Evaluating the Effect of Co-Registered Diagnostic MR Images Based CT Simulation on Target Volume Delineation and Dose Distribution for Tomotherapy of Rectal Cancer

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ABSTRACT

Background: Magnetic Resonance Imaging (MRI) has become a complementary imaging method for the treatment planning process due to the limitations of Computed Tomography (CT) imaging.

Objective: This study aimed to assess the effect of co-registered MRI and CT (MRI/CT)-based target delineation on the dose to the target, small bowel, bladder, and femoral heads during Helical Tomotherapy (HT).

Material and Methods: In this cross-sectional prospective study, MRI in a prone position were obtained for 12 patients with rectal cancer at one-day intervals with simulation CT. Following the co-registration process with the deformable algorithm, target volumes are defined. Gross Tumor Volume (GTV), Clinical Target Volume (CTV), and Planning Target Volume (PTV) were delineated for each CT and MRI/CT.

Results: GTV, CTV, and PTV mean values were significantly higher in the CT-based target delineation method than those in the MRI/CT-based method. In MRI/CT-based plans, the mean HI value was significantly lower, and the mean Conformity Index (CI) value was significantly higher than that in CT-based plans. In a small bowl, the most of dosimetric parameters (D_{max}, D_{mean}, $D_{50\%}$, $D_{50\%}$, $V_{40\%}$, and $V_{45\%}$) were significantly higher for the CT-based plans. In the bladder, all dosimetric parameters, except $V_{30\%}$, were statistically higher in CT-based plans.

Conclusion: Co-registered MRI/CT-based treatment planning can produce better dose coverage for the target and reduce the delivered dose to the Organs at Risk (OARs) when compared to CT-based planning.

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Keyword

Magnetic Resonance Imaging; Computed Tomography; Rectal Neoplasms; Radiotherapy; Helical Tomotherapy

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Introduction

The rate of Rectal Cancer (RC), the tenth most lethal cancer, has dramatically increased worldwide. The number of new rectal cancer cases was estimated at 732,210 in 2020 [1]. In recent

years, the use of preoperative chemoradiotherapy for localized rectal cancer has widely become accepted due to some advantages, such as tumor down-staging, reduction of local recurrence risk, and improved overall survival [2]. However, radiotherapy as a therapeutic option has significant clinical benefits, and some significant risks are associated with treatment-related adverse events [3].

Modern Radiotherapy (RT) techniques can help to reduce the side effects of radiation, such as modern radiotherapy technique (Helical Tomotherapy (HT)), yielding highly conformal distributions of radiation dose to the target and minimizing the level of radiation exposure to the Organs at Risk (OARs) [4]. The treatment of rectal tumors primarily aimed to achieve adequate radiation dose to the rectum and sparing of OARs, such as bladder, small bowel, and femoral heads, and accurate delineation of Gross Tumor Volume (GTV), and Clinical Target Volume (CTV) [5].

Tumor delineation and treatment planning in rectal tumors are based on Computed Tomography (CT) images. However, there are some limitations of CT images in the delineation of treatment volumes in pelvic structures, including poor contrast between soft tissues, artifacts from large bony structures or metal prostheses, and partial volume effects [6]. Recently, Magnetic Resonance Imaging (MRI) can complement CT imaging by improving soft tissue contrast, reducing large bony structure artifacts, and enhancing better contrast resolution [7,8].

Moreover, MR images provide better visualization of tumor extent and nodal involvement in some sites. For these reasons, co-registered MRI and CT images (MRI/CT) can be used for a better definition of treatment goals. The effect of co-registered MRI/CT images is investigated on tumor volume delineation [9,10], showing that delineated volumes based on CT images were not always the same as delineated volumes based on MRI/CT images. Some studies have reported that smaller GTV and CTV based on MRI/CT images and differences between treatment volumes can impress delivered radiation dose to the OARs [11,12]. Bird et al. [11] demonstrated that smaller delineated GTV-based MRI/CT images in anorectal tumors cause a reduction of delivered doses to the OARs, such as the bladder and small bowel.

Using MR images based on CT simulation instead of CT images alone is challenging in radiation therapy departments. Therefore, assessment of the role of co-registered MRI/CT images in HT treatment planning for rectal cancer is important for dose delivery of the target and reduction dose of OARs.

To the best of our knowledge, there is no published work on the evaluation of MRI/CT images in rectal cancer patients for HT treatment planning. For this reason, HT treatment plans were analyzed for comparison of both planning methods in the present study. This study aimed to compare volumetric and dosimetric parameters between MRI/CT and CT images alone for treatment planning of rectal cancer tomotherapy, and also to assess the influence of co-registered MRI/CT-based target delineation on the dose to the target and OARs, such as small bowel, bladder, and femoral heads during tomotherapy.

Material and Methods

Patients

In this cross-sectional prospective study, 12 patients with rectal cancer including 7 males and 5 females with a mean age of 60 years (range of 30-81 years) were selected after approval by the Isfahan University of Medical Sciences ethics committee. All patients were referred to the Department of Radiation Oncology, Seyed Al-Shohada Hospital, Isfahan for pre-operative chemo-radiation therapy between February 2022 and December 2022. All tumors were staged by echo endoscopy, diagnostic MRI, and CT.

Scanning methods

All patients underwent simulation CT and diagnostic MR images. Simulation CT scans were obtained using Siemens SOMATOM (Confidence® RT, Pro) with and without contrast enhancement. Patients were scanned with bladder filling protocol in the prone position, and all scans were obtained at 3 mm slice thickness. The MR images were obtained on a 1.5 T (Siemens MAGNETOM, Symphony) scanner with T_2W 2D turbo spin echo and T_1W 2D turbo spin echo sequences.

Image Fusion and Contouring

All images were imported into Radixact-X9® tomotherapy machine TPS (accuracy precision treatment planning system V2.0.1.1) for image fusion, contouring, and treatment planning. Both imaging methods were matched using a deformable fusion algorithm [13]. Then, all fused images were visually reviewed by a Radiation Oncologist and a Medical Physicist. An expert radiation oncologist delineated GTV, CTV, and OARs according to the Radiation Therapy Oncology Group (RTOG) protocols [14]. Based on the CT and MRI/CT images, two different GTVs were delineated for each patient: GTV_{CT} and $GTV_{MRI/CT}$, respectively. At first, GTV_{CT} was manually delineated in all slices, in which the tumor was visible, and $GTV_{MRI/CT}$ was then delineated at a week interval by the same radiation oncologist. In the same way, CTV_{CT} and $CTV_{MRI/CT}$ were defined. Clinical target volume included the GTV mesorectal, presacral, common, and internal iliac lymph nodes [14]. In addition, some OARs were contoured, including the bladder, small bowel, and femoral heads. In the end, the PTV was generated with a 3-mm margin around the CTV.

Treatment planning

Following the contouring process, tomotherapy plans were performed for all cases. The prescription dose for PTV was 45 Gy in 25 fractions of 1.8 Gy. Also, dose constraints are defined as covering ≥98% of the PTV with ≥93% of the prescribed dose, V35<180 cc for small bowel, V40<40% for femoral heads, and V40<40% for bladder. All plans were generated using a 5-cm field width, a pitch ranging from 0.28 to 0.43, and a modulation factor of 2 to 3. For each patient, planning was defined for two PTVs (CT and MRI/CT) under the same condition. All plans were reviewed by the Physicist and Oncologist. Treatment plans were compared after analyzing the Dose Volume Histogram (DVH) and target volumes.

Plan evaluation

For volumetric comparison, GTV_{CT} and $GTV_{MRI/CT}$ were calculated by the treatment planning software, and CTV and PTV volumes were compared. To evaluate the plans, dosimetric parameters were calculated using DVH data. For PTV, the Conformity Index (CI) and Homogeneity Index (HI) were calculated according to the following equations [15,16]:

$$CI = \frac{V_{45}Gy}{V_{PTV}} \qquad (1)$$

$$HI = \frac{I_{max}}{RI} \qquad (2)$$

where V_{45} Gy is the volume of PTV that receives 45 Gy radiation dose, V_{PTV} is the volume of PTV, I_{max} is the maximum isodose in the target, and RI is the reference isodose. For OARs, such as bladder, both femoral heads and small bowel, D_{mean} (mean dose) and D_{max} (maximum dose) were analyzed; Also, $V_{n\%}$ (percent volume of the organ that receives at least dose of n Gy) and $D_{n\%}$ (a dose received by n% of the volume of organ) were reported in various levels.

Statistical analysis

For all volumetric and dosimetric parameters of MRI/CT and CT-based plans, normality tests were performed. Paired Wilcoxon tests were used to compare the

variables since none of the parameters showed normal distribution. The data analysis was carried out using SPSS version 22.0 statistical software and a *P*-value<0.05 was considered statistically significant.

Results

As stated in methods section, the tumors were staged and their outputs are shown in Table 1.

Volume comparisons

The results of the volumetric analysis are shown in Figure 1. According to both volume delineation methods, Table 2 presents GTV, CTV, and PTV mean volumes. In GTV_{CT}, the mean value was significantly higher than in $GTV_{MRI/CT}$ (243.00±145.00 vs. 219.02±131.00, P<0.001). CTV_{CT} showed a significantly higher mean value than $CTV_{MRI/CT}$ (504.00±241.00 vs. 461.00±249.00, P<0.001). In addition, the mean value of the PTV_{CT} was significantly higher in the CT-based planning method compared to MRI/CT-based planning method (675.00±263.00 vs. 602.00±266.03, P=0.019). The PTV_{CT} was larger than the $PTV_{MRI/CT}$ in 9 cases (75%) and smaller in only 3 cases (25%).

Table 1: Tumor node metastasis or staging system in rectal cancer.

Patient	1	2	3	4	5	6	7	8	9	10	11	12
Stage	$T_3N_2M_0$	$T_3N_1M_0$	$T_3N_2M_0$	$T_2N_1M_0$	$T_3N_2M_1$	$T_3N_2M_0$	$T_3N_0M_0$	$T_4N_2M_0$	$T_4N_1M_0$	$T_2N_2M_1$	$T_3N_1M_0$	$T_4N_1M_0$

T: Shows the size of the tumor and any spread of cancer into nearby tissue, N: Shows the spread of cancer to nearby lymph nodes, M: Shows metastasis

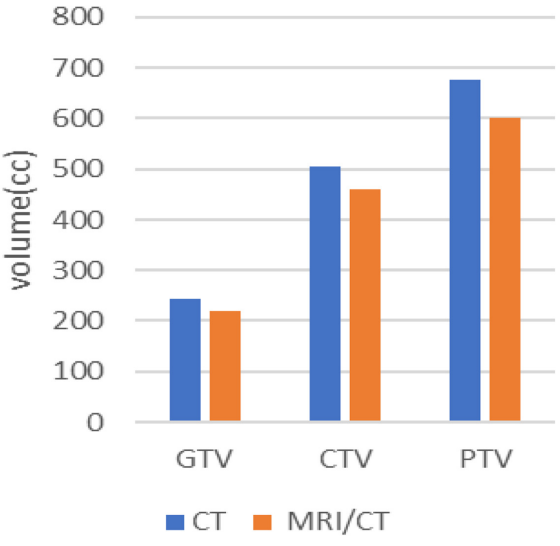

Figure 1: Volumetric comparison between CT-based and MRI/CT-based treatment volume delineation. (CT: Computed Tomography, MRI: Magnetic Resonance Imaging, GTV: Gross Tumor Volume, CTV: Clinical Target Volume, PTV: Planning Target Volume)

Table 2: Mean gross tumor volume, clinical target volume, and planning target volumes

Structure	CT		MRI/CT		*P*-value
	Mean (cc)	SD	Mean (cc)	SD	
GTV	243.00	145.00	219.02	131.00	<0.001
CTV	504.00	241.00	461.00	249.00	<0.001
PTV	675.00	263.00	602.00	266.03	0.019

CT: Computed Tomography, MRI: Magnetic Resonance Imaging, GTV: Gross Tumor Volume, CTV: Clinical Target Volume, PTV: Planning Target Volume, SD: Standard Deviation

Dosimetric comparisons

1. Planning target volume (PTV)

Table 3 shows the results of D_{mean}, CI, and HI parameters for CT- and MRI/CT-based plans. The mean HI value in CT-based plans was significantly higher than that in MRI/CT-based plans (1.08±0.03 vs. 1.06±0.02,

Table 3: Comparison of dosimetric parameters for organs at risk and planning target volume.

Structure	Parameters	CT		MRI/CT		*P*-value
		Mean	SD	Mean	SD	
PTV	D_{mean} (cGy)	4613.00	79.00	4620.00	99.00	<0.001
	HI	1.08	0.03	1.06	0.02	0.005
	CI (%)	90.00	11.00	92.00	8.00	0.042
Bladder	D_{max} (cGy)	4545.00	655.00	4401.00	639.00	0.004
	D_{mean} (cGy)	3360.00	610.03	3198.00	593.00	0.005
	$D_{50\%}$	75.00	21.00	71.00	22.00	0.015
	$D_{98\%}$	41.09	18.00	36.00	18.00	0.019
	$V_{30\%}$	57.00	29.00	53.00	24.00	0.099
	$V_{40\%}$	47.00	21.00	41.00	18.00	0.010
	$V_{45\%}$	29.00	20.00	24.00	18.00	0.026
Small bowel	D_{max} (cGy)	4553.00	957.00	4409.00	996.00	0.028
	D_{mean} (cGy)	2105.00	850.00	2080.00	867.00	<0.001
	$D_{50\%}$	39.00	24.00	39.00	25.00	<0.001
	$V_{20\%}$	45.00	24.00	46.00	24.00	<0.001
	$V_{30\%}$	31.00	18.00	31.04	15.00	<0.001
	$V_{40\%}$	22.00	14.00	21.00	12.00	<0.001
	$V_{45\%}$	15.00	12.00	13.00	10.00	<0.001
Left femoral head	D_{max} (cGy)	3817.00	770.00	3541.00	812.00	0.034
	D_{mean} (cGy)	2322.00	623.00	2197.00	695.00	0.084
	$D_{50\%}$	55.00	18.00	49.00	23.00	<0.001
	$V_{20\%}$	71.00	20.07	65.00	22.00	0.004
	$V_{30\%}$	29.00	28.00	30.01	28.00	0.99
Right femoral head	D_{max} (cGy)	3991.00	650.00	3755.00	791.00	0.034
	D_{mean} (cGy)	2361.00	623.00	2240.00	753.00	0.099
	$D_{50\%}$	55.00	15.00	49.00	20.00	0.055
	$V_{20\%}$	73.00	20.00	69.00	21.00	0.093
	$V_{30\%}$	29.00	27.00	27.00	25.08	<0.001

CT: Computed Tomography, MRI: Magnetic Resonance Imaging, PTV: Planning Target Volume, HI: Homogeneity Index, CI: Conformity Index, D_{max}: Maximum Dose, D_{mean}: Mean Dose, $V_{n\%}$: Percent Volume of the Organ That Receiving At Least Dose of N Gy, $D_{n\%}$: A Dose Received by N% of the Volume of the Organ, SD: Standard Deviation

P=0.005). Additionally, the mean value for the D_{mean} parameter was significantly lower in PTV_{CT} than in $PTV_{MRI/CT}$ (4613.00±79.00 vs. 4620.00±99.00). Also, Figure 2 shows the radiation dose distribution in PTV_{CT} and $PTV_{MRI/CT}$.

2. Bladder

D_{max}, D_{mean}, $D_{50\%}$, and $D_{98\%}$ for bladders in CT-based plans were significantly higher than in MRI/CT-based plans (*P*-value =0.004, *P*-value=0.005, *P*-value=0.015, and *P*-value=0.019, respectively) (Table 3). For both $V_{40\%}$ and $V_{45\%}$ parameters, CT-based plans had significantly higher mean values than those of MRI/CT-based plans (*P*-value=0.010 and *P*-value=0.026, respectively). However, no significant difference was found between the two planning methods in $V_{30\%}$ (*P*-value =0.099).

3. Small bowel

D_{max}, D_{mean}, $D_{50\%}$, $V_{40\%}$, and $V_{45\%}$ mean values for both planning methods are mentioned in Table 3. All mean values were significantly higher in CT-based plans (*P*-value=0.028, *P*-value<0.001, *P*-value<0.001, *P*-value<0.001, *P*-value<0.001, respectively).

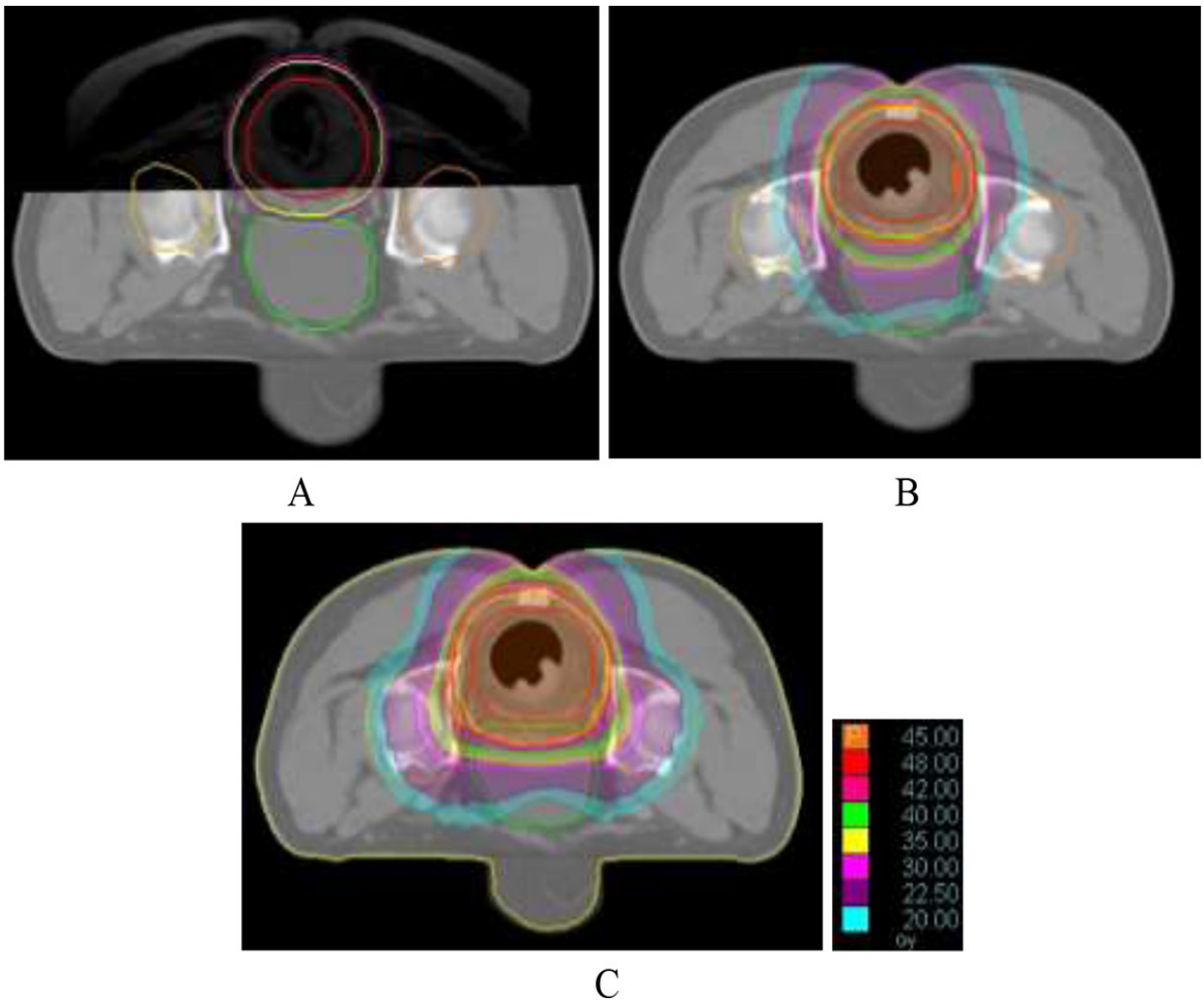

Figure 2: (**A**) Image fusion with deformable registration algorithm. (**B** and **C**) Dose distribution comparison between MRI/CT-based contour (**B**) and CT-based contour (**C**) in the same patient and same slice. (CT: Computed Tomography, MRI: Magnetic Resonance Imaging)

However, the opposite results were obtained for the $V_{20\%}$ and $V_{30\%}$ parameters.

4. Femoral heads

In Table 3, the mean values of D_{max}, D_{mean}, $D_{50\%}$, $V_{20\%}$, and $V_{30\%}$ were presented for femoral heads. For the left femoral head, the mean values of D_{max}, $D_{50\%}$, and $V_{20\%}$ parameters were significantly higher in the CT-based planning method compared to MRI/CT-based planning method (*P*-value=0.034, *P*-value<0.001, *P*-value=0.004, respectively). On the other hand, there was no significant difference in D_{mean} and $V_{30\%}$.

In the right femoral head, the mean value of D_{max} and $V_{30\%}$ was significantly lower in the MRI/CT-based planning method than in the CT-based planning method (*P*-value=0.034 and *P*-value<0.001, respectively). In addition, no significant difference was observed in other parameters.

Discussion

Accurate target volume delineation is a critical issue in rectal radiotherapy, with the use of the HT technique. This study aimed to compare volumetric and dosimetric parameters between MRI/CT- and CT-based treatment plans for rectal cancer tomotherapy.

Due to CT limitations, it has recently become more common to use MR imaging for treatment planning. Better soft tissue contrast, lower large bony structure artifacts, and better contrast resolution are some of the advantages of MRI over CT [17]. The MRI scan can be acquired in the treatment position or the diagnostic position. For using MRI/CT for treatment planning, it is recommended that the MRI scan be acquired in the treatment position. However, some clinical centers do not have access to MRI scanners that can scan the patient in the treatment position [18].

In this study, a deformable image registration algorithm was used to register diagnostic MRI images with CT simulation images (Figure 2A). The target volumes derived from MRI/CT and CT images were compared and their delivered dose of target and OARs in both planning methods were analyzed.

B. O'Neill et al. [19] showed tumor volumes on MRI were smaller, shorter, and more distal from the anal sphincter than those defined on CT. Tan et al. [10] showed that rectal treatment volumes are lower in co-registered MRI and CT images than only CT images. In addition, Bird et al. [11] released that MRI data in rectal radiotherapy, either in MRI-only planning or MRI/CT planning can lead to a decrease in target volume and delivered doses to OARs. However, research results may be affected by new radiotherapy techniques. According to the results, the GTVs, CTVs, and PTVs delineated with simulation CT were significantly larger than those delineated with MRI/CT. In the present study, CT significantly overestimates target volumes in rectal cancer (Table 2), due to poor soft tissue contrast in CT, leading to defining larger volumes in an attempt to minimize regional misses [10,11].

The correct target volumes delineating is essential for achieving a better target volume dose distribution and reducing doses to the OARs. Consequently, it is expected that the dose delivered to the OARs decreases due to the smaller PTV in MRI/CT-based planning. The present study also compared CT- and MRI/CT-based planning methods based on dosimetric parameters. The findings of the present work showed that HI and CI parameters were significantly improved in $PTV_{MRI/CT}$ compared to PTV_{CT}. Additionally, D_{mean} was significantly higher in $PTV_{MRI/CT}$ than in PTV_{CT}.

Results of this study showed the MRI/CT-based planning method achieves better results than CT-based planning in terms of dose conformity and dose homogeneity in the PTV. In rectal cancer radiotherapy, the small bowel is the most important organ, which is dose-limited and causes toxicity in patients [20].

This study also showed most of the dosimetric parameters (D_{max}, D_{mean}, $D_{50\%}$, $D_{50\%}$, $V_{40\%}$, and $V_{45\%}$) were significantly higher in the CT-based plans than in the MRI/CT-based plans in the small bowel. Also, in the bladder, all dosimetric parameters except $V_{30\%}$ (*P*-value=0.099) were statistically higher in CT-based plans than in MRI/CT-based plans. In femoral heads, several of the dosimetric parameters showed higher mean values in CT-based plans compared to MRI/CT-based plans, reducing the probability of avascular necrosis occurring [21]. However, the difference between the two methods was not as great as in other organs at risk. In the present study, the smaller MRI/CT-based target volumes delivered less dose to the OARs, especially the small bowel. The MRI/CT-based planning method also improved dose distribution in the PTV, which confirms the results of previously studies [10,11]. Findings of this work showed it is possible to define safer treatment planning by using deformable registration of MRI/CT-based plans than only CT-based plans.

The present study has some limitations as follows: 1) the small number of patients, 2) a change in tumor volume due to the one-day interval between the CT and MRI scans, and 3) contouring by two or more radiation Oncologists, separately, instead of one radiation Oncologist.

Conclusion

In this work, mean values of GTV, CTV, and PTV are lower in CT-based plans in comparison with MRI/CT-based plans. In addition, MRI/CT-based plans may lead to better dose coverage and dose homogeneity for the target and also reduce the delivered dose to the bladder, small bowel, and femoral heads in comparison with CT-based plans. Accordingly, co-registration of diagnostic MRI images with CT simulation images can improve the efficiency of tomotherapy treatment plans for rectal cancer patients.

Authors' Contribution

B. Rahmani contributed to idea formation, proposal writing, data collection, and drafting of the manuscript. D. Shahbazi-Gahrouei contributed to idea formation and development, data interpretation and analysis, editing of the manuscript, and supervised the research project as the principal person. M. Roayaei contributed to idea development and data collection. All the authors read, modified, and approved the final version of the manuscript.

Ethical Approval

This work was approved by the Isfahan University of Medical Sciences Ethics Committee (IR.MUI.MED.REC.1401.052).

Informed Consent

Before entering the study, each participant signed a consent form.

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Conflict of Interest

None

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