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Scientific Article

Real-World Data on Barrigel and SpaceOAR Rectal Spacers in Prostate Cancer Radiation Therapy: A Comparative Analysis

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Purpose: : Hydrogel rectal spacers are in widespread and routine clinical use for prostate cancer radiation therapy. Theses spacers separate the prostate from the rectum, thereby reducing the radiation dose to the rectum. Two major hydrogels are in use, SpaceOAR and Barrigel, yet there are no real-world data comparing these two. This study aims to compare these gels with respect to quality of insertion and dosimetric outcomes.

Methods and Materials: A multicenter retrospective analysis was performed on all men with prostate cancer undergoing radiation therapy from 2017 to 2023. Demographic, radiation therapy, and magnetic resonance imaging details were imported for analysis. Each multiparametric magnetic resonance imaging was scored on rectal spacing placement by 2 independent observers.

Results: Eight hundred twenty-two patients were included for dosimetric and 605 for quality of insertion analysis. The median SpaceOAR volume (13.80 cc) was larger than the median Barrigel volume (5.10 cc) ($P < .01$). SpaceOAR was more likely to achieve a higher Spacer Quality Score (SQS) compared to Barrigel (5-fraction odds ratio [OR], 6.25; >5 fractions OR, 2.16; $P < .01$ for both respectively). SpaceOAR achieved lower irradiated rectal volumes for 20 fractions, at v60, v46, v38, and v30 ($P < .01$ for all) and 5 fractions, v30 ($P = .04$), v20 ($P = .01$). After accounting for spacer volume, Barrigel achieved better rectal dosimetric outcomes for 20 fraction patients compared to SpaceOAR for volumes between 6 and 13 cc, v57 ($P = .01$), v54 ($P = .01$). Higher SQS correlated with improved dosimetric outcomes ($P < .05$), whereas no similar monotonic trend was observed with the Fischer-Valuck (FV) score across evaluated dose levels, including v36 ($P = .10$), v32 ($P = .26$), and v30 ($P = .45$). Incidence of rectal wall infiltration among SpaceOAR patients was 7/287 (2.44%) compared to none for Barrigel.

Conclusions: Real-world data show that SpaceOAR achieves better dosimetry than Barrigel likely due to larger insertion volumes. At similar insertion volumes, Barrigel achieves lower irradiated rectal volumes compared to SpaceOAR. Dosimetric outcomes are more

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likely impacted by volume rather than symmetry of insertion. The SQS scoring method may have better utility than the FV scoring method for assessing dosimetric outcomes. Our data also indicate that Barrigel has a lower incidence of rectal wall infiltration compared with SpaceOAR.

Introduction

Prostate cancer (PC) is the most commonly diagnosed malignancy in Australia.[1] External beam radiation therapy (EBRT) is a curative approach to PC that offers high local control rates at up to 99% at 5 years.[2,3] Dose escalation to improve PC tumor control is supported throughout radiation therapy literature, with strong evidence from the FLAME trial[4] however is restricted by normal healthy adjacent organs at risk.[4] The application of hydrogel rectal spacers in EBRT has emerged as an innovative method to reduce potential rectal toxicities and allow for greater ability to dose escalate. By introducing hydrogel into the perirectal fat, posterior to Denonvilliers' fascia, a temporary protective cushion is created, effectively increasing the distance between the prostate and rectum. This separation helps minimize the high radiation therapy doses to the anterior rectal wall, reducing the potential for side effects such as bowel dysfunction or radiation-associated vascular ectasia which may adversely impact quality of life (QOL).[5,6]

Two rectal spacing gels (RSGs) are in widespread use—SpaceOAR and Barrigel.[5] These 2 gels differ significantly in composition, leading to distinct advantages and disadvantages. SpaceOAR is 90% water and 7% polyethylene glycol.[7] Polyethylene glycol is a synthetic material, polymerizing within 8 to 15 seconds. Once inserted, it can remain in situ for 3 months before being naturally absorbed.[5,8] On the other hand, Barrigel is made from nonanimal stabilized hyaluronic acid. Unlike SpaceOAR, Barrigel does not undergo polymerization, and therefore hydrodissection is not required prior to insertion. Additionally, Barrigel can be enzymatically degraded by hyaluronidase,[9] whereas no such agent exists for SpaceOAR.[10,11]

Although randomized control trials (RCTs) have demonstrated the efficacy and safety of each gel in reducing rectal radiation doses, no studies have directly compared the 2 products.[12,13] A systematic review by Miller et al[14] found that although RSGs effectively reduced rectal radiation exposure, the clinical impact of hydrogel placement symmetry on rectal dose reduction remains uncertain. To improve patient outcomes, it is important to understand this relationship to determine the ideal placement of RSG to maximize rectal dose reduction. In the literature, 2 semiqualitative metrics have been developed to assess RSG placement: the FV score proposed by Fischer-Valuck et al[15], and the Spacer Quality Score (SQS) developed by Grossman et al.[16] Throughout this paper, we refer to these as the FV score and SQS, respectively. Due to differences in their design, the 2 methods have had varying success in correlating spacer placement to rectal outcomes, and as a result, there remains discussion around which is better for defining quality of insertion.

RCTs of both products evaluated QOL across 4 domains: bowel, urinary, sexual, and hormonal. The SpaceOAR RCT showed statistically significant improvements in bowel QOL up to 3 years, whereas the Barrigel RCT showed a numerical trend toward improved bowel QOL at 3 to 6 months, but this was not statistically significant. The SpaceOAR RCT also found a slight benefit of hydrogel to improved urinary QOL, but this difference did not meet the minimally important difference. There were no notable findings in both studies regarding sexual and hormonal QOL.[12,13] Currently, RSGs are not publicly subsidized by Medicare in Australia.

Although evidence supports the clinical benefit of RSGs, they are not without potential complications, with procedure-related complications following insertion having been documented.[17] Two recent reviews of the Manufacturer and User Facility Device Experience database have shown rates of infection and rectal ulceration at 17.6% and 10.5%, respectively. Three patients had profound complications that resulted in death, although the exact events of these are unknown.[18,19]

This retrospective multicenter study looks to assess real-world data on the 2 major hydrogels in use, SpaceOAR and Barrigel. This study aims to compare these gels with respect to quality of insertion and dosimetric outcomes.

Methods and Materials

Study design and patients

A retrospective multicenter cross-sectional cohort study was performed on patients treated in the Hunter New England Local Health District (HNELHD), Australia at GenesisCare.

The study was approved by the local ethics committee 2022/ETH00247 GenesisCare Oncology Outcomes Project (GCOP).

All patients who had received EBRT for PC between 2017 and 2023, at the two GenesisCare facilities in HNELHD were included for analysis. In total, 856 patients were identified and collated into a large database.

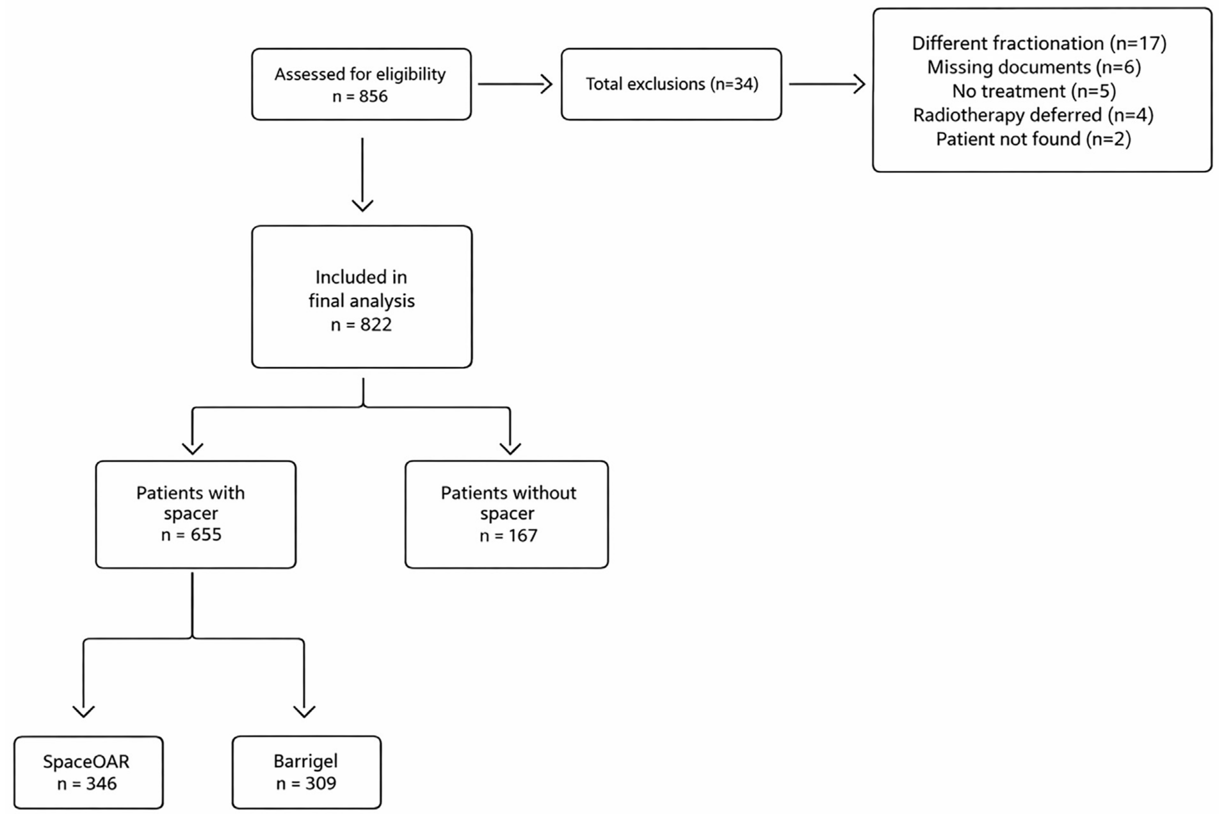

Figure 1 Consolidated standards of reporting trials diagram.

Patients were assessed for eligibility for dose-volume histogram (DVH) analysis. Thirty-four patients were excluded from DVH analysis—17 patients were excluded due to enrollment in specialized treatment trials (eg, the Prometheus trial[3]) requiring different fractionation schedules. Other reasons for exclusion included the decision not to undergo treatment (patient preference), deferral of radiation therapy due to complications from prior procedures (such as chronic constipation and lower urinary tract symptoms), missing documentation, or if the patient was unable to be located on the electronic medical record (Fig. 1).

For quality of insertion analysis, a further 50 patients were excluded. Forty-eight exclusions were due to scans being unavailable—either missing from archives or patient-related factors preventing acquisition, such as claustrophobia, anxiety, or the presence of metallic foreign bodies (eg, pacemakers, cardiac loop monitors, or aneurysm clips). Additionally, 2 patients were excluded due to unclear imaging which rendered scoring unreliable. In total, 605 patients were included for quality of insertion analysis (287 SpaceOAR, 202 Barrigel).

Demographic data (age, treatment data, stage) and DVH data (prescription, clinical target volume, planning target volume, dosimetric information) were obtained through retrospective review of MOSAIQ documentation.

For quality of insertion analysis, multiparametric magnetic resonance imaging (MRI) was obtained for each patient. These were performed 1 week post spacer insertion to allow image fusion. Contouring and assessments were conducted using the T2 weighted image.

We specify 2 coprimary endpoints: first, the difference between Barrigel and SpaceOAR in terms of rectal dose exposure, analyzed separately for 20 and 5 fractionation schedules, and second, the difference between Barrigel and SpaceOAR in terms of spacer insertion quality assessed using the FV and SQS scores. Secondary endpoints include differences between the RSGs after adjusting for insertion volume, incidence of rectal wall infiltration (RWI), and intraobserver variability with the quality of insertion metrics.

Quality of insertion analysis

A semiqualitative assessment of rectal spacer placement was analyzed using 2 scoring methods—the FV scoring system outlined by Fischer-Valuck et al[15] (Tables E1a, b) and the SQS (Table E2) developed by Grossman et al.[16] The FV score ranged from 1 (best) to 5 (worst). The SQS ranged from 0 (worst) to 2 (best). For 5-fraction patients, we retained the original SQS criteria outlined by Grossman et al.[16] However, for patients with >5 fractions, the criteria were modified from 0.3 cm to 0.5 cm to account for larger margins, differences in interfraction management, and less steep dose gradients typical of more conventional courses.

For each patient's multiparametric MRI, 2 observers assessed a SQS and FV score. Where there was a discrepancy between Observer 1 and Observer 2's scoring of an image (SQS or FV scores or both), a third observer scored the image. The final SQS was calculated by evaluating the mode of observer 1,2, and3's scores. If a mode could not be calculated, a fourth observer reviewed the scan, and a mode was calculated using all 4 scores.

Where RWI was observed on multiparametric MRI, the RWI score as outlined by Fischer-Valuck et al[15] was used to grade the degree of infiltration.

DVH analysis and rectal spacer volume stratification

As SQSs are primarily derived by grading measurements of the prostate-rectal interface (PRI) (see Table E2), rectal spacer volume (RSV) was identified as a confounding variable in DVH analysis, as larger volumes can result in a thicker PRI. Groups were reassessed using 2 revised subgroups restricting for RSV range. The first of these groups included RSVs of 6 to 13 cc, to account for 6- and 9-cc insertions of Barrigel. The second group included RSVs of 7.5 to 9 cc—this was calculated to be the common range for both Barrigel and SpaceOAR, after exclusion of outliers which may influence the results. This was applied to 20-fraction patients only, to allow for effective comparison.

Statistical analysis

Using standard procedures, we calculated baseline descriptive statistics, including medians with interquartile ranges for continuous parameters (ie, age, rectal volume, gel volume) and frequencies for categorical variables (ie, cohorts, treatment year, and staging). To evaluate the relationship between RSG and SQS/FV scores, the χ^2 test was used. Fisher's exact test was used when there was a low count. Simple ordinal logistic regression modeling was performed to further analyze these associations. For analysis of dosimetric outcomes, medians were calculated, and the Kruskal−Wallis and Wilcoxon 2-sample test was used to determine differences between cohorts. Generalized regression modeling was also performed to analyze the relationship between gel and dosimetric outcomes as a function of RSV. The relationship between dosimetric outcomes and SQS was evaluated using the Kruskal−Wallis and Jonckheere−Terpstra tests. Intraobserver variability was assessed using Cohen's kappa (κ). Results were deemed statistically significant if $P < .05$. Computations were performed using Google Sheets and JMP Version 18.

Results

Demographics

Of the 822 patients included in this study, 346 received SpaceOAR, 309 received Barrigel and 167 did not receive spacer (Table 1). The most common fractionation schedule was 20 fractions (63.83%), followed by 39 fractions (20.27%) then 5 fractions (14.96%). Among 20-fraction patients, the majority (98.4%) received prescription doses between 60 and 66 Gy. Among 5-fraction patients, prescription dose ranged from 36 to 45 Gy; the majority (61.8%), received 40 Gy. All 39 fraction patients received 78 Gy.

The majority of patients treated between 2017 and 2020 received SpaceOAR, as Barrigel was only implemented into clinical practice from 2021. From 2021 onward, most patients (75%) were treated with Barrigel.

The median SpaceOAR volume (13.80 cc) was significantly larger than the median Barrigel volume (5.10 cc) (Wilcoxon $P < .01$). The median rectal volume for the Barrigel cohort (62.07 cc) was significantly lower than the SpaceOAR and no-spacer cohorts (66.82, $P = .01$; 64.82, $P = .05$ respectively).

Spacer insertion quality analysis

Six hundred five patients were included in quality of insertion analysis. The median SQS for both 5-fraction and >5-fraction groups was 1 and the median FV score for both groups was 2. For both groups the association between spacer type and the SQS was statistically significant (likelihood ratio $P < .01$). There appeared to be more SQS differences between the 2 RSGs within the 5-fraction group (Fig. 2a) compared to the >5 fraction group (Fig. 2b). Patients with SpaceOAR had a greater proportion of SQS 2 scores across both 5-fraction and >5-fraction groups (Fig. 2a, b) and were consequently more likely to achieve higher SQS compared to Barrigel (5-fraction cohort: odds ratio = 6.25, $P < .01$; >5 fraction cohort: odds ratio = 2.16, $P < .01$).

With the FV metric, there was no statistically significant association between spacer type and FV scores (likelihood ratio $P = .27$) (Fig. 2c).

Intraobserver variability

Of the 605 patients who were evaluated for an SQS, 121 (20%) required a third observer and 6 (1%) required a fourth observer. Among the 605 patients evaluated for a

Table 1 Demographics.

Characteristic	Number (%)			
	All patients (n = 822)	SpaceOAR (n = 346)	Barrigel (n = 309)	No spacer (n = 167)
Fractions				
5 fractions	123 (14.96)	26 (7.51)	92 (29.77)	5 (2.99)
20 fractions	503 (61.19)	236 (68.21)	177 (57.28)	89 (53.29)
39 fractions	166 (20.19)	81 (23.41)	30 (9.71)	55 (32.93)
Other fractions	30 (3.65)	3 (0.87)	10 (3.24)	18 (10.78)
Treatment year				
2017	20 (2.43)	17 (4.91)	0 (0)	3 (1.80)
2018	68 (8.37)	53 (15.32)	1 (0.32)	14 (8.38)
2019	84 (10.22)	80 (23.12)	1 (0.32)	3 (1.80)
2020	111 (13.50)	94 (27.17)	0 (0)	17 (10.24)
2021	181 (22.02)	54 (15.61)	69 (22.33)	58 (34.73)
2022	199 (24.21)	27 (7.80)	120 (38.83)	52 (31.14)
2023	159 (19.34)	21 (6.07)	118 (38.19)	20 (11.98)
AJCC T-stage				
Unknown	13 (1.58)	4 (1.16)	2 (0.65)	7 (4.19)
T1a	3 (0.36)	3 (0.87)	0 (0)	0 (0)
T1b	9 (1.09)	6 (1.73)	1 (0.32)	2 (1.20)
T1c	244 (29.68)	144 (41.62)	89 (28.80)	11 (6.59)
T2a	163 (19.83)	62 (17.92)	85 (27.51)	18 (10.78)
T2b	55 (6.69)	32 (9.25)	16 (5.18)	7 (4.19)
T2c	147 (17.88)	36 (10.40)	81 (26.21)	28 (16.77)
T3a	121 (14.72)	33 (9.54)	25 (8.09)	63 (37.72)
T3b	53 (6.45)	19 (5.49)	10 (3.24)	24 (14.37)
T4	13 (1.58)	6 (1.73)	0 (0)	7 (4.19)
Median (IQR)				
Age, y	74.95 (70.09-78.99)	75.49 (71.27-79.41)	74.04 (69.07-77.50)	76.76 (71.38-80.25)
Rectal volume (cm^3)	64.30 (52.24-79.23)	66.82 (53.92-82.36)	62.07 (50.48-75.25)	64.82 (53.40-83.19)
Spacer gel volume (cm^3)		13.80 (11.82-15.82)	5.10 (3.10-6.4)	

Abbreviations: AJCC = American Joint Committee on Cancer; IQR = interquartile range.

FV score, 177 (29.3%) needed a third observer and 15 (2.5%) required a fourth observer.

There was an almost perfect level of agreement between Observer 1 and Observer 2 in the SQS scoring of 5-fraction and >5-fraction patients (5 fractions: $\kappa = 0.83$; >5 fractions $\kappa = 0.91$; $P < .01$ for both). For the FV scores, there was borderline substantial agreement, although still statistically significant ($\kappa = 0.61$, $P < .01$).

Dosimetric outcomes

For the 20-fraction patient group, there were significant differences in rectal volume exposed between the groups (no spacer, Barrigel, SpaceOAR) across all dose levels (v60 to v20) (Kruskal−Wallis $P < .01$). However, for the 5-fraction regimen, fewer significant differences were observed, with v32, v30, and v20 showing significance ($P = .03$, .01, .04, respectively), whereas v36 and v34, approached significance ($P = 0.08$, $P = .06$). SpaceOAR had statistically significantly lower irradiated rectal volumes than Barrigel for 20 fractions patients at several dose levels (Fig. 3a), including v60, v46, v38, and v30 ($P <$ .01 for all). This trend was not observed at v57 ($P = 0.32$) or v54 ($P = .31$) where differences were not statistically significant.

For 5-fraction patients, SpaceOAR consistently had lower irradiated rectal volumes than Barrigel across all

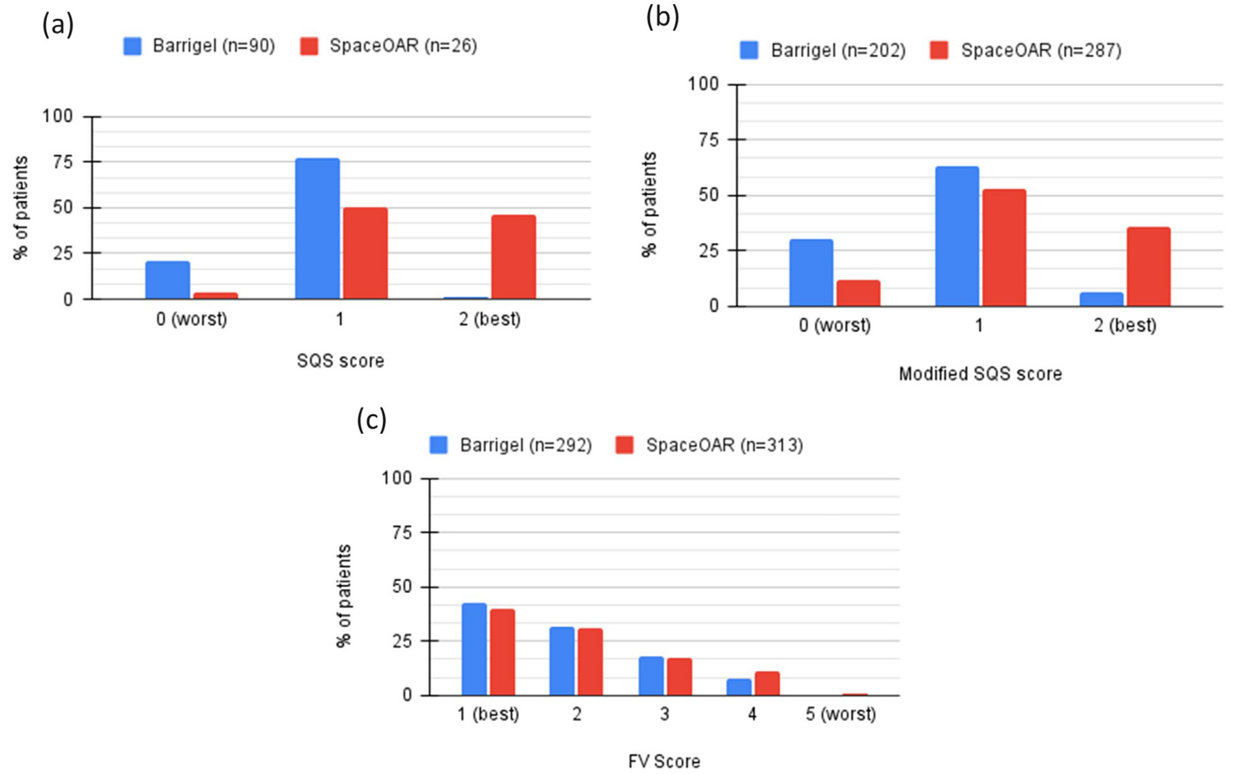

Figure 2 (a) Distribution of Spacer Quality Score (SQS) for patients receiving 5 fractions. (b) Distribution of modified SQS for patients receiving more than 5 fractions. (c) Distribution of Fischer-Valuck (FV) scores for all patients.

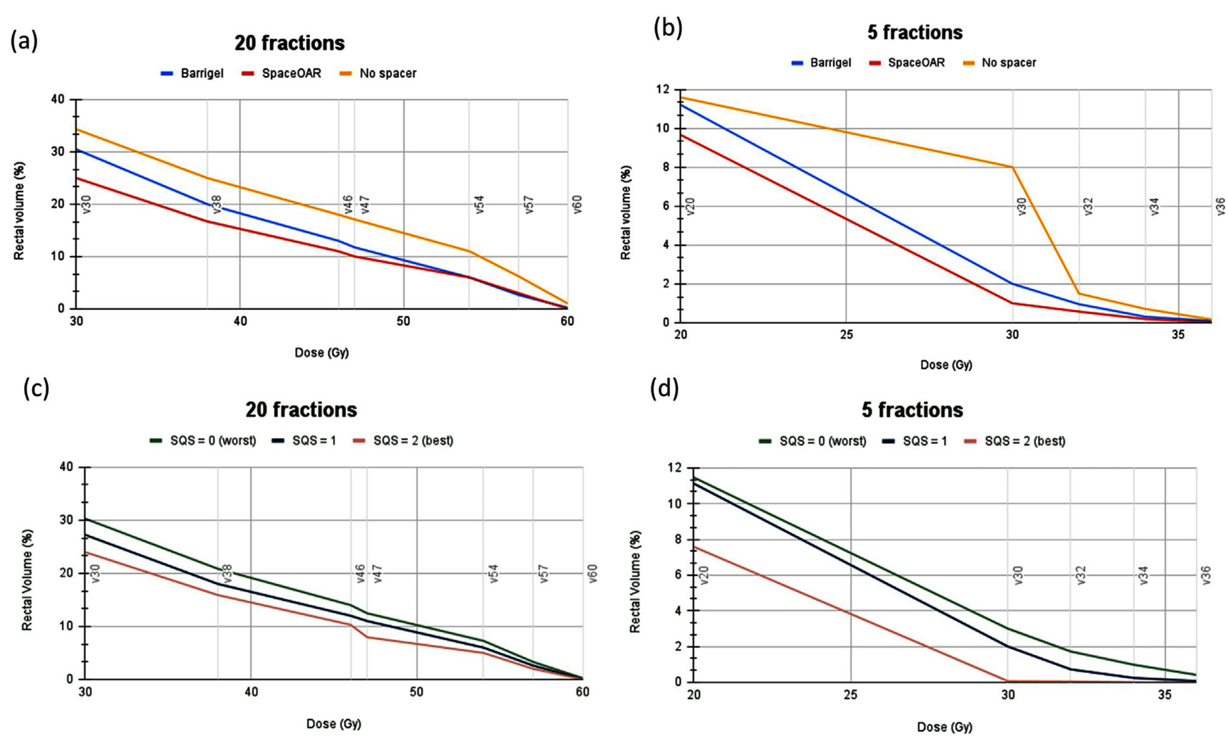

Figure 3 Comparison of median dosimetric outcomes as a function of spacer type for (a) 20-fraction patients, (b) 5-fraction patients. Comparison of median dosimetric outcomes as a function of Spacer Quality Score (SQS) for (c) 20-fraction patients, (d) 5-fraction patients. Medians (IQRs) for Fig. 3a-d are listed in Tables S3a-S3d, respectively.

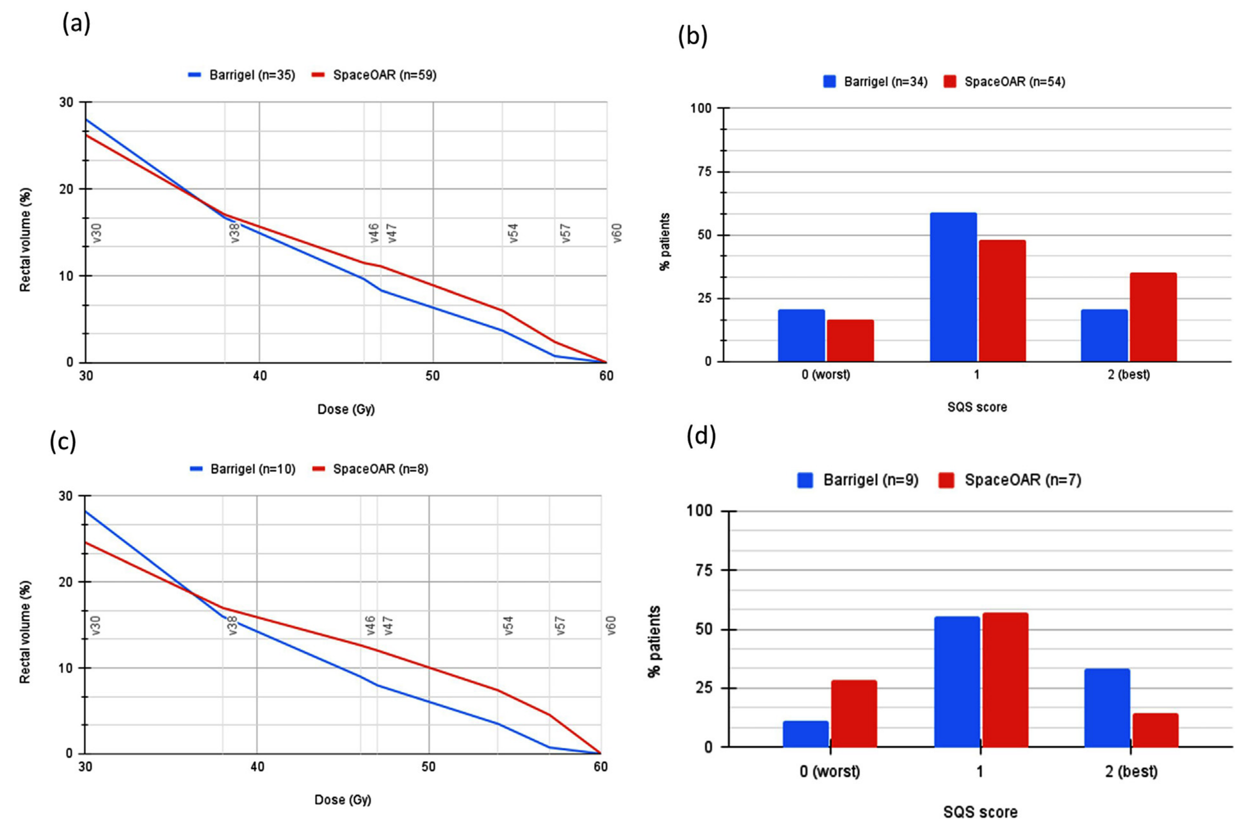

Figure 4 For 20-fraction patients where rectal spacing volume is 6 to 13 cc: (a) comparison of median dosimetric outcomes, (b) comparison of Spacer Quality Score (SQS) distributions. For 20-fraction patients where rectal spacing volume is 7.5 to 9 cc: (c) comparison of median dosimetric outcomes, (d) comparison of SQS distributions.

dose levels (Fig. 3b). Statistically significant differences were observed at v30 (P = .04) and v20 (P = .01), whereas v36 (P = .25), v34 (P = .14) and v32 (P = .06) did not reach significance.

SQSs were associated with dosimetric outcomes in both the 20-fraction and 5-fraction patient groups across all levels (v30-v60) (Kruskal−Wallis $P < .05$). Higher SQS were linked to lower dosimetric outcomes (Jonckheere−Terpstra $P < .05$) across all dose levels for 20 and 5 fraction patients (Fig. 3c, d).

No significant association was observed between FV scores and rectal dose levels in the 20-fraction group (Kruskal−Wallis) at v60 (P = .23), v57 (P = .41), v54 (P = .97), v47 (P = .93), v46 (P = .77), v38 (P = .79), and v30 (P = .90). In the 5-fraction group, FV scores showed differences at v36 (P = .04), v32 (P = .01), and v30 (P = .024), whereas v34 (P = .31) and v20 (P = .66) were not significant. However, these differences did not follow a monotonic trend (Jonckheere−Terpstra); v36 (P = .10), v32 (P = .26), and v30 (P = .45) (Figure E4a, b).

When RSV was restricted to ranges of 6 to 13 cc, Barrigel achieved better median rectal doses for v57 and v54 (P = .01 for both), and nearing significance for v47 (P = .06, Fig. 4a). This was despite SpaceOAR achieving more SQS 2s than Barrigel (Fig. 4b). When RSV was further restricted to ranges between 7.5 to 9 cc, to limit outliers, Barrigel achieved better median rectal doses for v57, v54, v47 with P values of 0.01, 0.04, and 0.02, respectively (Fig. 4c). Distribution of SQS scores between Barrigel and SpaceOAR cohorts in the 7.5- to 9-cc range was similar (Barrigel n = 10, SpaceOAR n = 9; Fisher's exact test, P = .84, Fig. 4d).

A generalized regression model using log distributions was fitted to model dosimetric outcomes after accounting for RSV for the 20-fraction patient group. RSV was restricted to a common range between SpaceOAR and Barrigel. Our model showed that for every unit increase in RSV, Barrigel had an effect at dose reduction which was greater than SpaceOAR. This trend was observed across v60 to v38, only meeting significance at v54 (P = .04) (see Table E5 for model coefficients). Barrigel's dose reduction appeared most meaningful at volumes >6 cc, especially at dose levels of v47, v54, and 57 (Fig. 5).

Rectal wall infiltration

Seven patients were identified with RWI, all recipients of SpaceOAR (7/287, 2.44%). As per the RWI scoring

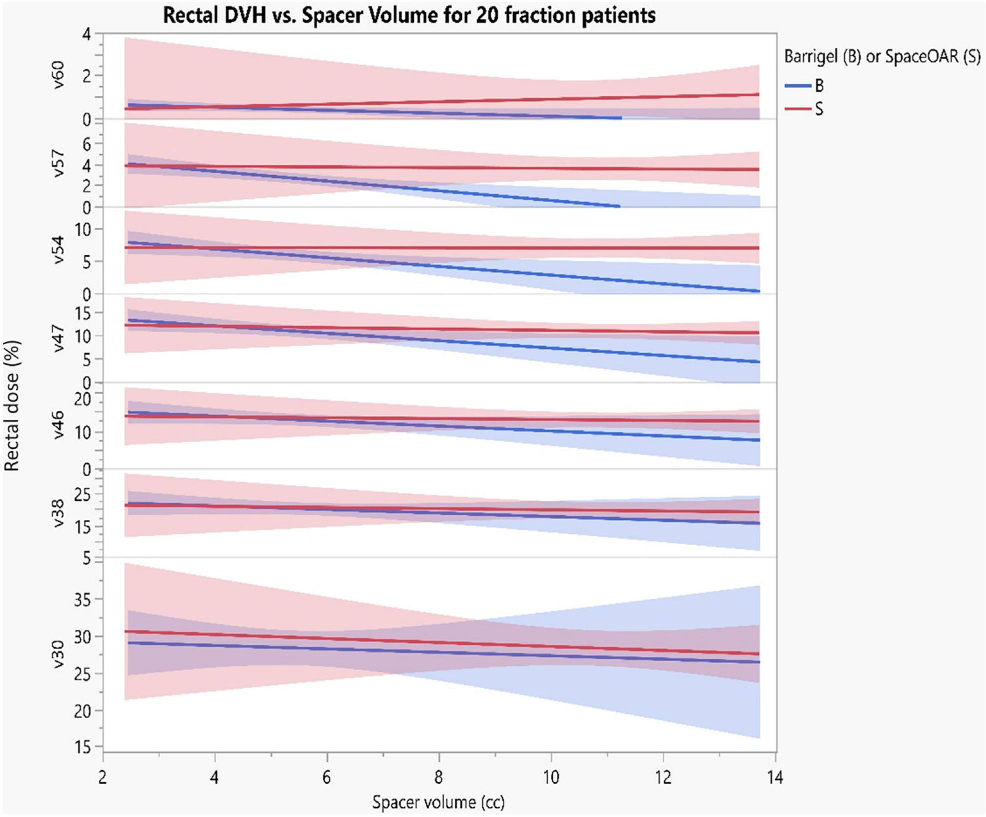

Figure 5 Comparison of Barrigel and SpaceOAR in terms of dosimetric points as a function of rectal spacer volume for patients receiving 20 fractions.

criteria, 3 patients were identified with grade 1, 2 with grade 2, and 2 with grade 3. No hyaluronidase reversals were recorded during this timeframe from data given by Teleflex Medical Australia.

Discussion

In this real-world study, we have found that SpaceOAR implantation offers better SQSs and rectal DVHs compared to Barrigel without consideration of RSV. We found that at higher RSVs (>6 cc), Barrigel then outperforms SpaceOAR in terms of dosimetric outcomes.

The SQS system may be better than the FV scoring method when assessing rectal dosimetry. Unlike the SQS method, FV scores had no correlation with spacer type nor dosimetric outcomes. This is most likely due to the FV method accounting more for symmetry of insertion which does not always equate the thickness of the PRI, as discussed by Grossman et al.[16] The SQS scoring was less subjective to observer discrepancy compared to FV ($\kappa = 0.91$ vs 0.61, respectively).

Patients with SpaceOAR were more likely to achieve higher SQS scores in both the 5-fraction and >5-fraction groups. This may be attributed to the larger RSG volumes inserted, allowing for thicker PRI. Although SQS directly measures PRI thickness, it is also indirectly affected by symmetry of gel placement where better symmetry would allow for higher SQS.[20] In our study, where volumes were similar, there was no statistically significant difference concerning SQS distributions between cohorts, suggesting that one gel type is not associated with better symmetry of insertion. This suggests the presence of other confounding variables such as intrinsic properties of the gel (eg, composition or density) or other aspects of placement (eg, whether the gel is concentrated more at the apex) which may be impacting these results. This study used overall SQS for analysis of outcomes, but this may mask important variations in gel insertion—for example, a patient with substantial gel at the prostate base but minimal at the apex could yield the same SQS as a patient with the opposite distribution despite very different dosimetric outcomes. Barrigel at volumes 6 cc or above likely had greater PRI at the apex which enabled the lower rectal dosimetry compared to SpaceOAR. This is supported by the improved sculpting ability of this RSG compared to SpaceOAR.[21] Given the lack of correlation with the FV score, it is unlikely symmetry of insertion is largely influencing dosimetric outcomes compared to RSG volume. SQS differences were noted between the 5-fraction and >5-fraction groups, which may reflect differences in the criteria used to assess SQS between these cohorts rather than a true influence of fractionation on spacer insertion quality.

In the subset of patients when RSG volumes >6 cc, Barrigel's effect compared to SpaceOAR was most meaningful at higher rectal dose levels of v57, 54, and 47. There was minimal impact at lower dose levels (eg, v30). This likely relates to the inverse square law, with a principle of diminishing returns for lower radiation therapy doses the further the distance is. The challenge is correlating this with toxicity. Despite clear reduction in rectal irradiated volumes, this may not translate to improved toxicities based on the already low rectal dosimetry that is achieved using today's volumetric modulated arc radiation therapy without RSG.[22] With such high efficacy in controlling PC using radiation therapy, future trials are needed to focus on improving QOL outcomes. Examples include the ASTuTE trial, which aims to de-escalate short-term androgen deprivation therapy using artificial intelligence[23] or trials using virtual high-dose-rate (HDR) boosts.[24] We await stronger toxicity and QOL data to prove the utility of RSG insertion.

No incidence of RWI was seen among Barrigel patients (0/202) and no use of the enzyme, hyaluronidase, was employed during this time. This is consistent with previous findings, including 0% reported in the Barrigel pivotal trial and 0.32% in the study by Hong et al.[13,25] The incidence of RWI among SpaceOAR patients (2.44%) was substantially higher than Barrigel, though lower than 6% previously reported in the SpaceOAR pivotal trial.[15] These findings suggest that Barrigel may have a more favorable safety profile compared to SpaceOAR. This may be due to the nature of the product itself or larger volumes of insertion which can exert greater rectal wall stress.[15] Although the relationship between RWI and application technique has not been studied thus far,[15] insertion process may also be a relevant consideration. For example, Barrigel does not polymerize in situ so clinicians are not time-restricted during application, and this may lead to better control and better placement of the gel. Although we have reported the incidence of RWI, studies have not found correlation between RWI and patient complications[15,26] although larger volume RWIs may lead to delays in radiation therapy treatment.[25]

Clinician experience may impact the incidence of procedural complications. In this study, data regarding which clinicians performed the procedures were not collected so the role of this factor remains unknown. It is overall unlikely for inserter inexperience to have influenced the results as SpaceOAR had been incorporated into clinical practice for 5 years prior to the start of this trial and the urologists performing spacer insertions remained consistent throughout the 5-year period analyzed. This stability reduces the likelihood of our results being impacted by factors specific to an individual clinician (eg, varying levels of experience, differing techniques, etc).

A key limitation of our study is that most Barrigel insertions did not adhere to the manufacturer's recommended volume. Barrigel recommends a 9-cc insertion volume regardless of prostate size; however, in this study, several patients received volumes of 3 cc or 6 cc. Although SpaceOAR is typically inserted at 10 cc, the median volume in our cohort was 13.80 cc. This discrepancy may be attributed to timing of MRI acquisition which was performed one week post spacer insertion. Factors such as saline from the insertion procedure or potential product volume changes over time may have also contributed to this observed variation. Additionally, MRI measurements of spacer volume may have been systematically biased relative to the true insertion volume.

Furthermore, the scoring systems used (FV and SQS) are semiqualitative, and therefore, inclined to subjective error. To minimize this, observer 1 and 2 allocations were evenly distributed among 5 observers. Discrepancies were resolved via a third observer. A high level of agreement was generally noted between Observer 1 and Observer 2 suggesting a high level of reliability in the data collection process. Regardless, both scoring systems are naturally impacted by image quality, rotation of the patient, and physiological variability of anatomic structures within the body.

Moreover, the study did not consider intrafraction motion differences caused by the different RSGs which may have impacted true rectal dose exposure during treatment. As a retrospective analysis, our study is subject to incomplete/missing data and potential learning curve effects over the study period that may have affected consistency of technique; however, the impact of this is likely minimal because all urologists at the center had been inserting SpaceOAR for several years before 2017. Finally, patient-reported outcomes and long-term toxicity data were unavailable, so clinically meaningful differences could not be established to correlate the impact of dosimetry on QOL; this presents an area for future investigation.

Overall, real-world data show that SpaceOAR performed better at reducing rectal dose compared to Barrigel. However, this was likely volume dependent and after accounting for this confounding variable, it appears Barrigel may achieve more favorable dosimetry compared to SpaceOAR at insertion volumes of 6 cc or higher.

Disclosures

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Supplementary materials

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