NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: IP1919 Intraoperative electron beam radiotherapy for locally advanced and locally recurrent colorectal cancer

Your information

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Job title:	Professor of Surgical Oncology; Honorary consultant General and colorectal surgeon
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Professional organisation or society membership/affiliation:	GMC, ACPGBI, BACR, EACR
Nominated/ratified by (if applicable):	Click here to enter text.
Registration number (e.g. GMC, NMC, HCPC)	4212164

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☒ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

Please note that questions 10 and 11 are applicable to the Medical Technologies Evaluation Programme (MTEP). We are requesting you to complete these sections as future guidance may also be produced under their work programme.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology?	Yes I am familiar with it and have experience of using the technology in the USA and Europe while on fellowships, and now since 2017 at the institution I practice in clinically in the UK namely University Hospital Southampton where we have been applying the technique.
	Have you used it or are you currently using it? − Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? − Is this procedure/technology performed/used by clinicians in specialities other than your own? − If your specialty is involved in patient selection or referral to another specialty for this	This procedure is not used to my knowledge outside of Southampton in the UK, however it is standard of care in Europe and North America and part of the EU ESTRO guidelines and the North American NCCN cancer guidelines for the indications described above as well as others. In the UK there is lots of interest in it as a modality amongst units that offer complex pelvic exenteration surgery for locally advanced and locally recurrent rectal cancer, as well as units interested in advanced pancreatic cancer surgery and sarcoma surgery. It would be very easy to take this technology up in the NHS. Prior to developing the technology we had referred patients abroad at times for this in highly selected cases both as part of and independent to the IFR program.

	procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure. I have done clinical research on this procedure involving patients or healthy volunteers. Other (please comment) Currently also conducting a clinical trial on the subject matter.
3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Radiotherapy by electron beams is not innovative in itself and is a cornerstone treatment modality in the NHS and internationally for cancer and especially advanced and recurrent rectal cancer. Intraoperative radiotherapy also is not in itself novel in the NHS, in that this was part of the process of treatment with kilovoltage devices (as opposed to megavoltage devices) in breast cancer as part of the TARGIT trial. However Intraoperative radiotherapy with Electron beams using a mobile self shielded Linac for locally advanced and locally recurrent rectal cancer is innovative in the NHS (internationally this is regarded as a standard of care however – see notes above) in that it allows the combination of maximal surgery with synchronous intraoperative radiotherapy which is not conducted in the UK. This facilitates several advantages for patients and their treatment in that firstly it allows greater treatment dose escalation while synchronously protecting and shielding radiation sensitive structures during the surgical procedure; secondly it facilitates the possibility of de-escalation of certain ultra-radical operations to less radical procedures with the concerning tumour margin being mitigated for by radiotherapy rather than further margin extensions into non-expendable territories potentially; and thirdly it allows the consideration and testing for de-escalation of neoadjuvant radiation protocols at times. Nevertheless, intraoperative electron beam radiotherapy for locally advanced and locally recurrent rectal cancer is in my opinion only a minor variation on concept and approach towards treatment and dose escalation in radiotherapy management of these tumours.

		Established practice and no longer new. – yes internationally this is now established practice and not new (although not so in the NHS),
4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	As an addition only at present and not as a replacement, although it helps open the doors to trials that may allow de-escalation of neoadjuvant chemoradiotherapy regimes potentially in the future.

Current management

5	Please describe the current standard of care that is used in the NHS.	For locally advanced rectal cancer (LARC), the UK standard of care would represent Neoadjuvant chemotherapy, neoadjuvant chemoradiotherapy, followed by extended margin surgery. IOERT would be an addition at the time of surgery for LARC and would not otherwise change the standard of care. For Locally recurrent rectal cancer (LRRC), the standard of care in the UK varies between neoadjuvant chemotherapy followed by extended margin surgery vs neoadjuvant chemotherapy followed by reirradiation followed by extended margin surgery. In both cases IOERT would be an extra addition to the time of surgery. Consequently, whether combined with conventional external beam Radiotherapy in long course chemoradiotherapy or with reirradiation, IOERT represents an extra treatment boost for both LARC and LRRC, allowing dose escalation without side effects to

		deep radiation sensitive structures which are shielded at the time of surgery during delivery of the treatment.
6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	No. the closest technology represents SABR treatment which cannot be given at the time of surgery and is occasionally used for the treatment of disease recurrence or involved margins. However, in the management of disease recurrence, this is NOT combined with surgery and given the heterogenous nature of cancer response to radiotherapy and neoadjuvant treatments many will not be cured and experience recurrence/persistence of tumour despite SABR treatment. In the management of positive margins at surgery, treating patients with SABR post operatively exposes patients to the same risks of external beam radiotherapy and damage to surrounding structures such as the ureter or small bowel many of whom will be adjacent to the zone of treatment. Finally, it is important t note that SABR is a “relatively” new technique and has not been tested in randomised high quality studies in these settings. The comparison with SABR is timely also as it has seemingly gained traction and commissioning despite the lack of high quality randomised trials in the field. IOERT should technically be subjected to the same standards and in fact has a much larger and more mature data set associated with its use.

Potential patient benefits and impact on the health system

7	What do you consider to be the potential benefits to patients from using this procedure/technology?	Abbreviations used below: IOERT – Intraoperative Electron Beam Radiotherapy As described above, radiotherapy is clearly a cornerstone treatment modality in the management of advanced solid organ malignancies, and especially locally advanced and locally recurrent rectal cancers. Historically, the greater the dose of radiotherapy given, the more cancer cells have been eradicated. However the dose that can be safely delivered is limited by radiation damage to surrounding structures, and this especially applies for deep-seated tumours such as in the pelvis. Consequently, the efficacy of radiotherapy can be improved by either increasing the dose or protecting radiation-sensitive structures, and IOERT in the deep pelvis utilises both these effects to achieve more radical local treatment, and therefore offers a therapeutic edge in very challenging tumours and works synergistically with radical surgery by delivering a high dose of radiotherapy to the area of highest risk tumour cell persistence, while physically displacing and protecting radiation sensitive structures (eg small bowel, ureter) from the radiotherapy field of treatment by the operating surgical team. As a result it is a treatment modality most suitable for tumours with the likelihood of a close or involved surgical resection margin in order to improve local control. In this situation, IOERT is being used as an additive to existing standard of care. However there are several instances where IOERT may also have clinical utility which are being currently explored. These include using IOERT to de-escalate existing neoadjuvant radiotherapy regimens; and using IOERT to potentially de-escalate surgical margins to reduce surgical morbidity. Examples of the both are provided below: 1. IOERT to reduce neoadjuvant radiotherapy doses. Currently standard of care neoadjuvant chemoradiation methods involve a 45 Gy dose of radiotherapy fractionated in such a manner that patients have to attend hospitals for treatment more than 26 times. For some elderly patients or those not near a radiation centre this can at times be prohibitive and it has been our experience that some patients are greatly put off by this process and have expressed an interest in reducing this. The ability to deliver

		IOERT may potentially facilitate trials in this arena aiming to de-escalate external beam radiotherapy usage. 2. IOERT may also enable de-escalation of the surgery. Currently the gold standard surgical outcome in treatment of LARC and LRRC is the resection margin status, as achieving a tumour free resection margin (R0) is associated with better oncological outcomes compared to close or involved margins (R1). However achieving an R0 resection may at times necessitate surgical resection of non expendable vessels and bones and nerves which will have significant reconstructive consequences or functional consequences for patients. As a result, IOERT has at times been used by some centres as a measure to de-escalate the surgical procedure. The current albeit low quality evidence suggests that in these cases the patients having an R1 resection with IOERT achieve an oncological outcome close to an R0 without IOERT. Consequently it is for all the reasons above that IOERT has become part of the recommended standards in ther NCCN cancer treatment guidelines for North America, as well as the guidelines for various countries in the EU such as the Netherlands and Germany. Finally, in addition to the above, there are several reported but more hypothetical beneficial measures outlined below: - IOERT is radio-biologically believed to be equivalent to 3x the biological dose of conventional External Beam radiotherapy (EBRT) – and so can improve the therapeutic ratio even further (hence 10Gy IOERT is equivalent to 20-30 Gy fractionated EBRT given in 1.8-2 Gy fractions) - In a solid non-operated tumour, hypoxia-induced radio-resistance is the most important feature in the tumour microenvironment responsible for failure of radiotherapy, as the central core of such tumour nodules are quite hypoxic. However, at surgery, after nearly complete resections of the tumour with minimal residual cells at a positive margin, and under the circumstances of oxygenation of tissues in a ventilated patient, this underlying hypoxia is eradicated and so the efficacy of any peroperative radiation treatment can be theoretically enhanced greatly. - High dose radiotherapy (hypo-fractionated or single large boosts) also has significant anti-tumourigenic immune effects which are at present rather poorly understood mechanistically. These can lead to both direct local tumour cell killing and can lead to abscopal/systemic tumour cell killing also through the activated immune system.

8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Yes – patients with LARC and LRRC with disease in the sidewall and posterior compartments.
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Yes – death from uncontrolled pelvic cancer from LARC and LRRC is one of the worst wasy of dying and affects many young patients nationally. Better management and treatment of these patients with the ability to deliver IOERT in a few select centres would prevent loss of life and improve quality of life.
10 - MTEP	Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	Cost for treatment delivery is very minimal, however the initial outlay costs for having a machine able to deliver this is not insignificant. This outlaty cost would be recouped by the cost per life saved and contribution to society made by often very young tax-paying patients.
11 - MTEP	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)?	Likely to cost more in the short term and then less eventually after time.
12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Modifications to the theatres in which this would be delivered in
13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes – our staff needed training and multiple visits to expert international centres and then adoption of their standard operating procedures and modifications to those for the purposes of use in the NHS.

Safety and efficacy of the procedure/technology

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	Ureteric strictures Wound complications Bony necrosis Mirnezami R, Chang GJ, Das P, Chandrakumaran K, Tekkis P, Darzi A, Mirnezami AH. Intraoperative radiotherapy in colorectal cancer: systematic review and meta-analysis of techniques, long-term outcomes, and complications. Surg Oncol. 2013 Mar;22(1):22-35.
15	Please list the key efficacy outcomes for this procedure/technology?	IOERT field local control
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	None – in our experience of over 170 cases it has been exceptionally safe. The main complications and morbidity come from the major radical surgery and the IOERT component does not seem to add to the risk so far.
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Extent of efficacy in margin close tumours is unclear. In Margin positive tumours this is not the case.
18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Fewer than 10 specialist centres in the UK.

Abstracts and ongoing studies

19	Please list any abstracts or conference proceedings that you are aware of that have	Since January 2017, this treatment has been funded at University Hospital Southampton by a

	been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	charitable organisation for such patients with a view to establishing real life NHS experience into its safety and feasibility. To date the results have confirmed the international findings and shown a very low local recurrence rate and no morbidity attributable to the IOERT treatment. These have been presented at the NIHR meeting as an oral presentation and a conference video synopsis of this may be found on the Video Journal of Oncology: https://www.youtube.com/watch?v=MuzXhQ7zIvc
20	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Yes – the ELECTRA trial. 1. https://www.isrctn.com/ISRCTN48105173 2. https://www.southampton.ac.uk/ctu/trialportfolio/listoftrials/electra.page 

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an	It is difficult to make a precise calculation of the population however the figures below provide an estimate of the likely numbers of patients with LARC and LRRC that IOERT would apply to. Colorectal cancer represents the fourth most common cause of cancer in the UK with around

	estimated number, or a proportion of the target population)?	42,300 new cases every year (1). The majority (over 30%; 12690 cases) take place within the rectum. Locally advanced rectal cancer typically affects approximately 10-15% of the population of patients with rectal cancer (1903 patients) and locally recurrent rectal cancer can affect up to 12% of patients who have previously undergone rectal cancer surgery (2). Questionnaire analyses within the UK surgical community have also previously shown the incidence of LRRC to be 688 patients per annum (3). Only 50% of these figures will typically be amenable to surgery and represent true localised and resectable disease however, equating to 951 cases of LARC and 344 cases per year of LRRC. In addition, the proportion of cases that are in the lateral and posterior pelvic compartments for which IOERT principally applies, represents 30-40% (personal experience from our own series and personal communications with other specialists in the UK), and so the number of potentially eligible cases for IOERT in the current PPP proposal is likely to be approximately 30-40% of the sum of LARC and LRRC cases representing 518 patients in total. 1. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancertype/bowel-cancer 2. Sebag-Montefiore D, Stephens RJ, Steele R, Monson J, Grieve R, Khanna S, Quirke P, Couture J, de Metz C, Myint AS, Bessell E, Griffiths G, Thompson LC, Parmar M. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. Lancet. 2009 Mar 7;373(9666):811-20. 3.Harji DP, Griffiths B, McArthur DR, Sagar PM. Current UK management of locally recurrent rectal cancer. Colorectal Dis. 2012 Dec;14(12):1479-82.

22	Are there any issues with the usability or practical aspects of the procedure/technology?	Applying this in compliance with UK radiation safety guidance
23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	No
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Yes – use of the technique for de-escalating surgery or reducing extent of external beam neoadjuvant radiotherapy
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	Beneficial outcome measures: IOERT field local control at 2 or 3 years Overall survival at 5 years Adverse outcome measures: Ureteric strictures – within 6 months (although maybe a consequence of surgery alone also) Bony necrosis (within 2-3 years) Wound infections (within 90 days)
26	Is there any other data (published or otherwise) that you would like to share with the committee?	

Further comments

26	Please add any further comments on your particular experiences or knowledge of the procedure/technology,	We have now used the technology for LARC and LRRC cases for over 5 years. We are preparing our experience for publication Since January 2017, this treatment has been funded at University Hospital Southampton by a charitable organisation for such patients with a view to establishing real life NHS experience into its safety and feasibility. To date the results have confirmed the international findings and shown a very low local recurrence rate and no morbidity attributable to the IOERT treatment. These have been presented at the NIHR meeting as an oral presentation and a conference video synopsis of this may be found on the Video Journal of Oncology, (https://www.youtube.com/watch?v=MuzXhQ7zIvc). Importantly, to date, patient and public involvement thus far has shown a high level of interest and enthusiasm for the application of such a modality with many patients championing their local MPs for this modality. Patients undergoing the treatment have found it to be very acceptable and in the words of many of them, there appear to be no downsides and only advantages, especially in the setting of such advanced and life threatening situations with littel other alternatives. To quote one patient: *"In the setting of imperfect preop information, abnormal and hard to judge tissues at surgery, and a well tolerated treatment that doesn't add hugely to an already long operation, is there much to lose?"*

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Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Non-financial professional	Chief investigator of ELECTRA trial	**May 2022**	
Choose an item.			
Choose an item.			

☒ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Alex Mirnezami**
Dated:	**21/07/2022**

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Professional Expert Questionnaire

Technology/Procedure name & indication: IP1919 Intraoperative electron beam radiotherapy for locally advanced and locally recurrent colorectal cancer

Your information

Name:	Jim Khan
Job title:	Consultant Surgeon
Organisation:	Portsmouth Hospitals University NHS trust
Email address:	[redacted]
Professional organisation or society membership/affiliation:	General Medical Council
Nominated/ratified by (if applicable):	BASO
Registration number (e.g. GMC, NMC, HCPC)	6049414

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Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

Please note that questions 10 and 11 are applicable to the Medical Technologies Evaluation Programme (MTEP). We are requesting you to complete these sections as future guidance may also be produced under their work programme.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? − Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? − Is this procedure/technology performed/used by clinicians in specialities other than your own? − If your specialty is involved in patient selection or referral to another specialty for this	I have been a practicing colorectal cancer surgeon for over 14 years and work in a teaching hospital with a significant cancer workload. This technology is a relatively new innovative technique which has been used for locally advanced rectal cancer in a very few selected centres. I am aware fo how this works, have seen some results for my patients but dont have this in my hospital and i don’t manage the direct delivery of this treatment to my cancer patients. This tehcniquye can be used in colorectal and irology and gyanecology We do refer the selected cases for this treatment to an other centre

	procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research. I have had no involvement in research on this procedure. Other (please comment)
3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Established practice and no longer new. A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy. Definitely novel and of uncertain safety and efficacy. The first in a new class of procedure.
4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	Perhaps yes for a small subset of patients with rectal cancer

Current management

5	Please describe the current standard of care that is used in the NHS.	External beam radiotherapy and chemotherapy followed by surgery
6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	No

Potential patient benefits and impact on the health system

7	What do you consider to be the potential benefits to patients from using this procedure/technology?	May increase the chances of a complete cancer resection and hence reduce local recurrence and regrowth of cancer
8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Yes those with locally advanced rectal cancer beyond local resection margins in the pelvis
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Yes all of these
10 - MTEP	Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	I dont fully know but would think it will cost similar
11 - MTEP	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)?	Some extra resources in theatre will be needed as it is delivered during the operation
12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Installation of the kit, specified theatre build up (radiation proof) and then extra allocated times in theatre

13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes

Safety and efficacy of the procedure/technology

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	Tissue trauma, injury to other organs, collateral damage and increased risk of complications
15	Please list the key efficacy outcomes for this procedure/technology?	Complete cancer resection
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	effectiveness
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Unsure, lack of data
18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Most or all district general hospitals. A minority of hospitals, but at least 10 in the UK. Fewer than 10 specialist centres in the UK.

		Cannot predict at present.

Abstracts and ongoing studies

19	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	
20	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	I am not aware

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	10% of patients with rectal cancer in this country
22	Are there any issues with the usability or practical aspects of the procedure/technology?	no

23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	no
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Registry data on patients treated so far
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	Beneficial outcome measures: Adverse outcome measures:
26	Is there any other data (published or otherwise) that you would like to share with the committee?	

Further comments

26	Please add any further comments on your particular experiences or knowledge of the procedure/technology,	

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Print name:	**Jim Khan**
Dated:	**12/08/2022**

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Professional Expert Questionnaire

Technology/Procedure name & indication: IP1919 Intraoperative electron beam radiotherapy for locally advanced and locally recurrent colorectal cancer

Your information

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Email address:	[redacted]
Professional organisation or society membership/affiliation:	BASO, ACPGBI, RCS Edinburgh, GMC
Nominated/ratified by (if applicable):	BASO
Registration number (e.g. GMC, NMC, HCPC)	6024769

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Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

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1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? − Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? − Is this procedure/technology performed/used by clinicians in specialities other than your own? − If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	Experience of technology in 2010-12 as part of clinical evaluation in rectal cancer. Project led by Professor A Munro (University of Dundee). Series of 20 patients using a mobile device. Leeds Teaching Hospital Trust currently has one of the largest locally advanced and recurrent practices in the UK. The technology is however only available in limited centres in the UK. Leeds Teaching Hospital Trust does not have access to IORT currently and so not part of my routine practice. We do however, have a locally advanced and recurrent rectal cancer MDT with multimodal radiotherapy options including SABR (Stereotactic Ablative Radiotherapy).
2	− Please indicate your research experience relating to this procedure	I have done bibliographic research on this procedure.

	(please choose one or more if relevant):	Other (please comment)
3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Established practice and no longer new. Intra-operative radiotherapy (IORT) is not a new concept. It was introduced in the 1970s and 1980s as a technique to improve local control in locally advanced and unresectable tumours. It is typically combined with pre- or postoperative external beam radiotherapy (EBRT). Today it is used in conjunction with preoperative and, at times, repeat preoperative pelvic radiation therapy which is then followed by IORT.
4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	Addition to existing standard of care

Current management

5	Please describe the current standard of care that is used in the NHS.	Surgical resection with clear margins is the current stand of care but can only be achieved in 70% of cases. Early recurrence, poor quality of life and limited survival are expected following a positive margin resection. IORT is an adjunctive strategy to salvage cancer specific survival in light of a predicted positive margin.

6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	SABR radiotherapy is an alternative to surgical resection of pelvic recurrence in a limited number of cases. There are very specific indications for SABR, however this limited technique does not offer cure. There are no intraoperative adjuncts to improve survival in predicted positive margin cases.

Potential patient benefits and impact on the health system

7	What do you consider to be the potential benefits to patients from using this procedure/technology?	1. Improved cancer specific survival and reduced local recurrence 2. Possible reduced long-term morbidity if major neurovascular resection avoided.
8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	IORT is indicated for borderline-resectable tumours and tumours where the resection margin is predicted to be close – for both primary and recurrent cancers. It is useful when the resection margins, despite multivisceral or extended resection, are threatened.
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	IORT has the potential to improve cancer specific survival and reduce local recurrence for these complex cases. This will of course lead to improved quality of life and survivorship. It could also increase the number of patients eligible for radical surgery in those with borderline resectability due to threatened margins. To me the key unanswered questions are: Can IORT improve outcomes following resection of borderline resectable tumours? Can it facilitate organ preservation? For example, can an anterior tumour threatening the prostate or a posterior tumour abutting the sacral bone be resected using IORT in order to avoid the morbidity of exenteration or composite bone resection?
10 - MTEP	Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	There is no equivalent technology. The adjunct of IORT to radical surgery will come with an increased cost.
11 - MTEP	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)?	1. Equipment 2. Radiotherapy delivery suite/operating room 3. Staff 4. Operating time A significant investment in equipment would be required to make IORT technology available across the National Health Service The available methods of delivering IORT are low-energy X-ray systems, electron beam radiation therapy, high dose rate after loaders or specific balloon devices. Tungsten-impregnated sheets are used to shield the wound prior to treatment. These block 95% of radiation, but radiation doses within the operating room remain potentially

		significant and necessitate control of access to the room during treatment and further shielding for the anaesthetist and medical physicists. Existing walls will often provide sufficient shielding for the low-energy X-rays, and thus, it is often possible to use existing operating rooms. In terms of cost-effectiveness, in other tumour types, despite the higher initial device-related costs, the cost per patient treated with IORT by using electron beams linear accelerators is effective when considering the reduction in radiotherapy waiting lists, pre-treatment planning and delay. However, a specific cost-effective analyses is required in locally advanced and recurrent rectal cancer. The delivery of IORT should be by an appropriately trained multi-professional team including clinical oncologists, radiographers, surgeons and physicists. Two operators under IRMER would be required for checking/setting up purposes. Radiotherapy should be prescribed by a clinical oncologist. The delivery of IORT is also likely to increase operating time. Typically standard operation times are prolonged by 45-60 mins for the required treatment (beam on) time (30 minutes) and applicator placement, preparation and clear up (30 minutes). This will significantly impact on theatre throughput and capacity.
12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Access to or construction of operating suite with specification required to safely deliver radiotherapy
13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes

Safety and efficacy of the procedure/technology

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	The primary toxicity of IORT appears to be wound related with an increased risk of wound toxicity with the addition of IORT. Potential for normal tissue toxicity effecting nerves, bone and urogenital structures. Recent metanalysis however reported no reported clinically significant neuropathy or ureteral stenosis reported. IORT was not shown to be associated with higher rates of wound infection, pelvic abscess, anastomotic leak or need for surgical reintervention
15	Please list the key efficacy outcomes for this procedure/technology?	Local recurrence Normal tissue toxicity – nerve, ureter, bone
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	The results from our meta-analysis suggest that there is an improvement in local control with the addition of IORT and that it comes with no increase in morbidity. However, these results must be interpreted with caution. Unfortunately, due to a paucity of data in the individual studies it is unclear why patients were chosen to undergo IORT and it was not possible to analyse the effect of IORT in subgroups of patients who underwent an R0 compared to an R1 resection, nor was it possible to distinguish between primary and recurrent cases.
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Heterogeneity in the application of IORT is another factor which limits the interpretation of trial data. Dosing regimens differ quite significantly, ranging from 10 Gy to 25 Gy.
18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	A minority of hospitals, but at least 10 in the UK.

Abstracts and ongoing studies

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	100-200
22	Are there any issues with the usability or practical aspects of the procedure/technology?	
23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	1. Clinical effectiveness of IORT is, as yet, unproven 2. No cost effectiveness analysis 3. The training costs and capital required to implement could be a costly financial risk for the NHS and divert funding from existing services.
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Currently, no randomised evidence.
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.	Beneficial outcome measures: 1. Improved cancer specific survival 2. Reduced local recurrence Adverse outcome measures:

	– Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	1. Surgical morbidity 2. Ureteric stenosis 3. Nerve dysfunction 4. Operating time
26	Is there any other data (published or otherwise) that you would like to share with the committee?	

Further comments

26	Please add any further comments on your particular experiences or knowledge of the procedure/technology,	

NICE National Institute for Health and Care Excellence

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Non-financial professional	Specialist interest in locally advanced and recurrent rectal cancer with one of largest practices in UK.	**2015**	
Choose an item.			
Choose an item.			

X☐ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Aaron Quyn**
Dated:	**21/7/22**

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **IP1919 Intraoperative electron beam radiotherapy for locally advanced and locally recurrent colorectal cancer**

Your information

Name:	Sathish Harinarayanan
Job title:	Consultant Clinical Oncology
Organisation:	University Hospital of Southampton NHS Trust
Email address:	[redacted]
Professional organisation or society membership/affiliation:	MRCP (Royal college of Physicians, UK), FRCR (Clinical Oncology with Royal College of Radiologists, UK), Member BAHNO (British Association of Head and Neck Oncology)
Nominated/ratified by (if applicable):	Click here to enter text.
Registration number (e.g. GMC, NMC, HCPC)	6083771

How NICE will use this information: the advice and views given in this questionnaire will form part of the information used by NICE and its advisory committees to develop guidance or a medtech innovation briefing on this procedure/technology. Information may be disclosed to third parties in accordance with the Freedom of Information Act 2000 and the Data Protection Act 2018, complying with data sharing guidance issued by the Information Commissioner's Office. Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of the process of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice.

☒ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

Please note that questions 10 and 11 are applicable to the Medical Technologies Evaluation Programme (MTEP). We are requesting you to complete these sections as future guidance may also be produced under their work programme.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology?	Observed closely under supervision with senior colleagues since 2017 Started practicing as an independent practitioner since 2018 at University Hospital of Southampton NHS Trust First National UK IOERT symposium conducted at University Hospital of Southampton on 21/6/2019
	Have you used it or are you currently using it?	We have been using this technology since 2017 and currently using it.
	− Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?	This is the first in NHS, likely other trusts may adopt it. But due to resources needed to co-ordinate in between multiple specialities and specialists, unfortunately did not gain popularity in the NHS, whereas it is considered as a standard in few biggest cancer centres across the world.
	− Is this procedure/technology performed/used by clinicians in specialities other than your own?	No, only by clinical oncologist with FRCR (clinical oncology) qualification
	− If your specialty is involved in patient selection or referral to another specialty for this	

	procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g., device-related research). We are doing clinical research currently with this procedure. It's called ELEKTA clinical trial. Principal Investigator: Prof. Alex Mirnezami, consultant colorectal surgery and co-investigators: Dr Andrew Bateman and Dr Sathish Harinarayanan (consultant clinical oncologists)
3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	New, the one and only available in the NHS, which is the best option available for patients with locally advanced disease, where surgery could not be offered previously. Whereas now, we can offer complex surgery with IOERT to reduce the local recurrence of the disease and improve the survival as well. Established practice in other countries and in UHS for the past five years. Very safe to deliver and no complications reported so far within our patient population group who received the procedure over past five years. Definitely safe to deliver. The first in a new class of procedure in the NHS and in the country.
4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	It's an addition to existing care

Current management

5	Please describe the current standard of care that is used in the NHS.	Patients with locally recurrent rectal cancers- either palliative chemotherapy alone which is still standard of care across the UK currently Vs Pelvic exenteration with IOERT to surgically worrying margins which does improve survival significantly compared to palliative chemotherapy/surgery alone.
6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	No other alternative treatments available for similar type of cases

Potential patient benefits and impact on the health system

7	What do you consider to be the potential benefits to patients from using this procedure/technology?	To improve local control rate by reducing the cancer relapse locally To improve the survival of patients who otherwise no alternative curative options of treatments with a poor prognosis estimated around 9 to 12 months versus 40 to 50% five years survival chances by having complex surgery with IOERT.
8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Yes, Previously treated rectal cancer patients with local recurrence and surgically inoperable due to worrying margins.
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Yes, certainly. It gives confidence for surgeons who could not remove the cancer as a whole previously now can remove the cancer as a whole without worrying about microscopic positive margin as the worrying tumour bed can receive RT through IOERT without potential damage to neighbouring structures, which happens with external beam RT.
10 - MTEP	Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	Procedure overall may cost a little more as it involves co-ordinating and bringing staff together including surgical operation team, an hour extra in theatre for anaesthetists, co-ordinating and bringing radiographers, physicists and clinical oncology consultant into theatre.
11 - MTEP	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)?	Likely to cost a little more as above
12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Radiotherapy safe purpose-built operation theatres, QA process to go through each week with the machine by physicist, creating safe environment for staff as it includes ionising radiation

13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes Radiation safety precautions

Safety and efficacy of the procedure/technology

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	None so far within the population treated. As ionising radiation, risks could be a small damage to neighbouring structures in the body like muscles, nerves, and vessels though they are negligible compared to cancer causing that anyway if untreated. Small possibility of damage to bowel So far none from our centre's experience As above damage to neighbouring structures (if precautions not taken during directing the RT)
15	Please list the key efficacy outcomes for this procedure/technology?	Reducing the cancer relapse locally Improving the survival from cancer
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Occasionally it is unclear if surgically removed completely or not, but will be guided by surgeons and MRI scan which we discuss in our complex cancer MDT
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	
18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Not in district general hospitals. A minority of hospitals, (but at least 10 in the UK) where complex pelvic cases can be handled by complex pelvic surgeons alongside with clinical oncology experts.

Abstracts and ongoing studies

19	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	First National (UK) IOERT symposium held at University Hospital of Southampton NHS Trust on 21st of June 2019 Please check Intraop.com where links to all literature and resources and evidence available More recent paper about pancreatic cancer: 5.2-year median follow-up time, 46-month median overall survival for R0+R1 patients, 83% local control at 5 years, 1/3 of patients are alive at 5 years This is something we never heard of in pancreatic cancers. PACER trial, also showed improved survival in PancFORT trial HNSALV trial for Head and neck cancer-treatment option for salvage Head&Neck cancer, which we could not provide currently due to restriction in resources at UHS For rectal cancer: Please go through this paper where multivariate analysis with lot of evidence been done showing improving survival advantages. https://doi.org/10.1016/j.ctro.2020.06.007 ESTRO/ACROP IORT recommendations for intraoperative radiation therapy in locally recurrent rectal cancer (Felipe A.Calvo et al., ctRO vol.24, Sept.2020, pages 41-48)
20	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Yes ELECTA trial currently in progress at University Hospital of Southampton

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	~50 But there is a capacity to increase more if operation theatre could be modified a bit more, which we are planning to currently.

22	Are there any issues with the usability or practical aspects of the procedure/technology?	Yes, the staff are not paid and been doing voluntarily, which may need to take into consideration as it's not a commissioned like for radiographers, physicists etc..,
23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	Funding as above. Currently PLANETS charity is funding us
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	ELECTA trial should give us some more answers
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: – Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. – Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	Beneficial outcome measures: To monitor and audit the patients who received it so far and compare with patients who did not receive it. Audit process on its way to see the benefits with our centre's experience, survival rate and local control rates Adverse outcome measures: Literature reports says: Neuropathy 3%, ureter dysfunction in 56% if in the field, but we always move it out of the field, late toxicities: would infection/breakdown in 9%, fistula in 8%, bladder dysfunction in 7%, sexual dysfunction in 6%,
26	Is there any other data (published or otherwise) that you would like to share with the committee?	Lot of literature on it and been standard of care in major cancer centres in the US, Switzerland, Germany etc..., Also adopted in few recognised guidelines in the world like NCCN, ESTRO..,guidelines

Further comments

26	Please add any further comments on your particular experiences or knowledge of the procedure/technology,	It's a game changing procedure if done with all expertise including complex pelvic surgical team, clinical oncology team, complex pelvic radiology team with dedicated complex pelvic cancer MDT deciding about the patients who gets maximum benefit.

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Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.	None		
Choose an item.			
Choose an item.			

☒ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Dr Sathish Kumar Harinarayanan**
Dated:	**24th August 2022**

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: IP1919 Intraoperative electron beam radiotherapy for locally advanced and locally recurrent colorectal cancer

Your information

Name:	Campbell Roxburgh
Job title:	Consultant Colorectal Surgeon and Clinical Senior Lecturer
Organisation:	University of Glasgow
Email address:	[redacted]
Professional organisation or society membership/affiliation:	General Medical Council, Fellow of the Royal College of Surgeons of Edinburgh
Nominated/ratified by (if applicable):	N/A
Registration number (e.g. GMC, NMC, HCPC)	GMC 6076119

How NICE will use this information: the advice and views given in this questionnaire will form part of the information used by NICE and its advisory committees to develop guidance or a medtech innovation briefing on this procedure/technology. Information may be disclosed to third parties in accordance with the Freedom of Information Act 2000 and the Data Protection Act 2018, complying with data sharing guidance issued by the Information Commissioner's Office. Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of the process of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice.

☒ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

Please note that questions 10 and 11 are applicable to the Medical Technologies Evaluation Programme (MTEP). We are requesting you to complete these sections as future guidance may also be produced under their work programme.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology?	I am familiar with the literature on the technology. I undertook a fellowship at MSKCC in New York City in 2015/20216 and was directly involved in operations in which intra-operative radiotherapy was used.
	Have you used it or are you currently using it?	I am not currently using this technology. I am aware IORT is only available in selected UK centres and this fact has limited its uptake.
	− Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? − Is this procedure/technology performed/used by clinicians in specialities other than your own? − If your specialty is involved in patient selection or referral to another specialty for this	IORT is used by other specialities (other than general surgery). A clinical oncologist is required to participate in administration of IORT regardless of operative speciality. Appropriate cases would be discussed at a multi-disciplinary meeting in order to plan treatment strategy.

	procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research. I have had no involvement in research on this procedure. X. I have presented at departmental meetings on IORT and so have appraised the literature for this topic. Other (please comment)
3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	This is innovative treatment incorporating significant organisational issues and extra theatre time in already complex cancer cases. Established practice and no longer new. A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy. X Definitely novel and of uncertain safety and efficacy. The first in a new class of procedure.

4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	Used in addition to standard of care

Current management

5	Please describe the current standard of care that is used in the NHS.	Major complex cancer surgery – accepting the risk of close or involved surgical margins.
6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	No

Potential patient benefits and impact on the health system

7	What do you consider to be the potential benefits to patients from using this procedure/technology?	Mitigates against the local recurrence risk from close or involved surgical margins.
8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Patients at highest risk of a positive surgical resection margin in cancer surgery.
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Could reduce local recurrence and improve cancer outcomes. Local recurrence is associated with high cost and negative patient outcome.
10 - MTEP	Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	Cost more (hardware is expensive)
11 - MTEP	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)?	There are initial capital outlay and then maintainence costs associated with the equipment/ hardware. Additional staff costs (oncologist to plan and administer the RT). Depending on the equipment used, there may need to be changes to theatre infrastructure to protect staff and shield from RT.
12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	A theatre with the appropriate safety measures to administer RT. Infrastructure works may be required.

13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes - The surgical and anaesthetic team mucst train in delivery of IORT and ensuring successful patient monitoring during treatment. Clinical oncologists and radiographers must also train in IORTdosing and administration.

Safety and efficacy of the procedure/technology

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	RT toxicity to patient (low risk). Radiation exposure to staff (low risk)
15	Please list the key efficacy outcomes for this procedure/technology?	Local recurrence rate, long term cancer outcomes.
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Lack of prospective clinical trials. Published data comes from prospective series only.
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	There remains uncertainty over the addition of a single fraction of RT and whether this truly improves outcomes.
18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Most or all district general hospitals. A minority of hospitals, but at least 10 in the UK. Fewer than 10 specialist centres in the UK. X

		Cannot predict at present.

Abstracts and ongoing studies

19	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	I am not aware of specific recent abstracts that would be relevant here.
20	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Not aware of any

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	In a tertiary referral centre performing 50-70 major resections per year I would estimate approx. 10-20 would be appropriate for IORT.
22	Are there any issues with the usability or practical aspects of the procedure/technology?	Requires a large item of equipment to be implemented in theatres, stored and maintained. A team mist be trained to deliver the treatment.

23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	Cost of the technology and the relative low level of evidence for benefit.
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Prospective clinical trials are required.
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	Beneficial outcome measures: Post operative complications (clavian dindo grading) Length of stay in hospital Length of time in theatre Long term oncological outcome, local recurrence, overall and cancer specific survival Adverse outcome measures: See above
26	Is there any other data (published or otherwise) that you would like to share with the committee?	None

Further comments

26	Please add any further comments on your particular experiences or knowledge of the procedure/technology,	None

NICE National Institute for Health and Care Excellence

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Non-financial professional	I run a research laboratory which has received research funding for an investigator initiated research project from Varian, a company that manufacture external beam radiotherapy machines.	**2021**	**2024**
Choose an item.			
Choose an item.			

☒ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**CAMPBELL ROXBURGH**
Dated:	**14/07/2022**