Factors Affecting Isocenter Displacement and Planning Target Volume Margin for Patients With Rectal Cancer Receiving Radiation Therapy

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Abstract

Purpose: 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 interfraction random and systematic errors and hence propose the optimum planning target volume (PTV) in patients with rectal cancer.

Methods and Materials: Translational and angular isocenter displacements were retrospectively collected for 189 patients. Random and systematic errors were determined, and 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 no-daily image-guided radiotherapy (IGRT) and daily IGRT respectively.

Results: Before the online correction, the systematic errors were 2.5, 2.8, and 3.0 mm for superior-inferior (SI), right-left (RL), and anterior-posterior (AP) directions, respectively, compared with 2.1, 1.7, and 1.8 mm after online correction. The random errors were 6.2, 7.4, and 8.2 mm in SI, RL, and AP, respectively, before online correction, compared with 4, 4.2, and 4.5 mm after online correction. The recommended PTV margin was 0.7 and 1.0 cm for daily IGRT and no-daily IGRT, respectively. The prone position and BMI >30 kg/m² warrant higher margins in no-daily IGRT cases, 1.2 and 1.4 cm, respectively.

Conclusions: The prone position, BMI >30 kg/m², 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.

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Introduction

Precise and reproducible daily placement of treatment isocenter has been the main target for radiation therapy (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.\(^3\) RT is recommended for patients with stage II-III rectal cancer as a neoadjuvant concurrent with chemotherapy. The radiation treatment is delivered either as a short course with a dose of 25 Gy in 5 fractions per week\(^4\) or as a long course with a dose of 50 to 50.4 Gy in 25 to 28 fractions every 5 to 5.5 weeks.\(^6\) 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.\(^11\) 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 the (more comfortable) supine position is superior, especially with the use of advanced RT techniques that allow sparing of the small bowel. Intensity modulated RT (IMRT) or volumetric modulated arc therapy (VMAT) can achieve the constraint of small bowel volume receiving 45 Gy to \(<195 \text{ cm}^3 (V_{45} \leq 195 \text{ cm}^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 patients with obesity. 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 recommends prone positioning with a belly board device for pelvic RT and expects emerging evidence shortly.\(^17\) Ninety percent of the panel, given the lack of clear literature evidence, recommends daily image guided RT (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 with 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 patients with rectal cancer is of major concern.

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

**Methods and Materials**

This study was approved by the institutional review board (IRB) at King Fahad Medical City, Riyadh, Saudi Arabia (IRB 22-029), and registered with the Office for Human Research Protections, National Institute of Health (IRB00010471; approval number, Federal Wide Assurance National Institute of Health: FWA00018774).

Upon IRB approval, the daily portal images—before and after online correction—for patients with rectal cancer 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, patients with rectal cancer were advised to have an empty rectum and full bladder before computed tomography (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 RT verification protocol for patients with rectal cancer**

Kilovoltage portal images using the onboard imaging system were acquired. Then, online matching with digitally reconstructed radiographs—created from CT simulation images—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 3 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 3 days for each patient was routinely evaluated by a senior radiation technologist to decide on either daily IGRT or no-daily IGRT (ie, keep the same portal image frequency).
Estimation of reproducibility

The isocenter shift was computed using the Offline Review of the ARIA Radiation Therapy Management software system (version 16.0120; Varian Medical Systems). Automatch of digitally reconstructed radiographs and the portal images before and after the online correction was done to calculate the setup errors (Fig. 1).

The translational setup errors, including the 3 directions (SI, RL, and AP) were calculated, and the total vector error (TVE) was computed for each patient. TVE reflects the overall treatment isocenter shift from the planned isocenter. It is a mathematical function that takes the 3 directions’ displacements into account simultaneously and computed for each patient \(i\) from the mean displacements \(m\):

\[
TVE(i) = \sqrt{m_{SI}^2 + m_{RL}^2 + m_{AP}^2}
\]  

(1)

The rotational displacement was calculated separately and measured in angular degrees. Systematic (Σ)
and random \( (\sigma) \) errors were calculated according to Stroom et al\(^{18} \) and Van Herk et al.\(^{19} \) Systematic error is the average setup variations of the target volume for all fractions for a certain patient. The random errors are unpredictable and unavoidable interfractional variations.

A certain direction systematic error for each patient \((i)\) is the standard deviation (SD) of the mean \((m)\) displacement in that direction (SI, RL, or AP):

\[
\Sigma_{SI} = SD(m_{i, SI})
\]  

A certain direction random error \((\sigma)\) for each patient \((i)\) is the square root of this direction displacement squared SD:

\[
\sigma_{SI} = \sqrt{SD_{i, SI}^2}
\]

We calculated PTV margins based on the suggested formula by Stroom et al.\(^{18} \). This formula ensures that 99% of the clinical target volume (CTV) volume receives 95% of the prescribed dose \( (V_{99\%} \text{ covered by } \geq 95\% \text{ dose}) \).

\[
Margin = 2\Sigma + 0.7\sigma
\]

### Statistical analysis

The translational and rotational mean displacements for all patients were collected. The data were compared for treatment positions (supine vs prone), BMI groups \((\leq 30 \text{ kg/m}^2 \text{ vs } >30 \text{ kg/m}^2)\), and fixation aids (Vac-Lok vs belly board). Shapiro-Wilk’s and Levine’s tests were used to calculate the normal distribution of data and equal variances, respectively. Two-tailed independent sample \( t \) test was performed to compare the data between different groups. A \( P \) value \( \leq 0.05 \) was considered significant. The systematic error and random errors were calculated, and then PTV margins were computed using Stroom et al’s\(^{18} \) formula.

Matching images before online correction was used to assess the recommended PTV margin for no-daily IGRT treatment, and matching images after online correction was used to assess the PTV margin for daily IGRT treatment. The PTV margins for the different subset of patients as per treatment position, BMI, and fixation aids were computed and studied.

### Results

One hundred eighty-nine patients with rectal cancer, treated between 2011 and 2021, were included in the final analysis. We excluded patients treated by short-course RT or due to unavailability of images of both before and after online corrections.

### Patients’ characteristics

The mean age was 54 ± 15 years (range, 19-93 years). Sixty-five patients (34%) were women, and 124 (66%) were men. The mean BMI was 27 ± 5 kg/m\(^2\) (range 13-44.5 kg/m\(^2\)). Underweight patients having BMI under 18.5 kg/m\(^2\) were 10% of the studied group, and normal-weight patients having BMI between 18.5 and 24.9 kg/m\(^2\) were 26%. Overweight patients with BMI between 25 and 29.9 kg/m\(^2\) were 36% of the studied group of patients. The obese group having BMI >30 kg/m\(^2\) was 53 patients, representing 28% of the studied group, as shown in Table 1.

One hundred ten patients (58%) were treated in the supine position, whereas 42% were treated in the prone position. The belly board device was used for 50 patients (26%), and Vac-Lok was used for 20 patients (11%).

### Table 1 Patient characteristics (\(n = 189\))

| Variable                  | n   | %   |
|---------------------------|-----|-----|
| Sex                       |     |     |
| Male                      | 124 | 66  |
| Female                    | 65  | 34  |
| Position                  |     |     |
| Supine                    | 110 | 58  |
| Prone                     | 79  | 42  |
| Immobilization            |     |     |
| Belly board               | 50  | 26  |
| Vac-Lok                   | 20  | 11  |
| None                      | 119 | 63  |
| BMI grouping, kg/m\(^2\)  |     |     |
| \(\leq 20\)               | 19  | 10  |
| 20-25                     | 49  | 26  |
| 26-30                     | 68  | 36  |
| 31-35                     | 42  | 22  |
| >35                       | 11  | 6   |
| Treatment technique       |     |     |
| 3D-CRT                    | 63  | 33  |
| VMAT                      | 126 | 67  |
| Verified RT sessions      | 2345 (average, 12.4 sessions/patient; range, 5-23 sessions) |   |
| Patient age (y), mean ± SD (range) | 54 ± 15 (19-93) |   |
| BMI (kg/m\(^2\)), mean ± SD (range) | 27 ± 5 (13-44.5) |   |

**Abbreviations:** 3D-CRT = 3-dimensional conformal radiation therapy; BMI = body mass index; RT = radiation therapy; SD = standard deviation; VMAT = volumetric modulated arc therapy.
## Table 2  Mean isocenter shift before and after online correction and the effect of different variables

| Displacement direction | n  | Displacement before online correction | P value | Displacement after online correction | P value |
|------------------------|----|--------------------------------------|---------|--------------------------------------|---------|
|                        |    | Mean ± SD, cm                        |         | Mean ± SD, cm                        |         |
| SI                     |    |                                      |         |                                      |         |
| Fixation aid           |    |                                      |         |                                      |         |
| BB                     | 50 | 0.12 ± 0.14                          | .1      | 0.15 ± 0.16                          | .8      |
| Vac-Lok                | 20 | 0.07 ± 0.12                          |         | 0.14 ± 0.11                          |         |
| Position               |    |                                      |         |                                      |         |
| Supine                 | 110| 0.12 ± 0.3                           | .9      | −0.01 ± 0.23                         | .06     |
| Prone                  | 79 | 0.11 ± 0.12                          |         | 0.14 ± 0.15                          |         |
| BMI, kg/m²             |    |                                      |         |                                      |         |
| ≤30                    | 136| 0.11 ± 0.26                          | .83     | 0.06 ± 0.21                          | .9      |
| <30                    | 53 | 0.11 ± 0.24                          |         | 0.06 ± 0.22                          |         |
| All patients           | 189| 0.11 ± 0.25                          |         | 0.06 ± 0.21                          |         |
| RL                     |    |                                      |         |                                      |         |
| Fixation aid           |    |                                      | .005    |                                      | .8      |
| BB                     | 50 | 0.24 ± 0.25                          |         | 0.11 ± 0.14                          |         |
| Vac-Lok                | 20 | 0.07 ± 0.2                           |         | 0.13 ± 0.16                          |         |
| Position               |    |                                      | .001    |                                      | .01     |
| Supine                 | 110| 0.06 ± 0.3                           |         | −0.06 ± 0.17                         |         |
| Prone                  | 79 | 0.22 ± 0.26                          |         | 0.12 ± 0.15                          |         |
| BMI, kg/m²             |    |                                      | .02     |                                      | .5      |
| ≤30                    | 136| 0.10 ± 0.28                          |         | 0.01 ± 0.18                          |         |
| <30                    | 53 | 0.21 ± 0.27                          |         | 0.03 ± 0.19                          |         |
| All patients           | 189| 0.13 ± 0.28                          |         | 0.02 ± 0.18                          |         |
| AP                     |    |                                      | .6      |                                      | .1      |
| Fixation aid           |    |                                      |         |                                      |         |
| BB                     | 50 | 0.12 ± 0.20                          | .001    | 0.11 ± 0.12                          | .001    |
| Vac-Lok                | 20 | 0.09 ± 0.2                           |         | 0.06 ± 0.14                          |         |
| Position               |    |                                      | .01     |                                      |         |
| Supine                 | 110| −0.14 ± 0.32                         |         | 0.01 ± 0.21                          |         |
| Prone                  | 79 | 0.12 ± 0.20                          |         | 0.11 ± 0.13                          |         |
| BMI, kg/m²             |    |                                      | .05     |                                      | .3      |
| ≤30                    | 136| −0.02 ± 0.28                         |         | 0.06 ± 0.17                          |         |
| <30                    | 53 | −0.06 ± 0.38                         |         | 0.03 ± 0.21                          |         |
| All patients           | 189| −0.03 ± 0.31                         |         | 0.05 ± 0.18                          |         |
| Rotation               |    |                                      | .07     |                                      | .06     |
| Fixation aid           |    |                                      |         |                                      |         |
| BB                     | 50 | 1.5 ± 0.14                           | .001    | 1.5 ± 1.0                            | .001    |
| Vac-Lok                | 20 | 2.0 ± 0.9                            |         | 2.0 ± 0.8                            |         |
| Position               |    |                                      | .01     |                                      |         |
| Supine                 | 110| 0.01 ± 0.3                           |         | 0.01 ± 0.42                          |         |
| Prone                  | 79 | 1.6 ± 0.9                            |         | 1.63 ± 0.95                          |         |
| BMI, kg/m²             |    |                                      | .08     |                                      | .08     |
| ≤30                    | 136| 0.60 ± 1.00                          |         | 0.60 ± 1.00                          |         |
| <30                    | 53 | 0.89 ± 1.13                          |         | 0.91 ± 1.11                          |         |
| All patients           | 189| 0.7 ± 1.0                            |         | 0.6 ± 1.0                            |         |

(continued on next page)
patients treated using the belly board and Vac-Lok were lying in the prone position.

The IMRT/VMAT technique was used for treating 126 patients, representing 67% of the whole studied group, and 33% were treated with 3-dimensional conformal RT. The total number of verified sessions was 2345 (52%) of 4515 treated sessions. The average verified sessions per patient was 12.4 (range, 5-25 sessions). The verification images included megavoltage images, kilovoltage, and CBCT images.

**Setup errors before and after online correction**

The mean translational, angular, and TVE displacements for the whole group of patients and different subgroups before and after online correction are shown in Table 2. The mean SI displacement was 0.11 ± 0.25 cm before online correction, compared with 0.06 ± 0.21 cm after online correction.

The mean RL displacement was 0.13 ± 0.28 cm before online correction, compared with 0.02 ± 0.18 cm after online correction. The mean AP displacement was −0.03 ± 0.31 cm, compared with 0.05 ± 0.18 cm before and after online correction, respectively. Figures E1 and E2 show the clear difference between SI, RL, and AP displacements before and after online correction.

The mean rotational displacement was 0.7° ± 1.0° before online correction compared with 0.6° ± 1.0° after online correction, as shown in Table 2.

The mean TVE was higher at 0.45 ± 0.26 cm before online correction compared with 0.32 ± 0.14 cm after online correction, as shown in Fig. 2.

The patients treated in the supine position showed significantly lower mean RL, AP, rotational, and TVE displacement before online correction compared with those treated in the prone position, with P values of .001, .001, .001, and .05, respectively. The same is valid after online correction, except for TVE, which did not show a significant difference between the supine and prone positions, with a P value of .21, as shown in Table 2.

The patients with BMI >30 kg/m² showed significantly higher mean RL, AP, and TVE displacement before online correction compared with patients with BMI ≤30 kg/m², with P values of .02, .05, and .05, respectively. However, there was no significant difference after online correction between the same groups, as shown in Table 2.

The belly board device showed higher mean RL and TVE displacement before online correction compared with Vac-Lok, with P values of .005 and .03, respectively. However, these differences were lost after online correction, as shown in Table 2.

**Systematic, random errors and recommended PTV margins**

The systematic and random errors were computed as per Stroom et al. The SI, RL, and AP random errors before online correction were 6.2, 7.4, and 8.2 mm, respectively, compared with 4.4, 4.2, and 4.5 mm, respectively, after online correction. The SI, RL, and AP systematic errors before online correction were 2.5, 2.8, and 3.0 mm, respectively, compared with 2.1, 1.7, and 1.8 mm, respectively, after online correction.

The CTV-PTV margin was computed per Stroom et al. The recommended PTV margin for the patients to be treated with no-daily IGRT was 0.9 cm for the SI direction, 1.0 cm for the RL direction, and 1.1 cm for the AP direction. The PTV margin for patients to be treated with

| Displacement direction | n  | Mean ± SD, cm | P value | Mean ± SD, cm | P value |
|------------------------|----|---------------|---------|---------------|---------|
| TVE                    |    |               |         |               |         |
| Fixation aid           |    |               |         |               |         |
| BB                     | 50 | 0.42 ± 0.2    | .03     | 0.30 ± 0.13   | .6      |
| Vac-Lok                | 20 | 0.32 ± 0.15   | .05     | 0.29 ± 0.12   | .21     |
| Position               |    |               |         |               |         |
| Supine                 | 110| 0.48 ± 0.3    | .05     | 0.33 ± 0.15   | .4      |
| Prone                  | 79 | 0.40 ± 0.2    |         | 0.30 ± 0.12   |         |
| BMI, kg/m²             |    |               |         |               |         |
| ≤30                    | 136| 0.43 ± 0.25   | .05     | 0.31 ± 0.13   | .4      |
| <30                    | 53 | 0.51 ± 0.26   |         | 0.33 ± 0.16   |         |
| All patients           | 189| 0.45 ± 0.26   |         | 0.32 ± 0.14   |         |

*Abbreviations: AP = anterior posterior; BB = belly board; BMI = body mass index; RL = right-left; SI = superior-inferior; TVE = total vector error.*
daily IGRT was 0.7 cm for the SI direction, 0.66 cm for the RL direction, and 0.68 cm for the AP direction (Table 3).

For treatment without daily IGRT, the required PTV margin for patients treated in the supine position was 0.9 cm, compared with 1.2 cm for those treated in the prone position. Also, patients with a BMI >30 kg/m² required a PTV margin of 1.4 cm, compared with 1.0 cm for patients with BMI ≤30 kg/m². For treatment with daily IGRT, the previous differences were lost, and all patients could be treated with a PTV margin of 0.7 cm. The fixation aid did not affect the PTV margin for daily IGRT and no-daily IGRT treatments (Table 3).

The random and systematic errors were higher before online correction compared with after online correction regardless of the treatment position. Interestingly, the systematic errors were higher for the supine position compared with the prone position in contrast to random errors (Table 4).

**Discussion**

In this study, we retrospectively reported the setup error for 189 patients with rectal cancer who underwent RT. Most pelvic RT setup error studies include a diversity of diseases; however, we believe that each one warrants a dedicated study due to different setups, types of patients, and disease factors. For patients with rectal cancer,
immobilization devices widely used for the sake of reproducibility and decreasing irradiated bowel volume failed to reduce setup errors and affected the needed PTV margin.20-22 Also, the increasing trend of using VMAT for those cases mandates examining the isocenter displacement and the recommended PTV margin precisely. The logical assumption of having a lower PTV margin for daily IGRT cases compared with no-daily IGRT cases is valid but not standardized yet due to a lack of evidence in the literature.

Studying portal images before online correction (first taken images) and after online correction for the same patients made the comparison of the 2 data sets homogeneous enough to assess the difference properly. The high number of patients in our study compared with other studies lends more validity to this study’s results.

As most of the studies are concerned with patients with gynecologic and prostate cancer, we tried our best to highlight only rectal cancer studies to compare to our study, as shown in Table 4.

Kasabasic et al23 reported 11 patients with pelvic malignancy, including rectum cases, and showed higher systematic and random errors compared with our data before online correction. They reported systematic errors ranging from 2.4 to 12 mm, and random errors reached up to 18 mm. They recommended margins of 11, 13, and 14 mm in the RL, SI, and AP directions, respectively, which is nearly the same as our recommended margins for the prone setup position using a belly board device without IGRT.23

Tamponi et al24 showed systematic and random errors of 2 to 3 mm in the patients with prostate, rectum, and gynecologic cancers receiving RT. The calculated CTV-PTV margins were 10 mm in the RL direction and 20 mm in the SI direction. In comparison, our setup errors were lower than these numbers, and the recommended PTV margins for non-IGRT were within 10 mm, and for IGRT they were within 6 to 7 mm.

Thasanthan et al25 studied 50 cancer rectum patients with portal images taken on the first 2 days of treatment only. They used the corrected images for the assessment of isocenter shifts and showed mean AP, SI, and RL displacements of 1.0, −1.8, and 0.8 mm, respectively. The systematic errors reported in this study were higher compared with ours, in contrast to the random errors, which were lower. The systematic errors were nearly 3 mm in all directions, whereas the random errors were 2.3, 1.6, and 1.6 mm for the AP, SI, and RL directions, respectively. Thasanthan et al recommended PTV margins of 0.84 cm for AP, 0.9 cm for SI, and 0.76 cm for RL directions. They concluded that the routinely used PTV margin of 0.5 cm was not enough for approximately 22% of treatment sessions.

Rajeev et al26 studied 20 patients with rectal cancer and compared the supine and prone positions. Systematic

| Table 3 | Recommended PTV margins for daily and no-daily IGRT with the effect of different variables |
|---------|-----------------------------------------------|
| Variable | PTV margin (mm) for no-daily IGRT | PTV margin (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-Lok | 20   | 8.2  | 11.6 | 13.5 | 5.3  | 6.8  | 7.0  |
| Body mass index |      |      |      |      |      |      |      |
| ≤30 |      |      |      |      |      |      |      |
| 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  |

Abbreviations: AP = anterior posterior; IGRT = image guided radiation therapy; PTV = planning target volume; RL = right-left; SI = superior-inferior.
| Study and treatment sites | Patients, n | Position | Fixation aid | Systematic errors $\Sigma$ (mm) | Random errors $\sigma$ (mm) |
|--------------------------|-------------|----------|--------------|-------------------------------|-----------------------------|
|                          |             |          |              | AP   | LR  | SI  | AP   | LR  | SI  |
| Kasabasic et al $^{23}$  | 11          |          |              | 9    | 12  | 2.4 | 17   | 22  | 18  |
| Rectum                   | 1           | Prone    | BB           |      |     |     |      |     |     |
| Uterus                   | 4           | Prone    | BB           |      |     |     |      |     |     |
| Cervix                   | 6           | Prone    | BB           |      |     |     |      |     |     |
| Tamponi et al $^{24}$    | 100         |          |              |      |     |     |      |     |     |
| 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 et al $^{25}$ | 50          |          |              |      |     |     |      |     |     |
| Rectum                   | -           | -        |              | 2.7  | 3.3 | 2.6 | 2.3  | 1.6 | 1.6 |
| Rajeev et al $^{26}$     | 20          |          |              |      |     |     |      |     |     |
| Rectum                   | -           | Prone    | BB           | 1.3  | 0.6 | 1.2 | 2    | 1.2 | 3.1 |
| Supine                   | -           |          |              | 0.9  | 0.7 | 1.6 | 1.8  | 1.7 | 1.8 |
| Bouchra et al $^{27}$    | 44          |          | FF, UK       | 1.4  | 2   | 1.2 | 1.7  | 2.9 | 1.3 |
| Cervix                   |             | Supine   | FF, Uk       | 1.3  | 1.9 | 2.9 | 1.3  | 2.3 | 1   |
| Rectum                   |             |          |              |      |     |     |      |     |     |
| Bansal et al $^{28}$     | 7           |          | TTM          | 4.7  | 1.2 | 2.1 | 9.6  | 2.3 | 2   |
| Present study, before correction | 189     |          | FF, UK       | 3.2  | 2.8 | 3.1 | 3.6  | 4.8 | 4   |
| Rectum                   |             | Supine   | FF, UK       | 2    | 2.6 | 1.4 | 12   | 9.9 | 8.3 |
| Prone                    |             | BB, VL   |              | 3    | 2.8 | 2.5 | 8.2  | 7.4 | 6.2 |
| Present study, after correction | 189     |          | FF, UK, BB, VL | 2.1  | 1.7 | 2.3 | 3.2  | 3.2 | 3.5 |
| Rectum                   |             | Supine   | FF, UK       | 1.3  | 1.5 | 1.5 | 5.7  | 5.4 | 4.6 |
| Prone                    |             | BB, VL, no |            | 1.8  | 1.7 | 2.1 | 4.5  | 4.2 | 4   |

Abbreviations: BB = belly board; FF = foot fix; TTM = thermoplastic mask; UK = under knees; VL = Vac-Lok.
errors for the supine position were 0.87 mm for the AP direction, 0.66 mm for the RL direction, and 1.6 mm for the SI direction. These values were lower than our current study. The prone position’s systematic errors were 1.3, 0.59, and 1.17 mm for the AP, RL, and SI directions, respectively. Rajeev et al reported random errors of 1.81 mm (AP), 1.73 mm (RL), and 1.83 mm (SI) for the supine position, compared with 2.02 mm (AP), 1.21 mm (RL), and 3.05 mm (SI) for the prone position. Consequently, the recommended PTV margins were 3.45, 2.87, and 5.31 mm for the AP, RL, and SI directions, respectively, in the case of the supine position. The prone position’s recommended margins were 4.9, 2.3, and 5.1 mm for the AP, RL, and SI directions, respectively. The non-practical recommended PTV margins of 2 mm in some directions was a result of very low random error values in this study. We think Rajeev et al followed a strict protocol for online correction and that they used the confirmation image after this correction for measuring the setup errors; however, it is not clearly stated.

Bouchra et al studied 44 patients, including 12 patients with rectal cancer treated in the supine position. The reported mean displacements were nearly 3.9 mm in all directions. The systematic errors proved to be 1.3, 1.9, and 2.9 mm for the AP, RL, and SI directions, respectively, and the random errors were 1.25, 2.33, and 1.04 mm for the AP, RL, and SI directions, respectively. Bouchra et al recommended PTV margins of 8 mm for the RL direction and 5 mm for the SI and AP directions based on their clinical routine work.

Bansal et al studied 7 patients with rectal cancer treated in the prone position using a thermoplastic mask. The prone position’s systematic and random errors were nearly comparable to our data, apart from the higher value of the SI direction, which could be related to the use of the thermoplastic mask. PTV margins calculated were found to be 0.5, 1.8, and 0.7 cm in the lateral, longitudinal, and vertical directions, respectively.

In summary, our data showed a significant statistical difference between the supine and prone positions, with superiority of the supine position regarding reproducibility and higher margins recommended for the prone position. Our results match Adli et al, who studied gynecologic tumors. They concluded that the valuable effect of the prone position on reducing the irradiated bowel volume outweighed its setup uncertainties.

The interfractional rectal and bladder filling variation was not studied in our patients due to the unavailability of CBCT for all of them. However, the previous point is well-studied by others for prostate stereotactic body RT (SBRT), with contradictory results. Byun et al studied 85 patients with prostate carcinoma who received SBRT with 510 acquired CBCT. Patients were instructed to maintain a full bladder and empty rectum before simulation and daily RT. They reported a difference in the bladder and rectal volumes at the time of treatment compared with the planning scans. They doubt the need for excessively strict bladder filling and rectal emptying protocols in the context of IGRT-SBRT.

Studies endorsing rectal RT with daily CBCT-IGRT are needed to determine whether the daily variation of bladder and rectal filling will affect the PTV margins. However, we can extrapolate cautiously from Byun et al’s study that the effect of this factor will be small with the current practice of bladder filling and rectal emptying.

### Conclusion

The computed PTV margins for daily IGRT are lower compared with no-daily IGRT. Prone position and BMI >30 kg/m² require a higher PTV margin in the case of no-daily IGRT; however, this is not the same with the use of daily IGRT. The use of immobilization devices such as belly boards should be studied by each department to find the optimal PTV margins for their use.

We recommend using daily IGRT for rectal cancer radiation treatment and applying a PTV margin of 7 mm. However, in the case of no-daily IGRT, the margins should be 1.0 cm to 1.4 cm based on the BMI, treatment position, and fixation tool. We encourage further studies examining the effect of bladder and rectal filling on the recommended PTV margins.

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### Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2022.101060.

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