Use of hydrogel spacer for improved rectal dose-sparing in patients undergoing radical radiotherapy for localized prostate cancer: First Canadian experience

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Abstract

We describe the initial experience using a hydrogel spacer (SpaceOAR) to separate the prostate-rectum interspace in patients planned to undergo radical hypofractionated, image-guided, intensity-modulated radiotherapy (IG-IMRT). We depict and discuss the impact of SpaceOAR in the context of hypofractionated IG-IMRT, and the particular considerations for its applications in the Canadian setting.

Introduction

Prostate cancer.is the most common non-cutaneous malignancy in Canadian men.[1] External beam radiotherapy (EBRT) is a mainstay of treatment across the localized disease spectrum. Dose-escalation has lead to improved outcomes in prostate cancer, but has been associated with increased risk of gastrointestinal, and in particular, rectal toxicity.[2] Recent advances in radiation technology and delivery, including image-guided, intensity-modulated radiation therapy (IG-IMRT) have improved the therapeutic index;[3] however, in a proportion of cases, it remains difficult to adequately spare the surrounding organs at risk (OAR). Moreover, in patients where dose constraints for OAR can be achieved, they still may be vulnerable to such toxicities, and this appears to be related to the volume of normal tissue encompassed within the high-dose region.

In recent years, there has been a growing interest in placing biomaterials in the prostate-rectum interface, creating a separation between the target (prostate) and the OAR (rectum) that can potentially reduce rectal doses. Of these, polyethylene glycol (PEG) hydrogels have been the most widely studied.[4] Once within the perirectal space, cross-linked PEG rapidly polymerizes into a soft hydrogel, which after three months begins to hydrolyze until complete reabsorption in approximately 6–8 months. SpaceOAR (Augmenix Inc., U.S.) is an FDA- and Health Canada-approved PEG hydrogel rectal spacer that demonstrated >98% successful placement rate, with none or only mild symptoms (i.e., tenderness, fullness) at the site of injection resolving within 24 hours after the procedure. Importantly, the resulting space rendered better radiotherapy plan dosimetry, which improved late rectal toxicity and bowel-domain health-related quality of life in a randomized study comprising more than 200 men.[5,6]

Herein, we report our initial experience using SpaceOAR, the impact on IG-IMRT plan dosimetry, and discuss potential uses in the Canadian healthcare system setting.

Methods and results

Five patients with localized prostate cancer planned for radical radiotherapy underwent rectal spacer insertion after providing informed consent. In brief, the patient was placed in the lithotomy position and perineal skin prepped in a sterile manner. The skin and deep tissues up to the prostatic apex bilaterally were infiltrated with 20 cc of 1% lidocaine under transrectal ultrasound (TRUS) guidance. Three gold fiducials were inserted transperineally at the prostate base, mid-gland, and apex by TRUS guidance. Subsequently, the SpaceOAR injection needle (18 G, 15 cm length) was inserted parallel to the TRUS probe affixed to the brachytherapy stepper. The tip of the needle was positioned at the mid-gland level between Denonvilliers' fascia and the anterior rectal wall. Hydrodissection was performed with 5–15 cc of saline to confirm correct positioning. Under direct visualization, the assembled SpaceOAR kit was attached, and while maintaining the needle position, 10 cc of hydrogel was injected in one continuous motion over 8–10 seconds. The total procedure time ranged between 15 and 25 minutes. All patients tolerated the procedure well, with only mild discomfort related to the TRUS probe and initial lidocaine injection.

Patients underwent computed tomography (CT) and magnetic resonance (MR) simulation for EBRT planning, 3–10 days after SpaceOAR insertion. CT was acquired, without intravenous contrast, at 2 mm slice thickness per institutional practice. MR (3 Tesla) without endorectal coil consisted of axial T2-weighted (T2w) and.diffusion-weighted imaging (DWI) sequences for prostate and tumour delineation, and three-dimensional constructive interference in steady state (3D-CISS) sequence for optimal fiducial identification and CT-MR registration (Fig. 1). The resultant distance between the anterior rectal wall and prostate measured in T2w MR sequence at the base, mid-gland, and apex ranged between 10–13, 9–11, and 8–14 mm, respectively. Radiotherapy planning was performed in RayStation (RaySearch Laboratories, Sweden) following departmental (i.e., PROFIT) dose goals and constraints. All plans met criteria for approval. The resultant dose-volume histograms (DVH) of the five patients were averaged and compared to five randomly selected historical cases treated with the same IG-IMRT schedule (60Gy in 20Fx) for illustrating the differences in rectal doses (Fig. 2).

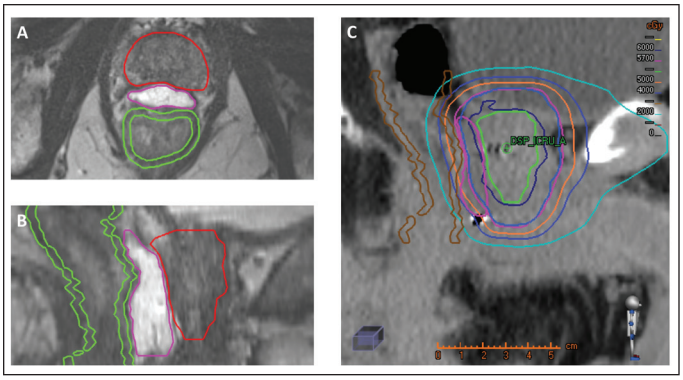

Fig. 1. (A, B) Axial and sagittal MR-T2w images showing the prostate (red), rectum (green), and space OAR (magenta). A separation of 11 mm between the anterior rectal wall and the prostate was achieved with SpaceOAR. ***(C)*** Dose distribution on the corresponding co-registered planning-computed tomography sagittal image depicts the ability of SpaceOAR to exclude a significant proportion of the rectal wall from the higher-dose region.

Discussion

This report represents the first experience using SpaceOAR in Canada. Insertion as a short outpatient procedure under local anesthesia, translated into excellent results and patient tolerance. The dosimetric results of hypofractionated IG-IMRT compared favourably to historical plans. Our experience and planned future use of a rectal spacer for IG-IMRT have unique considerations in our setting.

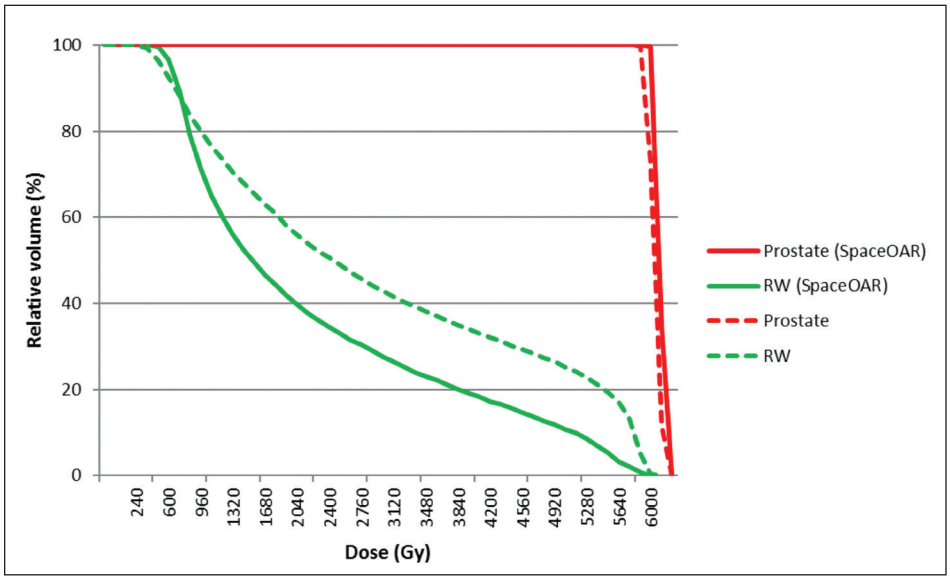

Fig. 2. Averaged dose-volume histograms (DVH) of prostate and rectal wall (RW) in the five patients with SpaceOAR (continuous lines), and five randomly selected historical cases treated with identical dose schedule (dotted lines). Mean dose to 30% and 50% of the rectal wall significantly decreased from 45.8 and 26.9 Gy in the historical group compared to 27.8 and 15.3 Gy in the SpaceOAR patients (t-test p=0.0001 and 0.0002, respectively).

The recently published Canadian PROFIT study demonstrated 60 Gy in 20 fractions to be non-inferior to conventionally fractionated dose-escalation (78 Gy in 39 fractions).[7] Based on this and other studies,[8,9] mild hypofractionation has become an accepted and increasingly adopted dose schedule at ours and many other institutions. Nonetheless, in approximately 10–25% of cases, strict rectal dose-constraints are not met, generating a concern for increased risk of late toxicities, particularly in the context of higher-dose per fraction. Furthermore, with increasing number of stereotactic ablative body radiotherapy (SABR or SBRT) schemes that employ more extreme forms of hypofractionation being investigated, there may be greater concern with regard to treatment toxicity. In these scenarios, the possibility of rectal sparing with a single, mildly invasive procedure may be appealing to maximize the therapeutic index.

Although cost-effectiveness analyses in other jurisdictions suggest routine use of SpaceOAR in every patient,[10] this would be challenging to justify in the current Canadian environment. Moreover, it would likely be clinically unjustified considering only 6% of the control arm experienced Grade 2 or greater gastrointestinal toxicity (only one case [1.3%] of Grade 3) in the SpaceOAR pivotal randomized study.[6] Therefore, clinical feasibility and performance data in the Canadian setting will allow economic modelling accounting for the costs of rectal spacer, repeated

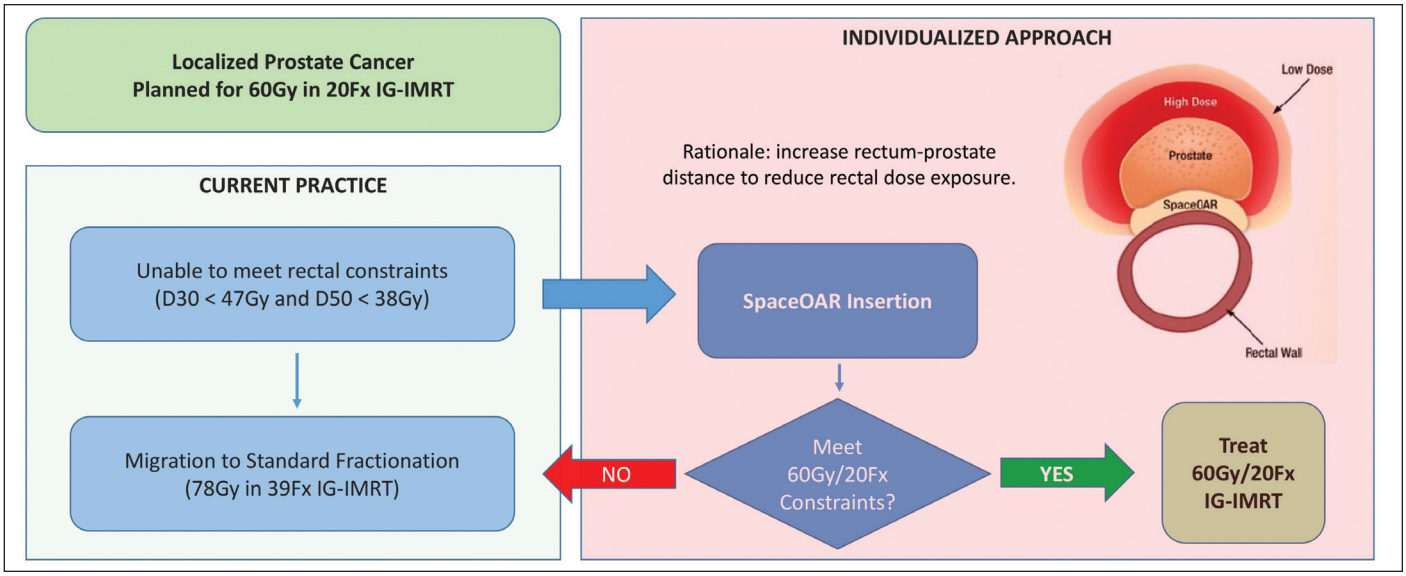

Fig. 3. Schematic representation of our proposed individualized use of SpaceOAR in patients undergoing curative-intent hypofractionated, image-guided, intensity-modulated radiotherapy (IG-IMRT) for localized prostate cancer.

planning imaging studies, shorter vs. longer treatment duration, and associated toxicities over the full cycle of care.

We envisage an individualized approach for SpaceOAR use in patients undergoing hypofractionated IG-IMRT (Fig. 3). In our institution, cases in which hypofractionated OAR dose-volume constraints are not met, a new plan is generated with conventional fractionation (78 Gy in 39 fractions) and treated accordingly. Tailored use of rectal spacer in these cases may offer the opportunity of hypofractionation, with its logistic advantages, a reduced rectal dose, and a decrease in the associated risk of toxicity.

In summary, we report the first experience with SpaceOAR use for hypofractionated IG-IMRT treated patients with prostate cancer. Determining the clinical scenarios applied in the Canadian healthcare setting, where rectal spacers may be judiciously used to achieve the most cost-effective solution in terms of toxicity reduction is warranted.

Competing interests: The authors reports no competing personal or financial interests.

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This paper has been peer-reviewed.

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