First report of transperineal polyethylene glycol hydrogel spacer use to curtail rectal radiation dose after permanent iodine-125 prostate brachytherapy

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ABSTRACT

PURPOSE: To demonstrate the feasibility of transperineal polyethylene glycol (PEG) hydrogel insertion into anterior perirectal fat for reducing rectal radiation dose in patients with suboptimal rectal dosimetry after permanent iodine-125 prostate brachytherapy.

METHODS AND MATERIALS: Five patients with suboptimal rectal dosimetry after iodine-125 seed brachytherapy implant underwent a single transperineal injection of PEG hydrogel into the anterior perirectal fat under general anesthetic using transrectal ultrasound guidance. Prostate—rectum separation and rectal radiation dose before and after PEG hydrogel spacer insertion were measured. Toxicity because of spacer insertion was assessed at Days 0—1 and 4—6 weeks using National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.

RESULTS: All patients experienced a clinically significant reduction in the volume of rectum receiving greater than or equal to the prescription dose (RV100) on the postspacer postimplant dosimetry, compared with the prespacer postimplant dosimetry. Mean prostate—rectum separation that was achieved with the insertion of the spacer was 15.1 mm (±3.4). The mean difference in separation from before to after spacer insertion was 12.5 mm (±4.5). This was associated with a reduction in mean RV100 from 3.04 (±1.2) to 0.06 (±0.1) cc. Toxicities were limited to Grade 1 (National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0) perineal pain and rectal discomfort (3/5 patients). There were no Grade 2 or greater toxicities reported after insertion of the spacer.

CONCLUSIONS: PEG hydrogel is safe and effective at reducing rectal radiation dose in select patients with suboptimal rectal dosimetry after prostate seed brachytherapy. © 2013 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Polyethylene glycol hydrogel; Seed brachytherapy; Spacing agent; Transperineal spacer

Introduction

Prostate cancer is the commonest male malignancy. Definitive treatment options for prostate cancer include radical prostatectomy, external beam radiotherapy (EBRT), and brachytherapy. Permanent interstitial prostate brachytherapy has been shown to confer at least equivalent oncologic outcomes to radical prostatectomy or EBRT in most series, with low rates of urinary incontinence and rectal toxicity, as well as acceptable rates of sexual dysfunction (1). All forms of prostate radiation, however, carry a risk of chronic radiation proctitis, which, although less common with brachytherapy, is still a dreaded treatment complication.

The focus of modern radiation treatment has been on dose escalation while simultaneously minimizing treatment-related toxicity. Dose escalation has been demonstrated to improve biochemical control in localized prostate cancer in several large randomized trials (2—6). The major structure limiting radiotherapy dose escalation for prostate...
cancer is the anterior rectal wall. Reported rates of acute and late Grade 2 or greater rectal toxicity range from 3% to 20% and 5% to 21%, respectively (7, 8). The risk of late rectal toxicity has been shown in large prospective series to correlate with rectal radiation dose, as measured by dosimetric parameters, such as $V_{70}$ (volume of rectum receiving a radiation dose of 70 Gray [Gy]) and $D_{2cc}$ (maximum dose received by 2 cc of rectum). A rectal $V_{70} > 26.2\%$ has been shown to result in 54% incidence of Grade 2 or greater chronic rectal toxicity, as compared with 13% in those with $V_{70} < 26.2\%$ (9). Unfortunately, the area most commonly involved with prostate adenocarcinoma, the peripheral zone, lies immediately anterior to the rectum. This has been a long-standing dilemma of prostate EBRT, in terms of ensuring adequate expansions to account for daily variations in treatment set up and organ motion, while respecting rectal dose constraints (7, 8).

Interstitial prostate brachytherapy has become an increasingly popular method of radiation dose escalation because it confers major biologic and dosimetric advantages in terms of organ confinement and rapid dose fall off with increased distance from the source. Rectal dosimetry remains critical with this technique, however, as radiation proctopathy still occurs in 2–10% of patients, and can potentially be more serious, with a small proportion of these patients developing a rectal ulcer or fistula (10, 11). The risk of rectal complications has consistently been linked to greater rectal wall doses (11–14). In a series by Tran et al. (10), in which 503 patients were treated with permanent interstitial prostate brachytherapy using iodine-125 ($^{125}$I) or palladium-103, 44 patients developed persistent rectal bleeding, including 2 patients with fistula formation. In both these cases, the volume of rectum receiving greater than or equal to the prescription dose ($RV_{100}$) exceeded 1 cc (10). Recently updated American Brachytherapy Society Guidelines recommend that $RV_{100}$ should not exceed 1 cc on Day 1 dosimetry or 1.3 cc on Day 30 dosimetry (15).

Hence, even with brachytherapy, rectal dose is fundamental in determining the quality of an implant and estimating the risk of late rectal toxicity. In seed brachytherapy patients, postimplant CT-based dosimetry can predict which patients are at higher risk of radiation-related morbidity (16). Patients whose $RV_{100}$ exceeds 1.3 cc are likely to be at greater risk of rectal complications and may benefit from an intervention to curtail radiation dose to the rectum.

A number of small single-institution series have looked at injecting a biocompatible spacer to physically increase the separation between the rectum and prostate before prostate radiotherapy (17–22).

Susil et al. (17) used a polyethylene glycol (PEG) hydrogel injected into the space between the rectum and prostate via a transperineal approach in cadaveric specimens. The injection of 20 mL of PEG hydrogel produced an average of 12.5 mm of prostate–rectum separation, and the average rectal volume receiving 70 Gy decreased from 19.9% to 4.5% ($p < 0.05$). A prostate—rectum separation of 10 mm was sufficient to reduce mean rectal $V_{70}$ by 83.1% ($p < 0.05$) (17).

Wild et al. (18) were able to achieve an additional 8–18 mm of separation by injecting hyaluronic acid between the prostate and rectum in patients receiving prostate intensity-modulated radiotherapy (IMRT). Rectal $V_{70}$ was decreased from 25% to 4% ($p = 0.005$).

Prada et al. (19) randomized 54 patients receiving high-dose-rate brachytherapy to receive a hyaluronic acid injection into the anterior perirectal space ($n = 27$) at the time of their prostate implant. A prostate—rectum separation of 15 mm was created, and the resultant mean rectal $D_{max}$ (maximum dose to the rectum) was reduced from 7.08 to 5.07 Gy ($p < 0.001$). No rectal or other toxicities were reported as a result of the injection itself.

Previous studies have consistently shown that rectal radiation dose can significantly be reduced by injecting a spacing agent into the anterior perirectal fat under transrectal ultrasound (TRUS) guidance. Although this has mainly been described in the setting of EBRT, our hypothesis was that, by injecting a spacer into the anterior perirectal space in seed brachytherapy patients with inadequate postimplant rectal dosimetry, this could equally reduce any further radiation dose to the rectum in this group during the remaining life of the isotope, thereby helping to ameliorate associated rectal complications. The spacer being investigated in this study (SpaceOAR; Augmenix, Inc., Waltham, MA) is PEG based, polymerizes within seconds of injection, and is designed to maintain separation in the body for 3 months, with gradual degradation thereafter and renal excretion (22).

Methods and materials

Target population

Patients with histopathologically confirmed localized prostate cancer, who had undergone permanent prostate $^{125}$I seed brachytherapy according to St George Hospital Prostate Cancer Institute guidelines, were approached for participation in this study, if their Day 30 postimplant dosimetry showed an $RV_{100} > 1.3$ cc. Our seed implantation technique comprises a preplanned peripheral loading pattern, as described previously by the Seattle group (23). Stranded $^{125}$I sources were used. This was an institutional ethics board approved protocol-based intervention.

PEG hydrogel insertion

TRUS images of the prostate from base to apex were acquired before spacer insertion to determine prespacer prostate—rectum separation. A single transperineal injection of PEG hydrogel was administered under general anesthetic using TRUS guidance, according to the technique.
described by Pinkawa et al. (22). The 18-gauge PEG hydrogel needle was inserted into the perineum and positioned at midline in the transverse plane into the space between the rectum and prostate (posterior to Denovilliers’ fascia and anterior to the rectal wall) (22). After verifying correct placement of the needle tip, the perirectal space was hydrodissected from apex to midgland by injecting 10 mL of normal saline. The hydrogel precursor and accelerator solutions were then prepared according to manufacturer instructions and simultaneously injected into the anterior perirectal space. The total volume of injectable solution when prepared was approximately 15 mL.

Rectal separation and dose

At this institution, postimplant dosimetry is routinely undertaken at Day 30. This involves a CT scan using 5-mm scan intervals with aerated lignocaine gel and contrast per urethrum. Sources are identified by the physicist, and the images then manually coregistered by the radiation oncologist with the preoperative TRUS using urethral and rectal contours. Additionally for the purpose of this study, MRI scans were undertaken on Days 0–1 postspace insertion and coregistered with the CT. This was because the PEG hydrogel is not well visualized on CT, and the TRUS images became distorted after insertion of the spacer. The MRIs were used to assess rectal separation prespacer to compare rectal dosimetry with the postspacer dosimetric assessment as for the dosimetric assessment oncologist with the preoperative TRUS using urethral cist, and the images then manually coregistered by the radiologist. The VariSeed version 8.0 planning software (Varian Medical Systems, Inc., Palo Alto, CA) was used to undertake all postimplant dosimetric evaluations. The VariSeed version 8.0 planning software uses seed activity on the day of implantation to calculate the dose. Hence, the same seed activity was assumed for the postspacer dosimetric assessment as for the dosimetric assessment prespacer to compare rectal dosimetry with and without spacer. In particular, $R_{100}$ (cc) postspacer was compared with the preimplant prespacer $R_{100}$.

We also undertook to estimate the proportion of dose received by the rectum during the varying conditions (before spacer insertion, with spacer, and after dissolution of the spacer) in the life of the $^{125}$I implant. This was calculated by determining seed activity at the time of spacer insertion (Day 35) and spacer dissolution (Day 125) and using a committed dose equation to estimate what proportion of the total dose has been received at that time point.

As an additional quality assurance measure, the PEG hydrogel was also contoured on the MRI, and this volume in situ was compared with the volume of PEG hydrogel actually injected.

Toxicity evaluation

Patients were assessed for toxicity because of spacer injection at Days 0–1 and 4–6 weeks after PEG hydrogel insertion. Clinician assessment of toxicity included allergic reactions, injection site pain or discomfort, bleeding, thromboembolic complications, infection, and urinary or rectal complications. Treatment-related toxicities were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (24).

Statistical analysis

Given the limited number of patients, descriptive statistics (mean, range, and standard deviation) were used to summarize prostate—rectum separation and dosimetric parameters before and after spacer insertion. Prostate—rectum separations at 5-mm intervals along the length of the prostate—rectum interface were used to determine the mean prostate—rectum separation before and after spacer insertion for each patient.

Results

Patient characteristics

All patients had Gleason 7 prostate adenocarcinoma, clinical stage T1c, and prostate-specific antigen level less than 10 ng/mL (Table 1).

Prostate—rectum separation and rectal dosimetry

Table 2 illustrates mean separation along the length of the prostate—rectum interface for each of the 5 patients. The broad range of values was a reflection of the large natural variation in separation that occurs at different positions along the prostate—rectum interface, the greatest separation being at the prostatic base, with closer apposition of prostate and rectum at midgland and apex. The combined mean difference in separation that was achieved with the spacer was 12.5 mm ($\pm$4.5). The mean ($n = 5$) volume of spacer that was injected was 14.6 mL. This was because in 1 patient, the precursor solutions were prematurely advanced into the Y-connector during preparation of the kit. The Y-connector was replaced immediately,

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>58</td>
<td>60</td>
<td>60</td>
<td>65</td>
<td>57</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>3.5</td>
<td>4.8</td>
<td>2.6</td>
<td>5.2</td>
<td>4.2</td>
</tr>
<tr>
<td>Gleason score</td>
<td>7 (3 + 4)</td>
<td>7 (3 + 4)</td>
<td>7 (4 + 3)</td>
<td>7 (3 + 4)</td>
<td>7 (3 + 4)</td>
</tr>
<tr>
<td>Clinical stage</td>
<td>T1c</td>
<td>T1c</td>
<td>T1c</td>
<td>T1c</td>
<td>T1c</td>
</tr>
<tr>
<td>Baseline IPSS</td>
<td>6</td>
<td>9</td>
<td>4</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>(0–35)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormonal therapy (Y/N)</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Prostate volume on TRUS (cc)</td>
<td>46</td>
<td>38</td>
<td>34</td>
<td>38</td>
<td>59</td>
</tr>
</tbody>
</table>

PSA = prostate-specific antigen; IPSS = International Prostate Symptom Score; TRUS = transrectal ultrasound; Y = yes; N = no.
Table 2  Prostate—rectum separation before and after spacer insertion

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Prespacer separation (mm)</th>
<th>Postspacer separation (mm)</th>
<th>Difference in separation (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (range) ± SD</td>
<td>Mean (range) ± SD</td>
<td>Mean (range) ± SD</td>
</tr>
<tr>
<td>1</td>
<td>4.4 (1−12) ± 3.8</td>
<td>15.4 (8−29) ± 7.0</td>
<td>11 (5−17) ± 4.1</td>
</tr>
<tr>
<td>2</td>
<td>2.9 (0−10) ± 3.2</td>
<td>10.6 (8−15) ± 2.0</td>
<td>7.7 (3−10) ± 2.5</td>
</tr>
<tr>
<td>3</td>
<td>3.6 (0−8) ± 3.5</td>
<td>13.4 (12−15) ± 1.1</td>
<td>9.9 (4−15) ± 4.4</td>
</tr>
<tr>
<td>4</td>
<td>0.6 (0−2) ± 1.0</td>
<td>19.6 (8−33) ± 9.2</td>
<td>19 (6−35) ± 10.0</td>
</tr>
<tr>
<td>5</td>
<td>1.7 (1−5) ± 1.4</td>
<td>16.5 (12−20) ± 3.4</td>
<td>14.8 (10−19) ± 3.2</td>
</tr>
<tr>
<td>Mean</td>
<td>2.6 ± 1.5</td>
<td>15.1 ± 3.4</td>
<td>12.5 ± 4.5</td>
</tr>
</tbody>
</table>

(n = 5)

SD = standard deviation.

and the remaining 13 mL of spacer constituents was injected. The mean (n = 5) volume of spacer that was accounted for in situ on MRI was 14.4 mL. Figure 1a is an example of the separation that was achieved with the spacer on axial MRI views. For the same patient, Fig. 1b is a representative section from the postimplant postspacer dosimetry (coregistered postimplant, postspacer MRI and CT images).

Table 3 shows the reduction in rectal radiation dose that was achieved for all 5 patients with the spacer. The uncorrected mean \(R_{V_{100}}\) as determined by VariSeed (which infers that the postspacer prostate—rectum separation is present throughout the entire life of the implant) was decreased from 3.04 to 0.06 cc in the presence of the spacer (±0.1). To obtain corrected \(R_{V_{100}}\) values (Table 3), and hence illustrate more accurately the true impact of spacer on rectal dosimetry, we selected matching rectal dose points from the VariSeed-generated prespacer and postspacer dose volume assessments. The prespacer dose—volume histogram (DVH) values were adjusted for isotope decay to determine the proportion of the dose that would actually be delivered to each selected point in the absence of the spacer (Days 0–35 before its insertion, and Days 125 onward, after spacer dissolution). The process was repeated using the postspacer DVH values to calculate the proportion of dose that would be delivered to the same points during Days 35–125 (spacer present). The decay-adjusted doses received in the intervals with and without spacer were then summated to give the corrected total dose to each selected rectal point. Figure 2 illustrates the uncorrected prespacer and postspacer DVHs as determined by VariSeed for the example patient, and their corrected DVH (adjusted for isotope decay and variable presence of spacer throughout the life of the \(^{125}\)I implant), which was obtained by plotting the corrected rectal doses. Corrected \(R_{V_{100}}\) values (Table 3) for each patient were obtained from their corrected DVH. Note that to plot the corrected DVH, total rectal volume was assumed to remain constant across the three time intervals. Our available software did not allow us to summate DVHs with time, dose, and volume, all being variable.

Table 3  Rectal dosimetry before and after spacer insertion

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Uncorrected prespacer (R_{V_{100}}) (cc)</th>
<th>Uncorrected postspacer (R_{V_{100}}) (cc)</th>
<th>Difference (cc)</th>
<th>Corrected (R_{V_{100}}) (cc)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.04</td>
<td>0</td>
<td>4.04</td>
<td>0.75</td>
</tr>
<tr>
<td>2</td>
<td>4.67</td>
<td>0.09</td>
<td>4.58</td>
<td>0.8</td>
</tr>
<tr>
<td>3</td>
<td>2.01</td>
<td>0.12</td>
<td>1.89</td>
<td>0.35</td>
</tr>
<tr>
<td>4</td>
<td>2.15</td>
<td>0.1</td>
<td>2.05</td>
<td>0.2</td>
</tr>
<tr>
<td>5</td>
<td>2.32</td>
<td>0</td>
<td>2.32</td>
<td>0.3</td>
</tr>
<tr>
<td>Mean</td>
<td>3.04 ± 1.2</td>
<td>0.06 ± 0.1</td>
<td>2.98 ± 1.2</td>
<td>0.48 ± 0.28</td>
</tr>
</tbody>
</table>

(n = 5) ± SD

SD = standard deviation; \(R_{V_{100}}\) = volume of rectum receiving greater than or equal to the prescription dose.

* Rectal dose adjusted for variable presence of spacer throughout the life of the iodine-125 implant and isotope decay in the intervals before spacer insertion (Days 0–35), with spacer (Days 35–125), and after spacer dissolution (Days 125 onward).
to selected rectal points were plotted to give the corrected DVH throughout the 5 months (Day 125 after implantation). Decay-adjusted cumulative doses for a spacer was inserted 35 days postimplantation, and will degrade in 3 months postspacer DVH does not take into account isotope decay, or that the dosimetry throughout the life of the iodine-125 implant. The uncorrected rectal dosimetry before and after spacer insertion and corrected rectal doses with higher
toxicity.

Fig. 2. Rectal dose—volume histograms (DVHs) showing uncorrected rectal dosimetry before and after spacer insertion and corrected rectal dosimetry throughout the life of the iodine-125 implant. The uncorrected postspacer DVH does not take into account isotope decay, or that the spacer was inserted 35 days postimplantation, and will degrade in 3 months (Day 125 after implantation). Decay-adjusted cumulative doses to selected rectal points were plotted to give the corrected DVH throughout the life of the iodine-125 implant.

Toxicity

No patients complained of rectal toxicity in association with higher RV_{100} values before the insertion of the spacer. The main acute toxicity reported on Days 0—1 after the insertion of the spacer was mild rectal discomfort (2/5 patients), which was scored as Grade 1 proctitis using National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. One patient also reported Grade 1 perineal pain. These symptoms had all resolved within 1 week of spacer insertion and were believed to be the result of injection site trauma as well as the combined volume of saline for hydrodissection and the spacer itself. Both these acute toxicities were self-limited and did not warrant intervention. There were no other reported adverse events either at Days 0—1 or 4—6 weeks after the insertion of the spacer.

Discussion

The use of an anatomic spacer to increase separation between the prostate gland and rectum has been described in several studies. Spacing substances used have ranged from hyaluronic acid and PEG-based hydrogels to human or animal collagen injections (17—22). The focus of available studies, however, has generally been on using the spacer during prostate IMRT, with less data on the risks and potential benefits in terms of rectal dosimetry in brachytherapy patients. The single available clinical study at the time of reporting using PEG-based spacer was performed in prostate cancer patients (n = 18) receiving either IMRT or three-dimensional conformal radiotherapy, not brachytherapy (21).

This is the first report of PEG-based spacer use in permanent 125I prostate interstitial brachytherapy patients. In keeping with the results of previous studies, we were able to achieve an additional 12.5 mm of separation in these patients with the use of PEG hydrogel (17—22). The resultant dosimetric benefits were a consistent reduction in rectal radiation dose in all 5 patients.

This intervention was pertinent to our practice as historically, a lower activity seed of 0.383 milliCurie (mCi) was used, and higher rectal dose constraints than present were accepted (RV_{100} up to 2 cc). Since 2009, however, seed activities ranging from 0.35 to 0.45 mCi have been used at our institution, depending on prostate volume (0.35 mCi for volumes less than 30 cc, 0.4 mCi for 30—50 cc, and 0.45 mCi for prostate volumes greater than 50 cc). With the use of higher activity seeds, more conservative rectal dose constraints have been adopted to maintain our standard of low toxicity. Long-term radiation proctitis rates at our institution are estimated to be below 5%, but with the large body of evidence correlating rectal toxicity with dose (11—14), and to remain consistent with updated American Brachytherapy Society Guidelines, we have endeavored to keep RV_{100} below 1 cc on the preoperative plan and less than 1.3 cc on the Day 30 dosimetric assessment (15). Since 2009, our records indicate that less than 10% of patients had a Day 30 RV_{100} greater than 1.3 cc, and of these, only a fraction have developed significant rectal toxicity. Although long-term followup and a larger patient cohort will be required to assess how a rectal dose reduction will impact on late rectal toxicity in patients undergoing PEG hydrogel insertion, there is already good evidence as mentioned previously, correlating rectal dosimetric parameters with toxicity (10—14). In a series of 212 patients treated with 125I seed brachytherapy, Snyder et al. (25) reported that if the volume of rectum receiving the prescribed dose was ≤1.3 cc, then the risk of proctitis at 5 years was 5%, as compared with 18% if the volume of rectum receiving the prescribed dose exceeded 1.3 cc.

The timing of postimplant dosimetric analysis varies among centers. Although our practice is to undertake dosimetry at Day 30, the utilization rates of the spacer could be potentially greater in centers that perform their dosimetric assessment on Days 0—1, as this allows a greater window for therapeutic intervention and making use of the spacer before the major portion of the dose has already been delivered. If comparable reductions in rectal dose can be assumed to those that were seen in our patients, this would support the use of PEG hydrogel in all patients with suboptimal rectal dosimetry provided it is inserted within the first half-life of the isotope, after which 50% of the dose has already been delivered.

Our seed brachytherapy planning software (VariSeed, version 8.0) uses source activity on the day of implantation to calculate dosimetry, and this would be the same activity used when undertaking both the prespacer and postspacer dosimetric assessments. Although this may be
an oversimplification of the actual dosimetry, it is a valid assumption for highlighting that the reduction in rectal radiation dose seen with the spacer is not simply because of the isotope being of lower activity at the time of spacer insertion. This dosimetric assessment, however, remains incomplete because it does not take into account that the PEG hydrogel was not present for the first 30 days of the implant’s life or that the PEG hydrogel is expected to degrade after 3 months. Clearly, a more accurate representation of the cumulative rectal dose would need to take into account the total dose received by the rectum before spacer insertion, followed by further dose received in the next 3 months during which the spacer is expected to retain its composition in situ and subsequent rectal dose when the spacer has degraded (although the rectal dose contribution from the $^{125}$I sources beyond the latter 4-month time point would be negligible). Our calculation of a corrected rectal DVH taking these factors into consideration, and the differing activity of the isotope at these time points, illustrates that there is still a therapeutic advantage to be gained from using the spacer, as most contributions to rectal dose occurs in the spacer’s absence. One assumption that was made to determine corrected rectal dose throughout the life of the $^{125}$I implant was that total rectal volume remained constant at the time points considered. Although clearly rectal volume does vary over time, this assumption was necessary to determine the proportion of total dose that is received at corresponding rectal dose points during each of the three time intervals. At the time of writing, we did not have the software that would allow us to summate DVHs with rectal volume, time, and dose, all being variable.

No serious adverse events occurred after the insertion of the spacer, with the exception of Grade 1 perineal pain and rectal discomfort. Both these toxicities were self-limited and resolved within days of the injection. The main risks reported with transperineal spacer injections have included infection, allergic reactions, and injection site pain, bruising, or bleeding (17–22). This risk is estimated to be less than 5% (18). The volume of spacer injected in one prior study was reduced from 15 to 10 mL, to minimize these potential complications (22). Theoretically, although embolization of the gel through the bloodstream is also a possibility, it is extremely unlikely (18). We took additional precautions during injection of the spacer by aspirating to ensure that the needle was not intravascular before injection of the compound.

In selecting a spacer for our study, durability of separation was sought to ensure a consistent and systematic displacement during the biologic life of the isotope (19). Both collagen and hyaluronic acid are associated with long residence times in the body, with hyaluronic acid implants largely unchanged after 1 year. Although their stability during the treatment period is advantageous, persistence long after this time may be associated with increased toxicity (19). Animal-based collagen injections have also been associated with immunologic reactions, and, although human-derived collagen has better biocompatibility, it is very expensive and difficult to obtain. Synthetic PEG-based hydrogels are composed of more than 90% water by weight and are thin injectable liquids that polymerize in situ to form a soft hydrogel when the two precursor solutions mix. PEG-based hydrogels are also less expensive and have excellent biocompatibility. The PEG compound chosen for this study (SpaceOAR; Augmenix, Inc., Waltham, MA) is an anatomic spacer approved by the Therapeutic Goods Administration for use in this setting. It is composed of PEG and water, giving it excellent tissue compatibility, without local or systemic toxicity. It also maintains its form for up to 3 months, which is ideal in the setting of prostate radiotherapy of any form.

**Conclusion**

This study demonstrates that transperineal insertion of PEG-based hydrogel is a safe and effective strategy for reducing rectal radiation dose in seed brachytherapy patients with suboptimal postimplant rectal dosimetry. Further followup is required to assess the impact of this rectal dose reduction on toxicity and quality of life.

**References**


