National Institute for Health and Care Excellence

IP1919 Intraoperative electron beam radiotherapy for locally advanced and locally recurrent colorectal cancer

IPAC date: 9th February 2023

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1	Consultee 1 NHS clinician (Professional expert)	General	Thank you for the detail in the document. As someone who delivers this treatment and who understands the challenges of such a review process in a rare area this is a difficult task. However we must be mindful that this process has already taken place in North America and in the EU and this modality has become standard practice for them now (in North America since 2018). Consequently a discrepancy from the UK would also create significant challenges from patients many of whom now demand this as a modality to be available to them as part of their healthcare rights. Indeed before we were able to offer this we had several very challenging discussions with patients who wished to be referred abroad for this treatment. Consequently a situation that allows and supports the conduct of this therapy within specific specialist NHS units and encourages the best available research and participation in international trials would be a better outcome and more representative of the existing body of information.	Thank you for your comment. Consultee disagrees with the main recommendation. Consultee notes that the procedure is standard practice in North America and Europe. Consultee advocates for the procedure to be performed in specialist NHS units. The Committee's recommendation was made on the basis of peer-reviewed published data on safety and efficacy. The committee is informed about the content of other international guidelines and practices, however the committee's recommendation is focused on the UK context and is independent of international practices.

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				The current guidance states that the procedure should only be done in the context of research **preferably** in the form of randomised controlled trials.
2	Consultee 1 NHS clinician (Professional expert)	1.1	Please see my comment below also. Two of the main international committees in North America and the EU now recommend this based on the existing level of evidence and so it seems contrary that we would not recommend this in the UK. We have had a number of patients request being referred abroad for this and have in the past completed IFR forms also for them. With such a degree of complexity, in a small but significant number of patients, setting the high bar of randomised studies only being acceptable seems illogical, especially when randomised studies can be conducted poorly and be subject to poor patient selection.	Thank you for your comment. Consultee disagrees with the main recommendation. Consultee notes that feasibility of randomised studies is challenging given the complexity of the procedure and small number of patients. The complexity of the procedure is noted in section 3.5 of the guidance. The current guidance states that the procedure should only be done in the context of research **preferably** in the form of randomised controlled trials.
3	Consultee 1 NHS clinician (Professional expert)	1.2	This is a major challenge in common surgical procedures let alone more rare situations which this relates to. Existing evidence in the form of high quality systematic reviews have been accepted as sufficient evidence by the North American National Comprehensive Cancer Network and therefore this is now a recommended treatment modality in North America. Similarly in Europe the EU guidelines published by ESTRO now recommend this based on the same data. In addition the very high level of	Thank you for your comment. Consultee disagrees with the main recommendation. The committee's view was that the quality of the evidence was mixed and that the clinical outcomes of IORT were not

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			evidence suggested for this is contrary to many other interventions now accepted such as SABR radiotherapy which have not been subjected to the same rigour and indeed do not have data going back as long as IOERT does.	demonstrated to be superior to surgery/EBRT in the highest quality evidence.
4	Consultee 2 NHS clinician	1.1	I agree the evidence for safety and also feasability for IOERT is adequate in colorectal cancer, but especially n locally advanced rectal and locally recurrant rectal cancer	Thank you for your comment. Consultee agrees that evidence on safety is adequate.
5	Consultee 2 NHS clinician	1.2	Further research is greatly encouraged and should be funded by relevant funding bodies as a priority stream as this technique might have the potential for large patient benefit when could with standard of care treatment	Thank you for your comment. Consultee agrees that further research would be helpful.
6	Consultee 2 NHS clinician	3.1	NICE should consider an exclusive review on locally advnaced and locally recurrant rectal cancer alone including most of the literature excluded from this review with a focus on disease freee survival and local recurrance within the IOERT field as primary outcomes.	Thank you for your comment. Most of the evidence considered by the committee was on locally advanced and locally recurrent rectal cancer although there was also some evidence on colon cancer. The Committee considered a rapid review of the evidence, in which the most valid and relevant studies were selected for detailed presentation. Other relevant studies are included in the appendix.
7	Consultee 2 NHS clinician	3.2	Specific within IOERT field recurrance and disease related treatment failure outcome (see RAPIDO trial) should also be included	Thank you for your comment.

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				The Committee considered this comment but decided not to change the guidance. Section 3.2 currently includes the following key efficacy outcomes: local recurrence, disease-free survival, overall survival, quality of life.
8	Consultee 2 NHS clinician	3.8	This comment is very underplayed by NICE and should be rectified. One of the strongholds of using IOERT in this patient population is the ablity to offer a curtailed treatment strategy eg in frailer, older, unfit individuals that would not be able to withstand multi-compartment, non-expendable structures or large boney resection. Adding IOERT as a treatment option to spare/mitigate against non-expendable vessels/nerve or large boney resection (high sacrectomy)is a priorty for patients. They specifically request that alternatives to large multi-visceral operations should be discussed as part of the shared decision making process especially with alternatives that include gold-standard resections and no-treatment options. Using IOERT to plan a curtailed / de-esclated surgery in treating LARC/LRRC cancers when radiologically predicted involved margins (R1) include non-expendable vessles/nerves or large boney surfaces should be investigated. These opptions should be put to the patient as achieving R0 (although gold standard of treatment) might place the patient at significant risk of non-rescuable complications, risks from large scale reconstructions after non-expendable vessel resection or large risks form the empty	Thank you for your comment. Section 3.8 of the guidance states: 'The committee was informed that this procedure can reduce the extent of surgery needed.'

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			pelvis syndrome especially when considering large boney resections.	
9	Consultee 3 Patient representative	General	I am responding to this consultation on behalf of two patients who have asked for my support to upload their accounts online. 1.) [redacted] My journey began on the [redacted] September when I met [redacted] who was to explain how far my cancer had gone and what treatment was on offer. After viewing the scans with the professor and a very detailed explanation of how far the tumor had spread, I was basically offered three options. One option chemotherapy/radiotherapy was removed as the tumor was too advanced for it to be of any real use. The other two options were to do nothing and await the inevitable end or have extensive surgery that would not be without its own risks. Of course I took the surgery as that would hopefully buy me more time. At this point we spoke about how the tumor would be removed and the likely end results. One of the things that was explained at this point were "margins" when removing the tumour. We spoke about removing the bladder and prostate, as well as the bowel. Then this led onto to issue of my right leg as the tumor had travelled into the pelvic area and there was a risk to the legs, nerves and main blood arteries. It was at about this point that we spoke about a trial that was being run that used a new treatment called IORT. It was also explained that Southampton was the only place in the country that had one which had been bought by Planets Cancer Charity.	Thank you for your comment. The Committee very much welcomed hearing from patients who have undergone this procedure and considered these experiences and views in their deliberations.

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			Anyway after a bit more explaining I decided to sign up to the trial. After all I had nothing to lose and if anything it gave me real hope that it would help give me a positive outcome from the surgery. So on the 1st December I went into surgery. When I finally woke after the surgery I was somewhat weak but within a few days I was up walking - albeit with the aid of a frame and not very far. But each day I managed a bit more and now, nearly three weeks later I'm walking unaided and reasonable distances. The pain has mostly subsided just some discomfort left now. I've ended up with two stomas which I'm already getting used too and infact doing reasonably well in emptying and changing the bags etc. Now while I may never know what dose of radiation I got through the IORT trial, I had real hope and confidence in a good outcome due to knowing I had the best surgical team in this field and knowing that the IORT machine would be used. I will be forever grateful to all the surgical team and Planets Charity for raising the money to buy the machine in the first place. The evidence for it seems to be strong and growing. I was made aware that 190 patients in the UK have been treated with the technology in Southampton since its introduction with impressive results, such as preliminary results for colorectal patients reported by the Video Journal of Oncology (https://www.vjoncology.com/video/muzxhq7zivc-role-of-intra-operative-electron-radiotherapy-in-abdominopelvic-malignancies/) in 2018 and those for pancreatic cases reported in the British Journal of Surgery (https://academic.oup.com/bjs/advance-article/doi/10.1093/bjs/znab335/6377876) last year.	

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			Now I need to get back to full health and start looking forward to many more years, in which my wife and I intend to make the most of and travel the world visiting all those places we've dreamed of. Thank you. 2.) [redacted] Just before Christmas of 2017 at the age of 74 it was discovered that I had a tumour on the sacrum bone of my spine close to the organs of my pelvic area. The medical team in my local hospital were very negative about my future stating that surgery would be too risky and the surgeons were not prepared to undertake any action. Palliative care was spoken about. I was very unhappy about this and mentally stamped my feet. I asked to see the lead consultant. I said I most definitely wanted to investigate all risks fully as it was my life and I wanted to make decisions about what should happen to me. The consultant then agreed to send all my history to [redacted] hospital. I was invited to meet with [redacted], colorectal surgeon and research professor. My heart was heavy and I was anticipating bad news. After a long discussion he confirmed that it was possible to operate but there would be some risks and life changing outcomes. – but he could do it. WELL……I wanted to hug him and cheer! [redacted] insisted that I talk openly and frankly with my family and that all were in agreement about the way forward for me. So it was agreed that surgery would go ahead.	

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			It was at this point that intra operative radiotherapy and PLANETS charity was discussed. Before it was agreed that surgery would commence and IORT using the Mobetron machine would be used, my details were presented for assurance that I was fit enough and the prognosis for recovery was good. Fortunately for me my case was accepted and surgery was planned for [redacted] 2017. My very grateful thanks to [redacted] and PLANETS charity for providing this life-saving opportunity. The use of the Mobetron machine and IORT are amazing innovations. It would be excellent if these were available to all those for whom it would be suitable. Now, at the age of 80, I lead a full and very busy life. The activities I enjoy include volunteering with the Foodbank and my parish, singing in a choir, a pilates class, socialising and holidaying with friends and spending as much time as possible with my lovely family. Thank you.	
10	Consultee 4 NHS clinician	General	Anecdotal evidence has some value in situations where the numbers treated are small. At the Royal Berkshire Hospital in Reading we have referred patients to surgery with IOERT to Southampton where this is carried out. We refer 3 groups of patients: 1. Patients with ongoing locally advanced disease following long course chemoradiotherapy 2. Patients with locally advanced disease where external beam pelvic radiotherapy is not possible (eg previous pelvic radiotherapy) or advisable and primary surgery is considered	Thank you for your comment. Consultee describes the outcomes in a cohort of 10 patients who all survived 90 days post-op. The description does not include long-term outcomes, nor does it provide information on potential bias. The Committee welcomed the comment, but it does not meet

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			3. Patients with recurrent and locally advanced disease following previous surgery or previous complete clinical response with radiotherapy who have subsequently relapsed Our cohort of 10 patients who have undergone full or partial pelvic exenteration with IOERT have all survived beyond 90d post-op. We have seen no significant post-operative complications requiring re-operation and no significant side effects from the IOERT. IOERT in conjunction with exenteration techniques offer patients an option of cure in some cases and in others a quality of life without significant pelvic cancer which is an awful disease to treat in palliation	the evidence requirements of the NICE IP Methods Guide.

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