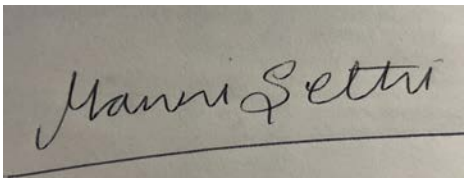
Prior Authorization Review Panel
MCO Policy Submission

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	**Submission Date**: 1/1/2024
Policy Number: ccp.1476	**Effective Date:** 12/2020 **Revision Date:** November 1, 2023
Policy Name: Hydrogel spacer use during radiotherapy for prostate cancer	
Type of Submission – Check all that apply: **New Policy** **x 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): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Keystone First
Family of Health Plans

Hydrogel spacer use during radiotherapy for prostate cancer

Clinical Policy ID: CCP.1476

Recent review date: 11/2023

Next review date: 3/2025

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

Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First's 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 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's 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's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First's clinical policies are not guarantees of payment.

Coverage policy

Hydrogel spacer is clinically proven and, therefore, may be medically necessary for reducing exposure of the rectum to radiotherapy in members with prostate cancer (Morgan, 2019; National Comprehensive Cancer Network, 2023).

Polyethylene glycol hydrogel spacers are covered once in patients with clinically localized prostate cancer when any of the following are present:

- Low* or favorable intermediate prostate cancer risk group.
- Dose escalated (≥ 76 Gy) conventional fractionation (1.8 – 2 Gy fractions) or moderate hypofractionation (2.4 – 3.4 Gy fractions) image-guided, intensity-modulated radiation therapy planned.
- Eastern Cooperative Oncology Group performance status ≤ 1.
- Modern localization techniques would be insufficient to improve oncologic cure rates and/or reduce side effects due to at least one of the following:
    - Anatomic geometry precluding ideal rectal constraints (V70 < 10%, V65 < 20%, V40 < 40%):
- Conventional fractionation (V70 < 10%, V65 < 20%, V40 < 40%).
- Moderate HPX (dose constraints not yet standardized; employ those used in the supporting phase III trials).
    - Medication usage (e.g., anticoagulants).
    - Comorbid conditions (e.g., increased age, history of myocardial infarction or congestive heart failure).

None of the following exclusion criteria are present:

- Less than five-year life expectancy and asymptomatic.
- Prior prostate cancer treatment (surgery or radiation therapy).
- Active bleeding disorder or clinically significant coagulopathy.
- Active inflammatory or infectious disease in the perineum or injection area (e.g., prostatitis, anorectal inflammatory bowel disease).
- Prostate volume > 80 cc.

*Life expectancy ≥ 20 years (very low risk); ≥ 10 years (low risk)

Limitations

All other uses of hydrogel spacer are investigational/not clinically proven.

Alternative covered services

Endorectal balloon.

Background

Prostate cancer is the most commonly diagnosed cancer among American males, with an estimated 288,300 cases in 2023. The estimated annual number of deaths from the disease in the United States is 34,700 (American Cancer Society, 2023).

Prostate cancer patients 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).

SpaceOAR™ (Augmenix) is a polyethylene glycol hydrogel, injected through a trans-perineal approach into the Denonvilliers' space, under general or local anesthesia. The gel hardens to a soft hydrogel within 10 seconds, creating a separation of at least 10 mm between the prostate and rectum, in the attempt to limit rectal toxicity from relatively high doses of radiation; forms of toxicity include rectal urgency, diarrhea, bleeding, and pain (Forero, 2018). After three months (during radiotherapy) the gel undergoes hydrolysis, liquefaction, and absorption into the bloodstream, where it leaves the body through renal filtration (Karsh, 2018).

In April 2015, the U.S. Food and Drug Administration gave de novo clearance to Augmenix Inc. to use SpaceOAR in prostate cancer patients before they received radiation therapy. Previously, SpaceOAR was already approved for use in Europe and Australia (WGC FDA News, 2015). Augmenix was acquired by Boston Scientific Corporation (Marlborough, Massachusetts) in 2018. The Food and Drug Administration allowed legal marketing of the device in July 2019 (U.S. Food and Drug Administration, 2019). The company claims that 150,000 procedures using SpaceOAR for prostate cancer have been performed worldwide (Spaceoar.com, 2022).

Another product used in hydrogel spacer procedures for prostate cancer is DuraSeal® (Covidien, Mansfield, Massachusetts). It has no Food and Drug Administration 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

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” (National Comprehensive Cancer Network, 2023).

The American Urological Association, American Society for Radiation Oncology, and American Society for Clinical Oncology collaborated on a guideline on hypofractionated radiation therapy for localized prostate cancer. The guideline supported use of one or more of the following: protocols to ensure that the bladder is comfortably full at time of treatment; prostate-rectal spacers to allow rectal dose sparing; and rectal balloon devices to assist in prostate immobilization (Morgan, 2019).

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 (Eastham, 2022).

The National Institute for Health and Care Excellence issued a guidance supporting use of inserting biodegradable spacers in persons with prostate cancer prior to radiotherapy to reduce rectal toxicity, only with “special arrangements for clinical governance, consent, and audit or research” (National Institute for Health and Care Excellence, 2023).

An interdisciplinary consensus statement after a meeting of radiation oncologists and urologists experienced in hydrogel spacer injections concluded that the treatment’s main indication was dose-escalated radiotherapy for histologically confirmed low- or intermediate-risk prostate cancer. The group did not recommend the treatment in cases of locally advanced prostate cancer (Muller, 2016).

A study (n = 483) of males with early-stage prostate cancer treated with brachytherapy included 30 who received SpaceOAR after radiation treatment. After 12 months follow-up, both groups had similar International Prostate Symptom Score, Overactive Bladder Symptom Score, quality of life due to urinary symptoms and uroflowmetry, and post-voided residual urine (Taniguchi, 2022),

A systematic review of eight studies (n = 780) males treated for early-stage prostate cancer revealed that compared to no spacer, SpaceOAR reduced the radiation to the rectum by 29% to 56%. Authors report 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 with localized prostate cancer 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) of outcomes in prostate cancer patients 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 of nine studies (n = 1,208) of males with prostate cancer randomized 671 patients and 537 controls according to whether they did or did not receive polyethylene glycol hydrogel spacer (DuraSeal or SpaceOAR) prior to brachytherapy. Insertion failure was 1%. The acute gastrointestinal complication rate was 33.7% for grade 1-2 toxicity, and 0.22% for grade 3-4 toxicity (Vaggers, 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 < 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).

A systematic literature review of 21 studies addressing various rectal displacement devices during prostate external beam radiation therapy included four on hydrogel spacer effects. Compared with the endorectal balloon, the hydrogel spacer significantly reduced rectal dose and toxicity without influencing prostate immobilization (Afkhami Ardekani, 2020). Authors also found hydrogel spacers, compared with endorectal balloons, significantly reduced rectal dose and toxicity, with no effect on prostate immobilization (Afkhami Ardekani, 2021).

A review by the Canadian Agency for Drugs and Technology in Health was based on an October 4, 2017, literature search. Evidence was used from three systematic reviews, one randomized controlled trial, seven non-randomized studies, two economic evaluations, and three evidence-based guidelines. Authors found most studies were not of good quality. While acknowledging spacers led to reductions in rectal radiation dose, authors assert reduced rectal dose “did not translate into clinically important reductions in acute or long-term rectal toxicity, quality of life, and rectal bleeding within the first year of follow-up (Chao, 2019).

A Cochrane review of 92 studies on gastrointestinal effects of pelvic radioactivity for primary pelvic cancers included a statement that low-certainty evidence suggests balloon and hydrogel spacers for prostate cancer radiotherapy may make little or no difference to gastrointestinal outcomes (Lawrie, 2018).

A study (n = 70) given an escalated dose (82 Gy) of radiation for prostate cancer after insertion of a perirectal spacer found minimal gastrointestinal and genitourinary adverse events and minimal reduction in quality of life after being tracked up to 37.5 months (See, 2022).

References

On August 10, 2023, 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.

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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.