Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: Keystone First Community HealthChoices	**Submission Date**: 1/2/2025
Policy Number: ccp.1476	**Effective Date:** 12/2020 **Revision Date:** November 1, 2024
Policy Name: Hydrogel spacer use during radiotherapy for prostate cancer	

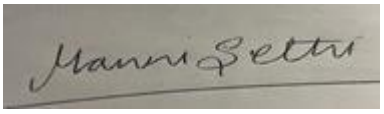
Type of Submission – Check all that apply:

- ☐ **New Policy**
- ☒ **Revised Policy***
- ☐ **Annual Review – No Revisions**
- ☐ **Statewide PDL**

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

See tracked changes below.

Name of Authorized Individual (Please type or print):	**Signature of Authorized Individual:**
Manni Sethi, MD, MBA, CHCQM	

Keystone First
Community HealthChoices

Hydrogel spacer use during radiotherapy for prostate cancer

Clinical Policy ID: CCP.1476

Recent review date: 11/2024

Next review date: 3/2026

Policy contains: hydrogel spacer; polyethylene glycol; radiotherapy; prostate cancer; rectum; brachytherapy

Keystone First Community HealthChoices has developed clinical policies to assist with making coverage determinations. Keystone First Community HealthChoices' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First Community HealthChoices, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First Community HealthChoices' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First Community HealthChoices' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First Community HealthChoices will update its clinical policies as necessary. Keystone First Community HealthChoices' clinical policies are not guarantees of payment.

Coverage policy

A hydrogel spacer is clinically proven and, therefore, may be medically necessary for reducing exposure of the rectum to radiotherapy in members with organ-confined prostate cancer (American Urology Association/American Society for Radiation Oncology [Eastham, 2022]; National Comprehensive Cancer Network, 2024).

Limitations

All other uses of a hydrogel spacer in prostate care are investigational/not clinically proven and, therefore, not medically necessary.

Hydrogel spacers are investigational/not clinically proven and, therefore, not medically necessary for members undergoing hypofractionated or ultra hypofractionated radiation therapy, because their effectiveness has not been established in this population (Eastham, 2022).

Members with grossly apparent posterior extraprostatic extension should not undergo perirectal spacer implantation, but marginal or suspected early extension is not a clear contraindication (National Comprehensive Cancer Network, 2024).

Alternative covered services

Endorectal balloon.

Background

Prostate cancer is the most commonly diagnosed cancer among American males, with an estimated 299,010 new cases and 35,250 deaths in 2024 (American Cancer Society, 2024).

Patients with prostate cancer can be treated with external beam radiotherapy (including intensity-modulated radiotherapy or stereotactic body radiation therapy), or with hypofractionated radiotherapy, proton beam therapy, and brachytherapy. The proximity of the rectum to the prostate gland raises the risk of rectal toxicity after radiation therapy for prostate cancer, prompting research on ways to minimize this adverse effect (Afkhami Ardekani, 2020; Forero, 2018).

Various materials, including collagen, polyethylene glycol hydrogel spacers, and absorbable balloons have been evaluated to reduce rectal radiation exposure. Radioprotective spacers, first reported 30 years ago for radiotherapy of tongue and abdominal cancers, have been developed for prostate cancer (Tang, 2018).

The U.S. Food and Drug Administration (2024) has issued 510(k) premarket approval to several absorbable perirectal spacers: SpaceOAR® Hydrogel System and the SpaceOAR Vue™ Hydrogel (formerly Augmenix Inc., Bedford, Massachusetts, now Boston Scientific Corp., Marlborough, Massachusetts); Barrigel Injectable Gel (Palette Life Sciences, Santa Barbara, California); and the BioProtect Balloon Implant™ System (BioProtect, Ltd., Philadelphia, Pennsylvania). As a minimally invasive procedure, each spacer is implanted by injecting a bioabsorbable gel through a dedicated delivery system under transrectal ultrasound guidance. These radioprotective spacers are intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer, thereby reducing the radiation dose delivered to the anterior rectum. The gel is generally absorbed into the system within a few months after implantation.

Another product used in hydrogel spacer procedures for prostate cancer is DuraSeal® (Covidien, Mansfield, Massachusetts). It has no regulatory approval for this use, but is used off-label, having been approved in 2005 as an adjunct to sutured dural repair during spinal surgery (Afkhami Ardekani, 2020).

Findings

Guidelines

The National Comprehensive Cancer Network guideline on prostate cancer includes a section on radiation therapy. The section states 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 in order to displace the rectum from high radiation dose regions.” For patients undergoing brachytherapy, perirectal spacer materials may be employed when efforts to improve oncologic cure rates and/or reduce side effects due to anatomic geometry or other patient-related factors are insufficient. Patients with grossly apparent posterior extraprostatic extension should not undergo perirectal spacer implantation, but marginal or suspected early extension is not a clear contraindication (National Comprehensive Cancer Network, 2024).

An American Urology Association/American Society for Radiation Oncology guideline on clinically localized prostate cancer endorses several means of optimizing the therapeutic ratio of radiation therapy, including rectal spacers, but point out that the utility of rectal spacers has not been examined in conjunction with hypofractionated or ultra hypofractionated radiation therapy (Eastham, 2022).

Evidence reviews

The evidence from the following systematic reviews consists of retrospective, observational studies of generally low quality and one randomized controlled trial. The majority of studies examined polyethylene glycol hydrogel spacers (SpaceOAR and DuraSeal). The characteristics of study participants were not always well described,

but men with clinically localized prostate cancer were included. The randomized controlled trial provides some guidance on additional selection criteria in men who underwent prostate image-guided intensity modulated radiation therapy: prostate volumes ≤ 80 mL, no extracapsular extension, and no prior radiation or surgery (Mariados, 2015). However, these criteria may not be applicable to recipients of other types of radiation therapy or therapy protocols.

Hydrogel spacers increase the distance between the prostate and rectum, reduce rectal radiation exposure, and compare favorably to endorectal balloons in reducing prostate motion. The randomized controlled trial (Mariados, 2015) with long term follow-up demonstrated significant reductions in late gastrointestinal and genitourinary toxicities, and observational studies generally confirm these findings across a range of radiation therapy modalities. The effect of hydrogel spacers on quality of life, oncologic outcomes, and other adjacent organ toxicity is less clear.

Implantation is feasible and well-tolerated with a favorable safety profile. The overall complication rate is low, but serious complications have been reported outside of clinical studies. For example, of the more than 206,000 SpaceOAR and SpaceOAR Vue devices sold from 2015 to 2022, one analysis examined 981 events reported to the Manufacturer and User Facility Device Experience database from January 2015 to May 2023, along with other manufacturer data. Device malfunction (e.g., device positioning problem) and patient injuries (e.g., device-related abscesses, rectourethral fistulas, and rectal ulcers) were the most common post-approval complications and adverse events. In total, 470 (50.2%), 344 (36.7%), 123 (13.1%) of the adverse events were Common Terminology Criteria for Adverse Events grade 1, 2, and 3 or higher, respectively (Millot, 2024).

A systematic review of eight studies of 780 males treated with stereotactic body radiation therapy for early-stage prostate cancer revealed that compared to no spacer, SpaceOAR reduced the radiation to the rectum by 29% to 56% regardless of radiation dose. Freedom from biochemical failure ranged from 96.4% to 100% after a median follow-up of 16 months (Payne, 2021).

A systematic review of eight studies of patients undergoing external beam radiation therapy for localized prostate cancer found SpaceOAR reduced rectal radiation dose volume. Four studies analyzed toxicity; SpaceOAR decreased acute Grade 1 diarrhea in one study and decreased late Grade 1 and Grade ≥ 2 rectal toxicities in two others. One study reported fewer large declines in bowel quality of life at three years among SpaceOAR patients, but another reported no benefit after five years (Babar, 2021).

A systematic review of 19 studies (n = 3,622) revealed SpaceOAR significantly reduced rectal radiation dose, regardless of type of radiation therapy. Use of the device also reduced gastrointestinal and genitourinary toxicities. Only one of the 19 studies was randomized (Armstrong, 2021).

A systematic review and meta-analysis of seven studies (one randomized, n = 1,011) of prostate cancer compared 486 subjects who received a hydrogel spacer prior to radiotherapy to 525 who did not. Mean follow-up was 26 months. The success rate of placement was 97.0%. Procedural complications were observed in less than 10% of patients and were mild and transient. The treatment group received 66% less v70 rectal irradiation versus controls (3.5% and 10.4%, $P = .001$). The risk of grade 2 or higher rectal toxic effects was similar in early follow-up (4.5% and 4.1%, $P = .38$), but was 77% lower in the treatment group in late follow-up (1.5% vs 5.7%, $P = .05$). Changes in bowel-related quality of life were similar ($P = .92$) but greater in the hydrogel spacer group in late follow-up ($P < .001$) (Miller, 2020).

Compared with the endorectal balloon, polyethylene glycol hydrogel spacers significantly reduced rectal dose and toxicity without influencing prostate immobilization in patients receiving external beam radiation therapy and brachytherapy (Afkhami Ardekani, 2020, 2021).

Results of two recent observational studies with long term follow-up provide conflicting results regarding the effect of hydrogel spacers on quality of life after prostate radiation therapy. In one study, hydrogel spacer use

was associated with better sexual quality of life, less measurable decline in sexual quality of life, and higher rates of adequate erectile function (Seymour, 2023).

Another study found patients undergoing low-dose-rate brachytherapy alone experienced no significant improvement in urinary, bowel or sexual quality of life when using a hydrogel spacer. In patients undergoing low-dose-rate brachytherapy in combination with intensity-modulated radiotherapy, a hydrogel spacer did significantly improve bowel quality of life, but not sexual or urinary quality of life (Nakia, 2024).

In 2024, we updated the references, deleted older references, and modified the coverage criteria and limitations based new guideline information.

References

On September 20, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “hydrogel spacer,” “polyethylene glycol,” “radiotherapy,” “brachytherapy,” “prostate cancer,” and “rectum.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Afkhami Ardekani M, Ghaffari H. Optimization of prostate brachytherapy techniques with polyethylene glycol-based hydrogel spacers: A systematic review. *Brachytherapy*. 2020;19(1):13-23. Doi: 10.1016/j.brachy.2019.08.009.

Afkhami Ardekani 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.

American Cancer Society. Key statistics for prostate cancer. https://www.cancer.org/cancer/types/prostate-cancer/about/key-statistics.html#:~:text=About%20288%2C300%20new%20cases%20of,34%2C700%20deaths%20from%20prostate%20cancer. Last updated January 19, 2024.

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: 10.1016/j.urology.2021.05.013.

Babar M, Katz A, Ciatto M. Dosimetric and clinical outcomes of SpaceOAR in men undergoing external beam radiation therapy for localized prostate cancer: A systematic review. *J Med Imaging Radiat Oncol*. 2021;65(3):384-397. Doi: 10.1111/1754-9485.13179.

Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically localized prostate cancer: AUA/ASTRO guideline, Part II: Principles of surgery, and follow-up. *J Urol*. 2022;208(1):19-25. Doi: 10.1097/JU.0000000000002758.

Forero DF, Almeida ND, Dendukuri N. Hydrogel spacer to reduce rectal toxicity in prostate cancer radiotherapy: A health technology assessment. Technology Assessment Unit of the McGill University Health Centre. Report number 82. https://muhc.ca/sites/default/files/micro/m-TAU/SpaceOAR.pdf. Published April 16, 2018.

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):971-977. Doi: 10.1016/j.ijrobp.2015.04.030.

Miller LE, Efstathiou JA, Bhattacharyya SK, Payne HA, Woodward E, Pinkawa M. 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*. 2020;3(6):e208221. Doi: 10.1001/jamanetworkopen.2020.8221.

Millot JC, Arenas-Gallo C, Silver E, et al. Major complications and adverse events related to use of SpaceOAR hydrogel for prostate cancer radiotherapy. *Urology*. 2024;188:94-100. Doi: 10.1016/j.urology.2023.12.034.

Nakai Y, Tanaka N, Asakawa I, et al. Efficacy of a hydrogel spacer for improving quality of life in patients with prostate cancer undergoing low-dose-rate brachytherapy alone or in combination with intensity-modulated radiotherapy: An observational study using propensity score matching. *Prostate*. 2024;84(12):1104-1111. Doi: 10.1002/pros.24744.

National Comprehensive Cancer Network. Prostate Cancer. Version 4.2024. www.nccn.org. Published May 17, 2024.

Payne HA, Pinkawa M, Peedell C, Bhattacharyya SK, Woodward E, Miller LE. SpaceOAR hydrogel spacer injection prior to stereotactic body radiation therapy for men with localized prostate cancer: A systematic review. *Medicine (Baltimore)*. 2021;100(49):e28111. Doi: 10.1097/MD.0000000000028111.

Seymour ZA, Pinkawa M, Daignault-Newton S, et al. A pooled long-term follow-up after radiotherapy for prostate cancer with and without a rectal hydrogel spacer: Impact of hydrogel on decline in sexual quality of life. *Front Oncol*. 2023;13:1239104. Doi: 10.3389/fonc.2023.1239104.

Tang Q, Zhao F, Yu X, Wu L, Lu Z, Yan S. The role of radioprotective spacers in clinical practice: A review. *Quant Imaging Med Surg*. 2018;8(5):514-524. Doi: 10.21037/qims.2018.06.06.

U.S. Food and Drug Administration. 510(k) premarket notification database. Searched using product code OVB. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. Page last updated September 16, 2024.

Policy updates

11/2020: initial review date and clinical policy effective date: 12/2020

11/2021: Policy references updated.

11/2022: Policy references updated.

11/2023: Policy references updated.

11/2024: Policy references updated. Coverage modified.