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Expanding access to rectal spacers in the United Kingdom: an examination of current evidence and an early review of data from a single institution

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Editorial

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Abstract

Background: Prostate cancer is a common malignancy with rising incidence in Western countries such as the United Kingdom. In localised disease there are a variety of curative treatment modalities. Patients can be referred for surgery, or for a combination of hormonal therapies and radiotherapy (external beam radiotherapy or brachytherapy). Each treatment option comes with side effects and in the case of radiotherapy one potential complication is bowel toxicity from radiation exposure. New technologies are being developed to try and mitigate the side effects and long term morbidity of this treatment, and to expand access to radiotherapy for patients who may previously have been excluded (i.e those with inflammatory bowel disease). Rectal Spacers are absorbable polyethylene glycol hydrogels injected into the perirectal space. These position the anterior rectal wall away from the prostate, subsequently minimising radiation dose to the rectum. Rectal Spacers have been introduced to National Healthcare Service (NHS) practice as part of the Innovation and Technology Payment (ITP) programme, however, their use is now under review.

Methodology and Results: In this editorial we conduct a narrative review of some of the available evidence for Rectal Spacers, discuss their utilization within the NHS and the barriers to their wider use. We also explore preliminary dosimetry and quality of life data for use of Rectal Spacers in our centre where we have been part of the NHS ITP programme. Dosimetry data and Quality of life questionnaires were gathered from 22 treated patients and 11 matched controls. This indicated lower radiation doses to the prostate in those treated with Rectal Spacers.

Conclusion: Rectal Spacers are an effective method to reduce radiation dose to the prostate in men treated for localised prostate cancer, however, their use remains under review in the NHS and there are a variety of barriers to upscaling their use.

Introduction

Prostate cancer is the most common malignancy affecting men in the United Kingdom.[1] In localised disease, radical treatment options include prostatectomy or radiotherapy (external beam radiotherapy or brachytherapy). For this patient, cohort both treatment modalities have similar oncological outcomes.[2] While radiotherapy is an excellent radical treatment option for localised disease, it can risk long-term bowel toxicity.[3] Therefore, patients also diagnosed with inflammatory bowel disease (IBD) may be steered away from this option due to the risk of worse bowel-related quality of life (QOL) post-radiotherapy. Equally, patients with IBD are at higher risk of secondary malignancies, and therefore, radiation exposure should be avoided. While patients are carefully counselled about the risks of IBD and concurrent radiotherapy, there remains little supporting literature.[4–6]

Recognition of the bowel-related side effects arising from prostate radiotherapy has resulted in the development of new technologies to mitigate these impacts including the use of rectal spacers. In this editorial, we will review the concept of rectal spacers and the evidence behind their introduction. We will examine their current uptake within the United Kingdom and explore some of the potential barriers to their use. Finally, we present some real-world data from the introduction of a programme for rectal spacers in our regional centre, including dosimetric data and QOL outcomes from our patient cohort.

Background

While radiotherapy to the prostate is a widely used curative treatment in those with localised prostate cancer, the spatial proximity of the bowel, prostate and bladder can result in side effects.

In particular, the focus of radiation on the prostate can result in a high radiation dose to the anterior rectal wall. This can cause symptoms of diarrhoea, incontinence and ulceration of the rectal mucosa[7]—and for this reason, prostate radiotherapy is often used cautiously in those with inflammatory bowel disease or pre-existing troubling gastrointestinal symptoms. In the United Kingdom, treatment of prostate cancer is audited nationally by the National Prostate Cancer Audit.[8] Their review includes toxicity and patient experiences after treatment, and thus, finding ways to minimise radiation side effects is an important issue that falls under national scrutiny and provides further impetus for clinicians to find new treatment ideas in this area.

Rectal spacers, such as SpaceOAR, are absorbable polyethylene glycol hydrogels injected into the perirectal space[9] to position the anterior rectal wall away from the prostate and minimise radiation dose to the rectum. The procedure is performed as an outpatient appointment, usually taking around 30 minutes. The urology or interventional radiology team use an ultrasound-guided technique to ensure correct placement of the spacer material, which is inserted using an injection of two liquids that together form a hydrogel. The procedure can be done under general, local or spinal anaesthesia.[10] Other biodegradable substances, that is, hyaluronic acid and human collagen or biodegradable balloon spacers, can be used. In all cases, the result is a physically increased distance between the prostate and rectum that aims to reduce the dose of radiation delivered to the rectum and thereby reduce bowel-related side effects.

The spacers degrade over an average of 3 months and are absorbed by the body, with spacer material being eliminated via the urine. The insertion of spacers is typically a safe and well-tolerated procedure. There have been a few adverse outcomes reported. Potential side effects include the insertion of spacer material causing needle penetration of the bladder or rectum, pain post-insertion, hydrogel being injected into other organs such as the bladder and bleeding.[11–13] In one case study, the patient received an intravascular injection of a hydrogel spacer, and the patient remained well and was treated with anticoagulation. Other adverse events have included injection into the rectal wall resulting in focal rectal mucosal necrosis and a separate case of a haematoma behind the bladder.[14]

Review of the evidence-based research

Rectal spacer devices are still relatively novel with most research published from 2013 onwards. Here we present some key findings from early trials, accessing relevant literature from literature resources including PubMed, EMBASE and Cochrane. Early clinical trial data show patients demonstrate excellent tolerability[15] during radiotherapy treatment and improved rectal dosimetric outcomes and QOL measures[16] when using spacer devices.

Data in recently published trials show evidence to support the rationale of spacer devices, demonstrating spacers significantly increase the physical distance between the prostate and anterior rectal wall. An early multicentre randomised control trial included 222 patients with early clinical stage T1 and T2 prostate cancer where rectal spacers were inserted. Respectively, the perirectal spaces were measured at 12·6 ± 3·9 mm (spacer group) against 1·6 ± 2·0 mm (control group).[15] No complications were reported following spacer insertion. In a systematic review of early spacer studies, the authors reviewed 6 trials that reported spacing distance. The combined data compared 671 patients who had hydrogel spacers (of 2 different types) with 537 controls, and mean prostate rectum space varied between 7·7 mm and 16 mm, respectively (though a variety of techniques were used to measure spacing distance).[17]

The tolerability of spacers in prostate patients has been evaluated in many early clinical trials. The previously mentioned multicentre randomised trial published by Maridos et al assessed both acute and late rectal adverse events. Acute rectal toxicity was found to be similar between the spacer and control groups. However, the spacer group had a significant reduction in the late rectal toxicity (3–15 months),[15] and measures of bowel QOL indicated that 11·6% of spacer patients and 21·5% of controls had a 10-point decline in bowel QOL based on QOL scoring systems. Long-term follow-up of this cohort at 3 years confirmed reduced late rectal toxicity in the spacer arm compared to controls for both grade ≥1 (9·2 versus 2·0%; $p = .028$) and grade ≥2 (5·7 versus 0%; $p = .012$) complications.[18] In the study, the use of QOL questionnaires in the men in the spacer arm reported improved bowel QOL compared to controls. There was also a trend towards better urinary symptoms in the intervention group.

The improvement in QOL through the use of spacer devices has been replicated in other studies. A prospective study of 59 patients examined baseline Expanded Prostate Cancer Index Composite (EPIC-26) scores along with baseline American Urology Association Symptom Index (AUA-SI) scores.[19] No significant changes in the AUA-SI score ($p = 0·69$) or EPIC-26 domain scores ($p = 0·19$) during the study period were demonstrated. This indicates that the use of the spacers led to maintenance of QOL-reported outcomes, perhaps as a result of reduced toxicity.

The current findings of the efficacy and tolerability of spacers have been examined in a recent systematic review article published in 2021. This analysed 19 studies and found that regardless of the radiotherapy technique used the introduction of spacers both decreased the rectal radiation dose and improved not only the late gastrointestinal and genitourinary toxicities but also led to improvement in sexual QOL compared to controls.[16] This review also acknowledged the paucity of research that has been undertaken into rectal spacers and hypofractionated radiotherapy.

Use of spacers within the United Kingdom

Spacers provided by the manufacturer Boston Scientific are now available as part of the NHS England Innovation and Technology Payment programme (ITP).[20] This NHS programme aims to assist the nationwide introduction of technologies that have been shown to be clinically effective but are not yet widely available. It aims to remove some of the financial barriers to hospital services and allow wider access for patients. Currently, the majority of insertions take place in private hospitals in the United Kingdom where funding for these treatments is at the patient's cost.

Rectal spacers were included on the ITP in 2019–20 and have subsequently been extended on the programme. However, despite this the uptake of rectal spacers remains low within the public health service. A questionnaire sent to urologists within the United Kingdom indicated that only 37% of surgeons had inserted a rectal spacer, despite 68% saying that they would be open to using them in the future.[21] Furthermore, most of those who had inserted spacers before had used them within the private sector or for those with pre-existing bowel conditions. This is forcing many patients to apply to the private sector to get a spacer or to travel long distances to undergo spacer insertion in the public health service. This is an area of frequent discussion in patient prostate cancer forums.[22,23]

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Table 1. A comparison of rectal radiation doses in patients with a spacer and controls.

	n			Radiation dose (median, IQR)		
Dose type	Total	Spacer	Control	Spacer	Control	*p**
V58·6	29	18	11	0·76 (0·09 – 1·33)	5·26 (4·78–6·61)	<0·0001
V60	29	18	11	0 (0–0·06)	0·31 (0·15–0·80)	<0·0001

*Wilcoxon rank-sum (Mann-Whitney) test.

There may be several reasons why uptake within the United Kingdom remains low. The application for the spacers can be complex, and it requires a large volume of patients arriving at the service to make it cost-effective. Furthermore, it requires additional training for staff, both with simulators and in clinics. Spacers are also difficult to identify on standard CT imaging; therefore, patients may require an additional magnetic resonance imaging (MRI) alongside the CT scan to help delineate the hydrogel spacer and facilitate contouring by the oncologist and planning team. This is an additional scan at added cost to NHS trusts and requires time to set up a new scan pathway. Access to MRIs can be limited, and long waitlists have been a burden to cancer treatments due to staff shortages and COVID restrictions, in turn generating potential delays to treatment which would cause oncologists and patients to decline the use of rectal spacers as part of their treatment. Advances in CT visible rectal spacers will reduce the potential barrier to use. In our centre, patients undergoing rectal spacer insertion will also have intra-prostatic fiducial markers inserted to facilitate image-guided radiotherapy (IGRT). Patients undergo daily cone beam CT matching to fiducial markers and soft tissue to ensure the geometric accuracy of treatment. Retrospective studies have established the importance of IGRT to reduce toxicity during prostate radiotherapy, and this is a fundamental consideration for patients with rectal spacers.[23]

The routine use of rectal spacers is currently being reconsidered by The National Institute for Health and Care Excellence (NICE) who held an expert panel in March 2022 into the use of this technology.[24] They have conducted a rapid review of the evidence and have concluded that public coverage for SpaceOAR is not yet supported. Their cited reasons for this include the following:

- The limitations in the evidence, including the absence of data for groups considered to be at higher risk for rectal toxicity.
- The risk-benefit ratio, which does not appear to support the use of this technology.
- The possibility of major complications for patients.
- The possibility of an increased risk of complications for patients at increased risk for rectal toxicity.
- The observed dosimetric benefit (sometimes significant) in the evidence presented, which appears to offer only a small clinical benefit.
- The contradiction between the positions taken by other organisations.
- The potential difficulty of access to MRI.

As part of their review process, they have gathered questionnaire responses from several patients who have had rectal spacers, most of whom have had very positive experiences. 82% said that they felt the procedure worked, and 91% would recommend it to another patient with their condition.[25] This has been echoed by patient groups involved in this discussion including Tackle Prostate Cancer. This group has surveyed members and concluded that, for many individuals, radiation-induced bowel damage can be one of the most significant impacts of post-radiotherapy. In their concluding points, they noted that *'Undoubtedly most patients would take a "Better Safe than Sorry" approach to any new technology that can produce potential improvement in quality of life during and after treatment with radiotherapy. Currently they do not even have a choice to make'*.[25]

Opening a rectal spacer programme on the NHS is a complex and nuanced issue. Many patients have testified that they would like this service to be more widely available and to help improve patient choice. The early clinical trials have also supported the use of spacers to help reduce radiation dose to the rectum and to improve late bowel toxicity. However, the NHS must carefully consider the cost-benefit of all new treatments, and a thorough review of the evidence is underway.

It is also important to acknowledge that the introduction of this technology has led to innovations in other fields of radiotherapy. As with many scientific advances, the positive impacts may not just be felt in the intended field of use. A recent technical report highlighted the role of spacer gels in a case of recurrent hypopharyngeal cancer. In this case, a gel spacer was used to protect the carotid artery during irradiation of a previously radiated area.[26] By broadening access and training in the user of spacers, we may help to improve outcomes across several tumour groups and complex cases.

Our experiences and recommendations to take this forward

Our institution developed a rectal spacer service, primarily for patients with inflammatory bowel disease who either opted against or were felt inappropriate for, radical prostatectomy. We also received personal requests from patients treated elsewhere who wished to explore the option of rectal spacers. We applied to the ITP funding initiative and received SpaceOAR kits along with support in training for their use from Boston Scientific.

Since implementing this service in April 2021, we have monitored QOL metrics and analysed dosimetric planning data. We have treated 22 patients and have 11 matched controls all receiving 60 Gy in 20 fractions (Table 1). We excluded 4 patients in the spacer group from dosimetry analysis as they had radiotherapy to the prostate and nodes.

QOL data were gathered at six time points: spacer insertion, planning CT, first fraction of radiotherapy, last fraction of radiotherapy, 3 months after completion of treatment, 6 months after completion of treatment. We do not yet have data at all time points for our patients as the earliest date of Spacer insertion was 09 April 2021, and the most recent insertion was on 29 April 2022. Questionnaires utilised for QOL information include Fact-P (version 4), EPIC-CP, IPSS. These questionnaires were used as they

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have been validated in other prostate cancer research[27–29] and have been used in rectal spacer trials previously. The data were inputted onto spreadsheets, and trends in QOL were monitored, focussing on overall scores and bowel-related questions. QOL scores for patients with rectal spacers appear stable. Our cohort of patients are at different points in their treatment; however, in the 6-month group, bowel toxicity remains low.

Dosimetry data were gathered from the summary of the completed Radiotherapy Plan (Pinnacle planning). Volumes were collected based on final locked plans for spacer, prostate, rectum, bladder and bowel. Dosimetric data were gathered for the rectum (V24·3 Gy, V32·5Gy, V40·6 Gy, V56·8 Gy and V60 Gy), bladder and bowel. We analysed V56·8 Gy doses and V60 Gy doses as these high doses are likely to be associated with toxicity. These doses were also used in other studies reviewing the effects of rectal spacers.[15,30–32]

None of our spacer patients developed post-procedural complications. In the SpaceOAR group, the mean rectal V60Gy was 0·0% compared to 0·31% in controls ($p < 0·0001$) (Table 1). The mean V58·6 Gy dose in the spacer group was 0·76% compared to 5·26% in controls ($p < 0·001$). Therefore, we were able to demonstrate that the reduced rectal radiation dose seen in clinical trials of rectal spacers was maintained in our 'real-world' cohort.

Conclusion

Radical radiotherapy to the prostate is a gold-standard treatment offered to patients with organ-confined disease. While it offers excellent long-term local control and cancer-specific survival, a proportion of patients will experience significant bowel toxicity that can impact their daily lives years later. The emerging technology of rectal spacers has been shown to reduce the radiation dose to the bowel and allows patients to have better QOL post-treatment. While the early research into their use has been promising, there is still a limited amount of evidence producing conflicting results. There are also barriers to their introduction including cost, which is demonstrated by the majority of United Kingdom spacers currently being inserted in a private healthcare setting. Their use also involves the logistical challenges of developing a multi-speciality service and changes to existing treatment pathways such as the use of additional imaging. This is adding to already strained waiting lists.

Here we have explored the evidence base for the use of spacers and some of the factors limiting their use. Moving forward, we hope to see more conclusive evidence on whether this should be offered to all prostate patients or just those with inflammatory bowel disease, as well as its use and improvement in toxicity in patients undergoing hypofractionated treatment as well as brachytherapy. We have also outlined the success of introducing this new technology in our regional centre. We hope that this article helps to broaden the discussion around the use of this new technology, and we await the outcome of the NICE interventional procedure consultation which will be published in June 2022.

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