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Original Article

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

C. Rao [*][†], A. Stewart [‡], A.P. Martin [§], B. Collins [¶], D.M. Pritchard [||], T. Athanasiou [†], A. Sun Myint [||][**]

[*] Queen Elizabeth Hospital, London, UK
[†] Department of Surgery and Cancer, Imperial College London, UK
[‡] St Luke's Cancer Centre, Royal Surrey County Hospital, Guildford, UK
[§] HCD Economics, Daresbury, UK
[¶] Department of Public Health and Policy, University of Liverpool, Liverpool, UK
[||] Department of Cellular and Molecular Physiology, University of Liverpool, Liverpool, UK
[**] The Clatterbridge Cancer Centre, Bebington, UK

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Abstract

Aims: Emerging evidence suggests that contact X-ray brachytherapy (CXB) may increase the clinical complete response rate and durability when administered after standard chemoradiotherapy in patients with rectal cancer. The addition of CXB in partial responders is therefore probably cost-effective. The affordability of widening access to CXB in the UK, however, has not been evaluated.

Materials and methods: Decision analytical modelling with Monte Carlo simulation was used to evaluate long-term costs for the management of patients with rectal cancers who were given a CXB boost when a clinical complete response was not initially achieved following chemoradiotherapy in order to facilitate a watch and wait approach. A third-party payer (National Health Service) perspective was adopted, probabilistic sensitivity analysis was carried out and a scenario analysis was performed to investigate the effect of the number of referral centres and number of patients treated with CXB.

Results: We estimate that 818 (95% confidence interval 628–1021) patients per year are eligible for CXB as an adjunct to a watch and wait approach in England and Wales. As this management is less costly than surgical management for each individual patient, the more patients treated, the more affordable the technology. Even if as few as 125 patients are treated nationally in 15 centres, the cost of implementing this technology would be less than £4 million. If the average number of patients treated in each centre is 30, this technology would be cost saving within 5 years.

Conclusions: The cost of CXB is not prohibitive according to the National Institute for Health and Care Excellence threshold for implementation of new technology and may even be cost saving within 5 years compared with standard surgical management, depending on the uptake of the technology and the number of referral centres.

Key words: Contact brachytherapy; cost-effectiveness; organ preservation; radiotherapy; rectal cancer; watch and wait

Introduction

The standard of care for rectal cancer threatening the circumferential resection margin is currently neoadjuvant chemoradiotherapy followed by radical surgery. There is now emerging evidence, however, that patients with a clinical complete response (cCR) to chemoradiotherapy who are intensively monitored for early signs of recurrence and treated with curative salvage surgery should recurrence occur (commonly referred to as 'watch and wait' management) may have comparable long-term survival and

Author for correspondence: C. Rao, Department of Surgery, Queen Elizabeth Hospital, Woolwich, London SE18 4QH, UK. Tel: +44-7796954284.
E-mail address: christopher.rao@nhs.net (C. Rao).

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oncological outcomes to patients initially treated with surgical resection [1].

The cCR rate in rectal cancer after conventional chemoradiotherapy using external beam radiotherapy (EBRT) and concurrent fluoropyrimidine chemotherapy in the UK may be as low as 12% [1]. A contact X-ray brachytherapy (CXB) boost enables high doses of radiation to be delivered directly to the tumour with minimal damage to adjacent tissue [2–4]. There is evidence that CXB can be used in addition to EBRT to increase the proportion of patients who achieve a cCR [2,5–8]. CXB may therefore avoid the need for surgery and associated perioperative mortality, morbidity and need for stoma in patients who do not achieve a cCR after EBRT. There is also emerging evidence to suggest that dose escalation may increase the durability of a cCR after chemoradiotherapy [7,8]. In a recent study we have shown not only that CXB is cost-effective, but is also likely to be cost saving [9]. Wider implementation of CXB will inevitably, however, require investment in the infrastructure and equipment to deliver this service. In a climate of static or falling healthcare expenditure in the UK [10] the affordability of CXB is therefore uncertain. Therefore, in this study we aim to perform a budget impact analysis (BIA) for the wider implementation of CXB as an adjunct to watch and wait management for rectal cancer for patients who do not achieve a cCR after EBRT, from a UK National Health Service (NHS) perspective, adapting our previously published decision analytical model [9,11,12]. We also aim to investigate and quantify uncertainty associated with investment in this technology.

Materials and Methods

A BIA was carried out for implementing a strategy for NHS patients in England and Wales who are undergoing neoadjuvant chemoradiotherapy for rectal cancer where a CXB boost is performed for those patients who do not achieve a cCR, thereby increasing the chance that they will achieve a cCR and be suitable for a watch and wait, organ-preserving approach. According to standard management paradigms, these patients would have no alternative but to undergo surgical resection. Patients who do not achieve a cCR after CXB or have tumours that are too large for CXB will undergo surgery. This strategy will henceforth be referred to as watch and wait with CXB boost (WW_{CXB}). The cost of implementing this strategy in this study will be compared with current standard management in the UK where radical surgery is carried out for all patients after chemoradiotherapy with EBRT irrespective of whether a cCR is achieved.

Long-term costs for patients following chemoradiotherapy, treated with WW_{CXB} and standard surgical management were modelled using a decision analytical model consisting of a combined decision tree and Markov chain simulation. Details of the Markov chain simulation have previously been described [9,11,12] and are described in detail in Supplementary Data File A. Additional model parameters and assumptions required for BIA are described in Table 1 and Figure 1. The analysis was carried out from a third-party payer perspective (NHS) according to the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) guidelines on BIA [13]. Costs are reported in UK pounds sterling (£). The BIA was carried out for a 10 year time horizon, the expected lifetime of the technology. Costs were discounted at 3.5% per annum. The analysis was carried out using decision analytical software (TreeAge-Pro, TreeAge; Williamstown, MA, USA).

Model Parameters

The incidence of rectal cancer and the proportion of patients undergoing neoadjuvant chemoradiotherapy prior to radical surgery was extracted from the National Bowel Cancer Audit (NBOCA) report (Table 1) [14]. The exact number of patients who would be eligible for treatment with CXB as an adjunct to a watch and wait approach, who would otherwise be candidates for radical curative surgery is unknown, and consequently this was modelled from NBOCA estimates of the number of patients undergoing chemoradiotherapy before surgery for rectal cancer, estimates of the cCR after EBRT and estimates of the proportion of patients without cCR who would be suitable for CXB (Table 1).

The purchase and maintenance costs of the Papillon Plus machine were based on manufacturer's data (Ariane Medical Systems, UK). The cost of individual patient treatment with CXB was based on a micro-costing study undertaken at out institution (Supplementary Data File B). Estimates of other healthcare costs were obtained from several sources, including NHS reference costs to model the long-term costs associated with competing treatment strategies [15–17] (Table 2). Unlike in our previously published cost-effectiveness analysis [9], fixed annual costs and capital investment expenses for each centre, such as the purchase and maintenance cost of the Papillon Plus machine, were considered separately to the incremental treatment costs for each patient. The initial cost of training the team is covered by the manufacturer as part of the contract to purchase the machine. It was then conservatively assumed that the first 20 cases would be undertaken by the whole team under supervision. The capital investment cost of establishing the existing four UK centres was excluded, but fixed and variable treatment costs for these centres were included in the analysis. A summary of all economic parameters is given in Table 2.

Sensitivity Analysis

Alternative analyses were carried out to explore the effect of uptake of CXB on the affordability of this technology nationally. Analyses were carried out assuming 125, 250 and 500 patients a year nationally would receive CXB boost after EBRT. In the first scenario, patients were treated in five centres; in addition to the four existing UK centres, one additional centre was established. In the second scenario, patients were treated in 10 centres; in addition to the four existing UK centres, six additional centres were established.

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Table 1
Model parameters. Transition probabilities were described by beta distributions based on the listed expected value and range

Model parameter	Expected value	Range	Distribution	α	β
% of patients without cCR who are suitable for CXB [8]	71%	50–100%	Beta	115	46
% of patients with cCR after CRT with EBRT alone [1]	12%	0–50%	Beta	31	228
% of patients with cCR after CXB boost [8]	65.2%	25–80%	Beta	75	40
% of patients who have abdominoperineal resection (rather than anterior resection of the rectum) [14]	27.7%	10–50	Beta	3240	8459
% of patients where cCR corresponds to a pCR after chemoradiotherapy (see Supplementary Data File A for references)	70%	0–100%	Beta	4.44	3.40
No. patients with rectal cancer who receive CRT for rectal cancer in England and Wales [14]	1305	870–1740	Triangular	–	–

cCR, clinical complete response; CRT, chemoradiotherapy; CXB, contact X-ray brachytherapy; EBRT, external beam radiotherapy; pCR, pathological complete response.

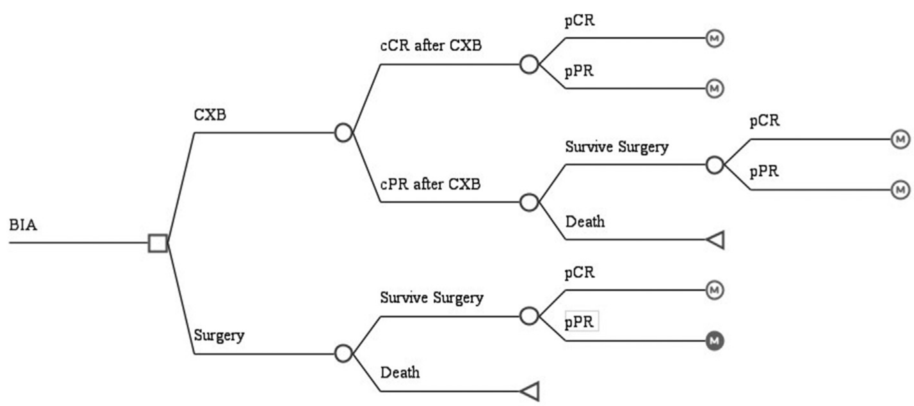

Fig 1. Schematic representation of our decision analytic model, consisting of a decision tree and Markov chain simulation to investigate the long-term outcomes associated with the competing interventions. Decision nodes are represented by boxes and chance nodes are depicted by circles. The decision tree terminates either with the patients dying (in the case of patients who do not survive surgery), shown by a triangle, or a Markov chain simulation, shown by a circle with an 'M' inside. The model parameters are described in Table 1. The structure of the Markov simulation has previously been described and is detailed in Supplementary Data File A. BIA, budget impact analysis; cCR, clinical complete response; cPR, clinical partial response; CXB, contact X-ray brachytherapy; pCR, pathological complete response; pPR, pathological partial response.

In the final scenario, patients were treated in 15 centres, with 11 additional centres being established. We conservatively assumed that it would take 4 years for each new centre to become fully established. In the first year we assumed that each new centre would have 25% of their final caseload, increasing to 50% in the second year, 75% in the third year and 100% by year 4. Although treating 125 patients nationally in 15 centres does not represent a practical configuration of services, this represents a pessimistic scenario for the uptake of this technology in relation to investment costs.

In order to estimate the combined effect of uncertainty associated with all model parameters, a probabilistic sensitivity analysis was carried out using Monte Carlo simulation [18]. Briefly, all parameters were randomly sampled from assigned distributions (Tables 1 and 2; Supplementary Data File A). The model was then run to simulate a 'virtual' cohort of 1000 'matched' patients for each intervention. All model parameters were then resampled and the model was then run again to generate data for a further virtual cohort of 1000 patients. This process was repeated until data had been generated for 1000 matched virtual cohorts of 1000 patients. This allowed costs to be estimated for both treatment strategies. Importantly, however, it also allowed estimates of the uncertainty associated with these outcomes to be calculated. As cost parameters may be correlated, it is possible that the assumption that all model parameters are independent may overestimate the uncertainty.

Results

We estimate that 818 (95% confidence interval 628–1021) patients per year are eligible for CXB as an adjunct to a watch and wait approach in England and Wales (Figure 2).

As WW_{CXB} management is less costly than standard surgical management for each individual patient, implementation of this technology is most expensive in the first year that the technology is implemented and then the cost of implementation subsequently declines. A further

Table 2

Economic parameters relating to the cost of implementation of contact X-ray brachytherapy and the costs incurred by individual patients in the Markov simulation described in Supplementary Data File A

Model parameter (HRG code)	Mean (£)	Lower quartile (£)	Upper quartile (£)	Distribution	α	Λ
Investment costs						
Papillion Plus System (manufacturer)	300 000	–	–	–	–	–
Papillion Mono System (manufacturer)	170 000	–	–	–	–	–
Team training	7060	5295	8826	Gamma	7.290000002	0.001032512
Fixed costs (per annum)						
Annual maintenance contract (parts and labour) (manufacturer)	20 000	–	–	–	–	–
Other costs (Supplementary Data File B)	1616	1212	2020	Gamma	7.290000002	0.004511
Variable costs						
Cost of contact brachytherapy (3 fractions) (Supplementary Data File B)	921	691	1152	Gamma	7.290000002	0.007912281
Cost of radical surgery (abdominoperineal resection) – comorbidities (FZ74E) [15]	8602	6706	10 113	Gamma	11.60054808	0.001348587
Cost of radical surgery (abdominoperineal resection) – without comorbidities (FZ74F) [15]	7298	5866	8361	Gamma	15.57006829	0.002133471
Cost of liver resection – comorbidities (GA04C) [15]	10 576	8133	12 040	Gamma	13.33459903	0.001260836
Cost of liver resection – without comorbidities (GA04D) [15]	8118	6077	9386	Gamma	10.95288326	0.00134921
Cost of palliative surgery – comorbidities (FZ27E) [15]	4302	1917	5568	Gamma	2.526626492	0.000587314
Cost of palliative surgery – without comorbidities (FZ27F/G) [15]	3101	2056	3710	Gamma	6.39670645	0.002062788
Cost of examination under anaesthesia (FZ23A) [15]	794	558	976	Gamma	6.566173299	0.00826974
Cost of rigid sigmoidoscopy (FZ57Z) [15]	194	138	219	Gamma	10.43896212	0.053809083
Cost of flexible sigmoidoscopy (FZ54Z) [15]	410	319	489	Gamma	10.58507087	0.025817246
Endoscopic treatment of radiation proctitis (FZ89Z) [15]	959	521	1168	Gamma	3.998089872	0.00416902
Cost of colonoscopy (FZ52Z) [15]	602	486	726	Gamma	11.44970767	0.019019448
Cost of magnetic resonance imaging of pelvis (RD01A) [15]	146	108	167	Gamma	11.14360187	0.07632604
Cost of computerised tomography of chest, abdomen and pelvis (RD26Z) [15]	125	84	145	Gamma	7.641599202	0.061132794
Cost of multidisciplinary discussion of patient management (CMDT_C) [15]	126	75	144	Gamma	6.068296718	0.048161085
Cost of outpatient appointment (WF01A_104) [15]	122	85	158	Gamma	5.082739366	0.041661798
Cost of palliative chemotherapy [17]	30 800	23 100	38 500	Gamma	7.279204003	0.000236338
Cost of annual stoma care [16]	1100	700	2100	Gamma	1.125195166	0.001022905

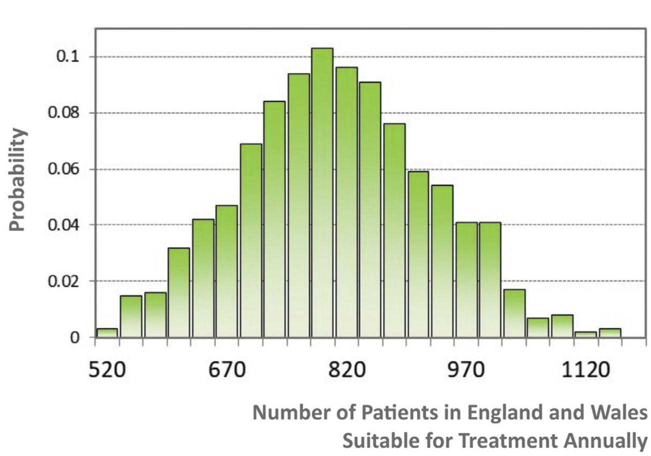

Fig 2. Estimate of the population suitable for watch and wait with contact X-ray brachytherapy boost management annually in England and Wales and the associated uncertainty.

consequence of the fact that WW_{CXB} management is less costly than standard surgical management for each individual patient is that the more patients are treated, the more affordable implementation of this management strategy becomes nationally. Even if as few as 125 patients annually are treated nationally in as many as 15 centres, the cost of implementing this technology would be £3 521 000 (95% confidence interval £3 364 000–£3 655 000). This falls well below the 'budget impact test' of £20 million and would be considered of 'low or not significant cost' as defined by the National Institute of Health and Care Excel-

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Table 3
Summary of scenario analysis for the annual incremental costs associated with implementation of a watch and wait with contact X-ray brachytherapy boost (WW_{CXB}) strategy

	Number of Centres	Annual incremental cost of CXB compared to open management									
		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
125 Patients a Year	5	£ 73,942.25 (−219,237.07 −318,478.33)	£ −169,717.05 (−685,746.92 −292,113.03)	£ −196,645.14 (−888,244.63 −387,270.64)	£ −251,661.80 (−1,060,062.33 −409,585.38)	£ −289,453.86 (−1,160,647.37 −414,425.61)	£ −318,617.55 (−1,199,877.12 −398,958.82)	£ −341,998.03 (−1,222,932.41 −387,553.35)	£ −360,723.01 (−1,239,857.27 −377,178.12)	£ −374,836.18 (−1,241,951.47 −351,459.19)	£ −384,987.61 (−1,235,888.50 −348,836.43)
	10	£ 1,837,678.07 (1,646,819.65 −1,998,115.86)	£ −10,875.91 (−364,974.11 −307,990.29)	£ −63,965.00 (−611,840.19 −395,469.63)	£ −136,858.18 (−844,602.51 −441,778.04)	£ −156,809.28 (−979,064.05 −502,335.77)	£ −188,225.61 (−1,057,944.62 −518,265.05)	£ −217,569.25 (−1,119,453.05 −504,202.03)	£ −240,879.40 (−1,117,496.16 −494,324.45)	£ −257,643.06 (−1,118,065.53 −479,037.19)	£ −270,049.18 (−1,124,878.77 −458,038.71)
	15	£3,521,143.73 (3,364,263.62 −3,654,697.52)	£114,091.39 (−186,831.70 −387,850.90)	£52,281.96 (−447,356.47 −468,211.10)	£ −26,570.05 (−684,802.15 −525,978.74)	£ −40,574.16 (−848,378.59 −611,517.37)	£ −72,741.38 (−942,830.33 −626,682.08)	£ −104,072.74 (−998,146.46 −617,116.45)	£ −128,911.27 (−1,002,686.80 −605,684.08)	£ −146,558.43 (−1,017,024.74 −581,994.19)	£ −159,716.12 (−1,017,374.26 −566,492.70)
250 Patients a Year	5	£ −267,205.92 (−852,691.86 −219,806.15)	£ −447,464.48 (−1,477,520.37 −478,746.41)	£ −501,320.66 (−1,883,591.65 −666,668.05)	£ −611,353.97 (−2,224,759.78 −708,959.11)	£ −686,938.09 (−2,432,110.35 −717,829.17)	£ −745,265.49 (−2,506,066.74 −691,386.81)	£ −792,026.44 (−2,551,238.01 −666,628.35)	£ −829,476.41 (−2,585,405.86 −649,222.79)	£ −857,702.75 (−2,597,259.34 −593,106.92)	£ −878,005.60 (−2,582,631.18 −588,587.31)
	10	£1,616,935.13 (1,237,443.12 −1,938,212.38)	£ −237,812.57 (−940,849.29 −403,281.53)	£ −343,990.76 (−1,434,346.89 −569,179.24)	£ −489,777.11 (−1,901,020.59 −668,957.73)	£ −529,679.31 (−2,181,223.62 −782,729.89)	£ −592,511.99 (−2,338,521.23 −819,213.65)	£ −651,199.27 (−2,457,872.49 −799,085.26)	£ −697,819.55 (−2,450,893.83 −775,927.29)	£ −731,346.87 (−2,448,743.77 −730,121.07)	£ −756,159.12 (−2,461,366.33 −702,522.08)
	15	£3,340,535.87 (3,028,871.83 −3,604,386.51)	£ −95,908.35 (−691,321.72 −449,098.99)	£ −219,527.21 (−1,213,109.10 −611,886.23)	£ −377,231.24 (−1,691,745.95 −736,901.60)	£ −405,239.46 (−2,031,400.48 −886,845.70)	£ −469,573.90 (−2,218,383.58 −920,579.67)	£ −532,236.62 (−2,324,135.39 −915,209.46)	£ −581,913.68 (−2,333,956.97 −886,194.23)	£ −617,208.00 (−2,352,648.41 −846,319.26)	£ −643,523.38 (−2,356,261.87 −803,551.03)
500 Patients a Year	5	£ −949,502.26 (−2,119,174.09 −22,285.15)	£ −1,002,959.33 (−3,061,067.27 −849,749.63)	£ −1,110,671.69 (−3,874,285.68 −1,229,302.72)	£ −1,330,738.32 (−4,554,154.69 −1,307,014.60)	£ −1,481,906.56 (−4,975,036.32 −1,324,636.30)	£ −1,598,561.35 (−5,118,445.98 −1,273,451.74)	£ −1,692,083.27 (−5,207,849.20 −1,225,064.86)	£ −1,766,983.19 (−5,276,503.03 −1,193,312.13)	£ −1,823,435.88 (−5,307,378.18 −1,076,402.38)	£ −1,864,041.57 (−5,276,116.54 −1,069,198.72)
	10	£1,175,449.27 (416,811.76 −1,812,833.57)	£ −691,685.89 (−2,090,482.87 −595,411.81)	£ −904,042.28 (−3,079,360.30 −916,564.16)	£ −1,195,614.98 (−4,008,548.47 −1,120,521.45)	£ −1,275,419.38 (−4,585,542.77 −1,346,300.71)	£ −1,401,084.73 (−4,899,674.46 −1,421,110.86)	£ −1,518,459.29 (−5,130,311.51 −1,388,745.20)	£ −1,611,699.87 (−5,117,689.18 −1,339,132.95)	£ −1,678,754.51 (−5,120,178.45 −1,232,692.85)	£ −1,728,379.00 (−5,140,639.93 −1,193,206.90)
	15	£2,979,320.16 (2,358,097.44 −3,504,714.70)	£ −515,907.83 (−1,698,900.63 −570,504.67)	£ −763,145.55 (−2,747,921.83 −906,527.58)	£ −1,078,553.62 (−3,706,730.79 −1,146,302.62)	£ −1,134,570.07 (−4,397,444.24 −1,440,798.18)	£ −1,263,238.93 (−4,764,447.21 −1,516,085.39)	£ −1,388,564.38 (−4,976,408.93 −1,516,248.93)	£ −1,487,918.50 (−4,996,498.04 −1,447,558.42)	£ −1,558,507.13 (−5,023,895.74 −1,360,249.10)	£ −1,611,137.90 (−5,035,679.80 −1,277,700.73)

lence (NICE) [19]. In all scenarios, the cumulative cost of implementation of WW_{CXB} management fell below the NICE threshold with 100% certainty at 3 years and 98.5% certainty at 10 years. The annual incremental costs associated with WW_{CXB} are shown in Table 3 and Figure 3. The cumulative costs of implementing WW_{CXB} are shown in Table 4 and Figure 3.

If the average number of patients treated in each centre is about 30, this technology may become cost saving within 5 years (with 68.6% certainty if 125 patients are treated in five centres, 45.9% certainty if 250 patients are treated in 10 centres and 41.3% certainty if 500 patients are treated in 15 centres). Figure 4 shows the certainty with which the implementation of WW_{CXB} is cost saving as the time horizon, number of centres and number of patients treated with WW_{CXB} change.

Discussion

The results of the BIA suggest that WW_{CXB} will probably be affordable according to the NICE threshold for implementation of new technology. Furthermore, our analysis suggests that within 5 years, the capital expenditure needed to implement WW_{CXB} may be offset by the reduction in healthcare costs incurred by individual patients depending on assumptions about the uptake of the technology and the provisions made to ensure geographical equity. In the field of oncology, few innovations offer the prospect of cost savings. The finding that a WW_{CXB} strategy is affordable adds weight to the argument that access to this technology should be widened based on existing evidence of its cost-effectiveness [9] and clinical efficacy [5,7,8].

All studies based on decision analytical modelling necessarily represent crude simplification of complex real-world scenarios and, consequently, the results of these studies must be interpreted with significant caution. The accumulated errors and assumptions that are necessitated for modelling longer-term outcomes mean that these findings must be treated with a degree of caution. As all models are vulnerable to uncertainty associated with model parameters, we have endeavoured to populate our model with the most relevant and robust estimates and to fully quantify the uncertainty associated with these model parameters. As no study has directly compared CXB and surgery for treatment of patients who do not achieve a cCR, and in particular there is no randomised evidence currently,

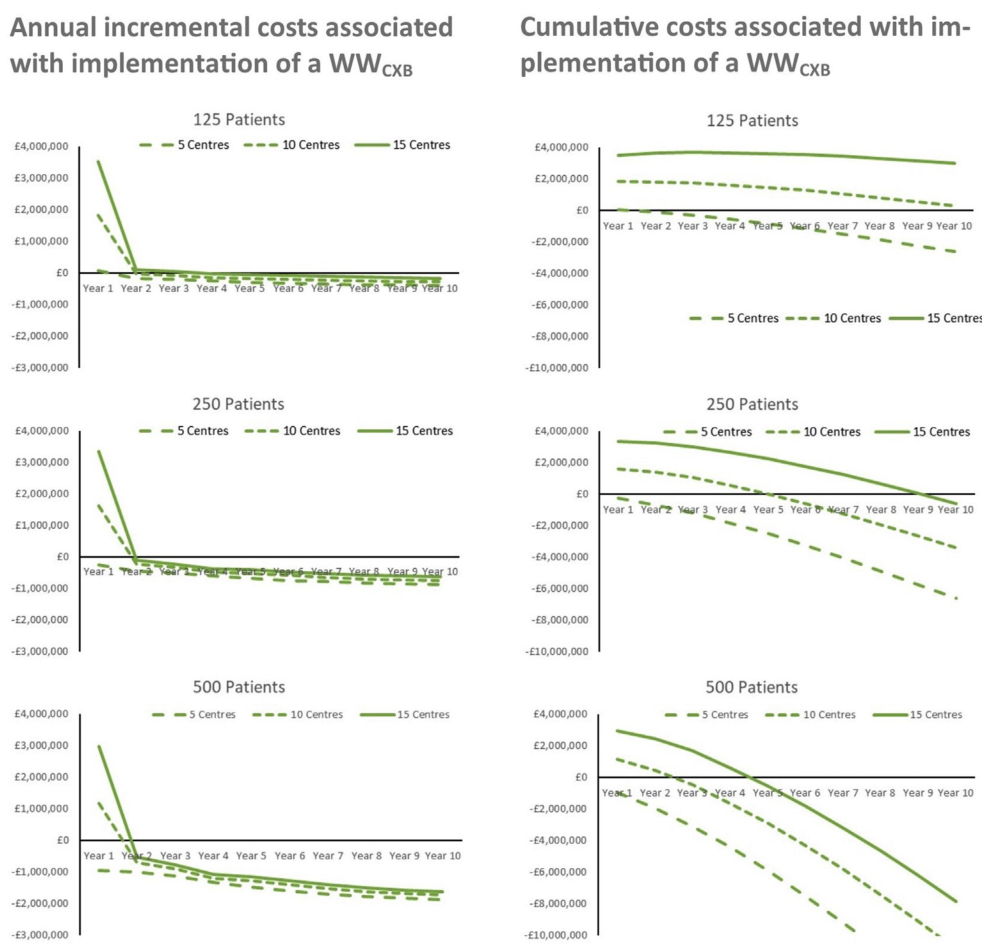

Fig 3. The left-hand panel shows the effect that patient volume and the number of centres have on the annual incremental costs associated with the implementation of a watch and wait with contact X-ray brachytherapy boost (WW_{CXB}) strategy. The right-hand panel shows the effect that patient volume and the number of centres have on the cumulative costs associated with implementation of a WW_{CXB} strategy.

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Table 4
Summary of scenario analysis for the cumulative costs associated with implementation of a watch and wait with contact X-ray brachytherapy boost (WW_{CXB}) strategy

	Number of Centres	Cumulative incremental cost of CXB compared to open management									
		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
125 Patients a Year	5	£ 73,942.25 (−219,237.07 −318,478.33)	£ −95,774.80 (−796,145.65 −541,456.15)	£ −292,419.94 (−1,627,012.49 −900,151.54)	£ −544,081.73 (−2,721,748.64 −1,302,074.54)	£ −833,535.59 (−3,846,620.01 −1,697,853.03)	£ −1,152,153.14 (−5,103,281.85 −2,058,165.79)	£ −1,494,151.18 (−6,446,866.89 −2,416,877.59)	£ −1,854,874.19 (−7,693,020.93 −2,793,207.30)	£ −2,229,710.38 (−8,897,318.44 −3,144,119.37)	£ −2,614,697.98 (−10,067,374.48 −3,482,131.09)
	10	£ 1,837,678.07 (1,646,819.65 −1,998,115.86)	£ 1,826,802.16 (1,336,405.31 −2,278,341.17)	£ 1,762,837.16 (793,560.17 −2,641,015.11)	£ 1,625,978.98 (−65,633.02 −3,087,273.81)	£ 1,469,169.71 (−1,003,579.36 −3,588,632.85)	£ 1,280,944.09 (−2,079,554.19 −4,083,423.55)	£ 1,063,374.84 (−3,357,668.65 −4,570,349.18)	£ 822,495.44 (−4,439,585.49 −5,029,185.27)	£ 564,852.38 (−5,617,789.17 −5,521,918.89)	£ 294,803.20 (−6,672,805.90 −5,976,859.23)
	15	£ 3,521,143.73 (3,364,263.62 −3,654,697.52)	£ 3,635,235.12 (3,213,288.56 −4,031,887.08)	£ 3,687,517.09 (2,842,064.69 −4,472,386.31)	£ 3,660,947.03 (2,132,881.27 −4,978,802.11)	£ 3,620,372.87 (1,296,853.00 −5,603,798.06)	£ 3,547,631.49 (351,417.42 −6,211,052.55)	£ 3,443,558.75 (−767,878.41 −6,807,842.72)	£ 3,314,647.47 (−1,722,968.17 −7,413,436.67)	£ 3,168,089.04 (−2,826,446.99 −7,983,481.92)	£ 3,008,372.92 (−3,805,267.31 −8,547,136.00)
250 Patients a Year	5	£ −267,205.92 (−852,691.86 −219,806.15)	£ −714,670.40 (−2,117,151.90 −566,621.83)	£ −1,215,991.05 (−3,876,224.13 −1,172,783.66)	£ −1,827,345.02 (−6,169,424.45 −1,869,654.56)	£ −2,514,283.11 (−8,536,294.95 −2,529,561.98)	£ −3,259,548.60 (−11,132,818.37 −3,159,595.87)	£ −4,051,575.04 (−13,988,463.64 −3,738,270.85)	£ −4,881,051.45 (−16,532,467.31 −4,393,479.46)	£ −5,738,754.20 (−19,076,748.73 −4,987,300.87)	£ −6,616,759.80 (−21,488,683.19 −5,551,745.96)
	10	£ 1,616,935.13 (1,237,443.12 −1,938,212.38)	£ 1,379,122.56 (388,960.80 −2,271,740.49)	£ 1,035,131.81 (−897,371.68 −2,796,605.02)	£ 545,354.69 (−2,820,479.39 −3,470,532.40)	£ 15,675.38 (−4,897,863.45 −4,246,006.37)	£ −576,836.60 (−7,286,364.10 −5,026,940.78)	£ −1,228,035.87 (−9,998,247.00 −5,774,733.30)	£ −1,925,855.42 (−12,387,417.21 −6,425,338.90)	£ −2,657,202.30 (−14,986,115.48 −7,216,056.90)	£ −3,413,361.42 (−17,357,976.73 −7,910,566.76)
	15	£ 3,340,535.87 (3,028,871.83 −3,604,386.51)	£ 3,244,627.52 (2,400,515.63 −4,019,311.00)	£ 3,025,100.32 (1,327,801.79 −4,590,090.61)	£ 2,647,869.08 (−383,011.21 −5,318,927.22)	£ 2,242,629.61 (−2,383,403.35 −6,217,115.13)	£ 1,773,055.71 (−4,603,147.45 −7,102,664.51)	£ 1,240,819.09 (−7,137,375.77 −7,967,903.23)	£ 658,905.41 (−9,432,291.66 −8,765,284.23)	£ 41,697.41 (−11,988,969.97 −9,645,408.22)	£ −601,825.97 (−14,241,802.14 −10,447,727.00)
500 Patients a Year	5	£ −949,502.26 (−2,119,174.09 −22,285.15)	£ −1,952,461.59 (−4,763,593.93 −617,446.88)	£ −3,063,133.28 (−8,374,895.75 −1,716,969.13)	£ −4,393,871.60 (−13,065,950.78 −3,005,462.32)	£ −5,875,778.16 (−17,915,644.84 −4,205,897.41)	£ −7,474,339.51 (−23,191,891.40 −5,362,456.02)	£ −9,166,422.78 (−29,015,778.82 −6,381,057.37)	£ −10,933,405.98 (−34,211,360.07 −7,594,023.79)	£ −12,756,841.85 (−39,435,609.31 −8,673,663.86)	£ −14,620,883.43 (−44,331,300.61 −9,690,975.72)
	10	£ 1,175,449.27 (416,811.76 −1,812,833.57)	£ 483,763.37 (−1,497,457.93 −2,271,652.06)	£ −420,278.91 (−4,268,047.79 −3,114,169.18)	£ −1,615,893.89 (−8,340,475.57 −4,223,391.72)	£ −2,891,313.27 (−12,686,431.64 −5,553,581.61)	£ −4,292,398.00 (−17,699,983.92 −6,906,715.46)	£ −5,810,857.29 (−23,279,403.70 −8,153,741.12)	£ −7,422,557.15 (−28,420,246.52 −9,217,646.15)	£ −9,101,311.66 (−33,692,830.30 −10,609,243.14)	£ −10,829,690.67 (−38,729,796.13 −11,795,128.12)
	15	£ 2,979,320.16 (2,358,097.44 −3,504,714.70)	£ 2,463,412.33 (765,438.06 −3,991,925.76)	£ 1,700,266.78 (−1,687,870.27 −4,828,464.85)	£ 621,713.16 (−5,445,935.62 −5,953,598.23)	£ −512,856.91 (−9,744,173.17 −7,397,245.29)	£ −1,776,095.84 (−14,520,123.25 −8,875,388.28)	£ −3,164,660.22 (−19,810,924.54 −10,259,877.03)	£ −4,652,578.72 (−24,987,423.25 −11,469,715.37)	£ −6,211,085.86 (−30,168,459.32 −12,939,184.14)	£ −7,822,223.75 (−35,101,094.29 −14,220,749.55)

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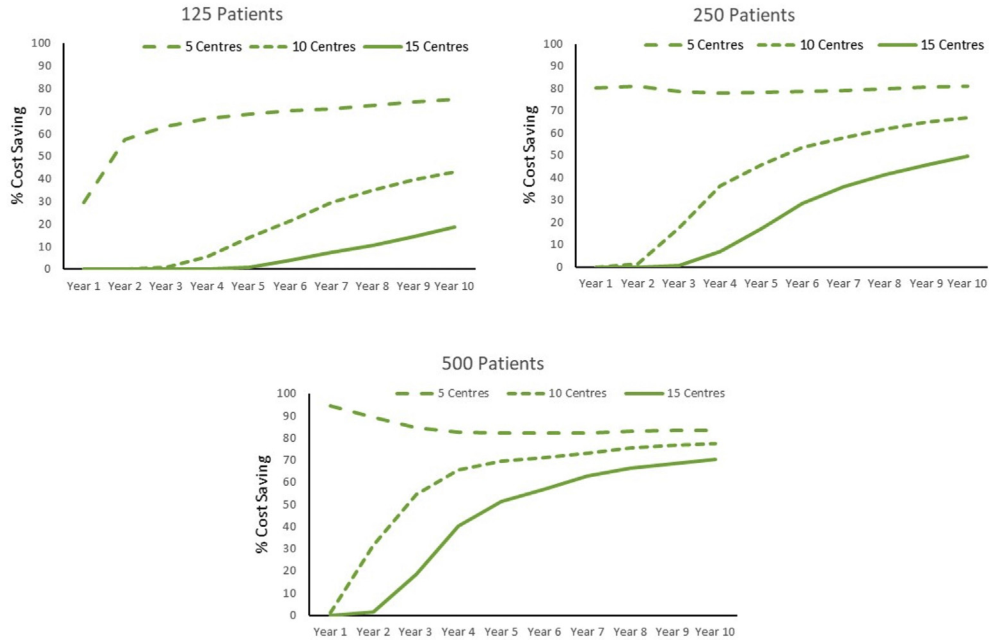

Fig 4. The effect that patient volume, the number of centres and the time horizon have on the certainty that implementation of a watch and wait with contact X-ray brachytherapy boost strategy will be cost saving.

these findings must be interpreted with caution. Similarly, sensitivity analyses cannot readily investigate the effect of factors external to the modelling paradigm, such as changing patient preferences, oncological paradigms, evolving technology and demographic factors. Consequently, long-term predictions of affordability must be treated with caution.

In many respects, however, our BIA is quite conservative about the potential affordability of CXB. For example, the assumptions we made that it would take 4 years to establish a service is quite pessimistic based on the experience of the more recently established UK services [5]. Finally, estimates of the affordability of CXB that are described in our BIA must be considered conservative given that the role that commissioned CXB centres could have in treating patients with other cancers, or rectal cancer for other indications (salvage and treatment of local regrowth, palliation, treatment of surgically unfit patients, treatment of T1 polyp cancers, for example), was not considered. Although it is likely that wider application of the technology would offset the cost of implementation, formal BIA analysis has not been undertaken for these applications.

In conclusion, this study suggests that the wider implementation of WW_{CXB} in England and Wales would be considered to be of ‘low or non-significant cost’ and may even be cost saving. This has significant implications both for clinicians working in this field, policy makers and commissioners of cancer services in the UK. It remains to be seen how decision making bodies, like NICE, SIGN and the NHS, respond to the growing body of evidence that CXB is a cost-effective treatment option and that the budget needed to establish new CXB services is not prohibitive.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clon.2018.06.010.

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