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Brachytherapy ■ (2017) ■

BRACHYTHERAPY

Improved rectal dosimetry with the use of SpaceOAR during high-dose-rate brachytherapy

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ABSTRACT

PURPOSE: Hydrogel spacers have been suggested to limit rectal radiation dose with improvements in clinical outcomes in patients undergoing external beam radiation treatment for prostate cancer. No studies to date have assessed the utility and dosimetric effect of SpaceOAR (Augmenix, Inc, Waltham, MA), the only Food and Drug Administration−approved hydrogel rectal spacer, for high-dose-rate (HDR) brachytherapy.

METHODS: Eighteen consecutive patients scheduled for HDR brachytherapy in the treatment of prostate cancer underwent transperineal ultrasound-guided placement of 10 cc of SpaceOAR hydrogel following catheter implantation. Treatment plans were generated using an inverse planning simulated annealing algorithm. Rectal dosimetry for these 18 patients was compared with the 36 preceding patients treated with HDR brachytherapy without SpaceOAR.

RESULTS: Fifty-four plans were analyzed. There was no difference in age, pretreatment prostate-specific antigen, Gleason score, clinical stage, prostate volume, or contoured rectal volume between those who received SpaceOAR and those who did not. Patients who received SpaceOAR hydrogel had significantly lower dose to the rectum as measured by percent of contoured organ at risk (median, $V_{80} < 0.005\%$ vs. 0.010%, $p = 0.003$; $V_{75} < 0.005\%$ vs. 0.14%, $p < 0.0005$; V_{70} 0.09% vs. 0.88%, $p < 0.0005$; $V_{60} = 1.16\%$ vs. 3.08%, $p < 0.0005$); similar results were seen for rectal volume in cubic centimeters. One patient who received SpaceOAR developed a perineal abscess 1 month after treatment.

CONCLUSIONS: Transperineal insertion of SpaceOAR hydrogel at the time of HDR brachytherapy is feasible and decreases rectal radiation dose. Further investigation is needed to assess the clinical impact of this dosimetric improvement and potential toxicity reduction. © 2017 Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: Prostate cancer; Brachytherapy; Hydrogel; Rectal protection; Dosimetry

Introduction

Prostate cancer remains the leading cancer in men with over 180,000 estimated new cases in 2016, accounting for 10.7% of all new cancer diagnoses, and approximately 26,000 deaths (1). High-dose-rate (HDR) brachytherapy is used in the treatment of prostate cancer as monotherapy in low or favorable intermediate-risk patients, as well as in conjunction with external beam radiation in the definitive and in the salvage settings (2–5). Given potential cost savings along with results demonstrating an improvement in disease free survival (6–8), interest in incorporating brachytherapy into the treatment paradigm for prostate cancer has increased (9).

Primary side effects of HDR brachytherapy include rectal and urinary toxicity. For single-fraction HDR in combination with external beam radiation or as monotherapy, acute Grade 2 gastrointestinal (GI) toxicity occurs in up to 6.5% of patients treated with combination therapy and in up to 5% of patients treated with HDR monotherapy

Received 12 August 2017; received in revised form 23 October 2017; accepted 23 October 2017.

Financial disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Augmenix did not contribute to or support this work in any way. No authors have disclosures to report.

Conflict of interest: The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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1538-4721/$ - see front matter © 2017 Published by Elsevier Inc. on behalf of American Brachytherapy Society.
https://doi.org/10.1016/j.brachy.2017.10.014

(10, 11). Late Grade 2 GI toxicity occurs in approximately 10% of patients (11), whereas acute or late Grade 3 toxicity is uncommon (12). Brachytherapy in the salvage setting has been associated with rates of Grades 3−4 rectal toxicity of 20%, with up to 12% of patients requiring surgical intervention for rectal fistulas (13). In the external beam setting, Grade 2 GI toxicity is predicted by rectal dose—particularly V_{60}−V_{80} (14, 15).

Several studies have evaluated the use of rectal spacers injected between the anterior rectal wall and the prostate to improve dosimetry and rectal mucosal injury (16−18). SpaceOAR is the only polyethylene glycol−based hydrogel approved by the Food and Drug Administration for use in the treatment of prostate cancer. Given increased gel polymerization time that facilitates injection, dimensional stability following placement, and more durable effect compared to previously used hydrogels, SpaceOAR offers specific benefits that are particularly relevant in the treatment of prostate cancer. To our knowledge, this is the first study to assess feasibility of and dosimetric differences due to SpaceOAR injection at the time of HDR brachytherapy.

Methods and materials

Eighteen consecutive patients scheduled to receive HDR brachytherapy to the prostate and seminal vesicles at the University of California, San Francisco for treatment of biopsy-proven localized prostate cancer were consented to receive SpaceOAR at the time of catheter insertion. Dosimetric parameters for these 18 patients were compared with the 36 consecutive preceding patients who were treated to the whole prostate and seminal vesicles before the adoption of SpaceOAR at our institution. Patients treated in the salvage setting who received focused brachytherapy (i.e., to the left seminal vesicle or right lobe of the prostate) were excluded from this analysis. All patients received 2 g of cefoxitin or in the case of a penicillin or cephalosporin allergy, clindamycin 600 mg before the procedure.

All patients were instructed to perform an enema before their procedure. The rectums were assessed before Betadine prep and fecal matter was manually removed from the rectum if necessary before insertion of the transrectal ultrasound. Following insertion of HDR catheters under ultrasound guidance in the dorsal lithotomy position, intraoperative cystoscopy was used to ensure no catheters were within the urethra or bladder. Catheters were advanced under gentle pressure to result in mucosal tenting at the bladder neck, ensuring adequate coverage at the base of the prostate.

Following catheter placement, an 18-guage needle was inserted through the perineum approximately 1 cm above the ultrasound probe and into the anterior rectal space posterior to Denonvilliers' fascia under ultrasound guidance. Sterile saline of 5−10 cc was used to hydrodissect the anterior rectal space at the level of the apex and midgland. This was followed by injection of 10 cc of hydrogel (comprised two liquids including the precursor and accelerator, which mix during the injection and polymerize over 8−10 s) into the space. The SpaceOAR application technique has been previously described (19).

Treatment planning

Following the procedure, patients underwent CT scan with 3-mm slices for HDR treatment planning. Patients who received SpaceOAR also had 50 cc of 10% iodinated contrast instilled into the bladder via Foley catheter, which was clamped during the planning CT scan to better visualize the bladder−prostate interface. The target planning treatment volume and organs at risk (OARs) (the prostatic urethra, rectum to the rectosigmoid junction, penile bulb, and bladder) were contoured on planning CT scan. Rectums were contoured from the anus at the level of the ischial tuberosity superiorly to the rectosigmoid flexure. The bladders were contoured from dome to base. The urethra was contoured using the outer surface of the Foley catheter. Treatment plans were optimized using an anatomy-based dwell time optimization approach (inverse planning simulated annealing method) (20−22) with constraints for OARs based on Radiation Therapy Oncology Group 0321 (V_{125} urethra <1 cc, V_{75} bladder <1 cc, and V_{75} rectum <1 cc) (23, 24). Patients were prescribed 15 Gy (boost in conjunction with external beam radiation, $n = 27$), 18 Gy (salvage brachytherapy of 18 Gy in three fractions per implant for two implants, $n = 5$), or 19−21 Gy (brachytherapy monotherapy, $n = 22$) per implant to cover at least 90% of the clinical target volume, which was defined as the prostate and seminal vesicles without a planning target volume expansion.

Dosimetric parameters for the 18 patients who received SpaceOAR were compared with the 36 consecutive preceding HDR brachytherapy patients treated to the prostate and seminal vesicles without SpaceOAR. The primary study objectives were to demonstrate feasibility of SpaceOAR injection at the time of HDR brachytherapy and compare rectal radiation dosimetry in patients who received SpaceOAR compared to those who did not.

Statistical analysis

Descriptive statistics were used to characterize variables of interest. The Shapiro−Wilk test was used to assess normality of all variables. For nonnormally distributed variables, the Mann−Whitney U test was used to compare means. All statistics were 2-sided and a p-value 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics (version 24.0.0.0).

Results

Treatment plans for 54 patients were analyzed (18 with SpaceOAR and 36 without). The average age at the time of treatment was 65.3 years (SD 6.6 years). The demographics of our study population are described in Table 1. There