Molina Clinical Policy
Hydrogel Spacer for Prostate Radiotherapy (SpaceOAR)
Policy No. 425

Last Approval: 2/8/2023
Next Review Due By: February 2024

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 anticipated 248,530 cases in 2021 (Siegel et al. 2021). A range of treatment approaches, including as radical prostatectomy, radiation therapy (RT), and close observation, are standardized by national guidelines (NCCN, 2022). Surgical procedures, chemotherapy, cryosurgery, and RT 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 RT, stereotactic body radiotherapy (SBRT), or intensity modulated RT (IMRT) and image-guided RT (IGRT). 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 (GI) toxicity.

The position of the prostate gland in front of the rectum 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 RT (Pinkawa, 2015). To shield the anterior rectum from radiation, rectal spacers may be placed between the prostate and rectum. Multiple different space-creating solutions have been developed over the past 10-15 years, including an implanted bio-absorbable balloon, hyaluronic acid, human collagen, and polyethylene glycol (PEG) based hydrogel (Repka et al. 2022). However, while the use of rectal displacement devices has increased in recent years, the standard of care for prostate cancer RT remains to provide treatment without a spacer. Medical interventions for the treatment of rectal toxicity secondary to RT for the treatment of prostate cancer may include anti-inflammatory drugs, antidiarrheal agents, laxatives, polypectomy, sclerotherapy, endoscopic coagulation of hemorrhoids, and endoscopic evaluation (Hayes, 2022).

The **SpaceOAR System** (Spacing **O**rgans **A**t **R**isk; Boston Scientific Corporation) is single-use device that consists of a PEG 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 RT. 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 RT (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. Potential complications that may be associated with the use of the SpaceOAR system include, but are not limited to pain and discomfort associated with SpaceOAR or hydrogel injection; needle penetration and/or injection of the hydrogel into the bladder, prostate, rectal wall, rectum, or urethra; infection or local tissue inflammatory reactions; urine retention, bleeding, rectal mucosal damage, ulcers, necrosis, constipation; rectal urgency; injection of air, fluid or SpaceOAR hydrogel intravascularly; device functional failure or its inability to maintain the space stability during the course of RT; prolonged or delayed procedure; and incomplete absorption of the hydrogel (FDA Decision Summary).

Regulatory Status

The FDA completed its review of the de novo request (DEN140030) for classification of the **SpaceOAR** system as a class II device under the device name *hydrogel spacer* with product code OVB (21 CFR 892.5725). FDA identifies this generic type of device as an "absorbable perirectal spacer."

The FDA granted premarket notification clearance for the device on April 1, 2015. The approved indication is as follows:

> SpaceOAR System is intended 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 composed of biodegradable material and maintains space for the entire course of prostate radiotherapy treatment and is completely absorbed by the patient's body over time. No contraindications are listed.

Augmenix Inc. received de novo approval from the FDA in April 2015 to use SpaceOAR in prostate cancer patients prior to RT. Augmenix was purchased by Boston Scientific Corporation (Marlborough, Massachusetts) in 2018. In July 2019, the FDA approved legal marketing of the device. According to Boston Scientific, 50,000 procedures for prostate cancer using SpaceOAR have been performed globally (SpaceOAR.com, 2022).

The SpaceOAR System consists of the following components: powder vial with a blue label, diluent syringe with a blue label, accelerator syringe, Y connector, syringe holder, plunger cap, and 18 gauge x 15 cm needle.

DuraSeal® (Covidien, Mansfield, Massachusetts) is another product used in hydrogel spacer procedures for prostate cancer. It does not have FDA approval for this use, but it is used off-label after being approved in 2005 as an adjunct to sutured dural repair during spinal surgery.

Rectafix (Scanflex Medical AB) has been studied for the same indications as the SpaceOAR APS (Wilton et al., 2017); however, the device is not currently approved by the US Food and Drug Administration.

**De Novo premarket review: a regulatory pathway for low- to moderate-risk devices of a new type.*

COVERAGE POLICY

Hydrogel Spacer for Prostate Radiotherapy (e.g., SpaceOAR) to reduce rectal and urinary toxicity in men with prostate cancer who are receiving radiotherapy **may be considered medically necessary** when **ALL** of the following clinical criteria with documentation are met:

1. Diagnosis of localized or locally advanced prostate cancer with no lymph node involvement, **AND**
2. Treatment plan includes EBRT (including IMRT or SBRT), **AND**
3. Prostate volume is less than 80 cc, **AND**
4. Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1; **AND**
5. Documentation of the following: A recent history and physical exam, and any medical progress notes related to the medical treatment and planned surgical and radiation interventions; **AND**
6. Member does **not** have the following conditions:
    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.

LIMITATIONS AND EXCLUSIONS

The use of a prostate hydrogel spacer for any other indication is considered **experimental and investigational** and therefore not medically necessary.

The following conditions are considered **contraindications/exclusions** based on insufficient evidence:

1. Prior surgery or radiation for prostate cancer treatment
2. Prostate volume > 80 cc
3. T3 or T4 disease with posterior extension into the peri-rectal space

PRESCRIBER REQUIREMENTS: The procedure is performed by a board-certified urologist, radiation oncologist, interventional radiologist or physician experienced with ultrasound-guided transperineal procedures or certified in SpaceOAR procedures.

MONITORING PARAMETERS: Member will be monitored according to FDA-approved labeling.

QUANTITY LIMITATIONS: The prostate hydrogel spacer will be authorized for a one-time patient application.

ADMINISTRATION: The APS is typically placed in an outpatient or ambulatory setting. Hospital stay is not indicated for placement of the APS.

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 GI toxicities (Chao, 2018; Chao, 2019a; Chao, 2019b; Hedrick, 2017a and 2017b; Juneja, 2015; Pinkawa, 2011; Pinkawa, 2017b; Ruggieri, 2015; Schorghofer, 2019; Te Velde, 2019; van Gysen, 2014; Whalley, 2016; Wilton, 2017; Wu, 2018).

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 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 QOL were evaluated. The hydrogel placement success rate for spacer application was 99%. There were no device-related adverse events (AEs), rectal perforations, serious bleeding, or infections in either group, according to the authors. Overall, the rates of acute rectal AEs 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 RT 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 RT, whereas patients with prior radiation or surgery may develop perirectal scarring, limiting space creation. The use of spacers in these populations, the authors noted, should proceed cautiously in separate clinical trials.

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 RT. Additional long-term outcomes are required to determine the benefits of hydrogel spacers.

Payne et al. (2021) published a meta-analysis and systematic review evaluating the clinical utility of hydrogel spacers placed prior to SBRT 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 RT 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 EBRT. 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 considerably 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 EBRT 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.

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.

A Health Technology Assessment (HTA) concluded that while published evidence suggests a potential benefit of an APS during RT for prostate cancer, there is significant uncertainty about its safety and efficacy; future studies are needed to assess the APS clinical usefulness and cost-effectiveness (Hayes, 2022).

Low-quality published evidence suggests some potential benefit for the APS for preventing rectal toxicity and enhancing QOL in prostate cancer patients receiving EBRT compared with no spacer. Due to conflicting results and limited evidence for the clinical benefit, the efficacy and safety of the APS compared to other rectal displacement devices, and the impact of the APS on local control, the efficacy and safety of the APS in this patient population are uncertain. The HTA found insufficient evidence for the efficacy and safety of APS in prostate cancer patients undergoing proton beam or low-dose-rate brachytherapy. The report also concluded that there is insufficient evidence exists to develop definitive patient selection criteria for APS use in prostate cancer RT.

National and Specialty Guidelines

DiBiase and Roach (2022) in an updated evidenced-based peer-review, highlighted the following (UpToDate, 2022):

The AUA/ASTRO/SUO and ASCO guidelines endorse shared decision making, which explicitly considers cancer severity (risk stratification), patient values and preferences, life expectancy, pretreatment general functional status and genitourinary symptoms, expected post-treatment functional status, and salvage treatment (Sanda et al. 2018a, 2018b).

The AUA/ASTRO/SUO has provided the following recommendations regarding the specific role of RT, which ASCO has largely endorsed (Bekelman et al. 2018):
- Clinicians may offer single-modality EBRT or brachytherapy for patients who elect RT for low-risk prostate cancer.
- Clinicians may offer EBRT or brachytherapy, alone or in combination, for favorable intermediate-risk prostate cancer.

DiBiase and Roach (2022) further recommended: 'SBRT (or ultrahypofractionated RT) is an appropriate alternative to conventional fractionation RT for carefully selected men with low- or intermediate-risk prostate cancer who do not require nodal irradiation. Patients may choose this option if they value a shorter treatment duration and are willing to accept a potentially higher toxicity profile, particularly in the short term. We do not recommend SBRT to men with high-risk prostate cancer outside of a clinical trial.'

American Urological Association (AUA) / American Society for Radiation Oncology (ASTRO) / Society of Urologic Oncology (SUO)

The 2017 AUA/ASTRO/SUO Guideline on Clinically Localized Prostate Cancer was recently updated and is now titled, Clinically Localized Prostate Cancer: AUA/ASTRO Guideline (2022). The guidelines refer to toxicity associated with RT for the treatment of prostate cancer. However, there was no mention of perirectal spacer materials (Sanda et al., 2018).

American Society of Clinical Oncology (ASCO) / AUA / ASTRO

A discussion of perirectal spacer materials was not located in the 2018 'Hypofractionated Radiation Therapy for Localized Prostate Cancer: An ASTRO, ASCO, and AUA Evidence-Based Guideline.'

National Comprehensive Cancer Network (NCCN)

The NCCN Clinical Practice Guidelines for prostate cancer (V1.2023) includes recommendations on EBRT, noting:

> "Biomaterials have been developed, tested, and FDA approved to serve as spacer materials when inserted between the rectum and prostate. In a randomized phase 3 multicenter clinical trial of patients undergoing image-guided IMRT (IG-IMRT), where the risk of late (3-year) common terminology criteria for adverse events (CTCAE) was grade 2 or higher, physician-recorded rectal complications declined from 5.7% to 0% in the control versus hydrogel spacer group. The hydrogel spacer group had a significant reduction in bowel QOL decline. No significant differences in adverse events were noted in those receiving hydrogel placement versus controls. Results of a secondary analysis of this trial suggest that use of a perirectal spacer may decrease the sexual side effects of radiation.'

The panel added the following:

> "Spacer implantation, however, is quite expensive and may be associated with rare complications such as rectum perforation and urethral damage. Retrospective data also support its use in similar patients undergoing brachytherapy. 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."

NCCN Guidelines recommend selective use of the PEG spacer (standard EBRT or Hypofractionation) when modern EBRT localization techniques are "insufficient to improve oncologic cure rates and/or reduce side effects due to anatomic geometry or other patient related factors, such as medication usage and/or comorbid conditions."

National Institute for Health and Care Excellence (NICE)

NICE issued Interventional Procedure Guidance (IPG590) supporting the use of biodegradable spacers in patients with prostate cancer prior to radiotherapy to decrease rectal toxicity and performed exclusively by professionals with the appropriate training and experience (NICE, 2017). The guidance states: "current evidence on the safety and efficacy of insertion of a biodegradable spacer to reduce rectal toxicity during radiotherapy for prostate cancer is adequate to support the use of this procedure provided those standard arrangements are in place for clinical governance, consent and audit."

The IPG designation allows UK radiation oncologists and urologists to recommend using a hydrogel spacer, such as SpaceOAR, as an alternative for men with prostate cancer who want to lower their risk of AEs from radiotherapy, including rectal toxicity, incontinence, and loss of sexual function. It should be noted that the use of hydrogel spacers with CE Marking was mentioned as providing most of the evidence; there is no specific mention of SpaceOAR APS.

ECRI Institute Health Technology Assessment

ECRI (2017) concludes in a custom product brief that SpaceOAR hydrogel is well-tolerated, reduces long-term, but not acute, rectal toxicity, and improves bowel QOL based on one RCT and four prospective nonrandomized comparative studies. There was no reduction in acute rectal toxicity found. According to the report, studies with longer term follow-up of more than five years comparing different spacers are required.

SUPPLEMENTAL INFORMATION

Risk Stratification Schema for Localized Prostate Cancer (NCCN)

Very Low Risk

- T1c AND
- Grade group 1 AND
- PSA <10 ng/mL AND
- Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core AND
- PSA density <0.15 ng/mL/g.

Low Risk

- T1 to T2a AND
- Grade group 1 AND
- PSA <10 ng/mL AND
- Does not qualify for very low risk.

Favorable Intermediate Risk

- No high or very high risk features
- No more than one intermediate risk factor:
  - T2b to T2c OR
  - Grade group 2 or 3
  - PSA 10 to 20 ng/mL

AND

- Grade group 1 or 2

AND

- Percentage of positive biopsy cores <50%

Unfavorable Intermediate Risk

- No high or very high risk features
- Two or three of the intermediate risk factors:
  - T2b to T2c
  - Grade group 2 or 3
  - PSA 10 to 20 ng/mL

AND/OR

- Grade group 3

AND/OR

- ≥50% of positive biopsy cores

High Risk

- No very high-risk features

AND

- T3a OR
- Grade group 4 or 5 OR
- PSA >20 ng/mL

Very High Risk

- T3b to T4 OR
- Primary Gleason pattern 5 OR
- Two or three high-risk features OR
- >4 cores with Grade group 4 or 5

Reference: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Prostate Cancer.

CODING & BILLING INFORMATION

CPT Code

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

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

2/8/2023 New policy. IRO Peer Review. November 16, 2022. Practicing physician. Board-certified in Radiation Oncology.

REFERENCES

Government Agencies

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database (search: spaceoar OR hydrogel OR absorbable perirectal spacer OR prostate rectal spacer). Available from CMS.
   - No NCD was identified for the use of the SpaceOAR APS with radiation therapy for prostate cancer.
   - LCD 37485: Prostate Rectal Spacers
2. Food and Drug Administration (FDA)
   a. 510(k) Premarket Notification Database. Summary of Safety and Effectiveness. Rockville, MD: FDA. SpaceOAR Vue Hydrogel. K182971. July 17, 2019. Available at: FDA
   b. Device Classification under Section 513(f)(2) (denovo). Hydrogel Spacer. De Novo Number: DEN140030. SpaceOAR System, 04/01/2015, Updated 10/03/2022. Available at: FDA
3. ClinicalTrials.gov
   a. SpaceOAR System Pivotal Study. ClinicalTrials.gov identifier: NCT01538628

Manufacturer Website

1. SpaceOAR for Healthcare Professionals. Boston Scientific. Accessed October 2022.

Other Evidence Based Reviews and Publications

1. DynaMed. Registration and login required.
   a. Oral Appliances in the Treatment of Sleep-disordered Breathing. EBSCO Information Services. Accessed September 8, 2022.
   b. Surgical Management of Obstructive Sleep Apnea (OSA) in Adults. EBSCO Information Services. Accessed September 8, 2022.
   c. Obstructive Sleep Apnea (OSA) in Adults. EBSCO Information Services. Accessed September 8, 2022.
2. Hayes, Inc. Health Technology Assessment. Absorbable Perirectal Spacer (SpaceOAR System; Boston Scientific) During Radiation Therapy for Prostate Cancer. Sep 27, 2021. Annual Review: Nov 4, 2022.
3. DiBiase SJ and Roach M. External beam radiation therapy for localized prostate cancer. Available from UpToDate. Updated October 19, 2022. Accessed December 2022. Registration and login required.

Peer Reviewed Publications

1. Afkhami Ardenkani M, Ghaffari H, Navaser M, Moghaddam SHZ, Refahi S. Effectiveness of rectal displacement devices in managing prostate motion: A systematic review. Strahlenther Onkol. 2021;197(2):97-115. DOI: 10.1007/s00066-020-01633-9.
2. Aminsharifi A, Kotamarti S, Silver D, Schulman A. Major complications and adverse events related to the injection of the SpaceOAR Hydrogel System Before radiotherapy for prostate cancer: review of the manufacturer and user facility device experience database. J Endourol. 2019;33(10):868–871.
3. Armstrong N, Bahl A, Pinkawa M, et al. SpaceOAR hydrogel spacer for reducing radiation toxicity during radiotherapy for prostate cancer. A systematic review. Urology. 2021; 156:e74-e85. DOI:https://doi.org/10.1016/j.urology.2021.05.013.
4. 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):976-985. PubMed 28209443.
5. Mariados, N, Sylvester, J, Shah, 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):971-977. doi: 10.1016/j.ijrobp.2015.04.030. PubMed 26054865.
6. Miller LE, Efstathiou JA, Bhattacharyya SK, et al. Association of the placement of a perirectal hydrogel spacer with the clinical outcomes of men receiving radiotherapy for prostate cancer: A systematic review and meta-analysis. JAMA Netw Open. Jun 01 2020; 3(6): e208221. PMID 32585020.
7. Pinkawa M. Current role of spacers for prostate cancer radiotherapy. World J Clin Oncol. 2015;6(6):189-193. doi:10.5306/wjco.v6.i6.189
8. Repka MC, Creswell M, Lischalk JW, et al. Rationale for utilization of hydrogel rectal spacers in dose escalated SBRT for the treatment of unfavorable risk prostate cancer. Front Oncol. 2022 Mar 31;12:860848. doi: 10.3389/fonc.2022.860848. PMID: 35433457; PMCID: PMC9008358.
9. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin (2021) 71(1):7–33. doi: 10.3322/caac.21654
10. Yu T, Zhang Q, Zheng T, et al. The effectiveness of intensity modulated radiation therapy versus three-dimensional radiation therapy in prostate cancer: A meta-analysis of the literatures. PLoS One. 2016;11(5):e0154499. doi:10.1371/journal.pone.0154499

National and Specialty Organizations

1. American Urological Association (AUA) / American Society for Radiation Oncology (ASTRO) / Society of Urologic Oncology (SUO)
   a. Sanda MG, Cadeddu JA, Kirkby E, et al. Clinically localized prostate cancer: AUA/ASTRO/SUO Guideline. Part II: Recommended approaches and details of specific care options. J Urol 2018; 199:990.
   b. Sanda MG, Cadeddu JA, Kirkby E, et al. Clinically localized prostate cancer: AUA/ASTRO/SUO Guideline. Part I: Risk stratification, shared decision making, and care options. J Urol 2018; 199:683. doi:10.1016/j.juro.2017.11.095

2. American Society for Radiation Oncology (ASTRO) / American Society of Clinical Oncology (ASCO) / American Urological Association (AUA)
   a. Morgan SC, Hoffman K, Loblaw DA, et al. Hypofractionated radiation therapy for localized prostate cancer: An ASTRO, ASCO, and AUA evidence-based guideline. J Clin Oncol. 2018:JCO1801097. doi: 10.1200/JCO.18.01097. Epub ahead of print. PMID: 30307776; PMCID: PMC6269129.
3. Bekelman JE, Rumble RB, Chen RC, et al. Clinically localized prostate cancer: ASCO clinical practice guideline endorsement of an American Urological Association/American Society for Radiation Oncology/Society of Urologic Oncology guideline. J Clin Oncol 2018; 36:3251.
4. ECRI Institute. Health Technology Assessment Information Service. SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for reducing exposure during prostate cancer radiation therapy. Product brief. Health Technology Assessment Information Service, May 2017.
5. National Comprehensive Cancer Network (NCCN).
   a. Prostate cancer (V1.2023). NCCN Evidence Blocks. September 16, 2022
   b. Prostate cancer (V3.2022). Revised January 10, 2022.
   c. Prostate cancer (V4.2019).
6. National Institute for Health and Care Excellence (NICE).
   a. Interventional procedures guidance (IPG-590): Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer. Available from NICE. Published August 23, 2017. Accessed October 2022.
   b. Interventional procedures guidance (IPG-752): Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer. Available from NICE. Published February 7023. Accessed October 2022.

Other Peer Reviewed and National Organization Publications (used in the development of this policy)

1. Chao M, Ho H, Chan Y, et al. Prospective analysis of hydrogel spacer for patients with prostate cancer undergoing radiotherapy. BJU Int. 2018; 122(3):427-433.
2. Chao M, Lim Joon D, Khoo V, et al. The use of hydrogel spacer in men undergoing high-dose prostate cancer radiotherapy: Results of a prospective phase 2 clinical trial. World J Urol. 2019a; 37(6):1111-1116.
3. Chao M, Ow D, Ho H, et al. Improving rectal dosimetry for patients with intermediate and high-risk prostate cancer undergoing combined high-dose-rate brachytherapy and external beam radiotherapy with hydrogel space. J Contemp Brachytherapy. 2019b; 11(1):8-13.
4. Hedrick SG, Fagundes M, Case S, et al. Validation of rectal sparing throughout the course of proton therapy treatment in prostate cancer patients treated with SpaceOAR®. J Appl Clin Med Phys. 2017; 18(1):82-89.
5. Hedrick SG, Fagundes M, Robison B, et al. A comparison between hydrogel spacer and endorectal balloon: An analysis of intrafraction prostate motion during proton therapy. J Appl Clin Med Phys. 2017; 18(2):106-112.
6. Juneja P, Kneebone A, Booth JT, et al. Prostate motion during radiotherapy of prostate cancer patients with and without application of a hydrogel spacer: a comparative study. Radiat Oncol. 2015; 10:215.
7. Pinkawa M, Corral NE, Caffaro M, et al. Application of a spacer gel to optimize three-dimensional conformal and intensity modulated radiotherapy for prostate cancer. Radiother Oncol. 2011; 100(3):436-441.
8. Pinkawa M, Berneking V, Schlenter M, Krenkel B, Eble MJ. Quality of life After radiation therapy for prostate cancer with a hydrogel spacer: 5-year results. Int J Radiat Oncol Biol Phys. 2017b; 99(2):374-377.
9. Ruggieri R, Naccarato S, Stavrev P, et al. Volumetric-modulated arc stereotactic body radiotherapy for prostate cancer: Dosimetric impact of an increased near-maximum target dose and of a rectal spacer. Br J Radiol. 2015; 88(1054):20140736.
10. Ruggieri R, Naccarato S, Stavrev P, et al. Volumetric-modulated arc stereotactic body radiotherapy for prostate cancer: Dosimetric impact of an increased near-maximum target dose and of a rectal spacer. Br J Radiol. 2015; 88(1054):20140736.
11. Schörghofer A, Drerup M, Kunit T, et al. Rectum-spacer related acute toxicity – endoscopy results of 403 prostate cancer patients after implantation of gel or balloon spacers. Radiat Oncol. 2019; 14(1):47.
12. Te Velde BL, Westhuyzen J, Awad N, et al. Late toxicities of prostate cancer radiotherapy with and without hydrogel SpaceAOR insertion. J Med Imaging Radiat Oncol. 2019.
13. van Gysen K, Kneebone A, Alfieri F, et al. Feasibility of and rectal dosimetry improvement with the use of SpaceOAR® hydrogel for dose-escalated prostate cancer radiotherapy. J Med Imaging Radiat Oncol. 2014; 58(4):511-516.
14. Whalley D, Hruby G, Alfieri F, et al. SpaceOAR hydrogel in dose-escalated prostate cancer radiotherapy: Rectal dosimetry and late toxicity. Clin Oncol (R Coll Radiol). 2016; 28(10):e148-154.
15. Wilton L, Richardson M, Keats S, et al. Rectal protection in prostate stereotactic radiotherapy: A retrospective exploratory analysis of two rectal displacement devices. J Med Radiat Sci. 2017; 64(4):266-273.
16. Wu SY, Boreta L, Wu A, et al. Improved rectal dosimetry with the use of SpaceOAR during high-dose-rate brachytherapy. Brachytherapy. 2018; 17(2):259-264.
17. Mashaqi S, Patel SI, Combs D, et al. The hypoglossal nerve stimulation as a novel therapy for treating obstructive sleep apnea – a literature review. Int J Environ Res Public Health. 2021 Feb 9;18(4):1642. doi: 10.3390/ijerph18041642. PMID: 33572156; PMCID: PMC7914469.