

Corporate Medical Policy

Perirectal Spacer Use During Radiotherapy for Prostate Cancer

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Last CAP Review:	5/2020
Next CAP Review:	5/2021
Last Review:	9/2020

Description of Procedure or Service

Radiation therapy for prostate cancer

Localized prostate cancer may be treated using surgery or definitive radiation therapy. Highly conformal radiation techniques are used in order to minimize toxicity to surrounding normal organs and structures, however, side effects can still occur. Radiation induced toxicity can cause acute symptoms (occurring during radiotherapy or within three months) and/or chronic symptoms (persisting or appearing after three months). Acute gastrointestinal (GI) symptoms can include diarrhea, abdominal pain, nausea, bloating, rectal bleeding and urgency. Chronic GI symptoms can include fecal incontinence, urgency, rectal bleeding, flatulence and abdominal pain.

Various factors contribute to the risk of toxicity to normal tissues, including the type of radiation therapy, the size of the treatment field and dose delivered. Dose escalation of radiation therapy may improve cancer outcomes but also increases the risk of toxicity to surrounding tissue. Image-guided radiation therapy and conformal radiation techniques may be used to limit margins and reduce toxicity but, in the case of prostate cancer, because the rectum lies in close proximity, the risk of rectal toxicity remains high.

Perirectal Spacers

One proposed approach to potentially decrease rectal toxicity associated with radiation therapy to the prostate is to increase the space between the two organs during radiation therapy. A variety of biomaterials, including collagen, hyaluronic acid, polyethylene glycol (PEG) hydrogels, and absorbable balloons have been evaluated as a means to reduce radiation exposure to the anterior rectal wall. The SpaceOAR System is the first PEG hydrogel that was cleared by the U.S Food and Drug Administration specifically for use during radiation therapy of the prostate. The chemical composition of the SpaceOAR is similar to a PEG-based hydrogel that is Food and Drug Administration approved as a dural sealant. Hydrodissection is achieved with saline between the retroprostatic (Denonvilliers') fascia and the anterior rectal wall using a transperineal approach. Once the needle placement is confirmed, two solutions in a two-channel syringe are injected into the perirectal space. The hydrogel then polymerizes to form a soft mass. The hydrogel maintains the space for approximately 3 months, the duration of radiotherapy, and is completely absorbed by 12 months. The PEG hydrogel may be injected at the same time as the placement of fiducial markers in the prostate.

Regulatory Status

In October 2014, SpaceOAR® (Augmenix) was cleared by the Food and Drug Administration through the De Novo process (DEN140030). "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."

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Policy

BCBSNC will provide coverage for transperineal placement of a biodegradable, perirectal spacer in individuals receiving radiotherapy for prostate cancer (ie SpaceOAR) when it is determined to be medically necessary because the medical criteria and guidelines shown below have been met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Perirectal Spacer Use in Radiotherapy for Prostate Cancer is covered

Transperineal placement of a biodegradable, perirectal spacer (ie SpaceOAR) may be considered **medically necessary** in individuals undergoing external beam radiation therapy (IMRT or SBRT) for organ-confined prostate cancer.

When Perirectal Spacer Use in Radiotherapy for Prostate Cancer is not covered

Transperineal, placement of a biodegradable perirectal spacer (ie SpaceOAR) is considered **investigational** when the above criteria are not met.

Policy Guidelines

The rectum lies in close proximity to the prostate and is at risk for toxicity due to radiation therapy. One proposed approach is to displace the rectum away from the prostate, increasing the space between the two and reducing the radiation dose to the rectum. A variety of biomaterials, including polyethylene glycol hydrogels (eg, SpaceOAR System) have been evaluated as perirectal spacers.

Evidence Summary

For individuals who have prostate cancer and are undergoing radiation therapy who receive a perirectal spacer, the evidence includes a pivotal randomized controlled trial with three year follow-up with use during IMRT and a systematic review with meta-analysis. Additional literature consists of non-randomized, smaller studies, including the use of perirectal spacers with low-dose-rate brachytherapy. The relevant health outcomes include symptoms, quality of life, and treatment-related morbidity. The randomized trial indicated the hydrogel spacer reduced the radiation dose to the rectum compared to the control group (no spacer). Acute rectal toxicities were similar between groups. There were few events of greater than grade 1 toxicity in either group, however, there was a reduction in rectal toxicity severity in the spacer group between 3 and 15 months. A meta-analysis of the study concluded that the evidence is of low-certainty and that hydrogel spacers may make little or no difference to GI outcomes. At three years, fewer patients in the spacer group had grade 1 or greater late toxicity, and patient-reported declines in rectal and urinary quality of life were statistically lower in the spacer group and met the threshold for a clinically significant difference. However, it is not clear if patients were blinded to treatment at the longer-term follow-up and only 63% of the patients from the original study were evaluated at three years. Additional study is needed to corroborate the findings of the pivotal randomized controlled trial, to determine which patients are likely to benefit from the use of a spacer, and to fully understand the long-term safety and efficacy of this technology.

Randomized Controlled Trial

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The phase 3 trial for the hydrogel spacer SpaceOAR randomized 222 men being treated for prostate cancer 2:1 to the spacer or control group (no spacer), respectively (Mariados 2015). Safety, toxicity and quality of life (QoL) were assessed through 15 months. All patients had clinical stage T1 or T2 prostate cancer, Gleason score ≤ 7 and received image-guided IMRT to the prostate, 79.2 Gy in 1.8 Gy fractions. The primary effectiveness outcome was the proportion of patients achieving $>25\%$ reduction in rectal volume receiving 70 Gy in dose planning studies, which was 3.3% with the spacer and 11.7% without ($p < 0.001$). Blinded adjudication identified no spacer-related adverse events. Acute rectal and urinary toxicity in the first three months and the rates of grade 1 or greater rectal or procedure adverse events in the first 6 months were similar in the spacer and control groups. Late rectal toxicity of grade 1 or greater at 3-15 months was observed in 2.0% of the spacer patients and 7.0% of the control patients (all were grade 1 with the exception of 1 grade 3 proctitis in the control group). No grade 4 toxicities were reported. Final results of the trial were reported with a median follow-up period of 3 years (Hamstra 2017), and included 63% of the original sample. It was unclear if the patients remained blinded to treatment group at the three year follow-up. Grade 1 or greater toxicities were reported as 2% vs 9%, in the spacer group vs the control group, respectively ($p < 0.03$).

Systematic Review

A 2018 Cochrane systematic review of interventions to reduce acute and late adverse gastrointestinal effects of pelvic radiotherapy for primary pelvic cancers assessed the evidence from two studies in men undergoing radiation for prostate cancer (Mariados 2015; Prada 2009). The 2009 Prada study included 69 men who underwent low-dose-rate brachytherapy for low or intermediate risk prostate cancer. A meta-analysis of the two studies reported the following results for a hydrogel spacer versus no spacer and the risk of GI toxicity: low-certainty evidence suggests that hydrogel spacers may make little difference to acute GI (rectal) toxicity grade 2+ (RR 0.51, 95% CI 0.08-3.38) [2 studies] and acute grade 1+ GI toxicity (RR 0.85, 95% CI 0.55 to 1.30) [1 study]. Low-certainty evidence suggests that hydrogel spacers may make little or no difference to late GI (rectal) toxicity grade 2+ up to 15 months post-radiation therapy (RR 0.16, 95% CI 0.01 to 3.96) [1 study] and at a median of three years (RR 0.07, 95% CI 0.00 to 1.34) [1 study]. Evidence on late GI toxicity grade 1+ up to 15 months post-radiation (RR 0.29, 95% CI 0.07 to 1.19) [1 study] and at a median of three years (RR 0.24, 95% CI 0.05 to 1.29) [1 study] is also of low certainty.

For quality of life (QoL), the authors found no continuous data that could be included in meta-analysis. The Mariados 2015 study reported that fewer participants in the spacer group “reported declines in QoL relative to those of the control, with 11.6% and 21.4% of hydrogel and control patients, respectively, experiencing 10-point declines at 15 months” post-radiation ($p = 0.087$). In the follow-up report to this study, which involved 63% of the original participants, at three years those in the spacer group were less likely to have a detectable change in GI QoL score on the expanded prostate cancer index composite scale than controls (five-point reduction: 41% vs 14%, $p = 0.002$; 10-point reduction: 21% vs 5%, $p = 0.02$).

Overall, the review concluded that low-certainty evidence on hydrogel spacers suggests that this intervention may make little or no difference to GI outcomes.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 55874

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

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Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.164, 1/17/2019

Hamstra DA, Mariados N, Sylvester J, et al. Sexual quality of life following prostate intensity modulated radiation therapy (IMRT) with a rectal/prostate spacer: Secondary analysis of a phase 3 trial. *Pract Radiat Oncol*. 2018 Jan - Feb;8(1):e7-e15.

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 Apr 1;97(5):976-985.

Lawrie TA, Green JT, Beresford M, et al. Interventions to reduce acute and late adverse gastrointestinal effects of pelvic radiotherapy for primary pelvic cancers. *Cochrane Database Syst Rev*. 2018 Jan 23;1:CD012529.

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 Aug 1;92(5):971-977.

Prada PJ, Gonzalez H, Menéndez C, et al. Transperineal injection of hyaluronic acid in the anterior perirectal fat to decrease rectal toxicity from radiation delivered with low-dose-rate brachytherapy for prostate cancer patients. *Brachytherapy*. 2009 Apr-Jun;8(2):210-217.

Medical Director review 3/2019

Specialty Matched Consultant Advisory Panel 5/2019

Medical Director review 5/2019

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.164, 1/16/20

Specialty Matched Consultant Advisory Panel 5/2020

Medical Director review 5/2020

Medical Director review 9/2020

Policy Implementation/Update Information

3/12/19 New policy developed. Perirectal spacer use during radiotherapy for prostate cancer is considered **investigational**. Medical Director review 3/2019. Reference added. Notification given 3/12/19 for effective date 5/14/19. (lpr)

5/28/19 Specialty Matched Consultant Panel review 5/15/2019. No change to policy statement. (lpr)

6/26/20 Specialty Matched Consultant Panel review 5/20/2020. Reference added. No change to policy statement. (lpr)

10/1/20 Under "When Covered" section: added medical necessity coverage for perirectal spacer use in prostate cancer: "Transperineal placement of a biodegradable, perirectal spacer (ie

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SpaceOAR) may be considered **medically necessary** in individuals undergoing external beam radiation therapy (IMRT or SBRT) for organ-confined prostate cancer.” Updated policy guidelines. Medical Director review 9/2020. (lpr)

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