해부 · 생물인류학 제 38 권 제 4 호
Anat Biol Anthropol Vol. 38, No. 4 (2025) pp. 273~281
https://doi.org/10.11637/aba.2025.38.4.273

Check for updates

Review Article

Minimizing Rectal Toxicity in Prostate Cancer Radiotherapy: From Anatomical Understanding to Modern Protective Strategies - A Narrative Review

Ye Won Kim[1], Seung Gyu Park[1,2], Euncheol Choi[1,2], Myeongsoo Kim[1], Byungyong Kim[1], Sang Jun Byun[1,2]

[1]*Department of Radiation Oncology, Keimyung University Dongsan Hospital*
[2]*Department of Radiation Oncology, Keimyung University School of Medicine*

Abstract : Rectal toxicity remains one of the major dose-limiting complications in prostate cancer radiotherapy. Due to the close anatomical proximity between the prostate and rectum, even modest dose escalation may induce mucosal and vascular injury, leading to acute or chronic proctitis. This narrative review summarizes the anatomical and physiological characteristics of the rectum, mechanisms of radiation-induced injury, and current strategies to minimize toxicity. Advances in intensity-modulated and image-guided techniques have significantly reduced rectal exposure; however, residual toxicity persists in a subset of patients. Clinical strategies to mitigate rectal injury include consistent bladder filling and rectal emptying protocols, which enhance treatment reproducibility and reduce high-dose exposure. Mechanical interventions, such as endorectal balloons and implantable rectal spacers, provide additional protection by stabilizing the prostate and creating physical separation from the rectum. Among available devices, hydrogel and biodegradable balloon spacers demonstrate the strongest evidence for lowering rectal dose and improving quality of life. Despite these advances, procedural variations, invasiveness, and limited data for pelvic nodal irradiation remain challenges. Future perspectives include the standardization of protocols, incorporation of adaptive image guidance, and the development of artificial intelligence-based predictive models for personalized rectal protection. A comprehensive understanding of rectal anatomy, dose-volume parameters, and emerging technologies is essential to optimize therapeutic outcomes in prostate cancer radiotherapy.

Keywords : Rectum, Anatomy, Prostate cancer, Radiotherapy, Toxicity

INTRODUCTION

Prostate cancer is one of the most prevalent malignancies worldwide and represents a major cause of cancer-related morbidity in men. Radiotherapy is one of the least invasive treatment options for prostate cancer, delivered with or without androgen deprivation therapy. With the development of intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT), dose escalation has become feasible while reducing exposure to surrounding normal tissues [1]. Furthermore, prostate cancer is characterized by a relatively low α/β ratio, estimated at approximately

The author(s) agree to abide by the good publication practice guideline for medical journals.
The author(s) declare that there are no conflicts of interest.
Received: November 21, 2025; **Revised:** December 23, 2025; **Accepted:** December 26, 2025
Correspondence to: Sang Jun Byun (Department of Radiation Oncology, Keimyung University School of Medicine, 1095 Dalgubeol-daero, Dalseo-gu, Daegu 42601, Republic of Korea)
E-mail: kryph@dsmc.or.kr

ISSN 2671-566X (Online)

1.5~3 [2,3]. This biological feature provides a rationale for hypofractionated schedules, which are now increasingly recommended in clinical practice guidelines [3,4]. Despite these advances, radiation-induced toxicity to adjacent normal organs remains a major dose-limiting factor [5].

Among pelvic organs, the rectum is particularly vulnerable due to its immediate anatomical proximity to the prostate [6]. Acute rectal toxicities such as diarrhea, tenesmus, urgency, and rectal discomfort are adverse effects that occur during treatment or within 3 months after the completion of radiotherapy [7,8]. In contrast, late toxicities, including chronic proctitis, bleeding, ulceration, stenosis, and fistula formation, may occur beyond 3 months after the completion of treatment and may appear even several years later. These toxicities are mediated by early mucosal inflammation and edema in the acute phase, progressing to vascular damage, ischemia, and fibrosis in the chronic phase [8,9]. The incidence of grade≥2 late rectal toxicity has historically been reported in 10% to 20% of patients receiving conventional external beam radiotherapy, although modern techniques have reduced this risk, particularly in selected cohorts [10,11].

Given these challenges, increasing attention has been directed toward strategies that minimize rectal irradiation to enhance treatment tolerability and preserve long-term quality of life [6,7]. Accordingly, this review highlights the anatomical and physiological features of the rectum, outlines the clinical manifestations of radiation-induced rectal injury, and examines current approaches to mitigation, with particular emphasis on clinical outcomes as well as advances in emerging technologies.

ANATOMICAL AND FUNCTIONAL ASPECTS OF THE RECTUM

The rectum is the terminal portion of the large intestine, extending approximately 12~18 cm from the rectosigmoid junction to the anal canal within the pelvis. Its superior third is partially covered by peritoneum, the middle third only on the anterior surface, while the inferior third lacks peritoneal covering. Anteriorly, the rectum is near the prostate, seminal vesicles, and bladder, with the average distance between the prostate and the anterior rectal wall being only 2~3 mm [12]. This anatomical relationship underscores its vulnerability to radiation-induced injury during pelvic radiotherapy [12,13].

In addition to its anatomical position, the rectum contains natural curvatures such as the sacral and anorectal flexures, which aid in stool distribution and continence. These functions are further supported by a complex innervation derived from both autonomic and somatic pathways, mediating rectal sensation, compliance, and sphincter control. Acting as a reservoir, the rectum maintains distensibility to accommodate variations in stool and gas volume, and coordinated mechanisms involving the internal and external anal sphincters together with the puborectalis muscle regulate continence and defecation. Radiation-induced fibrosis can impair these physiological properties, leading to urgency and frequency [13].

Denonvilliers' fascia, a multilayered fibromuscular structure located between the prostate and anterior rectal wall, plays a critical role as a natural anatomical barrier. Posterior to the rectal wall, the mesorectum—composed of adipose tissue, lymphatic structures, and vessels—provides additional cushioning that can influence rectal dose distribution. Understanding these anatomical interfaces is essential for optimizing rectal protection strategies, including the placement of rectal spacers [9].

Histologically, the rectal wall is composed of the mucosa, submucosa, and muscularis propria, and contains a rich submucosal vascular plexus that is highly sensitive to radiation. Microvascular damage and ischemia may initially manifest as acute inflammation but can progress over time to chronic proctitis, ulceration, or stricture formation [13].

TOXICITIES

The rectum is anatomically adjacent to the prostate and is one of the most critical organs at risk during radiation therapy [6]. Toxicities are generally graded according to the Common Terminology Criteria for Adverse Events (CTCAE) and the Radiation Therapy Oncology Group (RTOG) morbidity scoring system, which are widely used in clinical studies [14,15].

Acute rectal toxicities are pathophysiologically driven by superficial mucosal injury. Loss of the epithelial barrier exposes the lamina propria to luminal bacteria, thereby triggering an acute inflammatory response [9]. Clinically, these events manifest as diarrhea, tenesmus, urgency, and rectal discomfort. They occur during treatment or within three months of its completion and are generally self-limiting,

with most patients improving with supportive care [8,9].

Chronic rectal toxicities, in contrast, are characterized by persistent ischemia and progressive fibrosis. Radiation-induced vascular injury leads to intimal fibrosis, arteriosclerosis, and endothelial damage, culminating in obliterative endarteritis [9]. This process results in chronic ischemia, tissue atrophy, and full-thickness injury of the rectal wall, with repeated cycles of inflammation and repair further promoting fibrosis. Clinically, late toxicities may arise beyond three months after radiotherapy and can manifest even years later [9,10].

Reported incidences are approximately 15% for grade≥2 and about 2% for grade≥3 gastrointestinal events [10]. The incidence of late rectal toxicity has declined with advances in radiotherapy techniques. In the era of three-dimensional conformal radiotherapy (3D-CRT), rates of grade≥2 late rectal toxicity were reported as high as 15~25%. With the adoption of modern modalities such as IMRT and IGRT, these rates have decreased to approximately 5~15% [11].

Among predictive factors, dosimetric parameters remain the most reliable [16]. In particular, rectal V70 and V74 have been identified as strong predictors of late toxicity, while maintaining the rectal wall V70≤5% (and ideally ≤1%) has been associated with a substantially reduced risk of grade≥2 events [17]. By contrast, clinical factors such as age, PSA level, Gleason score, and the use of androgen deprivation therapy (ADT) have not consistently demonstrated predictive value [16,17].

STRATEGIES TO REDUCE RECTAL TOXICITY

1. Bladder control

The prostate lies anatomically between the bladder superiorly and the rectum posteriorly, variations in the volume of these two adjacent organs can directly affect prostate positioning and the resulting radiation dose distribution. For this reason, numerous strategies have been investigated to reduce rectal toxicity, which can be broadly divided into approaches that optimize bladder and rectal preparation and those that use devices to stabilize or physically separate the prostate and rectum.

Bladder control is one of the simplest and most widely adopted strategies to reduce rectal toxicity in prostate cancer radiotherapy. Variations in bladder volume can alter the relative position of the prostate and adjacent organs at risk, thereby influencing dose distribution to the rectum. In a dosimetric and positional analysis comparing full and empty bladder protocols, Pinkawa et al. demonstrated that bladder distension was associated with prostate positional changes and a reduction in prostate-rectum contact, resulting in decreased high-dose rectal exposure, particularly in the V60~70 range [18]. However, the study also highlighted a key limitation of the full bladder approach: maintaining a consistent degree of bladder filling throughout the treatment course was challenging, leading to increased inter-fraction variability. In contrast, the empty bladder protocol showed inferior rectal sparing but provided improved reproducibility and patient compliance, contributing to more stable treatment setup. These findings underscore the clinical trade-off between dosimetric benefit and treatment reproducibility when selecting bladder preparation strategies in conventional prostate radiotherapy.

2. Rectal emptying

The condition of the rectum is equally important. Gas or stool within the rectum can push the prostate anteriorly, creating discrepancies between the planned and delivered doses. In a prospective study of 20 patients, Arya et al. used daily cone-beam CT to monitor changes in bladder and rectal volumes as well as their effects on prostate displacement [19]. They reported that bladder volume showed large variations, averaging 101.9 cc across fractions, while rectal volume changes were smaller, around 10.2 cc. Nonetheless, these changes had distinct directional effects: a distended bladder displaced the prostate in the anterior-superior direction, while rectal distension caused anterior displacement. Importantly, their analysis emphasized that the bladder and rectum act in a complementary fashion—optimal rectal sparing requires not only a distended bladder but also an empty rectum to fully realize the benefit of bladder filling. Supporting this, a CBCT-based analysis by Umbarkar et al. showed significantly reduced rectal volume variation during morning radiotherapy sessions compared with afternoon sessions, indicating greater rectal reproducibility with earlier treatment delivery [20]. This suggests that even a practical factor such as scheduling treatment sessions earlier in the day may improve reproducibility of prostate positioning and maintain agreement with planned dose distributions.

3. Endorectal balloon (ERB)

In addition to patient preparation, mechanical interventions have been developed to stabilize the prostate and protect the rectum. The endorectal balloon (ERB) is inserted daily into the rectum and inflated to immobilize the prostate and displace the rectal wall posteriorly; the physical expansion of the balloon before and after air inflation is illustrated in Fig. 1. On treatment planning CT images, the inflated ERB occupies the rectal lumen and increases the separation between the prostate and the anterior rectal wall, thereby contributing to prostate stabilization and rectal sparing (Fig. 2). Systematic reviews have shown that ERB use reduces both intrafraction and interfraction prostate motion, which may allow for smaller planning target volume (PTV) margins [21]. Moreover, ERBs are associated with significant reductions in rectal wall high-dose exposure, including V60~70, as well as reductions in mean rectal dose. This is particularly relevant because rectal wall V70 (EQD2, $\alpha/\beta = 2.3$ Gy) has been identified as the most powerful predictor of late grade II rectal toxicity, especially proctitis [17]. Achieving a rectal wall V70 $\leq$ 5%, and ideally $\leq$ 1%, is considered critical to minimize risk. Nevertheless, despite these advantages, ERBs cannot completely prevent prostate motion and must be combined with image-guided corrections. In addition, their requirement for daily insertion creates logistical challenges and patient discomfort, which limit their routine use in clinical practice.

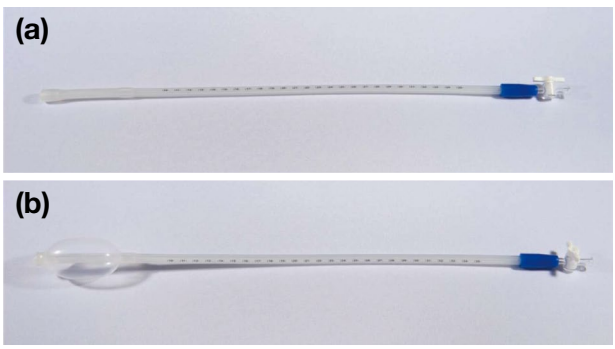

Fig. 1. Photographs of the endorectal balloon (ERB) used during prostate radiotherapy. The ERB before (a) and after (b) air inflation, demonstrating the expansion of the balloon.

4. Implantable rectal spacers (IRS)

Given the anatomic proximity between the prostate and rectum, high-dose regions ($\geq$ 70 Gy) during radiotherapy can easily overlap with the anterior rectal wall. Implantable rectal spacers (IRS) are biodegradable materials inserted into the perirectal space to create a physical distance of 1~2 cm separation, thereby reducing rectal dose and mitigating toxicity [22].

The NCCN Guidelines for Prostate Cancer (2025) recommend perirectal spacers for patients receiving definitive radiotherapy for localized disease. However, spacer implantation is contraindicated in cases of true posterior extraprostatic extension, where safe separation between the prostate and rectum cannot be achieved. Conversely, in high-risk patients without posterior extension, spacer use is permissible. Thus, spacer application should be determined based on anatomical suitability rather than risk classification alone [23].

With a single procedure performed before treatment, the IRS maintains a stable separation throughout the radiotherapy course, improving treatment reproducibility and reducing both acute and late rectal toxicities.

Recent systematic reviews have reported that IRS achieves a mean prostate-rectum separation of approximately 10~20 mm, reducing rectal V70 by 60~85% and lowering the inci-

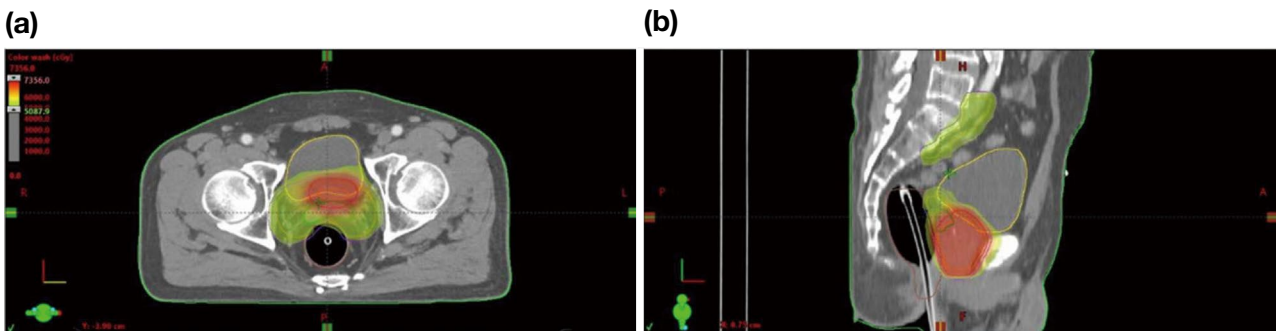

Fig. 2. Axial (a) and sagittal (b) treatment planning CT images of a patient with an inserted endorectal balloon (ERB) during prostate radiotherapy. The inflated ERB is visible within the rectum, stabilizing the prostate position and reducing high-dose exposure to the rectum.

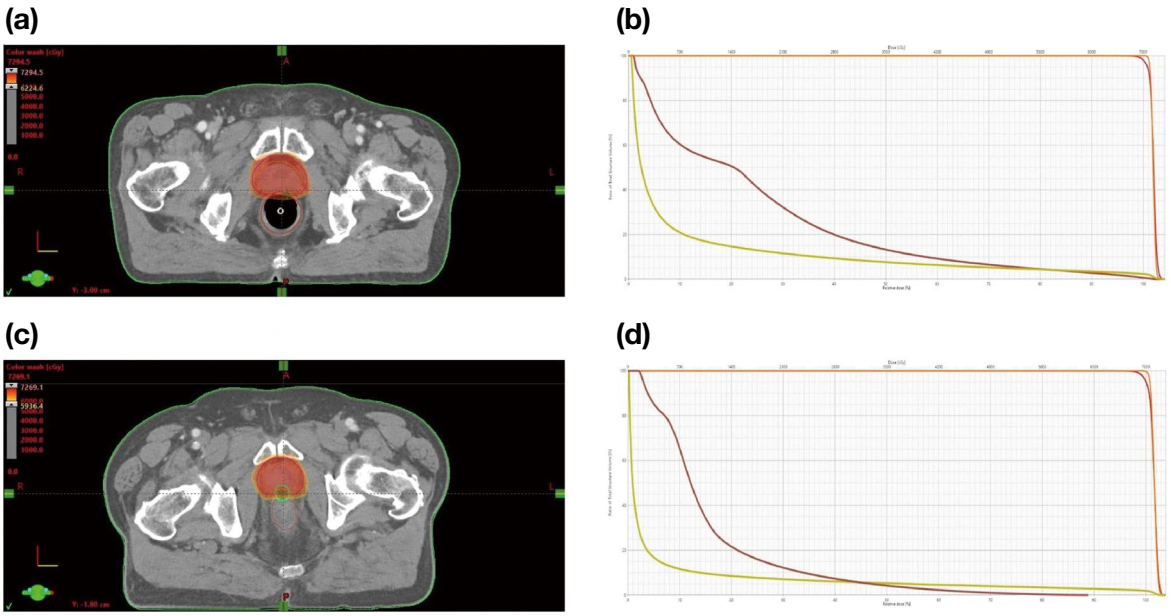

Fig. 3. Comparison of treatment plans with and without a hydrogel rectal spacer (SpaceOAR^{TM}) in prostate cancer radiotherapy. (a) Axial computed tomography (CT) image before spacer insertion, demonstrating the close anatomical proximity between the prostate and rectum. (c) Axial CT image after spacer insertion, showing increased separation between the prostate and rectum with posterior displacement of the rectum following hydrogel spacer placement. In each image, the bladder is contoured in yellow, the rectum in brown, and the hydrogel spacer in light green. (b, d) Dose-volume histograms (DVHs) before (b) and after (d) spacer insertion. After spacer placement, the rectal volume receiving high-dose radiation (e.g., V70, V75) is markedly reduced, providing a dosimetric rationale for rectal toxicity mitigation. In contrast, prescription dose coverage of the prostate target volume is maintained.

dence of grade ≥2 rectal toxicity to below 3~5%. Most insertion-related complications were mild and transient, such as minor pain, temporary urinary discomfort, or mild hematuria, occurring in fewer than 5% of cases.

IRSs are clinically available in four major forms: hydrogel spacer, hyaluronic acid (HA), human collagen (HC), and biodegradable balloon spacer. Among these, hydrogel and balloon spacers are the most widely used and have the strongest clinical evidence base [10,24].

1) Hydrogel spacer

Hydrogel spacers are polyethylene glycol (PEG)-based materials that polymerize within 3~10 seconds after injection, forming a gel that remains stable for more than 3 months. The conventional product (SpaceOAR^{TM}) is visible on MRI but has limited contrast on CT, whereas the iodinated version (SpaceOAR Vue^{TM}) provides enhanced visibility for CT-based planning and daily image guidance. The representative product, SpaceOAR^{TM} (Boston Scientific, Marlborough, MA, USA), provides approximately 1~1.5 cm of prostate-rectum separation, significantly reducing rectal wall dose [24]. This geometric separation and posterior displacement of the rectum are illustrated on axial planning CT images before and after spacer insertion (Fig. 3a and 3c).

In a multicenter randomized controlled trial, Mariados et al. evaluated patients with cT1~T2, PSA ≤20, and Gleason ≤7 prostate cancer, comparing the spacer and control groups. The mean prostate-rectum distance increased to 12.6 mm in the spacer group versus 1.6 mm in controls, with significant reductions in rectal V70 and V50 (both $p<0.0001$). Consistent with these findings, dose-volume histogram comparisons demonstrate marked reductions in rectal high-dose exposure after spacer placement while maintaining target dose coverage (Fig. 3b and 3d). Late rectal toxicity was significantly lower in the spacer group, and bowel quality of life, measured by EPIC scores, improved at both 6 months and 3 years ($p=0.002$, $p=0.02$) [25].

Multiple meta-analyses have consistently demonstrated that hydrogel spacers reduce both acute and late rectal toxicity, particularly in hypofractionated regimens. Although the reduction in severe (grade ≥3) toxicity is modest, the device significantly decreases grade 1~2 events and improves patient quality of life. However, most published studies have

Table 1. Characteristics of hydrogel and balloon spacer

Characteristic	Hydrogel spacer	Balloon spacer
Material	Polyethylene glycol (PEG)-based hydrogel	Biodegradable polymer balloon filled with saline
Insertion approach	Transperineal injection	Transperineal balloon insertion
Mean separation	1~1.5 cm	1.8~2 cm
Degradation time	Stable for >3 months	Absorbed within 6 months
Shape	Variable	Constant and symmetric
Reposition possible	No	Yes
Procedural complexity	Moderate	Higher
CT visibility	Limited (SpaceOAR™), Enhanced with iodine (SpaceOAR Vue™)	Intrinsic (salin-filled)

Comparison of commercially available rectal spacer systems used in prostate radiotherapy. The listed characteristics are derived from published clinical trials, systematic reviews, and manufacturer-provided technical specifications.

evaluated the dosimetric and clinical benefits of hydrogel spacers in patients receiving prostate±seminal vesicle radiotherapy. Evidence regarding its efficacy and safety when pelvic lymph nodes are included in the treatment field remains limited [26].

2) Balloon spacer

To overcome the limitations of hydrogels—such as their inability to be repositioned after injection and potential diffusion into surrounding tissue—a biodegradable balloon-type spacer has been developed. The BioProtect® biodegradable balloon spacer (BioProtect Ltd., Herzliya, Israel) system, inserted via a transperineal approach and inflated with saline, creates a stable and symmetric space between the prostate and rectum. The saline-filled balloon is inherently visible on CT without the need for additional contrast agents, facilitating treatment planning and daily verification [24].

In a multicenter randomized trial by Song et al. including 222 patients with localized prostate cancer, rectal V70 decreased from 7.0% to 1.1%, with 97.9% of patients showing ≥25% V70 reduction ($p<0.001$). The mean prostate-rectum separation was 19±3.7 mm, and device-related grade≥1 adverse events occurred in 18%, compared with 23% in controls. Grade≥2 rectal toxicity was 4.3% in the balloon group versus 6.5% in controls. The balloon spacer offers advantages including potential repositioning, symmetrical space formation, and complete absorption within six months (98.5%) [27].

Systematic reviews have shown that balloon spacers create slightly greater mean separation (approximately 18~20 mm) and more pronounced rectal dose reduction than hydrogel spacers, though the procedure is technically more demanding and long-term data remain limited. Nonetheless, recent evidence supports the safety and efficacy of balloon spacers, while emphasizing the need for further studies on long-term outcomes and cost-effectiveness [24].

Collectively, implantable rectal spacers represent the most direct and mechanical strategy for minimizing rectal toxicity in prostate radiotherapy. The key characteristics, advantages, and limitations of hydrogel and balloon spacers are summarized in Table 1. Their use significantly reduces rectal radiation dose and improves patients' quality of life, as demonstrated across multiple prospective studies and systematic reviews.

Taken together, these strategies demonstrate the multifactorial approach required to minimize rectal toxicity in prostate radiotherapy. Consistent bladder filling and rectal emptying protocols, attention to treatment timing, and the use of intrarectal or interspace devices all contribute to reducing high-dose rectal exposure. Although each method has specific strengths and limitations, their shared aim is to improve treatment reproducibility, reduce the risk of toxicity, and ultimately enhance the therapeutic ratio in prostate cancer radiotherapy.

LIMITATIONS AND FUTURE DIRECTIONS

Although numerous strategies have been developed to minimize rectal toxicity in prostate radiotherapy, current evidence is still limited by methodological and clinical factors. The following section summarizes the major challenges identified in the literature and outlines future directions to

enhance the effectiveness and applicability of rectal toxicity-reduction approaches.

Most studies have been single-institutional, retrospective, and small in scale, typically including fewer than 200 patients [24]. Such designs are inherently prone to selection bias, lack representativeness, and restrict the generalizability of findings across diverse clinical settings.

In terms of clinical applicability, the majority of available data are derived from patients receiving definitive prostate-only radiotherapy. Evidence addressing more complex scenarios-such as pelvic nodal irradiation, re-irradiation, or concurrent chemoradiotherapy—remains incomplete [27,28]. Consequently, the true efficacy and safety of these rectal protection strategies in broader or more advanced clinical contexts have yet to be established.

Procedural and technical limitations are also evident. Studies evaluating mechanical devices such as ERBs and implantable rectal spacers (IRSs) have reported procedural invasiveness, cost burden, and operator-dependent variability [24]. However, standardized implantation criteria and management protocols are still lacking. Moreover, evidence on long-term durability is insufficient, and the persistence of rectal protection after complete hydrogel absorption has not been clearly demonstrated [25].

Inter-institutional variability further complicates clinical translation. Bladder filling and rectal emptying protocols, the frequency of image guidance, and the selection criteria for spacer insertion differ substantially across centers [18]. As a result, reproducibility and consistent outcome comparisons between institutions remain challenging, underscoring the need for harmonized clinical standards.

To overcome these limitations, future research should prioritize the generation of high-quality evidence through multi-institutional, prospective, and randomized clinical trials [29]. These studies should specifically evaluate rectal toxicity-reduction strategies in contemporary treatment settings, including hypofractionation, stereotactic body radiotherapy (SBRT), pelvic nodal irradiation, and re-irradiation. Long-term follow-up is essential to characterize late toxicity patterns and to determine the sustained protective effects of these interventions.

Further technical refinement and optimization of mechanical devices are also required. Standardized investigations addressing insertion technique, spacer volume, CT/MRI visibility, maintenance duration, and timing relative to treatment initiation would improve reproducibility [24]. Clearer patient selection criteria should be established, and clinical trials should expand to include patients undergoing pelvic nodal irradiation, re-irradiation, or hypofractionated regimens [20]. In addition, prospective safety registries and cost-effectiveness analyses are also warranted to evaluate real-world applicability.

Moreover, the integration of artificial intelligence (AI) and machine learning offers promising opportunities for personalized toxicity prediction [29]. By incorporating anatomical, dosimetric, and clinical variables, AI-driven models may enable individualized risk stratification and guide proactive interventions such as preemptive spacer insertion or tailored bowel preparation. Beyond static DVH-based models, dynamic systems that integrate dose accumulation, adaptive planning, and real-time imaging data are expected to further improve precision and patient safety.

Collectively, these directions emphasize the need for evidence-based standardization, technological innovation, and personalized treatment planning to further reduce rectal toxicity and optimize clinical outcomes in prostate radiotherapy.

CONCLUSION

Rectal toxicity remains one of the major dose-limiting complications in prostate radiotherapy. A comprehensive understanding of rectal anatomy, dosimetric predictors, and organ motion is essential to minimize radiation-induced injury. Consistent bladder filling and rectal emptying protocols, together with modern image-guided techniques, contribute to improved treatment reproducibility and reduced inter-fractional uncertainty. Mechanical approaches, such as ERBs and implantable rectal spacers, have demonstrated substantial reductions in rectal dose exposure, with hydrogel spacers showing the most robust clinical evidence to date.

Despite these advances, severe (grade $\geq$2) gastrointestinal toxicity has not been completely eliminated, indicating that optimal patient selection, individualized preparation protocols, and precise integration of real-time image guidance remain critical. Future research should focus on integrating dosimetric and volumetric parameters with emerging predictive modeling—such as artificial intelligence-based risk stratification—to personalize rectal protection strategies and further enhance the therapeutic ratio in prostate cancer radiotherapy.

REFERENCES

1. Vanneste BG, Van Limbergen EJ, Van Lin EN, van Roermund JG, Lambin P. Prostate cancer radiation therapy: what do clinicians have to know? Biomed Res Int. 2016;2016: 6829875.
2. Brenner DJ, Hall EJ. Fractionation and protraction for radiotherapy of prostate carcinoma. Int J Radiat Oncol Biol Phys. 1999;43:1095-101.
3. Miralbell R, Roberts SA, Zubizarreta E, Hendry JH. Dose-fractionation sensitivity of prostate cancer deduced from radiotherapy outcomes of 5,969 patients in 25 randomized trials. Int J Radiat Oncol Biol Phys. 2012;82:e17-24.
4. Dearnaley D, Syndikus I, Mossop H, Khoo V, Birtle A, Bloomfield D, et al. Conventional versus hypofractionated high-dose IMRT for prostate cancer: 5-year outcomes of the randomised CHHiP trial. Lancet Oncol. 2016;17:1047-60.
5. Tree AC, Ostler P, van der Voet H, Chu W, Loblaw A, Ford D, et al. Intensity-modulated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): 2-year toxicity results from an open-label, randomised, phase 3, non-inferiority trial. Lancet Oncol. 2022;23:1308-20.
6. Michalski JM, Lawton C, El Naqa I, Ritter M, O'Meara E, Seider MJ, et al. Development of RTOG consensus guidelines for the definition of the clinical target volume for post-operative conformal radiation therapy for prostate cancer. Int J Radiat Oncol Biol Phys. 2010;76:361-8. https://doi.org/10.1016/j.ijrobp.2009.02.006
7. Folkert MR, Sato R, Yu JB, Vannan D, Bhattacharyya S, Noriega C, et al. Bowel disorder incidence and rectal spacer use in patients with prostate cancer undergoing radiotherapy. JAMA Netw Open. 2025;8:e250491.
8. Dahiya DS, Kichloo A, Tuma F, Albosta M, Wani F. Radiation proctitis and management strategies. Clin Endosc. 2022;55: 22-32.
9. Tzelves L, Protogerou V, Varkarakis I. Denonvilliers' fascia: the prostate border to the outside world. Cancers (Basel). 2022;14:688. https://doi.org/10.3390/cancers14030688
10. Ohri N, Dicker AP, Showalter TN. Late toxicity rates following definitive radiotherapy for prostate cancer. Can J Urol. 2012;19:6373-80.
11. Zelefsky MJ, Levin EJ, Hunt M, Yamada Y, Shippy AM, Jackson A, et al. Incidence of late rectal and urinary toxicities after 3D-CRT and IMRT for localized prostate cancer. Int J Radiat Oncol Biol Phys. 2008;70:1124-9.
12. Ajdžanović V, Miler M, Šošić-Jurjević B, Filipović B. The close proximity between the human rectum and prostate: anatomical and clinical significance. J Mens Health. 2023.
13. Rao SS. Pathophysiology of adult fecal incontinence. Gastroenterology. 2004;126(1 Suppl 1):S14-22.
14. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Published November 27, 2017.
15. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995;31:1341-6.
16. Swanson GP, Stathakis S. Rectal dose constraints for intensity modulated radiation therapy of the prostate. Am J Clin Oncol. 2011;34:188-95.
17. Spohn SKB, Radicioni G, Eisfelder M, Zamboglou C, Baltas D, Grosu AL, et al. Predictors of radiation-induced late rectal toxicity in prostate cancer treatment: a volumetric and dosimetric analysis. Front Oncol. 2024;14:1371384. https://doi.org/10.3389/fonc.2024.1371384
18. Pinkawa M, Asadpour B, Gagel B, Piroth MD, Holy R, Eble MJ. Prostate position variability and dose-volume histograms in radiotherapy for prostate cancer with full and empty bladder. Int J Radiat Oncol Biol Phys. 2006;64:856-61. https://doi.org/10.1016/j.ijrobp.2005.08.016
19. Arya R, Goyal H, Naik A, Gurjar OP. A prospective observational study to analyse the influence of bladder and rectal volume changes on prostate radiotherapy using IMRT. Rep Pract Oncol Radiother. 2020;25:312-17. https://doi.org/10.1016/j.rpor.2020.03.004
20. Umbarkar P, Kannan V, Anand VJ, Deshpande S, Hinduja R, Babu V, et al. A comparative study of rectal volume variation in patients with prostate cancer: a tertiary care center study. Radiography (Lond). 2023;29:845-50.
21. Smeenk RJ, Louwe RJ, Langen KM, van Lin EN, van der Heide UA. Endorectal balloon in prostate radiotherapy: a systematic review. Radiother Oncol. 2010;95:293-302. https://doi.org/10.1016/j.radonc.2010.05.004
22. Hamstra DA, Mariados N, Sylvester J, Shah D, Karsh L, Hudes R, et al. Continued benefit to rectal separation for prostate radiation therapy: final results of a phase III trial. Int J Radiat Oncol Biol Phys. 2017;97:976-85.
23. NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer. Version 2.2025.
24. Lippens J, Willems L, Boychak O, Michael Pinkawa M, Orio 3rd PF, Chao MWT, et al. Implantable rectal spacers in prostate cancer radiation therapy: a systematic review. Pract Radiat Oncol. 2025;15:e460-83. https://doi.org/10.1016/j.prro.2025.03.009
25. Mariados N, Sylvester J, Shah D, Karsh L, Hudes R, Beyer D, et al. Hydrogel spacer prospective multicenter randomized controlled pivotal trial: dosimetric and clinical effects of perirectal spacer application in men undergoing prostate image-guided intensity-modulated radiation therapy. Int J Radiat Oncol Biol Phys. 2015;92:971-7. https://doi.org/10.1016/j.

ijrobp.2015.04.030
26. Kwon JK, Jeon J, Bang S, Koo KC, Cho KS, Kim DK. Association of perirectal hydrogel spacer placement with clinical outcomes in patients with prostate cancer undergoing radiotherapy: a systematic review and meta-analysis. World J Mens Health. 2025;43:e250043.
27. Song D, Dabkowski M, Costa P, Nurani R, Kos M, Vanneste B, et al. Prospective, randomized controlled pivotal trial of biodegradable balloon rectal spacer for prostate radiation therapy. Int J Radiat Oncol Biol Phys. 2024;120:1410-20.
28. Serrano NA, Kalman NS, Anscher MS. Reducing rectal injury in men receiving prostate cancer radiation therapy: current perspectives. Cancer Manag Res. 2017;9:339-50
29. Parkinson C, Matthams C, Foley K, Spezi E. Artificial intelligence in radiation oncology: A review of its current status and potential application for the radiotherapy workforce. Radiography (Lond). 202127 Suppl 1:S63-8.