

BMJ Open Delphi study to identify consensus on patient selection for hydrogel rectal spacer use during radiation therapy for prostate cancer in the UK

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ABSTRACT

Objectives To identify consensus on patient prioritisation for rectal hydrogel spacer use during radiation therapy for the treatment of prostate cancer in the UK.

Design Delphi study consisting of two rounds of online questionnaires, two virtual advisory board meetings and a final online questionnaire.

Setting Radical radiation therapy for localised and locally advanced prostate cancer in the UK.

Participants Six leading clinical oncologists and one urologist from across the UK.

Interventions Rectal hydrogel spacer.

Primary and secondary outcome measures None reported.

Results The panel reached consensus on the importance of minimising toxicity for treatments with curative intent and that even low-grade toxicity-related adverse events can significantly impact quality of life. There was agreement that despite meeting rectal dose constraints, too many patients experience rectal toxicity and that rectal hydrogel spacers in eligible patients significantly reduces toxicity-related adverse events. However, as a consequence of funding limitations, patients need to be prioritised for spacer use. A higher benefit of spacers can be expected in patients on anticoagulation and in patients with diabetes or inflammatory bowel disease, but consensus could not be reached regarding patient groups expected to benefit less. While radiation therapy regimen is not a main factor determining prioritisation, higher benefit is expected in ultrahypofractionated regimens.

Conclusion There is a strong and general agreement that all patients with prostate cancer undergoing radical radiation therapy have the potential to benefit from hydrogel spacers. Currently, not all patients who could potentially benefit can access hydrogel spacers, and access is unequal. Implementation of the consensus recommendations would likely help prioritise and equalise access to rectal spacers for patients in the UK.

INTRODUCTION

Prostate cancer burden

Prostate cancer is the second most common cancer in men globally¹ and the most common in the UK.² More than 47 500 UK

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The Delphi panel is a recognised method in developing National Institute for Health and Care Excellence guidelines and is used here to gather insights from a diverse panel of UK radiation oncology and urology experts who are experienced users of hydrogel spacers.
- ⇒ This study included seven panel experts, and their experiences may not reflect all users of hydrogel spacers.
- ⇒ To help reduce bias, answers and opinions were assessed by two researchers working independently.

men are diagnosed with prostate cancer every year, and over 400 000 men are living with and after prostate cancer.³ The 5-year survival rate for localised prostate cancer in the UK is almost 100%,⁴ with three-quarters of men diagnosed at any stage expected to survive 10 years.² In England, 97%, 87% and 78% of men diagnosed with prostate cancer survive their disease for more than 1, 5 and 10 years, respectively.² Given the high likelihood of curative therapy, a key treatment goal is to prevent potential adverse events from impacting patient quality of life after treatment.

In addition to the patient burden, prostate cancer is a costly disease with the European costs of care for prostate cancer estimated at €199 billion in 2018.⁵

Radiation therapy (RT) for prostate cancer

Choice of treatment for prostate cancer is complex and involves multifactorial considerations including presenting cancer stage (localised, locally advanced or metastatic), risk stratification, life expectancy, comorbidities and other patient-specific factors, such as lifestyle, patient preference and treatment goals.⁶ For localised and locally advanced

prostate cancer, treatment options include active surveillance, surgery, brachytherapy (BT) and RT, with or without hormone treatment, as well as multimodality treatment combining surgery or RT with systemic therapy.⁷⁻⁹ RT with radical intent is a first-line treatment for localised and locally advanced prostate cancer.⁸ Intensity-modulated RT (IMRT) with image guidance RT is considered the gold standard form of external beam RT (EBRT).¹⁰ Of the circa 18000 men identified as having received radical RT for prostate cancer in England and Wales between April 2018 and March 2019, over 90% were treated with IMRT.¹¹ While stereotactic body RT (SBRT, or stereotactic ablative radiotherapy (SABR)) is not currently routine practice in the UK, its use is increasing, and it is now delivered in several National Health Service (NHS) centres.¹² Circa 95% of UK men with intermediate-risk disease receive a hypofractionated radiotherapy regimen.¹¹

The success and clinical outcomes of RT depend on several factors, including radiation dose to the tumour and the extent of irradiation affecting nearby normal tissue, particularly the rectum.¹⁰ Dose-escalated EBRT is a highly effective curative treatment, with higher doses providing better biochemical control.¹³ Higher doses can, however, increase radiation toxicity to nearby tissues. Despite substantial advancements in RT, acute and reversible, as well as rare but severe, long-term adverse effects of radiation toxicity such as urinary and bowel incontinence remain problematic. The National Prostate Cancer Audit reported that 11% of patients with prostate cancer experienced ≥ 1 severe gastrointestinal complication within 2 years after radical RT. This outcome factor derived from hospital records data is defined as a confirmed diagnosis of radiation toxicity \geq grade 2 according to National Cancer Institute Common Toxicity Criteria for Adverse Events in addition to a documented procedure to the large bowel.^{11 14} Late \geq grade 2 gastrointestinal toxicity has been explored in numerous randomised clinical trials. The 2016 Hypofractionated versus conventionally fractionated radiotherapy for patients with prostate cancer trial found an incidence of gastrointestinal toxicity at 3 years of 17.7% in standard fractionation and 21.9% in hypofractionation.¹⁵ In 2017, results from the ASCENDE-RT (Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy) trial showed a cumulative incidence of 5-year gastrointestinal side effects ranging from 20.2% (dose-escalated EBRT) to 31.3% (low dose rate (LDR) prostate BT).¹⁶ Due to its proximity to the prostate, the anterior rectal wall is especially vulnerable to irradiation effects, and the rectum is a dose-limiting organ at risk.¹⁷

Hydrogel spacers

One way of reducing the unwanted radiation dose to the rectum is by increasing the space between the prostate and the rectal wall. This can be achieved by use of a rectal spacer, with three currently indicated for use during RT for prostate cancer in the UK: biodegradable balloons, hyaluronic acid gel and polyethylene glycol (PEG)

hydrogel.¹⁸ In the UK, the use of biodegradable spacers to reduce rectal toxicity during RT for prostate cancer is accepted (IPG590) by NICE, based on safety and efficacy data on the use of PEG hydrogel spacers.¹⁸ Use of rectal hydrogel spacers has been evaluated in a single-blind, phase III trial in image guided IMRT (n=222).¹⁹ The spacer-placement success rate was 99%, and no device-related adverse events occurred.¹⁹ Late (3–15 months) rectal toxicity severity was significantly reduced in the spacer group.¹⁹ At 3-year follow-up, decreased bowel toxicity and fewer declines in urinary and bowel quality of life were observed in the spacer group (41% men in the control group experienced a minimally important difference (MID) in decline in bowel quality of life vs 14% in the spacer group; p=0.002). The risk of large decline (twice the MID) was 21% (control) versus 5% (spacer; p=0.02) in bowel quality of life and 23% (control) versus 8% (spacer; p=0.02) in urinary quality of life, respectively.²⁰

Lack of routine reimbursement has led to restricted patient access to hydrogel spacers in the UK. Therefore, there is a requirement to prioritise patients for hydrogel spacer use in the UK, and attempts have been made to identify optimal usage. A secondary analysis of the hydrogel spacer trial data tried to identify the patient subgroups most and least likely to benefit from the intervention but found generally homogeneous results in bowel quality of life with benefits in all assessed subgroups.²¹

The aim of this study was to identify consensus on patient prioritisation for rectal hydrogel spacer use during RT for the treatment of prostate cancer in the UK.

METHODS

The Delphi technique and panel experts

The Delphi technique is a structured, iterative, multi-stage process using rounds of questionnaires to collect opinions and to stepwise develop consensus among a predefined panel of experts.²² For this study, experts were approached and asked to participate in the panel based on being a UK radiation oncologist or urologist having experience with rectal hydrogel spacers. To ensure a diverse panel, experts were sought to represent different geographies within the UK and use different types of RT modalities. There is no defined optimal panel size for a Delphi study,²³ but the selection of an odd number of experts ensured that a majority outcome could be reached.

Steps in the Delphi process

There is no fixed number of rounds in a Delphi survey.²³ As depicted in [figure 1](#), our study adopted a five-stage approach to elicit consensus, consisting of two preadvisory board questionnaires administered through a web-based survey programme, two virtual advisory board discussions and a final concluding questionnaire.

The first questionnaire provided some background information on the experts, such as their most used RT modalities and open-ended questions to capture a broad understanding. The open-ended questions related to key

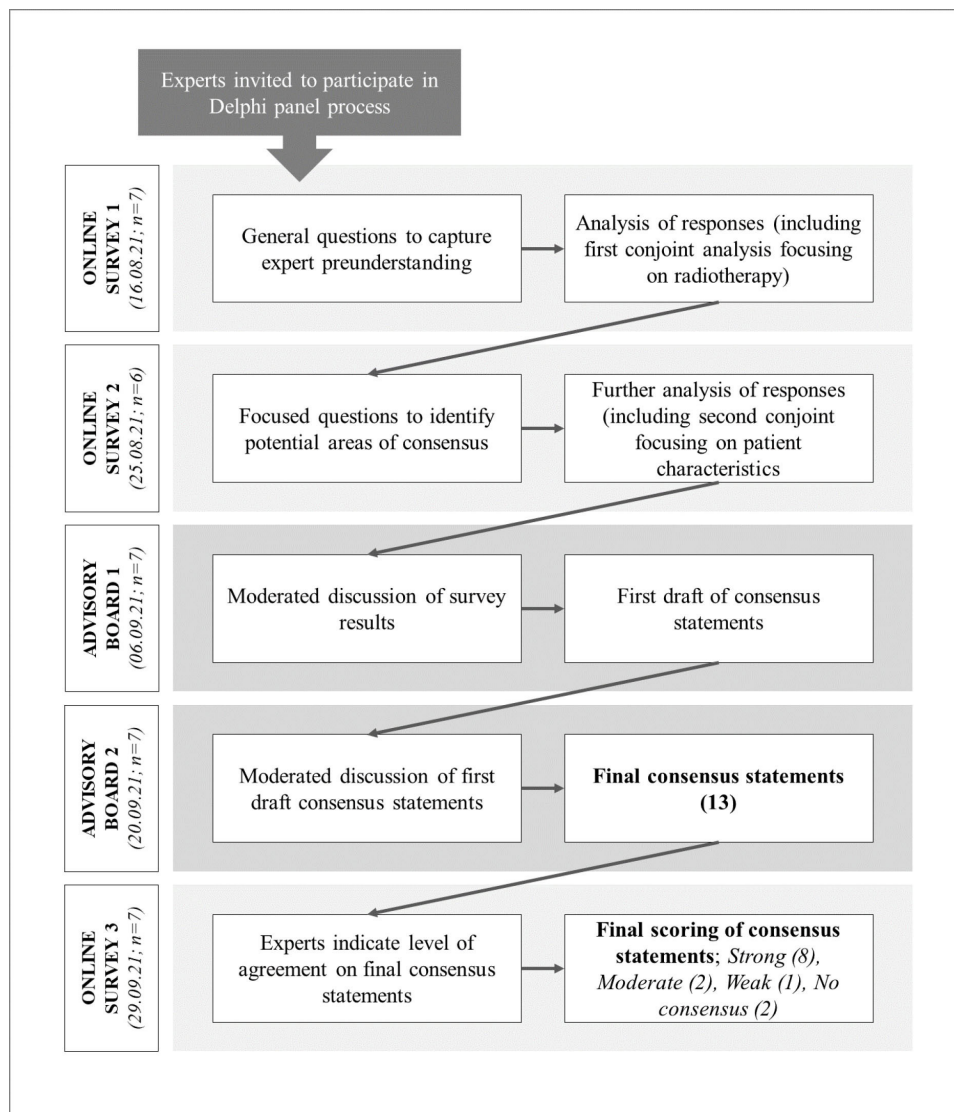


Figure 1 Overview of Delphi panel process.

treatment aims, which patient and treatment characteristics to consider when prioritising hydrogel spacer, factors typically deterring them from recommending hydrogel spacer use and factors predictive for toxicity. Additionally, experts were asked to rank treatment modalities in order of how much patient benefit they would expect from hydrogel spacer use, on a scale from 0 (no patient benefit) to 100 (maximal patient benefit).

In the second questionnaire, the responses to the open-ended questions from the previous questionnaire were presented, and the experts asked to rank them by order of importance. In addition to follow-up questions, the second questionnaire included questions on perceived barriers to hydrogel spacer use.

Analysis and scoring

Qualitative content analysis was used to analyse responses to open-ended questions. Two researchers independently analysed responses and interpreted consensus. At the advisory board meetings, results from the questionnaires were presented together with initial drafted consensus

statements for discussion. Then followed moderated discussions that led to revisions of the consensus statements. In the final online questionnaire, the consensus statements were presented, and the experts asked to select a level of agreement: ‘I fully agree’, ‘I partially agree’ or ‘I disagree’. On selecting ‘I partially agree’, experts were asked to give a comment and/or update the wording of the statement. The responses were linked to an agreement score, based on the answer selected, and the comment given if ‘I partially agree’ was selected (table 1).

Table 1 Consensus statement scoring key

Score	Answer selected	Description
4	‘I fully agree’	
3	‘I partially agree’	With minor word change
2	‘I partially agree’	With minor change to statement interpretation/meaning
1	‘I disagree’	

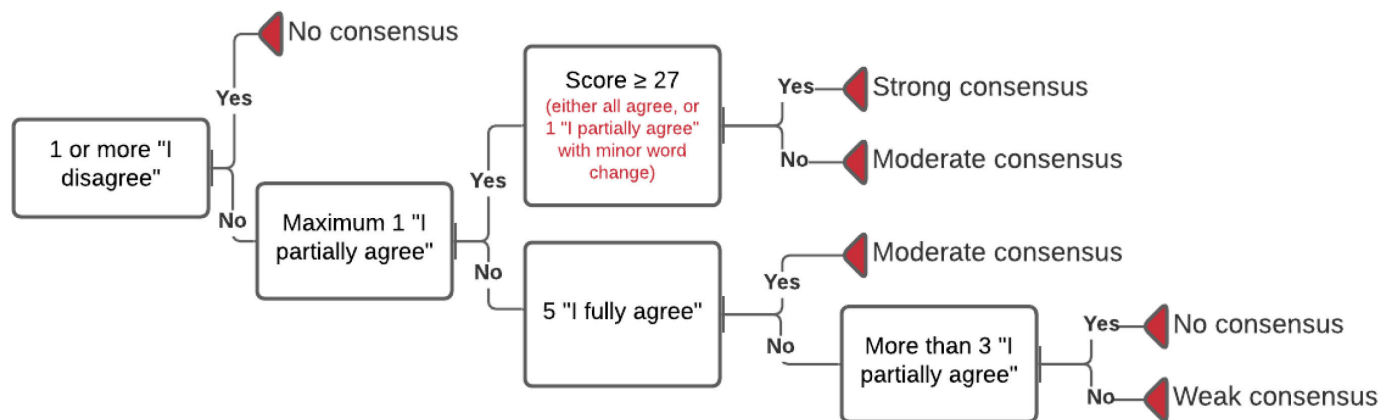


Figure 2 Consensus statement scoring, decision tree. Strong consensus could only be reached if all experts indicated that they ‘fully agree’ or all except one ‘fully agree’, with the last respondent ‘partially agree’ with only a minor word change (score ≥ 27). Moderate consensus could only be reached if at least five respondents ‘fully agree’ and with no ‘disagree’. Weak consensus was reached where a maximum of three respondents ‘Partially agree’ and with no ‘disagree’. No consensus was indicated where at least one respondent ‘disagree’ or if four or more respondents ‘partially agree’.

Consensus definitions vary between studies,^{24–28} with percent agreement being one of the more common approaches.²⁸ Based on the results of our final online survey, statements were categorised into four levels of consensus (strong, moderate, low and no consensus). This study scored the level of consensus in terms of percent agreement, and additionally that consensus could not be reached in case any expert disagreed with a statement. **Figure 2** depicts the consensus statement scoring for this study. Only statements grouped as either strong or moderate are considered statements where consensus was reached. Weak or no consensus mean that there was still substantial discussion or divergence of opinion among the experts.

Consent, privacy and data security

The panel experts were informed about and consented to the full Delphi process, including length and time of surveys and details on the data collected, stored and deleted. The retention periods of collected data were predefined. Questionnaire responses were anonymised and securely stored on the survey software provider’s server in Germany. Audio recordings were stored for 60 days on the conference provider’s European-Union-based server. All experts were contracted for this study and reimbursed at fair, local market rates for their time commitment during the Delphi process.

Patient and public involvement

No patients involved.

RESULTS

Panel expert characteristics

All approached experts agreed to participate (n=7). Details on the panel experts’ treatment practices are presented in **table 2**. The majority of the panel (n=6) exclusively use rectal hydrogel spacers in their practices. One uses rectal hydrogel spacers as well as biodegradable

balloons. Participation rates were high, with only one dropout (one expert did not complete the second questionnaire but participated in all other steps).

Key treatment aims, besides curing or controlling cancer and increasing overall survival, were to minimise the risk of side effects and toxicity.

Questionnaire outcomes shaping the consensus statement discussion

Questionnaire outcomes showed that the panel estimated considerably less toxicity in patients with hydrogel spacer, as compared with those without (**figure 3**). All experts

Table 2 Panel experts treatment practice

Geographical setting, n (%)	
England	5 (57)
Northern Ireland	1 (14)
Wales	1 (14)
Public or private setting, n (%)	
Public only	1 (14)
Private only	0 (0)
Both	6 (86)
Most frequently used RT modalities, % of patients (N experts using modality)	
IMRT	25–95 (6)
EBRT (not specified)	90 (1)
IMRT and HDR BT boost	15–30 (2)
SBRT	45 (1)
BT monotherapy (LDR)	10–20 (2)
PBT	10 (1)

BT, brachytherapy; EBRT, external beam radiation therapy; HDR, high dose rate; IMRT, intensity-modulated radiation therapy; LDR, low dose rate; PBT, proton beam therapy; SBRT, stereotactic body radiation therapy.

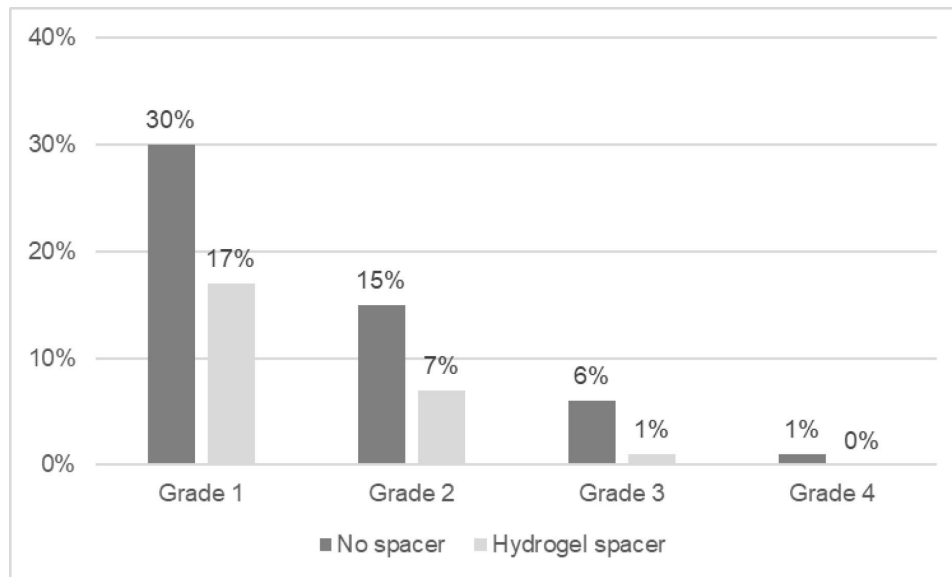


Figure 3 Expected level of late (after 3 months) rectal toxicity in patients with and without hydrogel spacer.

agreed that hydrogel spacers reduce grade 1 and 2 late rectal toxicity, 86% agreed that it reduces grade 3 toxicity and 71% grade 4 toxicity.

The panel considered toxicity a considerable issue and underlined that also low-grade toxicity-related adverse events may significantly worsen patient’s lives:

I ask them [my patients], when you’re out and about, is the first thing you think of where the toilet is?... And a remarkable number of patients say yes to that question, and it is affecting their quality of life.

In the first questionnaire, the panel estimated that an average of 83% (SD: 13%) patients who could potentially benefit from a hydrogel spacer were denied access. Throughout the discussions, patient access in general and equal access in particular were central themes. The panel voiced their concern, for example, regarding differences between NHS and private practice:

In my private practice, every patient gets it [hydrogel spacer] unless there is a reason why they should not get it. Whereas in my NHS practice, unfortunately no patient gets it, unless there is a reason why they should get it.

The main barrier to hydrogel spacer use was funding and resource constraints, followed by lack of trained staff.

The ideal way to go would be to offer it to every eligible patient. But given that this is not currently feasible in our centre, there has to be some kind of categorisation.

As seen in figure 4, a trend towards hypofractionated external beam regimens, with potential increased bowel dose and toxicity being associated with more potential benefit for spacers was apparent. This was also reflected in the outcome of the conjoint analysis. The absolute

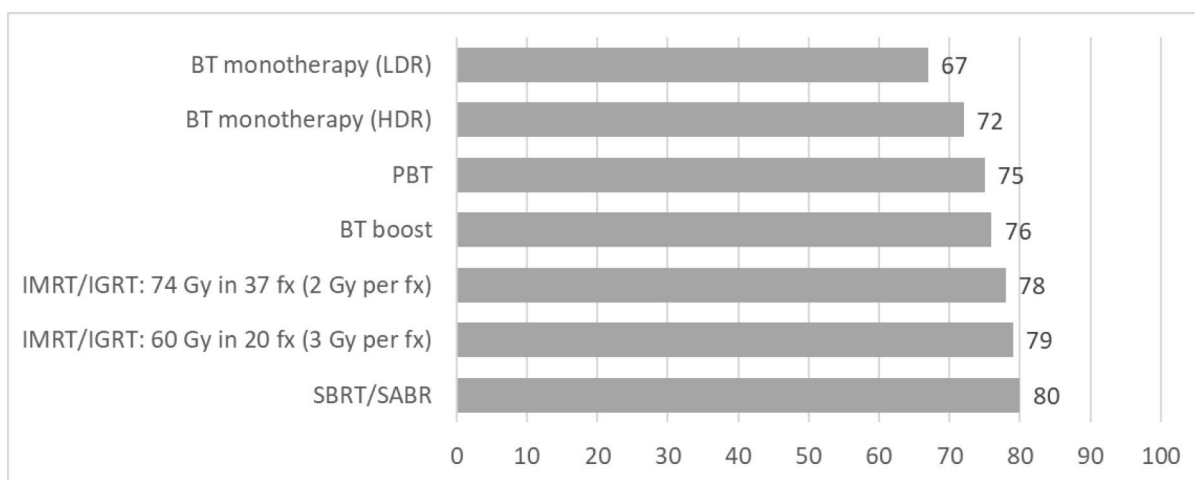


Figure 4 Expected patient benefit from hydrogel spacer use by treatment modality. BT, brachytherapy; HDR, high dose rate; LDR, low dose rate; IGRT, image guided radiation therapy; IMRT, intensity-modulated radiation therapy; PBT, proton beam therapy; SABR, stereotactic ablative radiotherapy; SBRT, stereotactic body radiation therapy.

variation between expected benefit was, however, relatively low, ranging from 67 (BT monotherapy LDR) to 80 (SBRT/SABR) on average. This was reflected in later discussions, where experts agreed that RT modality is not the main consideration when prioritising patients for hydrogel spacer use.

When asked about patient characteristics to consider when deciding whether to recommend using hydrogel spacer the experts gave a wide range of suggestions, including comorbidities (age, diabetes, high bleeding risk, hip prosthesis, inflammatory bowel disease and rectal and bowel problems and normal erectile function), cancer stage, localisation and heavy smoking. This was narrowed down in subsequent discussion, with general agreement that patients with certain comorbidities (diabetes and inflammatory bowel disease) or on anticoagulation may have higher benefit from hydrogel spacers.

Consensus statements

On being shown the results of the questionnaires, two rounds of moderated discussion followed, resulting in 13 consensus statements. These statements were subsequently voted on in a final questionnaire, and a final scoring was assigned as described in the Method section.

The following eight statements reached strong consensus:

- ▶ Our consensus opinion is that for treatments with curative intent, focus should be on minimising toxicity and the risk of side effects.
- ▶ Our consensus opinion is that use of spacers in eligible patients significantly reduces radiation dose to the rectum and toxicity-related adverse events.
- ▶ Our consensus opinion is that despite meeting rectal dose constraints, too many patients continue to experience rectal toxicity.
- ▶ Our consensus opinion is that certain grade one toxicity-related adverse events (bowel frequency and urgency, diarrhoea, flatulence, radiation cystitis, radiation proctitis, rectal bleeding and rectal mucus) can still have a significant impact on patient quality of life.
- ▶ Our consensus opinion is that any toxicity grading system in use should be complemented by patient-reported outcomes.
- ▶ Our consensus opinion is that patients receiving long-term anticoagulation therapy with medications such as direct oral anticoagulants (DOACs) (The reason for prescribing the DOAC, rather than the medication itself, is more important for the decision. All patients on DOACs, except for cardiac stent and prosthetic valve replacement patients, may be able to safely pause their anticoagulation.) should be considered for spacer use if their anticoagulation can be safely paused.
- ▶ Our consensus opinion is that spacers are useful in eligible patients with T1-T2 disease. Spacer use in patients with T2+ disease should not be excluded but should be assessed on an individual basis by a team proficient in inserting spacers.

- ▶ Our consensus opinion is that patients should have the opportunity to take part in the discussion regarding the use of a spacer.²⁹

For the following two statements, moderate consensus was reached. Each statement is followed by an explanation on why strong consensus was not reached.

- ▶ Our consensus opinion is that a higher benefit of spacers is expected in eligible patients with certain comorbidities (anticoagulation, diabetes, inflammatory bowel disease (ulcerative colitis and Crohn's disease)) and/or longer expected overall survival.

Six experts (86%) fully agreed with the statement. One expert (14%) only partially agreed and suggested removing 'and/or longer expected overall survival'. This was deemed a change to the statement interpretation.

- ▶ All eligible radiotherapy patients should have equal opportunity to access spacers, independent of socioeconomic factors.

Five experts (71%) fully agreed with the statement. While there was an overall agreement that lack of equality in access to spacers is currently an important issue, two experts (29%) had rewording suggestions that would have impacted the statement interpretation. One proposed to add more detail on eligibility and to add that patients suitable for a spacer implant should have access, irrespective of whether they can afford it. The other expert expressed some uncertainty regarding the term 'socioeconomic factors' and would have preferred the wording 'irrespective of post-code'.

Statements where no consensus was reached

One statement was categorised as a weak consensus statement:

- ▶ While we support the use of spacers in all eligible patients, our consensus opinion is that if resource constraints exist, patients receiving ultrahypofractionated or hypofractionated radiotherapy should be prioritised for access to a spacer.

Four experts (57%) fully agreed with the statement. The remaining three (43%) partially agreed but had additional comments. One expert expressed that individual risk factors should be considered, rather than the RT modality. The second expert agreed on the need to identify a group at higher risk of rectal toxicity and suggested combination of RT modality considerations and patient characteristics (eg, age) and comorbidities. The third respondent only agreed that patients receiving ultrahypofractionated RT should be prioritised.

For the following two statements, no consensus was reached.

- ▶ Our consensus opinion is that for patients with anticipated short overall survival but who will receive radical radiotherapy, use of a spacer should only be considered after careful evaluation of potential benefit.

Three experts (43%) fully agreed. Four (57%) partially agreed but had additional comments. Two experts made the point that it is unlikely that patients with short anticipated overall survival would be indicated for radical

radiotherapy. Two experts expressed uncertainty with the wording 'overall survival'. One of them suggested a rewording that some carefully selected patients with short expected survival who are offered radical radiotherapy may benefit from spacer use after careful consideration. The second expressed that the statement was too unclear. Additionally, in subsequent discussions, the experts agreed that the term 'anticipated shorter life expectancy' would have been preferred over 'anticipated short overall survival', so as not to imply that the use of hydrogel spacers affects survival. On subsequent discussion, experts agreed that the statement would have been improved by adding 'and side effects' to the end of the statement.

► Our consensus opinion is that there are a limited number of patients with risk factors, or combination of risk factors, in which use of a spacer should only be considered after careful evaluation of potential benefits.

Four experts (57%) fully agreed, two (29%) partially agreed and one (14%) disagreed. Those who partially agreed expressed that an addition should be made to the statement that the majority of patients who receive radical RT would also be suitable for a spacer, noting that patients who are not fit enough for a spacer likely are also not fit for RT. The second partially agreeing expert wanted to add a recommendation to discuss such cases with a mentor with extensive experience in spacer insertion. On subsequent discussion, experts agreed that the statement would have been improved by adding 'and side effects' to the end of the statement.

DISCUSSION

Statement of principal findings

There was strong consensus that rectal toxicity is a considerable issue and that minimising the risk of radiation side effects is an important treatment aim. Rectal hydrogel spacers can reduce the toxicity burden and benefit patients undergoing radical RT for the treatment of prostate cancer in the UK. Currently, the NHS does not routinely fund hydrogel spacers. Limited funding leads to limited resources and therefore limited access. Experts estimated that, on average, 83% of their patients that could benefit from a spacer are not currently getting access. There was moderate consensus that a higher benefit is expected in patients on anticoagulation, patients with diabetes and patients with inflammatory bowel disease (ulcerative colitis or Crohn's disease). However, experts expected the majority of patients to benefit from use of a spacer, and it was not possible to reach consensus on those patients with lower expected benefit. Key takeaways from discussions around statements where no consensus was reached are that individual patient characteristics are more important for informing the decision on whether to prioritise the use a spacer than the RT regimen selected. However, a higher level of benefit from spacer use is expected with ultrahypofractionated RT compared with standard RT, a conclusion in line with current clinical evidence.³⁰

Meaning of the study: possible explanations and implications for clinicians and policy makers

Currently, patient selection is driven by limitations in the healthcare system rather than patient needs. This highlights the importance of developing guidance on spacer use to ensure fair and equal access to healthcare. The COVID-19 pandemic has lengthened already substantial NHS waiting times, further exacerbating issues with access and underscoring the need for formal guidance. Additionally, practical issues (eg, availability of trained staff and theatre capacity) need to be considered when preparing a clinic to start using hydrogel spacers. As is important for all techniques to be introduced, audit of practice and quality improvement is recommended.

Strengths and weaknesses

This study only included seven experts who are all experienced users of hydrogel spacers. Naturally, a broader selection of experts could have resulted in different answers. However, including non-users as panel experts would not have been feasible for the purposes of this study, as they would have not possessed the relevant experience required. Additionally, the RT modality used by panel members could influence their view on when to prioritise hydrogel spacer use. However, the diversity of the panel in terms of modalities used likely safeguarded the balance of the resulting consensus.

The main strengths of this study are the scientific rigour applied following a well-defined and proven Delphi methodology and the experience and diversity of the panel. The Delphi method allowed gathering insights from leading experts in the field from different UK countries using a mix of RT modalities, while reducing bias and separating the evaluation by tasking two independent researchers with analysis and scoring.

Comparison with other studies

To the best of our knowledge, no previous attempts have been done to establish consensus for rectal hydrogel spacer use in the UK. A study published in 2016 used a model-based approach to identify patients expected to benefit the most from implantable rectum spacers among 26 patients with localised prostate cancer treated at a German hospital. The clinical risk factors found relevant were anticoagulant use, hormonal therapy, antihypertensive use, diabetes, haemorrhoids, pelvic nodal RT and prior abdominal surgery.³¹ Single-centre studies of rectal spacers in Crohn's and ulcerative colitis patients suggest benefit of spacers.^{32 33} One study conducted secondary analyses of a single-blinded, phase III randomised trial, with the aim of identifying patients benefitting the least from hydrogel rectal spacer during prostate RT.²¹ In line with this study, no subgroup without potential benefits of hydrogel spacers could be identified. The benefit of hydrogel spacers perceived by the experts is in line with current clinical evidence.²⁰

Unanswered questions and future research

As well as hydrogel rectal spacers, other materials including hyaluronic acid, saline-filled balloon and

human collagen have been used to create space between the rectum and prostate. Readers should familiarise themselves with the available evidence on each product when considering between the different options. This study offers guidance to later adopters of rectal hydrogel spacers, building on the expertise of leading UK radiation oncologists and urologist. Future research should focus on implementing formal guidance on hydrogel spacer use and strive towards reaching a consensus on patient prioritisation. A larger follow-up consensus study would be of value, asking all UK domain experts their opinion on the consensus statements. With growing interest in hydrogel spacers, it is increasingly important to study the impact of the quality of the implant. There is an ongoing debate on what a good implant is and how it is measured. Similarly, it would be valuable to reach an agreement on which toxicity data to generate and follow-up through including hydrogel spacers in cancer treatment trials, or through the development of a quality registry. Finally, it is of utmost importance to investigate the availability and equality in access to spacers. For this aim to be reached, further cost-effectiveness research and a continued discussion on willingness to pay should be undertaken. Analyses of spacers in prostate cancers have shown cost-effectiveness in certain radiation modalities in US^{34,35} and Dutch³⁶ contexts.

CONCLUSION

Rectal toxicity is a considerable issue, and focus should be on minimising side effects of curative treatment. There is a strong and general agreement that all patients with prostate cancer undergoing radical RT have the potential to benefit from hydrogel spacers. Currently, not all patients who could potentially benefit can access hydrogel spacers, and access is unequal. Implementation of the 10 strong and moderate consensus recommendations would likely help prioritise and equalise access to rectal spacers for patients in the UK. In particular, prioritising access towards patients on anticoagulation, with diabetes, and/or patients with inflammatory bowel disease would, in our opinion, be a strong starting position.

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Contributors EW conceptualised the idea. RS and AHH designed and ran the questionnaires and implemented data protection measures. EW reviewed the study design. AHH and RS analysed the responses. RS moderated the advisory boards. SJ, JAT, AE, AB, PD, CP and HAP responded to the questionnaires and participated in the advisory boards. AHH and RS drafted the manuscript, in collaboration with SJ, JAT, AE, AB, PD, CP and HAP. All authors critically reviewed the manuscript outline and manuscript drafts. All authors approved the final manuscript. RS acts as guarantor of this work.

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Competing interests RS is the owner of Coreva Scientific, a health economics and value-based healthcare consultancy that focuses on medical devices. AHH is an employee of Coreva Scientific. Coreva Scientific received consultancy fees from Boston Scientific for work related to this manuscript. The authors did not receive direct payment as a result of this work outside of their normal salary payments. EW is an employee of Boston Scientific.

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REFERENCES

- Sung H, Ferlay J, Siegel RL, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209–49.
- Cancer Research UK. Prostate cancer statistics. Available: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer#heading-Zero> [Accessed 23 Nov 2021].
- Prostate Cancer UK. Prostate information. About prostate cancer 2019. Available: <https://prostatecanceruk.org/prostate-information/about-prostate-cancer> [Accessed 23 Nov 2021].
- Hamdy FC, Donovan JL, Lane JA, *et al*. 10-Year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *N Engl J Med* 2016;375:1415–24.
- Hofmarcher T, Lindgren P, Wilking N, *et al*. The cost of cancer in Europe 2018. *Eur J Cancer* 2020;129:41–9.
- Nazim SM, Fawzy M, Bach C, *et al*. Multi-disciplinary and shared decision-making approach in the management of organ-confined prostate cancer. *Arab J Urol* 2018;16:367–77.
- Cancer Research UK. Prostate cancer treatment statistics. Available: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer/diagnosis-and-treatment> [Accessed 26 Oct 2021].
- National Institute for Health and Care Excellence (NICE). Prostate cancer: diagnosis and management NICE guideline 2019.

- 9 Moris L, Cumberbatch MG, Van den Broeck T, *et al.* Benefits and risks of primary treatments for high-risk localized and locally advanced prostate cancer: an international multidisciplinary systematic review. *Eur Urol* 2020;77:614–27.
- 10 Mottet N, van den Bergh RCN, Briers E, *et al.* EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate Cancer—2020 update. Part 1: screening, diagnosis, and local treatment with curative intent. *Eur Urol* 2021;79:243–62.
- 11 National Prostate Cancer Audit (NPCA). Annual report 2020 results of the NPCA prospective audit in England and Wales for men diagnosed from 1 April 2018 to 31 March 2019 2021.
- 12 Prostate Matters. Where to access SBRT. Available: <https://prostatematters.co.uk/prostate-cancer/where-to-access-sbirt/> [Accessed 26 Nov 2021].
- 13 Miller LE, Efstathiou JA, Bhattacharyya SK, *et al.* Association of the placement of a perirectal hydrogel spacer with the clinical outcomes of men receiving radiotherapy for prostate cancer: a systematic review and meta-analysis. *JAMA Netw Open* 2020;3:e208221.
- 14 National Prostate Cancer Audit (NPCA). Annual report 2020 methodology supplement 2021.
- 15 Aluwini S, Pos F, Schimmel E, *et al.* Hypofractionated versus conventionally fractionated radiotherapy for patients with prostate cancer (HYPRO): late toxicity results from a randomised, non-inferiority, phase 3 trial. *Lancet Oncol* 2016;17:464–74.
- 16 Rodda S, Tyldesley S, Morris WJ, *et al.* ASCENDE-RT: an analysis of treatment-related morbidity for a randomized trial comparing a low-dose-rate brachytherapy boost with a dose-escalated external beam boost for high- and intermediate-risk prostate cancer. *Int J Radiat Oncol Biol Phys* 2017;98:286–95.
- 17 Afkhami Ardekani M, Ghaffari H. Optimization of prostate brachytherapy techniques with polyethylene glycol-based hydrogel spacers: a systematic review. *Brachytherapy* 2020;19:13–23.
- 18 National Institute for Health and Care Excellence (NICE). Interventional procedures programme equality impact assessment IPG590 biodegradable spacer insertion to reduce rectal toxicity during radiotherapy for prostate cancer 2016.
- 19 Mariados N, Sylvester J, Shah D, *et al.* Hydrogel spacer prospective multicenter randomized controlled pivotal trial: dosimetric and clinical effects of perirectal spacer application in men undergoing prostate image guided intensity modulated radiation therapy. *Int J Radiat Oncol Biol Phys* 2015;92:971–7.
- 20 Hamstra DA, Mariados N, Sylvester J, *et al.* Continued benefit to rectal separation for prostate radiation therapy: final results of a phase III trial. *Int J Radiat Oncol Biol Phys* 2017;97:976–85.
- 21 Quinn TJ, Daignault-Newton S, Bosch W, *et al.* Who benefits from a prostate rectal spacer? secondary analysis of a phase III trial. *Pract Radiat Oncol* 2020;10:186–94.
- 22 Keeney S, Hasson F, McKenna H. Consulting the oracle: ten lessons from using the Delphi technique in nursing research. *J Adv Nurs* 2006;53:205–12.
- 23 Keeney S, McKenna H, Hasson F. *The Delphi technique in nursing and health research*. John Wiley & Sons, 2011.
- 24 Courtenay M, Deslandes R, Harries-Huntley G, *et al.* Classic e-Delphi survey to provide national consensus and establish priorities with regards to the factors that promote the implementation and continued development of non-medical prescribing within health services in Wales. *BMJ Open* 2018;8:e024161.
- 25 Howarth E, Vainre M, Humphrey A, *et al.* Delphi study to identify key features of community-based child and adolescent mental health services in the East of England. *BMJ Open* 2019;9:e022936.
- 26 Snape D, Kirkham J, Preston J, *et al.* Exploring areas of consensus and conflict around values underpinning public involvement in health and social care research: a modified Delphi study. *BMJ Open* 2014;4:e004217.
- 27 Taylor RM, Feltbower RG, Aslam N, *et al.* Modified international e-Delphi survey to define healthcare professional competencies for working with teenagers and young adults with cancer. *BMJ Open* 2016;6:e011361.
- 28 Diamond IR, Grant RC, Feldman BM, *et al.* Defining consensus: a systematic review recommends methodologic criteria for reporting of Delphi studies. *J Clin Epidemiol* 2014;67:401–9.
- 29 General Medical Council (GMC). Good medical practice 2019. Available: https://www.gmc-uk.org/-/media/documents/good-medical-practice-english-20200128_pdf-51527435.pdf
- 30 Jain S. NCT04905069: effectiveness of the SpaceOAR Vue system in subjects with prostate cancer being treated with stereotactic body radiotherapy (sabre), 2021. Available: <https://clinicaltrials.gov/ct2/show/NCT04905069?term=spaceoar&draw=2&rank=1>
- 31 Vanneste BGL, Hoffmann AL, van Lin EN, *et al.* Who will benefit most from hydrogel rectum spacer implantation in prostate cancer radiotherapy? A model-based approach for patient selection. *Radiother Oncol* 2016;121:118–23.
- 32 Vanneste BGL, Van Limbergen EJ, Marcelissen T, *et al.* Is prostate cancer radiotherapy using implantable rectum spacers safe and effective in inflammatory bowel disease patients? *Clin Transl Radiat Oncol* 2021;27:121–5.
- 33 Vanneste BGL, Van Limbergen EJ, van de Beek K, *et al.* A biodegradable rectal balloon implant to protect the rectum during prostate cancer radiotherapy for a patient with active Crohn's disease. *Tech Innov Patient Support Radiat Oncol* 2018;6:1–4.
- 34 Hutchinson RC, Sundaram V, Folkert M, *et al.* Decision analysis model evaluating the cost of a temporary hydrogel rectal spacer before prostate radiation therapy to reduce the incidence of rectal complications. *Urol Oncol* 2016;34:291.e19–291.e26.
- 35 Levy JF, Khairnar R, Louie AV, *et al.* Evaluating the cost-effectiveness of hydrogel rectal spacer in prostate cancer radiation therapy. *Pract Radiat Oncol* 2019;9:e172–9.
- 36 Vanneste BGL, Pijls-Johannesma M, Van De Voorde L, *et al.* Spacers in radiotherapy treatment of prostate cancer: is reduction of toxicity cost-effective? *Radiother Oncol* 2015;114:276–81.