A Prospective Analysis of SpaceOAR® Hydrogel Rectal Spacing and Rectal Toxicity in the Treatment of Prostate Cancer


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Introduction

In spite of recent advances in radiotherapy for prostate cancer, rectal toxicity still remains one of the major limitations to effective dose delivery due to the close proximity of the anterior rectal wall to the high dose region. It is well documented that the late rectal toxicity is correlated with the volume of the anterior rectal wall being treated, particularly V70.

Reducing the volume of the anterior rectal wall being treated will minimize the rectal toxicity and one of the most simple and effective methods to achieve this is to increase the distance between the rectum and the prostate by inserting hydrogel anterior to the rectal wall.

We prospectively analyzed a group of prostate cancer patients and reported on the benefit of SpaceOAR® hydrogel and associated gastrointestinal (GI) toxicities.

Method and Materials

A prospective, non randomized, single institution study involving 76 confirmed prostate cancer patients treated at Radiation Oncology Victoria from December 2013 to December 2015. Median age was 74 years. Disease stage ranged from T1c to T3a.

Under transrectal ultrasound guidance, all patients underwent transperineal insertion of gold seed fiducial markers into the prostate and injection of 8ml of SpaceOAR® hydrogel posterior to the Denonvillier’s fascia prior to CT planning (Fig. 1).

To maintain consistency in hydrogel placement, volume marking and toxicity assessment, only one Radiation Oncologist was involved in the study.

CT planning for IMRT with full bladder and empty rectum was performed approximately 5 days post procedure. Dose prescribed was 78.00Gy - 80.00Gy in 2.00Gy fractions; treatment was delivered using either IMRT or VMAT (Fig. 2).

Degree of separation achieved between the anterior rectal wall and posterior edge of prostate was quantified at apex, mid-gland and base. Rectal V70g, V75g, V100g, V60g and V50g were assessed for correlation between dosimetric endpoints and any GI toxicity.

Patients were assessed at baseline, weekly throughout treatment, and followed up at 3, 6, 12 months then annually post treatment. Toxicity was assessed according to CTCAE v4.0.

Results

Overall, all of our patients tolerated the SpaceOAR® and gold seed insertion procedure well with no report of adverse events. Analysis of our patient cohort indicated a mean rectal spacing of 1.3mm, 8mm and 5mm at base, mid-gland and apex respectively as indicated in Table 2. below. Rectal spacing achieved was similar for all of our patients irrespective of prostate size.

Dosimetric analysis demonstrated that all rectal dose constraints were well below the acceptable tolerance for our entire patient cohort as shown in Table 3 below.

Comparison with our institution’s current rectal DVH constraints for non SpaceOAR® plans demonstrated a significant improvement in the SpaceOAR® plans, particularly in the high dose regions.

Detailed analysis of variation in prostate size indicated comparable mean rectal volume constraints achieved across our patient cohort (Fig. 3).

79% of our patients reported acute grade 0 GI toxicity; 21% developed acute grade 1 GI toxicity. No patient experienced acute grade 2+ GI toxicity (Table 4). At a median follow up of 14 months post treatment, 97% of patients had resolution of their grade 1 acute GI toxicities. One patient developed late grade 1 rectal haemorrhage at 9 months post treatment; one patient developed late grade 1 proctitis at 8 months post treatment. No patients developed early late GI toxicity of Grade 2+.

Our results are very comparable with the recently published randomised trial by Mariados et al(1). The acute toxicity rate was high in both groups. Of note the rate of late toxicity dropped significantly at 3 months follow up which is consistent with our results of no Grade 2+ toxicity in our patient cohort.

Conclusion

In our experience SpaceOAR® hydrogel has been found to be easy and safe to use with no adverse effects associated with the device, nor any rectal complications reported in our patient cohort group.

This study has demonstrated that spacer hydrogel was effective in increasing the perirectal space in all of our patients, irrespective of prostate size, thus significantly reducing the volume of rectum being irradiated.

Our study has demonstrated very encouraging results with significant rectal dose reduction in both the low and high dose regions particularly the rectal V70g. Clinical reduction in rectal volume has validated a correlation between rectal sparing and associated GI toxicity.

References


Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Stage</th>
<th>Patient Number</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>16% (12/76)</td>
</tr>
<tr>
<td>II</td>
<td>57% (43/76)</td>
</tr>
<tr>
<td>III</td>
<td>17% (13/76)</td>
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<table>
<thead>
<tr>
<th>Prostate Size</th>
<th>Patient Number</th>
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<tbody>
<tr>
<td>&lt;50 cc</td>
<td>38% (29/76)</td>
</tr>
<tr>
<td>50-100 cc</td>
<td>45% (34/76)</td>
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<tr>
<td>&gt;100 cc</td>
<td>17% (13/76)</td>
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Table 2. Peri Rectal Space Results

<table>
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<tr>
<th>OAR Constraints</th>
<th>SpaceOAR Mean (%)</th>
<th>Non SpaceOAR Mean (%)</th>
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<tbody>
<tr>
<td>Rectum V50Gy50%</td>
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<td>28.5</td>
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<td>Rectum V60Gy35%</td>
<td>14.4</td>
<td>19.0</td>
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<td>Rectum V70Gy20%</td>
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<td>Rectum V75Gy15%</td>
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<td>9.5</td>
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<tr>
<td>Rectum V78Gy5%</td>
<td>0.4</td>
<td>4.5</td>
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Table 3. Rectal Volume Dose Comparison between SpaceOAR® and Non SpaceOAR® Plans

Fig. 3. Mean Rectal Volume

Table. 4. Radiation Toxicity

Table 5. Mariados et al, 2015

Fig. 1. SpaceOAR® Injection (Ref. Augmenxis)

Fig. 2. IMRT Beam Arrangements
The Use of TraceIT® as a Fiducial Marker in Bladder Radiotherapy

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Introduction

Accurate localization for radiation therapy to bladder malignancies is a challenge due to uncertainty in daily variation of bladder volume. This uncertainty can pose a significant risk in accurately identifying the tumour target volume which in turn can impact on radiation damage to surrounding healthy tissues. Lipiodol has been used as a fiducial marker in the treatment of bladder cancer. However, injection of Lipiodol as discrete fiducial markers into the bladder submucosa can be technically difficult. In addition, diffusion of Lipiodol into the submucosa can make it difficult to clearly identify the markers on CBCT images (Fig. 1).

Background and Objectives

Recently, TraceIT® Tissue Marker has attracted more interest as an alternative soft tissue fiducial marker for the bladder wall. TraceIT® Tissue Marker is an absorbable radiopaque hydrogel consisting of iodinated polyethylene glycol (PEG) hydrogel particles in a viscous carrier (Fig. 2). The PEG iodination property enables TraceIT® to be visible on both CT and CBCT without any artefacts; the high water content allows the gel to be visible on MRI and Ultrasound. Following injection into the bladder wall, the hydrogel particles form a "bleb" that remains in-situ and visible for 3 months. These "blebs" then hydrolyse, which causes them to liquefy, be re-absorbed and cleared from the body via renal filtration after 7 months.

In this case study, we evaluated:
• The safety of TraceIT®
• The suitability of TraceIT® as a stable fiducial marker in the treatment of bladder cancer

Method and Materials

84 year old male presented with a newly diagnosed unilateral invasive high grade transitional cell carcinoma (TCC) of his posterior bladder wall with a past history of prostate cancer treated more than 5 years ago with iodine-125 low dose rate (LDR) brachytherapy. His PSA was now <0.1ng/ml.

In view of the patient's prior prostate brachytherapy and concomitant multiple co-morbidities, a non-surgical management option was chosen. Due to the potential of overlap with his previous LDR of 145.00Gy, a course of concurrent chemotherapy and targeted partial bladder irradiation was prescribed. Under general anaesthetic, a rigid 20F cystoscopic injection needle was introduced into the bladder. Systematic cystoscopy was performed and the bladder tumour was localised. All macroscopic tumours were resected via TURBT. Using a 23G flexible Cook Williams Cystoscopic Injection Needle, 0.3 – 0.4 ml of TraceIT® was injected into 6 locations around the tumour bed within 1 cm of the tumour border. A total of 2ml of TraceIT® tissue marker was injected into the bladder mucosa (Fig.3)

CT planning for bladder IMRT was performed 5 days post procedure. The patient was catheterised at CT. The bladder was drained of urine then refilled with 240ml of saline to displace the tumour bed away from the previously irradiated prostate. Dose prescribed was 64.0 Gy in 2.0 Gy per fraction.

Results

The patient tolerated the TraceIT® injection procedure well with no adverse event reported. With a similar density value to tissue of 1.03g/cm³ and owing to its radiopaque property, TraceIT® blebs were clearly visible on CT images without any artefacts. This further enabled easy delineation and contouring of TraceIT® blebs for planning and verification images.

Daily matching of TraceIT® blebs on CBCT was straightforward as the blebs were very distinct and remained stable throughout the entire course of treatment (Fig. 7).

Conclusion

In our experience, TraceIT® was found to be straightforward to inject cystoscopically into the bladder submucosa with no reported post operative complications. TraceIT® blebs remained stable throughout the entire course of treatment and there were no issues reported with identifying and matching TraceIT® blebs on CBCT images. TraceIT® can be considered as a feasible option to clearly demarcate the exact tumour location and margins to facilitate the delivery of targeted focal bladder IMRT.

References