Molina Clinical Policy
Perirectal Spacer for Prostate Radiotherapy
Policy No. 425

Last Approval: 12/10/2025
Next Review Due By: December 2026

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members.[1] References included were accurate at the time of policy approval and publication.

OVERVIEW

Prostate cancer is the most prevalent cancer among males, with an estimated 3.3 million men in the United States living with this cancer as of 2020 (NCI date unknown). Surgical procedures, chemotherapy, cryosurgery, and radiation therapy are among the available treatments for prostate cancer. Radiotherapy is an effective treatment for localized and locally advanced prostate cancer. It can be administered internally as brachytherapy, or externally as external beam radiotherapy (EBRT). Brachytherapy, also known as internal radiation, can be delivered at either a low or high dose rate, with low dose rates used alone or in conjunction with EBRT. EBRT to treat localized prostate cancer are commonly delivered using image-guided conformal radiation therapy, stereotactic body radiotherapy, or intensity modulated radiation therapy and image-guided radiation therapy. Studies indicate that EBRT is highly effective for patients with localized disease, and that increasing the dosage improves biochemical control in patients at intermediate risk; however, increasing the dose may also increase the risk of urinary and gastrointestinal toxicity.

The position of the prostate gland enhances its susceptibility to clinically significant problems from radiation toxicity and is therefore a dose-limiting factor in prostate radiation dose escalation. The establishment of a safety space margin of 4 to 10 millimeters between the prostate and rectum is thought to reduce the risk of rectal toxicity during prostate radiation therapy (Pinkawa 2015). To shield the anterior rectum from radiation, rectal spacers may be placed between the prostate and rectum. However, while the use of rectal displacement devices has increased in recent years, the standard of care for prostate cancer radiation therapy remains to provide treatment without a spacer.

The **SpaceOAR System** is single-use absorbable perirectal spacer device that consists of a polyethylene glycol powder, buffer solution, and specialized tools for mixing and implantation. The mixture forms a synthetic hydrogel spacer intended to protect the anterior rectum during prostate irradiation by temporarily pushing the rectum away from the prostate to reduce the radiation dose delivered to the anterior rectum and reduce rectal complications related to radiation therapy. The radiation oncologist inserts the hydrogel mixture between the rectum and the prostate using transrectal ultrasound guidance, where it remains intact for the duration of the patient's radiation therapy (about three months), after which it is absorbed by the body and eliminated via urine. The device has no intended effect on prostate cancer therapy, other than to protect the rectum.

Barrigel Injectable Gel is intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer to reduce the radiation dose delivered to the anterior rectum. Barrigel is a sterile, transparent, biodegradable gel of stabilized hyaluronic acid at a concentration of 20 mg/mL in phosphate buffered saline. Barrigel utilizes a single syringe system and does not require pre-mixing prior to use.

The **BioProtect Balloon Implant System** is intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer to reduce the radiation dose delivered to the anterior rectum. The BioProtect Balloon Implant System is composed of a balloon made of a biodegradable material that maintains the space for the entire course of prostate radiotherapy treatment and is absorbed by the patient's body in approximately 6 months. The balloon is implanted transperineally in a minimally invasive procedure in the space between the prostate and the rectum under transrectal ultrasound guidance using a dedicated delivery system. Balloon height can be controlled depending on desired spacing, by controlling the amount of saline injected prior to balloon sealing.

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Regulatory Status

The SpaceOAR System (Augmenix Inx, Waltham MA) DEN140030 was approved via the Device Classification Under Section 513(f)(2)(De Novo) database on April 1, 2015 under the product code OVB, for the indication to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer and in creating this space it is the intent of SpaceOAR System to reduce the radiation dose delivered to the anterior rectum. The SpaceOAR System is a polyethylene glycol-based hydrogel that is injected transperineally that maintains space for the entire course of prostate radiotherapy treatment and is completely absorbed by the patient's body over time.

The U.S. Food and Drug Administration (FDA) has cleared additional rectal spacer devices under its 510(k) Premarket Notification process. These biodegradable devices are also placed transperineally and maintain space between the anterior rectal wall and prostate for the entire course of prostate radiotherapy treatment. These devices are absorbed by the patient's body over time. Barrigel Injectable Gel (Palette Life Sciences) K220641 received approval on May 26, 2022. Barrigel is a biodegradable hyaluronic based gel that is injected transperineally. The Bioprotect Balloon Implant System (BioProtect, Ltd.) K222972 received approval on August 25, 2023. This is a balloon spacer that is placed transperineally, filled with up to 17 mL saline, sealed and left in situ.

COVERAGE POLICY

Placement of a biodegradable/biocompatible transperineal spacer (e.g., Space OAR, Barrigel) may be **considered medically necessary** to reduce rectal, urinary, and gastrointestinal toxicity in Members undergoing radiotherapy for prostate cancer when ALL the following clinical criteria are met:

1. Diagnosis of localized or locally advanced prostate cancer with no lymph node involvement
2. Treatment plan includes external beam radiotherapy (including stereotactic body radiotherapy or intensity modulated radiation therapy)
3. Prostate volume is less than 80 ml
4. Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1
5. Documentation of a recent history and physical exam, medical progress notes related to the medical treatment, and any planned surgical and radiation interventions
6. Member is free from ALL the following contraindications:
   a. Active bleeding disorder
   b. Tumor invasion into the rectum and no posterior extraprostatic extension (local tumor growth beyond the fibromuscular pseudocapsule of the prostate gland into the periprostatic soft tissues).
   c. Prior surgery or radiation for prostate cancer treatment
   d. Prostate volume > 80 ml
   e. T3 or T4 disease with posterior extension into the peri-rectal space

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or rendering a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Multiple prospective studies on the use of SpaceOAR have demonstrated reduced radiation exposure and rectal and gastrointestinal toxicities (Chao 2018; [1-2]Chao 2019; [1-2]Hedrick 2017; Juneja 2015; Pinkawa 2011; Pinkawa 2017; Ruggieri 2015; Schorghofer 2019; Te Velde 2019; van Gysen 2014; Whalley 2016; Wilton 2017; Wu 2018).

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Randomized Controlled Trials

Mariados et al. (2023) conducted a randomized, patient-blinded clinical trial to assess whether a hyaluronic acid (HA) perirectal spacer can improve rectal dosimetry and reduce acute grade 2 or higher gastrointestinal (GI) toxicity during hypofractionated radiation therapy (HFRT) for prostate cancer. The study included 201 patients with T1 to T2 prostate cancer, a Gleason score of 7 or less, and a PSA level of 20 ng/mL or less. Participants were randomly assigned in a 2:1 ratio. 136 patients received the HA spacer plus fiducial markers, while 65 patients in the control group received fiducial markers. Both groups subsequently underwent HFRT. Results indicated that 131 patients in the spacer group (98.5%) had at least a 25% reduction in rectum V54, significantly surpassing the 70% acceptable primary endpoint, with an average reduction of 85%. The study also noted reductions in all rectal dose volume histogram (DVH) metrics, including those for the bladder and penile bulb. In the spacer group 4/136 patients experienced grade 2 or higher GI toxicity, compared to 9/65 patients in the control group, representing a significant difference. The authors concluded that the use of an HA-based rectal spacer improves rectal dosimetry and reduces the incidence of grade 2 or higher GI toxicity during HFRT for prostate cancer. This information suggests that incorporating an HA perirectal spacer could provide significant benefits in reducing radiation-induced GI side effects for prostate cancer patients.

Hamstra et al. (2017) published a 3-year follow-up of the pivotal RCT study conducted by Mariados et al. (2015), the single-blind phase 3 trial of IG-IMRT (n = 222). The mean follow-up period was 3 years, involving 63% of the original cohort (46 in control group and 94 in spacer group). Those who received the hydrogel had a smaller volume of rectum treated to volumes from V50 to V80 (P<0.0001 for all). For V50, a 54% relative reduction was found (21% vs 10% for control vs spacer), with increasing relative reductions at higher doses. These included a 79% relative reduction in V70 (10% vs 2 % for control vs spacer) and a 96% reduction in the V80 (4% vs 0.1% for control vs spacer). No differences were found in the dosimetry values for the bladder, bladder wall, or bladder/bladder wall within 1 or 2 cm of the prostate. Grade ≥1 rectal toxicity at 3 years of follow-up was decreased by 75% in the spacer arm (control: 9%, 95% confidence interval; spacer 2%, 95% CI). No grade ≥2 rectal toxicity was observed in the spacer arm (3-year rate: control, 6%; spacer 0%). The authors reported that the benefit of a hydrogel spacer in reducing rectal dose, toxicity, and QOL declines after IG-IMRT for prostate cancer was maintained or increased with a longer follow-up period, providing stronger evidence for the benefit of hydrogel spacer use in prostate radiation therapy. Additional long-term outcomes are required to determine the benefits of hydrogel spacers.

The largest published peer-reviewed study involving the use of the SpaceOAR device was reported by Mariados et al. (2015). This pivotal manufacturer sponsored, prospective, multicenter, single-blind, randomized, controlled trial (RCT) involved 222 subjects (n=222) with clinical stage T1 or T2 prostate cancer who were randomized in a 2:1 fashion to receive image-guided IMRT (79.2 Gy in 1.8-Gy fractions) either with (n=149) or without (n=73) placement of the SpaceOAR system and were followed for 15 months.

Mariados et al. (2015) assessed 222 participants (n=222: 149 with spacer versus 73 without spacer [control]) patients with clinical stage T1 or T2 prostate cancer (NCCN low or intermediate risk). Patients also had Gleason score of ≤ 7, PSA ≤ 20 ng/mL, Zubrod performance status 0 to 1, who were planning to undergo image guided intensity modulated radiation therapy (IG-IMRT). For treatment planning, CT and MRI scans were performed, and this was followed by the implantation of fiducial markers. Participants were randomly assigned to either a spacer injection or no injection: 149 patients received perirectal injection of a hydrogel between the prostate and rectum prior to IG-IMRT and 73 patients received only fiducial markers inserted in the prostate prior to IG-IMRT. Both groups received IG-IMRT at a dosage of 79.2 Gy in 44 segments and were followed for 15 months. Throughout a 15-month period, spacer safety and its impact on rectal irradiation, toxicity, and quality of life (QOL) were evaluated. The hydrogel placement success rate for spacer application was 99%. There were no device-related adverse events, rectal perforations, serious bleeding, or infections in either group, according to the authors. Overall, the rates of acute rectal adverse events were comparable across groups, with fewer spacer patients experiencing rectal pain (p =.02). In the spacer group, there was no late rectal toxicity greater than grade 1. At 15 months, 11.6% of spacer patients and 21.4% of control patients, respectively, had 10-point declines in bowel QOL. At 12 months, MRI scans confirmed spacer absorption. The authors concluded that the use of spacers was well-tolerated. Increased perirectal space reduced rectal irradiation, rectal toxicity severity, and the proportion of patients experiencing bowel QOL declines. The spacer appears to be an effective tool, with the potential to enable advanced prostate radiation therapy protocols. The short follow-up period is a study limitation, as the median time to late GI grade > 2 toxicity was 17 months. The study was also limited by the exclusion of patients with prostate volumes greater than 80 mL, those with extracapsular extension, and those who had previously undergone radiation or surgery. Patients with extracapsular extension run the risk of pushing posterior extracapsular disease further away from the prostate during radiation therapy, whereas patients with prior radiation or surgery may

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develop perirectal scarring, limiting space creation. The use of spacers in these populations, the authors noted, should proceed cautiously in separate clinical trials.

Systematic Reviews and Meta-Analysis

Kwon et al. (2025) published a systematic review and meta-analysis of 35 studies evaluating the impact of perirectal hydrogel spacer placement in 4,664 men receiving external beam radiotherapy for prostate cancer. The review included studies that directly compared patients treated with and without a spacer and reported measurable outcomes related to rectal dosimetry and gastrointestinal or genitourinary toxicities. Overall, men who received a spacer had significantly lower radiation exposure to the rectum, including meaningful reductions in both the highest ($p = 0.02$) and average doses ($p = 0.002$). In addition, the spacer group experienced fewer short-term digestive side effects, with a 36% lower risk of any-grade acute GI symptoms ($p < 0.00001$) and fewer long-term mild symptoms ($p = 0.02$), with the greatest benefit seen in men treated with more intensive radiation schedules. However, the use of a spacer did not significantly reduce serious complications, such as severe digestive or urinary side effects, and results in these categories were not statistically significant. The authors noted that many of the included studies were not randomized, used different treatment techniques, and had varying follow-up times, which limits the strength of the evidence. Overall, the review found that spacers reliably reduce radiation exposure to the rectum and lower the risk of mild side effects, but current research does not show a clear benefit in preventing serious toxicity, and more high-quality studies are needed.

Payne et al. (2021) published a meta-analysis and systematic review evaluating the clinical utility of hydrogel spacers placed prior to stereotactic body radiation therapy in patients with localized prostate cancer. There were 11 prospective and retrospective studies in total. The perirectal space in individuals with SpaceOAR ranged from 9.6 to 14.5 mm across all studies, and rectal irradiation was 29% to 56% lower in those with SpaceOAR compared to those without. The authors noted:

> "Grade ≥ 2 GI toxicity complications were uncommon. In early follow-up, grade 2 GI complications were reported in 7.0% of patients and no early grade 3+ complications were reported. In late follow-up, the corresponding pooled mean rates were 2.3% for grade 2 and 0.3% for grade 3 GI toxicity."

Armstrong et al. (2021) conducted a systematic review of 19 studies (n = 3,622; 1 RCT and 18 nonrandomized comparative studies) of outcomes in prostate cancer patients found that SpaceOAR significantly reduced rectal radiation dose, regardless of radiation therapy type. The device also reduced GI and genitourinary toxicity. Only 1 of the 19 studies was randomized (Mariados et al. 2015). The studies also showed improvements in most urinary, bowel, and sexual QOL measurements, with increases in Expanded Prostate Cancer Index Composite Health-Related QOL Questionnaire domains, although most were not statistically significant. Since no hypofractionation studies were included, additional research is warranted in this area.

Ardekani et al. (2020) performed a systematic literature review on 21 studies that addressed various rectal displacement devices during prostate external beam radiation therapy. Four of these studies focused on the effects of hydrogel spacers. The hydrogel spacer, when compared to the endorectal balloon, significantly reduces rectal dose and toxicity without affecting prostate immobilization. Hydrogel spacers reduced rectal dose and toxicity when compared to endorectal balloons, but had no effect on prostate immobilization, according to the authors' findings.

Miller et al. (2020) published a manufacturer-sponsored systematic review and meta-analysis of the 7 studies (1 RCT and 6 cohort studies) that evaluated the safety and efficacy of the absorbable perirectal spacer (APS) to prevent rectal toxicity in patients with prostate cancer undergoing external beam radiation therapy compared with patients who did not receive a spacer prior to prostate radiotherapy in 1100 men (n=1100). The reviewers found that perirectal hydrogel spacer placement was associated with less rectal irradiation, fewer rectal toxic effects, and higher bowel related QOL in long-term follow-up.

- The percentage of rectal radiation above 70 Gy was 3.5% with SpaceOAR versus 10.4% in controls.
- The spacer did not reduce the risk of early grade 2 or higher rectal toxicity, but it was associated with a reduced risk of late grade 2 or higher rectal toxicity (1.5% vs. 5.7%; 0.06 to 0.99; p =.05).
- Mariados et al. (2015) and Pinkawa et al. (2015) were primarily responsible for these findings. The other two studies included for this outcome (te Velde et al. 2019; Whalley et al. 2016) were imprecise and did not show a significant reduction in rectal toxicity.
- Only two studies (Mariados et al. 2015 and Pinkawa et al. 2017) reported bowel related QOL, with patients treated with SpaceOAR reporting higher QOL.

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The interpretation of these findings is limited by the small number of included studies, the majority of which were non-randomized, and the short duration of follow-up for detecting long-term outcomes of rectal irradiation.

Non-Randomized Studies, Retrospective Reviews and Other Evidence
Lin et al. (2021) conducted a retrospective case-control cohort study that analyzed the rectal dosimetry and toxicity outcomes for 70 men with prostate cancer treated with iodine-125 low-dose-rate brachytherapy (LDR-BT). Patients were enrolled between October 2017 and July 2019. Of these patients, 28 (40%) had a rectal spacer (RS) inserted, while 42 (60%) did not. The study used descriptive statistics to compare the safety and dosimetric effects on the rectum and urethra, and the gastrointestinal (GI) and genitourinary (GU) toxicities between the patients with and without the hydrogel spacers. SpaceOAR®, (Boston Scientific, MA, USA) was used for insertion prior to 2020, while after 2020 Barrigel® (Palette Life Sciences, Stockholm Sweden) was used. The patients were then followed up every 3 to 4 months for the first year by the treating radiation oncologist, and every 6 months for the next 5 years. Median follow-up was 23.5 months. There was significantly reduced rectal dosimetry in RS-group vs. non-RS group; the median RV100 was 0.0 cc (IQR, 0.0-0.0 cc) vs. 0.4 cc (IQR, 0.1-1.1 cc) ($p < 0.001$), respectively. The mean rectal D1cc and D2cc were 52.4% vs. 84.2% ($p < 0.001$) and 45.7% vs. 70.0% ($p < 0.001$) for RS and non-RS group, respectively. There were no significant differences in mean urethral dosimetry between groups. Significantly lower incidence of grade-1 acute and late GI toxicities were seen in the RS group compared to the non-RS group (acute: 0% vs. 24%, $p = 0.004$ for acute GI toxicity; late: 4% vs. 33%, $p = 0.003$ for late GI toxicity. There were no reported acute or late grade-2 or above GI toxicities. The study concluded that RS insertion is safe and leads to a significant reduction in rectal dosimetry, which translates into reduced acute and late GI toxicities. The authors disclosed a potential conflict of interest: the corresponding author Associate Professor Michael Chao is an advisory board member for Palette Life Sciences Pty Ltd.

A Hayes Health Technology Assessment (2024) concluded that the overall body of published evidence is of low quality and suggests some potential benefit for use of an absorbable perirectal spacer for the prevention of rectal toxicity and improvement of quality of life in patients undergoing external beam radiation therapy for the treatment of prostate cancer compared with no spacer. The assessment does highlight that there is substantial uncertainty regarding the efficacy and safety of the absorbable perirectal spacer in this patient population due to conflicting results and limited evidence for extent of the clinical benefit, comparative efficacy, and safety of the absorbable perirectal spacer relative to other rectal displacement devices, and impact of absorbable perirectal spacer on local control. There is insufficient evidence supporting the efficacy and safety of the absorbable perirectal spacer for use in patients with prostate cancer undergoing proton beam therapy or low dose rate brachytherapy.

National and Specialty Guidelines

The **National Comprehensive Cancer Network (NCCN)** (2024) published the NCCN Clinical Practice Guidelines in Oncology for Prostate Cancer (v 4.2024) stated “Overall, the panel believes that biocompatible and biodegradable perirectal spacer materials may be implanted between the prostate and rectum in patients undergoing external radiotherapy with organ-confined prostate cancer to displace the rectum from high radiation dose regions. Patients with obvious rectal invasion or visible T3 and posterior extension should not undergo perirectal spacer implantation.” The guidelines noted that spacer implantation is expensive and may be associated with rare complications such as rectum perforation and urethral damage.

The **National Institute for Health and Care Excellence (NICE)** (2023) issued an Interventional Procedure Biodegradable Spacer Guidance (IPG752) *Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer* stating “Evidence on the safety and efficacy of biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer is limited in quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research.”

The **American Brachytherapy Society** (King et al. 2021) provided an evidence-based consensus opinion on the use of rectal spacers: "Acceptable rectal dosimetry is indicated by a rectal V100 (RV100) <1 cc, given the increased risk of late Grade 2+ rectal toxicity if this constraint is not met. If this constraint is not met, a rectal spacer could be considered to increase the distance between the prostate and rectum.”

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CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
55874	Transperineal placement of biodegradable material, peri-prostatic, single, or multiple injection(s), including image guidance, when performed

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APPROVAL HISTORY

12/10/2025	Policy reviewed. No changes to coverage criteria. Updated Summary of Medical Evidence and References.
12/11/2024	Policy revised. Coverage criteria updated to include Barrigel Injectable Gel and the BioProtect Balloon Implant System. Title changed from Hydrogel Spacer for Prostate Radiotherapy (SpaceOAR) to Perirectal Spacer for Prostate Radiotherapy. Updated Overview, Summary of Medical Evidence, and References.
02/14/2024	Policy reviewed. No changes to coverage criteria.
02/08/2023	New policy. IRO Peer Review. November 16, 2022. Practicing physician. Board-certified in Radiation Oncology.

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