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Expanding the Utilization of Rectal Spacer Hydrogel for Larger Prostate Glands (>80 cc): Feasibility and Dosimetric Outcomes

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Expanding the Utilization of Rectal Spacer Hydrogel for Larger Prostate Glands (>80 cc): Feasibility and Dosimetric Outcomes

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Purpose: The Hydrogel Spacer Prospective Randomized Pivotal Trial achieved mean rectoprostatic spacing of 12.6 mm resulting in lowering of rectal V70 from 12.4% (without spacer) to 3.3% (with spacer) in patients with glands up to 80 cm^3. The value of this approach in patients with larger glands is inadequately established. This study assesses the feasibility and dosimetric outcomes of perirectal spacing in patients with prostate cancer with larger glands (>80 cm^3).

Methods and Materials: Between January 2017 and December 2019, 33 patients with prostate glands >80 cm^3 (mean 108.1 cm^3; range, 81.1-186.6 cm^3) were treated, 15 with glands >80 to 100 cm^3 and 18 >100 cm^3. Median follow-up was 10 months (range, 3-26). The median international prostate symptom score was 9 (range, 1-18). Hydrogel was placed under local anesthesia in all cases. Treatment modality included intensity modulated radiation therapy in 15 and proton therapy (PT) in 18 patients. Treatment targeted the prostate plus seminal vesicles in 21 patients and 12 also had elective nodal irradiation. Conventional fractionation (CF) to 78 Gy in 39 fractions was used in 16 and moderate hypofractionation (HF) to 70 Gy in 28 fractions in 17 patients.

Results: In the CF group, mean rectum (r) V75, 70, 60, 50 was 0.87%, 2.25%, 5.61%, and 10.5%, respectively. For glands >80 to 100 cm^3 and >100 cm^3, rV70 was 2.55% and 2%, respectively. In HF patients, mean rV65, 63, 60, and 50 was 1.67%, 2.3%, 3.4%, and 8.6%. For glands >80 to 100 cm^3 and >100 cm^3, rV63 was 2% and 2.56%, respectively. Overall, the mean midgland rectoprostatic hydrogel separation was 9.3 mm (range, 4.7-19.4 mm). All patients tolerated treatment well; no acute grade 2 or higher adverse gastrointestinal events were observed.

Conclusions: Hydrogel placement is feasible in prostate glands larger than 80 cm^3 with favorable dosimetric outcomes.

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Data Sharing Statement: Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

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Introduction

External beam radiation therapy (EBRT) is commonly used in the curative treatment of localized prostate cancer. Despite advances in image guided treatment delivery with increasing tumor targeting precision, the rectum remains an organ at risk for radiation-induced toxicity.[1-9]

Both prospective multi-institutional studies[10-12] and retrospective studies demonstrated the feasibility of rectal spacer application to improve rectal sparing and mitigate rectal toxicity, but essentially all of these have limited the use of the spacer to glands <80 cm^3.[13-17]

The SpaceOAR System (Augmenix, Inc, Waltham, MA) is a slowly absorbable hydrogel injected into Denonvillier's space, which temporarily displaces the rectum away from the prostate and thus decreases rectal dose. The SpaceOAR Pivotal Trial[11] compared patients receiving EBRT treated with or without rectal spacer. Postspacer plans significantly reduced mean rV70 (12.4% to 3.3%, $P < .0001$) with a reduction in rectal toxicity.[11]

To date, there remains a scarcity of published data on the feasibility, outcomes, and technical aspects pertaining to hydrogel application in patients with larger glands. The present study reports on the feasibility and dosimetric outcomes of patients with large prostate glands (>80 cm^3) with a subset larger than 100 cm^3, treated with conventional as well as moderately hypofractionated EBRT and rectal spacer.

Methods and Materials

Between January 2017 and December 2019, 33 patients with localized prostate cancer with gland volume exceeding 80 cm^3 (median 101.2 cm^3; range, 81.1-186.6 cm^3) received definitive EBRT with curative intent. Fifteen patients had glands >80 to 100 cm^3 and 18 had glands >100 cm^3. The median international prostate symptom score was 9 (range, 1-18) with a mean value of 8.8. Median patient age was 73 years (range, 59-83). Median follow-up was 10 months (range, 3-26 months). The mean interval from hydrogel injection to computed tomography (CT) simulation was 1.6 days (range, 1-5). Planning magnetic resonance imaging (MRI) for image fusion was obtained after the CT simulation on same day, consisting of axial T1, fat suppression T2, and sagittal T2 sequences. Fused MRI was used to assist in target contouring and hydrogel delineation. Rectoprostatic hydrogel separation was first measured at midgland, defined as half distance between base and apex along prostate sagittal midline. Additional measurements were performed at 1 and 2 cm cephalad and caudad of midgland along midline.

There were no hydrogel procedure-related complications. During treatment, patients were assessed weekly toxicities were recorded using Common Terminology Criteria for Adverse Events, version 4.0 (available online at https://doi.org/10.1016/j.ijrobp.2020.01.026). After completion of treatment, patients were seen in follow-up at 3-month and subsequently at 6-month intervals.

Pretreatment patient characteristics are displayed in (Table 1). No patients had extraprostatic disease extension. Before hydrogel placement, 11 patients (33.3%) were on aspirin and another 4 (12.1%) were either on Plavix or Eliquis. Patients on aspirin or Plavix held the medication 7 days before the procedure and Eliquis was held 2 days prior; all resumed medication within 24 hours after hydrogel placement. This retrospective review was approved Baptist Health South Florida Institutional Review Board.

Hydrogel procedure

All procedures were performed under local anesthesia. Bowel preparation included a fleet enema 3 to 4 hours before the procedure. One hour before the procedure, Emla topical anesthetic (lidocaine/prilocaine cream) was applied on the perineum and patients were given oral premedication consisting of a single dose of prophylactic antibiotic consisting of cefadroxil 500 mg by mouth. Patients with history of allergy to penicillin or cephalosporin were given a single dose of Bactrim DS. In addition, oral premedication for pain consisted of acetaminophen 500 mg single dose given with antibiotics in 24 of 33 patients (72.7%). Nine patients received hydrocodone/acetaminophen 5 to 300 mg single dose. Patients were asked to empty their bladder just before the procedure.

Interstitial numbing was performed using mixed 2% plain lidocaine buffered with sodium bicarbonate 8.4% solution in a 20-mL syringe in a ratio of 10:1. Numbing was performed along the midline, corresponding to the path of the hydrogel needle and up against the capsule of the prostate apex on both sides using a median total volume of 10 cm^3 (range, 10-18 cm^3). After transperineal fiducial marker placement, the hydrogel needle was inserted.

The hydrogel application technique has been described by Hatiboglu et al.[12] We describe additional steps used at our institution to optimize hydrogel placement, particularly useful in larger glands, which include (1) maximize anatomic delineation, (2) steps to optimize needle placement, (3) and hydrogel dissipation during injection.

Maximize anatomic delineation

Because large glands tend to compress the rectoprostatic space (Figs 1A-B), it is important to lower the probe to increase the prostate-rectum separation to improve hydrogel needle access. On lowering the probe, air artifact may develop obscuring the ultrasound image. In the case shown, artifact was located at the apex entrance level

Table 1 Patient characteristics

Characteristics	n (%)
Mean age (y)	73 (59-83)
Mean follow up (mo)	10.7 (3-26)
Prostate size	
>80-100 cm^3	15 (45.4%)
>100 cm^3	18 (54.6%)
IPSS score	
Mean (range)	8.8 (1-18)
Median	9
PSA	
<10	20 (60.6%)
10-20	10 (30.3%)
>20	3 (9.1%)
Stage	
T1c	23 (69.7%)
T2a	4 (12.1%)
T2b	4 (12.1%)
T2c	2 (6.1%)
Gleason score	
6	5 (15.2%)
7 (3 + 4)	13 (39.4%)
7 (4 + 3)	7 (21.2%)
8 (4 + 4)	7 (21.2%%)
9 (4 + 5)	1 (3%)
NCCN risk group	
LR	4 (12.1%)
IR	19 (57.6%)
HR	10 (30.3%)
Dose regimen	
CF 78 Gy/39 fractions	16 (48.4%)
HF 70 Gy/28 fractions	17 (51.6%)
Radiation therapy modality	
IMRT	15 (45.4%)
Proton	18 (54.6%)
ADT (duration)	
LR	0/4
IR (6 mo)	7/19
HR (18 mo)	10/10
Hydrogel procedure	
Local anesthesia	33 (100%)
Aspirin	11/33 (33.3%)
Anticoagulants	4 /33 (12.1%)
History of hemorrhoid surgery	4 /33 (12.1%)
History of Transurethral procedure	
HoLEP	1/33 (3%)
MRI staging	33 (100%)
Negative capsule invasion or extraprostatic extension	33 (100%)

Abbreviations: ADT = androgen deprivation therapy; CF = conventional fractionation; HF = moderate hypofractionation; HoLEP = Holmium laser enucleation of prostate; HR = high risk; IMRT = intensity modulate radiation therapy; IPSS = international prostate symptom score; IR = intermediate risk; LR = low risk; MRI = magnetic resonance imaging; NCCN = National Comprehensive Cancer Network; PSA = prostate-specific antigen.

(Fig 1C). An ultrasound probe standoff saline balloon can be employed to mitigate artifact and improve anatomic delineation (Fig 1D).

Steps to optimize needle placement

On sagittal view, the needle is introduced and advanced up to midgland avoiding the rectal wall (Figs 2A-C). Hydrodissection is initiated with a small puff of saline (0.5-1 cm^3) injected first in the sagittal plane to confirm that rectoprostatic space opens (Fig 2D).

The ultrasound is then switched to axial plane and probe is moved caudally, such that the needle tip is visualized. Next, the needle tip is slowly and gently wiggled approximately 2 mm back and forth in the anteroposterior direction to make sure the needle is not catching or "dragging" the outer layers of the rectal wall or the rectoprostatic fascia. Another puff (0.5-1 cm^3) is injected on axial plane to visualize the actual right-to-left symmetry of saline dissipation (Fig 2E). We also evaluate whether the rectoprostatic space is clearly opening resulting in a dark "water" ultrasound signal and at the same time displacing the rectal wall (Fig 2E). Saline permeation into the rectal wall would be suggested by a gray ultrasound signal blurring the rectal wall. Hydrodissection is then completed on sagittal view with a total volume rarely exceeding 6 cm^3.

Whenever saline distribution is asymmetrical, despite having needle at midline, we consider adjusting the needle laterally by 5 to 10 mm to the side with less saline to correct the asymmetry. Such adjustment requires pulling the needle back to just above apex and readvancing it to the intended side. This maneuver should be performed on the sagittal plane only to ensure that the needle does not drop toward the rectum or rise toward the prostate fascia, with the needle tip always in view.

Hydrogel dissipation during injection

To maximize hydrogel dissipation from base to apex, especially in the larger glands, we start the hydrogel injection 1 cm cephalad of midgland and perform a cephalocaudad needle pull back during continuous injection to just caudad of midgland (Figs 3A-C). When needle pull back is employed during injection, caution must be exercised to avoid over injection at the apex or caudal of the prostate.

Applicability of standoff saline balloon

We typically use a condom to cover the ultrasound probe. An ultrasound standoff saline balloon is useful in selected instances when there is artifact created by gas obscuring the image, which cannot be cleared by raising the probe anteriorly

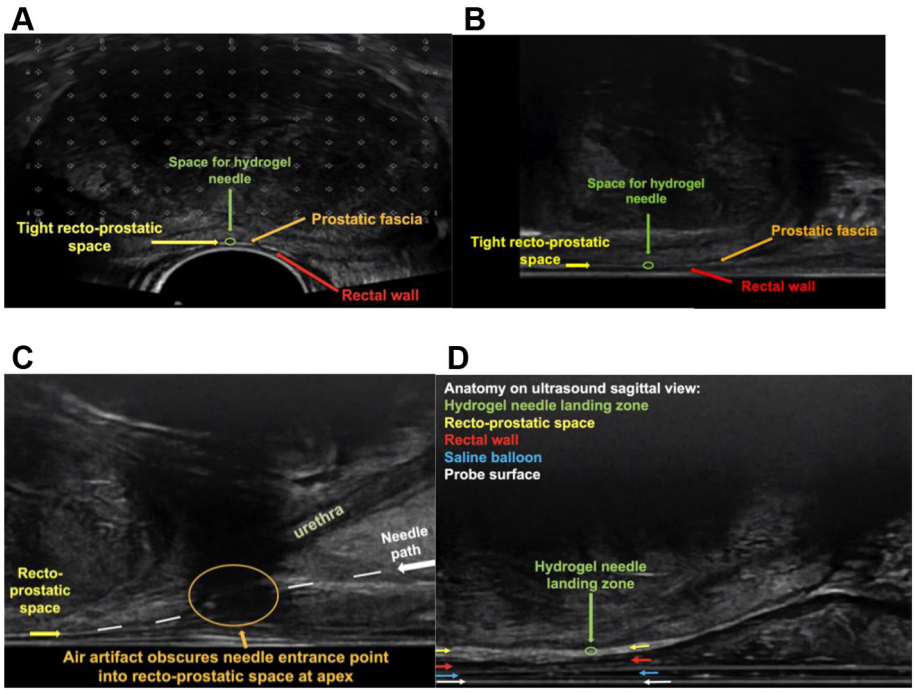

Figure 1 (A-B) Axial and sagittal views of large gland (186.6 cm^3) illustrate a tight rectoprostatic space. (C) Sagittal view of 186.6 cm^3 gland demonstrates air artifact obscuring anatomy at crucial needle entrance into rectoprostatic space at the apex. Dashed white line demarcates the intended hydrogel needle path. (D) Sagittal view of the gland with standoff saline balloon which mitigates air artifact; pertinent structures abutting rectoprostatic space are illustrated: rectoprostatic space (yellow), rectal wall and underlying mucosa (red), saline balloon (blue), ultrasound probe surface (white), and needle landing zone (green circle). (A color version of this figure is available at https://doi.org/10.1016/j.adro.2021.100651.)

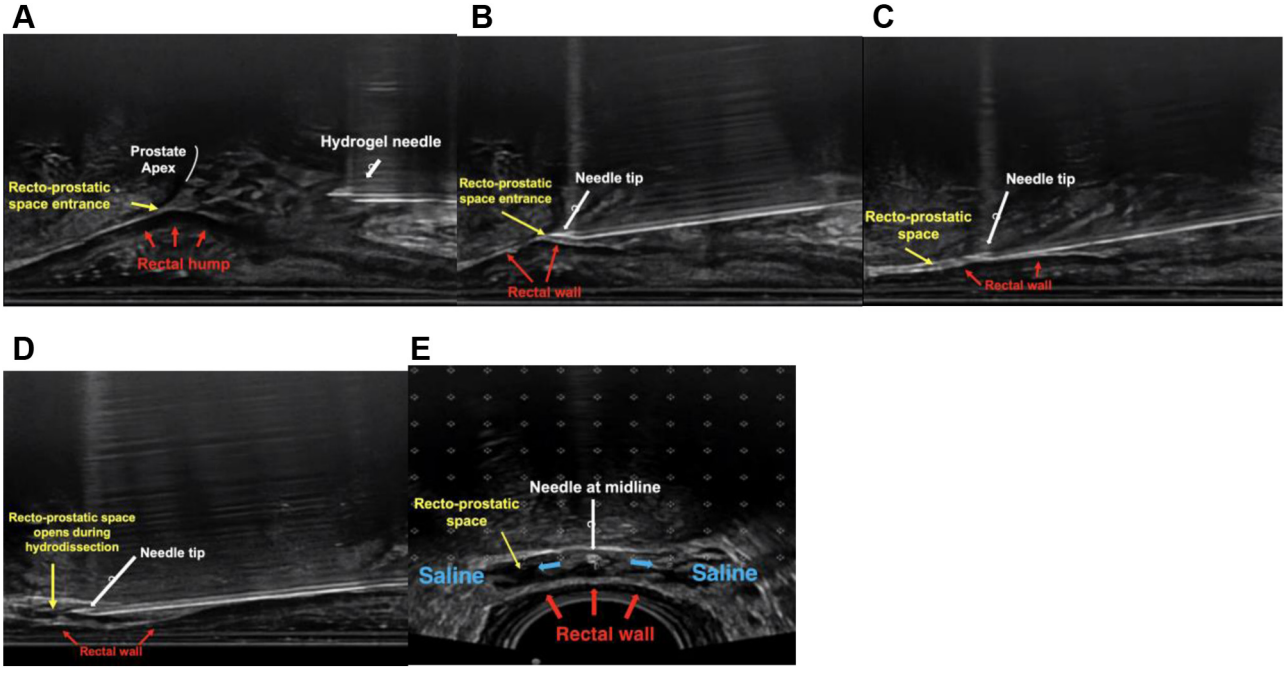

Figure 2 (A) Sagittal view illustrates needle approaching rectoprostatic space entrance point at apex. Needle will be angled posteriorly after passing rectal hump such to avoid transecting rectal wall at this point. (B) Needle entering rectoprostatic space at apex. (C) Needle in rectoprostatic space approaching midgland. Needle must be kept off rectal wall as it advances. (D) Hydrodissection opens rectoprostatic space. (E) Axial plane verification illustrates needle at midline, in free space, off rectal wall, with good symmetry of saline dissipation.

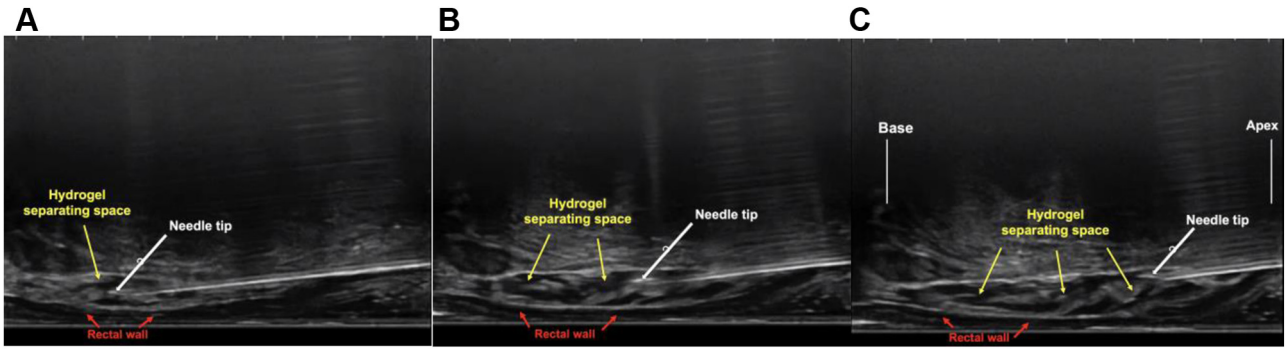

Figure 3 (A) Hydrogel injection (needle just cephalad of midgland); (B) needle at midgland; and (C) needle just caudal of midgland.

against the prostate or when raising the probe would result in significant narrowing of the rectoprostatic space. The largest gland we treated in this series, measuring 186.6 cm^3, is illustrated in Figure 1A-B. There were 2 reasons to use a standoff balloon in this case. First, there was air artifact obscuring the critical needle entrance point at the apex (Fig 1C). The balloon cleared the air artifact providing visibility of the rectal wall and fascia at the apex (Fig 1D). Second, the balloon improved the definition of the rectal mucosa and wall, providing even more confidence in the needle tip position and ability to avoid penetration of the rectal wall during needle insertion, a crucial concern in cases with very tight rectoprostatic space (Figs 1D, 2A-C). The fill volume of the balloon must be kept to a minimum (4-5 cm^3), enough to improve rectal wall visibility. After hydrodissection begins, the saline balloon should be completely deflated to eliminate any volume that would impede hydrogel separation (Figs 3A-C).

Simulation

Bowel preparation included fleet enema 3 to 5 hours before CT scan. Patient we also asked to maintain looser stools with the aid of stool softeners and low gas diet. Before CT and MRI, patients were instructed to empty their bladder and drink 24 ounces of water, seeking to achieve a "comfortable bladder fill" of 250 to 350 cm^3. Mean interval between hydrogel placement and simulation was 1.6 days (range, 1-5 days).

Target definition and dose regimens

Intensity modulated radiation therapy (IMRT) planning and delivery used volumetric arc therapy technique. Proton therapy employed pencil beam scanning technique delivered with lateral opposed fields. Prostate clinical target volume (CTV) was defined on CT after MRI fusion. CTV to planning target volume (PTV) expansions were 4 mm posteriorly and 6 mm elsewhere.

In low-risk patients, the CTV included the prostate + proximal seminal vesicles (1 cm cephalad from origin and 1 cm left and right of midline) defined as (prostate CTV + SVprox). In intermediate-risk patients, 2 CTV and PTV volumes were created; the smaller volume defined as (PTV_*P* + SVprox) received the full prescription dose and a larger volume including the entire seminal vesicles received a minimum of 54 to 56 Gy. For those treated with conventional fractionation (CF) to 78 Gy in 39 fractions, the first phase targeted the (PTV_*P* + SV) to 54 Gy in 27 fractions, followed by a boost to the (PTV_*P* + SVprox) to 78 Gy. In patients treated hypofractionation (HF) to 70 Gy in 28 fractions, we used a simultaneously integrated boost approach where (PTV_*P* + SVprox) received 2.5 Gy per fraction to 70 Gy and the distal seminal vesicle received 56 Gy in 2 Gy per fraction.

High-risk patients were treated with 78 Gy in 39 fractions in 2 phases: the high-dose volume (PTV_*P* + SVprox) received 24 Gy in 12 fractions. The second phase used a simultaneously integrated boost approach targeting the (PTV_*P* + SV) prostate + seminal vesicles to 54 Gy in 27 fractions and pelvic nodes received 48.6 Gy in 1.8 Gy fractions. Pelvic nodes included obturator, iliac, presacral and common iliac nodes to L4 to L5 junction.

Risk groups and treatment delivered

Of the 33 patients, 4 were low risk (12.1%), 19 intermediate risk (57.5%), and 10 high risk (30.3%). All 4 low-risk patients were treated to 70 Gy in 28 fractions, 2 with IMRT and the other 2 with proton therapy. Of the 19 intermediate-risk patients, 2 patients (10.5%) met the minimum threshold risk of 15% for lymph node metastasis and received elective pelvic lymph treatment performed in conventional fractionation. Lymph node risk was estimated using the Memorial Sloan Kettering - Cancer Center pelvic lymph node nomogram and Briganti nomograms.[18,19] The remaining 17 patients treated to prostate + seminal vesicles, 6 (31.6%) with HF and 13 (68.4%) with CF. Ten of 33 patients (30.3%) had high-risk disease, all of whom were treated to 78 Gy in 39 fractions with a minimum dose of 48.6 Gy to elective pelvic lymph nodes. Overall, 12 patients were treated to prostate, seminal vesicles, and pelvic nodes.

Table 2 Mean and median rectoprostatic hydrogel separation (mm)

Prostate size	All		>80-100 cm^3		>100 cm^3	
Sagittal midline separation	Mean	Median	Mean	Median	Mean	Median
Cephalad 2 cm	7.8	8.0	11.9	8.4	7.6	8.0
Cephalad 1 cm	10.1	9.9	10.8	11.2	9.6	9.7
Midgland	9.3	8.9	10.5	9.9	8.3	8.3
Caudad 1 cm	8.6	8.6	7.6	9	8	8.2
Caudad 2 cm	5.9	6.3	6.7	6.8	5.3	5.6

Dietary recommendations during treatment

Patients were routinely instructed to maintain loose stools with the aid of over-the-counter stool softeners and to follow a low-gas-producing diet. This recommendation was derived from early observations using rectal spacer where rectal distension during treatment by either constipation or gas was correlated with increased rectal dose.[20]

For IMRT patients, setup used cone beam computed tomography for all fractions. For proton patients, cone beam computerized tomography was performed on first treatment and then weekly thereafter, and 2 orthogonal x-rays were obtained daily to confirm all fiducials were within the 2 mm tolerance expansion.[21]

Results

Overall, the mean midgland rectoprostatic hydrogel separation along the anterior to posterior axis was 9.3 mm (4.7-19.4 mm). The separation was 9.9 mm (range, 6.6-19.4 mm) for glands measuring >80 to 100 cm^3 and 8.8 mm (range, 4.7-12.3) for glands >100 cm^3.

Rectoprostatic hydrogel separation was also measured 1 and 2 cm both cephalad and caudad from the midgland along the sagittal plane. The mean cephalad 1 and 2 cm separation was 10.1 and 7.8 mm and the caudad 1 and 2 cm separation was 8.6 and 5.9 mm, respectively. Table 2 displays the corresponding values for patients with glands >80 to 100 cm^3 and >100 cm^3.

In patients treated with CF, the mean rV70 was 2.55% (range, 0.73-4.7) and 2% (range, 0.3-3.0) for glands >80 to 100 cm^3 and >100 cm^3, respectively (Table 3). In patients treated with HF, the rV63 was 2% (range, 0.17-6.7) and 2.56% (range, 0.16-5.8), for glands >80 to 100 cm^3 and >100 cm^3.

In the CF group, the overall mean rV75, 70, 60, and 50 were 0.84%, 2.25%, 5.61%, and 10.5%, respectively. In patients for whom treatment included elective pelvic lymph nodes, the mean rV75, 70, 60, and 50 were 0.87%, 2.3%, 5.66%, and 10.7%, respectively (Table 4). In the moderately HF group, the overall mean rV65, 63, 60, and 50 were 1.67%, 2.3%, 3.4%, and 8.6%, respectively (Table 4).

Bladder and penile bulb dosimetry were also tracked. With respect to bladder dosimetric outcomes in the CF group, mean bladder (b) V70, 60, and 50 were 13.5%, 19.4%, and 25.3%, respectively. In the moderately HF group, mean bV70, 60 and 50 were 11%, 17.4%, and 20%, respectively. Mean penile bulb dose was 14.8 Gy and 18 Gy for those treated with CF and moderately HF regimens, respectively.

EBRT was completed within the planned interval in all patients. Patients tolerated treatment well without any acute grade 2 or higher adverse rectal or other gastrointestinal (GI) adverse events. Only 3 of 33 patients (9%) experienced grade 1 diarrhea, one of whom was treated to pelvic nodes. To date, no significant late rectal toxicities have been observed; however, the relatively short median follow-up of 10 months (range, 3-26 months) limits such assessment.

With respect to genitourinary outcomes, it should be noted that 18 of 33 patients (54.5%) were on α-blockers at baseline before hydrogel injection and radiation therapy initiation. None of these patients required α-blocker dose escalation. During radiation therapy, 9 of 15 patients (60%) previously not on α-blockers were prescribed Flomax for grade 2 acute urinary flow adverse events.

Table 3 Prostate size and dosimetric outcomes

Prostate size	Patients	Mean size (range)	Midgland separation	Mean rV70 (78 Gy/39 fractions)	Mean rV63 (70 Gy/28 fractions)
All patients	33	108.1 cm^3 (81.1-186.6)	9.4 mm (6.6-12.3)	2.25% (0-4.7%)	2.33% (0.16-6.7)
>80-100 cm^3	15	89 cm^3 (81.1-98.3)	9.9 mm (6.6-19.4)	2.55% (0.73-4.7)	2% (0.3-6.7)
>100 cm^3	18	124 cm^3 (100.1-186.6)	8.8 mm (4.7-12.3)	2% (0-3.07)	2.56% (0.16-5.8)

Table 4 Dosimetric outcomes

Conventional fractionation (78 Gy/39 fractions)					
	Pts	rV75	rV70	rV60	rV50
All	16	0.84% (0-2.7)	2.25% (0-4.7)	5.61% (1.7-9.5)	10.5% (2.39-15.2)
P + SV	4	0.75% (0.06-1.77)	2% (0.75-4.4)	5.47% (2.5-9.5)	10.1% (6.4-15.2)
P + SV + Lns	12	0.87% (0-2.7%)	2.3% (0-4.7)	5.66% (1.7-8.9)	10.7% (2.3-14.9)
P + SV (IMRT)	2	0.58% (0.06-1.1)	1.61% (0.93-2.3)	4.95% (4.5-5.4)	9.45% (9.4-9.5)
P + SV (PT)	2	0.93% (0.09-1.77)	2.57% (0.75-4.4)	6% (2.5-9.5)	10.8% (6.4-15.2)
Moderate hypofractionation (70 Gy/28 fractions)					
	Pts	rV65	rV63	rV60	rV50
All P + SV	17	1.67% (0-5.8)	2.3% (0.1-6.7)	3.4% (0.4-9.6)	8.6% (3.3-15.7)
P + SV (IMRT)	9	1.16% (0-4.6)	1.65% (0.1-5.8)	2.5% (0.3-7.8)	6.9% (2.46-15)
P + SV (PT)	8	2.24% (0.7-5.8)	3.1% (1.3-6.7)	4.48% (2.4-9.6)	10.5% (4.9-15.7)

Abbreviations: IMRT = intensity modulated radiation therapy; (P + SV) = prostate plus seminal vesicles; (P + SV + Lns) = prostate plus seminal vesicles plus lymph nodes; PT = proton therapy; Pts = patients.

Discussion

Despite improvements in prostate EBRT with widespread adoption of IMRT, radiation-induced rectal toxicity remains a concern.[8,22,23] Randomized trials using various dose regimens show that rectal complications have not been eliminated.[24-26] Furthermore, radiation-induced rectal toxicities remain an obstacle in dose escalation strategies.[1-8,27] hydrogel rectal spacer is an innovation to mitigate radiation-induced rectal toxicity.[11,28]

The process of transperineal percutaneous ultrasound-guided hydrogel placement is relatively simple as described by Hatiboglu et al.[12] Displacement of the rectum with a relative reduction in rectal V70 of 60.9% was achieved in 28 of 29 patients (96.6%).

In the study by Pinkawa et al,[13] the authors report on a learning curve with increasing hydrogel symmetry and improved distribution through the base, middle, and apex detected when comparing the first 15 cases performed with subsequent cases. Mean distance between prostate and anterior rectal wall increased from 0.8 cm, 1.1 cm, and 0.8 cm (first 15 cases) at the base, middle, and apex to 1.3 cm, 1.5 cm. and 1.2 cm (subsequent cases), respectively, resulting in significant decrease in rV70 (from 6% vs 2%; $P < .01$).

Several prospective multi-institutional studies[10,11] and a number of retrospective clinical or dosimetric studies have demonstrated the feasibility of rectal spacer application with improvement in rectal sparing.[13-16,29-33]

Song et al[10] reported the results of a multi-institutional study where hydrogel resulted in >7.5-mm prostate-rectal separation in 95.8% of patients with 95.7% achieving a reduction in rV70 of >25%. Eligibility was limited to prostate glands <80 cm^3. In the prospective randomized phase 3 trial reported by Mariados et al,[11] >97% of men had a clinically significant 25% relative reduction in the rectal V70. Mean rV70 reduced from 12.4% to 3.3% postspacer.

The dosimetric effect of rectal spacer with proton therapy planning to 78 Gy in 39 fractions was evaluated in a study of 10 patients comparing planning CT scans before and after spacer placement. Mean rectal V70 was significantly reduced from 4.62% to 0.68% ($P < .001$).[31] A subsequent analysis of 146 patients treated with proton therapy to 78 Gy in 39 fractions with endorectal balloon or rectal spacer demonstrated significant reduction in rectal V70 favoring rectal spacer (5.7% vs 1%, $P < .001$).[30]

Our study focused on the feasibility, technical aspects, and dosimetric outcomes of patients with large prostate glands (>80 cm^3) with a subgroup of very large glands (>100 cm^3) treated with EBRT and rectal spacer. This study is unique in that it includes technical details with illustrative ultrasound images of key steps used at our institution to optimize hydrogel placement especially in larger glands. Our experience evolved with pursuit of midline needle placement to optimize left to right saline and ultimately hydrogel symmetry as well as base to apex spacer dissipation. It should be noted that the procedure is even more meticulous in patients with large glands due to tight rectoprostatic space (Fig 1) and requires high level of attention to detail.

The rectal spacing achieved in our series resulted in rV70 of 2.55% and 2% for glands measuring >80 to 100 cm^3 and >100 cm^3, respectively, for patients treated with CF. When looking at the 12 patients whose treatment included elective pelvic nodes, favorable rV70 of 2.3% was also achieved. Similarly, within the moderate HF group the rV63 corresponding to the 90% prescription dose was 2% and 2.56% for glands >80 to 100 cm^3 and >100 cm^3, respectively.

Our dosimetric outcomes are in line with the results reported by Mariados et al[11] from the Pivotal trial, which demonstrated an overall mean rV70 of 3.3% posthydrogel injection. Of note, a secondary analysis of this trial described a small subset of patients with prostate glands of 80 to 100 cm^3 with the postspacer rV70 of 2%, reduced from 12% in the comparison prespacer scans.[34] The authors concluded that regardless of prostatic volume, there was consistent relative reduction in rectal V70 after spacer placement between 70% to 84%.

Radiation exposure of the rectum and use of aspirin or anticoagulants are correlated with increased risk of grade 2 rectal bleeding.[35,36] Conceivably, patients at higher risk for complications due to preconditions, such as use of aspirin/anticoagulants, could benefit even more from such rectal radiation dose exposure mitigation strategies. Thus, we consider these patients potential candidates for hydrogel placement to maximize rectal sparing. In our series, aspirin or anticoagulants did not preclude hydrogel placement.

The 5-year follow-up results from the pivotal phase 3 trial confirmed that the benefit of rectal spacer hydrogel in reducing the rectal dose, toxicity, and quality of life declines after image guided intensity modulated radiation therapy was maintained or increased with a longer follow-up period.[37] In addition, interest has emerged in evaluating the potential benefits of hydrogel spacer in other clinical outcome domains, such as sexual function. Hamstra et al[38] reported a correlation between use of hydrogel spacer and a decrease penile bulb dose, which was associated with improved erectile function compared with a nonhydrogel control group based on patient-related quality of life assessment.

The growing body of data in support of the benefits of rectal spacer led to the establishment of a new procedural terminology code for periprostatic implantation of hydrogel as of 2018.[11,37] The newly established reimbursement rates vary depending on type of facility where the procedure is performed. Given the variables in payment schedule coupled with the updated clinical data, Levy et al[39] sought to develop a decision-making analytical model to evaluate the cost-effectiveness of hydrogel spacer in radiation therapy for prostate cancer from the perspective of the US payers. The authors proposed the development of quality-adjusted life years and costs modeled for a 5-year period after radiation therapy, taking into consideration the potential benefits of hydrogel in various domains, such as gastrointestinal, genitourinary, and sexual function to better assist in decision making. Finally, we believe this report builds on existing literature and could provide useful technical guidance to appliers who consider expanding rectal spacer utilization in patients with large glands.

Conclusions

In our experience, hydrogel placement is feasible in large glands >80 cm^3, even when including a subgroup of patients with prostates >100 cm^3 (100.1-186.6 cm^3) with very favorable dosimetric outcomes which are in line with benchmark published results with smaller glands.[11,34]

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