



SpaceOAR™ Hydrogel is Associated with Lower Rectal Toxicity and Higher Bowel Quality of Life in Late Follow-up: Systematic Review & Meta-Analysis¹


The purpose of this value analysis brief is to highlight key findings from a systematic literature review and meta-analysis that demonstrates the clinical benefits of SpaceOAR Hydrogel compared with no spacer.


SUMMARY

In a pooled analysis of **1,011 patients** receiving **radical radiotherapy** from 7 clinical studies, SpaceOAR Hydrogel when compared to control demonstrates:

 **66% less v70 rectal irradiation**

 **77% reduction in the risk of** rectal toxicity (grade ≥2) in late follow-up

 **70% reduction in the risk of** rectal toxicity (grade ≥1) in late follow-up

 **Better patient quality of life** in late follow-up exceeding the threshold for a minimal clinically important difference (mean difference = 5.4).

BACKGROUND

Radical radiotherapy is a well-established and highly effective curative treatment option for patients with prostate cancer.² Due to its proximity to the prostate, the rectum is vulnerable to radiation induced treatment toxicity, which can in turn cause gastrointestinal complications.¹

Symptoms of radiation toxicity often begin during radiation therapy, but sometimes do not appear until several years later.³

The SpaceOAR Hydrogel System (Figure 1) is a biodegradable polyethylene glycol hydrogel intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy in prostate cancer patients.⁴

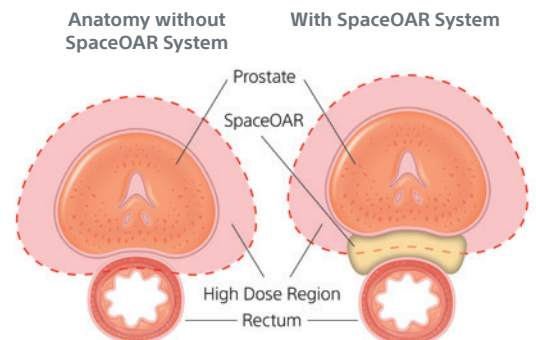


Figure 1: SpaceOAR Hydrogel System

LOWER RECTAL TOXICITY AND IMPROVED BOWEL QUALITY OF LIFE (QOL) WITH SPACEOAR HYDROGEL

Clinical trials in the U.S.^{5,6,7} and Europe^{3,8} have demonstrated that SpaceOAR Hydrogel is safe and that the space created with hydrogel spacers significantly reduces the radiation delivered to the rectum. The randomised SpaceOAR Hydrogel U.S. Clinical Trial found that patients who received SpaceOAR Hydrogel reported significantly less rectal pain during radiotherapy⁵ and had significantly fewer severe long-term rectal complications.^{6,7}

WHY IS THIS SYSTEMATIC REVIEW EVIDENCE IMPORTANT?

Systematic review and meta-analyses are categorised as the highest quality or most robust type of evidence because they allow pooling of data from a large number of treated patients to minimise the effects of bias in studies.⁹ This type of evidence is important to clinicians, payers, providers, HTA organisations and other funding bodies to ensure SpaceOAR Hydrogel is safe and effective. This is the first systematic review with quantitative analysis of the existing SpaceOAR Hydrogel clinical trial data.

METHODS

The systematic review was conducted and reported according to the PRISMA guidelines.¹⁰ Searches were performed in Cochrane Central Register of Controlled Trials, Medline, and Embase up to September 2019 to identify comparative studies of men receiving radiotherapy for localised or locally advanced prostate cancer, with and without hydrogel spacing. Randomised control trials and cohort studies with >10 patients were included. Out of 475 articles identified, 73 full-text papers were reviewed with 7 studies included (Table 1) comprising 1,011 patients (486 SpaceOAR Hydrogel vs 525 no spacer) for analyses across different radiotherapy protocols.¹

Table 1: Included primary studies in systematic literature review

Primary Study, Year	No. patients	Follow-up (months)	RT protocol
	SpaceOAR hydrogel/control		
Chao ¹¹ , 2019	32/65	42/65	BT, IMRT
Mariados ⁵ , 2015	149/73	37/37*	IMRT
Pinkawa ¹² , 2017	101/66	63/63	IMRT
Tagger ¹³ , 2018	79/136	<12	BT ± EBRT
Te Velde ¹⁴ , 2019	65/56	<36	IMRT
Whalley ¹⁵ , 2016	30/110	28/26	IMRT
Wolf ¹⁶ , 2015	30/19	3	IMRT

RT, radiotherapy; BT, brachytherapy; EBRT, external beam radiotherapy; IMRT, intensity modulated radiation therapy; *data includes secondary study Hamstra et al.⁸

OUTCOMES

Outcomes were based on procedural results, rectal irradiation, rectal toxicity, and bowel QoL.

Procedural Outcomes

A well tolerated procedure, SpaceOAR™ Hydrogel demonstrates a 97% placement success rate¹ with mild procedural complications occurring in 0% to 10% of patients within studies.¹

Rectal Irradiation Outcomes

Men who received SpaceOAR Hydrogel prior to radiotherapy showed a **66% reduction of v70 rectal irradiation** (Figure 2) (3.5% vs 10.4%, p=0.001) when compared to men without a hydrogel spacer. There is a strong correlation between rectal v70 and rectal toxicity.¹

Rectal Toxicity Outcomes

SpaceOAR Hydrogel was associated with a **reduction in rectal toxicity** of any severity (grade ≥1) in the short and long-term (≤3 months, 20.5% vs 29.5%, p=0.005; median 40 months, 4.8% vs 16.2%, p<0.001)¹ and a **77% lower risk of grade ≥2 severity at late follow-up** (1.5% vs 5.7%, p=0.05)¹ (Figure 3).

Bowel QoL Outcomes

Two studies^{3,5} reported bowel QoL, and demonstrated **higher bowel QoL scores at late follow-up** vs control (median 48 months) (Figure 4) that exceeded the threshold for a minimal clinical importance difference.

Figure 2: Rectal Irradiation with vs. without SpaceOAR Hydrogel¹

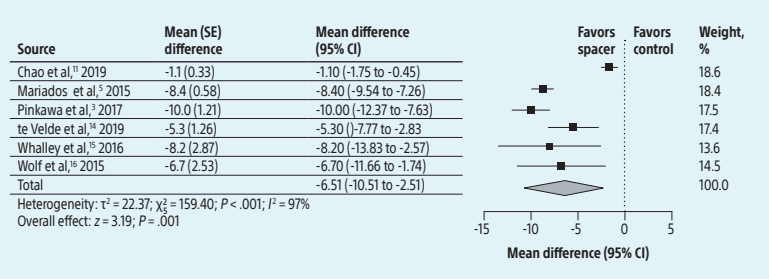


Figure 3: Rectal toxicity in late grade ≥2 complications¹

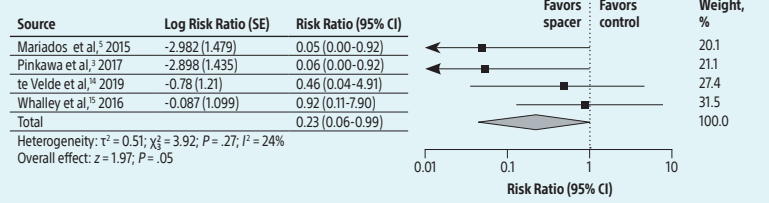
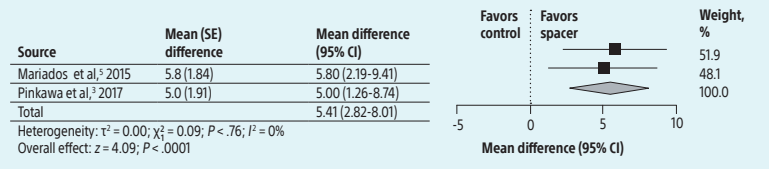


Figure 4: Late bowel QoL with vs. without SpaceOAR Hydrogel¹



STRENGTHS & LIMITATIONS

Strengths of the review include following PRISMA guidelines, careful identification of studies with overlapping patients and sensitivity analysis to explore potential sources of heterogeneity. Limited number of studies, non-randomised study designs and short follow-up time, which may not accurately capture radiation toxicity manifestations limit this review.

CONCLUSIONS

Among men planning to receive radiotherapy for localised or locally advanced prostate cancer, injection of a SpaceOAR Hydrogel was safe, provided prostate-rectum separation sufficient to reduce v70 rectal irradiation, and was associated with lower rectal toxicity and higher bowel quality of life in late follow-up.

WHAT IS THE PROFESSIONAL CLINICAL GUIDANCE?

Professional clinical guidelines recommend the use of biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer in adults.^{2,17}

- Miller L, Efstathiou J, Bhattacharya S, Payne H, Woodward E, Pinkawa M. Association of Perirectal Hydrogel Spacer with Safety and Efficacy Outcomes in Prostate Cancer Radiotherapy: A Systematic Review and Meta-Analysis. JAMA 2020
- National Institute of Health and Care Excellence. Guideline: Biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer. Interventional procedures guidance [IPG752]. <https://www.nice.org.uk/guidance/ipg752>
- Pinkawa M, Bemeking V, Schlienter M, Krenkel B, Eble MJ. Quality of Life After Radiation Therapy for Prostate Cancer With a Hydrogel Spacer: 5-Year Results. International Journal of Radiation Oncology 2017;99(2):374-377
- Data on file with Boston Scientific
- Mariados Sylvester J, Shah D, et al. N. Hydrogel Spacer Prospective Multicenter Randomized Controlled Pivotal Trial: Final Results of Phase III Trial. Dosimetric and Clinical Effects of Perirectal Spacer Application in Men Undergoing Prostate Image Guided Intensity Modulated Radiation Therapy. International Journal of Radiation Oncology 2015;92(5):971-977.
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- Hamstra DA, Mariados N, Sylvester J, Shah D, Gross E, Hudes R, 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;8(1):e7-e15.
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- te Velde BL, Westhuizen J, Awad N, et al. Late toxicities of prostate cancer radiotherapy with and without hydrogel SpaceOAR insertion. J Med Imaging Radiat Oncol. 2019.
- Whalley D, et al. SpaceOAR Hydrogel in Dose-escalated Prostate Cancer Radiotherapy: Rectal Dosimetry and Late Toxicity. Clin Oncol (R Coll Radiol). 2016;28:e148-154.
- Wolf F, Gaisberger C, et al. Comparison of two different rectal spacers in prostate cancer external beam radiotherapy in terms of rectal sparing and volume consistency. Radiother Oncol. 2015;116:221-225.
- National Comprehensive Cancer Network (NCCN). NCCN Guidelines: prostate cancer v. 4.2022. <https://www.nccn.org/patientresources/patient-resources/guidelines-for-patients>

SpaceOAR Hydrogel 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 Hydrogel to reduce the radiation dose delivered to the anterior rectum. SpaceOAR Hydrogel contains polyethylene glycol (PEG). Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions and potential adverse events. As with any medical treatment, there are some risks involved with the use of SpaceOAR Hydrogel. Potential complications associated with SpaceOAR Hydrogel include, but are not limited to: pain associated with SpaceOAR Hydrogel injection, pain or discomfort associated with SpaceOAR Hydrogel, local inflammatory reactions, infection (including abscess), urinary retention, urgency, constipation (acute, chronic, or secondary to outlet perforation), rectal tenesmus/muscle spasm, mucosal damage, ulcers, fistula, perforation (including prostate, bladder, urethra, rectum), necrosis, allergic reaction (localized or more severe reaction, such as anaphylaxis), embolism (venous or arterial embolism is possible and may present outside of the pelvis, potentially impacting vital organs or extremities), syncope and bleeding. The occurrence of one or more of these complications may require treatment or surgical intervention. URO-989608-AB
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