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Placement of an absorbable rectal hydrogel spacer in patients undergoing low-dose-rate brachytherapy with palladium-103

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ABSTRACT

PURPOSE: Rates of rectal toxicity after low-dose-rate (LDR) brachytherapy for prostate cancer are dependent on rectal dose, which is associated with rectal distance from prostate and implanted seeds. Placement of a hydrogel spacer between the prostate and rectum has proven to reduce the volume of the rectum exposed to higher radiation dose levels in the setting of external beam radiotherapy. We present our findings with placing a rectal hydrogel spacer in patients following LDR brachytherapy, and we further assess the impact of this placement on dosimetry and acute rectal toxicity.

METHODS AND MATERIALS: Between January 2016 and April 2017, 74 patients had placement of a hydrogel spacer, immediately following a Pd-103 seed-implant procedure. Brachytherapy was delivered as follows: as a monotherapy to 26 (35%) patients; as part of planned combination therapy with external beam radiotherapy to 40 (54%) patients; or as a salvage monotherapy to eight (11%) patients. Postoperative MRI was used to assess separation achieved with rectal spacer. Acute toxicity was assessed retrospectively using Radiation Oncology Therapy Group radiation toxicity grading system. Rectal dosimetry was compared with a consecutive cohort of 136 patients treated with seed implantation at our institution without a spacer, using a 2-tailed paired Student's t test ($p < 0.05$ for statistical significance).

RESULTS: On average, 11.2-mm (SD 3.3) separation was achieved between the prostate and the rectum. The resultant mean rectal volume receiving 100% of prescribed dose ($V_{100\%}$), dose to 1 cc of rectum (D_{1cc}), and dose to 2 cc of rectum (D_{2cc}) were 0 (SD 0.05 cc), 25.3% (SD 12.7), and 20.5% (SD 9.9), respectively. All rectal dosimetric parameters improved significantly for the cohort with spacer placement as compared with the nonspacer cohort. Mean prostate volume, prostate V_{100} and dose to 90% of gland (D_{90}) were 29.3 cc (SD 12.4), 94.0% (SD 3.81), and 112.4% (SD 12.0), respectively. Urethral D_{20}, D_{5cc}, and D_{1cc} were 122.0% (SD 17.27), 133.8% (SD 22.8), and 144.0% (SD 25.4), respectively. After completing all treatments, at the time of first the followup, 7 patients reported acute rectal toxicity—6 experiencing Grade 1 rectal discomfort and 1 (with preexisting hemorrhoids) experiencing Grade 1 bleeding.

CONCLUSIONS: Injection of rectal spacer is feasible in the post-LDR brachytherapy setting and reduces dose to the rectum with minimal toxicity. Prostate and urethral dosimetries do not appear to be affected by the placement of a spacer. Further studies with long-term followup are warranted to assess the impact on reduction of late rectal toxicity.

Keywords: Prostate cancer; Low-dose-rate brachytherapy; Rectal spacer

Background

Modern radiation techniques, such as intensity-modulated radiotherapy, image-guided radiotherapy, and proton therapy, have made dose escalation possible for treatment of prostate cancer associated with superior tumor control outcomes (1, 2). However, the proximity of the rectum to the prostate and the sensitivity of rectal

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mucosa to radiation is often a dose-limiting factor. Contemporary series and well-controlled prospective trials suggest incidence of Grade 2 or higher acute- and long-term rectal toxicity to be <10−47% and 6.4−24%, respectively (3−5). The placement of a biodegradable gel has been used to increase the distance between the prostate and the rectum for patients who are undergoing prostate radiotherapy for this purpose. Placement of a hydrogel spacer between the prostate and the rectum has been proven in a randomized controlled trial to reduce rectal dose resulting in decreased acute- and long-term rectal toxicity and improvement in bowel-related quality of life (6, 7).

Brachytherapy is an accepted single-modality treatment for low-risk and favorable intermediate-risk prostate cancer or as part of a combination regimen for unfavorable intermediate- and high-risk prostate cancer (8). Overall Grade 1, 2, and 3 acute rectal toxicity from seed implantation are reported to be in range of 15.8−36.5% (9−11). A randomized trial demonstrated much higher rates of acute gastrointestinal (GI)/rectal toxicity rates (G1: 46.2%, G2: 39.2%, and G3: 9.0%) with combination of low-dose-rate (LDR) + external beam radiotherapy (EBRT) as compared with that from LDR alone (reported above) (12). Toxicity, however, is dependent on rectal dose which is ultimately associated with rectal distance from the prostate and seeds implanted within the gland. This is especially important among patients who are treated with a combined regimen of brachytherapy and EBRT. Therefore, it was hypothesized that placement of a rectal spacer would reduce rectal dose and toxicity in patients undergoing LDR brachytherapy alone or in combination with EBRT.

In this report, we present our experience with placement of rectal hydrogel spacer following LDR brachytherapy with Pd-103 seeds and assess its impact on dosimetry as well as acute rectal toxicity.

Methods

Patient selection

Between January 2016 and April 2017, 79 patients were planned for placement of a food and drug administration (FDA)-approved hydrogel rectal spacer, SpaceOAR (Augmenix Inc., Waltham, MA). Spacer placement was done based on disease characteristics, treatment modality, and patient preference. Demographics and treatment characteristics are outlined in Table 1.

Procedure and postimplant assessment

After completion of intraoperatively planned seed implantation as per institutional practice described previously (13, 14), the spacer was placed between the prostate and the rectum during the same procedure as described by Pinkawa *et al.*(15). Briefly, a needle was advanced into the retroprostatic space below the Denonvillier's fascia and above the anterior rectal wall using the sagittal plane of the transrectal ultrasound. We took care not to puncture the rectal wall. The midprostate placement of the needle was confirmed on the transverse plane. We injected saline to hydrodissect the fascia and maintained the needle tip within the sagittal view. The SpaceOAR was injected as two separate liquids that solidified into a gel within 7−10 s of instillation. A CT scan for postimplant dosimetry was performed immediately after the procedure (Day 0 CT scan). Patients receiving a spacer also underwent a postimplant MRI (axial, coronal, and sagittal T2 sequences and a T1-weighted sequence for seeds/gold marker identification) either on Day 0 (monotherapy or salvage patients) or Day 14 (combination patients). Separation achieved with the rectal spacer was measured at midgland using axial T2 sequences shown schematically in Fig. 1a.

Postimplant dosimetry was performed using VariSeed (Varian Medical System, Palo Alto, CA) software after identifying seeds and after drawing the contours of the prostate, urethra, bladder, and rectum on the Day 0 CT scan. Because patients undergoing monotherapy or combination therapy are prescribed different doses, the percentage of each prescribed dose is documented and reported. Dosimetric parameters for prostate (dose to 90% of the target volume [D_{90}], volume receiving 100%, 150%, and 200% of the prescribed dose [V_{100}, V_{150}, and V_{200}]), dose

Table 1
Patient, disease, and treatment characteristics

Parameter	Spacer cohort (n = 79)	Nonspacer cohort (n = 136)
Median age	68.9	69.1
Clinical stage, n (%)		
T1	48 (60.8)	72 (52.9)
T2	19 (24.1)	38 (27.9)
T3	1 (1.3)	7 (5.2)
Recurrent	11 (13.9)	19 (14.0)
Gleason score, n (%)		
3+3	4 (5.1)	11 (8.1)
3+4	33 (41.8)	70 (51.9)
4+3	24 (30.4)	27 (20.0)
4+4	9 (11.4)	11 (8.1)
4+5	7 (8.9)	15 (11.1)
5+4	2 (2.5)	1 (0.08)
Pretreatment PSA (ng/ml) (range)	7.2 [1.1−211.0]	6.6 [0.5−88.7]
Baseline IPSS (range)	5 [0−20]	6 [0−30]
LDR implant intent, n (%)		
Monotherapy	26 (32.9)	44 (32.3)
Combination with external beam	42 (53.2)	73 (53.7)
Salvage monotherapy	11 (13.9)	19 (14.0)

PSA = prostate-specific antigen; IPSS = international prostate symptom score; LDR = low-dose-rate.