SpaceOAR System (Augmenix, Inc.)
Hydrogel Spacer for Reducing Exposure during Prostate Cancer Radiation Therapy

The SpaceOAR™ System is a single-use device consisting of a polyethylene glycol 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. The radiation oncologist uses ultrasound to insert the hydrogel mixture between the rectum and the prostate. The hydrogel is absorbed by the patient’s body within three months.

The Evidence Bar™: Evidence is somewhat favorable

Executive Summary

Conclusions: SpaceOAR hydrogels are well tolerated and work as intended to reduce rectal irradiation, long-term (but not acute) rectal toxicity, and improve bowel quality of life (QOL), based on 1 randomized controlled trial (RCT) and 3 non-RCTs. A comparative study found that neither SpaceOAR nor a competing spacer (BioProtect Prospace) reduced acute rectal toxicity (<3 months). Studies with longer follow-up (>5 years) that compare different spacers are needed; an ongoing study will provide 5-year data.

- SpaceOAR hydrogel increases perirectal space and reduces rectal irradiation, severity of late rectal toxicity, and the proportion of patients experiencing poor bowel QOL, based on results of a multicenter RCT that reported 3-year results and 3 non-RCTs of radiotherapy groups reporting shorter 3- to 12-month follow-up. No studies are available that compare SpaceOAR with hyaluronic acid or human collagen spacers.
- SpaceOAR does not appear to reduce acute rectal toxicity during and shortly after radiation therapy (<3 months) based on controlled trial results. A study comparing SpaceOAR with the BioProtect Prospace balloon spacer found that neither device reduces acute rectal toxicity (<3 months).
- Clinicians may need to perform at least 32 procedures before achieving optimal SpaceOAR insertion and patient outcomes, based on evidence from a retrospective, single-center comparison study.
- SpaceOAR placement and hydrogel material appear to be well tolerated based on results from the RCT and case series. RCT authors reported that no rectal perforation, hemorrhage, or infection were associated with use of SpaceOAR. Most events were mild, transient, and similar between groups. Case series (n = 683) reported few adverse events: 4 rectal wall penetrations (with dose escalation), 1 Grade 3 telangiectasia, and 1 asymptomatic necrotic rectal lesion.
- Longer-term (>5 years) and comparative data are needed because late effects can occur many years after prostate irradiation. A single-arm postmarketing study is collecting 5-year data on 250 patients.

Evidence: Search dates: January 1, 2000, to May 17, 2017. We identified 12 published studies reported in 14 publications and reviewed full text of 7 articles and abstracts of 7 articles.

- 7 controlled trials: 1 RCT (n = 222) reported in 3 publications compared intensity modulated radiation therapy (IMRT) with and without SpaceOAR; 4 non-RCTs (n = 516) compared various radiation therapy modes with and without SpaceOAR; 1 non-RCT (n = 78) compared external beam radiation therapy (EBRT) with and without SpaceOAR or BioProtect Prospace balloon; and 1 non-RCT (n = 64) compared the first 32 and next 32 SpaceOAR injections to assess clinician learning curve.
- 4 case series (n = 683) assessed SpaceOAR use in patients receiving prostate radiation therapy.
- 1 cost model compared costs associated with rectal toxicity over 10 years in patients with and without SpaceOAR.
- The longest reported follow-up is 3 years; no studies compared SpaceOAR with hyaluronic acid or human collagen injection spacers.

Safety: Unable to assess MAUDE reports of technology-related events due to few and vague reports.

Ongoing trials: Trials may partially address evidence gap.

- 2 single-arm studies (n = 279) on rectal complications are expected to end in January 2019 and December 2020.
**Product Overview**

The **SpaceOAR hydrogel spacer** (Augmenix, Inc., Waltham, MA, USA) is intended to protect the anterior rectum during prostate cancer radiation therapy by temporarily positioning the rectum away from the prostate, thereby reducing the radiation dose delivered to the anterior rectum and reducing rectal complications related to radiation therapy. The SpaceOAR maintains space for the entire course of prostate radiotherapy. The device has no intended effect on prostate cancer therapy, other than to protect the rectum.

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.

During a short procedure with transrectal ultrasound guidance, the radiation oncologist uses the SpaceOAR single-use dual syringe with injection needle to combine the system components and place the mixture in the space between the rectum and the prostate via a transperineal approach. The mixture forms a malleable hydrogel. According to the instructions for use, “The Precursor solution is formed by mixing the Diluent solution (Trilysine buffer solution) with the PEG [polyethylene glycol] powder. The Accelerator solution is a simple salt buffer solution. When mixed together, the solutions cross-link to form a soft hydrogel.” The Y-connector of the syringe has a static mixer that allows mixing of the two solutions before passing through the injection needle. The soft hydrogel forms the spacer between the prostate and the anterior rectal wall. According to Augmenix, the spacer is biodegradable and “remains in place for about three months, after which it liquefies by hydrolysis, and is absorbed and cleared in the patient’s urine.”

**Purported Benefits/Advantages According to Manufacturer Information***

- “SpaceOAR System reduces rectal injury in men receiving prostate cancer radiation therapy (RT) by acting as a spacer – pushing the rectum away from the prostate.”
- “SpaceOAR System is the first absorbable hydrogel spacer designed to reduce unintentional rectal injury in men undergoing prostate radiotherapy (RT).”
- “SpaceOAR claims to provide “patients the confidence to undergo prostate radiotherapy.”
- “Once in place, patients typically can’t feel the SpaceOAR hydrogel.”

*Note: This is a list of the main benefits described by the manufacturer and does not imply endorsement or validation by ECRI Institute.

**Regulatory Status**

In April 2015, FDA granted marketing clearance for the SpaceOAR hydrogel spacer through the 513(a) (1) (de novo) process (DEN140030). 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.

According to the FDA Reclassification order, FDA completed its review of the de novo request for classification of the SpaceOAR system, a prescription device under 21 CFR 801.109. FDA identifies this generic type of device as an "absorbable perirectal spacer."

**Current Treatments**

Prostate cancer is one of the most common types of cancer in older men. Prostate cancer treatment options include surgery, chemotherapy, cryosurgery, and radiation therapy. Prostate radiotherapy usually results in the rectum receiving high-dose radiation, leaving the organ at risk. Rectal spacers may be placed between the prostate and rectum to protect the anterior rectum from radiation. Different spacer materials intended to prevent radiation damage include hyaluronic...
SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer

Acid, human collagen, inflatable balloons, and hydrogel. (For more information, see the article by Pinkawa, “Current Role of Spacers for Prostate Cancer Radiotherapy.”)

Clinical Literature

We searched PubMed, EMBASE, and selected web-based resources for documents relevant to this topic and published between January 1, 2000, and May 17, 2017. We specifically searched for evidence addressing any reduction in radiotherapy toxicity in nearby organs, especially the rectum and gastrointestinal (GI) tract, as well as patient injury that may result from the hydrogel injection procedure. We included RCTs, non-RCTs, and case series that assessed 30 or more patients. We identified 14 relevant publications. We reviewed full text of seven studies (six available through open access and one available by subscription only) and the abstracts of seven studies. See Table 1 for summaries.

- 1 RCT (n = 222) with results in 3 publications compared IMRT with and without a SpaceOAR spacer (longest follow-up 3 years). (1-3)
- 4 non-RCTs (n = 516) compared radiation therapy (image-guided IMRT, volumetric modulated arc therapy, or 3-dimensional conformal radiation therapy) with and without a SpaceOAR spacer. (4-7)
- 1 nonrandomized controlled study (n = 78) compared EBRT without radioprotection with EBRT after a SpaceOAR injection and EBRT after insertion of a BioProtect Prospace balloon. (8)
- 1 nonrandomized controlled study (n = 64) compared IMRT and the first 32 SpaceOAR injections with IMRT and the second 32 SpaceOAR injections to assess learning curve with the spacer insertion procedure. (9)
- 4 case series (n = 683) assessed SpaceOAR spacer use in patients receiving radiation therapy to the prostate. (10-13)
- 1 cost model compared costs associated with rectal complications because of rectal toxicity over a 10-year period in patients with and without a SpaceOAR injection before conformal radiation therapy or stereotactic body radiotherapy. (14)

We also identified a patient selection decision model (15) and a 2014 systematic review of literature on different types of commercially available prostate-rectum spacers. (16)

RCT Findings

The multicenter RCT compared patients undergoing IMRT who were randomly assigned to receive SpaceOAR injection (n = 149) and those who received no injection (n = 73). (1) The study reported no device-related adverse events, rectal perforations, serious bleeding, or infections in either group. The authors found the spacer to be an effective tool that led to increased perirectal space and reduced rectal irradiation, rectal toxicity severity, and the number of patients experiencing declines in bowel QOL. This study was also described in the FDA Decision Summary as part of the de novo clearance process. This document states that “the evaluation of the safety data determined that the SpaceOAR procedure and hydrogel material were demonstrated to be well-tolerated. There were no unanticipated adverse device effects and no events attributed to the device based on independent review.” Also according to this document,

There were no CTCAE [Common Terminology Criteria for Adverse Events] Grade 3 or Grade 4 procedural or rectal events within the SpaceOAR treatment group and there were no serious procedure-related rectal events. In particular, no incidences of true rectal perforations, rectal hemorrhaging or infections in either group. The majority of the procedural-events that were observed were mild and transient and typical for men undergoing a transperineal injection or fiducial marker placement. The event rates for the two groups were comparable with 34.0% for the SpaceOAR treatment group vs. 31.9% for the control group (p=0.6862).

Hamstra et al. published final results of the RCT and found that the SpaceOAR benefits reported earlier were maintained or increased at 3-year follow-up. (3)
SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer

Non-RCT Findings

Radiation Therapy with and without SpaceOAR Injection

Pinkawa et al. 2017 (n = 167) reported that the SpaceOAR spacer did not affect acute rectal toxicity during and shortly after radiation therapy. However, a year after radiation therapy, patients with a spacer had significantly fewer treatments for bowel symptoms than patients without a spacer. Also, compared with baseline, mean bowel function scores did not change for patients with a spacer in contrast to patients without a spacer who had a mean decrease of 5 points.(4)

Te Vilde et al. 2017 (n = 125) reported that patients who received a SpaceOAR spacer experienced significantly less diarrhea in the month after IMRT than patients without a SpaceOAR spacer.(5)

Whalley et al. 2016 (n = 70) reported that patients who received a SpaceOAR spacer experienced significantly less diarrhea in the month after IMRT than patients without a SpaceOAR spacer. However, late Grade 1 GI toxicity was significantly less frequent in patients with the spacer than in patients without the spacer.

Pinkawa et al. 2012 (n = 84) reported that initial bowel impairment scores were similar between groups, but 2 to 3 months after radiation therapy, patients in the group that received a SpaceOAR spacer had less severe bowel symptoms.(7)

SpaceOAR Spacer versus Balloon Spacer

Wolf et al. reported that overall acute toxicity in all 3 study groups (i.e., SpaceOAR spacer, BioProtect Prospace balloon, no radioprotection) was low, with no Grade 3 toxicity, and “there was no statistical difference between groups in cumulative incidence up to 90 days after radiotherapy of any genitourinary, [GI], or combined Grade 2 toxicities.”(8)

Learning Curve

Compared with the first 32 patients who received SpaceOAR spacers at 1 institution, Pinkawa et al 2013 (n = 64) reported improved and more symmetrical spacer placement, improved treatment planning, and less treatment-related acute toxicity in a second group of 32 patients who received subsequent SpaceOAR spacers.(9)

Case Series Findings

Three case series reported rectal/GI toxicity rates in patients who had radiation therapy after the SpaceOAR injection:

Grade 1 acute (37.4% to 39.6%)(11,12), Grade 2 acute (2.8% to 12.5%)(11,12), Grade 1 late (4.3% to 12.7%)(11,12), Grade 2 late (1.4% to 2%)(10,11), and Grade 3 late (0.7%).(11)

One case series(12) reported acute and late genitourinary toxicity rates in patients who had radiation therapy after the SpaceOAR injection: Grade 1 acute (41.7%), Grade 2 acute (35.4%), Grade 3 acute (2.1%), Grade 1 late (17%), and Grade 2 late (2.1%).

Three case series described specific adverse events: rectal wall penetrations (1.6% with dose escalation)(10), a Grade 3 telangiectasia (1.9%)(12), and an asymptomatic necrotic rectal lesion (2.1%).(13)

Cost Study Findings

The cost model found that the incremental cost of adding a spacer before conformal radiation therapy was $518, assuming the rectal toxicity reduction seen at 15 months was maintained for 10 years. The model estimated a savings of $2,640 when the SpaceOAR spacer was added to high-dose stereotactic body radiotherapy.(14)

Ongoing Trials

Our search of ClinicalTrials.gov identified two ongoing trials. Both are single-arm observational studies examining late (five-year) rectal complications. See Table 2 for details.

Safety

We also searched ECRI Institute’s Health Devices Alerts database for product-specific alerts or recalls and FDA's MAUDE database for similar information. We did not identify any relevant information in the Health Devices Alerts database. We identified four MAUDE records of injury submitted between January 1, 2014, and May 16, 2017. These injury reports describe the following: unintentional intravascular injection of the spacer (two cases), post bowel movement pain six
months after spacer placement (possibly due to foreign body reaction) (one case), and transperineal pain/infection (specific cause unknown) (one case).

FDA’s MAUDE database consists of mandatory and voluntary user facility, distributor, and manufacturer reports. The data are not intended for adverse event rate evaluation because FDA does not verify the validity or completeness of these reports, and it has no record of the total universe of procedures performed to establish a denominator and calculate an event rate. Thus, the information must be considered in that context.

Table 1. Product-specific Clinical Literature

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study Type and Patients</th>
<th>Treatment(s)</th>
<th>Results as Reported by Authors</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mariados et al. 2015(1) Reviewed full text Pieczonka et al. 2016(2) Reviewed abstract</td>
<td>Multicenter, RCT 222 patients with confirmed diagnosis of clinical stage T1 or T2 prostate cancer</td>
<td>Image-guided intensity modulated radiation therapy (IMRT) SpaceOAR spacer injection (n = 149) vs. No injection (n = 73)</td>
<td>“Spacer application was rated as &quot;easy&quot; or 'very easy' 98.7% of the time, with a 99% hydrogel placement success rate. Perirectal spaces were 12.6 +/- 3.9 mm and 1.6 +/- 2.0 mm in the spacer and control groups, respectively. There were no device-related adverse events, rectal perforations, serious bleeding, or infections within either group. Pre-to post-spacer plans had a significant reduction in mean rectal V70 (12.4% to 3.3%, P&lt;.0001). Overall acute rectal adverse event rates were similar between groups, with fewer spacer patients experiencing rectal pain (P=.02). A significant reduction in late (3-15 months) rectal toxicity severity in the spacer group was observed (P=.04), with a 2.0% and 7.0% late rectal toxicity incidence in the spacer and control groups, respectively. There was no late rectal toxicity greater than grade 1 in the spacer group. At 15 months 11.6% and 21.4% of spacer and control patients, respectively, experienced 10-point declines in bowel quality of life. MRI [magnetic resonance imaging] scans at 12 months verified spacer absorption.”</td>
<td>“Spacer application was well tolerated. Increased perirectal space reduced rectal irradiation, reduced rectal toxicity severity, and decreased rates of patients experiencing declines in bowel quality of life. The spacer appears to be an effective tool, potentially enabling advanced prostate RT [radiation therapy] protocols.” “Hydrogel spacer application was straightforward and repeatable, resulting in consistent perirectal space creation and rectal dose reduction. Spacer application has the potential to improve prostate radiotherapy outcomes and enable advanced radiotherapy protocols.”</td>
</tr>
</tbody>
</table>
### SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study Type and Patients</th>
<th>Treatment(s)</th>
<th>Results as Reported by Authors</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamstra et al. 2017(3)</td>
<td>Multicenter RCT</td>
<td>IMRT SpaceOAR spacer injection (n = 149) vs. No injection (n = 73)</td>
<td>&quot;The 3-year incidence of grade &gt;/=1 (9.2% vs 2.0%; P=.028) and grade &gt;/=2 (5.7% vs 0%; P=.012) rectal toxicity favored the spacer arm. Grade &gt;/=1 urinary incontinence was also lower in the spacer arm (15% vs 4%; P=.046), with no difference in grade &gt;/=2 urinary toxicity (7% vs 7%; P=0.7). From 6 months onward, bowel QOL [quality of life] consistently favored the spacer group (P=.002), with the difference at 3 years (5.8 points; P=.05) meeting the threshold for a MID. The control group had a 3.9-point greater decline in urinary QOL compared with the spacer group at 3 years (P&lt;.05), but the difference did not meet the MID threshold. At 3 years, more men in the control group than in the spacer group had experienced a MID decline in urinary QOL (41% vs 14%; P=.002) and urinary QOL (30% vs 17%; P=.04). Furthermore, the control group were also more likely to have experienced large declines (twice the MID) in bowel QOL (21% vs 5%; P=.02) and urinary QOL (23% vs 8%; P=.02).&quot;</td>
<td>&quot;The benefit of a hydrogel spacer in reducing the rectal dose, toxicity, and QOL declines after image guided intensity modulated radiation therapy 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.&quot;</td>
</tr>
<tr>
<td>Non-RCTs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pinkawa et al. 2017(4)</td>
<td>Retrospective single-center comparison 167 consecutive patients with an indication for prostate treatment</td>
<td>RT with 2 Gy fractions 76-80 Gy with SpaceOAR spacer injection (n = 101) vs. Up to 76 Gy without injection (n = 66)</td>
<td>&quot;Baseline patient characteristics were well balanced. Treatment for bowel symptoms (0 vs. 11%; p &lt; 0.01) and endoscopic examinations (3 vs. 19%; p &lt; 0.01) were performed less frequently with a spacer. Mean bowel function scores did not change for patients with a spacer in contrast to patients without a spacer (mean decrease of 5 points) &gt;1 year after RT in comparison to baseline, with 0 vs. 12 % reporting a new moderate/big problem with passing stools (p &lt; 0.01). Statistically significant differences were found for the items ‘loose stools,’ ‘bloody stools,’ ‘painful bowel movements’ and ‘frequency of bowel movements.’&quot;</td>
<td>&quot;Spacer injection was not found to affect acute rectal toxicity during and shortly after RT. A considerable advantage in terms of bowel problems resulted &gt;1 year after RT, including the same mean bowel quality of life score as before treatment and an absence of treatment for bowel problems. Thus, the application of a spacer has been shown to prevent rectal toxicity in this study within the evaluated time period. These results encourage further evaluation of this concept in larger patient groups.&quot;</td>
</tr>
</tbody>
</table>
# SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study Type and Patients</th>
<th>Treatment(s)</th>
<th>Results as Reported by Authors</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Te Velde et al. 2017(5) Reviewed abstract</td>
<td>Retrospective single-center comparison 125 patients with localized prostate cancer</td>
<td>IMRT 81 Gy in 45Fx over 9 weeks SpaceOAR spacer injection (n = 65) vs. No injection (n = 60)</td>
<td>“Rectal volume parameters were all significantly lower in the SpaceOAR group, with an associated reduction in acute diarrhea (13.8% vs 31.7%). There were no significant differences in the very low rates of acute and late fecal incontinence or proctitis, however, there was a trend towards increased hemorrhoid rate in the SpaceOAR group (11.7% vs 3.1%, P = 0.09).”</td>
<td>“A SpaceOAR program in a regional setting with urologists performing low volumes of insertions (&lt;1 per month on average) is of clinical benefit, and was associated with significantly lower radiation doses to the rectum and lower rates of acute diarrhea.”</td>
</tr>
<tr>
<td>Whalley et al. 2016(6) Reviewed abstract</td>
<td>Prospective, multicenter case-control 140 patients with prostate cancer</td>
<td>IMRT or volumetric modulated arc therapy (VMAT): 80 Gy in 40 fractions SpaceOAR spacer injection (n = 30) vs. Contemporary control group without spacer injection (n = 110)</td>
<td>“There were no perioperative complications. Rectal doses were significantly lower for the post-hydrogel plans, especially above 65 Gy (V82 = 0.2% versus 1.3%; V80 = 0.8% versus 5.3%; V75 = 2.2% versus 9.5%; V70 = 3.7% versus 12.3%; V65 = 5.4% versus 14.7%; V40 = 22.9% versus 32% and V30 = 42.7% versus 49.4%). There was no significant difference in acute grade 1 and 2 gastrointestinal toxicity, which was 43% versus 51% and 0% versus 4.5% in the hydrogel and control groups, respectively. Late grade 1 was significantly less frequent in the hydrogel group (16.6% versus 41.8%, P = 0.04).”</td>
<td>“SpaceOAR hydrogel was inserted with minimal side-effects. Dosimetric benefits were greatest at higher rectal doses (V65 to V82). Late grade 1 gastrointestinal toxicity was significantly lower than that seen in patients treated without hydrogel.”</td>
</tr>
<tr>
<td>Wolf et al. 2015(8) Reviewed full text (available by subscription only)</td>
<td>Prospective single-center comparison 78 consecutive patients with prostate cancer</td>
<td>External beam radiation therapy (EBRT) SpaceOAR spacer injection (n = 30) vs. Prospace balloon insertion (n = 29) vs. No radioprotection (n = 19)</td>
<td>“Overall acute toxicity in all groups was low with no grade 3 toxicity. Rectal acute toxicity was very low with no grade 2 (increase 4–6 stools/d) and 16.6%, 16% and 9% grade 1 (increase &lt;4 stools/d) for gel, balloon and control groups, respectively. Genitourinary toxicity grade 2 (urinary frequency and incontinence) was 36.6% (gel), 20% (balloon) and 28.5% (control). However, if compared to baseline at start of RT, worsening by 1 grade was only 12.5%, 13% and 21%, respectively. There was no statistical difference between groups in cumulative incidence up to 90 days after radiotherapy of any GU, GI [gastrointestinal] or combined grade 2 toxicities. Vienna rectal toxicity scores were very low with a score of 0 in 90.6% over all groups and timepoints. 2 patients had a once-only score of 3, one in the control group and one in the gel group, resolving to zero 3 months thereafter.”</td>
<td>“During EBRT following implantation of a balloon spacer, although slightly superior in regard to dose distribution of the rectum, monitoring of the balloon’s filling status throughout the duration of the treatment is recommended so that relevant deflation of the balloon can be detected and re-planning can be performed if necessary. In addition, we think that the balloon spacer might be superior for short course treatment regimens such as HDR [high dose rate] brachytherapy or hypofractionation schedules, whereas the gel spacer might be a better option for standard EBRT treatment of the prostate due to its more consistent nature over a longer period of time.”</td>
</tr>
<tr>
<td>Author/Year</td>
<td>Study Type and Patients</td>
<td>Treatment(s)</td>
<td>Results as Reported by Authors</td>
<td>Authors’ Conclusions</td>
</tr>
<tr>
<td>---------------------------</td>
<td>----------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Pinkawa et al. 2013(9)</td>
<td>Retrospective single-center comparison</td>
<td>5-field intensity-modulated radiotherapy technique to 76-78 Gy First 32 SpaceOAR spacer injections vs. Second 32 SpaceOAR spacer injections</td>
<td>“Rectum volume could be entirely excluded from the planning target volume in 31% in G1 vs 56% in G2 (P = .04). Increasing symmetry was detected comparing the first 15 patients to the subsequent rest, with mean differences between right and left of 0.6 cm vs 0.3 cm at the midgland (P = .03). Mean distance between prostate and anterior rectal wall increased from 0.8 cm/1.1 cm/0.8 cm (G1) at the base/middle/apex to 1.3 cm/1.5 cm/1.2 cm (G2), respectively, so that the dose to the rectum decreased significantly (6% vs 2% of the volume inside the 70 Gy isodose; P &lt;.01). Bowel function and bother score changes were smaller comparing baseline with last day of radiotherapy levels (mean 16/18 in G1 vs 9/12 in G2).”</td>
<td>“A learning curve could be demonstrated in our patient population, respecting improved and more symmetrical spacer placement, improved treatment planning, and less treatment-related acute toxicity. Several important technical aspects need to be considered.”</td>
</tr>
<tr>
<td>Pinkawa et al. 2012(7)</td>
<td>Prospective single-center comparison</td>
<td>Median 78 GY in 2 GY fractions after SpaceOAR spacer injection (n = 28) vs. 3-dimensional conformal radiation therapy (3DCRT) 70.2 GY (n = 28) vs. IMRT 76 GY (n = 28)</td>
<td>“Baseline mean bowel bother scores were 96 points in all subgroups. Similar mean changes (SP 16, 3DCRT 14, IMRT 17 points) were observed at the end of radiotherapy. The smallest difference resulted in the spacer subgroup 2-3 months after radiotherapy (SP 2, 3DCRT 8, IMRT 6 points). Bowel bother scores were only significantly different in comparison to baseline levels in the [SP]. The percentage of patients reporting moderate/big bother with specific symptoms did not increase for any item (urgency, frequency, diarrhea, incontinence, bloody stools, pain).”</td>
<td>“Moderate bowel quality-of-life changes can be expected during [RT] irrespective of spacer application or total dose. Advantages with a spacer can be expected a few weeks after treatment.”</td>
</tr>
<tr>
<td>Case Series (n ≥30)</td>
<td></td>
<td>Dose-escalated RT after SpaceOAR spacer injection</td>
<td>“The main indication for hydrogel application was dose-escalated radiotherapy for histologically confirmed low or intermediate risk prostate cancer. It was not recommended in locally advanced prostate cancer. The injection or implantation was performed under transrectal ultrasound guidance via the transperineal approach after prior hydrodissection. The rate of injection-related G2-toxicity was 2% (n = 5) in a total of 258 hydrogel applications. The most frequent complication (n = 4) was rectal wall penetration, diagnosed at different intervals after hydrogel injection and treated conservatively.”</td>
<td>“A consensus was reached on the application of a hydrogel spacer. Current experience demonstrated feasibility, which could promote initiation of this method in more centers to reduce radiation-related gastrointestinal toxicity of dose-escalated IGRT. However, a very low rate of a potential serious adverse event could not be excluded. Therefore, the application should carefully be discussed with the patient and be balanced against potential benefits.”</td>
</tr>
</tbody>
</table>

**SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer**
**SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer**

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Study Type and Patients</th>
<th>Treatment(s)</th>
<th>Results as Reported by Authors</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeh et al. 2016(11)</td>
<td>Prospective single-center series 326 patients with prostate carcinoma</td>
<td>Combination high-dose-rate brachytherapy average dose 15.5 Gy and external beam radiotherapy average dose 60.2 Gy and SpaceOAR spacer injection</td>
<td>“Median follow-up was 16 months. The mean anterior-posterior separation achieved was 1.6 cm (SD = 0.4 cm). Rates of acute Grade 1 and 2 rectal toxicity were 37.4% and 2.8%, respectively. There were no acute Grade 3/4 toxicities. Rates of late Grade 1, 2, and 3 rectal toxicity were 12.7%, 1.4%, and 0.7%, respectively. There were no late Grade 4 toxicities.”</td>
<td>“PEG [polyethylene glycol] rectal spacer implantation is safe and well tolerated. Acute and chronic rectal toxicities are low despite aggressive dose escalation.”</td>
</tr>
<tr>
<td>Uhl et al. 2014(12)</td>
<td>Prospective, multicenter, series 52 patients with localized prostate cancer</td>
<td>SpaceOAR hydrogel spacer and IMRT (78 Gy delivered, 2 Gy per fraction).</td>
<td>“Of the patients treated 39.6% and 12.5% experienced acute Grade 1 and Grade 2 GI toxicity, respectively. There was no Grade 3 or Grade 4 acute GI toxicity experienced in the study. Only 4.3% showed late Grade 1 GI toxicity, and there was no late Grade 2 or greater GI toxicity experienced in the study. A total of 41.7%, 35.4% and 2.1% of the men experienced acute Grade 1, Grade 2 and Grade 3 GU toxicity, respectively. There was no Grade 4 acute GU toxicity experienced in the study. Late Grade 1 and Grade 2 GU toxicity was experienced in 17.0% and 2.1% of the patients, respectively. There was no late Grade 3 or greater GU toxicity experienced in the study. Seventy one percent of the patients had a VRS [Vienna Rectoscopy Scoring] score of 0, and one patient (2%) had Grade 3 telangiectasia. There was no evidence of ulceration, stricture or necrosis at 12 months.”</td>
<td>“The use of PEG spacer gel is a safe and effective method to spare the rectum from higher dose and toxicity.”</td>
</tr>
<tr>
<td>Klotz et al. 2013(13)</td>
<td>Prospective series 47 patients with prostate cancer</td>
<td>IMRT up to a dose of 80 Gy SpaceOAR spacer injection</td>
<td>“No early side effects specific for the application were observed. The achieved distance between rectum and the midplane of the prostate gland was on average 13.8 (6-24, SD=3.8) mm. Calculated V70 (rectal volume irradiated with 70.0 Gy or more) could be reduced to an average of 1.5 (0-8, SD=1.7) %. One patient showed an asymptomatic lesion of the rectal mucosa after irradiation with 38.0 Gy. This lesion was closely controlled and gel penetration was found. As a result [RT] was discontinued. Without further treatment the necrosis had completely healed 3 months later.”</td>
<td>“Hydrogel application between prostate and rectum allows dose escalation up to 80,0 Gy and seems to reduce morbidity in patients with localized prostate cancer receiving [RT]. However, before final judgement of the new technique further studies must follow.”</td>
</tr>
</tbody>
</table>

**Cost Study**
**Table 2. Ongoing Trials Identified in ClinicalTrials.gov**

<table>
<thead>
<tr>
<th>Study Name/Identifier from ClinicalTrials.gov</th>
<th>Planned Enrollment (n per group)</th>
<th>Study Design</th>
<th>Stated Objectives</th>
<th>Primary Endpoints to Be Reported</th>
<th>Estimated Date of Completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-marketing Surveillance Regarding Efficacy and Safety of SpaceOAR™ NCT01999660</td>
<td>n = 250</td>
<td>Prospective, observational study intended as “surveillance for the investigation of the Efficacy and Safety of SpaceOAR to Maintain Space Between the Rectum and Prostate During Radiation Therapy”</td>
<td>Primary endpoint: Rectal complication rate (late toxicity) at 6 months and yearly thereafter for 5 years</td>
<td>January 2019</td>
<td></td>
</tr>
<tr>
<td>Stereotactic Ablative Radiotherapy (SABR) for Low Risk Prostate Cancer With Injectable Rectal Spacer NCT02353832</td>
<td>n = 29</td>
<td>Phase II, open-label study to determine whether use of rectal spacers are effective at improving protection of rectum from high-dose radiation, using rate of rectal ulceration as a surrogate measure of acute effects, and to determine whether it provides sufficient dosimetric benefits to warrant further clinical investigation in future stereotactic ablative body radiation–related clinical studies. Primary endpoint: Acute periprostatic rectal ulcer events. To reduce acute periprostatic rectal ulcer events from 90%+ to ≤20% (particularly in the anterior rectum).</td>
<td></td>
<td>December 2020</td>
<td></td>
</tr>
</tbody>
</table>

**Selected References and Resources**

References Reviewed (PubMed and EMBASE search dates were January 1, 2000, through May 17, 2017)


SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer


ECRI Institute Resources

- Intensity-modulated radiation therapy compared with proton beam radiation therapy for treating prostate cancer. [Hotline]. 2014 Feb.
- Proton beam therapy for prostate cancer. [Hotline]. 2013 Sep.
- Stereotactic body radiation therapy for prostate cancer. [Hotline]. 2015 Apr.


We identified one de novo clearance for the SpaceOAR System. We also identified four Manufacturer and User Facility Device Experience (MAUDE) records and no recalls for this device.
SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer


- Manufacturer and User Facility Device Experience (MAUDE) Database. [searched January 1, 2014 through May 16, 2017]. Note: to access records, enter spaceoar in the brand name field.

Manufacturer Website (Augmenix, Inc. Waltham, MA, USA)

- SpaceOAR. [cited 2017 May 16].
  - SpaceOAR instructions for use. [cited 2017 May 16].
  - Why it matters (physicians). [cited 2017 May 16].
- Peer reviewed papers/Journal articles. [cited 2017 May 16].

We identified registered clinical trials on this device. See the list of ongoing trials and the comprehensive list of ongoing, complete, and terminated trials.

Additional Resources

- Medscape. [cited 2017 May 17]. Note: may require free registration to view documents.
SpaceOAR System (Augmenix, Inc.) Hydrogel Spacer for Reducing Exposure during Radiation Therapy for Prostate Cancer

The Evidence Bar™
ECRI Institute developed The Evidence Bar™ to provide a visualization of our judgment about the balance of benefits and harms of the technology after assessing the available published clinical evidence in light of key outcomes and comparisons of interest. The Evidence Bar™ rubric shows five possible choices for our expert judgment. After review of the evidence identified through literature searches conducted by master’s level medical librarians, ECRI Institute research analysts, extensively trained in methods of evidence assessment, weigh potential benefits and harms of a technology to arrive at their expert judgment.

Balance of evidence unfavorable

Balance of evidence raises concerns

Balance of evidence inconclusive because of no available evidence, mixed results, or too few data

Balance of evidence favorable

Balance of evidence very favorable

Policy Statement
This Product Brief addresses a specific inquiry from an ECRI Institute Health Technology Assessment Information Service member about a particular brand-name healthcare product and its safety and efficacy. The information contained in this Product Brief is highly perishable and reflects the available information we identified at the time this Product Brief was prepared. The comments and opinions expressed were accurate to the best of our knowledge at the time of preparation, but are subject to change if and when new information is published. Information was identified through searches conducted by medical librarians and compiled by research analysts from the available, published peer-reviewed clinical literature, conference proceedings, regulatory agencies, trade publications, World Wide Web sites, and manufacturer information. The Product Brief summarizes the identified clinical literature (i.e., human studies) and other information that we deemed relevant to the topic within the search dates noted in the clinical literature description. The clinical studies were reviewed by ECRI Institute in one or more of the following forms: full published articles, article abstracts, FDA summaries of safety and effectiveness data, and/or conference abstracts or posters. Conference abstracts and posters of clinical studies typically do not provide complete information by which to assess study design or validity of the final published results of a study. Therefore, results presented in these sources of information must be considered with caution. Any and all product claims described in this Product Brief were made by the manufacturer in materials it has presented or published about its products. ECRI Institute’s description of these claims in this Product Brief does not imply any endorsement or agreement. This Product Brief is not intended to provide specific guidance for the care of individual patients. ECRI Institute makes no express warranties or any implied warranties regarding the products discussed in this Product Brief, including any implied warranty of merchantability or fitness for a particular use. ECRI Institute assumes no liability or responsibility for how members use the information, comments, or opinions contained in Product Briefs.