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Hydrogel spacer use during prostate RT: Community experience

Data support product's use in protecting organs at risk for radiation exposure

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For urologists and radiation oncologists alike, when treating prostate cancer, one recurring theme is "protect the rectum." As surgeons, we learn meticulous techniques to avoid rectal injuries, and our radiation colleagues have long strategized on how to optimally deliver the maximum dose of tolerable radiation while minimizing radiation exposure to "organs at risk" such as the bladder, rectum, urethra, and penile bulb. In this era of dose escalation and hypofractionation, rectal toxicity is of paramount consideration.

In this article, we discuss one particular new product and how it may herald a significant change in the landscape of radiation therapy for prostate cancer.

A novel solution to reduce rectal dosing is to physically push the rectum away from the prostate during radiation treatment, which can be achieved with the transperineal injection of a hydrogel "spacer" that solidifies in seconds and stays in place through radiation therapy before fully resorbing in approximately 6 months. The concept is not new, but the first product of its kind to receive FDA approval, SpaceOAR hydrogel, was introduced by Augmenix in April 2015 and is now widely available for routine use.

Our large single-specialty urology group, UroPartners in Chicago, has been utilizing SpaceOAR hydrogel since its introduction, and we now have one of the largest series with the product in the United States. When we looked at our own experience with SpaceOAR, we reported on a retrospective series of 105 men receiving intensity-modulated radiation therapy (IMRT) monotherapy for low- and intermediate-risk prostate cancer (81Gy, 45 fractions) who received SpaceOAR hydrogel. We examined the dose-volume histograms (DVHs) with respect to rectal dosing and compared them to the non-spacer control arm in the SpaceOAR randomized clinical trial (Huang et al. Poster presentation, AUA annual meeting [Engineering in Urology], May 2016).

With the spacer hydrogel, we were able to achieve a mean rV70 (the percent volume of rectum that received 70 Gy) of 1.1% +/- 1.7% (0-8.3), which represents a 94% reduction in rectal dose compared to a published control arm and markedly below the recommended limit of 20% by QUANTEC safety guidelines. Likewise, we also saw large dose reductions to the penile bulb in our cohort (9.0 +/- 5.2 Gy), which is 82% lower than dosing guidelines.

After more than 250 SpaceOAR applications to date at the UroPartners Radiation Center in Chicago, we have not experienced any complications directly related to SpaceOAR placement. In one patient, SpaceOAR injection was well tolerated, but the patient then developed significant irritative voiding issues upon starting radiotherapy from what appeared to be exquisite bladder radiosensitivity. He stopped radiotherapy and instead underwent an uneventful robot-assisted laparoscopic radical prostatectomy. We do not feel the SpaceOAR hydrogel was responsible for his voiding issues and the gel placement did not complicate the surgery.

Recently published data

Recently published clinical studies in the radiation oncology literature have been very encouraging as well. In a landmark pivotal phase III trial on SpaceOAR hydrogel use in IMRT monotherapy study, Hamstra et al provided the first Level 1 evidence of a radiation technique for prostate cancer to demonstrate reductions in rectal dosimetry as well as improvements in quality of life (QoL) and toxicity (*Int J Radiat Oncol Biol Phys* 2017; 97:976-85). In this 222-patient series (randomly assigned 2:1 SpaceOAR vs. control arm) of men treated at 20 U.S. sites, cumulative 3-year Grade 1 rectal toxicity decreased by 75% in the spacer arm. Likewise, the incidence of Grade >2 rectal toxicity favored the spacer arm (5.7% in controls vs. 0% in spacer arm, p=.02). All patients were biochemically free of disease at publication, and no differences in PSA nadir were found in either arm.

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Similar to our own group's data, Hamstra et al reported a 73.5% relative reduction in mean rectal V70 dose (p<.0001) and a 48.8% relative reduction in median penile bulb dose (p=.0358). In their study, the number needed to treat (NNT) analysis revealed that 3.7 patients needed placement of SpaceOAR to avoid one patient from suffering a significant drop in bowel QoL. Likewise, 17.5 patients needed to receive SpaceOAR to prevent one Grade >2 bowel toxicity event.

In the Hamstra series, the control groups were more likely to have experienced large declines in bowel QoL (21% vs 5%; p=.02) and urinary QoL (23% vs 8%; p=.02) compared to the hydrogel spacer arm. With a median follow-up of 3 years, their study provided compelling evidence that patients receiving hydrogel spacer had a demonstrably protective effect and helped preserve urinary, sexual, and bowel QoL for radiation patients in a durable fashion. This well-designed trial provides strong support that SpaceOAR gel placement can be considered for routine use, particularly in a busy, high-volume radiation oncology clinic like ours.

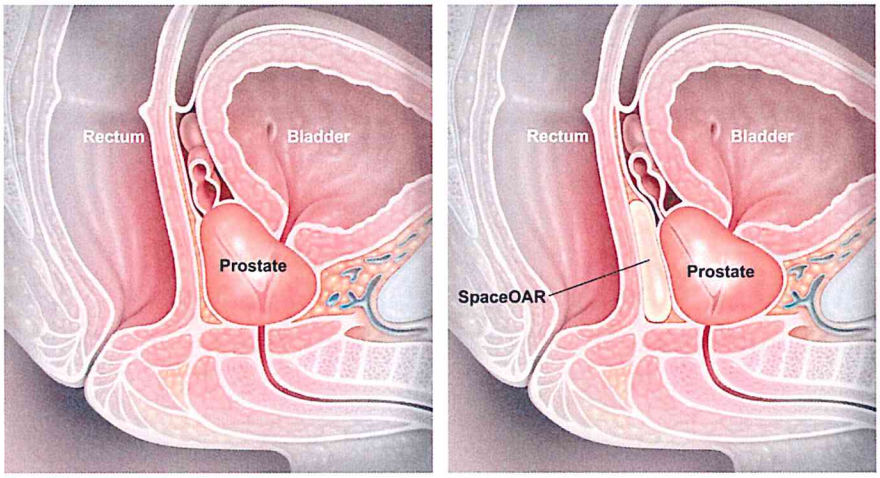
Likewise, Pinkawa et al reported QoL data in 114 patients with SpaceOAR hydrogel at 5 years using EPIC questionnaire instruments, with results mirroring other published work (*Int J Radiat Oncol Biol Phys* 2017; 99:374-7,) When comparing spacer versus non-spacer patients, a statistically significant number of patients who received radiotherapy without spacer placement had bowel urgency and overall problems with their bowel habits at 1.5 years and 5 years after randomization. A bowel bother score change >10 points was found in 6% versus 32% (p<.01) at 1.5 years. Most impressive, not one patient in the spacer cohort reported "moderate or big problems" with his bowel habits overall in their study.

Technique

SpaceOAR hydrogel requires a transperineal injection, so prior to insertion, a topical 1% lidocaine cream is applied to the perineum for 20 minutes. The SpaceOAR kit is assembled and mixed while the patient is positioned symmetrically on the table in a dorsal lithotomy position, and a transrectal ultrasound probe (stabilized on a brachytherapy stepper unit) is placed for visualization. A local anesthetic can be injected into the skin to anesthetize the perineum. A syringe with 10 cc of saline is connected to the SpaceOAR 18-gauge needle, which is inserted 2.5 cm above the anus through the perineal raphe. The needle is angled 15 degrees posteriorly under direct sagittal visualization into the perirectal fat.

Once into the space between Denonvilliers' fascia and the anterior rectal wall, the saline is injected for hydrodissection. Placement of the needle is verified in the sagittal and axial planes via ultrasound. This also allows verification of adequate hydrodissection throughout the posterior aspect of the gland. Using the same needle, SpaceOAR hydrogel is then injected over 8 to10 seconds and the needle is removed. In our experience, the rectal-prostate separation is typically about 1 cm and we have achieved a minimum of 5 mm in all cases (figure).

FIGURE SAGITTAL VIEW OF ANATOMY, PRE- AND POST-HYDROGEL PLACEMENT



Illustrations show sagittal view of the male anatomy before (left) and after hydrogel placement (right).

(Illustrations courtesy of Paul M. Yonover, MD, and Par Mehta, MD)

To date, we have not had a single case of transrectal puncture at the time of placement. No cases have been aborted due to patient discomfort or inability to identify the target insertion area. This is similar to the 99% successful placement rate noted by Mariados et al in the prospective multicenter controlled pivotal trial (*Int J Radiat Oncol Biol Phys* 2015; 92:971-7). One of our patients developed a fever 2 days after SpaceOAR placement that was treated successfully with oral antibiotics. Pain medication has not been necessary after placement, although a minority of patients have noted rectal fullness for a few days after SpaceOAR hydrogel insertion.

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Initially, we used conscious sedation for all patients at the time of placement, but now the majority of cases at our institution are performed quickly and tolerated well with local anesthesia with a periprostatic block alone, without sedation or general anesthesia. For patients with lower pain thresholds, anxiolytics can be used prior to SpaceOAR insertion. For our brachytherapy patients, after completion of the seed implant while the patient is still under general anesthesia, we place SpaceOAR hydrogel at the end of the case.

Conclusion

While we find that significant rectal toxicity with prostate radiation is relatively uncommon, when it occurs, it can be devastating for the patient and difficult to treat. The available data would suggest that a safe and easy maneuver such as SpaceOAR hydrogel injection can help avoid a severe episode of rectal toxicity without adding significant cost or morbidity to the radiation treatment. SpaceOAR has become a useful tool in our practice to "protect the rectum" and other organs at risk during radiotherapy for prostate cancer treatment. UT

DISCLOSURES

Dr. Yonover is a consultant and speaker for Augmenix, Astellas, and MDxHealth. Dr. Mehta is a consultant for Augmenix and trains/proctors physicians on SpaceOAR placement technique.