Interventional procedure overview of low-energy contact X-ray brachytherapy for rectal cancer

Contents

Table 1. Abbreviations

Abbreviation	Definition
BCSP	Bowel Cancer Screening Programme
cCR	Clinical complete response
CTCAE	Common Terminology Criteria for Adverse Events
CXB	Contact X-ray brachytherapy
DRE	Digital rectal examination
DSS	Disease-specific survival
EBRT	External-beam radiotherapy
ECOG	Eastern Cooperative Oncology Group
EORTC	European Organisation for Research and Treatment of Cancer
EQ-5D	EuroQol 5-Dimensional Questionnaire
EQ-VAS	EuroQol Visual Analogue Scale
Gy	International unit of radiation dose (1 Gy = 1 joule/kilogram)
HADS	Hospital Anxiety and Depression Scale
IPTW	Inverse probability of treatment weighting
MRI	Magnetic resonance imaging
nCR	Near-complete response
OS	Overall survival
PFS	Progression-free survival
PROM	Patient-reported outcome measure
QLQ-C30	Quality of life questionnaire Core-30
QLQ-CR29	Quality of life questionnaire Colorectal cancer module-29
QoL	Quality of life
RCT	Randomised controlled trial
RFS	Recurrence-free survival
TME	Total mesorectal excision
TNM	Tumour node metastasis

The procedure, condition, current practice and unmet need

Information about the procedure, condition, current practice and unmet need is available in section 2 and 3 of NICE's interventional procedures consultation document on low-energy contact brachytherapy for rectal cancer.

Outcome measures

The main efficacy outcomes were organ preservation (including avoiding a permanent stoma), clinical response, survival (including OS, PFS and disease-free survival), disease recurrence, distant metastases, change in tumour staging, need for further surgery, quality of life and functional outcomes. The main safety outcomes were mortality, proctitis, rectal bleeding and radiation toxicity. Some of the measures used are detailed in the following paragraphs.

Clinical complete response

No residual tumour is visible on endoscopy palpable on DRE or detected on MRI. No further treatment is necessary, and the person needs regular close follow-up only (similar to the 'watch-and-wait' policy).

EORTC QLQ-C30/CR29

EORTC QLQ-C30 is a questionnaire to measure the quality of life of people with cancer, which covers a person's physical, psychological and social functions. EORTC QLQ-CR29 is the colorectal cancer-specific module of the EORTC QLQ questionnaire.

LARS score

The LARS score is a scoring system for assessment of bowel dysfunction following a low anterior resection for rectal cancer.

Clavien–Dindo classification

The Clavien–Dindo Classification is used to rank the severity of a surgical complication, based on the type of therapy needed to correct the complication.

The scale consists of several grades (Grade I, II, IIIa, IIIb, IVa, IVb and V), whereby Grade I is the mildest and Grade V is the most severe.

Tumour staging

The TNM classification system for malignant tumours is used to describe the stage of a cancer. 'T' describes the size and location of the primary tumour, including whether it has invaded surrounding tissue. 'N' describes the extent of which the cancer has spread to local/regional lymph nodes. 'M' describes the degree of distant metastasis. The following classification applies to colorectal cancer:

- T0: There is no evidence of colorectal cancer.
- T1: The tumour has grown into the submucosa.
- T2: The tumour has grown into the muscularis propria.
- T3: The tumour has grown through the muscularis propria into pericolorectal tissues.
- T4a: The tumour has penetrated the surface of the visceral peritoneum, meaning that it has grown through all layers of the colon.
- T4b: The tumour has grown into, or has attached to, other organs or structures.

Evidence summary

Population and studies description

This interventional procedures overview is based on evidence from 1 systematic review and meta-analysis, 2 RCTs and 10 observational studies. The systematic review included a total of 5,447 people and the RCTs included a total of 236 people, 117 of whom had the procedure. The observational studies included a total of 1,932 people, but there was likely substantial overlap between these patient populations. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 13 studies as the key evidence in table 2 and table 3, and lists 17 other relevant studies in appendix B, table 5.

All the studies were done in Europe and almost all included at least 1 centre in the UK. Seven of the key studies included only a single centre, 6 of which were based in the UK. There were 4 multicentre studies, at least 3 of which included multiple centres from the UK. Median study follow-up duration ranged from 2 to 7 years. There was substantial heterogeneity in the study populations. The median age ranged from 70 to 81 years. One study reported the mean age of its participants (72 and 74 years for the 2 subgroups, respectively). In all the studies, the population was skewed towards males, which represented between 58% and 73% of all people who were included. There was substantial heterogeneity in terms of the stage of the tumours of the study populations. Most studies included all tumour stages, but overall T2 or T3 tumours were the most prevalent.

The key studies included people who had CXB at different points of the care pathway, for example before or after chemoradiotherapy, as a neoadjuvant or adjuvant treatment and in different doses (see the section on procedure technique). They included people with tumours of different radiological stages. Both RCTs investigated CXB as a boost, but one of them compared CXB plus EBRT with EBRT alone, whereas the other had a more complex intervention arm dependent on the tumour size. Table 2 presents study details.

Figure 1. Flow chart of study selection

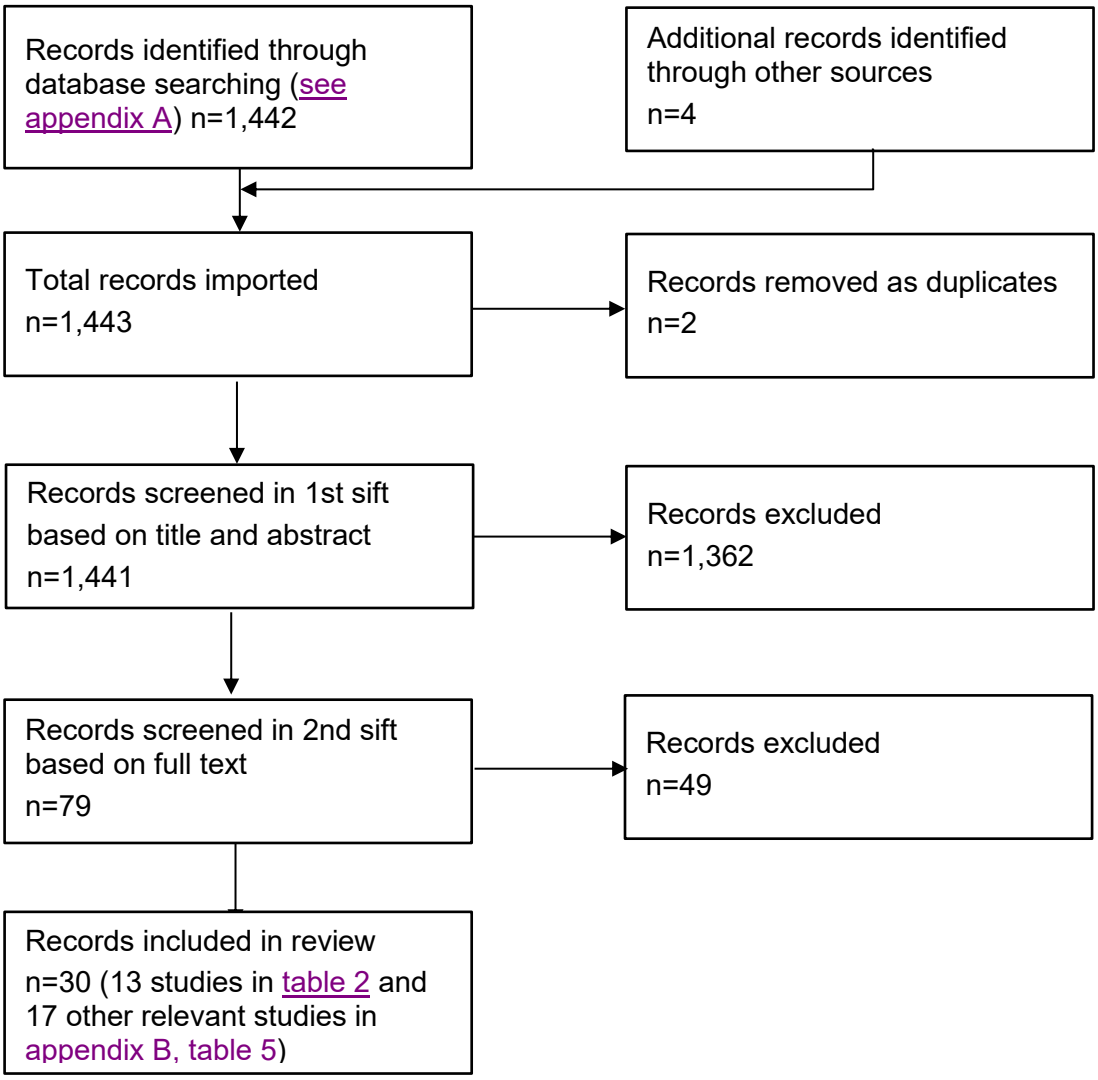

Table 2. Study details

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow-up
1	Baron 2025 Europe (17 centres)	N=148 [69 had a boost with EBRT at 9 Gy in 5 fractions (Arm A) compared with 72 having a boost with CXB at 90 Gy in 3 fractions (Arm B)] **Age** Arm A: 69 (61 to 74), Arm B: 70 (60 to 74) **Male sex** Arm A: 65%, Arm B: 58% **T2 lesions** Arm A: 64%, Arm B: 65% **N0 status** Arm A: 71%, Arm B: 76% **Distance from anal margin less than 6 cm** Arm A: 77%, Arm B: 74%	RCT (NCT025-05750)	Adults (18 or older) with biopsy proven adenocarcinoma with a cT2, cT3a or T3b tumour up to 10 cm from anal verge, less than 5 cm in diameter, and less than half the rectal circumference. They also had cN0 to cN1 disease (with lymph node less than 8 mm), no metastases and ECOG performance status of 0 or 1 and were fully operable	Boost with CXB at 90 Gy in 3 fractions (before or after chemo-radiotherapy if the tumour was less or more than 3 cm, respectively) the comparator arm was boost with EBRT only	5 years
2	Ortholan 2012 France	N=88 (45 CXB and EBRT compared with 43 EBRT alone) **Radiological stage**: T2 (n=22), T3 (n=62), unknown (n=4) **Nodal stage**: NO (n=37), N1 (n=46), unknown (n=1)	RCT	People with histologically confirmed adenocarcinoma of the lower rectum (located within 6 cm of the anal verge), classified as T2 or T3 by endorectal ultrasonography and involving less than two-thirds of the rectal	CXB Total dose of 85 Gy delivered in 3 fractions: 35 Gy, 30 Gy and 20 Gy on days 1, 8 and 21, respectively	10 years

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow-up
		Differentiation: well (n=39), moderate (n=42), poor (n=1), unknown (n=6) **CXB plus EBRT group**: median age 69 years (40 to 92 years); 62% (28 out of 45) male **EBRT-alone group**: median age 67 (29 to 79) years; 67% (29 out of 43) male		circumference; people with no signs of distant metastases		
3	Dhadda 2021 UK (2 centres), France (1 centre)	N=194 **Median age**: 69 (36 to 91) years **Male sex**: 65% **Tumour staging**: T1 (n=143), T2 (n=45), T3 (n=6)	Retrospective cohort study	People for whom standard therapy was unsuitable or refused; people with no signs of metastatic disease	Adjuvant CXB following local excision	77 months
4	Than 2024a UK (4 centres), Sweden (1 centre)	N=76 **Median age**: 78 (67 to 84) years **Male sex**: 65% **Tumour staging**: T1 (n=27), T2 (n=49)	Retrospective cohort study	People with stage 1 (T1 or T2-N0-M0) rectal cancer for whom surgery was unsuitable or declined	CXB Total dose of 90 Gy given in 3 fractions over 4 weeks, with a fourth 20-Gy dose (total 110 Gy) to selected people	26 months
5	Steinke 2023a	N=258 (N=226 who underwent CXB and short-course radiotherapy as primary treatment, and N=32	Retrospective cohort study	People who underwent CXB and short-course radiotherapy	CXB boost (ranging from 30 Gy to	24 months

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow-up
	UK (4 centres), Sweden (1 centre)	undergoing this immediately after local excision) **Median age**: 81 (49 to 103) years **Male sex**: 69% **Tumour staging**: T1 or T2 (n=182), T3 or T4 (n=72)			120 Gy) after short-course radiotherapy	
6	Than 2024b UK (1 centre)	N=328 (N=224 at low or intermediate risk and N=104 at high risk) **Median age**: 73 (62 to 80) years **Male sex**: 73% **Tumour staging**: T1 (n=1), T2 (n=117), T3 (n=188), T4 (n=22)	Retrospective cohort study	People who underwent (chemo)radiotherapy and CXB, including short- and long-course radiotherapy	CXB boost Total dose of 90 Gy given in 3 fractions over 4 weeks, with a fourth 20-Gy dose (total 110 Gy) to selected people	33 months
7	Steinke 2023b UK (1 centre)	N=193 **Median age**: 73 (33 to 103) years **Male sex**: 73% **Tumour staging**: T1 (n=27), T2 (n=98), T3 (n=64), T4 (n=3)	Retrospective cohort study	People who had at least 1 fraction of CXB	CXB Total dose up to 110 Gy in up to 4 fractions	31 months
8	Than 2024c UK (1 centre)	N=56 **Median age**: 76 (45 to 91) years	Retrospective cohort study	People who had CXB as salvage therapy for local rectal cancer	CXB Total dose up to 110 Gy in 3 to 4	37 months

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow-up
		Male sex: 71% **Tumour staging**: T2 (n=11), T3 or T4, N0 (n=14), T3 or T4, N1 or N2 (n=31) Early-stage regrowth (82%), late-stage regrowth (18%)		regrowth after a watch-and-wait approach	fractions over 4 to 6 weeks	
9	Than 2024d UK (1 centre)	N=251 (N=103 starting with EBRT and N=148 with CXB) **Mean age (before adjustment)**: EBRT first: 72 (plus or minus 11) years CXB first: 74 (plus or minus 11) years **Male sex (before adjustment)**: EBRT first: 73% CXB first: 68%	Retrospective analysis with propensity matching and IPTW	People with rectal adenocarcinoma (cT1 to cT3, N0 to 1, M0, grade 1 to 2, size of 3 cm or less) who had both EBRT and CXB, irrespective of treatment sequence	CXB Total dose up to 110 Gy in 3 to 4 fractions over 4 to 6 weeks	EBRT first: 37 months CXB first: 32 months
10	Sun Myint 2017 UK (1 centre)	N=200 **Median age**: 74 (32 to 94) years **Male sex**: 67% **Tumour staging**: cT1 (n=21), cT2 (n=89), cT3 (n=87), cT4 (n=3)	Retrospective cohort study	People with histologically proven, well to moderately well differentiated residual rectal cancer after EBRT for whom surgery was not suitable or who refused surgery; tumour situated less than	CXB boost Most people had no more than a total dose of 90 Gy delivered in 3 fractions every 2 weeks in 4 weeks	2.7 years

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow-up
				12 cm from the anal verge		
11	Powell 2025 Multiple countries	N=5,447 There is likely significant overlap with other studies included in this overview. The following studies reported in this systematic review have also been included separately in this overview: Baron (2025) Than (2024a) Than (2024b) Than (2024d) Steinke (2023a) Steinke (2024b) Sun Myint (2017)	Systematic review and meta-analysis	Randomised and non-randomised studies reporting original data regarding outcomes of people whose rectal cancer was treated with CXB	CXB using 50 kVp with a radiation dose of 80 to 110 Gy, where each session is 2 weeks apart over 4 to 6 weeks	N/A
12	Than 2025 UK (1 centre)	N=53 Median age: 71 (64 to 77.5) Male sex: 64% Tumour staging: Stage 1: 16 (30%)	Prospective observational study	All consecutive people who were referred to the Clatterbridge Cancer Centre, Liverpool, from January to October 2023, for CXB treatment either	N/A	6 and 12 months

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow-up
		Stage 2: 15 (28%) Stage 3: 19 (36%) Tx-Nx-Mx: 3 (6%)		before or after (chemo)radiation, were eligible to participate. People who had CXB as postoperative adjuvant treatment following local rectal cancer excision were excluded		
13	Ul Haq 2025 UK (1 centre)	N=323 **Median age (range)**: 71 (36 to 99) years **Male sex**: 64% **Pathologic T Stage**: T1 (n=223), T2 (n=93), T3 (n=7) **Submucosal Invasion grade (for pT1 tumours):** SM1 (n=223), SM2 (n=93), SM3 (n=7), Not available (n=179) **Clinical N stage:** N0 (n=312), N1 (n=9), N2 (n=1), NX (n=1)	Retrospective cohort study	Patients were identified from a prospectively maintained database at Clatterbridge Cancer Centre. This cohort comprises people with rectal cancer who, after local excision, were either medically unfit for completion surgery or opted to decline further operative management.	**CXB** A standard surface dose of 60 Gy was given in two 30 Gy fractions 2 weeks apart. People with minimal residual or palpable tumour after the second fraction had a third 30 Gy dose at 4 weeks, and, if needed, a fourth 20 Gy at 6 weeks. **EBRT** Regimens were tailored to patient fitness: long-course radiotherapy (40–	51 months

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow-up
					50.4 Gy in 20–25 fractions over 28–35 days) and short-course radiotherapy (25 Gy in five daily fractions). Among long-course patients, 75.1% had concurrent chemoradiotherapy, no chemotherapy was given to the short-course cohort.	

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Baron 2025	**Organ preservation rate (5-year)** EBRT group: 56% (95% CI 49 to 72) CXB group: 79% (95% CI 70 to 89) HR 0.4 (95% CI 0.21 to 0.75); p=0.003 **OS (5-year)** EBRT group: 91% CXB group: 92%; p=0.5	**Mortality** EBRT group: n=7 CXB group: n=5 **Proctitis** EBRT group: 6% (n=4) CXB group: 13% (n=9) **Radiation dermatitis** EBRT group: 9% (n=6) CXB group: 1% (n=1)

First author, date	Efficacy outcomes	Safety outcomes
	DSS (5-year) EBRT group: 46% (95% CI 34 to 61) CXB group: 73% (95% CI 63 to 85); p=0.003 **LARS score 30 or above** EBRT group: 24% (8 out of 34) CXB group: 17% (9 out of 52); p=0.5 **Distant metastases (5-year)** EBRT group: 14% CXB group: 13% **Local regrowth (5-year)** EBRT group: 33% (95% CI 19 to 44) CXB group: 16% (95% CI 7 to 24); p=0.02	**Rectal bleeding (CTCAE grade 1 or 2)** EBRT group: 17% (n=12) CXB group: 64% (n=46) **Clavien–Dindo score** EBRT group: 15% (4 out of 26) CXB group: 15% (2 out of 13)
Ortholan 2012	**cCR (5-weeks)** CXB plus EBRT group: 26% (11 out of 42) EBRT-alone group: 3% (1 out of 36) **Clinical response greater than 50% (5-weeks)** CXB plus EBRT group: 69% (29 out of 42) EBRT-alone group: 67% (24 out of 36); p<0.001 **Clinical response less than 50% (5-weeks)** CXB plus EBRT group: 5% (2 out of 43) EBRT-alone group: 31% (11 out of 36) **OS (10-year)** CXB plus EBRT group: 55% EBRT-alone group: 56% **Disease-free survival (10-year)** CXB plus EBRT group: 53% EBRT-alone group: 54%; p=0.99	**Mortality (10-year)** CXB plus EBRT group: 24% (11 out of 45) EBRT-alone group: 28% (12 out of 43)

First author, date	Efficacy outcomes	Safety outcomes
	Local recurrence rate (Kaplan–Meier estimate) (10-year) CXB plus EBRT group: 10% EBRT-alone group: 15%; p=0.69 **Distant recurrence (10-year)** CXB plus EBRT group: 27% EBRT-alone group: 26% **Sphincter saving procedures** CXB plus EBRT group: 76% EBRT-alone group: 44% **Need for abdominoperineal resection** CXB plus EBRT group: 24% EBRT-alone group: 56% **Actuarial colostomy rate (Kaplan–Meier estimate)** CXB plus EBRT group: 29% EBRT-alone group: 63%; p<0.001 **Need for a colostomy** CXB plus EBRT group: 31% EBRT-alone group: 63%	
Dhadda 2021	**Crude local relapse (median follow-up 77 months)** 7.7% (15 out of 194) **Distant metastases (median follow-up 77 months)** 9.3% (18 out of 194) **Organ preservation** 95% **Local relapse rate (Kaplan–Meier estimate) (6-year)** 9% (95% CI 4 to 13) **OS (6-year)** 81% (95% CI 75 to 87)	N/A

First author, date	Efficacy outcomes	Safety outcomes
	Local recurrence rate CXB prior to EBRT: 4.5% (6 out of 134) EBRT prior to CXB: 15% (9 out of 60); p=0.037	
Than 2024a	**cCR (median follow-up 14 months)** All people: 82% - T1 cancers only: 93% - T2 cancers only: 76%; p=0.05 • fit but refused surgery: 92% • high risk for surgery: 81% • history of prior pelvic radiotherapy: 70%; p=0.17 **Local regrowth rate (median follow-up 14 months)** All people: 18% - T1 cancers only: 16% - T2 cancers only: 19%; p=0.95 • fit but refused surgery: 22% • high risk for surgery: 29% • history of prior pelvic radiotherapy: 8%; p=0.03 **Actuarial local control rate (median follow-up 14 months)** All people: 84% - T1 cancers only: 90% - T2 cancers only: 80%; p=0.95 The actuarial local control rate did not statistically significantly differ for people based on the reason for not having surgery. **Disease-free survival** 1-year: 80% (95% CI 73% to 95%) 3-year: 70% (95% CI 60% to 82%) 5-year: 66% (95% CI 53% to 82%) **OS** 1-year: 97% (95% CI 94% to 100%)	**Late G1 to G2 rectal bleeding** 26% (12 out of 47) **Grade 3 bleeding** 4% (2 out of 47) **Acute proctitis (G1 to G2)** 9% (4 out of 47)

First author, date	Efficacy outcomes	Safety outcomes
	3-year: 75% (95% CI 70% to 87%) 5-year: 58% (95% CI 48% to 72%) Disease-free and OS were not statistically significantly different for people with T1 compared with people with T2 cancer. Disease-free survival did not statistically differ for people based on the reason for not having surgery. OS was statistically significantly lower in people who were at high risk for surgery [HR 2.54 (95% CI 1.17 to 5.59), p=0.02] and those with history of prior pelvic radiotherapy (HR 2.75 [95% CI 1.15 to 6.58], p=0.03) than those who were fit but refused surgery. **Regional relapse** All people: 3% (n=2, both had T1 tumours) **Distant relapse** All people: 3% (n=2, both had T2 tumours)	
Steinke 2023a	**cCR** 73.8% **nCR** 6.7% **cCR or nCR** - primary treatment CXB subgroup: 77.9% - CXB after local excision subgroup: 96.9%; p=0.01 • CXB first subgroup: 84.8% • EBRT first subgroup 72.2%, p=0.03 **Local relapse (in people with cCR)** - primary treatment CXB group subgroup: 16.0% - CXB after local excision subgroup: 3.2%; p<0.001	**Mortality at latest follow-up** 50%

First author, date	Efficacy outcomes	Safety outcomes
	Time to local relapse (median [range]) 14.2 (9 to 50) months; no statistically significant difference between subgroups **Distant metastasis** 2.7%; no statistically significant difference between subgroups **Permanent stoma rate** 6.2%; no statistically significant difference between subgroups **OS (2-year, 3-year, 5-year)** - primary treatment CXB subgroup: 67%, 55%, 33% - CXB after local excision subgroup: 86%, 64%, 32% **Disease-free survival (2-year, 3-year, 5-year)** - primary treatment CXB subgroup: 75%, 63%, 60% - CXB after local excision subgroup: 93%, 93%, 93%	
Than 2024b	**cCR** - low/intermediate risk: 78% - high-risk: 73%; p=0.32) **Local regrowth** - low/intermediate risk: 16.6% - high-risk: 22.4%; p=0.41 **Nodal relapse** - low/intermediate risk: 1.8% - high-risk: 5.8%; p=0.05 **Regional relapse** - low/intermediate risk: 1.3% - high-risk: 2.9; p=0.33 **Distant relapse** - low/intermediate risk: 10.7% - high-risk: 21.2%; p=0.01	**Late rectal bleeding (any grade)** 18% **Grade 3 rectal bleeding only** 1%

First author, date	Efficacy outcomes	Safety outcomes
	3-year organ preservation - low/intermediate risk: 80% - high-risk: 87%; p=0.25 **5-year disease-free survival** - low/intermediate risk: 62% - high-risk: 64%; p=0.46 **OS** - low/intermediate risk: 67% - high-risk: 64%; p=0.88	
Steinke 2023b	**cCR** - Treatment with radical intent: 82% (78 out of 95) - Treatment after local excision: 100% (28 out of 28) - Treatment of recurrent disease after previous EBRT: 40% (4 out of 20) - Treatment of recurrent disease after no previous EBRT: 83% (5 out of 6) **nCR** - Treatment with radical intent: 3% (3 out of 95) - Treatment after local excision: 0% (0 out of 28) - Treatment of recurrent disease after previous EBRT: 20% (2 out of 20) - Treatment of recurrent disease after no previous EBRT: 0% **Partial response** - Treatment with radical intent: 4% (4 out of 95) - Treatment after local excision: 0% (0 out of 28) - Treatment of recurrent disease after previous EBRT: 10% (1 out of 20) - Treatment of recurrent disease after no previous EBRT: 0% **OS (treatment with radical intent; n=119)** - 2 years: 81%	

First author, date	Efficacy outcomes	Safety outcomes
	- 3 years: 77% - 5 years: 65% **Disease-free survival (treatment with radical intent; n=119)** - 2 years: 90% - 3 years: 85% - 5 years: 75% **Relapse-free survival (treatment with radical intent; n=119)** - 2 years: 85% - 3 years: 79%	
Than 2024c	**Any regrowth (n=56)** **cCR (6 months)** 57% (32 out of 56) **Disease-free survival** 1 year: 69% 3 years: 51% 5 years: 51% **OS** 1 year: 100% 3 years: 82% 5 years: 65% **Early-stage regrowth subgroup (n=46)** **cCR or nCR (6 months)** 61% (28 out of 46) **Sustained local control (median follow-up 39 months)** 79% (22 out of 28) **Further local regrowth (median follow-up 39 months)** 21% (6 out of 28) **Advanced stage regrowth subgroup (n=10)**	Proctitis symptoms (erratic bowel habits) as acute reactions and late rectal bleeding occurred in only 10 people (18%) after CXB. All these symptoms were self-limiting (CTCAE grade 1 or 2), and none of these people needed any intervention for their symptoms. Impaired anal sphincter function was not observed in any of the people in our cohort.

First author, date	Efficacy outcomes	Safety outcomes
	cCR or nCR (6 months) 40% (4 out of 10) **Sustained local control (median follow-up 39 months)** 50% (2 out of 4) **Further local regrowth (median follow-up 39 months)** 50% (2 out of 4)	
Than 2024d	**Unadjusted analysis** **cCR** - EBRT first: 79% - CXB first: 88%; p=0.07 **Local regrowth** - EBRT first: 19% - CXB first: 15%; p=0.81 **Nodal/regional relapse** - EBRT first: 4% - CXB first: 3%; p=0.60 **Distant relapse** - EBRT first: 13% - CXB first: 8%; p=0.24 **Organ preservation rate (3-year)** - EBRT first: 69% (95% CI 55% to 78%) - CXB first: 75% (95% CI 63% to 79%) • HR: 0.82 (95% CI 0.51 to 1.32); p=0.29 **Disease-free survival (3-year)** - EBRT first: 78% (95% CI 72% to 82%) - CXB first: 80% (95% CI 75% to 85%) • HR (univariable analysis): 0.87 (95% CI 0.45 to 1.67); p=0.68 • HR (multivariable analysis): 0.84 (95 %CI 0.39 to 1.82); p=0.66	**Rectal bleeding** - EBRT first: 18% - CXB first: 32%; p=0.01

First author, date	Efficacy outcomes	Safety outcomes
	OS - EBRT first: 78% (95% CI 73% to 84%) - CXB first: 79% (95% CI 74% to 84%) • HR (univariable analysis): 0.88 (95% CI 0.63 to 1.22); p=0.44 • HR (multivariable analysis): 0.65 (95% CI 0.43 to 0.97); p=0.03 **Propensity score-matched analysis** **cCR** - EBRT first: 78% - CXB first: 85%; p=0.39 **Local regrowth** - EBRT first: 18% - CXB first: 12%; p=0.47 **Nodal/regional relapse** - EBRT first: 3% - CXB first: 1.4%; p=1.00 **Distant relapse** - EBRT first: 10% - CXB first: 6%; p=0.53 **Organ preservation rate (3-year)** - EBRT first: 70% (95% CI 55% to 80%) - CXB first: 75% (95% CI 72% to 85%) • HR: 0.66 (95% CI 0.35 to 1.26); p=0.20 **Disease-free survival (3-year)** - EBRT first: 78% (95% CI 72% to 90%) - CXB first: 82% (95% CI 78% to 97%) • HR (univariable analysis): 0.47 (95% CI 0.16 to 1.38); p=0.17 • HR (multivariable analysis): 0.50 (95% CI 0.16 to 1.55); p=0.23 **OS** - EBRT first: 77% (95% CI 73% to 83%)	

First author, date	Efficacy outcomes	Safety outcomes
	- CXB first: 85% (95% CI 80% to 95%) • HR (univariable analysis): 0.58 (95% CI 0.37 to 0.91); p=0.02 • HR (multivariable analysis): 0.44 (95% CI 0.28 to 0.73); p<0.01 **IPTW analysis** **cCR** - EBRT first: 86% - CXB first: 88%; p=0.57 **Local regrowth** - EBRT first: 19% - CXB first: 10%; p=0.20 **Nodal/regional relapse** - EBRT first: 3% - CXB first: 3%; p=1.0 **Distant relapse** - EBRT first: 8% - CXB first: 7%; p=0.75 **Organ preservation rate (3-year)** - EBRT first: 73% (95% CI 55 to 80) - CXB first: 80% (95% CI 72 to 90) • HR: 0.47 (95% CI 0.35 to 1.10); p=0.27 **Disease-free survival (3-year)** - EBRT first: 87% (95% CI 76% to 92%) - CXB first: 88% (95% CI 78% to 95%) • HR (univariable analysis): 0.46 (95% CI 0.16 to 1.51); p=0.20 • HR (multivariable analysis): 1.03 (95% CI 0.46 to 2.29); p=0.95 **OS** - EBRT first: 78% (95% CI 65% to 85%) - CXB first: 78% (95% CI 70% to 82%)	

First author, date	Efficacy outcomes	Safety outcomes
	• HR (univariable analysis): 0.70 (95% CI 0.48 to 1.03); p=0.06 • HR (multivariable analysis): 0.58 (95% CI 0.40 to 0.85); p<0.01	
Sun Myint 2017	**cCR** 72% (144 out of 200) **Clinical incomplete response** 28% (56 out of 200) **Local regrowth after initial cCR** 11% (16 out of 144) **Distant metastases** 8.5% (17 out of 200) **Disease-free survival** 2-year: 72% (95% CI 66% to 78) 3-year: 65% (95% CI 58% to 72) 5-year: 53% (95% CI 44% to 62) **OS** 2-year: 88% (95% CI 83% to 93%) 3-year: 82% (95% CI 83% to 93%) 5-year: 64% (95% CI 55% to 73%) **Local PFS** 2-year: 74% (95% CI 68% to 80%) 3-year: 66% (95% CI 59% to 73%) 5-year: 52% (95% CI 43% to 61%)	**CXB-related mortality** 0% **Rectal ulceration (grade 1) after CXB, healed within 3 to 6 months** 30% **Bleeding (grade 1) due to telangiectasia** 28% (56 out of 200) **Haemostasis (grade 2) needed argon beam therapy** 10.5 (21 out of 200) **Colostomy to teat gastrointestinal toxicity** 0%
Powell 2025	**cCR** 82% (95% CI 76% to 88%) **Local regrowth** 20% (95% CI 15% to 25%) **Long term disease control post salvage surgery**	**Overall proctitis occurrence** 17% (95% CI 12% to 22%) **Severe proctitis occurrence** 7% (95% CI 3% to 12%) **Rectal bleeding occurrence**

First author, date	Efficacy outcomes	Safety outcomes
	88% (95% CI 78% to 96%) **Organ preservation** 81% (95% CI 74% to 88%)	24% (95% CI 13% to 35%)
Than 2025	**N/A**	**N/A**
Ul Haq 2025	**Local recurrence** 2-year: 4% 3-year: 6% 5-year: 8% **Distant recurrence** 2-year: 2% 3-year: 3% 5-year: 7% **OS** 3-year: 93% (95% CI 90% to 96%) 5-year: 84% (95% CI 80% to 88%) **RFS** 2-year: 94% (95% CI 90% to 96%) 3-year: 92% (95% CI 89% to 95%) **No statistically significant difference between excision types or radiotherapy schedules.**	**Acute proctitis** Grade 1: 2% Grade 2: 2% **Rectal bleeding** Grade 1: 7% Grade 2: 7% Grade 3: 14% **Needed blood transfusion** 2%

Procedure technique

Ten of the 13 studies detailed the device used, although the device could be inferred with high likelihood in the remaining 3 studies. The majority of the studies used the Papillon-50 machine (Ariane Medical Systems) (Baron 2025, Dhadda 2021, Than 2024a, Than 2024b, Than 2024c, Than 2024d). The Papillon-50 machine was also likely used in Steinke 2023a and Steinke 2023b. Sun Myint (2017) reported using the Papillon-50 machine after 2009 and the Therapax machine (Pantak) between 1993 and 2009. Ul Haq (2025) also reported using the Papillon-50 after 2009 and the Therapax machine (Pantak) between 2003 and 2009). Two studies reported using the RT50 machine (Philips) (Ortholan 2012 and Powell 2025). All of the devices were reported to deliver a beam of 50 kV X-rays (half-value layer 0.64 mm Al, 2.7 mA). Experts informed NICE that a new Papillon Plus machine has recently become available. However, this new device was not used in any of the included studies.

Most studies reported details about the procedure. When reported, the procedure was delivered exclusively in an outpatient setting. The total dose varied but in most studies it was 85 to 90 Gy delivered in 3 to 4 fractions in 4 to 6 weeks. Some people had up to 110 Gy (Than 2024a, Than 2024b, Than 2024c, Than 2024d). In the study by Steinke (2023a) the total CXB doses ranged from 30 Gy to 120 Gy. People who had CXB after local excision of the tumour had a dose of 60 Gy in 2 fractions (Dhadda 2021).

Efficacy

Clinical response

Most studies reported outcomes related to clinical response. cCR was reported in 9 of the studies. Two studies also reported nCR and 2 studies reported a combined cCR and nCR. One study also reported partial response and another study reported clinical incomplete response.

Than (2024a) observed a cCR in 82% of people at a median follow-up of 14 months. The cCR was statistically significantly higher in those with T1 tumours than those with T2 tumours (93% compared with 76%; p=0.05). The cCR rate was also higher among people who were fit but refused surgery than in those who were at high risk for surgery and those with history of prior pelvic radiotherapy (92% compared with 81% and 70%; p=0.17). The study population was 76 people. Steinke (2023a) reported a cCR rate of 74% in a cohort of 258 people after a median follow-up of 2 years. The nCR rate in the same cohort was 7%. In this study, the combined cCR/nCR rate was statistically significantly lower in the primary treatment CXB subgroup (78%) than in the CXB after local excision subgroup (97%; p=0.01). The combined cCR/nCR rate was also statistically significantly higher in the CXB first subgroup (85%) than in the EBRT first subgroup (72%, p=0.03).

After a median follow-up of 33 months, Than (2024b) observed a higher cCR rate among people who were at low or intermediate risk (78%) than among people who were at high-risk (73%), but the results were not statistically significant.

Steinke (2023b) reported cCR rates of 82% among people having CXB with radical treatment intent, 100% among people having CXB after local excision, 40% among people having CXB as treatment of recurrent disease after previous EBRT and 83% among people having CXB as treatment of recurrent disease after no previous EBRT. nCR was achieved in 3%, 0%, 20% and 0% of the subgroups, respectively. Partial response was achieved in 4%, 0%, 10% and 0% of the subgroups. The second, third and fourth subgroup included a small number of people.

Ortholan (2012) reported a higher cCR rate at 5-weeks among people who had CXB along EBRT than among people who had only EBRT (26% versus 3%). The study included people who had T2 or T3 tumours only.

Sun Myint (2017) observed a cCR rate of 72% in a cohort of 200 people having CXB as a boost after a median follow-up of 2.7 years. The clinical incomplete response rate in the same cohort was 28%.

Than (2024c) reported a 6-month cCR rate of 57% among 56 people who had CXB as salvage therapy for local rectal cancer regrowth after a watch-and-wait approach. In the same study the authors observed a combined cCR/nCR rate of 61% among 46 people with early-stage regrowth. But the combined cCR/nCR rate was 40% among 10 people with advanced stage regrowth.

Than (2024d) compared the cCR rate among 103 people who had EBRT first and 148 people who had CXB first. The rate was higher (but not statistically significantly different) in the CXB first group in both the unadjusted analysis (79% compared with 88%; p=0.07), propensity-matched analysis (78% compared with 85%; p=0.39) and IPTW analysis (86% compared with 88%; p=0.57).

Ortholan (2012) also reported the rates of clinical response greater and less than 50% at 5 weeks. Clinical response greater than 50% rate was higher in the CXB plus EBRT group (69%) than in the EBRT-alone group: (67%) and the difference was statistically significant (p<0.001). Conversely, the clinical response less than 50% rate was lower in the CXB plus EBRT group (5%) than in the EBRT-alone group (31%) (no p-value stated).

Powell (2025) included 24 studies (N=2,365) reporting cCR. The pooled rate of cCR was 82% (95% CI 76% to 88%). Meta-analysis of two RCTs included in this systematic review showed a significantly higher rate of cCR when CXB has been combined with EBCRT compared to EBCRT with EBRT boost, with an overall odds ratio of 7.89 (95% CI 3.31 to 18.83, n=222, p <0.01). 17 studies (N=668) reported cCR rate according to T-stage. Early-stage disease has a higher rate of cCR compared with more advanced disease, with pooled cCR rates of 91%, 76% and 75%, respectively for T1, T2, and T3 disease. Increased cCR rates were also noted with the addition of concomitant therapies.

Organ preservation

Six studies reported outcomes related to organ preservation. Three of them reported an organ preservation rate. Baron (2025) compared the 5-year organ preservation rate between people randomised to have an EBRT boost or a CXB boost. The organ preservation rate was statistically significantly lower for people who had the EBRT boost (56% compared with 79%; HR 0.4, p=0.003). Than (2024d) found the 3-year organ preservation rate higher in people who had CXB first compared with people who had EBRT first. The organ preservation rates were 69% versus 75% (unadjusted analysis), 70% versus 75% (propensity-matched analysis) and 73% versus 80% (IPTW analysis). But, the difference was not statistically significant in any of the analyses. In another study, Than (2024b) found a 3-year organ preservation rate lower in people at low or intermediate surgical risk compared with those at high risk, but the difference was not statistically significant (80% versus 87%; p=0.25).

Dhadda (2021) reported an organ preservation rate of 95% among 194 people who had adjuvant CXB after local excision of a tumour across 3 centres with a median follow-up of 77 months.

Ortholan (2012) reported 4 outcomes relevant to organ preservation in the small RCT in France. The authors observed more sphincter saving procedures in the CXB plus EBRT group than in the EBRT-alone group (76% compared with 44%). They also reported fewer people needing a colostomy in the CXB plus EBRT group than in the EBRT-alone group (31% compared with 63%) and fewer people needing an abdominoperineal resection in the CXB plus EBRT group than in the EBRT-alone group (24% compared with 56%). It was not reported if the results were statistically significantly different. The authors observed a lower actuarial colostomy rate in the combined treatment group (29% compared with 63%; p<0.001). Finally, Steinke (2023a) reported a permanent stoma rate of 6% in a

cohort of 258 people after a median follow-up of 2 years. There was no statistically significant difference in the rate between people who had CXB and short-course radiotherapy as primary treatment those who had the procedure after local excision of a tumour.

Powell (2025) reported consolidated findings from 15 studies (N=1,133), 80% (95% CI 73% to 87%) of people whose rectal cancer was treated with CXB ultimately did not need resection of the rectum.

Survival

Twelve of the 13 studies reported OS estimates. The longest follow-up was reported by Ortholan (2012) who observed a nearly identical 10-year OS among people who had CXB and EBRT and people who had EBRT only (55% and 56%, respectively) in their small RCT. In the larger and more recent RCT, Baron (2025) observed no statistically significant difference in the 5-year OS between people randomised to have EBRT or CXB (91% versus 92%; p=0.5). Than (2024a) observed OS of 97% (1-year), 75% (3-year) and 58% (5-year) among 56 people with stage I cancer. OS did not statistically significantly differ for people with T1 compared with people with T2 cancer, but was statistically significantly lower in people who were at high risk for surgery (HR 2.54, p=0.02) and those with history of prior pelvic radiotherapy (HR 2.75, p=0.03) than in those who were fit but refused surgery.

Steinke (2023a) reported OS at 2 years, 3 years and 5 years, separately for people who had CXB as primary treatment and people who had CXB after local excision. The OS rates were 67% and 86%, 55% and 64%, 33% and 32%, respectively. The study included 4 centres. In a single centre analysis, Steinke (2024b) reported OS among people who had CXB as treatment with radical intent only. The OS at 2 years, 3 years and 5 years was 81%, 77% and 65%, respectively. Similarly, in a single centre Sun Myint (2017) recorded OS at 2 years, 3 years and 5 years for people having CXB after EBRT. The observed rates were 88%, 82% and 64%, respectively. Than (2024d) investigated whether

the OS differed for people in a single centre dependent on the sequence of treatment. OS was higher for people who had CXB first. The magnitude was high in the propensity-matched analysis, but small in the unadjusted and the IPTW analyses. The difference was statistically significant in the multivariable analyses in all 3 cases.

Another single-centre study observed no statistically significant difference between the 5-year OS of people at low or intermediate surgical risk and people at high surgical risk (67% compared with 64%; p=0.88) (Than 2024b).

Than (2024c) observed OS of 100% (1 year), 82% (3 years) and 65% (5 years) among people who having CXB as salvage therapy for local rectal cancer regrowth. Six-year OS among people having adjuvant CXB following local excision was 81% according to Dhadda (2021).

Ul Haq (2025) observed an OS of 95% (3 year), and 84% (5 year) in people who had post excision CXB with EB(C)RT. An RFS of 94% (2 year) and 92% (3 year) was also reported.

Eight of the studies also reported disease-free survival. The longest follow-up was again reported by Ortholan (2012) who observed no statistically significant difference for people in the CXB plus EBRT and EBRT-only group (10-year disease-free survival of 53% compared with 54%; p=0.99). Than (2024a) observed disease-free survival of 80% (1-year), 70% (3-year) and 66% (5-year) among 56 people with stage I cancer; it was not statistically significantly different for people with T1 compared with T2 cancer or based on the reason for not having surgery. Disease-free survival was similar in the primary treatment CXB subgroup observed by Steinke (2023a): 75%, 63% and 60% at 2, 3 and 5 years, respectively. But survival was higher in the CXB after local excision subgroup: 93%, 93% and 93% for the same timepoints. The number of people in the latter subgroup was notably smaller. In another study Steinke (2023b) reported the disease-free survival for people having CXB with radical intent only; the observed survival probabilities were 90% at 2 years, 85% at 3 years and 75% at 5 years.

The authors also reported relapse-free survival probabilities which were slightly lower: 85% at 2 years and 79% and 3 years. Sun Myint (2017) observed slightly lower disease-free survival at the same intervals: 72% (2 years), 65% (3 years) and 53% (5 years). The authors also reported very similar local PFS: 74% (2 years), 66% (3 years) and 52% (5 years).

Than (2024d) found disease-free survival to be higher for people who had CXB first rather than EBRT first in both the unadjusted, propensity-matched and IPTW analyses, but the results were not statistically significant in either the univariable or multivariable analyses. In another study, the author observed 5-year disease free survival of 62% for people at low or intermediate surgical risk and 64% for people at high surgical risk: 64% (Than 2024c). The difference was not statistically significant (p=0.46).

In their small retrospective study Than (2024c) recorded lower disease-free survival among people having CXB as salvage therapy: 69% (1 year), 51% (3 years) and 51% (5 years).

Instead of disease-free, the RCT by Baron (2025) reported DSS. DSS at 5 years was found to be statistically significantly higher among people randomised to the CXB group (73%) than that of people in the EBRT group (46%; p=0.003).

The reporting of survival outcomes within the included studies in Powell (2025) was inconsistent, primarily because of differences in follow-up durations. The most commonly cited survival outcomes were 3- and 5- year DFS and OS. A pooled analysis from 6 studies including 580 people revealed a 3-year DFS rate of 81% (95% CI 73% to 89%) and a 5-year rate of 69% (95% CI 60–78%) from 8 studies involving 781 people. Regarding OS, the data presented include a 3-year rate of 85% (95% CI 61% to 99%) from 3 studies with 175 people, and a 5-year rate of 73% (95% CI 65% to 82%) from 11 studies with 963 people.

Disease regrowth

Studies included data on local regrowth. Baron (2025) provided evidence for statistically significantly lower local regrowth at 5 years in people randomised to CXB compared with people having EBRT (16% versus 33%; p=0.02). Local regrowth after initial cCR was observed in 11% of people by Sun Myint (2017) after a median follow-up of 2.7 years. Than 2024a reported local regrowth rates at a median follow-up of 14 months. They were 18% for all people, 16% for people with T1 cancers only and 19% for people with T2 cancers only. The difference between the latter subgroups was not statistically significant (p=0.95). In a single-centre study the same author observed local regrowth rates of 17% and 22% for people at low/intermediate risk and high risk, respectively (but the difference was not statistically significant; p=0.41). The local regrowth rates were not statistically significantly different for people who had EBRT or CXB first in either the unadjusted, propensity-matched or IPTW analyses by Than (2024d).

The small retrospective study of people who had CXB as salvage therapy for local rectal cancer regrowth after a watch-and-wait approach observed further early-stage local regrowth after a median follow-up of 39 months in 21% of people (Than 2024c). Further advanced-stage local regrowth was observed in 2 out of 4 people (50%).

Data on local regrowth was available for 28 studies (N=2,963) included in Powell (2025). The pooled local regrowth rate was 20% (95% CI 15% to 25%). The results of this paper appear to suggest that EBCRT, when combined with CXB, appears to have a protective effect against the risk of local regrowth with a pooled estimate of 13% (95% CI 10% to 17%, n=494) for studies using CXB and EBCRT, compared with 24% (95% CI 16% to 32%, n=1,424) for studies using CXB and EBRT, and 22% (95% CI 12% to 33%, n=1,045) for CXB alone.

Disease recurrence

Local recurrence was reported in 4 studies. The longest follow-up was available from the small RCT by Ortholan (2012). The local recurrence rate (Kaplan–Meier

estimate) at 10 years was 10 in the CXB plus EBRT group and 15% in the EBRT-alone group. The difference was not statistically significant (p=0.69). Steinke (2023a) only reported local relapse in people who had achieved cCR. The respective rates were 16% in the CXB as a primary treatment subgroup and 3% in the CXB after local excision subgroup. The difference was highly statistically significant (p<0.001). The multi-centre study by Dhadda (2021) reported a crude local relapse at a median follow-up of 77 months of 7.7%. The local relapse rate (Kaplan–Meier estimate) was 9% at 6 years for people having adjuvant CXB following local excision. The local recurrence rate was lower for people who had CXB prior to EBRT (4.5%) than for those having EBRT prior to CXB (15%). The difference was statistically significant (p=0.037), but based on a small number of events. Ul Haq (2025) reported a local recurrence rate of 4% (2 year), 6% (3 year) and 8% (5 year).

In addition to the local relapse rate, Steinke (2023a) also reported that the median time to local relapse was 14 months. It was not statistically significant difference between subgroups (people who had CXB as a primary treatment and people who had CXB after local excision).

Three studies also estimated regional relapse. With a median follow-up of 2 years, Than (2024a) observed regional relapse in 2 out of 76 people with stage I cancer, which represented 3% of the study population. In a larger single-centre study the authors noted regional relapse in 1% of people who were at a low or intermediate surgical risk and 3% of people who were at high risk. The median follow-up was 33 months and the difference was not statistically significant (p=0.33).

One study reported nodal relapse, whereas another reported combined regional/nodal relapse. Nodal relapse was statistically significantly lower among people at low/intermediate risk compared with people at high risk (2% versus 6%; p=0.05) in the single centre, retrospective cohort study by Than (2024b). In another single centre, retrospective study by Than (2024d), nodal/regional

relapse was higher among people who had EBRT first in both the unadjusted analysis (4% versus 3%; p=0.60) and propensity-matched analysis 3% versus 1%; p=1.00). The rates were the same in the IPTW analysis (3% versus 3%; p=1.0).

Eight studies included data on distant recurrence. In the recent multicentre RCT, Baron (2025) observed similar rates of distant metastases among people randomised to EBRT (14%) and people randomised to CXB (13%) at 5 years. Similarly, another small RCT found very similar rates of distant recurrence at 10 years in people who had CXB with EBRT (27%) and people who had EBRT only (26%; Ortholan 2012). This trend was also observed by Than (2024d). Distant relapse was lower in the CXB first group and higher in the EBRT first group, but the difference was not statistically significant in the unadjusted, propensity-matched or IPTW analyses. Ul Haq (2025) reported a distant recurrence rate of 2% (2 year), 3% (3 year) and 7% (5 year).

The single-centre retrospective study by Sun Myint (2017) reported distant metastases in 8% of all cases at the end of study period, with a median follow-up of 2.7 years. In the small retrospective study by Than 2024a distant relapse occurred in 2 people (3%) only. The study population was only people with stage 1 (T1 or T2-N0-M0) rectal cancer and the median follow-up was slightly above 2 years (26 months).

Steinke (2023a) reported a rate of distant metastasis of 3% across 5 centres after a median follow-up of 2 years. The authors found no statistically significant difference between the 2 subgroups (people having CXB as primary treatment and people having CXB after local excision). But, in a large cohort from a single centre, distant relapse occurred statistically significantly less often in people at low or intermediate surgical risk than people at high surgical risk (11% compared with 21%; p=0.01).

The single-centre study by Dhadda 2021 reported distant metastases in 9% of people who had adjuvant CXB following local excision after a median follow-up of 77 months.

Local control

Two small retrospective studies reported rates of local control. The actuarial local control rate in 76 people with stage 1 rectal cancer was 84% (90% for people with T1 cancer and 80% for people with T2 cancer; Than 2024a). The local control rate did not statistically significantly differ based on the reason for not having surgery. Than (2024c) only reported the local control rates per subgroup. The rates were 79% among 28 people with early-stage tumour regrowth and 50% among 2 people with advanced stage tumour regrowth.

Bowel function

Only 1 study assessed bowel function (Baron 2025). The authors reported a slightly higher LARS score in people who were randomised to have an EBRT boost (24%) than in people who had a CXB boost (17%), but the difference was not statistically significant.

Safety

Mortality

Four studies contained data on mortality. Baron (2025) observed 7 deaths in the EBRT group and 5 in the CXB group at 5 years. Nine of those were cancer related. The small French RCT comparing CXB and EBRT with EBRT alone recorded 10-year mortality rates of 24% in the CXB plus EBRT group and 28% in the EBRT-only group (Ortholan 2012).

Steinke (2023a) reported that nearly half of 258 people who had CXB across 5 centres were dead at the latest follow-up timepoint (this was not reported; the median follow-up was 2 years). The number was extracted from a table with results, but the authors did not interpret it in the study.

Sun Myint (2017) reported only CXB-related deaths in a retrospective analysis of a single-centre cohort of 200 people. No CXB-related deaths were observed.

Rectal bleeding

Six studies recorded rectal bleeding. This outcome occurred in 17% of people randomised to EBRT and 64% of people randomised to CXB in the OPERA trial (Baron 2025). But the bleeding presented as CTCAE grade 1 or 2 only. Similarly, Than (2024d) observed higher rates of rectal bleeding in the CXB first group (32%) than in the EBRT first group (18%). The difference was statistically significant (p=0.01). Sun Myint (2017) observed grade 1 bleeding caused by telangiectasia in 56 out of 200 people (28%) in a single centre. Than (2024b) recorded rectal bleeding in 18% of people. Most of the cases were grade 1 or 2, but grade 3 bleeding, which needed blood transfusion, occurred in 3 people (1%). Slightly higher rates were observed by Than (2024a) in the small multicentre study of people with stage 1 cancer. Grade 1 or 2 rectal bleeding occurred in 26% of all people and grade 3 bleeding in 4%. In Ul Haq (2025), 14% of participants had grade 1–2 rectal bleeding, and a further 14% developed grade 3 bleeding.

Fourteen studies (N=1,119) in Powell (2025) reported rectal bleeding. Overall, the rate was moderate, at 24% (95% CI 13% to 35%). Most rectal bleeding was mild and self-limiting. 7% of people needed blood transfusion, and 6% had argon beam therapy to control rectal bleeding.

Proctitis

Proctitis was recorded by Ul Haq (2025), Powell (2025), Baron (2025), Than (2024a) and Than (2024c). The outcome occurred in 6% of people randomised to the EBRT group and 13% of people randomised to the CXB group. A similar rate (9%) was observed by Than (2024a) among 76 people with stage 1 cancer.

Than (2024c) noted that proctitis symptoms (erratic bowel habits) as acute reactions and late rectal bleeding occurred in 10 out of 56 people (18%) who had

CXB as salvage therapy for local rectal cancer regrowth after a watch-and-wait approach.

In Powell (2025) the overall occurrence of proctitis was moderate at 17% (95% CI 12% to 22%). But most cases were mild, with severe grade 3 or higher proctitis occurring in only 7% of people.

In Ul Haq (2025) the occurrence of proctitis was relatively low, with 2% of participants experiencing grade 1 proctitis, and 2% experiencing grade 2 proctitis.

Other safety-related outcomes

Radiation dermatitis was overall rare but occurred more often in people randomised to the EBRT group than with the CXB group in the OPERA trial (9% compared with 1%; Baron 2025). The Clavien–Dindo scores in this RCT were the same (15% in both groups).

Sun Myint (2017) observed grade 1 rectal ulceration in 30% of people in a single centre analysis. In the same study the team reported 0% of people needed a colostomy to teat gastrointestinal toxicity.

Anecdotal and theoretical adverse events

Expert advice was sought from consultants working in the field. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They listed the following anecdotal adverse events:

- rectal telangiectasia.

They listed the following theoretical adverse events:

- rectal stenosis/fistula
- rectal perforation
- infection

- diarrhoea
- tenesmus.

Thirteen professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Quality of life and patient reported outcomes

In Than (2025), QoL was assessed in 53 people who had CXB for various clinical indications, with 51, 47, and 42 remaining at the end of treatment, 6-month and 12-month follow-ups, respectively. Overall, symptom and functional scores from EORTC-QLQ-CR29 remained stable throughout the follow-up period. Significant improvements were observed in abdominal pain, flatulence, urinary frequency and body weight at 12 months. HADS and EQ-5D-3L scores remained stable, while EQ-VAS scores showed improvement, indicating a good overall quality of life following CXB treatment.

Validity and generalisability

- Only 2 of the studies were designed to include random assignment. The remaining studies were retrospective cohort analyses. But some of those compared subgroups; 1 of the studies (Than 2024d) performed statistical adjustment of those subgroups to improve comparability.
- There is a lack of long-term follow-up, with the longest available being 10 years, as reported in Ortholan (2012). But this was somewhat different from the other studies (see below). The next longest was 77 months, and the rest of the studies with follow-up details are between 1 and 5 years' follow-up.
- 11 out of 12 studies were fully or primarily from the UK. 1 small RCT was conducted in France (Ortholan 2012).
- Ortholan (2012) produced results that differed somewhat from those observed in the other studies included in this review. This may be because of the use of

older data, a different device, or a higher proportion of stage T2 or T3 people in the study population.

- There may be overlap in the populations of some studies, in particular the retrospective cohort studies and the systematic review. The potential for selection bias was also noted by expert advisers.
- The evidence is highly heterogeneous in terms of the position of CXB in the treatment pathway, and therefore in the type of care received before and along with CXB. Several of the studies have investigated CXB as immediate neoadjuvant treatment, with or without EBRT. A minority of studies included people having CXB as an adjuvant treatment.
- There was notable heterogeneity in terms of the stage of the tumours of the study populations. Most studies included all tumour stages, but overall T2 or T3 tumours were the most prevalent. Some studies based inclusion or exclusion criteria on tumour stages. Experts highlighted that this is a key consideration as there is variation in how tumour stages are defined. They agreed that cT1 or cT2 tumours can be classified as early stage. But, they disagreed with the previous definition of T3 or T4 tumours as locally advanced in NICE guidance IPG659. One expert adviser said that most clinicians will consider a T3 tumour as locally advanced only when the circumferential resection margin is involved. A T4 with N2 disease would also be considered locally advanced. In other words, T3 cancers without circumferential resection margin involvement would be considered early stage and immediate treatment with CXB would be appropriate. This definition of early-stage rectal cancer is consistent with the one used in the OPERA trial (Baron 2025).
- The size of the tumour is an important factor, which may affect treatment choice. Expert advisers gave different upper limits for the maximal tumour size for which CXB is safe and effective. Those upper limits ranged from 3.5 cm to 6 cm. But, they advised that the procedure should only be considered for tumours less than 3 cm if CXB is used as a boost (after there is significant shrinkage of the tumour following EBRT).

- Expert advisers also highlighted that there is a learning curve associated with the procedure. But the majority of the key evidence is from centres with a long expertise in CXB, so the learning curve is unlikely to be a confounding factor.
- There was no evidence on important efficacy outcomes, including rectal perforation and rectal necrosis. The evidence was limited for other outcomes such as radiation toxicity and rectal ulceration.
- There is a paucity of evidence available to validate the QoL and patient reported outcomes outlined in this overview. Larger prospective studies with homogeneous study populations and extended follow-up periods could be used to fully assess functional outcomes following CXB treatment.
- Powell (2025) included multiple older studies from as early as 1974. This may limit generalisability to the modern clinical context. New diagnostic approaches, surveillance and administration of adjuvant therapies introduces significant heterogeneity and may impact outcomes.
- Only 2 of the studies included in Powell (2025) are of a randomised nature.

Ongoing trials

NCT02505750: A multicentre, open-label, phase 3 RCT to evaluate a boost of EBRT with a boost with CXB in adults with cT2, cT3a or cT3b adenocarcinoma of low-mid rectum. The study is known as the OPERA trial; 5-year results are included in the key evidence. Sponsor: Centre Antoine Lacassagne, France. Estimated completion: 2030.

NCT05772923: A prospective phase 2 feasibility study to evaluate CXB compared with extension of the waiting interval with or without local excision in people with rectal cancer with a good clinical response after neoadjuvant (chemo)radiation. Sponsor: The Netherlands Cancer Institute. Estimated completion: 2029.

NCT06402864: A feasibility phase 3 trial to evaluate total neoadjuvant treatment and a CXB boost in people with T2 or T3 tumours. Sponsor: The Gustave Roussy, Cancer Campus, Grand Paris. Estimated completion: 2030.

Existing assessments of this procedure

Low energy contact X-ray brachytherapy (CXB) for the treatment of early-stage rectal cancer (2023). Health Technology Wales Guidance 53

Related NICE guidance

Interventional procedures guidance

Transanal total mesorectal excision for rectal cancer (2021). NICE interventional procedures guidance IPG731. (Recommendation:only in research)..

Low-energy contact X-ray brachytherapy (the Papillon technique) for locally advanced rectal cancer (2019). NICE interventional procedures guidance IPG659. (Recommendation: only in research. This guidance is currently under review).

Low energy contact X-ray brachytherapy (the Papillon technique) for early stage rectal cancer (2015). NICE interventional procedures guidance IPG532. (Recommendation: Recommended for use for people for whom surgery is not considered suitable. This guidance is currently under review).

Preoperative high dose rate brachytherapy for rectal cancer (2015). NICE interventional procedures guidance IPG531. (Recommendation: special arrangements).

NICE guidelines

Colorectal cancer (2015). NICE guideline NG151

Professional societies

- Association of Coloproctology of Great Britain and Ireland
- Royal Society of Medicine - Coloproctology section
- Royal College of Radiologists - Faculty of Clinical Oncology
- British Society of Gastroenterology

- Papillon Patient Support
- Bowel Cancer UK
- National Cancer Information Network and Christies Cancer survivorship group
- Royal College of Physicians
- Royal College of Surgeons
- Beating Bowel Cancer
- Cancer Research UK
- European Society for Therapeutic Radiation Oncology
- British Institute of Radiology

Evidence from people who have had the procedure and patient organisations

NICE received 51 questionnaires from people who have had the procedure (or their carers). The views of people who have had the procedure were consistent with the published evidence and the opinions of the professional experts.

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the interventional procedures technical team and any relevant points have been taken into consideration when preparing this overview.

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Appendix A: Methods and literature search strategy

IP1041/2 Low-energy contact X-ray brachytherapy (the Papillon technique) for rectal cancer

Methods and literature search strategy

NICE has identified studies and reviews relevant to Low-energy contact X-ray brachytherapy (the Papillon technique) for rectal cancer.

Search strategy design and peer review

This search report is informed by the Preferred Reporting Items for Systematic reviews and Meta-Analyses literature search extension (PRISMA-S).

A NICE information specialist ran the literature searches on 20 January 2025 and updated them on 21 July 2025. See the search strategy history for the full search strategy for each database. Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The principal search strategy was developed in MEDLINE ALL (Ovid interface). It was adapted for use in each of the databases listed in table 4a, taking into account the database's size, search functionality and subject coverage. The MEDLINE ALL strategy was quality assured by a NICE senior information specialist. All translated search strategies were peer reviewed to ensure their accuracy. The quality assurance and peer review procedures were adapted from the Peer Review of Electronic Search Strategies (PRESS) 2015 evidence-based checklist.

Review management

The search results were managed in EPPI-Reviewer version 5 (EPPI-R5). Duplicates were removed in EPPI-R5 using a 2-step process. First, automated deduplication was done using a high-value algorithm. Second, manual

deduplication was used to assess low-probability matches. All decisions about inclusion, exclusion and deduplication were recorded and stored.

Limits and restrictions

The CENTRAL database search removed trial registry records and conference material. The Embase search excluded conference material and when updated in July 2025 also excluded additional clinical trial records added to Embase.

English language limits were applied to the search in adherence to standard NICE practice for review topics.

The search was limited from 01 January 2000 to 31 January 2025. The date limit was included to update searches undertaken for an earlier version of this guidance.

The limit to remove animal studies in the searches is standard NICE practice, which has been adapted from Dickersin K, Scherer R, Lefebvre C (1994) Systematic Reviews: Identifying relevant studies for systematic reviews. BMJ 309(6964): 1286.

Main search

Table 4a Main search results

Database	Date searched	Database platform	Database segment or version	Number of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	20/01/25	Wiley	Issue 1 of 12, January 2025	108
Cochrane Database of Systematic Reviews (CDSR)	20/01/25	Wiley	Issue 12 of 12 December 2024	Trials 11 Protocols 2
MEDLINE ALL	20/01/25	Ovid	1946 to January 17, 2025	772
INAHTA International HTA Database	20/01/25	https://database.inahta.org/	N/A	20
Embase	20/01/25	Ovid	1946 to January 17, 2025	1176

Update search

There were no changes to the search strategies between the original and the update search. However, with the addition of clinical trials to Embase in between searches, these were removed within Ovid.

Table 4b Update search results

Database	Date searched	Database platform	Database segment or version	Number of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	21/07/25	Wiley	Issue 7 of 12, 2025	5
Cochrane Database of Systematic Reviews (CDSR)	21/07/25	Wiley	Issue 6 of 12, 2025	0
Embase	21/07/25	Ovid	1974 to 2025 July 18, 2025	30
INAHTA International HTA Database	21/07/25	https://database.inahta.org/	-	21
MEDLINE ALL	21/07/25	Ovid	1946 to July 18, 2025	20

Search strategy history

MEDLINE ALL search strategy

1, *rectal neoplasms/ or *anus neoplasms/, 49,685

2, *Colorectal Neoplasms/, 108,846

3, *Colonic Neoplasms/, 62,426

4, ((rect* or anus or anal or colorect* or colon* or bowel*) adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metasta*)).tw., 319,543

5, or/1-4, 348,591

6, Brachytherapy/, 22,494

7, brachytherap*.tw., 21,528

8, ((internal* or interstitial* or intracavit* or contact*) adj4 (radiotherap* or ((radiation or irradiation) adj4 therap*))).tw., 2,844

9, ((radiotherap* or ((radiation or irradiation) adj4 therap*)) adj4 (endorect* or endocavit* or Intraluminal* or transluminal*)).tw., 227

10, (curietherapy or endocurietherapy).tw., 446

11, (implant* adj4 therap*).tw., 9,975

12, (surface* adj4 therap*).tw., 2,180

13, (endorect* adj4 (applicat* or catheter* or needle)).tw., 23

14, papillon.tw., 692

15, CXB.tw., 318

16, plaque therapy.tw., 142

17, radio* plaque therapy.tw., 20

18, or/6-17, 44,287

19, 5 and 18, 1,365

20, Animals/ not Humans/, 5,263,238

21, 19 not 20, 1,338

22, limit 21 to ed=20000101-20250131, 860

23, limit 22 to english language, 772

Embase search strategy

1 , *rectum cancer/ , 29,772

2 , *anus tumor/ , 1,311

3 , *colorectal tumor/ , 18,894

4 , *colon tumor/ , 13,690

5 , ((rect* or anus or anal or colorect* or colon* or bowel*) adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metasta*)).tw. , 461,587

6 , or/1-5 , 469,726

7 , brachytherapy/ , 47,733

8 , brachytherap*.tw. , 38,315

9 , ((internal* or interstitial* or intracavit* or contact*) adj4 (radiotherap* or ((radiation or irradiation) adj4 therap*))).tw. , 4,379

10 , ((radiotherap* or ((radiation or irradiation) adj4 therap*)) adj4 (endorect* or endocavit* or Intraluminal* or transluminal*)).tw. , 296

11 , (curietherapy or endocurietherapy).tw. , 364

12 , (implant* adj4 therap*).tw. , 14,348

13 , (surface* adj4 therap*).tw. , 3,057

14 , (endorect* adj4 (applicat* or catheter* or needle)).tw. , 55

15 , papillon.tw. , 809

16 , CXB.tw. , 433

17 , plaque therapy.tw. , 164

18 , radio* plaque therapy.tw. , 26

19 , or/7-18 , 74,009

20 , 6 and 19 , 2,509

21 , Nonhuman/ not Human/ , 5,552,183

22 , 20 not 21 , 2,451

23 , limit 22 to english language , 2,275

24 , (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. , 6,126,811

25 , 23 not 24 , 1,381

26 , from 25 keep 1-1381 , 1,381

27 , limit 26 to dc=20000101-20250131 , 1,176

Cochrane Library (CDSR and CENTRAL) search strategy

#1 MeSH descriptor: [Rectal Neoplasms] this term only 2768

#2 MeSH descriptor: [Anus Neoplasms] this term only 212

#3 MeSH descriptor: [Colorectal Neoplasms] explode all trees 13094

#4 MeSH descriptor: [Colonic Neoplasms] this term only 2530

#5 ((rect* or anus or anal or colorect* or colon* or bowel*) near/4 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metasta*)) 31303

#6 #1 or #2 or #3 or #4 or #5 31367

#7 MeSH descriptor: [Brachytherapy] explode all trees 1084

#8 brachytherap* 2967

#9 ((internal* or interstitial* or intracavit* or contact*) near/4 (radiotherap* or ((radiation or irradiation) adj4 therap*))) 3331

#10 ((radiotherap* or ((radiation or irradiation) near/4 therap*)) near/4 (endorect* or endocavit* or Intraluminal* or transluminal*)) 41

#11 (curietherapy or endocurietherapy) 8

#12 (implant* near/4 therap*) 2989

#13 (surface* near/4 therap*) 1024

#14 (endorect* near/4 (applicat* or catheter* or needle)) 1

#15 papillon 34

#16 CXB 33

#17 (plaque therapy) 10254

#18 radio* plaque therapy 1000

#19 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 20040

#20 #6 AND #19 294

#21 conference:pt or (clinicaltrials or trialsearch or clinicaltrials.gov or www.who.int) 832310

#22 #20 NOT #21 121

INAHTA HTA Database search strategy

1 , "Rectal Neoplasms"[mh] , 35

2 , "Anus Neoplasms"[mh] , 7

3 , "Colorectal Neoplasms"[mh] , 323

4 , "Colonic Neoplasms"[mh] , 26

5 , ((rect* or anus or anal or colorect* or colon* or bowel*) AND (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metasta*)) , 550

6 , "Brachytherapy"[mh] , 80

7 , brachytherap* , 96

8 , ((internal* or interstitial* or intracavit* or contact*) AND (radiotherap* or ((radiation or irradiation) AND therap*))) , 29

9 , ((radiotherap* or ((radiation or irradiation) AND therap*)) AND (endorect* or endocavit* or Intraluminal* or transluminal*)) , 3

10 , (curietherapy or endocurietherapy) , 0

11 , (implant* AND therap*) , 187

12 , (surface* AND therap*) , 50

13 , (endorect* AND (applicat* or catheter* or needle)) , 0

14 , papillon , 3

15 , CXB , 1

16 , (plaque therapy) , 14

17 , (radio* plaque therapy) , 0

18 , #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 , 363

19 , #5 OR #4 OR #3 OR #2 OR #1 , 586

20 , #19 AND #18 , 20

Inclusion criteria

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events not available in the published literature.
- People with rectal adenocarcinoma.
- Intervention or test: CXB.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Appendix B: Other relevant studies

Other potentially relevant studies that were not included in the main evidence summary (tables 2 and 3) are listed in table 5 below.

Table 5. Additional studies identified

Study	Number of people and follow-up	Direction of conclusions	Reason study was not included in main evidence summary
Baker A, Buckley L, Misra V, Bridge P. (2019) Clinical audit of rectal cancer patient referrals for Papillon contact brachy-therapy. Journal of Radio-therapy in Practice. 19: 321-326.	Audit of referral patterns between 2013 - 2019 N=31 people referred for CXB treatment from a major cancer centre	cCR for the audit cohort was 93.6%	Larger and more relevant studies included in the summary of the key evidence.
Benezery K, Montagne L, Evesque L, Schiappa R, Hannoun-Levi JM, Francois E, Thamphya B, Gerard JP. (2020) Clinical response assessment after contact X-Ray brachytherapy and chemoradiotherapy for organ preservation in rectal cancer T2-T3 M0: The time/dose factor influence. Clinical and Translational Radiation Oncology. 24: 92-98.	Retrospective case series N=61 people with T2-3 rectal adenocarcinoma (40 people whose cancer was treated with CXB first and 21 with EBRT first [if the tumour exceeded 3.5 cm]) Median follow-up 61 months	At 6 months, with CXB first all people were in cCR; five with EBRT remained in partial response. The local recurrence rate was 10% (6 to 16) at 5 years. T3 and fungating tumours were at higher risk of local recurrence. Organ preservation with good function was achieved in 95% of cases	Larger and more relevant studies included in the summary of the key evidence.
Bennett H, Rao C, Batten L, Hasler E, Jarrom D, Prettyjohns M, Barrington C, Sun Myint A. (2024) Low energy contact X-ray brachytherapy for treatment of rectal cancer: a health technology appraisal by Health Technology	Cost-effectiveness analysis	In Wales, CXB was cost effective compared with external-beam boost at a cost of £4,463 per quality-adjusted life year gained. CXB was estimated to provide 0.2 quality-adjusted life years at an	The focus of the study is on cost-effectiveness, which is outside the remit of IP guidance.

Wales. Colorectal Disease. 26:1053-1058.		additional cost of £887 per person.	
Clements E, Kinsella J, Rao C, Myint AS. [AIC]. Exploring Patient Experiences and Quality of Life Following Low Energy Contact X-ray Brachytherapy (Papillon) Treatment for Rectal Cancer: A Thematic Analysis. [unpublished AIC]	Thematic analysis of free-text data from a population-based National Institute of Clinical Excellence (NICE) administered survey. N=61 108 comments analysed	Despite experiencing side effects, people would recommend this procedure to others, emphasizing the avoidance of major radical surgical resection and stoma formation	Have included QoL and PROM data from a more robust source.
Custers PA, Geubels BM, Huibregtse IL, Peters FP, Engelhardt EG, Beets GL, Marijnen CAM, van Leerdam ME, van Triest B. (2021) Contact X-ray Brachytherapy for Older or Inoperable Rectal Cancer Patients: Short-Term Oncological and Functional Follow-Up. Cancers. 13: 6333.	Prospective cohort study N=19 Median follow-up 13 months (range 6 to 32 months)	Nine people achieved a cCR and 4 achieved local control of the tumor. The 12-month organ-preservation rate, PFS, and OS were 88%, 78%, and 100%, respectively. A transient decrease in quality of life and bowel function was observed at 3 months, which was generally restored at 6 months	Larger and more relevant studies included in the summary of the key evidence.
Custers PA, Maas M, Lambregts DMJ, Beets-Tan RGH, Beets GL, Peters FP, Marijnen CAM, van Leerdam ME, Huibregtse IL, van Triest B. (2022) Features on Endoscopy and MRI after Treatment with Contact X-ray Brachytherapy for Rectal Cancer: Explorative Results. Cancers. 14: 5565.	Prospective cohort study N=36 Median follow-up 14 (2 to 43) months	No outcomes of interest reported	No outcomes of interest reported.

Dhadda AS, Martin A, Killeen S, Hunter IA. (2017) Organ Preservation Using Contact Radio-therapy for Early Rectal Cancer: Outcomes of Patients Treated at a Single Centre in the UK. Clinical Oncology. 29: 198-204.	Prospective cohort study N=42 Median follow-up 24 (5 to 54) months	Local recurrence free survival after CXB: 88% Disease free survival after CXB: 86% Overall survival after CXB: 88% with a median follow-up of 24 months. The LARS score for people whose organs were preserved revealed that 65% of all people retained reasonable to good bowel function (LARS score 0 to 20). Satisfaction with treatment: 92% (39 out of 42)	Larger and more relevant studies included in the summary of the key evidence.
Dunstan MJD, Rockall TA, Potter K, Stewart AJ. (2018) Radiological and clinical findings following rectal contact X-ray brachytherapy (Papillon technique) - how to assess response. Journal of Contemporary Brachytherapy. 10: 179-189.	Case series N=7	No outcomes of interest reported	No outcomes of interest reported.
Frin AC, Evesque L, Gal J, Benezery K, François E, Gugenheim J, Benizri E, Château Y, Marcié S, Doyen J, Gérard JP. (2017) Organ or sphincter preservation for rectal cancer. The role of contact X-ray brachytherapy in a monocentric series of 112 patients. European Journal of Cancer. 72: 124-136.	Observational study N=112 people with rectal adenocarcinoma treated with CXB; Group 1 (n=27): T1N0 tumours less than 3 cm treated with initial local excision; Group 2 (n=45): T2 or early T3, N0 (less than	Group 1: Organ preservation was achieved in 26 people (96%). Group 2: cCR was observed in 43 out of 45 (96%) of people and 3 people developed a local recurrence (11% at 5 years). The specific survival was 76% at 5 years and the	Larger and more relevant studies included in the summary of the key evidence.

	4 cm) treated with CXB plus CRT or EBRT; Group 3 (n=40): distal locally advanced T3N0-2 treated with neoadjuvant CXB plus CRT or EBRT Median follow-up: Group 1: 63 months; group 2: 60 months; group 3: 40 months	rate of organ preservation was 89% (40 out of 45) with good bowel function in 36 people. Group 3: Anterior resection (with sphincter preservation) was possible in 35 people (86%) with a 3-year local recurrence of 6%	
Gerard JP, Frin AC, Doyen J, Zhou FX, Gal J, Romestaing P, Barbet N, Coquard R, Chapet O, François E, Marcié S, Benezery K. (2015) Organ preservation in rectal adeno-carcinoma (T1) T2-T3 Nx M0. Historical overview of the Lyon Sud - Nice experience using contact x-ray brachytherapy and external beam radiotherapy for 120 patients. Acta Oncologica. 54: 545-551.	Retrospective cohort study N=120 people with stage T1 to T3 rectal cancer treated by low-energy CXB and EBRT Median follow-up 5.2 years	People who had CXB achieved a high rate of cCR. Rate of local recurrence at 5 years was 14 to 27%. The most frequent toxicity was rectal bleeding	Larger and more relevant studies included in the summary of the key evidence.
Lavertu S, Schild SE, Gunderson LL, Haddock MG, Martenson JA. (2003) Endocavitary radiation therapy for rectal adeno-carcinoma: 10-year results. American Journal of Clinical Oncology. 26: 508-512.	Retrospective cohort study N=35 Median follow-up 102 (range from 7 to 163) months	For people treated with curative intent, the survival rate was 65% at 5 years and 42% at 10 years. Median survival for these people was 67 months. One of the 6 people treated palliatively was alive 56 months	Larger and more relevant studies included in the summary of the key evidence.
Picardi C, Caparrotti F, Montemurro M, Christen D, Schaub NB, Fargier-	Retrospective cohort study	The organ preservation rate was 96% (23 out of	Larger and more relevant studies included in the

Voiron M, Lestrade L, Meyer J, Meurette G, Liot E, Helbling D, Schmidt J, Gutz-willer JP, Bernardi M, Matzinger O, Ris F. (2024) High Rates of Organ Preservation in Rectal Cancer with Papillon Contact X-ray Radiotherapy: Results from a Swiss Cohort. Cancers. 16: 2318.	N=24 people with rectal cancer and a minimum follow-up of 12 months, treated with a CXB boost, with or without chemotherapy Median follow-up 43 months	24), and the local relapse rate was 8% (2 out of 24). No people developed grade 3 or higher toxicities	summary of the key evidence.
Rao C, Stewart A, Martin AP, Collins B, Pritchard DM, Athanasiou T, Sun Myint A. (2018) Contact X-ray Brachytherapy as an Adjunct to a Watch and Wait Approach is an Affordable Alternative to Standard Surgical Management of Rectal Cancer for Patients with a Partial Clinical Response to Chemoradiotherapy. Clinical Oncology. 30: 625-633.	Budget impact analysis and cost-consequence analysis	A watch-and-wait policy with a CXB boost is less costly than standard surgical management. The technology would become cost saving within 5 years. In all scenarios, the cumulative cost of implementation of the intervention fell below the NICE threshold	No relevant outcomes reported.
Smith FM, Al-Amin A, Wright A, Berry J, Nicoll JJ, Sun Myint A. (2016) Contact radiotherapy boost in association with 'watch and wait' for rectal cancer: initial experience and outcomes from a shared programme between a district general hospital network and a regional oncology centre. Colorectal Disease. 18: 861-870.	Retrospective cohort study N=17 Median follow-up 20 (5 to 54) months	Of the 14 people who remain alive, 11 (79%) have a sustained complete (n=8) or partial (n=3) response	Larger and more relevant studies included in the summary of the key evidence.
Sun Myint A, Grieve RJ, McDonald AC, Levine EL, Ramani S, Perkins K, Wong H, Makin CA, Hershman MJ. (2007)	Retrospective cohort study N=220	124 of 220 people had CXB. There were 24 out of 220 people (11%) with residual disease	Larger and more relevant studies included in the summary of the key evidence. The study

Combined modality treatment of early rectal cancer: the UK experience. Clinical Oncology. 19: 674-681.	Median follow-up 4.6 (0.25 to 11.25) years	after initial radiotherapy. 21 people (87.5%) had immediate rescue surgery. There were 22 people with late recurrences (10%) and 11 people had local recurrence alone	population likely overlaps with those of larger and more recent studies included in the key evidence.
Sun Myint A, Smith FM, Gollins S, Wong H, Rao C, Whitmarsh K, Sripadam R, Rooney P, Hershman M, Pritchard DM. (2018) Dose Escalation Using CXB After External Beam Radiotherapy as Nonsurgical Treatment Option for Rectal Cancer: Outcomes From a Single-Center Experience. International Journal of Radiation Oncology Biology Physics. 100: 565-573.	Retrospective cohort study N=83 Median follow-up 2.5 (1.2 to 8.3) years	cCR was achieved in 53 people (63.8%) after CXB boost; among these, 7 people (13.2%) developed a relapse; the 6 people (11.6%) with nonmetastatic regrowth underwent salvage surgery. At the end of the study period, 69 of 83 people (83.1%) were cancer free	Larger and more relevant studies included in the summary of the key evidence.
Sun Myint A, Rao C, Barbet N, Thamphya B, Pace-Loscos T, Schiappa R, Magné N, Martel-Lafay I, Mineur L, Deberne M, Zilli T, Dhadda A., Gerard JP. (2023) The safety and efficacy of total mesorectal excision (TME) surgery following dose-escalation: Surgical outcomes from the organ preservation in early rectal adenocarcinoma (OPERA) trial, a European multicentre phase 3 randomised trial. Colorectal Disease. 25: 2160-2169.	RCT N=148 Median follow-up 38.2 months	Whilst there was a statistically significant decrease in the TME rate following CXB boost (HR 0.38, 95% CI 0.19 to 0.74, p = 0.00419) there was no difference in surgical outcomes between people who had EBRT and CXB boost	Study reporting later follow-up included in the key evidence summary.