National Institute for Health and Care Excellence

IP 1234 – Low-energy contact X-ray brachytherapy (the Papillon technique) for early-stage rectal cancer
Consultation Comments table

IPAC date: 14 May 2015

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1: Specialist adviser	**1**	Finally, the term used in your document 'ineligible' is ambiguous. It would be better to used patients 'not suitable ' for surgery or 'high risk' patients for surgery.	**Thank you for your comment.** The recommendations in section 1 have been changed to: "1.1 In patients for whom surgery is not considered suitable, current evidence on the efficacy and safety of low energy contact X ray brachytherapy (CXB; the Papillon technique) for early stage rectal cancer is adequate to support the use of this procedure, provided that normal arrangements are in place for clinical governance, consent and audit. 1.2 In patients for whom surgery is considered suitable, but who choose not to have an operation, the evidence on safety is adequate but the evidence on efficacy is inadequate. Therefore this procedure should only be used for these patients with special arrangements for clinical governance, consent and audit or research."
2	Consultee 2: Specialist adviser	**1**	Change ineligible to unable	**Thank you for your comment.** Please refer to the response to comment 1.
3	Consultee 3: NHS professional	**1**	I am very grateful for NICE looking at Contact radiotherapy in rectal cancer and on the whole agree completely with the draft recommendations. However, I do have a few comments on the accompanying literature review.	**Thank you for your comment.**

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4	Consultee 2: Specialist adviser	**2**	Brachytherapy is the placing of radioactive material temporarily (wires/ pellets) or permanently (seeds) in or next to a tumour or placing a low energy X ray tube in close contact with the cancer (contact X-ray Brachytherapy).	**Thank you for your comment.** Section 2 aims to outline treatment options other the procedure that is being assessed in the guidance. Thus, Section 2.3 refers to the general concept of radioisotope brachytherapy as opposed to specifically describing contact X-ray brachytherapy. It was amended to add more clarity: "Radioisotope brachytherapy involves inserting radioactive pellets or seeds directly into the tumour (interstitial brachytherapy), or placing an endorectal applicator near the tumour to deliver radiation from within the rectum (Endorectal high dose rate brachytherapy)."
5	Consultee 1: Specialist adviser	**2&3**	Contact X-ray brachytherapy (the Papillon technique) use low energy (50 KV) x-rays applied straight on to the tumour under direct visual guidance. It does not use x-ray emitting catheters nor a technique where radioactive catheter is applied in close contact with the tumour (section 2.3 and 3.1 on Page 4/9).	**Thank you for your comment.** With regard to section 2.3, please refer to the response to comment 4. Section 3.1 was amended to highlight that the procedure involves inserting an X-ray tube through the anus and placing it in close contact with the tumour, to kill cancer cells and reduce the size of the tumour.
6	Consultee 2: Specialist adviser	**3**	3.1 – Remove - low energy- and start with -" Contact X-Ray Brachytherapy…". Then change to ….aims to improve local control or chance of cure of rectal cancer….	**Thank you for your comment.** Studies state that low-energy X-rays are used to perform the procedure. Section 3.1 was changed to state that: "Low energy Contact X-ray brachytherapy aims to improve local control **or cure rectal cancer".**

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7	Consultee 1: Specialist adviser	**3**	Patients can be treated with contact x-ray brachytherapy (Papillon) in supine position in patients who cannot kneel in knee chest position (section 3.2 page 5/9).	**Thank you for your comment** Section 3.2 was changed to “With the patient positioned in a knee-to-chest, prone jack-knife, or supine position…”
8	Consultee 2: Specialist adviser	**3**	3.2 – remove Low energy . Remove -(or prone jack knife position and replace with -or supine) Your last sentence is slightly contradictory , given these patient usually are not suitable for surgery. Change to ‘If the tumour does not respond to Contact Therapy, or recurs after Contact therapy surgery may be recommended.	**Thank you for your comment** Please refer to the response to comment 7. Section 3.2 was changed to: “If the tumour does not respond to low-energy contact X-ray brachytherapy, or recurs after treatment, surgery may be performed.”
9	Consultee 1: Specialist adviser	**4**	Interstitial brachytherapy boost was mention in section 4 & 5 on several papers referred in section 4.1,4.2 (page 6/9) and 5.3,5.4,5.5 (page 8/9). The word ‘Interstitial brachytherapy’ is used when needles or seeds are implanted into the tissues and should not be used for contact X-ray brachytherapy (Papillon) which can be referred instead as CXB or just as ‘Papillon’.	**Thank you for your comment.** The authors of the included papers stated that patients were treated by contact X-ray brachytherapy. Some patients also received interstitial brachytherapy. The wording in the guidance (sections 4.1, 4.2, 5.3, 5.4 and 5.5) states that: “Patients were treated by contact X-ray brachytherapy with or without interstitial brachytherapy boost.”
10	Consultee 1: Specialist adviser	**4**	There was a case series report on 97 patients with only 39 days follow up (section 4.2 Page 6/9). I am not sure this is true or typo error. If correct should not include this case series. Too short FU.	**Thank you for your comment.** The study in question (Study 4 - Rauch 2001) had a total follow-up period of 10 years; the text referred to describes the findings at a median follow-up of 39 days (complete response was reported in 85% (82/97) of patients). The study went on to report different outcome measures at 6 week, 15 month and 10 year follow-up assessments.

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11	Consultee 3: NHS professional	**4**	You make reference quite a lot to the Lyon 96-02 study of 88 patients. It should be made clear that these patients all underwent surgery with the primary endpoint being sphincter preservation.	**Thank you for your comment.** Authors state that “the main endpoint was sphincter preservation”. Section 4.1 was changed to: In the randomised controlled trial of 88 patients treated by CXB and EBRT (n=45) or EBRT alone (n=43) **all patients underwent surgery (either sphincter saving procedures or abdominoperineal resections) after initial treatment**. Sphincter-saving procedures were needed in 76% (34/45) of patients in the CXB and EBRT group and 44% (19/43) of patients in EBRT-alone group (no p values reported). **Abdominoperineal resections were needed in 24% (11/45) of patients in the CXB and EBRT group and 56% (24/43) of patients in EBRT-alone group (no p values reported).** In the same study, the actuarial colostomy rates (Kaplan–Meier estimates) were 29% in the CXB and EBRT group and 63% in the EBRT-alone group at 10-year follow-up (p<0.001).
12	Consultee 1: Specialist adviser	**4&5**	There are over 1000 patients treated since early thirties in the last century with large number of patients (over two to three hundred) in each series which were not quoted. Case series chosen in your report has very small number of patients with short follow ups. Not sure how these case series were chosen for your report.	**Thank you for your comment.** Studies included in the guidance involved primary data collection or retrospectively reviewed patient records. These studies clearly described patient selection criteria and treatment techniques. Reviews that described or pooled results from different studies/publications (some from a single centre) were not included as there was no indication that studies were selected systematically. These studies were included Appendix A of the overview

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13	Consultee 1: Specialist adviser	**4&5**	There are two case series of 380 (UK cases) and 310 (international) due for publication shortly. There are broadly two groups. One post-operative after local surgery TEMS or EMR. The efficacy of CXB treatment in T1 and T2 cases are very high (90%) when CXB is used as post- operative treatment. The second group where CXB is used as radical for elderly or younger ones who are not fit or refuse extirpative surgery. Your guidance report need to be updated on efficacy when the results of these cohorts are published later in the year.	**Thank you for your comment.** The 2 case series are being completed and the results have not been submitted for publication. Authors are hoping to submit the study manuscripts for publication in the third quarter of 2015. IPAC may update guidance upon publication of new evidence.
14	Consultee 1: NHS professional	**5**	Please note toxicity section (13) in my 'Rectal cancer' review in GEC ESTRO Handbook(2014)	**Thank you for your comment.** The toxicity section in question is a brief review of previously published studies that evaluated contact X-ray brachytherapy and HDR endoluminal rectal brachytherapy. This type of publication would not normally be included in table 2 of the overview.
15	Consultee 1: Specialist adviser	**5**	Bleeding due to CXB was mentioned in section 5.1 as lasting for 3 years in misleading and alarming as most patients who had bleeding in our experience settles after 12-18 months spontaneously or if severe will be offered argon laser ablation with excellent results. In our experience 5% of cases needed argon treatment for persistent bleeding (ACPGBI Poster2013) largest report from the UK not mentioned in your review.	**Thank you for your comment.** This adverse event was reported as stated by the authors to ensure the intended meaning is maintained. The Committee considers adverse events reported in peer-reviewed publications. The submitted conference poster is not a peer-reviewed publication and does not highlight any adverse events additional to those reported in studies that have been included in table 2 of the overview. It states that: "The main toxicity was bleeding, occurring in 26% of patients."

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16	Consultee 3: NHS professional	**5**	Rectal bleeding – only 1 patient required blood transfusions which by CTC criteria equates to a G3 toxicity rate of 1.6%	**Thank you for your comment.** This adverse event was reported as stated by the authors. The Committee considers adverse events reported in peer-reviewed publications.
17	Consultee 2: Specialist adviser	**5**	Rectal necrosis mentioned in section 5.2 is misleading as necrosis means death of tissue which result in deep painful ulceration that do not readily heal. At the end of section 5.2 it was stated that 'necrosis healed within 3-6 months in all patients' which meant that the toxicity referred to is rectal superficial ulceration and not necrosis(see first picture on our poster attached)	**Thank you for your comment.** The Interventional Procedures Programme is required to report adverse events as they are stated by authors. In order to clarify that this is the case, section 5.2 will be amended and the text expanded. The section will now read as follows: "Authors reported that 'grade 2 rectal necrosis' occurred in 19% (12/63) of patients, at a median of 7 months after treatment, in the case series of 63 patients treated by low-energy CXB followed by EBRT and interstitial brachytherapy boost. Details about the type of grading system for rectal necrosis were not provided. Authors stated that some patients had rectal necrosis which was accompanied by urgency and minor soiling. They highlighted that necrosis healed within 3 to 6 months in all patients."
18	Consultee 2: Specialist adviser	**5**	What was reported was superficial radionecrosis or rectal ulceration. We do not see full thickness rectal ulceration after Contact Therapy. Rectal ulceration may result in symptoms of urgency, frequency, tenesmus and incontinence. Rectal ulceration heals in all patients over the course of 3-6 months.	**Thank you for your comment.** Please refer to the response to comment 17.
19	Consultee 3: NHS professional	**5**	Rectal necrosis is a poor description – necrosis is irreversible. Rectal ulceration would be the more correct term as it was reported this healed in all cases.	**Thank you for your comment.** Please refer to the response to comment 17.

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20	Consultee 1: Specialist adviser	**5**	Coccygeal fracture reported in one patient in a case series of 77 patients treated by CXB cannot be attributed to CXB as coccyx is usually situated more than 20mm from rectum. The dose of radiation from CXB at 20mm is less than 10% which cannot result in bone fracture. This statement is misleading and should be remove.	**Thank you for your comment.** Authors state that one patient had a coccygeal fracture that occurred during digital rectal examination. Authors do not make it clear if this was directly related to Contact X-ray brachytherapy. Considering comments from specialist advisers, this adverse event was removed from the guidance document but remains in the overview.
21	Consultee 2: Specialist adviser	**5**	It is not possible for contact Brachytherapy to cause a coccygeal fracture as the X-rays do not travel far enough into someone to do that. The coccygeal fracture may have been incidental. Coccygeal fractures can be caused by external beam radiotherapy.	**Thank you for your comment.** Please refer to the response to comment 20.
22	Consultee 3: NHS professional	**5**	Coccygeal fracture is not a complication of contact radiotherapy as the depth dose to the coccyx from 50KV x-rays would be miniscule if we follow the inverse square law. This should not really be in the document.	**Thank you for your comment.** Please refer to the response to comment 20.
23	Consultee 1: Specialist adviser	**General**	I would like to congratulate Prof Bruce Campbell and his team in assessing this difficulty interventional procedure. As surgery is still regarded as the standard of care many elderly patients has been forced to accept extirpative surgery with high mortality(14% for over 80 years and 25% for over 90 years) and high morbidity(30-50%). At least, your publication may allow a few surgical sceptics to refer some of these ‘high risk’ patients for contact x-ray brachytherapy in the future.	**Thank you for your comment.**

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24	Consultee 4: Public	**General**	As lead volunteer for Papillon support I have spoken to over 200 patients asking for information and support on this treatment. Many are referred from [redacted] and colleagues and wish to speak to one of our 'buddies', who have had the treatment. Other individuals ring for advise and information on how to access Papillon treatment. We have been supporting patients for four years so have heard many personal experiences during this time. Patients who have opted for Papillon because they feel their quality of life would be better than if they had chosen major surgery and a stoma for life. Patients that had been given the option because of their age or medical conditions meant that they might not have survived major surgery. All these patients have been the lucky and informed ones because their clinicians had known about Papillon treatment and they got the chance to choose their preferred option. We want everyone to be given the option of choosing their own treatment which means Papillon should be a standard treatment offered to all patients with low rectal cancer.	**Thank you for your comment.** The Committee is pleased to have received the views of people who help provide support for patients with rectal cancer. IPAC does not have the remit to propose where a procedure lies in the care pathway.

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25	Consultee 5: Patient	**General**	I cannot overstate the fear of being told that you have cancer then only to be given the option of a permanent stoma or 12 months to live, I was incredibly lucky to find [redacted] at [redacted] and his Papillon technique and now 12 years on I have no cancer and thankfully I still have my bottom. This was in 2003 so I would have had to have stoma care and the incremental cost of that for the past 12 years on top of the physical and emotional cost, having a stoma at the age of 31 would have had on my life. I really hope you pass this through and help the thousands of patients who could qualify for this treatment - it's not just about saving the life, it's about the quality of the life saved!	**Thank you for your comment.** The Committee is pleased to have received the views of patients.

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26	Consultee 6: Patient	**General**	I was treated with the Papillon technique at [redacted] Hospital in February 2009. I had had TEM surgery at [redacted] the previous September followed by EBRT and oral chemotherapy. I was lucky enough to be referred for the Papillon by my surgeon and remain very grateful to him as I had not heard of the treatment at that stage. I had been diagnosed and successfully treated for breast cancer in September 2007 and really wanted to be sure that I had the best possible treatment for this entirely unexpected second cancer. I remain convinced that I did have the best possible treatment and I now lead a normal and active life with my family and friends. I am so glad that I did not have to have a colostomy and the major surgery that would have been required. I had slight complications with bleeding following the treatment, which was dealt with quickly and painlessly during a routine sigmoidoscopy. If I knew anyone who had been referred for Papillon treatment, I would wholeheartedly recommend that they accepted that offer.	**Thank you for your comment.** The Committee is pleased to have received the views of patients.

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27	Consultee 7: Patient	**General**	I have no comment to make on the document but would like to offer my experience as a recipient of the treatment. I received the treatment in February 2012. My initial diagnosis was made at [redacted] Hospital where I was offered radical treatment which would result in a permanent Stoma. I thought the treatment on offer would ruin my life and asked for a second opinion. Iwas then offered Tems treatment at [redacted] preceded by external beam therepy. The Tems procedure was carried out 3, January 2012. Unfortuately the Tems had left behind some residual cancerous cells and [redacted] (Tems Consultant) recommended the Papillon treatment. The Papillon treatment proved to be successful and has allowed me to resume a very active retirement. After three years I am clear of cancer and do not have any untoward bowel problems. I am probably fitter now than when in my 40s. I am surprised and disappointed that the Papillon procedure is not more widely available. [redacted] for instance are still not informing Patients that there may be an alternative to radical treatment and life with a Stoma.	**Thank you for your comment.** The Committee is pleased to have received the views of patients.

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28	Consultee 8: Patient	**General**	I had 4 treatments with the final one being in February 2013. I was offered this treatment by my Correctol consultant after I had refused surgery (TEMS) owing to still recuperating from major surgery in the previous 8 weeks. I found the pro0cedure very much preferable to GA and surgery. I suffered no side effects and did not require stoma (permanent or otherwise) nor other procedures. I am now a volunteer for the Papillion service and after speaking to over 80 other patients, I feel the this should be the first option as treatment for all persons who qualify due to its no invasive, little or no side effects, short duration and not painful.	**Thank you for your comment.** The Committee is pleased to have received the views of patients.

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29	Consultee 9: Patient	**General**	I have been asked to make my comments to NICE with regard to the treatment I received at [redacted] Hospital in 2009/10. I have tried to do this on line, but have experienced difficulties and am therefore setting out below my comments:- I was diagnosed with bowel cancer in October 2009. I had radiotherapy and chemotherapy from December 2009 to January 2010. In March 2010 I saw the surgeon at [redacted] Hospital, who told me that the treatment had shrunk the tumour but that I was to have an operation and be fitted with a irreversible stoma and was told this was standard procedure. I was very reluctant to have the operation as I still enjoyed swimming and skiing and could not imagine being able to do these activities with a stoma. I was 79 at the time and when I asked how long I had if I did not have the operation I was told 2 to 3 years. I said I would accept that as I would be 82 or 83 and thought that a major operation at my age would be risky. The surgeon then told me that he thought [redacted] might have an alternative. I waited just an hour or two and [redacted] was able to see me at the end of his clinic. He told me about papillon and I was pleased to accept this treatment. I had the first treatment two days later and then a further two treatments with two weeks in between. I have been closely monitored by [redacted] for the last five years and there is no evidence that the tumour has returned. I am feeling very well indeed and continue to enjoy my skiing and swimming and other activities. I am eternally grateful to [redacted] (now Professor) as is my family, for giving me the quality of life I enjoy and hope that all suitable patients in the future have the opportunity to benefit from papillon.	**Thank you for your comment.** The Committee is pleased to have received the views of patients.