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Rectal wall sparing effect of a rectal retractor in prostate intensity-modulated radiotherapy

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ABSTRACT

Purpose: The objective of the study was to evaluate the effectiveness of a rectal retractor (RR) designed to protect rectal tissue in intensity-modulated radiotherapy (IMRT) by pushing rectal wall (RW) away from the prostate.

Materials and Methods: Twelve patients with localized prostate cancer were enrolled into this study. Patients underwent two computed tomography (CT) scans without and with RR. A prescription of 80 Gy in 40 fractions was planned on CT scans with and without RR. This study evaluates the ability of the RR in RW dose reduction, in particular reduction of the RW $V_{70Gy} \geq 25\%$ in comparison with the plan without RR dose-volume histograms were generated with and without RR. The patient's tolerance was assessed by patient-reported outcomes.

Results: The planning target volume coverage was equal for both without and with RR ($P = 0.155$). The mean dose to the RW was statistically significantly lower for the plan with RR than that for the plan without RR, a mean reduction of 5.8 Gy ($P = 0.003$). Significant relative reductions in rectal dose-volume parameters whether in absolute volume (cc) or as a percentage of contoured RW were detected. A relative reduction more than 25% in RW V_{70Gy} (%) in 100% of patients was achieved. The rectal retraction resulted in a significant increase in the prostate to the rectum space at the prostate midgland level, an absolute increase of 2.7 mm. The retraction of the rectum induced a mean (±standard deviation) pain score of 2.7 (±1.3) according to the visual analog score.

Conclusion: The application of a RR showed a remarkable rectal sparing effect during prostate IMRT. This may lead to reduced acute and late rectal toxicities in prostate IMRT.

KEY WORDS: Dose-escalated radiotherapy, intensity-modulated radiotherapy, prostate cancer, rectal retractor

INTRODUCTION

External beam radiation therapy (EBRT) is considered as a well-established treatment modality for localized prostate cancer. Dose-escalated prostate radiotherapy (RT) has shown improved treatment outcomes, but dose escalation is limited by rectal toxicity.[1,2] Despite the advent of advanced technologies such as intensity-modulated RT (IMRT) and image-guided RT (IGRT), rectal toxicity is still a challenging issue in prostate RT.[3,4] This toxicity is primarily associated with the spatial proximity of the prostate gland and rectum. Therefore, geometric rectum sparing can be a considerable interest to reduce the radiation exposure to the rectum.

Two main strategies in rectal sparing technology are endorectal balloons (ERBs) and hydrogel rectal spacers, which were widely reviewed.[5,6] An alternative to ERBs and hydrogel rectal spacers in reducing the dose to the rectum is using a rectal retractor (RR). Few studies have been investigated the impact of a RR on the rectal doses during prostate stereotactic body RT (SBRT), volumetric modulated arc therapy (VMAT), and proton boost with promising results.[7-9] However, one comparative treatment plan study did not find statistically significant reductions in rectal doses between the plan with and without a RR.[10] Many centers treat prostate cancer with IMRT and three-dimensional conformal RT (3DCRT) with standard regimens that rectal toxicity remains a challenge. We have previously

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developed a RR in-house and addressed the feasibility of the use of the RR during 3DCRT in 40 × 2 Gy.[11,12] Furthermore, the RR was capable to provide *in vivo* rectal wall (RW) dosimetry.[11] The efficacy of the RR in prostate 3DCRT has been demonstrated. Based on these, in this work, we purpose to evaluate whether the same dosimetric benefit is observed using IMRT as a modern RT technique. In addition, we investigate the ability of the RR in the reduction of the rectal V_{70Gy} (volume receiving ≥70 Gy) ≥25% in comparison with the plan without using an RR.

MATERIALS AND METHODS

Twelve patients with intermediate-risk prostate cancer were included in the current study. Patients with anorectal diseases such as hemorrhoid were excluded from this study. Informed consent was obtained from all patients. Table 1 summarizes the patient and tumor characteristics.

All patients underwent transrectal ultrasound (TRUS)-guided insertion of three gold seed fiducial markers. Within 7 days of the fiducial marker implantation, all patients received two computed tomography (CT)-based simulation in the supine position (slice thickness 3 mm) without RR and with RR. All patients were asked to follow an empty rectum and full-bladder (drinking 500 cc of water ½ h prior to CT simulation and treatment) protocol during planning CTs and RT. Rectal and bladder preparation protocol was previously described.[11] In the planning CT, a physician inserted the rectal rod of the RR system into the rectum to evaluate the patient's tolerance. The rectal rod was connected to the vertical locking column attached to the carbon fiber baseplate, as shown in Figure 1. The vertical locking column mechanically displaces the rectal rod, and as a consequence, the rectum retracts dorsally. One technologist (r.d) inserted the rectal rod into the rectum (in the same vertical depression that was indexed in the planning CT) during the RT treatment for all patients. The rectal rod was covered by a disposable condom and insertion was facilitated by lidocaine jelly. The diameter of the rectal rod was 1.5 cm. The rectal rod was also sterilized after each use. Instruction of the application of the RR in more detail was described in our previous study.[11] On the CT datasets, the prostate, seminal vesicles, bladder, RW, and femoral heads were delineated (Varian Eclipse v. 13.6, Varian Medical System Inc., Palo Alto, CA, USA). The clinical target volume (CTV) included the prostate and seminal vesicles. Magnetic resonance imaging (MRI) was used as support for contouring of the target and organ at risks, as shown in Figure 2. The planning target volume (PTV) was defined in 5 mm extensions in all directions margin to the CTV.[13] The RW was contoured from the bottom of the ischial tuberosity to the rectosigmoid flexure. The RW was generated using a 3 mm internal margin of outer RW contour,[14] as displayed in Figure 3.

IMRT was delivered with a mixed 6 MV photons of 7 dynamic ports using multileaf collimators. The dose prescribed to the PTV was 40 × 2 Gy. The 95% prescription isodose line covered at least 99% of the PTV in all cases. Daily pre-RT treatment electronic portal images were obtained to correct the prostate's gold seeds position based on reference digitally reconstructed radiographs. QUANTEC guidelines were used for dose-volume constraints.[15] To elucidate the role of the RR on the rectal dose during prostate IMRT, two similar plans were created for each patient, one without RR and one with RR. The following dosimetric parameters were used to compare the volume of the RW irradiated with and without

Table 1: Patient and tumor characteristics

Parameter	Value
Age (year)	
Mean (range)	70.9 (60-80)
PSA (ng/ml)	
Mean (range)	10.5 (1.7-16.2)
Gleason score (*n*)	
6	7
7	4
8	1
T-stage	
T2	12

PSA: Prostate-specific antigen

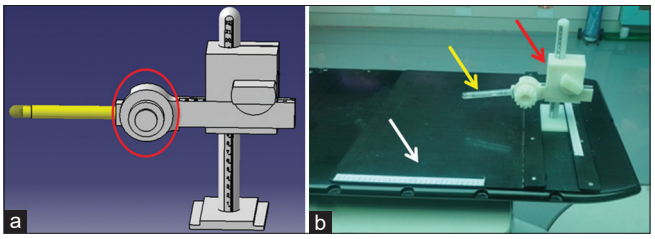

Figure 1: (a) Three-dimensional mechanical drawing of the rectal retractor system, red circle shows the angulation system of rectal rod, (b) rectal retractor system, rectal rod (yellow arrow), vertical locking column (red arrow) and carbon-fiber base plate (white arrow)

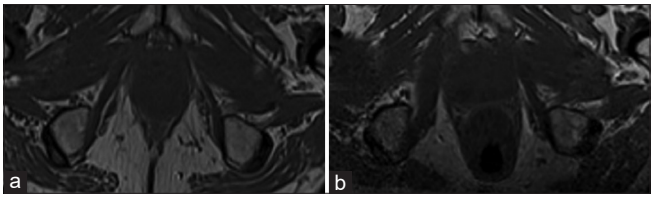

Figure 2: Magnetic resonance imaging without rectal retractor (a) and with rectal retractor (b)

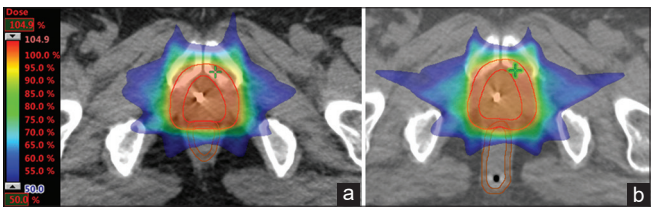

Figure 3: Planning computed tomography without rectal retractor (a) and with rectal retractor (b) for one representative patient, the clinical target volume (red), the planning target volume (orange) and the rectal wall (brown). Note that the rectal retractor pushes the posterior rectal wall away from prostate and does not increase the volume of the anterior rectal wall in the high dose regions

RR: mean dose to the RW (D_{mean}), the volume of the RW receiving 50 Gy (V_{50Gy}), 60 Gy (V_{60Gy}), 70 Gy (V_{70Gy}), 75 Gy (V_{75Gy}), and 78 Gy (V_{78Gy}) in percentage of contoured RW, the RW V_{50Gy} and V_{70Gy} in absolute volume (cc), dose to 30 and 50% of the RW volume (D30% and D50%), and dose to 5 cc of the RW volume (D_{5cc}). We have also investigated the ability of the RR in the reduction of the rectal V_{70Gy} ≥25% in comparison with the plan without using an RR. This was clinically relevant because the rectal V_{70Gy} is associated with late gastrointestinal toxicity, and the 25% reduction showed the improvement in rectal dosimetry when IMRT was employed instead of 3DCRT.[16] Furthermore, the evaluation of pain related to the retraction of the rectum was done with the visual analog score (VAS).

Statistical analysis

Statistical analysis was performed using the SPSS 16.0 software (SPSS, Chicago, Illiniois). Comparisons between without RR and with RR plan characteristics and doses were performed by the nonparametric Wilcoxon signed-rank test. We calculated mean difference, median difference, and 95% confidence interval of the mean over all patients to express relative reduction of the rectal V_{70Gy}. The confidence interval was computed using the *t*-distribution. Two-sided $P < 0.05$ was considered statistically significant.

RESULTS

There was no statistically significant difference in PTV volumes between the plan with RR and without RR (153.5 ± 42.5 cc vs. 145.8 ± 39.3 cc, $P = 0.695$). The mean ± standard deviation (SD) RW volumes with and without RR were 29.3 ± 5.9 cc and 28.8 ± 6.1 cc, respectively, and were not statistically significant difference ($P = 0.084$). The mean bladder volumes were 139.4 ± 61.7 cc with RR and 133.6 ± 58.2 without RR and did not differ statistically significant ($P = 0.074$).

The comparison of dosimetric parameters for PTV, bladder, and RW between the plan with RR and without RR is outlined in Table 2. The plan dosimetric parameters were not statistically significant differences between the plan with and without RR, as observable in Table 2 and Figure 4. The volume of PTV receiving 95% of the prescribed dose ($V_{95\%}$) was equal for both with and without RR ($P = 0.155$). The average of PTV mean dose was 80.5 ± 0.5 Gy with RR and 80.7 ± 0.4 Gy without RR ($P = 0.064$).

As shown in Table 2, the mean dose to the RW (RW D_{mean}) was statistically significant lower for the plan with RR than that for the plan without RR, a mean reduction of 5.8 Gy ($P = 0.003$). A pattern of reduction in the volume of RW (in percentage) receiving 50 Gy, 60 Gy, 70 Gy, 75 Gy, and 78 Gy was detected for a plan with RR in comparison with the plan without RR, as displayed in Table 2 and Figure 5a. Furthermore, RW D_{5cc} was significantly reduced using an RR, an absolute reduction of 11.9 Gy.

The mean rectal V_{70Gy} (%) reduced from 20.0% in the plan without RR to 8.5% in the plan with RR. The use of RR resulted in a relative reduction more than 25% in rectal V_{70Gy} in 100% of patients. Using an RR reduced rectal V_{70Gy} by 58.0% (95% confidence interval, 47.0%–68.7%; $P < 0.001$). The median (range) relative reduction in V_{70Gy} was 62.8% (34.0–81.0).

As displayed in Figure 5b, there is not a significant difference in the dose-volume parameters of the bladder with and without RR. On the other hand, using an RR has no effect on the dose distribution in the bladder. For example, the average bladder V_{70Gy} (±SD) with and without RR was 17.7 (±8.5) Gy and 21.5 (±9.1) Gy, respectively ($P = 0.328$).

The distance between the posterior borders of the CTV and the anterior wall of the rectum was measured for all scans without and with RR at prostate midgland on CT images together with magnetic resonance images as support. The retraction of the rectum resulted in a significant increase in the CTV to rectum space ($P = 0.002$). The mean ± SD (range) CTV to the anterior RW distances was 1.7 ± 1.5 mm (0–5) without RR and 4.4 ± 1.7 mm (2–7) with RR.

Using an RR did not result in serious complications, i.e., severe anal irritation or rectal bleeding, during planning CT. The retraction of the rectum led to a local pressure onto the posterior RW. The retraction of the rectum induced a mean (±SD) pain score 2.7 (±1.3) (range: 1–5). Therefore, the retraction of the rectum induces a mild pain according to the VAS. The RR was discomfort, but all patients tolerated it easily.

Table 2: Comparison of mean±SD dose-volume parameters for planning target volume (PTV), bladder, and rectal wall in plans with and without rectal retractor (*n*=12)

Structure	Mean ± SD		Δ	*P*
	With rectal retractor	Without rectal retractor		
PTV				
$V_{95\%}$ (%)	99.7±0.3	99.8±0.2	0.1	0.155
D_{mean} (Gy)	80.5±0.5	80.7±0.4	0.2	0.064
Bladder				
V_{70Gy} (%)	17.7±8.5	21.5±9.1	3.8	0.328
Rectal wall				
D_{mean} (Gy)	35.1±4.7	40.9±4.7	5.8	0.003
D_{5cc} (Gy)	58.6±6.2	70.5±8.9	11.9	0.003
$D_{30\%}$ (Gy)	45.0±6.2	55.3±6.6	10.3	0.002
$D_{50\%}$ (Gy)	32.4±8.2	38.7±6.0	6.3	0.005
V_{50Gy} (%)	25.8±5.1	35.1±6.7	9.3	0.002
V_{60Gy} (%)	15.1±3.3	26.0±5.7	10.9	0.002
V_{70Gy} (%)	8.5±4.2	20.0±5.0	11.5	0.002
V_{75Gy} (%)	5.6±4.3	16.8±4.6	11.2	0.002
V_{78Gy} (%)	3.5±3.8	14.2±4.3	10.7	0.002
V_{50Gy} (cc)	6.9±1.2	9.3±2.2	2.4	0.003
V_{70Gy} (cc)	2.6±1.5	5.3±1.5	2.7	0.002

PTV: Planning target volume; D_{mean}: Mean dose to the rectal wall; $D_{x\%}$: Dose to x% of the rectal wall volume, VxGy: Rectal wall volume receiving xGy; Dxcc: Dose to x cc of the rectal wall; Δ: Difference between mean without rectal retractor and with rectal retractor values

DISCUSSION

In the present study, using an RR resulted in remarkable reductions in key rectal dose metric parameters. This dosimetric advantage is owing to the retraction of the posterior RW away from the prostate gland as well as the anterior RW. An interesting consequence of using a RR was the absolute increase of 2.7 mm in distance between the CTV and the anterior RW that indicated a good agreement with the results reported by the previous study.[8] In a study by Nilsson *et al*., the average distance between the CTV and anterior RW was 4 mm with RR and 1 mm without RR.[8] As a consequence, a decrease in the volume of RW in high-dose regions can be associated with the narrow separation of the CTV and anterior RW, as well as changes in the shape of the rectum following the rectal retraction. Meanwhile, this prostate–rectum separation can lead to more surprising results in extreme conformal prostate RT techniques such as SBRT. As shown in Figure 5b, the application of an RR did not significantly change dose distribution in the bladder, which is consistent with our previous study.[11]

To the best of our knowledge, this is the first study that investigates the effect of the RR on RW doses during prostate IMRT. Utilizing an RR in the clinical practice may be limited by patient's tolerance, motivation of staff, and anal irritation associated with the daily insertion of the RR. In our previous study[11] and the current study, the RR was well tolerated, and no severe complications were observed owing to the daily insertion of the RR. The long shaft of the rectal rod was very helpful for the insertion and positioning of the RR. As displayed in Figure 1, scaling edges of fiber carbon baseplate in the longitudinal and lateral directions also were very helpful in patient setup and the reproducibility of the RR system position relative to the patient, respectively. Increasing experience has an effect on patient setup time, and complication related to the RR insertion. There is no definitive recommendation regarding optimal retraction of the rectum because it is limited by the patient's tolerance. Overall, at least a retraction of 1.5–2 cm is required to achieve the desired outcomes. With regard to postprostatectomy RT, the RR has a great potential to reduce the volume of the rectum in high-dose regions.[17] In addition, the hydrogel rectal spacer can be applied for postprostatectomy RT in specifically selected patients.[18]

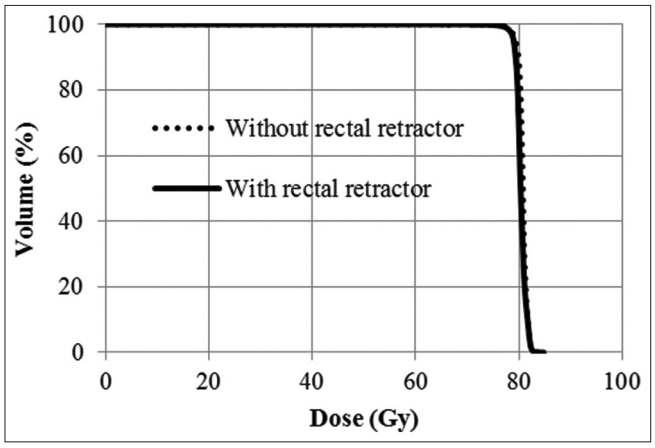

Figure 4: The average dose-volume histogram of the planning target volume (n = 12)

In the present study, the retraction of the rectum was successful in achieving clinical success (≥25% reduction in rectal V_{70Gy}) in 100% of patients, with a mean relative reduction of 58.0%. As outlined in Table 2, other rectal dosimetric parameters were significantly reduced by using a RR. However, a study by Nicolae *et al*. did not find a significant difference in rectal dosimetry using a RR ($P = 0.484$).[10] In that study, using a RR resulted in reducing the rectal V80% from 1.27 cc to 1.07 cc but not statistically significant. Of note, their study did not have a strong statistical plan in comparison with the present study. In addition, they contoured the rectum on CT images, without MRI as support, and stated that using MRI can better clarify the impact of the RR on rectal dosimetry. Previous reports in dose-escalated prostate RT have demonstrated an increase in rectal toxicity. Furthermore, these have shown that this risk can be correlated to the volume of the rectum receiving large radiation doses, including rectal V_{70Gy} >25%.[1,19] From our data, we expect rectal toxicities such as grade ≥2 late rectal toxicities following RT to be very low. From our results, it can be seen that the RR can reduce the volume of the rectum receiving high doses, as well as low and intermediate doses. As the RR reduces the radiation exposure to the rectum, it opens the door for dose-escalated prostate RT. Moreover, the previous study by our group showed that using an RR during

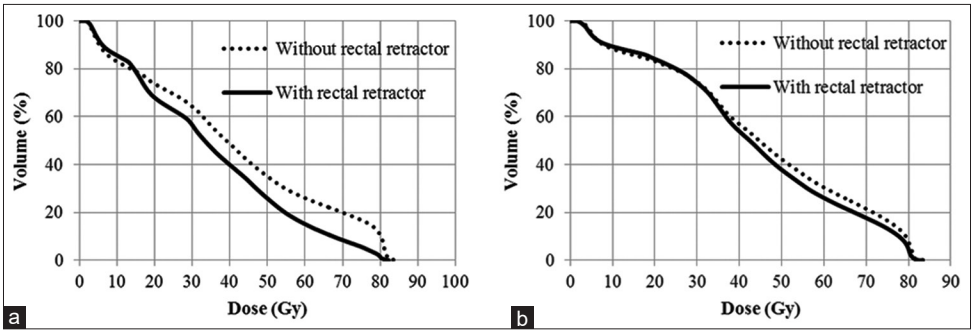

Figure 5: The average dose-volume histogram of the rectal wall (a), and bladder (b) (n = 12)

Table 3: Comparison of effect hydrogel rectal spacer and rectal retractor on rectal V_{70Gy} during prostate radiotherapy

Study	No. of patients	Type of RDD	RT technique	Mean rectal V_{70Gy} (%) without RDD vs. with RDD	Relative reduction (%)
Pinkawa *et al*., 2011[21]	18	PEG-hydrogel	IMRT and 3DCRT; 78 Gy in 2 Gy per fraction	IMRT: 17.2 vs. 7.5 3DCRT: 14.4 vs. 6.1	56 58
Hatiboglu *et al*., 2012[31]	29	PEG-hydrogel	IMRT; 78 Gy in 2 Gy per fraction	14.6 vs. 5.8	60.6
Weber *et al*., 2012[32]	8	PEG-hydrogel	IMRT; 78 Gy in 2 Gy per fraction	9.8 vs. 5.3	46.0
Song *et al*., 2013[22]	48	PEG-hydrogel	IMRT; 78 Gy in 1.8-2 Gy per fraction	13.0 vs. 5.1	60.0
Mahdavi *et al*., 2019[11]	21	Rectal retractor	3DCRT; 80 Gy in 2 Gy per fraction	24.1 vs. 8.8	63.5
Present study	12	Rectal retractor	IMRT; 80 Gy in 2 Gy per fraction	20.0 vs. 8.5	57.5

RDD: Rectal displacement device; PEG: Polyethylene glycol; RT: Radiotherapy; IMRT: Intensity modulated radiotherapy; 3DCRT: Three-dimensional conformal radiotherapy

dose-escalated prostate 3DCRT resulted in the reduction of acute rectal toxicities.[11]

Furthermore, there are other rectal displacement techniques, including ERBs and tissue spacers.[20-22] The deflated ERB inserts into the rectum and inflates with water or air that pushes the posterior RW away from the prostate. Furthermore, ERB moves the anterior RW toward the prostate. The use of ERB results in a significant reduction in the dose to the posterior RW, but a dose to the anterior RW can be increased.[20,23] In contrast to ERBs, using an RR did not lead to an increase in the anterior RW dose and did not deform the shape of the prostate gland [Figure 3]. As shown in Table 2, RW V_{70Gy} in absolute volume (cc) reduced from 5.3 cc in a plan without RR to 2.6 cc in plan with RR. These data show that the RR not only significantly reduces the whole RW doses but also significantly decreases the anterior RW doses. Meanwhile, the RR also significantly reduced radiation doses to the anterior RW in dose-escalated prostate 3DCRT.[11] There was concern about the daily reproducibility of the ERB position that can compromise PTV coverage.[24] Many studies reported the application technique of tissue spacers.[6,21,22] These materials inject or implant in the space between the prostate and anterior RW and create an average separation of 10 mm between the prostate and rectum. The procedure requires anesthesia (local or general) and the injection or implantation was performed by TRUS guidance. Several reports have shown that using tissue spacers significantly reduces the volume of the rectum receiving high doses. A drawback of this technology is an invasive procedure in comparison with ERBs and RR.[6,21,22] Meanwhile, reports showed that prostate–rectum spacers cannot lead to a decrease in the prostate motion and negate the need for IGRT.[25] The cost of these materials also is high.[26] The RR has the potential to reduce the surgical risk associated with tissue spacers for the patients. Economically, the RR is used with one purchase for all patients and reduces costs, while providing tissue spacers for every patient imposes a high cost on the health-care system and patient. Complications associated with the placement of hydrogel rectal spacers are rare, but rectal perforation and ulceration, perineal abscess, and a sense of fullness in the rectum following the hydrogel spacer implantation were reported by several studies.[27-30] Table 3 compares the studies on the effect of hydrogel rectal spacer and the RR on rectal V_{70Gy} during IMRT and 3DCRT. As observable in Table 3, the RR and hydrogel rectal spacers have a similar dose reduction effect on RW V_{70Gy}.

There are many challenges for RT physicists and radiation oncologists during prostate EBRT, including geometric uncertainties, conformal dose distribution, sparing of normal tissues, and prescription dose. With respect to previous studies, the RR can reduce the intrafractional prostate motion during prostate VMAT and also increase the reproducibility of the rectal position.[9,10,33,34] Thus, the use of RR can help to decrease the negative impacts of rectal motion. As shown in the current study, this technique with reduced rectal doses can provide dose escalation. Besides, patients can well tolerate RR. Taken together, these advantages make the RR to be a promising approach in prostate RT to resolve some of the above-mentioned challenges. Daily insertion of RR should be facilitated by lubricant gel or lidocaine jelly to prevent anal irritation. A good discussion and proper technique along with patient collaboration and willingness are factors that can facilitate the utilization of the RR into routine clinical practice. Furthermore, using an RR can be more effective during hypofractionated prostate RT.

CONCLUSION

Our data showed that the use of the RR results in significant dose reductions to the RW. The rectal retraction induced a mild pain but easily tolerable. This dose reduction may lead to a decrease in rectal toxicity. However, further clinical study with a large sample size will be required to elucidate the benefits of the application of the RR on reducing rectal toxicity.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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