Factors Affecting Isocenter Displacement and Planning Target Volume Margin in Rectal Cancer Patients Receiving Radiotherapy

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Title Page

1. Article Title:

Factors Affecting Isocenter Displacement and Planning Target Volume Margin for Rectal cancer Patients Receiving Radiotherapy

2. Short Running Title:

PTV margin for rectal cancer RT

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RM designed the study, reviewed the data, reviewed statistics, evaluated the results, edited the manuscript, and prepared the manuscript for publishing. **AAE** reviewed data collection and statistical analysis. Performed the computation of the margins and contributed to the drafting of the final manuscript. **NAl, MAl** performed the data collection. **MA** reviewed the results and final manuscript.

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Factors Affecting Isocenter Displacement and Planning Target Volume Margin in Rectal Cancer Patients Receiving Radiotherapy

Short running title:

PTV margin for rectal cancer RT

Type of the study

Retrospective study

Keywords:

Cancer- Rectum- Supine- Prone -Belly board

Abstract

Background: Setup errors are inherent in the process of daily radiation therapy (RT) delivery. Pelvic RT for rectal cancer is one of the body sites associated with the largest shift among other body sites. This study aimed to evaluate inter-fraction random and systematic errors and hence propose the optimum planning target volume (PTV) in rectal cancer patients.

Patients and methods: Translational and angular isocenter displacements were retrospectively collected for 189 patients. Random and systematic errors were determined, then the PTV margin was computed. Effect of

positioning, body mass index (BMI), and type of immobilization were studied. Portal images before and after online correction were used to define PTV for daily image-guided radiotherapy (IGRT) and no-daily IGRT respectively.

Results: Before the online correction, the systematic errors were 2.5 mm, 2.8 mm, and 3.0 mm for superior-inferior (SI), right-left (RL), and anterior-posterior (AP) directions respectively, compared to 2.1 mm, 1.7 mm, and 1.8 mm after online correction. The random errors were 6.2 mm, 7.4 mm, and 8.2 mm in SI, RL, and AP respectively before online correction, compared to 4 mm, 4.2 mm, and 4.5 mm after online correction. The recommended PTV margin was 0.7 cm and 1.0 cm for daily IGRT and no-daily IGRT respectively. The prone position and BMI > 30 kg/m^2 warrant higher margins in no-daily IGRT cases; 1.2 cm and 1.4 cm respectively.

Conclusion:

The prone position, BMI > 30 kg/m^2, and belly board device are associated with larger daily setup errors warranting higher PTV margins for no-daily IGRT; however, that can be avoided by using daily IGRT.

Background:

Precise and reproducible daily placement of treatment isocenter has been the main target for radiotherapy (RT) since its announcement as a medical discipline by Henry Coutard during the International Congress of Oncology in Paris in 1922 (1-2). Fixation aids, planning target volume (PTV), and electronic portal imaging devices (EPIDs) are the commonly used strategies to deal with the uncertainty of daily setup.

The overall lifetime risk of developing colorectal cancer is 4%, and it is considered the third most diagnosed cancer worldwide (3). Radiotherapy is recommended for stage II-III rectal cancer patients as a neoadjuvant concurrent with chemotherapy. The treatment is delivered either as a short course with a dose of 25Gy/5fx/1w (4-5), or a long course with a dose of 50-50.4 Gy/25-28fx/5-5.5w (6-10). Pelvic irradiation for rectal cancer is associated with large setup errors that are highly affected by body mass index (BMI) and treatment position.

Prone and supine positions are commonly practiced for rectal cancer RT, with no final agreement on the superiority of one over another (11-15). As the rectum is a posterior pelvic structure, the prone position is preferred by many centers to decrease bowel volume inside the RT field. On the other hand, others believe in the φ more comfortable φ supine position, especially with the use of advanced RT techniques that allow sparing of the small bowel. Intensity-modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) can achieve the constraint of small bowel volume receiving 45Gy to be less than 195 cm^3 (V_{45} ЖЧ мфр ŏY^3).

The belly board and Vac-Lok are commonly used with the prone position. The idea of using a belly board is to allow placement of the small bowel away from target volume and radiation beams in addition to providing a more comfortable positioning for obese patients.

Patients with high BMI are difficult candidates for accurate daily positioning, as skin tattoos are mobile and the weekly EPIDs are not enough to correct positioning errors (16).

The American Society of Radiation Oncology (ASTRO) recommends prone positioning with a belly board device for pelvic RT and expects emerging evidence shortly (17). Also, 90% of the panel φ with a lack of clear literature evidence φ recommends daily image-guided radiotherapy (IGRT) in addition to IMRT/VMAT technique.

The frequency of treatment verification using EPID differs from department to department based on the workload and even from time to time in the same department. The logical assumption of having a different PTV margin for daily IGRT compared to no-daily IGRT is valid for our targeted cohort of patients. The studies that have investigated this issue are still not enough to standardize the practice. Accordingly, analysis of setup errors during RT for rectal cancer patients is of major concern

Aim of the study

This study evaluated translational and rotational displacements before and after online correction for cancer rectum patients receiving RT. Different factors like treatment position, body mass index, and fixation aids were studied and correlated to the setup variations. Systematic errors, random errors, and the recommended PTV margin were computed.

Patients and methods:

Upon institutional review board (IRB) approval, the daily portal images φ before and after online correction φ for rectal cancer patients who received long-course RT were retrospectively reviewed. The isocenter displacement in the superior-inferior (SI), right-left (RL), and anterior-posterior (AP) directions were collected. The rotational displacement was also collected.

Per departmental policy, rectal cancer patients were advised to have an empty rectum and full bladder before CT simulation and daily treatment. The treatment positions practiced at our department included prone and supine as per physician preference and patient capability. The use of a belly board device, Vac-Lok cushion, or no fixation was discussed between the radiation oncologist and the radiation therapist and decided upon before CT simulation for each patient.

Departmental Radiation Therapy Verification Protocol for Rectal Cancer Patients:

Kilo-voltage (Kv) portal images using the onboard imaging (OBI) system were acquired. Online matching with digitally reconstructed radiographs (DRRs) φ created from CT simulation images φ was followed. Isocenter shift correction was applied as per departmental policy. A displacement of 3 mm shift is accepted without correction. The shift of 3 to 7 mm mandates applying shift correction before treatment. Re-setup is required for > 7 mm translational shift and > 3˙ rotational displacement. Another portal image was acquired after correction for documentation.

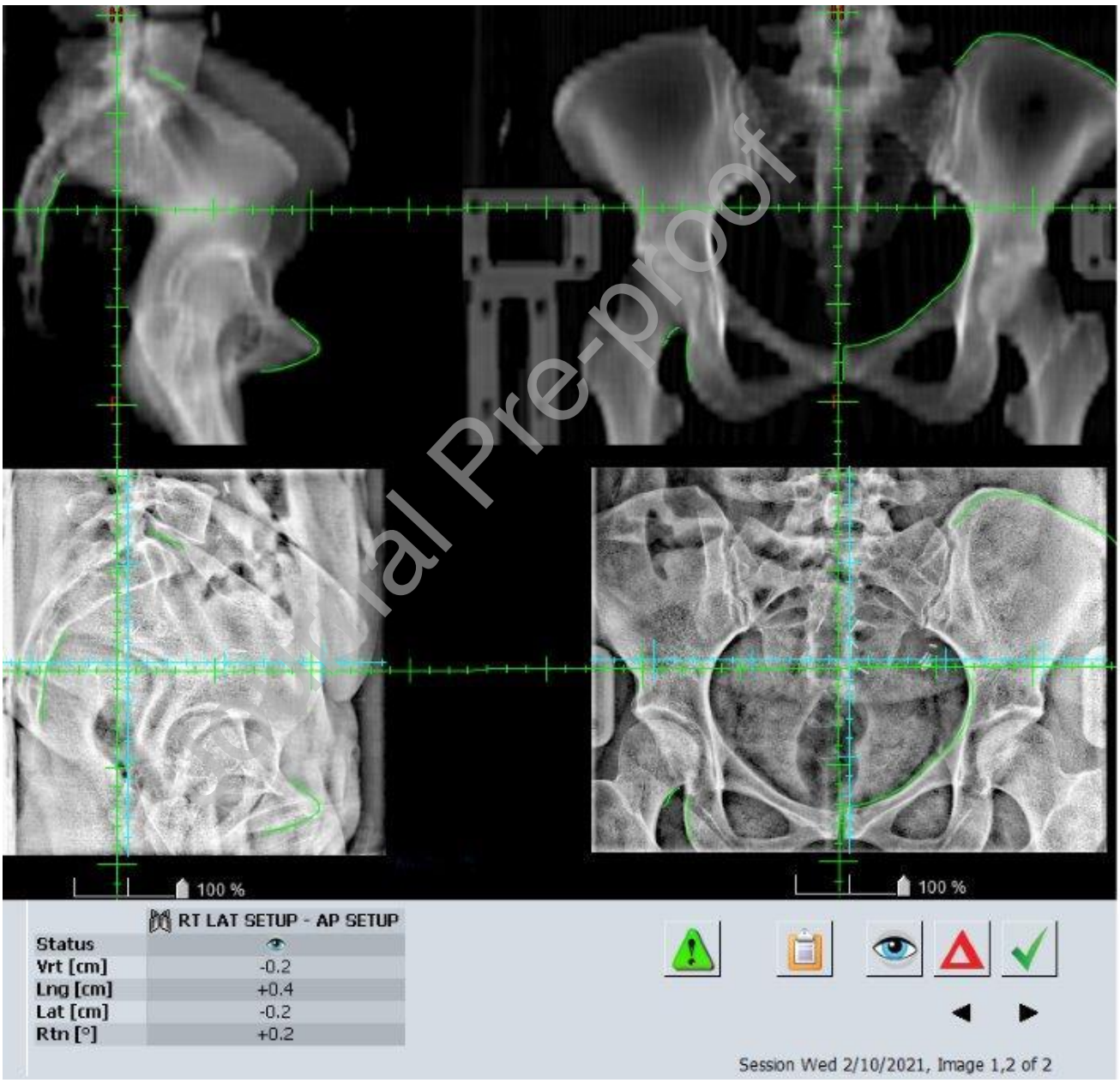
Frequency of Portal Images:

The portal images were acquired on the first three consecutive days of treatment and then twice weekly for each patient. Cone-beam CT (CBCT) was used for treatment verification at least once weekly. The trend of isocenter shifts in the first three days for each patient was routinely evaluated by a senior radiation technologist to decide on either daily IGRT or no-daily IGRT (keep the same portal image frequency).

Estimation of Reproducibility:

The isocenter shift was computed using the Offline Review of ARIA®Radiation Therapy Management software system (ARIA RTM version: 16.0120). Auto-match of DRR and the portal images before and after the online correction was done to calculate the setup errors (Figure 1).

***Figure 1**:* Matching of DRR with a portal image showing the isocenter shift for a patient with rectal cancer.



		The ocean coordinates represent the treatment isocenter for that day. The auto/manual matching generated table showed the isocenter shifts in Vrt (Anterior-Posterior), Lng (Superior-Inferior), Lat (Right-Left), and Rtn (Rotational) directions for that day.
Figure 2	tÌ·úʌŜyűăΩ ʌăƶÕŜyűŜℕ total vector error before and after online correction.	The figure shows total vector error (TVE) difference of treatment isocenter for all patients before (Fig 2A) and after (Fig 2B) online correction.

Tables

Table 1: tÌ·úʌŜyűăΩ ÕKÌ·ℕÌ·ÕűŜℕʌăúʌÕă

Variable	Total Number n=189	Percent %
Sex		
x Male	124	66
x Female	65	34
Position		
x Supine	110	58
x Prone	79	42
Immobilization		
x Belly board	50	26
x Vac-Loc	20	11
x None	119	63
BMI grouping		
x Ж нл	19	10
x 20-25	49	26
x 26-30	68	36
x 31-35	42	22
x > 35	11	6
Treatment technique		
x 3D-CRT	*63*	*33*
x VMAT	*126*	*67*

Number of verified RT sessions	*2345* *Average (12.4 session/patient)* *Range (5-23 session)*
Patient age (mean ±SD)	*54±15 (Range 19-93)*
BMI (mean ±SD)	*27±5 (Range 13-44.5)*

BMI= body mass index, VMAT= volumetric modulated arc therapy, RT= radiotherapy

Table 2: Mean isocenter shift before and after online correction and the effect of different variables.

Displacement Direction	Variable		N	Displacement before online correction		Displacement after online correction	
				Mean ± SD in cm	P value	Mean ± SD in cm	P value
SI	Fixation Aid	BB	50	0.12±0.14	0.1	0.15±0.16	0.8
		Vac Loc	20	0.07±0.12		0.14±0.11	
	Position	Supine	110	0.12±0.3	0.9	-0.01±0.23	0.06
		Prone	79	0.11±0.12		0.14±0.15	
	BMI	Ж ол kg/m^2	136	0.11±0.26	0.83	0.06±0.21	0.9

		> 30 kg/m^2	53	0.11±0.24		0.06±0.22	
	All patients		**189**	**0.11±0.25**		**0.06±0.21**	
RL	**Fixation Aid**	BB	50	0.24±0.25	0.005	0.11±0.14	0.8
		Vac Loc	20	0.07±0.2		0.13±0.16	
	Position	Supine	110	0.06±0.3		-0.06±0.17	0.01
		Prone	79	0.22±0.26	0.001	0.12±0.15	
	BMI	Жҥол kg/m^2	136	0.10±0.28		0.01±0.18	0.5
		> 30 kg/m^2	53	0.21±0.27	0.02	0.03±0.19	
	All patients		**189**	**0.13±0.28**		**0.02±0.18**	
AP	**Fixation Aid**	BB	50	0.12±0.20		0.11±0.12	0.1
		Vac Loc	20	0.09±0.2	0.6	0.06±0.14	
	Position	Supine	110	-0.14±0.32	0.001	0.01±0.21	0.001
		Prone	79	0.12±0.20		0.11±0.13	
	BMI	Жҥол kg/m^2	136	-0.02±0.28	0.05	0.06±0.17	0.3
		> 30 kg/m^2	53	-0.06±0.38		0.03±0.21	
	All patients		**189**	**-0.03±0.31**		**0.05±0.18**	
Rotation	**Fixation Aid**	BB	50	1.5±0.14	0.07	1.5±1.0	0.06
		Vac Loc	20	2.0±0.9		2.0±0.8	
	Position	Supine	110	0.01±0.3	0.001	0.01±0.42	0.001
		Prone	79	1.6±0.9		1.63±0.95	
	BMI	Жҥол kg/m^2	136	0.60±1.00	0.08	0.60±1.00	0.08
		> 30 kg/m^2	53	0.89±1.13		0.91±1.11	
	All patients		**189**	**0.7±1.0**		**0.6±1.0**	
TVE	**Fixation Aid**	BB	50	0.42±0.2	0.03	0.30±0.13	0.6
		Vac Loc	20	0.32±0.15		0.29±0.12	
	Position	Supine	110	0.48±0.3	0.05	0.33±0.15	0.21

		Prone	79	0.40±0.2		0.30±0.12	
BMI		Ж‹ол kg/m^2	136	0.43±0.25	0.05	0.31±0.13	0.4
		> 30 kg/m^2	53	0.51±0.26		0.33±0.16	
All patients			**189**	**0.45±0.26**		**0.32±0.14**	

SI=superior inferior, RL=right left, AP= anterior posterior, BB= belly board, BMI= body mass index, TVE=total vector error.

Table 3: Recommended PTV margins for daily IGRT and no-daily IGRT with the effect of different variables

Variable			N	PTV margin in mm for no-daily IGRT			PTV margin in mm for IGRT		
				SI	RL	AP	SI	RL	AP
Position	Supine		110	9.1	8.9	9.0	7.1	5.7	6.4
	Prone		79	8.6	12.2	12.4	6.2	6.7	6.5
Fixation Aid	Belly Board		50	8.7	11.9	12.2	6.5	6.6	6.4
	Vac Loc		20	8.2	11.6	13.5	5.3	6.8	7.0
Body Mass Index	Ж‹ол	All	136	9.3	10.4	10.8	7.0	6.4	6.3
		Supine	87	8.9	8.4	7.8	6.9	5.5	5.8
		Prone	49	8.6	12.2	12.4	6.2	6.7	6.5
	> 30	All	53	9.7	11.4	14.3	7.4	7.1	7.8
		Supine	23	9.7	10.2	11.4	7.7	6.4	7.9
		Prone	30	8.8	11.9	12.5	6.5	6.8	6.7
All rectal cases			189	9.0	10.0	11.0	7.0	6.6	6.8

SI=superior inferior, RL=right left, AP= anterior posterior, IGRT=image guided radiotherapy.

Table 4: Comparison of our data with other published studies

Study (Total number of	Treatment Site	Position	Fixation Aid	Systematic errors ٦ ٥YY٥	Random errors •(mm)

patients)	(No of Pts per site)			AP	LR	SI	AP	LR	SI
Kasabasic (23) 11 Patients	Rectum (1)	Prone	BB	9	12	2.4	17	22	18
	Uterus (4)	Prone	BB						
	Cervix (6)	Prone	BB						
Tamponi (24) 100 Pts	Rectum (8)	Prone	BB	1.8	0.4	1.6	2.5	1.5	2.8
	Uterus (9)	Supine	-	3.2	2.2	1.9	2	2.1	2.3
	Prostate (16)	Supine	-	1.7	1.3	1.5	1.8	1.9	1.8
Thasanthan (25)	Rectum (50)	-	-	2.7	3.3	2.6	2.3	1.6	1.6
Rajeev et al (26)	Rectum (20)	Prone	BB	1.3	0.6	1.2	2.0	1.2	3.1
		Supine	-	0.9	0.7	1.6	1.8	1.7	1.8
Bouchra et al (27) 44 patients	Cervix	Supine	FF/ UK	1.4	2.0	1.2	1.7	2.9	1.3
	Rectum			1.3	1.9	2.9	1.3	2.3	1.0
Bansal et al (28)	Rectum (7)	prone	TTM	4.7	1.2	2.1	9.6	2.3	2.0
Before correction (Present study)	Rectum (189)	Supine	FF/UK	3.2	2.8	3.1	3.6	4.8	4.0
		Prone	BB/VL	2.0	2.6	1.4	12.0	9.9	8.3
		All	FF,UK,BB,VL	3	2.8	2.5	8.2	7.4	6.2
After correction (Present study)	Rectum (189)	Supine	FF/UK	2.1	1.7	2.3	3.2	3.2	3.5
		Prone	BB/ VL/no	1.3	1.5	1.5	5.7	5.4	4.6
		All	FF,UK,BB,VL	1.8	1.7	2.1	4.5	4.2	4

BB = belly board, FF = foot fix, UK = under knees, TTM=thermoplastic mask, VL = Vac-Loc