KAISER PERMANENTE®

Kaiser Foundation Health Plan of Washington

Clinical Review Criteria
SpaceOAR (Spacing Organs at Risk)
- Rectal Protection during Prostate Cancer

Criteria
For Medicare Members
No review required.

For Non-Medicare Members
No review required.

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background
Prostate cancer is the most common cancer (excluding skin cancer) and the third leading cause of cancer death in men in the United States (American cancer Society Cancer facts and figures 2017). Treatment options for prostate cancer include active surveillance and watchful waiting, radical prostatectomy, radiation therapy, hormone therapy, chemotherapy, immunotherapy and other treatment modalities depending on the stage of the disease, patient age, health condition, and personal preference.

External beam radiation therapy (EBRT) remains one of the primary treatment modalities for patients with localized prostate cancer. Studies show that it is highly effective in patients with a localized disease, and that a dose escalation improves biochemical control in intermediate risk patients. However, dose escalation can also increase the risk of urinary and bowel toxicity (Pinkawa 2011, Uhl 2013, Chung 2016).

Advances in in radiotherapy treatment techniques including image-guided radiation therapy (IGRT) and intensity modulated radiation therapy (IMRT) that limit the margins and conform the high dose radiation volume, have allowed increasing the radiation dose to ≥78Gy while maintaining an acceptable toxicity profile. However, as the prostate is directly adjacent to the rectum, the anterior rectal wall cannot be completely spared from the high dose region regardless of the treatment technique. The rectum is the most radiation sensitive organ within the pelvic tissue and is the primary organ at risk (OAR) with external beam radiation therapy. Studies showed that rectal toxicity is associated with both the total radiation dose to a specific volume and the volume inside a specific isodose, and that Grade ≥2 rectal toxicity is significantly associated with the volume of rectum receiving >70Gy (V70) (Noyes 2012, Pinkawa 2013, Song 2013, Wolf 2015, Chung 2016, Hamstra 2017).

Researchers have been evaluating methods to create more space between the prostate and rectum to allow for prostate dose escalation while reducing anterior rectal wall radiation exposure. One of the promoted approaches involves the placement of a temporary injectable spacer to push the rectum away from the prostate before treatment planning and maintain the space throughout the treatment period. Different injectable agents including

Back to Top

human derived products (e.g. hyaluronic acid and collagen), synthetic polyethylene-glycol (PEG) hydrogel, and implantable absorbable balloons have been evaluated as spacing materials (Song 2013, Mariados 2015).

SpaceOAR (Spacing **O**rgans **A**t **R**isk), Augmenix, Inc., Waltham MA, USA, is an absorbable polyethylene glycol (PEG) hydrogel that expands the perirectal space as an injectable liquid and then solidifies into a soft absorbable spacer between the prostate and rectum. It consists of two liquid hydrogel precursors, that after hydro dissection with a saline solution, are injected using a small needle under transrectal ultrasound (TRUS) guidance through the perineum to the perirectal space (between the Dennonvilliers' Fascia and the frontal rectal wall). There, the liquid hydrogel polymerizes (solidifies) within seconds and creates a physical barrier between the prostate and rectum. The additional space created by the spacer has a volume of about 10-15 ml. The solidified hydrogel is compression resistant and is maintained for approximately three months. It should be absorbed in approximately six months and the degradation products cleared via renal filtration (Pinkawa 2011, Rucinski 2015, Wolf 2015).

Potential complications that may be associated with the use of the SpaceOAR system include, but are not limited to pain and discomfort associated with SpaceOAR or hydrogel injection; needle penetration and/or injection of the hydrogel into the bladder, prostate, rectal wall, rectum, or urethra; infection or local tissue inflammatory reactions; urine retention, bleeding, rectal mucosal damage, ulcers, necrosis, constipation; rectal urgency; injection of air, fluid or SpaceOAR hydrogel intravascularly; device functional failure or its inability to maintain the space stability during the course of radiation therapy; prolonged or delayed procedure; and incomplete absorption of the hydrogel (FDA decision summary, FDA website, accessed May 2017).

Medical Technology Assessment Committee (MTAC)

SpaceOAR

06/21/2017: MTAC REVIEW

Evidence Conclusion: The SpaceOAR pivotal trial (See Evidence Table 1) is a multicenter single-blinded phase III trial that evaluated the safety and effectiveness of SpaceOAR among 222 patients undergoing prostate image guided intensity modulated radiation therapy (IG-IMRT).The study included men with clinical stage T1 or T2 prostate cancer, Gleason score ≤7, and PSA concentration ≤20 ng/ml. Patients with prostate volume>80cm^3, extracapsular extension of the disease, >50% positive biopsy cores as well as those with prior prostate surgery or radiation therapy were excluded from the study. After undergoing initial treatment planning, and implantation of fiducial markers, the study participants were randomized in a 2:1 to receive spacer injection or no injection (control). Patients, but not the providers were blinded to their treatment allocation. Planning scans were then performed followed by image guided intensity modulated radiation therapy (79.2Gy in 1.8-Gy fractions). The primary effectiveness endpoint was the proportion of patients achieving >25% rectal volume receiving at least 70Gy (rV70) due to spacer placement, and the safety endpoint was the proportion of spacer and control patients with ≥grade 1 rectal toxicity or procedural adverse event (AEs) in 6 months. The results showed a significant reduction in the mean rectal V70 (>70Gy) in the post vs. pre- treatment plan. Overall 97.3% of spacer patients experienced ≥25% reduction in rectal volume receiving at least 70Gy (rV70).

Mean ± SD rectal dose volume at baseline and post- spacer dose plans

parameter	rV50	rV60	rV70	rV80
% before spacer	25.7 ± 11.1	18.4 ± 7.7	12.4 ± 5.4*	4.6 ± 3.1
% after spacer	12.2 ± 8.7	6.8 ± 5.5	3.3 ± 3.2**	0.6 ± 0.9
% absolute reduction	13.442	11.563	9.078	3.933
% relative reduction	52.3	62.9	73.3	86.3
P value	<0.0001	<0.0001	<0.0001	<0.0001

As regards the primary safety endpoint, the results showed no significant differences in the rates of ≥grade 1 rectal or procedural adverse event (AEs) in 6 months between spacer and control groups (34.2% and 31.5% respectively (p =0.7). 10% of the patients in the spacer group experienced mild transient procedural perineal discomfort and other symptoms.

Acute and late (up to 15 months) rectal toxicity

Rectal toxicity	Spacer (n=148)	Control (n= 73)	P value
Acute toxicity: from procedure through 3-months visit, n (%)			
Grade 0	108 (73.0%)	49 (68.0%)	0.525
Grade 1	34 (23.0%)	20 (27.8%)	
Grade >2	6 (4.1%)	3 (4.2%)	
Late toxicity Between the 3rd and 15th month visits			

Back to Top

Grade 0	145 (98.0%)	66 (93.0%)	0.044
Grade 1	3 (2.0%)	4 (5.6%)	
Grade >2	0 (0.0%)	1 (1.4%)	

The results show that the rate of rectal toxicity in the control group was low, which as the authors indicated was very low compared to earlier studies, and attributed that to several potential factors including the use of different toxicity scales, uniform use of both IMRT and IGRT, small PTV (planning target volume) margin, MRI planning, and strict dosimetric constraints with centralized pretreatment review of the plans. The extended follow-up reported by Hamstra and colleagues (2017), suggest that the benefit observed with the hydrogel spacer at 15 months was maintained at a median of 37 months of follow-up. However, this extended follow-up was optional and the long-term data were available for 66% of the patients at 30 months, and 17.5% at 40 months. The trial was randomized and controlled. However, it had its limitations. The providers were not blinded to the treatment allocation; the study had strict inclusion/exclusion criteria, which may limit generalization of its results, and the follow-p duration was insufficient to determine the long-term safety of the technology. The extended 3 years follow-up was voluntary and only 66% were followed up for 30 months, and 17.5% at 40 months, In addition the study was performed under an investigational setting, was sponsored by the manufactures, and the principal investigators had financial ties with the industry. Pinkawa and colleagues, 2017 compared the numbers of interventions resulting from bowel problems during the first 2 years after RT to assess the benefit of the using hydrogel spacer before prostate cancer radiotherapy (RT) according to patient's perspective. The study included 167 consecutive prostate cancer patients treated with radiotherapy (RT) in the years 2010 to 2013. 101 patients received 76-80Gy with hydrogel, and 66 were treated with up to 76Gy without hydrogel. All patients were surveyed prospectively before RT, at the last day of RT, and at a median of 2 and 17 months after RT using a validated questionnaire (Expanded Prostate Cancer Index Composite). The outcome was the difference between using and not using hydrogel on the rate of interventions resulting from bowel problems during the first 2 years after radiotherapy. The results show that treatment for bowel symptoms was performed less frequently with a using a spacer (0 with spacer vs. 11 % with no spacer; $p < 0.01$). Similarly there were less endoscopic examinations in patients receiving a spacer versus those who did not receive one (3 vs. 19 % respectively; $p < 0.01$). Mean bowel function scores did not change for patients with a spacer in contrast to patients without a spacer (mean decrease of 5 points) >1 year after RT in comparison to baseline. None of the spacer parents vs. 12% of those with no spacer reported a new moderate/big problem with passing stools ($p < 0.01$). The authors concluded that spacer injection is associated with a significant benefit for patients after prostate cancer RT. However, the study was only observational and patients were not randomized to the treatment groups.

Conclusion:

- There is insufficient published evidence to recommend for or against the use of SpaceOAR in prostate cancer patients treated with external beam radiotherapy.
- The only published RCT trial to date, had its limitations and does not provide sufficient evidence to determine the long-term safety and efficacy of the hydrogel spacer, or to determine its effect on the net health outcome outside the investigational setting.

Articles: The literature search for published studies on the efficacy and safety of injecting a temporary hydrogel spacer between the rectum and prostate in patients undergoing extremal beam radiotherapy revealed one randomized controlled trial (pivotal trial), a retrospective comparative study, observational studies with no controls, as well as a number of phase I/II studies investigating the feasibility, efficacy, safety, and/or dosimetric benefits of the spacers. The literature search also identified a small nonrandomized observational study that compared SpaceOAR to a saline inflated balloon (ProSpace) in terms of spacer volume, stability and radiation dose reduction to the anterior rectal wall. The pivotal RCT was selected for critical appraisal. 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. 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 Phy.* 2015; 92:971-977

The use of SpaceOAR (Spacing Organs at Risk) Hydrogel for Rectal Protection during Prostate Cancer Radiotherapy does meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Back to Top

Applicable Codes

Medical Necessity Review not required:

CPT® Codes	Description
55874	Transperineal placement of biodegradable material, peri-prostatic, single or multiple injection(s), including image guidance, when performed

***Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

****To verify authorization requirements for a specific code by plan type, please use the **Pre-authorization Code Check**.

Date Created	Date Reviewed	Date Last Revised
08/01/2017	08/01/2017[MPC], 07/10/2018[MPC], 07/09/2019[MPC], 07/07/2020[MPC], 07/06/2021[MPC], 07/05/2022[MPC], 07/11/2023[MPC], 04/02/2024[MPC]	07/07/2020

[MPC] Medical Policy Committee

Revision History	Description
01/08/2018	Medicare - No review required
07/07/2020	Removed deleted CPT code 0438T

Back to Top