CASE REPORT

Rectal ulcer associated with SpaceOAR hydrogel insertion during prostate brachytherapy

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Accepted 5 December 2014

SUMMARY

We present a case of rectal ulceration associated with SpaceOAR hydrogel insertion during low-dose-rate (LDR) brachytherapy in a patient with prostate cancer.

BACKGROUND

The insertion of the SpaceOAR hydrogel is an optional procedure offered to patients during prostate radiotherapy in an attempt to reduce risk of rectal toxicity. Owing to the proximity of the rectum to the prostate, curative radiotherapy for prostate cancer inevitably results in irradiation of the anterior rectal wall.^{1–2} The SpaceOAR System (Augmenix Inc, Waltham, Massachusetts, USA) is a synthetic polyethylene glycol hydrogel injected between the prostate and the rectum, thereby distancing the rectum away from the prostate, reducing irradiation of the anterior rectal wall.^{3–8}

The SpaceOAR is inserted trans-perineally under trans-rectal ultrasound (TRUS) guidance. When the precursor and the accelerator solutions that make up the SpaceOAR System are injected simultaneously into the perirectal space, the mixing of the two solutions initiates a cross-linking reaction that results in the formation of a soft polyethylene-glycol-based gel within seconds. After 12 weeks, the hydrogel hydrolyses and liquefies, and is absorbed.⁹

To the best of our knowledge, this is the first report of rectal ulceration following SpaceOAR hydrogel insertion with low-dose-rate (LDR) prostate brachytherapy. In this case report, we discuss possible mechanisms of rectal injury and technical manoeuvres that may help to reduce risk of rectal ulceration during SpaceOAR hydrogel insertion.

CASE PRESENTATION

A 66-year-old man was diagnosed with favourable intermediate risk prostate cancer. Baseline parameters included a prostate-specific antigen of 2.2 ng/mL and subtle non-specific firmness of the prostate gland bilaterally. On TRUS, the prostate had an estimated volume of 28 mL and prostate biopsies found evidence of multifocal Gleason score 3+4 adenocarcinoma. The patient was otherwise in good health although his history was relevant for a surgically resected atrial myxoma and coronary artery disease stenting. He also has a history of diverticulosis/diverticulitis and chronic renal impairment. Following consideration of management options, he elected to have treatment with LDR prostate brachytherapy.

TREATMENT

One month prior to LDR brachytherapy implant, a routine volume planning study was performed and three gold non-radioactive fiducial markers were inserted into the prostate. At the subsequent LDR brachytherapy implant, a total of 83 radioactive iodine-125 seeds were placed under TRUS guidance. The total prescribed dose was 145 Gy.

At the completion of the implant, SpaceOAR prosthesis was injected into the space between the prostate and the anterior rectal wall.

Postimplant CT scan was performed 24 h later demonstrating good seed placement within the prostate and in the immediate extraprostatic vicinity to allow adequate extraprostatic dose coverage.

The SpaceOAR was measured to have created a distance of 1.5 cm at the base of the prostate. A distance of 0.6 cm was created at the mid gland and 0.7 cm at the apex, where there was negligible space seen between the prostate and the rectum prior to SpaceOAR insertion.

Dose to the rectum achieved was very satisfactory, with maximum dose to the rectum of only 88.2% of prescribed dose (128 Gy), well under the recommended maximum dose to the rectum of 100%.¹⁰ Dose to the rectum achieved with SpaceOAR was reduced from what had been planned without SpaceOAR. The planned dose to the rectum (without SpaceOAR) was 75.4 Gy to 0.1 cc of the rectum, 63.2 Gy to 1 cc of the rectum and 55.2 Gy to 2 cc of the rectum. The achieved dose to the rectum (with SpaceOAR) was 69.3 Gy–0.1 cc of the rectum, 54.8 Gy–1 cc of the rectum and 47.9 Gy of the rectum.

OUTCOME AND FOLLOW-UP

Digital rectal examination (DRE) performed immediately following LDR brachytherapy and SpaceOAR implantation revealed submucosal induration in the anterior rectal wall as expected, consistent with presence of SpaceOAR. Rectal mucosa was intact.

On review at 1 month postimplantation, the patient reported increased bowel frequency and urgency, mucus discharge and occasional visible blood in the stools. DRE again revealed intact rectal mucosa, with the expected anterior submucosal induration from the SpaceOAR. There were no haemorrhoids. The patient was advised to follow a low-fibre diet at this point.

At review 2 months postimplantation, the patient described more frequent rectal bleeding and mucus discharge, associated with frequent bowel actions up to eight times a day. DRE now revealed a

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To cite: Teh AYM, Ko H-T, Barr G, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-206931

Figure 1 Anterior rectal wall necrotic rectal ulcer on sigmoidoscopy 2 months after low-dose-rate prostate brachytherapy and SpaceOAR insertion.

palpable tender 1 cm ulcer on the anterior rectal wall. Prompt gastroenterological review and sigmoidoscopy confirmed the presence of a necrotic ulcer consistent with DRE findings (figure 1). Of note, sigmoidoscopy findings were not consistent with that of radiation proctitis. The patient did not demonstrate constitutional symptoms, nor were there symptoms to suggest fistula formation. Thus, it was decided the patient be monitored closely by all three disciplines (radiation oncology, urology and gastroenterology) at this stage.

At 3 months postimplantation, the patient reported significant improvement in his bowel frequency down to once a day and with complete resolution of the passage of mucous and blood. By 6 months, DRE revealed a healed ulcer, with only a non-tender slit in the anterior rectal wall, without mucus discharge or bleeding. The submucosal induration from the SpaceOAR had resolved. At subsequent follow-up examinations out to 3 years since implantation, there has been no recurrence of bowel symptoms and the anterior rectal abnormality remains healed.

DISCUSSION

The rectum, given its proximity to the prostate, is the main dose-limiting organ during prostate radiotherapy. Excessive dose to the rectum can result in acute and possibly long-term bowel frequency, urgency, faecal incontinence, bleeding, ulceration and fistula formation.^{11–13} The risk of radiation proctitis is a function of dose delivered and volume of rectum irradiated.¹⁴ In LDR prostate brachytherapy, a form of prostate radiotherapy, Snyder *et al*¹⁵ reported 0% rate of proctitis when the volume of rectum receiving 160 Gy or more was kept under 0.8 cc. However, a 25.5% rate of proctitis was seen when volume of rectum receiving 160 Gy was greater than 2.3 cc. Thus, attempts have been made to reduce dose to the rectum during prostate radiotherapy and brachytherapy. Prada *et al*¹⁶ have shown that patients who received trans-perineal injection of hyaluronic acid spacer into their perirectal fat during iodine-125 LDR prostate brachytherapy had significantly smaller incidence of mucosal damage at proctoscopic examination (5% vs 36%, $p=0.002$) and no macroscopic rectal bleeding (0% vs 12%, $p=0.047$) than those who did not receive hyaluronic acid spacer insertion. In our case report, with insertion of SpaceOAR, the maximum dose to the rectum was only 128 Gy.

While the use of spacer technology has been shown to reduce rectal toxicity, it should not in itself compromise treatment or cause further complications. Klotz *et al*¹⁷ have described development of a rectal mucosal 'lesion' during external beam radiotherapy for prostate cancer after SpaceOAR insertion. As a

result, external beam radiotherapy was discontinued earlier than planned. The area of 'necrosis' did heal 3 months later. Thus, spacer technology needs to be used with care.

Possible mechanisms of rectal injury with SpaceOAR use include:

- ▶ Infection;
- ▶ Mechanical injury: Piercing of rectal wall by insertion needle, leading to leakage of SpaceOAR hydrogel into the rectal wall and the lumen;
- ▶ Ischaemic injury: Excessive tension from the SpaceOAR at the anterior rectal wall;
- ▶ Radiation injury: Ineffective placement of the SpaceOAR.

In this case, radiation injury was unlikely given the low dose to the rectum achieved with the insertion of SpaceOAR. Furthermore, sigmoidoscopic findings were inconsistent with that of radiation proctitis.

In our centre, precautions are taken to avoid infection, with insertions performed in the operating theatre in a sterile environment. Patients are routinely given intravenous cephazolin perioperatively and receive 5 days of norfloxacin 400 mg twice daily following brachytherapy and SpaceOAR insertion. In this case, the patient did not develop constitutional signs or symptoms to suggest an infective cause, and the ulcer resolved without further antimicrobial intervention.

Mechanical or ischaemic injury may be most likely. Precautions were taken to avoid mechanical injury to the rectum during SpaceOAR insertion.

First, SpaceOAR was inserted with clear imaging under TRUS guidance following adequate bowel preparation. The trans-perineal needle was clearly seen under sagittal TRUS imaging, and well-positioned between the prostate and the anterior rectum.

Patient and equipment positions were adjusted for optimal SpaceOAR needle placement. The perineum template used during iodine-125 seed implantation was removed prior to SpaceOAR insertion to improve manoeuvrability of the SpaceOAR needle. The needle was inserted with the bevel of the needle positioned away from the rectum to avoid the rectal wall perforation. Prior to needle placement, the TRUS probe was also lowered, to relax it away from the anterior rectal wall, reducing the pressure of the TRUS probe against the anterior rectal wall, yet ensuring adequate contact to allow good imaging. The technique of hydrodissection with normal saline was used to create the space before SpaceOAR was injected.

In this case, premature solidification of the SpaceOAR hydrogel within the delivery system did occur, requiring replacement of the delivery system. This is due to the downward angling of the needle (cranial–posterior direction) along the prostate–rectal space when the patient is lying horizontally, causing premature leaking of the precursor and accelerator solutions into the delivery system. Since this event, patient beds are now routinely tilted 'head up' prior to SpaceOAR insertion. This reduces the downward angling of the needle, and reduces risk of premature mixing and solidification of the solutions within the delivery system.

Another possible mechanism of injury is ischaemia of the anterior rectal wall due to the tension created by the SpaceOAR. Thus, recent recommendation is to limit the amount injected to 10 mL and stop injecting if resistance is felt. In this case, no resistance was felt, both during hydrodissection and SpaceOAR insertion.

At our centre, appropriate SpaceOAR placement is routinely confirmed with DRE performed immediately after the procedure. A further assessment of SpaceOAR placement is made on a CT scan performed 24 h later for radiotherapy dosimetry

purposes. SpaceOAR hydrogel has been shown to be more visible on MRI than CT scans.¹⁸ Thus MRI would be an additional modality to assess SpaceOAR placement. However, MRI would unlikely alter management routinely and thus the cost would not be justified. MRI evaluation could be considered at onset of rectal symptoms and signs. In this case, given spontaneous resolution of the patient with rectal ulcer, MRI was not performed and would unlikely have altered management.

In conclusion, SpaceOAR technology can reduce rectal irradiation during prostate LDR brachytherapy. This would likely translate to reduction in radiation rectal toxicity. However, care and consideration should be taken during SpaceOAR insertion so that the SpaceOAR in itself would not compromise treatment or cause further complications. Since 2011, 55 SpaceOAR insertions have been performed. This has been the only case of rectal ulceration.

Learning points

- ▶ Avoid infection: perform insertion in a sterile environment with antibiotics cover.
- ▶ Adequate imaging: perform insertion under trans-rectal ultrasound (TRUS) guidance on sagittal imaging with adequate bowel preparation.
- ▶ Appropriate needle positioning: remove low-dose-rate brachytherapy template to optimise needle manoeuvrability, and insert needle with bevel positioned away from the rectum to avoid rectal perforation. Consider tilting patient bed 'head up' to reduce downward angling of needle and delivery system.
- ▶ Allow space to be created: reduce pressure of TRUS probe against anterior rectal wall, and hydrodissect with normal saline before insertion of SpaceOAR.
- ▶ Avoid ischaemia: limit amount of SpaceOAR injected to 10 mL and stop if resistance is felt.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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