Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 1/1/25**
(See policy history boxes for previous effective dates)

Title: Perirectal Spacer for Radiation Therapy Treatment of Prostate Cancer (SpaceOAR®)

Description/Background

Prostate Cancer

Prostate cancer is the most common cancer (excluding skin cancer) among American men, with approximately 1 in 8 men diagnosed with prostate cancer over their lifetime.[1] The American Cancer Society estimates the United States will see over 240,000 new cases of prostate cancer in 2021. Approximately 6 in 10 cases are diagnosed in men 65 years of age and older; it is rare in men under the age of 40 years.[1] The 5-year survival rate for most men with local or regional prostate cancer is over 95%.[3]

Treatment of prostate cancer may include observation, active surveillance, surgery or radiation therapy. In most cases of newly diagnosed localized or locally advanced prostate cancer, treatment outcomes are similar for either surgery or radiation. External-beam radiation therapy (EBRT) for the treatment of localized prostate cancer is most often delivered using three-dimensional conformal radiation therapy (CRT), intensity modulated radiation therapy (IMRT), image guided radiation therapy (IGRT), stereotactic body radiation therapy (SBRT) or proton beam radiation therapy.[4,5]

There is evidence supporting dose escalation in selected patients with prostate cancer; specifically, improved local control, biochemical outcomes, and disease-free survival with doses above 70 grays (Gy). Advances in EBRT limit the margins and conform the high dose radiation volume; however, due to its proximity to the prostate, the anterior wall of the rectum cannot be completely spared.[5] Story et al (2000) reported that there were significantly more late rectal complications when 25% of the rectum received ≥70 Gy.[6] Early or acute rectal toxicities typically persist for fewer than 90 days following the end of treatment and include diarrhea, tenesmus, urgency, anorectal pain and bleeding. Late rectal toxicities persist or develop 90 days after treatment is completed; the most common symptom is rectal bleeding.

There is research interest in evaluating methods to create space between the prostate and rectum, allowing for prostate dose escalation while reducing anterior rectal wall radiation exposure. Transperineal materials have included blood patch (Morancy et al 2008), hyaluronic acid and collagen (Wilder et al 2010, 2011). Although these materials reduced the amount of radiation to the rectum, each material had limitations, such as short persistence, degradation during the course of radiation therapy and distribution that was not uniform. In response to these drawbacks, a polyethylene glycol (PEG)-based hydrogel (SpaceOAR®) was developed. Current research continues to evaluate the effectiveness of other potential spacers in radiation treatment of the prostate, such as DuraSeal® (a PEG-based hydrogel currently FDA approved for use as an adjunct to sutured dural repair during spinal / cranial surgery), implantable biodegradable balloons and hyaluronic acid.[7]

The SpaceOAR® (Spacing Organs At Risk) System consists of components for preparation of a synthetic, absorbable, polyethylene-glycol hydrogel spacer. The hydrogel is absorbable, water-soluble, non-toxic and non-immunogenic. Using ultrasound guidance, the gel is injected using a transperineal approach. The needle tip is positioned beyond the rectourethralis muscle and hydrodissection is achieved with saline between the retroprostatic (Denonvilliers') fascia and the anterior rectal wall. Once the needle placement is confirmed, the biodegradable spacer is injected into the perirectal space. It then polymerizes with the saline to form a soft absorbable hydrogel mass. The hydrogel spacer maintains space for approximately 3 months and is absorbed in about 6 months.[8]

Table 1. Prostate Cancer Grading Systems[2]

Grade Group	Gleason Score (Primary and Secondary Pattern)	Cells
1	6 or less	Well-differentiated (low grade)
2	7 (3 + 4)	Moderately differentiated (moderate grade)
3	7 (4 + 3)	Poorly differentiated (high grade)
4	8	Undifferentiated (high grade)
5	9 to10	Undifferentiated (high grade)

Regulatory Status

In October 2014, SpaceOAR™ (Augmenix, a subsidiary of Boston Scientific) was cleared by the U.S. Food and Drug Administration (FDA) through the De Novo process (DEN140030). Barrigel Injectable Gel (Palette Life Sciences) was approved by the FDA via the premarket approval process in March 2022 (K220641; FDA product code: OVB), followed by BioProtect Balloon Implant™ System (BioProtect, Ltd) in 2023 (K222972; FDA product code: OVB).The intended and approved use of SpaceOAR System, Barrigel, and BioProtect Balloon Implant is 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 these hydrogel spacers to reduce the radiation dose delivered to the anterior rectum.

On April 1, 2015 the FDA gave de novo clearance to the SpaceOAR® System (Augmenix, Inc.) as a class II device under the generic name of "Absorbable perirectal spacer."[9] 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 absorbable spacer maintains space for the entire course of prostate radiotherapy treatment and is completely absorbed by the patient's body over time.

On July 19, 2019, Augmenix, Inc. received FDA approval (K182971, Class II device) for the SpaceOAR Vue Hydrogel. The SpaceOAR Vue Hydrogel is a synthetic, absorbable polyethylene glycol (PEG)-based hydrogel that creates a space that temporarily positions the anterior rectal wall away from the prostate during radiotherapy.

DuraSeal® Exact (Integra) was approved by the FDA through the premarket approval process as a spine and cranial sealant (dura mater) and has been used off-label as a perirectal spacer.

Medical Policy Statement

The use of transperineal biodegradable material (SpaceOAR®) is considered established when criteria is met.

Inclusionary and Exclusionary Guidelines

The use of transperineal biodegradable material (SpaceOAR®) is considered established in men undergoing radiation therapy for prostate cancer.

The use of transperineal biodegradable material (SpaceOAR®) is considered experimental/ investigational for all other indications.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

55874

Other codes (investigational, not medically necessary, etc.):

N/A

Note: Code 55874 may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

Serrano et al (2017) reviewed evidence for reducing rectal injuries in men who are receiving radiation therapy for prostate cancer.[10] The first topic examined was advances in radiation therapy. Improved IMRT techniques have led to reduced margins and decreased injury. Studies that support this position include Zelefsky et al (2008), with a comparison of 3D conformal RT and IMRT in 1,571 patients; and Chung et al (2009) who examined 25 patients treated with high-dose IMRT, with and without IGRT with radio-opaque fiducials. The reviewers then evaluated the effect of endorectal balloons. As prostate immobilizers, there were conflicting reports regarding the impact on prostate motion. In regard to dosimetric effects, data on reported toxicities with the use of balloons is scarce. Finally, tissue spacers (hyaluronic acid, human collagen, interstitial biodegradable balloons and synthetic polyethylene glycol hydrogels) were reviewed. The reviewers concluded that the use of tissue spacers is promising; however, longer follow-up is needed. Current IMRT techniques result in relatively low rates of rectal toxicities and tissue spacers in IMRT may have little additional value in reducing rectal toxicity. However, spacers may be more beneficial when used with SBRT.

The patients were evaluated at baseline, weekly during IG-IMRT, and at 3-, 6-, 12- and 15-month follow-up visits. A significant reduction was found in late (3 to 15 months) rectal toxicity severity in the spacer and control groups (2.0% and 7.0%, respectively). There were similar acute toxicity rates between the groups. The primary study endpoint of >25% reduction of rectal volume exposure (receiving at least 70Gy) was met in 97.3% of spacer patients ($p<0.0001$).

Pinkawa et al (2015) reported on 5 year results of SpaceOAR. From 2010 to 2011, 114 patients received a five-field IMRT technique; 54 patients were selected for a hydrogel injection prior to RT.[11] Patients were surveyed before RT, the last day of RT, 2 months, 17 months and 63 months after RT using a validated questionnaire (Expanded Prostate Cancer Index Composite). For patients treated with a hydrogel spacer, mean bowel function and bother score changes of >5 points in comparison with baseline levels were found only at the end of RT (10-15 points; $P<.01$). No spacer patient reported moderate or big problems with his bowel habits overall. Mean bother score changes of 21 points at the end of RT, 8 points at 2 months, 7 points at 17 months, and 6 points at 63 months after RT were found for patients treated without a spacer. A bowel bother score change >10 points was found in 6% of those treated with a spacer versus 32% of those without a spacer ($P<.01$) at 17 months, and in 5% of those treated with a spacer versus 14% of those without a spacer ($P=.2$) at 63 months.

Hwang et al (2019) reported on safety and efficacy outcomes from their institutional prostate SBRT experience with SpaceOAR placement.[12] Fifty men with low- or intermediate-risk prostate cancer underwent SpaceOAR and fiducial marker placement. Toxicity assessments were conducted at least weekly while on treatment, 1 month after treatment and every follow-up visit thereafter. Median follow up time was 20 months. Mean prostate-rectum separation

achieved with SpaceOAR was 9.6 ± 4 mm at the prostate midgland. No grade ≥ 3 GU or GI toxicity was recorded. During treatment, 30% of men developed new grade 2 GU toxicity (urgency or dysuria). These symptoms were present in 30% of men at 1 month and in 12% of men at 1 year post-treatment. During treatment, GI toxicity was limited to grade 1 symptoms (16%), although 4% of men developed grade 2 symptoms during the first 4 weeks after SBRT. All GI symptoms were resolving by the 1 month post-treatment assessment and no acute or late rectal toxicity was reported > 1 month after treatment. The authors concluded that periprostatic hydrogel placement followed by prostate SBRT resulted in minimal GI toxicity, and favorable early oncologic outcomes. The authors stated that SBRT with periprostatic spacer is a well-tolerated, safe, and convenient treatment option for localized prostate cancer.

Mahal and Yu (2017) of the Yale School of Medicine discuss "… A decision analysis model using real-world costs and 2016 costs of Space-OAR conducted by Hutchinson et al [2016] found that although the rectal spacer resulted in an increase in cost of $518 over 10 years with conventional radiotherapy, significant reduction in rectal toxicity is observed. It is possible that the increase in cost is balanced by reduced toxicity and improved quality of life. Moreover, for high-dose SBRT the effect was amplified with immediate savings of $2332 due to higher rates of rectal toxicity with high dose SBRT. Thus, as increased emphasis is placed on reducing healthcare costs associated with delivery of radiotherapy or complications, SpaceOAR remains a viable option to achieve this goal."[13]

Miller et al (2020) performed a systematic review and meta-analysis of 7 studies and 1100 men receiving prostate cancer radiotherapy.[14] The reviewers found that perirectal hydrogel spacer placement was associated with less rectal irradiation, fewer rectal toxic effects and higher bowel-related quality of life in long-term follow-up.

Babar et al (2021) conducted a systematic review describing clinical outcomes of SpaceOAR in men undergoing EBRT for localized prostate cancer.[15] Eight studies were included, including all those analyzed in the systematic review by Miller et al (2020), plus an additional retrospective review by Navaratnam et al (2019) and a pooled analysis on long-term outcomes by Seymour et al (2020) (summarized in the Longer-term Follow-up section below). Unlike the publication by Miller et al (2020), a meta-analysis of the data was not performed. However, following a review of the available evidence, the authors concluded that SpaceOAR may be beneficial for those patients who 1) do not meet the standard rectal dose-volume criteria 2) have higher risk factors for the development of rectal toxicities post-radiation, and 3) wish to decrease the length and costs of radiotherapy by increasing the dose of radiation per fraction.

Published evidence supports the benefit of SpaceOAR for the prevention of rectal toxicity in patients treated with EBRT. SpaceOAR's safety and effectiveness is currently being studied in SBRT and brachytherapy modalities.

SUPPLEMENTAL INFORMATION

National Comprehensive Cancer Network (NCCN)
NCCN Clinical Practice Guidelines In Oncology, Prostate Cancer, Version 4.2024[16]
Definitive Radiation Therapy General Principles

“Ideally, the accuracy of treatment should be verified by daily prostate localization, with any of the following: techniques of image-gu9ided RT (IGRT) using CT, ultrasound, implanted fiducials, or electromagnetic targeting/tracking. Endorectal balloons may be used to improve prostate immobilization. Biocompatible and biodegradable perirectal spacer materials may be implanted between the prostate and rectum in patients undergoing external radiotherapy with organ-confirmed prostate cancer in order to displace the rectum from high radiation dose regions. A randomized phase III trial demonstrated reduced rectal bleeding in patients undergoing the procedure compared to controls. Retrospective data also support its use in similar patients undergoing brachytherapy. Patients with obvious rectal invasion or visible T3 and posterior extension should not undergo perirectal spacer implantation.”

National Institute for Health and Care Excellence
In 2023, NICE updated their guidance on the biodegradable spacer.[17,] The NICE recommendations state that: "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."

National Institute for Health and Care Excellence (NICE)
Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer - Interventional procedures guidance [IPG752] Published date: February 7, 2023[18]
Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer in adults. This involves using a liquid gel or a balloon to increase the distance between the prostate and the rectum to reduce the amount of radiation reaching the rectum.
1 Recommendations
.1.1 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. Find out what special arrangements mean on the NICE interventional procedures guidance page.

1.2Clinicians wanting to do biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer should:

- Inform the clinical governance leads in their healthcare organization.
- Give people (and their families and carers as appropriate) clear written information to support shared decision making, including NICE's information for the public.
- Ensure that people (and their families and carers as appropriate) understand the procedure's safety and efficacy, and any uncertainties about these.
- Audit and review clinical outcomes of everyone having the procedure. The main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes audit tool (for use at local discretion).

- Discuss the outcomes of the procedure during their annual appraisal to reflect, learn and improve.

1.3Healthcare organizations should:

- Ensure systems are in place that support clinicians to collect and report data on outcomes and safety for everyone having this procedure.
- Regularly review data on outcomes and safety for this procedure.

1.4The procedure should only be done by clinicians with training in and experience of transperineal interventional procedures.

1.5Further research could be in the form of randomized controlled trials or observational data studies including registry studies and real-world evidence. It should report details of patient selection, choice of radiotherapy technique and device used, improvement in quality of life, and long-term efficacy and safety. It should also identify high-risk groups who might benefit.

Government Regulations

National:

There is no National Coverage Determination found for biodegradable perirectal spacer.

Local:

There is no Local Coverage Determination found for biodegradable perirectal spacer.
The code 55874 has reimbursement amounts found in the 2024 CMS Physician Fee Schedule.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

IMRT of the Prostate

References

1. American Cancer Society. Key Statistics for Prostate Cancer. Key Statistics for Prostate Cancer | Prostate Cancer Facts | American Cancer Society Updated January 19,2024. Accessed 8/15/24
2. Gleason DF. Classification of prostatic carcinomas. Cancer Chemother Rep. Mar 1966; 50(3): 125-8. PMID 5948714
3. Centers for Disease Control. Prostate Cancer. https://www.cdc.gov/cancer/prostate/index.htm Accessed 8/15/24

4. American Cancer Society. Treating Prostate Cancer. https://www.cancer.org/cancer/prostate-cancer/treating.html Accessed 8/15/24.
5. DiBiase SJ and Roach III M. External beam radiation therapy for localized prostate cancer. UpToDate. Last update Apr 05, 2021. https://www.uptodate.com/contents/external-beam-radiation-therapy-for-localized-prostate-cancer?search=external%20beam%20radiation%20therapy%20for%20localized%20prostate%20cancer&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1 Accessed 8/15/24.
6. Storey MR, Pollack A, Zagars G, et al. Complications from radiotherapy dose escalation in prostate cancer: preliminary results of a randomized trial. Int J Radiat Oncol Biol Phys. Oct 1 2000; 48: 635–42. PMID 11020558
7. Hatiboglu G, Pinkawa M, Vallee, JP, et al. Application technique: placement of a prostate-rectum spacer in men undergoing prostate radiation therapy. BJU Int. Dec 2012;110(11 Pt B):E647-52. PMID 22788857
8. Hayes Health Technology Brief. Absorbable perirectal spacer (SpaceOAR System; Augmenix Inc.) during radiation therapy for prostate cancer. April 10, 2018.
9. Food and Drug Administration (FDA) de novo request, SpaceOAR System, https://www.accessdata.fda.gov/cdrh_docs/pdf14/den140030.pdf Accessed 8/15/24.
10. Serrano NA, Kalman NS, Anscher MS. Reducing rectal injury in men receiving prostate cancer radiation therapy: current perspectives. Cancer Manag Res. Jul 28 2017; 9: 339-350. PMID 28814898
11. Pinkawa M et al, Quality of life after radiation therapy for prostate cancer with a hydrogel spacer: five year results. International Journal of Radiation Oncology Biology Physics 2017; 99:(2), 374-377.
12. Hwang ME, Mayeda M, Liz M, et al. Stereotactic body radiotherapy with periprostatic hydrogel spacer for localized prostate cancer: toxicity profile and early oncologic outcomes. Radiat Oncol. Aug 2 2019;14(1):136 PMID 31375119
13. Mahal AR, Yu JB, Current and Emerging Standards in Radiation Therapy for Prostate Cancer. The American Journal of Hematology/Oncology June 2017 http://gotoper-com.s3.amazonaws.com/_media/_pdf/AJHO_June2017_prostate.pdf Accessed 8/15/24.
14. 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 1 2020;3(6):e208221. PMID 32585020
15. 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. Apr 14 2021. PMID 33855816
16. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Prostate Cancer Version 4.2024, May 17, 2024 https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf Accessed 8/15/24.
17. National Institute for Health and Care Excellence. Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer. IPG752 2023 Overview | Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer | Guidance | NICE accessed 8/15/24
18. National Institute for Health and Care Excellence (NICE), Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer, February 2023 Overview | Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer | Guidance | NICE Accessed 8/15/24.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 8/15/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
9/1/18	6/19/18	6/19/18	Joint policy established
9/1/19	6/18/19		Routine maintenance
9/1/20	6/16/20		Routine maintenance
9/1/21	6/15/21		Routine maintenance Ref 13, 15 added
3/1/22	12/14/21		Routine maintenance Ref added: 16
3/1/23	12/20/22		Routine maintenance (jf) • Vendor: AIM's criteria is more restrictive but there is no PA requirements for SpaceOAR. • Vendor: Code is not on the Evicore list for management.
1/1/24	10/17/23		Routine maintenance (jf) Vendor Managed: NA Replaced ref 1 and 17 Added ref 2
1/1/25	10/15/24		Routine maintenance (jf) Vendor Managed: NA

Next Review Date: 4th Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PERIRECTAL SPACER FOR RADIATION THERAPY TREATMENT OF PROSTATE CANCER (SPACEOAR®)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; policy guidelines apply.
BCNA (Medicare Advantage)	See Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.