ORIGINAL ARTICLE

The Effect of Injected and Oral Computed Tomography Contrast Agent on Helical Tomotherapy Dose Calculating in Rectal Cancer

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Abstract

Purpose: This study aimed to evaluate the impact of Contrast-Enhanced Computed Tomography (CECT) on treatment planning for rectal cancer using Helical Tomotherapy (HT).

Materials and Methods: A total of patients with known rectal tumors were included, and both CECT and non-CECT images were obtained. Patients adhered to a low-fat diet and received oral and intravenous iodine-based contrast agents. Target volumes, including Gross Tumor Volume (GTV), Clinical Target Volume (CTV), and Planning Target Volume (PTV), were delineated by a radiation oncologist using DICOM images. Intensity-Modulated Radiation Therapy (IMRT) techniques with Simultaneous Integrated Boost (SIB) methods were employed to optimize dose delivery while minimizing exposure to Organs at Risks (OARs).

Results: The analysis revealed that the use of CECT significantly increased. Hounsfield Unit (HU) values across all structures, enhancing visibility and accuracy in target volume delineation. Dosimetric evaluations indicated minimal differences in dose distributions between CECT and non-CECT plans. However, certain indices such as D_{max}, D_{min}, D_{mean}, Homogeneity Index (HI), and Conformity Index (CI) showed significant changes that could influence clinical outcomes.

Conclusion: The incorporation of CECT in radiation therapy planning for rectal cancer improves the delineation of critical structures, potentially leading to better treatment outcomes. The findings underscore the importance of using contrast media in enhancing imaging quality, which is crucial for effective target volume definition and OAR contouring. Future research should explore the long-term clinical implications of these findings on patient outcomes and quality of life post-treatment.

Keywords: Tomotherapy; Contrast Media; Radiotherapy Planning; Dosimetry; Rectal Cancer.

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1. Introduction

The use of CECT in radiotherapy for various cancer types has garnered significant attention due to its critical role in both diagnosis and treatment planning. CECT enhances tumor visualization in CT images by utilizing an intravenous contrast agent that increases electron density in highly vascularized organs, resulting in brighter regions on scans and clearer delineation of tumors from surrounding tissues [1]. During a CT scan, the contrast agent circulates, leading to increased HU in enhanced organs. While this change improves tumor visibility, it also introduces complexities in dosimetric calculations. Specifically, if CECT images are directly used for dose calculations, the increased tissue density must be accounted for, as dosimetric accuracy relies heavily on electron and mass densities derived from HU values. Treatment plans based on CECT may lead to discrepancies in dosimetric parameters—such as the Conformity Index (CI), Homogeneity Index (HI), and gamma index—when applied to patients without the contrast agent present, potentially resulting in treatment errors [2].

Many radiotherapy departments continue to rely on non-CECT for treatment planning while predominantly using CECT for target delineation. The administration of a contrast agent facilitates easier identification of target areas [3]. Studies indicate that tolerances of ± 20 HU for soft tissue and ± 50 HU for lung tissue can result in minimal dose changes (under 1%), despite slight increases in HU values being clinically insignificant [4]. However, research on the impact of varying HU values on dosimetric indices specifically for rectal cancer treated with tomotherapy remains limited. Research by Kim *et al.* assessed 22 CyberKnife treatment plans across various cancers using both CECT and non-CECT images, revealing dose differences ranging from 2% to 20% [5]. AlShurbaji *et al.* found no significant impact on calculated dose values between the two imaging modalities but noted an increase of approximately 2% in Monitor Units (MUs) for upper abdominal treatments [6]. Significant dose differences were observed in specific regions like the lower esophagus; however, no substantial variations were noted in critical structures or within the rectal region [7].

The influence of CT contrast agents appears to vary across different tumor types and anatomical locations [8]. In colon cancer radiotherapy, where beams traverse multiple contrast-enhanced organs, understanding the effect of CECT on dose distribution is crucial due to the vascularity of the colon and potential alterations in electron density caused by the contrast agent (Figures 1, 2). The surrounding organs also exhibit substantial blood supply, leading to notable differences in HU values between imaging sets. The relevance of these findings is amplified when considering Helical Tomotherapy (HT), recognized for its superior normal tissue sparing and precise dose distribution compared to traditional methods. However, the specific dosimetric effects of intravenous and oral contrast agents within CECT images during HT for rectal cancer patients have yet to be thoroughly investigated.

This study aims to elucidate how CECT influences dose calculations for rectal cancer HT techniques. We analyzed dosimetric parameters including CI, HI, and gamma index, alongside a comprehensive evaluation of Dose-Volume Histograms (DVHs) for both target volumes and Organs At Risk (OARs).

2. Materials and Methods

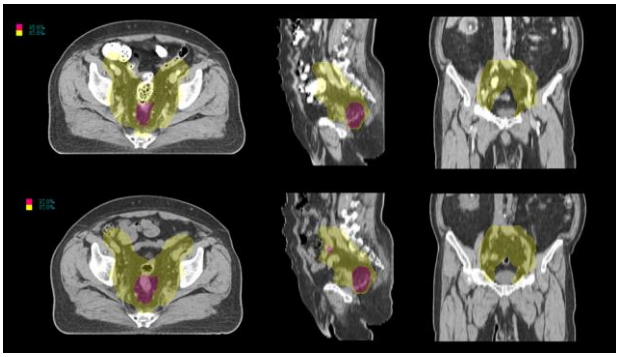

Figure 1. Illustration of the dose distribution of 95% (purple) and 85% (yellow) isodoses in two images with contrast (top) and without contrast (bottom)

2.1. Patients

This prospective study included patients with known rectal tumors who provided written informed consent between January 2023 and November 2024.

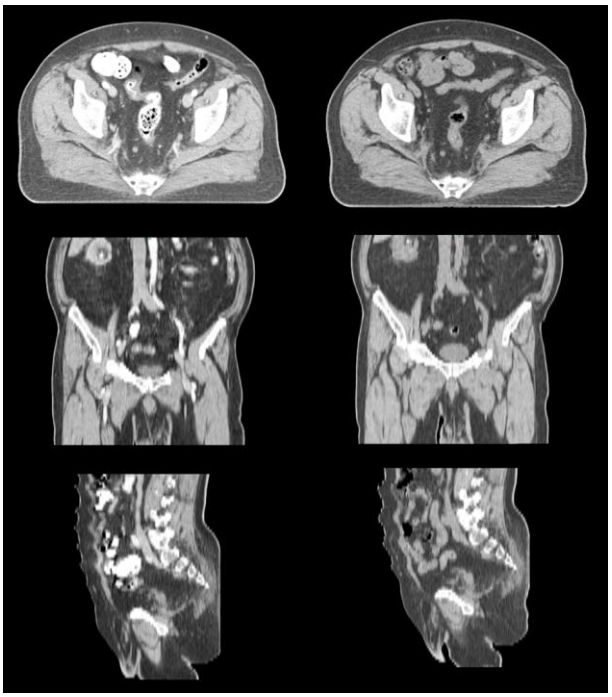

Figure 2. View of CT images with contrast (left) and without contrast (right)

Patients were included if they did not receive intravenous contrast agent injection, such as in cases with renal failure, serious liver function failure, hypersensitivity to iodinated contrast agents, etc. Overall, CT images of 15 patients were collected, but in the end, only a total of patients (7 males, 8 females) with healthy renal function and mean age (51.2 ± 4.8) met the necessity and were included in this study.

2.2. CT Image Acquisition

CT images with and without the contrast agent were acquired for each patient in the same position during the pelvic CT scans in a supine position using a 16-slice CT simulator (Somatom Emotion, Siemens AG, Forchheim, Germany). Initially, non-CECT images covering the entire treatment field were obtained. To minimize any positioning differences, the patients were kept in the same immobilization device after an unenhanced scan. The patients were asked to follow a low-fat and low-carbohydrate diet to empty the intestines as best as possible and instructed to drink an iodine-based liquid 250 mL every 60 min of approximately 1000 mL of oral contrast preparation at least 12 h before the CT scan in some determined time intervals so that a proper contrast of the intestine would be achieved. The patients remained in the same position as during non-contrast imaging and used bold tattoo markings to minimize positional deviations. For the intravenous Contrast Media (CM) administration, a small needle was inserted into a vein by an expert nurse connected the patient to an Intravenous (IV) automatic injector to enhance rectal tumor blood vessels and the soft tissues in the pelvis, making them more visible in the CT scan. The enhanced scan began immediately after the contrast injection. The amount of CM used for a CECT scan depended on the specific protocol and the patient's individual needs. Typically, the oral contrast of around 500-2000 mL of the Visipaque iodine-based liquid (15 mL Visipaque iodinated-based contrast diluted in 1500 mL water), while around 100-150 mL intravenous contrast was administered [9-11]. A similar scanning protocol and coordinates were applied for enhanced and unenhanced CT scans, and images were obtained for all patients. Further coordination was achieved by using 3 lead spot markers or tattoo markers placed on the right and left Anterior Superior Iliac Spines (ASIS) of the pelvic bone on the patient's skin. The slice thicknesses were 3 mm.

2.3. Target Volumes and OAR Delineation

CECT and non-CECT images in DICOM format were transferred to the Accuracy Precision treatment planning system (Accuray Incorporated, California, USA) version 2.0.1.1. for the structural contouring. Tumor-related contours (including the GVT, CTV, and PTV) and other OARs were delineated by a radiation oncologist on CECT images according to the ICRU-83 report [12].

2.3.1. Importance of Accurate Planning

Defining the GTV requires the meticulous identification of the primary tumor and involved lymph nodes. For CTV, it encompasses GTV the complete mesorectum, and the pelvic lymph node regions such as presacral, internal iliac, and obturator areas, extending up to the L5–S1 interspace [13]. This volume covers areas at risk for microscopic disease spread, not visible in imaging studies [14]. The PTV is then established by adding margins to the CTV to account for daily variations in patient setup and organ motion. Specifically, an 8 mm margin is added in the craniocaudal direction, and 6 mm in both anteroposterior and lateral directions [13]. This

ensures the CTV receives the prescribed tumoricidal dose despite potential movements and setup errors, which are particularly significant in pelvic radiation therapy for rectal cancer [15].

IMRT has transformed the treatment of pelvic malignancies by enhancing the conformality of radiation to the target volumes while significantly reducing the dose of OARs. IMRT plans consistently achieve targeted PTV coverage and show significantly lower doses across various dosimetric parameters of OARs compared to 3D-Conformal Radiation Therapy (3D-CRT) plans. For dose planning, the use of SIB techniques in IMRT, such as SIB7-IMRT and SIB9-IMRT, has been shown to maintain or reduce V35 values effectively, providing an optimal balance between efficacy and safety. These techniques also offer significant advantages in sparing the bladder and femoral heads from high-dose exposure, as evidenced by lower mean doses and reduced V40 values [16].

In terms of dose limits for OAR, specific maximal irradiation doses are maintained, such as keeping the bladder dose under 24 Gy, the bowel under 25 Gy, and the femur heads under 20 Gy. Additionally, the relative volumes of these organs receiving certain radiation thresholds are strictly controlled to minimize the risk of complications. This meticulous approach ensures that all OARs are protected effectively during the treatment, enhancing patient safety and treatment outcomes [17].

2.3.2. Modulation Factor, Pitch, and other Technical Parameters

Tomotherapy planning parameters include a field width of 2.5 cm, with a pitch set to 0.25 and a maximum modulation factor of 2.5, aiming to deliver at least 95% of the prescribed dose to 95% of the PTV [13]. The choice of a 2.5 cm Fan Beam Thickness (FBT) is strategic, minimizing the penumbra in the longitudinal direction and optimizing overall treatment time compared to other FBT options [17, 18]. Pitch values typically range from 0.287 to 0.31, adjusted according to the difficulty of meeting OAR constraints, while modulation factors can vary from 2 to 3, depending on desired homogeneity and conformity.

2.4. Tomotherapy Treatment Planning

The prescribed dose (5000 cGy in 25 fractions) and the number of treatment sessions were considered based on the RTOG 0529 phase II protocol [19]. HT treatment planning, optimization, dose constraints for OARs, and dose calculations based on CECT images were performed by an expert medical physicist to achieve 95% dose coverage in the PTV. By adhering to dose limits and carefully planning the tomotherapy treatment, healthcare professionals can ensure that the patient receives the necessary radiation therapy while minimizing the risk of side effects and complications. This meticulous planning and adherence to dose limits are essential to achieving successful outcomes in the treatment of rectum cancer with Tomotherapy.

Thereafter, all the extracted treatment plans of CECT images were applied to the same treatment plan (without changes in MU and fluence map) on non-CECT images by creating a Quality Assurance (QA) plan for each treatment plan, performing recalculations to determine the dose reached to the target volumes and OARs, and extracting the desired dosimetric parameters.

2.5. Dosimetric Evaluation Parameters

For each patient, different dosimetric indices of the CECT and non-CECT dose distributions were carefully analyzed and compared. The CI and HI parameters were employed as supplementary metrics to assess the CECT and non-CECT treatment plans. Various HT plans were designed for each patient, and finally, the optimal treatment plan was selected using a comprehensive evaluation of all plans through dosimetric indicators.

The CI, as an important criterion for determining the compliance of the prescribed dose with the target volume, is defined as follows according to the ICRU-62 report [20] (Equation 1):

$$CI_{paddick} = \frac{TV_{RI}}{TV} \times \frac{TV_{RI}}{V_{RI}} \quad (1)$$

Where TV_{RI} is the target volume covered by the reference isodose, and V_{RI} is the volume of the reference isodose and TV is the target volume.

The HI was calculated as a quantitative tool for analyzing the uniformity of the dose distribution in the

target volume. The following equations were used to calculate the above index (Equations 2-5):

$$HI(1) = \frac{D_{2\%} - D_{98\%}}{D_p} \quad (2)$$

$$HI(2) = \frac{D_{5\%} - D_{95\%}}{D_p} \quad (3)$$

$$HI(3) = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (4)$$

$$HI(4) = \frac{D_{5\%} - D_{95\%}}{D_{50\%}} \quad (5)$$

where D_2 = minimum dose to 2% of the target volume indicating the "maximum dose" [21], D_{98} = minimum dose to 98% of the target volume, indicating the "minimum dose" [22], D_5 = minimum dose in 5% of the target volume, D_{95} = minimum dose in 95% of the target volume [23] and D_p is the prescribed dose [24].

In this study, the dose distribution of treatment plans obtained from two cases with and without CECT was examined in terms of the degree of conformity of the evaluated dose distribution to the reference dose distribution [25]. This comparison utilized the gamma index. The gamma index dose comparison tool is widely utilized to compare two dose distributions. This is a computationally demanding task when dealing with 3D dose distributions. For each point in the assessed dose distribution, the gamma index, as a unit less quantity, combines both the dose and distance differences [26]. The two dose distributions were compared with the gamma acceptance criteria of 3%–3 mm. Also, the dose distribution without contrast agents was considered the reference dose distribution. In this regard, it is necessary to extract the dose distribution related to the plans from the Treatment Planning System (TPS) into the DICOM RT Dose file format, and after the necessary processing in the MATLAB environment, they were converted to an acceptable format in the VeriSoft software (MEPHYSTO software version 5.1, PTW, Freiburg, Germany) for gamma analysis. Then the files generated by MATLAB software were imported into gamma analysis software, and finally, two different dose distributions were evaluated in terms of gamma pass rate.

In addition, after completing treatment plans on CECT and non-CECT images and obtaining 3D dose distributions, other dosimetric parameters for the target and healthy and radiation-sensitive tissues were extracted. These parameters for the tumor included $D_{2\%}$, $D_{5\%}$, $D_{95\%}$, $D_{98\%}$, D_{min}, D_{mean}, and D_{max} indexes, and various V_x such as V_{100}, V_{95}, and V_{90}. For vital organs, the doses received by these tissues in different volumes were obtained with the help of the D_x index from D_{min}, D_{mean}, and D_{max} from the software.

2.6. Statistical Analysis

A paired t-test was employed for normally distributed data to compare calculated doses and other parameters in enhanced versus unenhanced CT plans with Graphpad Prism version 10.2.3. The non-parametric Wilcoxon signed-rank test was used in all other cases. It was considered statistically significant when $P < 0.05$. *p < 0.05, **p < 0.01, ***p < 0.001, and ****p < 0.0001 denote the significance level.

3. Results and Discussion

The analysis of dosimetric parameters for rectal cancer treatment planning using HT revealed minimal differences between plans with and without CM for most PTV dose parameters (Table 1). While none of these differences were statistically significant, the largest absolute difference was observed in D_{min}. D_{mean} showed a slight decrease without CM, approaching but not reaching statistical significance (p-value = 0.0645). For PTV volume parameters, V95 demonstrated a statistically significant increase (5.13%, p-value = 0.0006) without CM, while V100 and V90 showed slight, non-significant increases. V107 and V105 remained at 0% for both conditions, indicating good control of high-dose regions. Regarding HI, HI1, HI2, and HI3 showed minimal, non-significant changes, but HI4 exhibited a significant increase (122.22%, p-value= 0.0413) without CM, suggesting potentially less homogeneous dose distribution. For CI, CI100% showed a statistically significant decrease (p-value= 0.0051) without CM, indicating slightly less conformity, while CI98% showed a larger but non-significant decrease,

Table 1. Changes in dose delivered to the PTV before and after inserting oral and IV contrast medias. CN: contrast media and Δ: differences between with and without CM

Parameter	With CM	Without CM	Δ	Δ%	P-value
PTV					
D_{max} (cGy)	5240.60 ± 48.05	5244.67 ± 55.73	4.07	0.08	0.6928
D_{min} (cGy)	3965.87 ± 821.89	3944.73 ± 891.90	-21.13	-0.53	0.8865
D_{mean} (cGy)	5084.27 ± 33.79	5073.00 ± 43.17	-11.27	-0.22	0.0645*
D 98 (cGy)	4916.47 ± 144.67	4904.93 ± 148.59	-11.53	-0.23	0.1104
D 95 (cGy)	5022.80 ± 13.79	5018.73 ± 15.50	-4.07	-0.08	0.4783
D 90 (cGy)	5039.93 ± 13.03	5037.07 ± 12.28	-2.87	-0.06	0.4029
D 50 (cGy)	5114.73 ± 47.04	5111.93 ± 56.38	-2.80	-0.05	0.7110
D 5 (cGy)	5207.33 ± 44.05	5207.53 ± 45.49	0.20	0.00	0.8840
D 2 (cGy)	5190.07 ± 43.16	5191.00 ± 44.44	0.93	0.02	0.4456
V 107 (%)	0	0	0	-	-
V 105 (%)	0	0	0	-	-
V 100 (%)	238.74 ± 70.53	239.73 ± 70.44	0.99	0.42	0.3781
V 95 (%)	245.05 ± 76.61	250.18 ± 76.49	5.13	2.09	0.0006****
V 90 (%)	241.36 ± 51.64	242.23 ± 50.74	0.87	0.36	0.1464
HI					
HI 1	0.10 ± 0.14	0.10 ± 0.14	0.00	-0.85	0.1633
HI 2	0.05 ± 0.02	0.05 ± 0.02	0.00	1.63	0.0853
HI 3	0.06 ± 0.02	0.06 ± 0.02	0.00	0.90	0.4368
HI 4	0.04 ± 0.01	0.08 ± 0.11	0.04	122.22	0.0413**
CI					
100%	0.81 ± 0.08	0.78 ± 0.09	-0.03	-3.20	0.0051**
98%	0.84 ± 0.09	0.76 ± 0.10	-0.08	-9.10	0.4650*
95%	0.72 ± 0.03	0.72 ± 0.03	0.00	0.23	0.1189

The statistical significance levels are presented using the following notation, *p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001

and CI95% showed minimal change. These findings suggest that while the absence of contrast media affects some dosimetric parameters, particularly V95, HI4, and CI100%, the overall impact on the treatment plan may be limited but warrants consideration in treatment planning and delivery for rectal cancer patients using HT.

Furthermore, based on the provided data for the Small Intestine and Colon, the dosimetric parameters comparing plans with and without CM in HT planning for rectal cancer show minimal differences (Table 2). For the Small Intestine, most dose parameters (D_{max}, D_{min}, D_{mean}) exhibit slight variations, with the largest absolute difference observed in D_{mean} (-0.35%, p-value= 0.0901), which is not statistically significant. Volume parameters (V52, V50, V45, V40, V35, V30, V15) also show minor variations, with the most notable change in V45 (1.37% increase without CM), yet still not reaching statistical significance. Similarly, for the Colon, dose parameters display minimal differences, with the largest change in D_{max} (9.47 cGy increase without CM), again not statistically significant. Volume parameters for the Colon (V52, V50, V45, V40, V35) exhibit slight decreases without CM, with the largest percentage change in V35 (-0.34%, p-value = 0.0722), but none of these changes are statistically significant. These findings suggest that the presence or absence of contrast media does not significantly impact the dose distribution to these organs at risk in HT planning for rectal cancer, as the observed differences are minimal and lack statistical significance across all evaluated parameters.

The dosimetric analysis comparing plans with and without CM for rectal cancer treatment using HT revealed varying impacts on organs at risk. For the left femoral head, while D_{max} and D_{mean} showed minimal differences, D_{min} significantly decreased without CM (-18.91%, p-value = 0.0001), and volume parameters (V50, V45, V40) showed significant increases, with V50 increasing by 32.46% (p-value = 0.0034). The right femoral head exhibited less pronounced changes, with only V40 showing a significant increase without CM (8.43%, p-value = 0.0001). The bladder demonstrated minimal differences in D_{max} and D_{min}, but D_{mean} increased slightly without CM (0.55%, p-value = 0.0117), while volume parameters remained largely unaffected.

Table 2. Changes in dose delivered to the OARs before and after inserting oral and IV contrast medias. CN: contrast media and Δ: differences between with and without CM

Parameter	With CM	Without CM	Δ	Δ%	P-value
Small Intestine					
D_{max} (cGy)	5119.80 ± 78.16	5117.87 ± 77.96	-1.93	-0.04	0.0561
D_{min} (cGy)	4151.33 ± 901.07	4149.13 ± 901.51	-2.20	-0.05	0.3057
D_{mean} (cGy)	5035.33 ± 107.42	5017.73 ± 102.91	-17.60	-0.35	0.0901
V 52 (%)	248.41 ± 58.58	246.23 ± 58.48	-2.17	-0.88	0.0563
V 50 (%)	275.36 ± 43.20	275.65 ± 48.21	-4.07	-0.08	0.4783
V 45 (%)	303.86 ± 31.16	308.03 ± 40.44	4.17	1.37	0.2671
V 40 (%)	399.97 ± 10.29	399.57 ± 9.82	-0.40	-0.10	0.7925
V 35 (%)	383.52 ± 20.74	382.03 ± 19.30	-1.48	-0.39	0.1665
V 30 (%)	412.95 ± 18.66	410.61 ± 16.81	-2.34	-0.57	0.0645
V 15 (%)	413.17 ± 13.61	412.79 ± 12.38	-0.38	-0.09	0.7115
Colon					
D_{max} (cGy)	4930.80 ± 234.94	4940.27 ± 239.61	9.47	0.19	0.2309
D_{min} (cGy)	1995.33 ± 17.51	1996.53 ± 17.32	1.20	0.06	0.2305
D_{mean} (cGy)	2968.80 ± 63.51	2967.20 ± 63.48	-1.60	-0.05	0.2132
V 52 (%)	348.58 ± 13.81	347.86 ± 13.83	-0.73	-0.21	0.4789
V 50 (%)	464.91 ± 12.62	464.56 ± 12.87	-0.34	-0.07	0.7061
V 45 (%)	491.84 ± 5.55	490.41 ± 5.66	-1.43	-0.29	0.1157
V 40 (%)	573.21 ± 6.13	571.64 ± 6.04	-1.57	-0.27	0.1321
V 35 (%)	589.92 ± 6.33	587.93 ± 6.19	-1.99	-0.34	0.0722
Left femoral head					
D_{max} (cGy)	4693.87 ± 6.03	4693.60 ± 6.71	-0.27	-0.01	0.7513
D_{min} (cGy)	1993.73 ± 170.17	1616.27 ± 161.55	-377.47	-18.93	0.0001****
D_{mean} (cGy)	3002.00 ± 13.54	3003.40 ± 15.58	1.40	0.05	0.1306
V 50 (%)	62.69 ± 27.46	83.03 ± 21.00	20.35	32.46	0.0034**
V 45 (%)	90.51 ± 40.13	98.28 ± 39.75	7.77	8.59	0.0001****
V 40 (%)	96.12 ± 39.29	102.55 ± 38.77	6.44	6.70	0.0001****
Right femoral head					
D_{max} (cGy)	4810.80 ± 48.61	4816.27 ± 49.31	5.47	0.11	0.5164
D_{min} (cGy)	1973.53 ± 53.77	1974.27 ± 56.38	0.73	0.04	0.9239
D_{mean} (cGy)	2973.53 ± 28.83	2963.93 ± 44.95	-9.60	-0.32	0.2663
V 50 (%)	76.81 ± 2.23	78.22 ± 2.71	1.41	1.83	0.0551
V 45 (%)	154.75 ± 220.39	96.54 ± 5.12	-58.20	-37.61	0.2524
V 40 (%)	94.94 ± 38.99	102.94 ± 38.16	8.00	8.43	0.0001****
Bladder					
D_{max} (cGy)	4989.13 ± 78.43	4989.60 ± 73.77	0.47	0.01	0.0648
D_{min} (cGy)	1994.80 ± 2.34	1995.67 ± 1.96	0.87	0.04	0.0966
D_{mean} (cGy)	3107.60 ± 295.20	3124.80 ± 299.22	17.20	0.55	0.0117*
V 50 (%)	74.72 ± 2.88	75.16 ± 2.91	0.44	0.59	0.0668
V 45 (%)	55.17 ± 2.50	55.50 ± 2.33	0.32	0.58	0.1213
V 40 (%)	71.73 ± 13.21	71.45 ± 11.90	-0.29	-0.40	0.6788

The statistical significance levels are presented using the following notation, *p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001

These findings suggest that the absence of CM primarily affects the left femoral head's dosimetric parameters, with less impact on the right femoral head and bladder. Although some differences are statistically significant, their magnitude is generally small, indicating that contrast media use may have a minor influence on dose distribution to these OARs in HT planning for rectal cancer. However, the clinical relevance of these differences should be evaluated within the context of overall treatment objectives and potential toxicity risks, considering the specific dose constraints and treatment goals outlined in the study methodology. Shimizu RT *et al.* (2023) investigated the impact of contrast enhancement on CT imaging of the spinal cord and target volume in spine SBRT planning. They found that replacing the contrast-enhanced region with water-mass density in CT myelography images resulted in minimal changes to

the mean D0.035cc of the spinal cord. The study also showed that replacing the contrast-enhanced region with water-mass density had a minimal effect on the D98% for the planning target volume (p-value < 0.01). They concluded that using CT myelography images with the contrast-enhanced region replaced by water-mass density could provide more accurate dose calculations for the target volume of the spinal cord reducing uncertainty in treatment planning [27].

The analysis of HU differences between CECT and non-CECT images for various structures in rectal cancer radiotherapy planning reveals significant variations (Table 3). For the CTV, the maximum HU was higher with CM at 287.79 ± 45.40 compared to 189.00 ± 20.97 without CM, while the minimum HU also increased with CM, showing values of 9.64 ± 54.81 versus -84.79 ± 39.95, respectively. CM significantly enhances HU measurements, with remarkable percentage increases observed across CTV, planning target volume PTV, colon, and small intestine. The most dramatic transformations are evident in the colon, where maximum HU values surge by 348.9%, accompanied by a staggering 826.8% increase in mean HU. Similarly, the small intestine exhibits substantial HU modifications, with maximum HU escalating by 353.0% and mean HU rising by 432.3%. The CTV and PTV also display considerable HU alterations, with the PTV showing an extraordinary 791.6% increase in minimum HU and a 310.7% elevation in mean HU. These substantial percentage differences underscore the critical importance of contrast media in enhancing image contrast, tissue differentiation, and potentially improving target delineation accuracy during radiotherapy planning for rectal cancer patients. These results indicate that the use of contrast media consistently enhances HU values across all evaluated structures, particularly in the colon and small intestine, thereby improving visibility and delineation of critical structures essential for accurate target volume definition and OAR contouring in radiotherapy planning for rectal cancer. However, these differences in HU values between CECT and non-CECT images may influence dose calculations in TPS, highlighting the importance of considering these variations during the planning process as outlined in the study's methodology.

Choi *et al.* evaluated the impact of intravenous CA on dose calculations in IMRT for head and neck cancer. In their study involving 15 patients, they performed CT scans both with and without contrast enhancement. The results showed that doses calculated for planning target volumes (PTV70 and PTV59.4) from enhanced CTs were slightly lower than those from non-enhanced CTs, with differences less than 1% (p-value < 0.05). However, no significant differences were observed for PTV50, parotid glands, or spinal cord doses. The authors concluded that the minimal impact of CA on dose calculations supports its use in planning CT for head and neck IMRT, enhancing visualization without compromising dose accuracy [28]. Similarly, Li *et al.* investigated the impact of intravenous contrast on dose calculations in oesophageal cancer radiation treatment planning. Their study of 22 patients revealed that dose variations for PTV were less than 1.0%, with total lung and spinal cord variations under 0.5%. When blood stream HU values exceeded 245, heart V40 showed average variations exceeding 1.0%. In non-physiologic scenarios, PTV dose variations remained less than 1.0%, while organs at risk demonstrated dose variations greater than 2.0%. The researchers concluded that contrast agents minimally influence dose calculations for most structures, with potential

Table 3. Changes in amounts of HU in the PTV and OARs before and after inserting oral and IV contrast medias. CN: contrast media and Δ: differences between with and without CM

Parameter	HU_{max}		Δ% (P-value)	HU_{min}		Δ% (P-value)	HU_{mean}		Δ% (P-value)
	with CM	without CM		with CM	without CM		with CM	without CM	
CTV	287.79 ± 45.40	189.00 ± 20.97	<0.0001	9.64 ± 54.81	-84.79 ± 39.95	0/0009	213.92 ± 38.90	74.24 ± 18.22	<0.0001
PTV	393.36 ± 68.23	141.93 ± 31.47	<0.0001	63.21 ± 18.36	-9.14 ± 29.75	<0.0001	226.54 ± 64.90	55.16 ± 12.60	<0.0001
Colon	637.29 ± 71.82	141.93 ± 28.26	<0.0001	0.79 ± 16.17	-70.07 ± 25.35	<0.0001	426.68 ± 86.46	46.04 ± 16.04	<0.0001
Small intestine	649.29 ± 112.45	143.36 ± 41.36	<0.0001	96.71 ± 42.69	-74.14 ± 27.80	<0.0001	349.01 ± 116.52	65.56 ± 14.36	<0.0001

variations observed in specific organs like the heart [29]. The impact of oral and intravenous CA on dose calculations in radiotherapy planning for rectal cancer has been extensively studied. Oral CA (OCA) are commonly utilized in imaging protocols to improve the delineation of gastrointestinal structures, but their presence can significantly alter dosimetric outcomes [30]. A pivotal study examined the effects of OCA on dose calculations for rectal cancer patients. The findings indicated that including OCA in CT scan treatment planning resulted in an estimated reduction of approximately 5% in the delivered dose to the PTV compared to plans without OCA. This underestimation is primarily due to the increased electron density introduced by the contrast agent, which modifies the attenuation coefficients used in dose calculations. Consequently, this discrepancy may lead to insufficient radiation delivery to the tumor, potentially jeopardizing treatment outcomes. Additionally, the study highlighted an increase in the volume of adjacent OARs receiving high doses when using OCA, raising concerns about potential toxicity and side effects [31]. Elawadi *et al.* evaluated the impact of CA on dose calculations in Volumetric Modulated Arc Therapy (VMAT) for various cancer sites. Their study of 226 patients with both CECT and non-CECT scans revealed statistically significant HU variations for most structures, but these were not clinically significant. Dose distribution analysis showed that variations in target volumes' D2% and D98% were insignificant for most sites, except the brain and nasopharynx. Maximum dose differences were within 2% for the majority of critical structures and target volumes. 3D gamma analysis confirmed that most plans met the 2% and 2 mm criteria. These findings support the use of contrast-enhanced CT for treatment planning, as the differences in dose calculations are generally small and clinically acceptable [32]. In a related investigation, it was reported that treatment plans based on CT images with OCA resulted in lower radiation doses not only to target volumes but also to critical OARs such as the bladder and small intestine. Although these differences were statistically insignificant, they suggested a trend where OCA could subtly yet meaningfully influence dosimetric outcomes. The authors concluded that while OCAs enhance imaging quality, their impact on dose calculations necessitates careful scrutiny during treatment planning [33]. Conversely, studies focusing on Intravenous Contrast Agents (ICA) have shown that their influence on dosimetry is generally minor and manageable. For instance, a study comparing treatment plans generated with and without ICAs for head and neck cancers found minimal differences in dose distribution for critical structures like the spinal cord and parotid glands, with maximum dose differences typically around 0.5% [34]. The impact of ICA on dosimetry appears context-dependent. In scenarios involving large blood vessels or concentrated areas of contrast, more pronounced effects on dose calculations may occur. A Monte Carlo simulation indicated that while flat photon beams exhibited minimal dose increases due to contrast (less than 5%), unfiltered flat beams could experience increases up to 23% [35]. Jabbari *et al.* assessed the effect of intravenous CM on dose calculations in 3DCRT for lower esophageal and rectal cancers. The study involved 29 patients, with treatment plans based on CT scans both with and without IV contrast. They found that the use of contrast resulted in an average increase in MUs of 1.28% for 6 MV photon beams and 0.75% for 15 MV beams in the lower esophageal region, with these differences being statistically significant. In contrast, no significant differences were observed in the rectal region between the two sets of scans. They concluded that while the dose differences were small and clinically tolerable overall, the significant changes in the lower esophageal region should be considered in treatment planning [36]. In treatment planning systems that utilize CT scans, dose calculations are based on converting HUs into electron density. The use of CM during these scans can significantly influence the HUs of tissues, potentially leading to discrepancies in dose calculations. This effect may be more pronounced when the total dosage of CM is higher, as observed in some studies. For instance, while previous research on lung scans indicated that CM could alter CT numbers of vessels, it had minimal impact on overall radiation dose calculations. Consequently, although the differences in calculated doses may be small and clinically tolerable, careful consideration of CM concentration and its effects on HUs is essential for accurate treatment planning [37]. These findings are consistent with a recent prospective study indicating that contrast agents significantly influence radiation dose calculations in upper-abdominal radiation planning [38]. Additionally,

research by Burridge *et al.* demonstrated an average increase of 1.0% ± 0.8% in overall MUs when contrast media were used during dose computations in lung scans, with a maximum increase of 3.3%. These results highlight the importance of considering the effects of contrast media on dose calculations, as even small variations can have clinical significance, particularly in regions with high contrast uptake [39]. The implications of these findings for clinical practice are significant. Radiation oncologists must understand how both types of contrast agents can influence dosimetric calculations during treatment planning. Underestimating the relevance of OCA can lead to insufficient dosing if not properly accounted for in treatment plans. Conversely, while ICA may introduce variability in dosimetry, their effects are generally minor and manageable. Future research should focus on developing standardized protocols for integrating contrast materials into radiation therapy planning while quantifying the long-term effects of these discrepancies on treatment outcomes, including local control rates and toxicity profiles. By establishing a clearer connection between dosimetric accuracy influenced by contrast factors and clinical outcomes, physicians can better tailor treatment plans to meet patient needs. One key limitation of our study is the potential for selection bias due to the strict inclusion criteria, which may affect the generalizability of our findings. Additionally, variances in anatomy and response to treatment among patients could introduce confounding factors that we aimed to control through careful patient selection and imaging protocols. Future studies would benefit from larger, multi-institutional cohorts to better reflect broader patient demographics and treatment scenarios.

4. Conclusion

Contrast agents are crucial for enhancing image quality during radiation therapy planning and their influence on dose calculations must be carefully considered. This study demonstrates that the incorporation of CECT significantly improves the accuracy of treatment planning for rectal cancer using HT. The enhanced visibility of anatomical structures provided by CECT allows for more precise delineation of target volumes and better sparing of OAR, ultimately contributing to improved treatment outcomes. While the dosimetric parameters showed minimal differences in some cases, the overall enhancement in imaging quality underscores the importance of using contrast media in radiation therapy planning. Future research should continue to explore the clinical implications of these findings, particularly regarding patient outcomes and quality of life post-treatment. By adhering to meticulous planning protocols and utilizing advanced imaging techniques, healthcare professionals can optimize radiation therapy delivery while effectively managing potential side effects associated with treatment.

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