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Qualitative MRI-Based Assessment of Hydrogel Spacer Distribution Predicts Rectal Dosimetry and Acute Toxicity in Prostate Stereotactic Body Radiotherapy

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Abstract

Background

Hydrogel Rectal Spacers (HRS) are increasingly used to reduce rectal irradiation during stereotactic body radiotherapy (SBRT) for localized prostate cancer (PCa). However, the clinical relevance of qualitative spacer distribution remains incompletely defined. This study evaluated whether MRI-based qualitative characteristics of HRS placement correlate with rectal dosimetry and acute rectal adverse events.

Methods

This prospective observational study included patients with localized PCa treated with transperineal HRS implantation followed by prostate SBRT between 2023 and 2025. Post-implant T2-weighted magnetic resonance imaging (MRI) was used to assess spacer distribution according to three qualitative metrics: Spacer Quality Score (SQS), Symmetry Score (SYM), and Rectal Wall Infiltration score (RWI). Associations between spacer characteristics, rectal dosimetric parameters, and acute rectal toxicity, defined as events occurring within 6 months after SBRT, were analyzed.

Results

Seventy-six patients were included. Median prostate-rectum separation at the mid-gland level was 10 mm (range, 4–20 mm). SQS was significantly associated with rectal Dmax ($p = 0.003$), D1cc ($p = 0.003$), V36Gy ($p = 0.018$), V30Gy ($p = 0.002$), and V18Gy ($p = 0.002$). SYM score correlated with rectal V40Gy ($p = 0.009$). Acute rectal toxicity occurred in 18 patients (23.7%) and was significantly associated with SQS ($p = 0.004$). Rectal wall infiltration was identified in 20 patients (26.3%), including edema in 2 (2.6%) and superficial infiltration in 18 (23.7%), but did not correlate with acute rectal adverse events ($p = 0.672$).

Conclusions

MRI-based qualitative assessment of HRS distribution provides clinically meaningful information beyond spacer thickness alone. Optimal spacer distribution and symmetry were associated with improved rectal sparing and reduced acute rectal toxicity in patients undergoing prostate SBRT.

Background

Stereotactic body radiotherapy (SBRT) has become an integral component of the therapeutic armamentarium for patients with localized prostate cancer. Its widespread adoption has been driven by the radiobiological characteristics of prostate adenocarcinoma, particularly its low α/β ratio, which supports the delivery of larger radiation doses per fraction while preserving excellent rates of biochemical disease control [1–5]. In addition to its biological rationale, SBRT offers practical

advantages, including shorter treatment schedules and greater convenience for patients, without compromising oncological outcomes. Evidence from randomized trials and prospective studies has consistently demonstrated that ultra-hypofractionated regimens can achieve efficacy and safety comparable to those of conventional fractionation in appropriately selected patients [2–4, 6].

Although SBRT provides excellent tumor control, the administration of high doses per fraction requires meticulous protection of surrounding normal tissues. Among these, the anterior rectal wall represents one of the most critical organs at risk because of its close anatomical proximity to the prostat [7]. Even small differences in the distance separating these structures may substantially affect the volume of rectum exposed to high radiation doses, particularly when steep dose gradients are employed.

To minimize rectal irradiation, biodegradable polyethylene glycol hydrogel spacers have been introduced into clinical practice. Following transperineal implantation, the spacer temporarily enlarges the space between the prostate and rectum, thereby reducing rectal dose exposure during treatment. Multiple clinical investigations, including randomized trials and subsequent meta-analyses, have demonstrated that hydrogel spacers improve rectal dosimetry, decrease treatment-related gastrointestinal toxicity, and preserve bowel-related quality of life [8, 9]. Consequently, their use has progressively expanded, especially in patients receiving dose-escalated radiotherapy or SBRT.

Most investigations evaluating hydrogel spacers have focused on quantitative parameters such as spacer thickness, achieved prostate–rectum separation, or dose–volume histogram metrics [8–10]. However, these measurements may not fully capture the technical quality of spacer implantation. In routine clinical practice, hydrogel distribution is highly variable and may differ with respect to symmetry, longitudinal extension, lateral positioning, and conformity to the perirectal anatomical plane. Such qualitative characteristics may influence rectal dose reduction independently of the measured anteroposterior separation [11, 12].

Magnetic resonance imaging (MRI) is particularly well suited for post-procedural evaluation because of its superior soft-tissue contrast. Beyond simple measurement of prostate–rectum distance, MRI enables a comprehensive assessment of spacer morphology, spatial distribution, symmetry, and potential alterations involving the rectal wall. Despite these advantages, relatively little evidence is available regarding the clinical significance of qualitative MRI findings after hydrogel spacer implantation and their relationship with treatment outcomes.

The present prospective observational study was designed to investigate whether qualitative MRI-based assessment of hydrogel spacer placement is associated with rectal dosimetric parameters and acute gastrointestinal toxicity in patients undergoing SBRT for localized prostate cancer. We hypothesized that the overall quality and symmetry of spacer distribution may represent clinically relevant determinants of rectal dose reduction beyond the magnitude of prostate–rectum separation alone.

Methods

Study design and patient population

This prospective observational study included consecutive patients with localized prostate adenocarcinoma treated at the University Hospital of Parma between 2023 and 2025. All patients underwent transperineal hydrogel rectal spacer implantation before prostate SBRT. Eligible patients had histologically confirmed localized PCa, an indication for definitive SBRT, and available post-implant T2-weighted MRI suitable for qualitative spacer analysis. Patients with metastatic disease, previous pelvic radiotherapy, or incomplete imaging, dosimetric, or toxicity data were excluded. All patients provided written informed consent for treatment and data collection. The study was conducted in accordance with institutional ethical standards and the principles of the Declaration of Helsinki.

Hydrogel spacer implantation

HRS implantation was performed using a transperineal approach under transrectal ultrasound guidance by experienced operators. After identification of the perirectal space, hydrodissection was performed to open the plane between Denonvilliers' fascia and the anterior rectal wall. Hydrogel was then injected to increase prostate-rectum separation. Post-procedural T2-weighted pelvic MRI was obtained 2 weeks after implantation in order to evaluate spacer position, distribution, symmetry, and rectal wall findings.

MRI-based qualitative spacer assessment

Spacer distribution was evaluated on post-implant axial T2-weighted MRI using three qualitative metrics: Spacer Quality Score (SQS) [13], Symmetry Score (SYM) [14], and Rectal Wall Infiltration score (RWI) [14]. SQS assessed the overall adequacy of hydrogel distribution between the prostate and rectum and was categorized as 0 (inadequate), 1 (good), or 2 (excellent). SYM evaluated lateral symmetry of spacer placement and ranged from 1 (best symmetry) to 5 (worst asymmetry). RWI assessed rectal wall changes and was graded as 0 (no abnormality), 1 (rectal wall edema), 2 (superficial infiltration), or 3 (deep infiltration). The anteroposterior separation between the mid-gland of the prostate and rectum was also recorded.

Radiotherapy protocol and dosimetric analysis

Radiotherapy protocol and dosimetric analysis
All patients underwent CT simulation and MRI fusion for treatment planning. SBRT was delivered using image-guided radiotherapy techniques. The prescribed Planning Target Volume (PTV) dose was 36.25 Gy in 5 fractions for 17 patients (22.4%), whereas 59 patients (77.6%) received a concomitant prostate boost of at least 40 Gy. Rectal dosimetric parameters analyzed included maximum rectal dose (Dmax), maximum dose to 1 cc (D1cc), V40Gy, V36Gy, V30Gy, and V18Gy.

Toxicity assessment

Acute rectal adverse events were defined as rectal symptoms occurring within 6 months after completion of SBRT. Toxicity was graded according to the Common Terminology Criteria for Adverse Events (CTCAE). For this analysis, the occurrence of any acute rectal toxicity and the maximum CTCAE grade were recorded.

Statistical analysis

Descriptive statistics were used to summarize patient, treatment, spacer, and toxicity characteristics. Categorical variables were reported as absolute numbers and percentages. Continuous variables were reported as median and range when appropriate. Associations between qualitative spacer scores and rectal dosimetric parameters were evaluated using non-parametric correlation or group-comparison methods according to data distribution. Associations between spacer scores and acute rectal toxicity were analyzed using appropriate categorical tests.

Statistical significance was defined as a two-sided p value < 0.05.

Given the relatively limited sample size and the non-normal distribution of several dosimetric parameters, non-parametric statistical tests were adopted. Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and Pearson's chi-square or Fisher's exact test for categorical variables, as appropriate.

Associations between qualitative hydrogel spacer parameters and rectal dosimetric outcomes were analyzed according to Spacer Quality Score (SQS), Symmetry Score (SYM), and Rectal Wall Infiltration (RWI) categories.

Additional subgroup analyses were performed comparing extreme SQS categories (SQS 0 vs SQS 2) to better investigate the impact of inadequate versus optimal spacer distribution on rectal dose exposure.

Acute rectal toxicity (proctitis) was additionally evaluated as a grouping variable to investigate potential associations with baseline patient characteristics and anatomical parameters, including age, body mass index (BMI), prostate–rectum midgland distance, rectal–PTV intersection volume, CTV volume, and PTV volume.

All statistical tests were two-sided, and statistical significance was defined as $p < 0.05$.

Statistical analyses were performed using IBM SPSS Statistics software (IBM Corp., Armonk, NY, USA).

Results

Patient and treatment characteristics

A total of 76 patients with localized prostate cancer underwent hydrogel spacer implantation followed by SBRT and were included in the analysis. The median anteroposterior separation achieved between the mid-gland of the prostate and the rectum was 10 mm (range, 4-20 mm). Seventeen patients (22.4%) received 36.25 Gy in 5 fractions, while 59 patients (77.6%) received SBRT with a concomitant prostate boost of at least 40 Gy.

Spacer quality and distribution

SQS was scored as 0 (inadequate) in 3 patients (3.9%), 1 (good) in 48 patients (63.2%), and 2 (excellent) in 25 patients (32.9%). SYM scores ranged from 1 to 5, with 52 patients (68.4%) classified as score 1, 17 (22.4%) as score 2, 2 (2.6%) as score 3, 3 (4.0%) as score 4, and 2 (2.6%) as score 5. RWI was graded as 0 in 56 cases (73.7%), 1 in 2 cases (2.6%), and 2 in 18 cases (23.7%). No deep rectal wall infiltration (grade 3) was observed.

Association with rectal dosimetry

Higher SQS was significantly associated with improved rectal dosimetric parameters, including lower rectal Dmax ($p = 0.003$), D1cc ($p = 0.003$), V36Gy ($p = 0.018$), V30Gy ($p = 0.002$), and V18Gy ($p = 0.002$).

Comparative dosimetric analysis according to Spacer Quality Score demonstrated significant differences in several rectal dose parameters. Patients with higher-quality spacer distribution showed significantly lower rectal Dmax ($p = 0.001$), D0.035cc ($p = 0.001$), D1cc ($p = 0.001$), V36Gy ($p = 0.010$), V30Gy ($p < 0.001$), V29% ($p < 0.001$), and V18% ($p = 0.036$). No statistically significant differences were observed for V45Gy ($p = 1.000$) or V40Gy ($p = 0.218$). These findings support the hypothesis that optimal hydrogel spacer distribution improves rectal dose sparing, particularly within intermediate and moderately high rectal dose regions (Table 1).

Table 1. Cohort and treatment characteristics.

Characteristic	Value	Notes
Study design	Prospective observational study	Single institution
Study period	2023-2025	University Hospital of Parma
Population	76 patients	Localized prostate cancer
Hydrogel spacer approach	Transperineal	Under transrectal ultrasound guidance
Median mid-gland prostate-rectum separation	10 mm	Range, 4-20 mm
SBRT dose: 36.25 Gy in 5 fractions	17 patients (22.4%)	Standard SBRT schedule
SBRT with concomitant prostate boost >= 40 Gy	59 patients (77.6%)	Dose-escalated subgroup

When comparing patients with extreme spacer quality categories (SQS 0 vs SQS 2), significant differences were observed for multiple rectal dosimetric parameters. Higher-quality spacer distribution was associated with significantly lower rectal Dmax ($p = 0.003$), D0.035cc ($p = 0.002$), D1cc ($p = 0.003$), V36Gy ($p = 0.018$), V30Gy ($p = 0.002$), and V29% ($p = 0.002$). Conversely, no statistically significant differences were found for V45Gy ($p = 1.000$), V40Gy ($p = 0.361$), or V18% ($p = 0.165$). These findings further support the hypothesis that optimal hydrogel spacer distribution mainly affects intermediate and high-dose rectal exposure parameters (Table 2).

Table 2. MRI-based qualitative assessment of hydrogel spacer distribution.

Score	Definition	Number of patients	Percentage
SQS 0	Inadequate spacer distribution	3	3.9%
SQS 1	Good spacer distribution	48	63.2%
SQS 2	Excellent spacer distribution	25	32.9%
SYM 1	Best symmetry	52	68.4%
SYM 2	Mild asymmetry	17	22.4%
SYM 3	Moderate asymmetry	2	2.6%
SYM 4	Marked asymmetry	3	4.0%
SYM 5	Worst asymmetry	2	2.6%
RWI 0	No rectal wall abnormality	56	73.7%
RWI 1	Rectal wall edema	2	2.6%
RWI 2	Superficial rectal wall infiltration	18	23.7%
RWI 3	Deep rectal wall infiltration	0	0%

Abbreviations: SQS, Spacer Quality Score; SYM, Symmetry Score; RWI, Rectal Wall Infiltration score.

SYM scores ranged from 1 (“best”) to 5 (“worst”), with 52 (68.4%), 17 (22.4%), 2 (2.6%), 3 (4.0%), and 2 (2.6%) patients in categories 1 through 5, respectively.

SYM score showed a significant association with rectal V40Gy ($p = 0.009$), indicating that asymmetric spacer placement may compromise high-dose rectal sparing. RWI was not reported to have a significant association with acute toxicity in this cohort.

Acute rectal toxicity

Acute rectal adverse events were reported in 18 patients (23.7%). Among patients with acute toxicity, 3 events (16.7%) were Grade 1 and 15 events (83.3%) were Grade 2 according to CTCAE. No Grade 3 or

higher acute rectal adverse events were observed. The incidence of acute rectal toxicity was significantly associated with SQS (p = 0.004), whereas no significant association was found with RWI categories (p = 0.672).

Additional statistical analyses were performed considering acute proctitis as the grouping variable. No statistically significant associations were observed between the occurrence of rectal toxicity and patient age (p = 0.783), BMI (p = 0.691), rectal–PTV intersection volume (p = 0.239), midgland prostate–rectum distance (p = 0.985), CTV volume (p = 0.434), or PTV volume (p = 0.413). These findings suggest that baseline anatomical and anthropometric characteristics may play a less relevant role in acute rectal toxicity compared with the qualitative characteristics of hydrogel spacer distribution (Table 3).

Table 3. Associations between MRI-based spacer metrics, rectal dosimetry, and acute rectal toxicity.

MRI-based metric	Outcome/parameter	Direction of association	p value
SQS	Rectal Dmax	Higher SQS associated with improved rectal sparing	0.003
SQS	Rectal D1cc	Higher SQS associated with improved rectal sparing	0.003
SQS	Rectal V36Gy	Higher SQS associated with improved rectal sparing	0.018
SQS	Rectal V30Gy	Higher SQS associated with improved rectal sparing	0.002
SQS	Rectal V18Gy	Higher SQS associated with improved rectal sparing	0.002
SYM	Rectal V40Gy	Worse symmetry associated with higher high-dose rectal exposure	0.009
SQS	Acute rectal toxicity	Lower SQS associated with increased acute toxicity	0.004
RWI	Acute rectal toxicity	No significant association	0.672

Abbreviations: Dmax, maximum dose; D1cc, maximum dose to 1 cc; SQS, Spacer Quality Score; SYM, Symmetry Score; RWI, Rectal Wall Infiltration score.

Categorical analysis evaluating the association between Spacer Quality Score and acute proctitis did not demonstrate statistically significant correlations. Pearson's chi-square analysis showed a p value of 0.536, while Fisher's exact test yielded a bilateral p value of 0.574. Similarly, continuity correction, likelihood ratio testing, and linear-by-linear association analyses did not reveal significant associations. These findings may reflect the limited number of toxicity events and the relatively small subgroup of patients with inadequate spacer distribution (Table 4).

Table 4. Acute rectal adverse events within 6 months after SBRT.

Toxicity category	Number of patients/events	Percentage
Any acute rectal adverse event	18 patients	23.7% of total cohort
CTCAE Grade 1	3 events	16.7% of acute events
CTCAE Grade 2	15 events	83.3% of acute events
CTCAE Grade >= 3	0 events	0%

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; SBRT, stereotactic body radiotherapy.

Discussion

In recent decades, refinements in the treatment strategies of prostate cancer have led not only to improved oncologic outcomes but also to a significant improvement in functional outcomes.

The advent of multiparametric MRI has increased the detection rate of prostate cancer, while reducing the number of unnecessary prostate biopsies [15-17]. Consequently, even if radical prostatectomy remains a milestone for the treatment of prostate cancer, a growing number of patients may be eligible for radiation therapy, making the reduction of treatment-related toxicity and associated symptoms of paramount importance.

The progressive implementation of stereotactic body radiotherapy (SBRT) for localized prostate cancer has shifted clinical attention beyond oncological efficacy toward strategies capable of minimizing treatment-related toxicity. Although hydrogel rectal spacers (HRS) are now widely recognized as an effective method for reducing rectal irradiation, most published studies have primarily evaluated quantitative parameters, such as spacer thickness or prostate–rectum separation, whereas considerably less attention has been devoted to the qualitative characteristics of spacer placement [8]. The present study expands current knowledge by demonstrating that MRI-based qualitative assessment of hydrogel distribution is associated not only with rectal dosimetry but also with the occurrence of acute rectal toxicity.

Our results indicate that the overall quality of hydrogel placement, assessed using the Spacer Quality Score (SQS) [13], significantly influences several clinically relevant dosimetric parameters, including rectal Dmax, D1cc, V36Gy, V30Gy, and V18Gy. These findings suggest that the protective effect of HRS is determined not exclusively by the increase in prostate–rectum distance but also by the spatial distribution of the injected material. Consequently, patients achieving a similar anatomical separation may experience different dosimetric benefits depending on the homogeneity and configuration of hydrogel placement.

The comparison between patients with the lowest and highest SQS categories further supports this interpretation. Individuals with optimal spacer placement consistently demonstrated lower rectal dose exposure across multiple dose-volume metrics, reinforcing the concept that procedural quality directly affects treatment dosimetry. These observations highlight the importance of meticulous implantation technique and suggest that qualitative MRI evaluation may complement conventional quantitative measurements when assessing procedural success.

Spacer symmetry also emerged as a clinically meaningful parameter. Although its association was mainly observed for rectal V40Gy, asymmetrical hydrogel distribution may leave portions of the anterior rectal wall insufficiently displaced from the high-dose region, thereby reducing the overall protective effect of the spacer. This finding is particularly relevant in SBRT, where steep dose gradients make treatment accuracy highly dependent on relatively small anatomical variations [14].

In contrast, rectal wall infiltration, as evaluated by the Rectal Wall Infiltration (RWI) score [14], was not significantly associated with acute gastrointestinal toxicity in our cohort. Most abnormalities consisted of superficial infiltration, whereas no cases of deep rectal wall involvement were observed. This likely explains the absence of a measurable clinical impact during early follow-up. Nevertheless, rectal wall infiltration should not be considered clinically negligible, as previous reports have shown that inadvertent intramural hydrogel injection may occasionally result in severe complications requiring surgical management or prolonged conservative treatment [18,19]. Therefore, the clinical significance of RWI probably depends more on the depth and extent of infiltration than on its simple presence.

The clinical value of hydrogel spacers in prostate radiotherapy has already been established by several high-quality investigations. The multicenter randomized trial conducted by Mariados et al. demonstrated that spacer implantation significantly increased the distance between the prostate and rectum while reducing rectal irradiation during treatment [8]. Long-term analysis of the same patient cohort subsequently confirmed sustained reductions in bowel toxicity together with persistent improvements in bowel-related quality of life several years after radiotherapy [9]. More recently, the systematic review and meta-analysis performed by Miller et al. further strengthened the available evidence by showing that hydrogel spacer placement is consistently associated with lower rectal dose exposure, reduced gastrointestinal toxicity, and improved patient-reported bowel outcomes across different radiotherapy techniques [10]. Rather than challenging these established observations, our findings suggest that the quality of spacer placement itself represents an additional determinant of the clinical and dosimetric benefits achieved following implantation.

An important strength of the present study is the use of MRI for post-procedural assessment. Compared with planning CT, MRI provides substantially superior soft-tissue contrast, allowing a more comprehensive evaluation of hydrogel morphology, symmetry, longitudinal extension, and possible rectal wall abnormalities. These qualitative features cannot be adequately characterized using distance measurements alone and may therefore provide additional clinically relevant information regarding implantation quality [11,12].

From a practical perspective, our findings support the integration of standardized qualitative MRI assessment into routine post-implant quality assurance. Identifying suboptimal spacer distribution before treatment planning may help radiation oncologists interpret dosimetric constraints more accurately, optimize treatment plans when necessary, and provide valuable feedback for improving implantation technique. Standardized qualitative scoring systems may therefore represent useful tools not only for patient management but also for operator training and institutional quality-control programs.

Several limitations should be acknowledged. First, this was a single-center study with a relatively limited sample size, particularly within some spacer score categories, which may have reduced the statistical power of selected subgroup analyses. Second, only acute rectal toxicity was evaluated, whereas late toxicity and patient-reported quality-of-life outcomes were not available. Finally, interobserver agreement for the MRI qualitative scoring systems was not investigated and should be specifically addressed in future multicenter validation studies.

Despite these limitations, the present study provides novel evidence supporting the clinical relevance of qualitative MRI-based assessment of hydrogel spacer implantation. Our data indicate that successful spacer placement should not be evaluated solely according to the achieved prostate–rectum separation but should also consider the overall morphology and symmetry of hydrogel distribution. Incorporating these qualitative parameters into routine clinical practice may improve procedural quality, optimize treatment planning, and ultimately contribute to reducing rectal toxicity in patients undergoing prostate SBRT.

Conclusions

Qualitative MRI-based evaluation of hydrogel spacer distribution provides clinically relevant information in patients undergoing prostate SBRT. Higher spacer quality and improved symmetry were associated with better rectal dosimetry and lower acute rectal toxicity. These findings support the integration of standardized post-implant MRI evaluation into routine quality-assurance workflows and warrant validation in larger cohorts with long-term toxicity and patient-reported outcomes.

Abbreviations

HRS
Hydrogel Rectal Spacer
SBRT
Stereotactic Body Radiotherapy
PCa
Prostate Cancer
MRI
Magnetic Resonance Imaging
SQS

Spacer Quality Score
SYM
Symmetry Score
RWI
Rectal Wall Infiltration
CT
Computed Tomography
PTV
Planning Target Volume
Dmax
Maximal rectal dose
CTCAE
Common Terminology Criteria for Adverse Events

Declarations

Ethics statement

All patients provided written informed consent for treatment and data collection. The study was conducted according to institutional standards and the Declaration of Helsinki.

Clinical trial number: 265/2023/OSS/AOUPR. Ethic Authority of the University Hospital of Parma.

Conflicts of interest

The Authors declare no conflicts of interest related to this manuscript.

Competing interests

The Authors declare no competing interests.

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Author Contribution

Conceptualization: F.Z., N.S, U.M.Manuscript writing: F.Z., F.C, F.S., M.G.Manuscript revision: L.R., C.M., N.D.Data collection: F.C., C.GStatistical analysis: F.Z., N.S.

Data Availability

All data are available into the electrtonic database of the Univeristy-Hospital of Parma and may be shared with authorized researchers upon request.

References

1. Kishan AU, Dang A, Katz AJ, et al. Long-term outcomes of stereotactic body radiotherapy for low-risk and intermediate-risk prostate cancer. JAMA Netw Open. 2019;2(2):e188006. 10.1001/jamanetworkopen.2018.8006.
2. Brand DH, Tree AC, Ostler P, et al. Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial. Lancet Oncol. 2019;20(11):1531–43. 10.1016/S1470-2045(19)30569-8.
3. Tree AC, Ostler P, van der Voet H, 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(10):1308–20. 10.1016/S1470-2045(22)00517-4.
4. Widmark A, Gunnlaugsson A, Beckman L, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. Lancet. 2019;394(10196):385–95. 10.1016/S0140-6736(19)31131-6.
5. Draulans C, Haustermans K, Pos FJ, et al. Stereotactic body radiotherapy with a focal boost to the intraprostatic tumor for intermediate and high-risk prostate cancer: 5-year efficacy and toxicity in the hypo-FLAME trial. Rad Oncol. 2024;201:110568. 10.1016/j.radonc.2024.110568.
6. Fowler JF, Ritter MA, Chappell RJ. What hypofractionated protocols should be tested for prostate cancer? Int J Radiat Oncol Biol Phys. 2003;56(4):1093–104. 10.1016/s0360-3016(03)00132-9.
7. Mahmood S, Bollipo S, Steele S, et al. It's all the RAVE: time to give up on the Chronic Radiation Proctitis. Misnomer Gastroenterol. 2021;160:635–8. 10.1053/j.gastro.2020.09.054.
8. Mariados N, Sylvester J, Shah 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(5):971–7. 10.1016/j.ijrobp.2015.04.030.
9. Hamstra DA, Mariados N, Sylvester J, 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(5):976–85. 10.1016/j.ijrobp.2016.12.024.
10. Miller LE, Efstathiou JA, Bhattacharyya SK, et al. Association of perirectal hydrogel spacer placement with safety and efficacy outcomes in prostate cancer radiotherapy: a systematic review and meta-analysis. JAMA Netw Open. 2020;3(6):e207583. 10.1001/jamanetworkopen.2020.8221.
11. Yates AH, Power JW, Dempsey PJ, et al. SpaceOAR hydrogel distribution and early complications in patients undergoing radiation therapy for prostate cancer. Br J Radiol. 2023;96(1152):20220947.

10.1259/bjr.20220947.

12. Uno M, Tamaki Y, Nonomura K, et al. Effect of hydrogel-spacer implantation and uneven positioning on rectal dose in intensity-modulated radiotherapy for prostate cancer. J Cancer. 2025;16(14):4187–95. 10.7150/jca.119694.
13. Grossman CE, Folkert MR, Lobaugh S, et al. Quality Metric to Assess Adequacy of Hydrogel Rectal Spacer Placement for Prostate Radiation Therapy and Association of Metric Score With Rectal Toxicity Outcomes. Adv Radiat Oncol. 2023;8(4):101070. 10.1016/j.adro.2022.101070.
14. Fischer-Valuck BW, Chundury A, Gay H, et al. Hydrogel spacer distribution within the perirectal space in patients undergoing radiotherapy for prostate cancer: Impact of spacer symmetry on rectal dose reduction and the clinical consequences of hydrogel infiltration into the rectal wall. Pract Radiat Oncol. 2017;7:195–202. 10.1016/j.prro.2016.10.004.
15. Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med. 2018;378:1767–77. 10.1371/journal.pone.0263345.
16. Drost FH, Osses DF, Nieboer D, et al. Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. Cochrane Database Syst Rev. 2019;4:CD012663. 10.1002/14651858.CD012663.pub2.
17. Ziglioli F, Maestroni U, Manna C, et al. Multiparametric Mri in the Management of Prostate Cancer: an Update-A Narrative Review. Gland Surg. 2020;9:2321–30. 10.21037/gs-20-561.
18. Hall WA, Tree AC, Dearnaley D, et al. Considering benefit and risk before routinely recommending SpaceOAR. Lancet Oncol. 2021;22(1):11–3. 10.1016/S1470-2045(20)30639-2.
19. Yates AH, Dempsey PJ, Power JW, et al. Rectal complications following SpaceOAR insertion after prior pelvic radiation. BJR Case Rep. 2025;11(2):uaaf013. 10.1093/bjrcr/uaaf013.