatomical locations.[9] For this reason, dose analysis may be more accurate in more homogeneous groups in terms of anatomical location.

Movement-related dose changes may be of different importance for different patient groups. It may be appropriate to be more sensitive to intestinal doses in patient groups (anti-VEGF, anti- EGFR agents) where the fraction dose is high and simultaneous systemic targeted therapies are applied.[10]

Our study evaluated movement-related changes in data such as Dmax and D2 cc, which are dose-limiting parameters in SBRT and brachytherapy applications. In this area, a study assessing bowel complications in SBRT treatment applied to 84 abdominopelvic metastatic patients was presented in

Table 2. The planning and the administering bowel doses

	Mean (cGy)	**Range (cGy)**	**SD**	**p**
The planning total bowel maximum dose	1863	791-2817	548.3	0.615
The administering bowel maximum dose	1911	710-2972	572.2	
The planning fraction total bowel max dose	434	258-791	406.0	0.798
The administering fraction total bowel maximum dose	440	325-710	406.6	
The planning fraction bowel 2 cc dose	422	37-2960	191.4	0.580
The administering fraction bowel 2cc dose	321	206-518	284.9	
The planning total bowel 2cc dose	933	8.8-1940 cGy	504.1	0.016
The administering total bowel 2cc dose	1412	518-2731 cGy	439.2	

Abbreviations: SD= Standart Deviation; radiotherapy; cc=cubic centimeter; cGy= centiGray

Table 3. Planning and administering total bowel 2cc dose Wilcoxon test analysis

		N	Mean Rank	Sum of Runks
The planning total bowel 2cc dose The administering total bowel 2cc dose	Negative Ranks	10[a]	8.00	80.00
	Positive Ranks	3[b]	3,67	11.00
	Ties	0[c]	0	0
	Total	13		

[a]= *The planning total bowel 2cc dose < The administering total bowel 2cc dose*
[b]= *The planning total bowel 2cc dose > The administering total bowel 2cc dose*
[c]= *The planning total bowel 2cc dose = The administering total bowel 2cc dose*

2018. With the NCTP formula created in this study, it has been reported that the critical parameters in the development of grade 2 acute toxicity are related to the EQD2 (V30, V40, V50, and V65) data, but not with Dmax and D2 cc values. No correlation was found with any parameter for chronic toxicity.[5]

La Courte et al. have reported a trial which is a significant study on intestinal dose limitation in SBRT applications[11]; risk groups were established using the dose-volume histogram risk mapping method on case series belonging to different studies. According to this review, in the Timmerman study, the D5 cc= 16.2 Gy limit was found in 3 fractions for low risk and 2.5% risk. For cases requiring higher doses reported by Molinelli (2008), D5 cc= 21 Gy limit in 3 fractions was 6.5% risk.[11,12]

It is also a current issue which bowel contouring technique is correct or which new methods can be applied in cases where SBRT is used. In a study conducted for proton therapy, another treatment method with a sharp dose distribution, such as SBRT, dose data of 11 patients who underwent post-hysterectomy conventional doses of proton therapy were analyzed. It was reported that dose data obtained with bowel bag contouring and loop contouring gave different results depending on bladder fullness.[13]

There are also new studies on bowel contouring in cases with SBRT. New suggestions for bowel contouring have been made with the study published by Clark et al in 2020. Researchers reported that bowel loop drawing should be performed only within 3 cm circumferential and 2 cm upper-lower expansion of the PTV. The bowel loops distal to the SBRT area can be contoured as bowel bags, thus saving time during contouring.[14] The study's main weakness is that it does not include standardization and data on the factors affecting the bowel movements of the patients. After this study, a new prospective study was planned with a patient group standardized in terms of surgical status, premedication of simulation CT and primary disease site.

In conclusion, according to the findings of our study, the only parameter with a statistically significant dose difference is the intestinal D2cc dose. In this context, it is predicted that dose changes due to bowel movements will not differ significantly in different contouring styles in SBRT applications. However, more reliable results will be obtained with studies in which patients are evaluated anatomically more homogeneous and sufficient In cases where high fraction dose and simultaneous anti-VEGF treatments are applied, a more precise dose calculation can be made with loop and bowel bag drawings with new contouring techniques.

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