

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

### Interventional procedure consultation document

# Low-energy contact X-ray brachytherapy (the Papillon technique) for early-stage rectal cancer

Rectal cancer is a common form of bowel cancer that affects the rectum (the end part of the bowel). Low-energy contact X-ray brachytherapy involves placing an X-ray tube close to the cancer to shrink the tumour. Surgery may be needed if the procedure does not work well enough.

The National Institute for Health and Care Excellence (NICE) is examining low-energy contact X-ray brachytherapy (the Papillon technique) for early-stage rectal cancer and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made provisional recommendations about low-energy contact X-ray brachytherapy (the Papillon technique) for early-stage rectal cancer.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

**Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.**

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its provisional recommendations in the light of the comments received during consultation.

- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 21 April 2015

Target date for publication of guidance: 22 July 2015

## 1 Provisional recommendations

- 1.1 For patients ineligible for surgery, current evidence on the efficacy and safety of contact X-ray brachytherapy (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 For patients eligible for surgery, 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.

- 1.3 Clinicians wishing to undertake contact X-ray brachytherapy in patients eligible for surgery, who choose not to have an operation, should take the following actions:
- Inform the clinical governance leads in their NHS trusts.
  - Ensure that patients and their carers understand alternative options for treatment and the uncertainty about this procedure's efficacy and provide them with clear written information. In addition, the use of NICE's [information for the public](#) *[[URL to be added at publication]]* is recommended.
  - [Audit](#) *[[URL to audit tool to be added at publication]]* and review clinical outcomes of all patients having contact X-ray brachytherapy (see section 7.2).
- 1.4 Patient selection should be done by a colorectal cancer multidisciplinary team, which includes a clinical oncologist and a colorectal surgeon with expertise in local excision techniques.
- 1.5 Clinicians should enter details about all patients undergoing contact X-ray brachytherapy for early-stage rectal cancer onto the contact X-ray brachytherapy database *[[URL to be added at publication]]* and review local clinical outcomes.
- 1.6 NICE encourages further research into contact X-ray brachytherapy for early-stage rectal cancer. Research should clearly describe details of patient selection and treatment intent. It should document adjunctive treatments and subsequent procedures. Outcomes should include local recurrence, survival, disease-free survival and

quality of life. NICE may update the guidance on publication of further evidence.

## **2 Indications and current treatments**

- 2.1 Rectal cancer is a common form of bowel cancer. The likelihood of developing it rises sharply with age. Symptoms include rectal bleeding and change in bowel habit, although the early stages may be asymptomatic.
- 2.2 Surgery is the main treatment for patients with rectal cancer who are treated with curative intent. It involves resection of the affected part of the rectum and the mesorectum. The anal sphincter is preserved whenever possible: a colostomy is formed when this is not possible.
- 2.3 In some patients, radiotherapy or chemotherapy or both are used before, during or after surgery to decrease the chances of local recurrence and metastatic disease. Radiotherapy may take the form of external-beam radiotherapy (EBRT) or brachytherapy. EBRT uses radiation from outside the body, which is focussed on the cancer and surrounding lymph nodes. Brachytherapy involves inserting radioactive pellets or seeds directly into the tumour (interstitial brachytherapy), or placing a radioactive catheter in close contact with the tumour (contact brachytherapy).

## **3 The procedure**

- 3.1 Low-energy contact X-ray brachytherapy (the Papillon technique) aims to improve local control of rectal cancer while preserving the anal sphincter, so reducing the need for colostomy. The procedure involves inserting an X-ray emitting catheter through the anus and

placing it in close contact with the tumour, to kill cancer cells and reduce the size of the tumour.

- 3.2 Low-energy contact X-ray brachytherapy for rectal cancer is usually delivered in a day-care setting. The patient is given an enema before treatment, to clear the bowel. With the patient positioned in a knee-to-chest position (or prone jack-knife position), local anaesthesia and glyceryl trinitrate are applied to the anal sphincter to numb the area and relax the sphincter muscles. A sigmoidoscope is inserted to check the size and position of the tumour. A rigid endorectal applicator is then inserted and placed in contact with the tumour. A contact X-ray tube is introduced into the applicator and treatment commences. The tube emits low-energy X-rays that only penetrate a few millimetres. This minimises damage to deeper tissues that are not involved in the cancer. Surgery is done if the tumour does not respond to contact X-ray brachytherapy or if it recurs after treatment.

## 4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 In a randomised controlled trial of 88 patients treated by both contact X-ray brachytherapy (CXB) and external-beam radiotherapy (EBRT; n=45) or EBRT alone (n=43), overall actuarial survival rates (Kaplan–Meier estimates) were 55% and 56% respectively, at 10-year follow-up (p=0.85). In the same study, disease-free survival rates were 53% and 54% respectively, at 10-year follow-up (p=0.99). In a case series of 101 patients treated by IPCD: Low-energy contact X-ray brachytherapy (the Papillon technique) for early-stage rectal cancer

CXB with or without interstitial brachytherapy boost, overall actuarial survival rates (Kaplan–Meier estimates) were 83% and 63% at 5 and 8 years, respectively. In the same study, disease-specific survival rates were 94% and 89% at 5 and 8 years, respectively. Actuarial survival rates for patients with stage T1 and T2 tumours were 68% and 55%, respectively, at 8-year follow-up ( $p=0.73$ ). Disease-specific survival rates for patients with stage T1 and T2 tumours were 91% and 86%, respectively, at 8-year follow-up ( $p=0.82$ ).

- 4.2 In a case series of 97 patients treated by CXB with or without interstitial brachytherapy boost, a complete response (no definition provided) was reported in 85% (82/97) of patients at a median follow-up of 39 days. In a case series of 63 patients treated by CXB followed by EBRT and interstitial brachytherapy boost, a complete clinical response (no definition provided) was reported in 92% (58/63) of patients at 2-month follow-up.
- 4.3 In the randomised controlled trial of 88 patients treated by CXB and EBRT ( $n=45$ ) or EBRT alone ( $n=43$ ), actuarial local recurrence rates (Kaplan–Meier estimates) were 10% and 15%, respectively, at 10-year follow-up ( $p=0.69$ ). Distant recurrence was reported in 27% (12/45) of patients in the CXB and EBRT group and 26% (11/43) of patients in the EBRT-alone group at 10-year follow-up (no  $p$  value reported).
- 4.4 In the randomised controlled trial of 88 patients treated by CXB and EBRT ( $n=45$ ) or EBRT alone ( $n=43$ ), 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). 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 ( $p < 0.001$ ).

- 4.5 In a case series of 312 patients treated by CXB and interstitial brachytherapy boost, a permanent colostomy was needed in 3% (8/312) of patients.
- 4.6 Specialist advisers listed the following key efficacy outcomes: overall survival, disease-free survival, clinical response, local control rates, loco-regional and distant recurrence rates, avoiding a permanent stoma, quality of life, as well as bowel, urinary and sexual function.

## 5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 Rectal bleeding was reported in 38.1% (24/63) of patients, 6 months after treatment, in a case series of 63 patients treated by contact X-ray brachytherapy (CXB) followed by external-beam radiotherapy (EBRT) and interstitial brachytherapy. Bleeding lasted for up to 3 years. Patients were treated by unspecified oral medication or argon plasma coagulation. Only 1 patient needed occasional blood transfusions.
- 5.2 Rectal necrosis was reported in 19% (12/63) of patients, at a median of 7 months after treatment, in the case series of 63 patients treated by CXB followed by EBRT and interstitial brachytherapy. Details about the type and severity of rectal

necrosis were not provided. In some patients, necrosis was accompanied by urgency and minor soiling. Necrosis healed within 3 to 6 months in all patients.

- 5.3 Ulceration of the rectal mucosa was reported in 27% (27/101) of patients, at a median follow-up of 4 months, in a case series of 101 patients treated by CXB with or without interstitial brachytherapy boost. Ulceration healed in all these patients with no late sequelae.
- 5.4 Slight proctitis was reported in 10% (32/312) of patients in a case series of 312 patients treated by CXB and interstitial brachytherapy boost. The timing of occurrence was not reported.
- 5.5 Moderate tenesmus, urgency of bowel movement or diarrhoea was reported in 15% (15/101) of patients, during the course of treatment, in the case series of 101 patients treated by CXB with or without interstitial brachytherapy boost.
- 5.6 A coccygeal fracture was reported in 1 patient in a case series of 77 patients treated by CXB. The timing of occurrence was not reported.
- 5.7 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following anecdotal adverse events: bowel perforation, rectal stenosis, recto-vaginal fistula formation, incontinence. They considered that the following were theoretical adverse events: stricture formation, fistula formation, rectal perforation.



## **6 Committee comments**

- 6.1 The Committee noted recent and continuing changes in patterns of treatment for early-stage colorectal cancer.
- 6.2 The Committee noted that contact X-ray brachytherapy for early-stage rectal cancer is currently available in only a few specialist centres in the UK.

## **7 Further information**

- 7.1 For related NICE guidance, see the [NICE website](#).
- 7.2 This guidance requires that clinicians undertaking the procedure in patients eligible for surgery who choose not to have an operation, make special arrangements for audit. NICE has identified relevant audit criteria and is developing an audit tool (which is for use at local discretion), which will be available when the guidance is published.

Bruce Campbell

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