Deloitte.

Intraoperative radiotherapy for patients with early-stage breast cancer in New Zealand

An economic assessment

December 2016

Contents

Glossary

Acronym	Full name
APBI	accelerated partial-breast irradiation
ASTRO	American Society for Radiation Oncology
BCS	breast conserving surgery
BreastSurgANZ	Breast Surgeons of Australia and New Zealand
CTAG	Cancer Treatment Advisory Group (now disestablished)
DALYs	disability adjusted life years
DHB	district health board
EBC	early-stage breast cancer
EBRT	external beam radiotherapy
FCT	Faster cancer treatment (target)
GST	goods and services tax
Gy	gray
IHME	Institute of Health Metrics and Evaluation
IORT	intraoperative radiotherapy
linac	linear accelerator
LRR	local recurrence rates
MoH	Ministry of Health
MP	medical physicists
NHC	New Zealand National Health Committee
NICE	National Institute of Clinical Care and Education
NRCPC	Northern Regional Clinical Practice Committee
NZDGG	New Zealand Guidelines Group
PBI	partial-breast irradiation

PHARMAC	Pharmaceutical Management Agency
QALY	quality-adjusted life year
RANZCR	Royal Australian and New Zealand College of Radiologists
RCT	randomised controlled trials
ROWG	Radiation Oncology Work Group
RTOG	Radiation Therapy Oncology Group
UK	United Kingdom
US	United States

Executive summary

Breast cancer is the most common cancer for women in New Zealand. In 2012, the New Zealand Cancer Registry recorded 3,054 new cases of breast cancer. For women diagnosed with early stage breast cancer, current management options include mastectomy, or breast-conserving surgery (BCS) combined with a course of whole-breast external beam radiotherapy (EBRT). EBRT is the conventional radiation technique that delivers targeted radiation beams from outside the body to the whole breast or to the area where the cancer resides. EBRT is administered after complete healing of the surgical wound, and is typically delivered five days a week over three weeks in New Zealand.

In recent years, evidence from randomised controlled trials (RCTs) suggests that intraoperative radiotherapy (IORT) could be an alternative to EBRT. IORT consists of a single concentrated dose of radiation therapy to a tumour bed administered during BCS. The literature has noted various potential advantages of IORT over EBRT, including convenience to patients, improved quality of life, and a reduction in the overall costs of radiotherapy.

However, extant evidence for the efficacy and safety of IORT compared to EBRT remains equivocal. This is in part due to the lack of longer-term follow-up evidence (Picot et al. 2015). Furthermore, women receiving IORT in the RCTs had higher rates of local recurrence of cancer cells at follow-up than women who received EBRT. Although the differences in rates of local recurrence were within the pre-specified range considered to be statistically equivalent, many commentators remained cautious about the comparative clinical safety of IORT. For this reason, peak international clinical bodies have issued guidance recommending clinicians to weigh up the risks and benefits of IORT for patients, with IORT only being offered to women suitable for partial breast irradiation and whose breast cancer characteristics present low risk of local recurrence (Esposito et al. 2015; Zhang et al. 2015).

The New Zealand National Health Committee (NHC) (now disestablished) published a health technology assessment of IORT in 2015. This report had a primary focus on assessing the clinical effectiveness, safety and service provision of IORT, with considerations on costs and feasibility. Consistent with international guidelines, this report concluded that the evidence base for the comparative effectiveness of IORT was "immature" and current evidence has not demonstrated non-inferiority of IORT against EBRT (NHC 2015). This report also estimated that seven IORT machines would be needed in New Zealand to meet the estimated demand of 750 patients, at a capital cost of $8.4 million and $0.7 million of annual running cost.

About this project

The New Zealand Ministry of Health (MoH) has commissioned Deloitte to undertake an independent economic evaluation of introducing IORT to the public sector under three scenarios (Table i, p. ii), compared to the existing EBRT services, assuming that EBRT and IORT are clinically equivalent in the eligible populations. The purpose is to inform policy makers about the economic merits of and any issues relating to introducing IORT in New Zealand from the perspectives of the health system and society.

Table i: Modelling scenarios based on the location of IORT equipment

	Scenario 1	Scenario 2	Scenario 3
Number of complete IORT packages	2 (Auckland and Christchurch)	3 (Auckland, Hamilton and Christchurch)	2 (Auckland and Christchurch)
Number of permanent components	4 (Hamilton, Palmerston North, Wellington & Dunedin)	2 (Palmerston North and Wellington and)	2 (Hamilton, Palmerston North)

NOTE: **A complete package** includes a miniaturised linear accelerator, SQA tools, spherical applicator set and the permanent components. **Permanent components** comprise a control console, electrometer, cart, floor stand and shuttle container. Sites with the permanent components would share the linear accelerator, SQA tools and spherical applicator set with the sites with a complete package.

Estimated demand for IORT

The demand for IORT services was estimated based on recommended eligibility criteria and a number of factors influencing demand, as specified in the literature (Table ii). These factors include the proportion of women detected with early stage breast cancer at diagnosis, rate of BCS, rate of adjuvant radiotherapy post-BCS, patient preference, and the predicted year-on-year growth rate of incidence.

Under the base case scenario it was estimated that there would be 461 women clinically eligible and preferred to use IORT in 2017 if IORT were to be introduced in New Zealand (Table ii). This is projected to grow to 717 women in 2026. However, the estimated number of women using IORT would only be 80-125 patients if the assumptions under the low-demand scenario hold. In contrast, there would be 1,505 to 2,340 women using IORT under the high-demand scenario. The estimated numbers are comparable to the estimates by NHC and expert clinicians.

Table ii: Estimated demand by location of cancer centre and year

	Base case		Low demand		High demand	
Clinical eligibility						
Age	45-84 years		60-79 years		≥45 years	
Tumour size	≤3cm		<2cm		≤3cm	
Lymph node and metastasis	No		No		No	
Other factors influencing demand						
New cases with Stage 1 breast cancer at diagnosis	40.0%		29.3%		45.2%	
Stage 1 cases undergoing BCS	64.5%		56.3%		73.0%	
Post-BCS adjuvant radiotherapy	76.6%		71.2%		98.0%	
Patient preference for IORT	64.2%		16.0%		91.4%	
Estimated number of women using IORT						
Year / Region	**2017**	**2026**	**2017**	**2026**	**2017**	**2026**
Auckland	156	243	24	38	510	793
Hamilton	80	125	15	23	263	409
Palmerston North	58	90	11	17	188	293
Wellington	48	74	8	13	156	242
Christchurch	77	119	14	22	251	390
Dunedin	42	65	8	12	137	213
TOTAL number of women	**461**	**717**	**80**	**125**	**1,505**	**2,340**

Source: Deloitte Access Economics

Estimated financial and economic costs of introducing IORT

A model was constructed to assess the economic merits of introducing IORT during a 10-year period between 2017 and 2026, compared to the current provision of EBRT. The model assessed the three scenarios outlined in Table i, with consideration to the estimated demand (Table ii) and a range of variables and assumptions relating to equipment and consumables and provision of clinical services, as discussed in Section 4.

Assuming base case demand, the model found that providing IORT in the public sector under all three scenarios would generate net cost savings of $2.91 million to $17.61 million (in 2017 values) over 10 years, from both the health system and societal perspectives (Table ii). However, the savings may not be sufficient to offset the capital and operational costs associated with IORT if the demand were low. In this case, investing in IORT would incur costs to the health system under all three scenarios ($3.72 million to $4.72 million), even if the avoidance of patient travel costs and productivity losses were incorporated ($2.79 million to $4.24 million over 10 years) (Table iii). A further break-even analysis suggests that in order to be cost neutral from a health system perspective, demand would need to be at least 68.4% (3,939 over 10 years), 75.9% (4,365 over 10 years), and 55.1% (3,168 over 10 years) of the projected demand for scenarios 1, 2 and 3 (5,755 over 10 years) respectively.

Table iii: Incremental costs related to the provision of IORT in 2017-2026

	Scenario 1	Scenario 2	Scenario 3
Health system			
Capital			
IORT and related equipment	$4.56 m	$4.77 m	$3.59 m
Training and operating procedure development	$0.07 m	$0.07 m	$0.05 m
Operational			
Annual maintenance	$1.35 m	$1.90 m	$1.29 m
Replacement of Spherical applicators§	$0.36 m ($0.04 m ; $1.24 m)	$0.33 m ($0.04 m ; $1.24 m)	$0.36 m ($0.04 m ; $1.24 m)
Transportation, calibration and sterilisation§	$0.66 m ($0.40 m ; $1.35 m)	$0.63 m ($0.38 m ; $1.33 m)	$0.49 m ($0.24 m ; $1.18 m)
Clinical service			
Treatment with IORT, including disposables§	$27.46 m ($4.79 m ; $89.65 m)	$27.46 m ($4.79 m ; $89.65 m)	$27.46 m ($4.79 m ; $89.65 m)
Counterfactual - Treatment with EBRT§	$37.42 m ($6.52 m ; $122.15 m)	$37.42 m ($6.52 m ; $122.15 m)	$37.42 m ($6.52 m ; $122.15 m)
Incremental difference (IORT - EBRT) §	-$9.95 m (-$1.73 m ; -$32.49 m)	-$9.95 m (-$1.73 m ; -$32.49 m)	-$9.95 m (-$1.73 m; - $32.49 m)
Patient			
Travel costs§	-$6.04 m (-$1.05 m ; -$19.71 m)	-$6.04 m (-$1.05 m ; -$19.71 m)	-$6.04 m (-$1.05 m ; -$19.71 m)
Productivity losses from EBRT avoided§	-$7.43 m (-$1.20 m ; -$31.70 m)	-$7.43 m (-$1.20 m ; -$31.70 m)	-$7.43 m (-$1.20 m ; -$31.70 m)
Net impact			
Health system perspective§	-$2.91 m (+$4.72 m ; -$23.88 m)	-$2.22 m (+$5.44 m ; -$23.16 m)	-$4.15 m (+$3.49 m ; -$25.11 m)
Societal perspective§	-$16.38 m (+$4.24 m ; -$71.47 m)	-$15.69 m (+$5.49 m ; -$70.23 m)	-$17.61 m (+$2.79 m ; -$72.92 m)

Note: § Numbers are presented for base case and in parenthesis low-demand and high-demand estimates.

A series of one-way deterministic sensitivity analyses identified that investing in IORT would result in net cost to the health system if there is a paradigm shift of standard of care to five EBRT sessions (as per the FAST trial) and if the proposed cost of IORT with BCS would be $6,500. The analysis is not sensitive to other parameters tested.

Section 5 presents a discussion on a number of factors required for interpreting the findings and for further policy consideration. These include:

- **Demand side factors:** the number of patients receiving IORT would be heavily influenced by physician's acceptability of IORT as a replacement for EBRT, an emerging shift towards hypofractionation, and the clinical findings on using IORT as a boost therapy.
- **Supply side factors:** availability of IORT at major centres will have considerable impacts on surgical loads and service planning at these centres. This may have an impact on their ability to meet the MoH's "Faster cancer treatment" (FCT) targets. It will also have implications on the financial viability of smaller regional centres if BCS is a core part of their scope of service.
- **Procurement of IORT**: an effective procurement process would help with overall efficiency, but would require considerations on the ownership of the machine and how the costs were to be shared across district health boards for the shared component.
- **Local recurrence and other health outcomes**: the base case analysis presented in this report assumed clinical equivalence for EBRT and IORT, as requested by MoH. If IORT is proved to be clinically different to EBRT, a full economic analysis would need to consider differences in morbidity, mortality and quality of life outcomes arising from differences in local recurrence rates.
- **Use for other indications**: the significant start-up expenses may precipitate inappropriate uses of IORT for other clinical conditions for which there is less or insufficient evidence to support its use, in order to recover costs.

Conclusion

On the assumption of clinical equivalence, investing in IORT in the publicly funded radiation therapy centres according to the three scenarios would be likely to present cost savings for the New Zealand health system and society compared to the existing EBRT services, provided that estimated demand for IORT service is sufficiently high. In addition to the economic and financial considerations presented in this report, policy makers in New Zealand should consider other factors such as the overall policy objectives, acceptability to clinicians, impact on workforce and service capacity, the procurement arrangements, and potential indication 'creep' to other clinical conditions for which evidence remains insufficient. Furthermore, as evidence for the management of early breast cancer continue to evolve, policy makers should anticipate and be prepared for any future changes in the treatment recommendations, including the use or IORT or radiotherapy more generally, in women with low-risk early breast cancer.

1 Background

Breast cancer is the most common cancer for women in New Zealand. It affects 119.5 and 94.5 women per 100,000 women of Māori and non-Māori background in a year, respectively (Ministry of Health (MoH) 2015a). Breast cancer imposes a significant burden on New Zealand. The Global Burden of Disease Study (2015) estimated that breast cancer resulted in 20,297 disability adjusted life years (DALYs) in 2015 (95% uncertainty range: 24,135 DALYS; 18,177 DALYs). This represents 11.1% of the estimated total disease burden of cancer in New Zealand (Institute of Health Metrics and Evaluation (IHME) 2015).

Intraoperative radiotherapy (IORT) and whole-breast external beam radiotherapy (EBRT) are two modalities of radiation therapy for treating breast cancer. EBRT is the conventional radiation technique that delivers targeted radiation beams from outside the body to the whole breast or to the area where the cancer resides. IORT is a recently developed treatment modality that consists of a single concentrated dose of radiation therapy to a tumour bed during breast-conserving surgery (BCS).

The literature has noted various advantages of IORT over EBRT. These include that:

- IORT delivers a concentrated dose of radiation to a tumour site immediately after tumour removal thus helping to destroy any remaining microscopic tumour cells. In contrast, EBRT cannot commence until after complete healing of the surgical wound;
- IORT spares normal surrounding tissues, such as skin, that could otherwise be damaged, thus allowing a higher radiation dose to be delivered to the tumour bed;
- IORT, as a single treatment, may help some patients to finish treatment and resume normal activities faster. In contrast, EBRT is typically given five days per week for three to six weeks;
- IORT can be administered as a 'boost' to patients who may subsequently be provided EBRT; and
- IORT may reduce the cost of radiotherapy and improve quality of life.

However, current evidence for the efficacy and safety of IORT remains equivocal. This is partly due to a lack of longer-term follow-up data to ascertain long-term health outcomes; currently only five years of follow-up data is available. A meta-analysis of four major studies comparing IORT to EBRT involving 5,415 patients found that IORT had a significantly higher risk of ipsilateral breast tumour recurrence than EBRT (relative risk of 2.83; 95% confidence interval: 1.23-6.51, but with significant heterogeneity), although overall the mortality rates did not differ significantly (Zhang et al. 2015). It is currently recommended that the risks and benefits of IORT be weighed up for patients, with IORT only offered within agreed strict protocols to women with a low risk of local recurrence, and deemed suitable for partial breast irradiation (Esposito et al. 2015 and Zhang et al. 2015).

The working groups of the American Society for Radiation Oncology (ASTRO) and Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) have issued recommended clinical criteria for consideration by clinicians offering IORT. Treatment centres offering IORT are collecting further data on patient health outcomes and radiation toxicity on breast tissue, with a view to establishing further evidence (Massa et al. 2016). Furthermore, the longer-term safety and efficacy of IORT versus EBRT is being examined through a number of randomised controlled trials (RCTs)

(TARGIT-B, TARGIT-E, TARGIT-R, TARGIT-BQR and TARGIT-US) and registry trials. Results of these trials are expected to be available after 2020 (Picot et al.2015).

The findings on the comparative economic merits of IORT versus EBRT in patients with early-stage breast cancer (EBC) are inconclusive. For example, Alvarado et al. (2013) found IORT to be cost saving and produced greater quality-adjusted life years (QALYs) compared to EBRT (i.e. 'dominant' strategy to EBRT). However, Shah (2014) used data from two RCTs (TARGIT and ELIOT) and found that EBRT was more cost effective than IORT based on cost-per-QALY analyses. In their base case analysis, Picot et al. (2015) found that INTRABEAM was less expensive but also less effective than EBRT because it was associated with lower total costs but fewer total QALYs gained. Neither of these cost effectiveness analyses were conducted in a New Zealand context.

On the basis of the current evidence and while awaiting further evidence on longer term safety and efficacy from clinical trials, treatment centres in a number of countries, including in New Zealand, have introduced IORT as a treatment option for patients with early breast cancer.

1.1 National Health Committee's IORT Review

In March 2015, the New Zealand National Health Committee (NHC) published an evaluation of IORT to provide the New Zealand Government with advice regarding cost-effectiveness, organisational positions and feasibility of adopting IORT (NHC 2015).

This report concluded that the evidence base for the comparative effectiveness of IORT was "immature" and current evidence had not demonstrated non-inferiority of IORT against EBRT (NHC 2015). This report also estimated that seven IORT machines would be needed in New Zealand to meet the estimated demand of 750 patients, at a capital cost of $8.4 million and $0.7 million of annual running cost. It estimated that IORT would generate an annual cost savings of $0.4 million.

This report presented organisational positions by the Cancer Treatment Advisory Group (CTAG, now disestablished) and the Radiation Oncology Work Group (ROWG), the National Institute of Clinical Care and Excellence (NICE) in the United Kingdom (UK), United States (US) health insurers, the Northern Regional Clinical Practice Committee, the Faculty of Radiation Oncology of the Royal Australian and New Zealand College of Radiologists (RANZCR), and Breast Surgeons of Australia and New Zealand (BreastSurgANZ). These peak organisations reached a broad consensus that the TARGIT-A study needs longer follow-up in order to confirm positive outcomes for using IORT versus EBRT in breast cancer. The former CTAG and ROWG were opposed to public funding for IORT for women with early breast cancer, because investment in technology and infrastructure may become obsolete if IORT were shown to have poor longer term outcomes. Notwithstanding, these organisations emphasised that patients should have the right to choose IORT, but need to be aware of the uncertainty regarding the long-term outcomes of IORT. Some patients may accept the additional risks of IORT if they are outweighed by the benefits such as shorter length of treatment and improved quality of life (NICE cited in NHC 2015).

The NHC (2015) found that it could be technically feasible to adopt IORT in New Zealand if the evidence for IORT safety and efficacy could be established. It would depend on the trade-off between increased theatre utilisation with an extra 45-60 minutes during surgery to administer the IORT and reduced pressure on EBRT which has current shortages in the workforce and capital investment programmes. The NHC (2015) outlines additional consideration on feasibility, including:

- resource implications at referral centres for IORT given that a number of breast surgeries normally performed at a number of hospitals would be relocated to a few centres offering IORT;
- whether or not a formal inclusion and exclusion criteria for IORT should be developed and how this will impact equity of access; and
- that savings are unlikely to be accrued for several years after IORT equipment is purchased.

1.2 Purpose of the report

The New Zealand Ministry of Health has commissioned Deloitte New Zealand, working with Deloitte Access Economics Australia, to undertake an economic evaluation to assess the comparative costs of introducing IORT relative to EBRT for patients with EBC in New Zealand. The purpose is to inform policy makers about the economic merits and any issues relating to introducing IORT in New Zealand from an economic viewpoint.

1.3 Report structure

The remainder of this report contains the following structure:

- **Section 2** describes in detail the epidemiology of breast cancer in New Zealand. It presents the prevalence and incidence of breast cancer across New Zealand, with a view to understanding the distribution of breast cancer by geography and the potential demand for the two modalities of radiotherapy services. It also describes the supply of these two modalities of radiotherapy in New Zealand, focusing on describing the service models and resource requirements.
- **Section 3** outlines the method and findings for estimating the demand for IORT services in New Zealand based on the information presented in Section 2.
- **Section 4** presents a comparative cost assessment and reports the overall findings.

  Section 5 considers other issues pertinent to the implementation of the proposed expansion of IORT services and provides a conclusion to the report.

2 Breast cancer and radiotherapy

2.1 Breast cancer epidemiology

In 2012, the New Zealand Cancer Registry recorded 3,054 new cases of breast cancer. About three in four people with newly diagnosed breast cancer in 2012 lived in the North Island. The distribution of new cases is in line with the relative population distribution in the two islands (Table 2.1).

The majority of these people with newly diagnosed breast cancer were non-Māori (88.4%). However, the age-standardised rate of breast cancer per 100,000 population was higher in women of Māori (119.5) than non-Māori (94.5) background (MoH 2015).

Table 2.1: Number of new cases of breast cancer in New Zealand, 2012

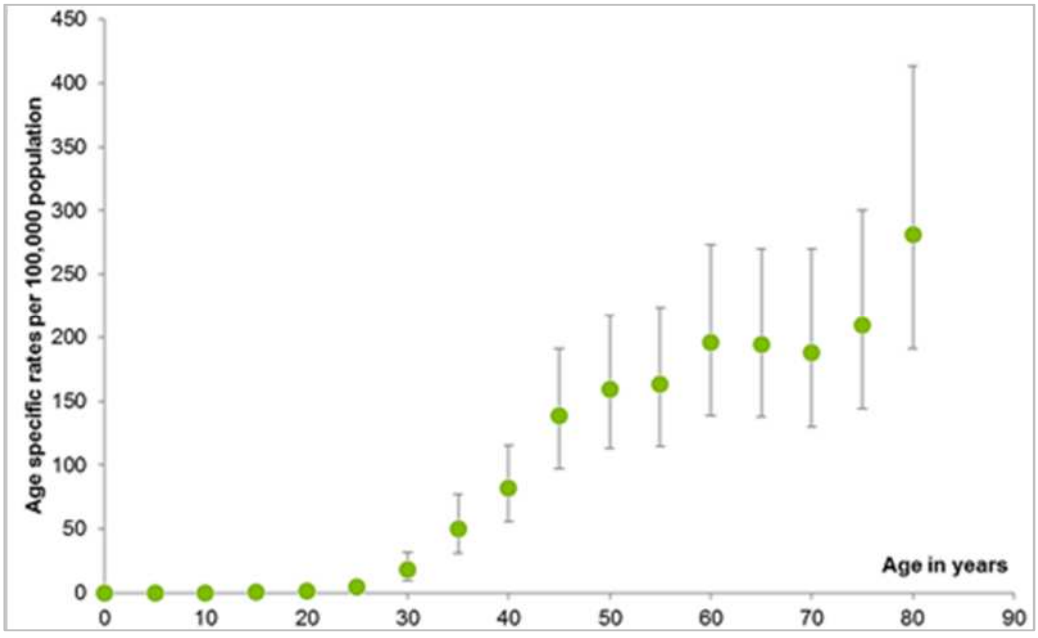
	Female	Male	Total
Total population			
All	3,025	29	3,054
Ethnic group			
Māori	351	3	354
Non- Māori	2,674	26	2,700
Life-stage (years)			
0–24	1	0	1
25–44	368	1	369
45–64	1,551	9	1,560
65–74	604	9	613
75+	501	10	511
District health board (DHB) of domicile			
Northland	124	0	124
Waitemata	384	3	387
Auckland	275	5	280
Counties Manukau	276	2	278
Waikato	268	3	271
Lakes	77	2	79
Bay of Plenty	162	0	162

	Female	Male	Total
Tairawhiti	28	1	29
Hawkes Bay	149	1	150
Taranaki	85	0	85
MidCentral	131	3	134
Whanganui	45	0	45
Capital & Coast	204	2	206
Hutt Valley	90	1	91
Wairarapa	32	0	32
Nelson Marlborough	97	1	98
West Coast	14	0	14
Canterbury	361	1	362
South Canterbury	40	1	41
Southern	183	**3**	186

Source: MoH (2015)

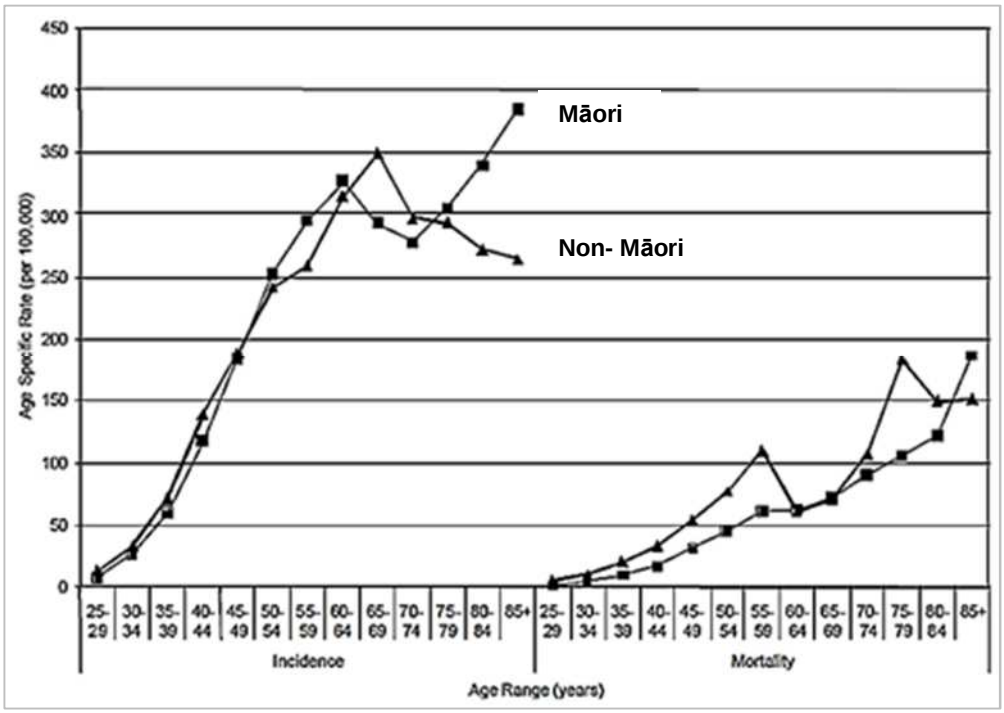
The number of people with newly diagnosed breast cancer aged over 45 years accounted for 87.9% of the total newly diagnosed population. This is broadly consistent with the distribution of breast cancer incidence rates by age in New Zealand reported by the IHME for 2015 (Chart 2.1) and Curtis et al. (2005) for 1996 to 2000 (Chart 2.2).

Chart 2.1: Estimated age-specific breast cancer incidence in New Zealand 2015



Source: IHME (2016)

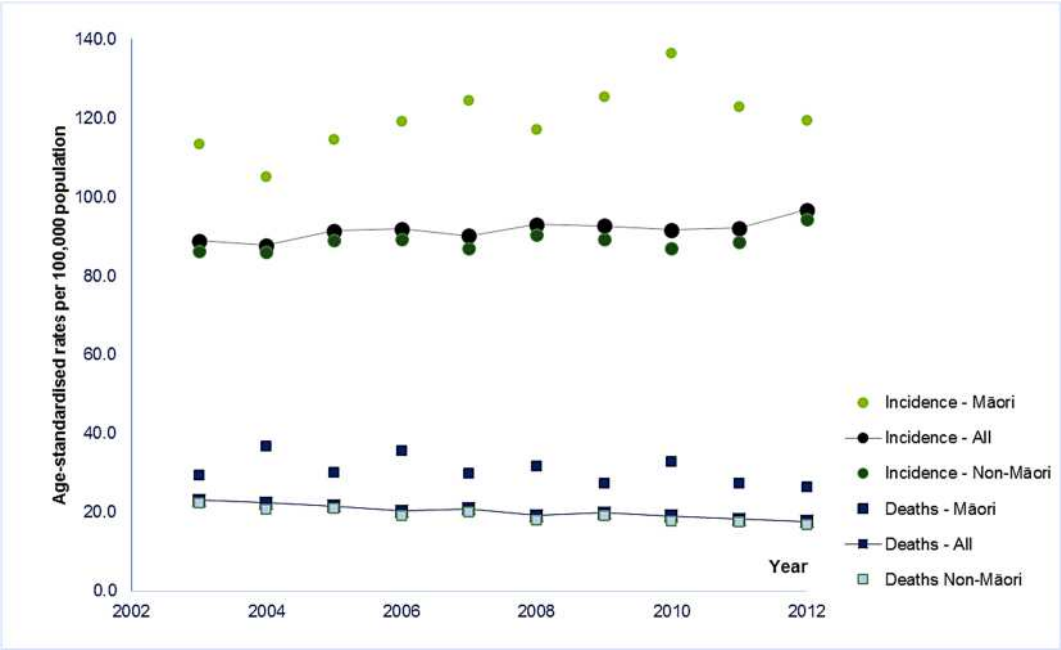
Chart 2.2: Age-specific breast cancer incidence and mortality rates for Māori and non- Māori women in New Zealand (1996-2000)



Source: Curtis et al. (2005)

Rates were adjusted for changes in age profiles of the populations in New Zealand over time (i.e. age standardisation') to assess the trend of breast cancer in New Zealand over time. Since 2003, there has been an increase in both the age-standardised rates for incidence of breast cancer and relative survival of individuals with breast cancer. As a result, there are more people than ever before living in New Zealand who have had a diagnosis of breast cancer. Chart 2.3 shows the increase in the age-standardised incidence rate and corresponding decrease in the age-standardised mortality rate between 2003 and 2012.

Chart 2.3: Age-standardised rates for new cases and deaths of breast cancers, by year and ethnicity



Source: Deloitte Access Economics analysis of data from the MoH (2015)

2.2 Staging and current clinical management for early breast cancer

2.2.1 Staging of breast cancer

'Staging' refers to the assessment of the extent of breast cancer in terms of tumour size and spread, with a view to informing treatment plan and prognosis. The TNM system is the most widely used cancer staging system where it assesses:

- **T**: size of the main or primary **t**umour;
- **N**: number of lymph **n**odes near to the primary tumour;
- **M**: whether the cancer has **m**etastasised.

Figure 2.1 presents the current recommended staging criteria for breast cancer. A patient is considered as having EBC if the cancer has characteristics classified as Stage I, Stage IIA or Stage IIB.

Figure 2.1: Staging of breast cancer

Tumour size (T)	Lymph node (N)				Spread	
	No	Yes (Category 1)	Yes (Category 2)	Yes (Category 3)	Nearby muscles and skin	Away from primary cancer (i.e. **m**etasis)
Not assessed	0	Not applicable				
<2cm	I	IIA	IIIA	IIIC	IIIB	IV
2-5cm	IIA	IIB	IIIA	IIIC	IIIB	IV
>5cm	IIB	IIIA	IIIA	IIIC	IIIB	IV
No cancer found in breast	-	IIA	IIIA	IIIC	IIIB	IV

2.2.2 Clinical management of early breast cancer

Treatment of breast cancer depends on the type of breast cancer, its size and position, the patient's age and general health and preferences. In general, surgery is recommended followed by additional treatments depending on the histopathologic findings. Additional treatments include radiotherapy, adjuvant chemotherapy and hormone therapy. Sometimes neoadjuvant chemotherapy and hormone therapy are given prior to surgery to decrease the tumour size and observe the response of the primary tumour prior to its removal.

A woman diagnosed with EBC will typically undergo BCS as their initial treatment option. This is often followed by adjuvant radiotherapy to destroy remaining cancer cells. This reduces the risk of local recurrence and breast cancer death (New Zealand Guidelines Group 2009).

BCS encompasses a range of different surgeries. These include wide local excision or 'lumpectomy' to remove the tumour, segmental excision or sector resection, quadrantectomy and partial mastectomy. Additionally, the axillary lymph nodes will be assessed for abnormalities indicating cancer nodal involvement. If nodal involvement is indicated, axillary lymph node dissection (removal) is also performed during BCS or in a second procedure (New Zealand Guidelines Group 2009; Senkus et al. 2015).

Although BCS is the preferred approach, if indicated, a patient with a diagnosis of EBC may instead undergo a full mastectomy (complete removal of the breast). This depends on factors such as the size and location of the tumour relative to the breast size; other disease factors; patient health and treatment history and preferences (New Zealand Guidelines Group 2009). Breast reconstruction surgery can be performed following mastectomy using a variety of techniques to rebuild the breast shape. The surgery may be done immediately following the mastectomy or delayed and performed in a subsequent surgery.

If cancer cells have not spread beyond the breast, then adjuvant whole-breast EBRT is initiated after BCS when the surgical wound has sufficiently healed. If cancer cells have spread beyond the breast, chemotherapy, biological therapy and hormone therapy will be administered prior to radiotherapy (Senkus et al. 2015). In general, EBRT will not be administered until two to three weeks after chemotherapy has been completed to minimize overlapping toxicities. Biological therapies and hormone therapies can be administered concurrently with EBRT (NICE 2009).

2.2.3 Adjuvant EBRT post breast conserving surgery

EBRT is the standard of care for all patients with early invasive breast cancer after BCS (NICE 2009, New Zealand Guidelines Group 2009; Senkus et al. 2015). EBRT directs high-energy photon beams through the skin directly at the tumour and surrounding cancer cells. For the patient, it is similar to having an X-ray but with stronger radiation. There is strong evidence that adjuvant EBRT reduces the 10-year risk of any first recurrence by 15.7% and the 15-year absolute risk of breast cancer mortality for patients with EBC by 3.8% compared to BCS alone (Early Breast Cancer Trialists Collaborative Group (EBCTCG) 2011).

There are immediate and longer-term adverse effects of radiotherapy associated with tissue damage[1] (New Zealand Guidelines Group, 2009). Additionally, radiotherapy treatment can be inconvenient for women to attend as they must attend a radiation oncology service up to five days a week for typically three weeks, and up to five or six weeks in exceptional clinical circumstances. This may pose difficulties for women who do not live close to the units. Notwithstanding, a number of shorter, 'hypofractionated' regimens exist which also have sufficient evidence supporting their efficacy in patients with EBC (ASTRO Guidelines; Cancer Australia 2011). An additional **boost course** of treatment to the tumour bed over a further one to two weeks may be delivered to patients considered to be at higher risk of local recurrence (e.g. less than 40 years of age, grade III disease and nodal involvement) (Sedlmayer et al. 2014; New Zealand Guidelines Group 2009).

In New Zealand, the most common EBRT used for patients with EBC is a hypofractionated regimen of 40 gray (Gy) in 15 fractions/sessions over three weeks (expert stakeholder advice, November 2016). This is also recommended by the NICE (NICE 2009). The NHC estimated that, on average, patients received 18.7 sessions of EBRT in New Zealand (NHC 2015).

2.2.4 Partial breast irradiation

Accelerated partial breast irradiation (APBI) refers to the irradiation of a limited amount of breast tissue around the tumour bed, using a number of techniques such as IORT or intra-cavity brachytherapy or balloon catheter devices. The rationale for PBI is that 44% to 86% of ipsilateral breast tumour recurrence occurs close to the lumpectomy bed (Njeh et al. 2010).

APBI delivers a larger dose per fraction than the standard 2 Gy delivered in each EBRT fraction, therefore allowing the overall treatment duration to be delivered in less than the standard three to five weeks required for EBRT (hence 'accelerated') (New Zealand Guidelines Group 2009). Guidelines from the ASTRO, the European society radiation oncology (ESTRO) and the European Society for Medical Oncology (ESMO) recommend that APBI is used in patients with a low risk of recurrence[2] (Polgar et al. 2010; Senkus et

[1] The immediate adverse effects include fatigue, skin erythema, skin breakdown, oedema, tenderness and pneumonitis. Longer-term adverse effects can include late tissue fibrosis, breast pain, telangiectasis, lung fibrosis, late cardiac morbidity, rib fractures and increased risk of contralateral breast cancer and non-breast cancer mortality. However, the risks of cardiac and lung morbidity and rib fractures is thought to be less with modern radiotherapy techniques.

[2] For example, patients at least 50 years old with unicentric, unifocal, non-metastatic, non-lobular invasive breast cancer with no nodal involvement, negative margins, without the presence of extensive intraductal components or vascular invasion.

al. 2015; Correa et al. 2017). The ASTRO recently updated consensus statement on APBI is summarised in Table 2.2.

Table 2.2: ASTRO guidelines for APBI eligibility

	Suitable	Cautionary	Unsuitable
Age	≥50 years	40-49 if all other criteria for suitable are met otherwise ≥50 years if patient has at least one of the factors below and none of the 'unsuitable' factors	<40 years
Tumour size	≤2 cm	2.1-3.0 cm	>3.0 cm
Grade	Any	-	-
N stage	N0	-	N1, N2, N3
T stage	Tis or T1	T2	T3-4
Oestrogen receptor (ER)	Positive	Negative	-

Source: Correa et al. (2017)

2.2.5 Clinical provision, workforce and equipment requirements for radiation therapy

EBRT is currently available in six DHB cancer centres in New Zealand: Auckland (Auckland DHB); Hamilton (Waikato DHB); Palmerston North (MidCentral DHB); Wellington (Capital and Coast DHB); Christchurch (Canterbury DHB) and Dunedin (Southern DHB). It is also available via three private providers at Auckland Radiation Oncology (a partnership between MercyAscot and Southern Cross hospitals in Auckland), St George's Cancer Care Centre in Christchurch; and Kathleen Kilgour Centre in Tauranga. EBRT is usually delivered as an outpatient treatment, but is centralised because of the technology required. Thus, treatment centres have a wide population catchment, a wide referral network and patients must travel daily over three to five weeks for treatment.

Central to the delivery of external radiation therapy is the linear accelerator (linac) which delivers the radiation to cancer cells. Linacs have a high capital cost and must be replaced every 10 years. They also require custom built facilities to protect staff from radiation (Health Partners Consulting Group, 2014). In 2015, there were a total of 31 linacs in New Zealand. Demand for linacs in New Zealand is projected to increase by an additional five to six linacs by 2023 based on increasing population and age. If the radiation therapy intervention rate for all cancers rises to 45% (equivalent to the highest reached by a DHB in 2013-2015), the number of linacs required will rise to 42 by 2023 (MoH 2016). Under this growth scenario, a total of $216 million will be needed for existing linac upgrades and replacements and additional new linacs to meet the projected demand (MoH 2016) [3]. It is worth-noting that linac is used for a broad range of cancers, not just breast cancer. Therefore, the capital and ongoing costs of linacs are shared across a range of cancers.

The core workforce required for the operation of radiotherapy treatment includes radiation oncologists, medical physicists, radiation therapists and nurses. Radiation oncologists are doctors that specialise in treating cancer with radiation therapy, Medical physicists are specialists in the therapeutic application of radiation sources and operating, calibrating and commissioning the equipment and Radiation therapists are involved in planning and delivering the radiation treatments and educating patients during their treatment in terms of managing side effects.

[3] Delaney et al. (2015) indicates that higher IRs, up to 48%, may contribute to a population health gain indicating that there may be room for increasing New Zealand's IR.

The Draft National Radiation Oncology Plan 2016-2021 (MoH 2016) states that workforce planning should aim for sufficient personnel resources to cover a 45% radiation therapy intervention rate by 2023. Based on demand and a 45.2% intervention rate, by 2022, RANZCR predicts that 44 linacs and 96 ROs will be needed, whereas, their projected supply of ROs was 61. In 2011, RANZCR noted that supply of radiation oncologists fell short of demand by seven. These calculations bring into question the ability of the New Zealand workforce to treat 45% of cancer patients with radiotherapy. Additionally, they do not consider the increased amount of time radiation oncologists may require to plan treatments which are becoming increasingly complex, nor the increased rate of graduate attrition due to the emergence of a more competitive Australian market (RANZCR 2013).

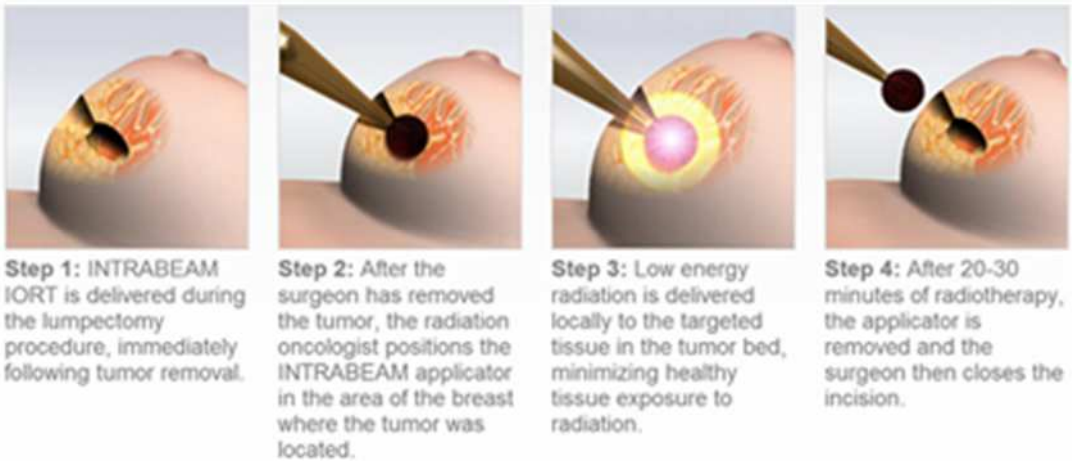
2.3 IORT

2.3.1 Radiotherapy during breast conserving surgery

IORT is a form of APBI. It requires specialised equipment and operation that enables the delivery of radiation therapy during BCS. There are a number of different IORT devices available on the market[4] with the INTRABEAM made by Carl Zeiss described in this report as a substitute for EBRT.

IORT is different from EBRT as IORT is delivered during the lumpectomy immediately after the tumour is removed directly to the exposed tissue via a specialised IORT applicator (Figure 2.2). Unlike EBRT, IORT does not require a shielded room.

Figure 2.2: Delivery of radiation with INTRABEAM



Source: Oncology Systems Limited (2016)

IORT is delivered during BCS and extends the time of surgery by around 30 to 45 minutes compared to BCS alone. The system must undergo a 10 to 30 minute quality assurance check performed by a medical physicist prior to it being used. Once checked, it can be used clinically for 36 hours. Additionally it will undergo a 10 to 15 minute quality assurance check prior to each procedure (Correspondence from Carl Zeiss, November 2016).

For patients with EBC and a low risk of recurrence, IORT can be used as a one-off radiation treatment therefore avoiding the need for further EBRT. Patients with a higher risk of recurrence[5] can have IORT as the tumour bed boost and subsequently receive the standard EBRT. This has been shown to have favourable toxicity and cosmetic outcomes and may be superior in terms of local control to conventional radiotherapy (Vaidya et al. 2016). IORT does not change the need for other adjuvant treatments which will be given as per normal depending on the indication.

[4] The US Food and Drug Administration approved INTRABEAM in 2005 and has also approved other systems including Mobetron, Novac7 and the Xoft Axxent system.

[5] e.g. invasive lobular carcinoma, extensive intraductal component, grade III, node involvement or close margins.

2.3.2 Safety and efficacy of IORT versus EBRT

Two pivotal RCTs examined the efficacy and safety of IORT as an alternative to EBRT in the treatment of breast cancer. These are the targeted intraoperative radiotherapy (TARGIT-A) trial which uses the INTRABEAM system to deliver IORT and the ELIOT trial which used the Novac7 system. Their inclusion criteria and overall results are summarised in Table 2.3.

Table 2.3 : Summary of TARGIT-A and ELIOT RCTs

Study	Inclusion criteria	Local recurrence	Mortality
TARGIT-A Vaidya et al, 2014 n=3,451	• Women ≥45 years • Operable invasive breast cancer tumour, nodes metastasis (TNM) – T1 and small T2 ≤ 3.5 cm, N0-1, M0), confirmed by cytological or histological examination; and • Suitable for BCS	• TARGIT was non-inferior to EBRT (threshold for non-inferiority was 2.5%). • 5-year risk of local recurrence in the conserved breast for TARGIT versus EBRT was 3.3% (95% CI: 2.1%-5.1%) versus 1.3% (95% CI: 0.7% -2.5%) respectively	• Breast cancer mortality similar for TARGIT compared to EBRT group (2.6% versus 1.9%). • Non-breast cancer mortality significantly lower with TARGIT (1.4% vs. 3.5%). • Overall mortality not significantly higher for EBRT versus TARGIT at 5.3% versus 3.9%.
ELIOT Veronesi (2013) n=1,035	• Women 48 to 75 years • T< 2.5cm • N0-≥4[6] • Suitable for BCS	• 5-year local recurrence rate was 0.4% for EBRT versus 4.4% for IORT which put the difference within the pre-specified equivalence margin • The pre-specified equivalence margin of 7.5% in the IORT group.	• Breast cancer and non-breast cancer survival and mortality rates did not differ between the two treatment modalities.

Source: Vaidya et al. (2014); Veronesi et al. (2013)

Future work for the TARGIT-A is planned with the aim for a median follow-up time for all trial participants of five years. This will mean that a substantial number of patients will provide data on health outcomes over a 10 year period (Vaidya et al. 2016). There are a number of other RCTs currently underway to confirm the efficacy and safety of IORT in specific sub-populations. These include: TARGIT-E(lderly); TARGIT-C(onsolidated) and TARGIT-B(oost).

2.3.3 Provision of IORT in New Zealand

One private specialist radiation therapy service in New Zealand currently provides IORT in conjunction with BCS using the INTRABEAM system. The service is located in Auckland and can be accessed by referral from a patient's general practitioner or via self-referral. Since introducing IORT to New Zealand in 2013, this provider has treated 100 patients with the inclusion criteria similar to that used in the TARGIT-A trial. IORT is currently paid for by the patient as an out-of-pocket cost or insurance coverage from three New Zealand private health insurers.

[6] All patients with positive sentinel node biopsy received axillary dissection and additional EBRT if indicated.

Options for publicly providing IORT within New Zealand have previously been explored by the NHC. The NHC (2015) estimated that a total of 10 INTRABEAM systems would be needed, seven to meet the demand for the substitution of EBRT in treating selected women with breast cancer[7] and an additional three to treat patients who receive IORT complementary to EBRT. The NHC (2015) discusses reducing the cost of introducing by sharing across multiple sites the portable parts of the equipment (Figure 2.3, circled in red). Therefore, treatment for eligible patients would be clustered into the days in which the complete system was available at a site. An expert in EBRT noted that patients with low-risk early breast cancer can wait up to six weeks for treatment without significantly impacting on health outcomes[8]. For this reason, a rotating schedule of IORT is possible to ensure that the patients receive timely treatment without compromising health outcomes.

Figure 2.3: Components of INTRABEAM

Source: Carl Zeiss (2016)

The miniaturised linear accelerator X-ray source weighs 3.4kg and its transfer case is around the size of a family suitcase along with the quality assurance instruments. Carl Zeiss confirms that it can be safely transferred by any sensitive freight provider and that there are numerous sites around the world that have adopted this approach to maximise its use, these include hospitals in Germany, Switzerland and France[9]. All components are recalibrated and serviced once per year by Carl Zeiss – the X-ray source must be serviced in Germany and the non-portable components are serviced on-site. During this time, Carl Zeiss provides another X-ray source to minimise service interruptions.

[7] This is based on NHC's demand projection that around 700 women with breast cancer would be clinically suited to IORT and would take up radiotherapy and each system has a capacity of 100 treatment deliveries per year (NHC, 2015)
[8] Expert advice received November 2016.
[9] Correspondence with Carl Zeiss, 4 November 2016

2.3.4 Training for using IORT

Expert stakeholders consulted estimated that each site using IORT would need two radiation oncologists and two breast surgeons trained in its operation and use. Carl Zeiss provides three-day training for two specialists in Germany or the United States per complete package purchased at no cost. Additional specialists can be trained onsite in New Zealand by specialists who have completed the training. Two medical physicists would also be required at each site, who would be trained on site by Carl Zeiss's staff members over 2.5 days during installation of the machine. Theatre nurses must also be familiarised with the equipment; which is estimated to take around three days.[10]

There are a number of other administrative requirements for consideration, including:

- documenting procedures and protocols for use, storage, handling, transport, disinfection and sterilisation, quality control, disposal of spherical applicators, disposal of de-ionized water, maintenance, electrical safety, radiation safety and printing data for patient record;
- log to record sterilisation;
- training design;
- identifying appropriate power sources, storage facility and operating theatres; and
- identifying a governance structure for review of protocols, equipment and so on.

An expert stakeholder estimated that an IORT service could be implemented in six weeks at a hospital. Some stakeholders may consider this estimate as optimistic because of the requirements to train workforce, establish referral pathways, and align resources and services across and within DHBs, prior to implementing IORT.

[10] Expert stakeholder advice, November 2016.

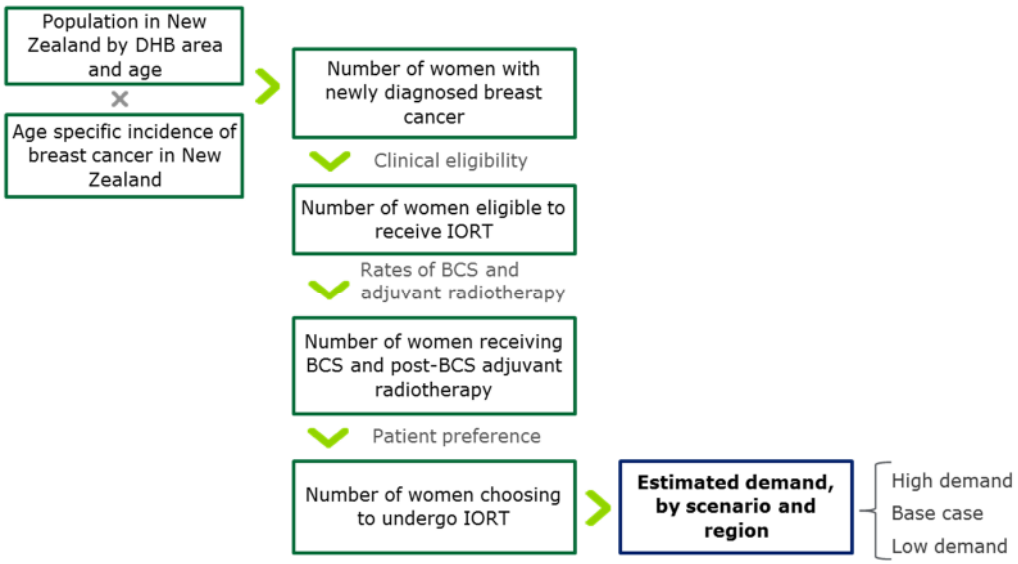
3 Assessing the demand for IORT

This Section describes an assessment of demand for IORT if this technology is introduced in public cancer centres in New Zealand. In assessing demand, the method accounts for the following groups of parameters:

- **demographics:** population in New Zealand by DHB area and age groups;
- **epidemiology:** incidence of breast cancer in New Zealand;
- **clinical eligibility:** criteria for receiving IORT, which include consideration for patient age, tumour size, lymph node involvement and whether the cancer has spread outside of the primary site;
- **clinical service provision**: parameters include rates of BCS and post-BCS adjuvant radiotherapy; and
- **patient preference** for IORT over EBRT.

The number of women who would use IORT was calculated by multiplying these factors, as illustrated in Figure 3.1. A targeted literature review and data scan was undertaken to ascertain parameters relating to these parameters. Where there were data gaps, appropriate assumptions were applied. As parameters are often presented as ranges, the model presents the estimated demand as "high demand", "base case demand" and "low demand", where "low demand" applies the most conservative assumptions.

Figure 3.1: Calculation of demand for IORT in New Zealand for each scenario



3.1 Variables and assumptions

3.1.1 Demographics and epidemiology of breast cancer

Deloitte Access Economics obtained population data by DHB and age from the 2013 Census (Statistics New Zealand 2016). Datasets from the Ministry of Health are available on the incidence of breast cancer in each DHB across New Zealand. However, the data presents age-standardised rates rather than age-specific rates. To obtain the number of new cases of breast cancer by age so that age-restriction could be applied, age-specific breast cancer incidence rates for New Zealand were taken from the Global Burden of Disease Study, as presented in Chart 2.1 (IHME 2015).

3.1.2 Clinical eligibility criteria

A review of the literature identified a variety of eligibility criteria for women to receive IORT. These were derived from both randomised controlled trials reported in the literature and different working groups (Table 3.1). In general these guidelines recommend the use of IORT in women over 50 years of age whose breast cancer tumour is less than 2-3cm in diameter and without lymph node involvement or metastasis.

Table 3.1: Eligibility criteria summary

Criteria	ESTRO	ASTRO	TARGIT-E(lderly)	TARGIT-C(onsolidation)	TARGIT-B(oost)	National Health Committee
Age (years)	>50	≥50	≥70	≥50	18-85	≥45
Tumour size	T1-2 (≤3cm)	T1 (≤2cm)	T1 (<2cm)	T1 or small T2 (≤3.5cm)	T1-2 (≤3.5cm)	T1-2 (≤3cm)
Lymph node	N0	N0	N0	N0	Not specified	N0 or N1 micro (0.2-2mm)
Metastasis	M0	M0	M0	M0	M0	M0

Source: ESTRO (Polgar et al. 2010); ASTRO (Correa et al. 2017); TARGIT-E(lderly) (Neumaier et al. 2012); TARGIT-C(onsolidation) (ClinicalTrials.gov); TARGIT-B(OOST) (ClinicalTrials.gov)

An assessment of these criteria and the relevant literature was undertaken to identify an appropriate synthesis of the criteria. Following consultation with the MoH, a base case clinical criteria for estimating demand for IORT as well as a low demand and high demand scenario were developed. 'Low demand' represented the most restrictive and 'high demand' represented the least restrictive criteria. The clinical criteria for each of these scenarios is summarised in Table 3.2.

It is worth noting that clinicians usually consider a much broader range of clinical criteria when assessing patient eligibility for receiving IORT, including observations during surgery. These include tumour free margins, extensiveness of in-site component and if there is unexpected invasive lobular carcinoma observed during surgery.

Table 3.2: Assumed eligibility clinical criteria by scenario

Criteria	Base case	Low demand	High demand
Age	45-84 years	60-79 years	≥45 years
Tumour size	T1-2 (≤3cm)	T1 (≤2cm)	T1 (≤3cm)
Lymph node and metastasis	No	No	No

3.1.3 Other parameters

Table 3.3 summarises the key parameters used in the calculation of the estimated demand for IORT, including the sources and assumptions. The lower and upper bounds of values that were identified in the literature have been used respectively as the parameters for the low and high demand scenarios.

Table 3.3: Key parameters and assumptions

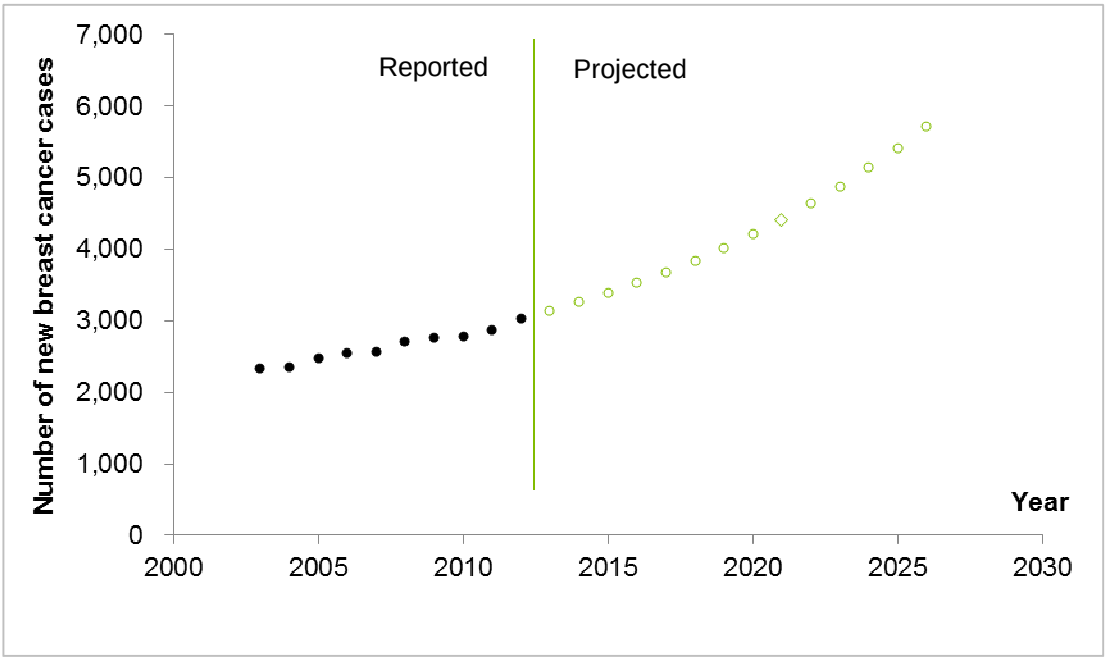
Source	Study method	Finding	Assumptions/Comments
What proportion of newly diagnosed breast cancer cases are at Stage 1?			
Walters et al. 2013	Analysed women diagnosed with breast cancer from 1995-2007 in Canada, Denmark, Norway, Sweden and the UK, with Australian data excluded.	Proportion of new cases at Stage 1 ranged between 29.3% and 45.2% after imputation.	A median value of the range (40%) was used as the base case estimate of the proportion of new cases with Stage 1 breast cancer at diagnosis.
What proportion of Stage 1 breast cancer cases undergo BCS?			
Ainsworth et al. 2013	Analysed data from the BreastSurgANZ National Breast Cancer Audit (Australia and New Zealand) relating to cases since 2001.	56.3% of episodes relating to invasive cancer involved undergoing BCS	The median value of the identified estimates (64.5%) was taken as the base case estimate of the proportion of Stage 1 cases undergoing BCS.
Kummerow et al. 2015	Analysed data from the National Cancer Data Base (US), from the period of 1998 to 2011.	64.5% of patients underwent BCS while 35.5% underwent mastectomy	
Lam et al. 2015	Analysed data for patients with EBC from New South Wales in Australia between 2010 and 2014.	73% of patients with ductal carcinoma in situ were found to have undergone breast-conserving treatment	
What proportion of patients with EBC undergo adjuvant radiotherapy after BCS?			
Wang et al. 2016	Analysed data from the National Cancer Data Base (US) pertaining to women aged 50 years and over with EBC and treated with BCS between 2004 and 2013	76.6% of patients had undergone adjuvant radiotherapy following BCS	The median value of the identified estimates (76.6%) was taken as the base case rate for post-BCS adjuvant radiotherapy
Ooi et al. 2012	Analysed New Zealand data from the National Breast Cancer Audit with a diagnosis date of 2008.	98.0% of early breast cancer patients in New Zealand underwent post-operative radiotherapy	
Daugherty et al. 2016	Analysed data from the Surveillance, Epidemiology and End Results database (US) for patients aged 70 years and over who had undergone BCS	71.2% of patients subsequently received radiotherapy	
What proportion of patients would elect to have IORT rather than EBRT if provided with evidence based information?			
Alvarado et al. 2014	Patient preference for IORT over EBRT using a trade-off technique to quantifying the additional accepted risk that patients were willing to bear to choose IORT instead of EBRT (US) Women in the sample were current and past candidates for BCS. A majority were aged 46-60 years (77.8%).	64.2% of patients accepted IORT with some additional risk of having a local recurrence with 10 years.	They had a range of different tumour grades (low, intermediate, high and unknown). Some of these patients would not be eligible for IORT. Patient preference may be influenced by advice from their treating doctors.

Source	Study method	Finding	Assumptions/Comments
Bonin et al. 2016	Study participants were presented with an educational tool containing comprehensive evidence based information regarding PBI versus WBI	Of those who chose PBI (N=27), 48% chose IORT which was 14.4% of the total sample. People with no-preference were divided equally between the remaining categories resulted in an overall figure of 15.3% of the total sample likely to choose IORT.	Preferences 'stated' in this study by participants would be in line with the subsequent 'revealed' preference. Patient preference may be influenced by advice from their treating doctors.

3.1.4 Projection of future incidence of breast cancer

The number of EBC cases from 2012 onwards was projected using data from the New Zealand Cancer Registry (MoH 2015) on the number of new breast cancer cases between 2003 and 2012. Based on these data points, a basic linear regression was modelled to estimate the year-on-year growth rates of EBC cases up to 2026 (Chart 3.1).

Chart 3.1: Reported and projected number of new breast cancer cases in New Zealand



Source: New Zealand Cancer Registry data and analysis by Deloitte Access Economics

3.2 Results

It was estimated that approximately 461 women underwent IORT in 2017, within a projected range of 83 to 1,505, based on low and high demand scenario estimates. This number is projected to rise to 717 women in 2026, within a range of 125 to 2,340. A breakdown of this estimate by cancer centres is provided in Table 3.4. Appendix A presents the full estimates by year.

Table 3.4: Estimated demand for IORT by cancer network in 2017 and 2026

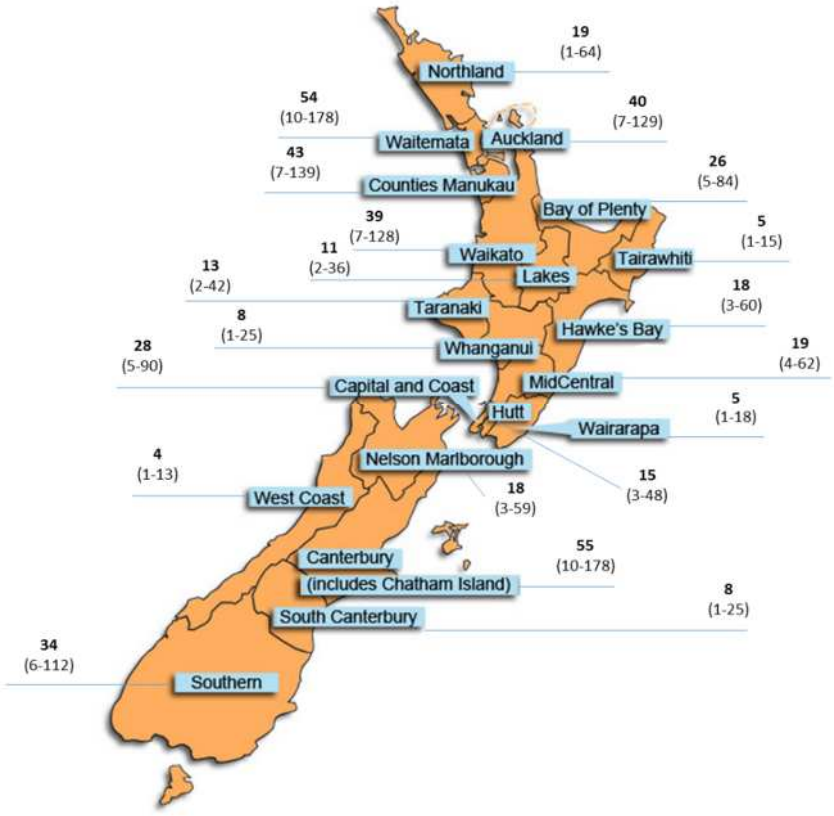
Cancer centres	2017	2026
Auckland	156 (24; 510)	243 (38; 793)
Hamilton	80 (15; 263)	125 (23; 409)
Palmerston North	58 (11; 188)	90 (17; 293)
Wellington	48 (8; 156)	74 (13; 242)
Christchurch	77 (14; 251)	119 (22; 390)
Dunedin	42 (8; 137)	65 (12; 213)
Total	461 (80; 1,505)	717 (125; 2,340)

Source: Deloitte Access Economics calculations.

Note: numbers are presented as base case and low demand and high demand estimates in parenthesis

The estimated demand for IORT in 2017 by DHB is presented in Figure 3.2.

Figure 3.2: Estimated number of people with IORT by DHB and scenario, 2017



Source: Deloitte Access Economics calculations and MoH (2016)

3.3 Summary

Table 3.4 presents a summary of the estimated demand based on the main assumptions discussed in this Section.

Table 3.5: Estimated demand for IORT by cancer network

	Base case	Low demand	High demand
Estimates based on 2013 data			
Number of women in New Zealand in 2013	**2,178,033**		
New cases of breast cancer Age specific breast cancer incidence per 100,000 women	**3,544** 15 years: 0.35 85+ years: 281	**2,456** 15 years: 0.14 85+ years: 190.8	**5,010** 15 years: 0.80 85+ years: 413.6
New cases of breast cancer eligible^ for IORT at diagnosis [Age, tumour size, and probability of detection with Stage 1 at diagnosis]	**1,238** [45-84 years; ≤3cm; and 40%]	**276** [60-79 years; ≤2cm; and 29.3%]	**1,962** [≥45 years; ≤3cm; and 45.2%]
Number of women undergoing BCS	**799** 64.5%	**155** 56.3%	1,432 73.0%
Number of women receiving adjuvant radiotherapy after BCS	**612** 76.6%	**111** 71.2%	**1,404** 98.0%
Number of women preferring IORT over EBRT	**393** 64.2%	**71** 16.0%	**1,282** 91.4%
Estimated number of women using IORT, 2017 and 2026*			

Year / Region	2017	2026	2017	2026	2017	2026
Auckland	156	243	24	38	510	793
Hamilton	80	125	15	23	263	409
Palmerston North	58	90	11	17	188	293
Wellington	48	74	8	13	156	242
Christchurch	77	119	14	22	251	390
Dunedin	42	65	8	12	137	213
TOTAL number of women	**461**	**717**	**80**	**125**	**1,505**	**2,340**

Note:*see projection method in Section 3.1.4

4 Financial and economic impacts

This Section provides an outline of the model developed to estimate the economic and financial impacts of introducing IORT in public cancer centres in New Zealand.

This Section first describes the types of variables used in the model, then outlines the sources and bases of various model assumptions. Broadly speaking the model consisted of four types of variables:

- demographic and demand variables;
- equipment and consumable variables;
- clinical service variables; and
- output variables.

The model forecasts the impacts during a 10-year period between 2017 and 2026, with an assumed introduction of IORT occurring from 2017. The MoH specifies three scenarios for assessment, as specified in Table 4.1

Table 4.1: Modelling scenarios based on the location of IORT equipment

	Scenario 1	Scenario 2	Scenario 3
Number of complete IORT package	2	3	2
Number of permanent component	4	2	2
Location of equipment			
Auckland	Complete	Complete	Complete
Hamilton	Permanent	Complete	Permanent
Palmerston North	Permanent	Permanent	Permanent
Wellington	Permanent	Permanent	-
Christchurch	Complete	Complete	Complete
Dunedin	Permanent	-	-

Note: **The complete package** includes a miniaturised linear accelerator, SQA tools, spherical applicator set and the permanent components. **Permanent components** comprise a control console, electrometer, cart, floor stand and shuttle container. Sites with a permanent component would share the linear accelerator, SQA tools and spherical applicator set with the sites with complete package.

The expected impacts were estimated by taking the difference between output variables under the base case and under each of the three scenarios when the IORT is made available at the locations as specified. The base case counterfactual assumed the status quo where IORT is not available in the public radiation therapy centres in New Zealand and eligible patients would continue to receive EBRT.

The findings are presented from the health system perspective and societal perspective where impacts on patients are included. A series of one-way deterministic sensitivity analyses were undertaken to test a set of input parameters with different assumed values.

For the base case analysis, all values were discounted at 6% annually (New Zealand Treasury 2016). All figures are presented as net present values in 2016 New Zealand Dollars. In view of the equivocal evidence, the MoH has requested the model to consider the efficacy and safety of IORT and EBRT as equivalent for the base case.

4.1 Variables and assumptions

4.1.1 Demographic and demand variables

Demographic and demand variables in this model were presented in Section 3. To reiterate, the demand estimates account for:

- **demographics:** population in New Zealand by DHB area and age groups;
- **epidemiology:** incidence of breast cancer in New Zealand;
- **clinical eligibility:** criteria for receiving IORT, which include consideration for age, tumour size, lymph node involvement and whether the cancer has spread outside of the primary site;
- **clinical service provision**: parameters include rates of BCS and post-BCS adjuvant radiotherapy; and
- **patient preference** for IORT over EBRT.

The estimated number of patients using IORT was presented as base case estimates by year, bounded by the low- and high-demand scenarios.

4.1.2 Equipment and consumable variables

Equipment and consumable variables represent characteristics of INTRABEAM equipment, and the consumables and services required for its use. For the base case, the model assumed the values outlined in Table 4.2. These values are based on the manufacturer's product description and published estimates in the NICE's Health Technology Assessment (NICE 2015).

Table 4.2: Model parameter values for equipment variables

Parameter	Base case	Sources and assumptions
Life time of INTRABEAM	10 years	Carl Zeiss and NICE (2015)
Complete IORT package	$1,316,590*	Carl Zeiss: $1,144,861 (ex goods and services tax (GST)). Volume discount is provided at 5%, 7%, 10%, and 12% for 2, 3, 4 and 5 units purchased, respectively.
Permanent components	$567,095*	Carl Zeiss: $493,126 (ex GST). Volume discount as per above.
Radiation screen	$3,500 per site	Estimate from informant
Lifespan and replacement of spherical applicator	100 uses ($26,565 per 300 uses)	Carl Zeiss and informant: each applicator can be only be sterilised 100 times. According to an informant consulted, the average size of applicator used was 3.5cm and 2.5cm was used once in 100 cases. For simplicity, it was assumed that for 3 new applicators are required for every 300 procedures performed. Carl Zeiss quoted the costs of each applicator as $7,700 (ex GST)
Quality assurance check of core device	2 times per week ($52)	Carl Zeiss: quality assurance checks are required every 36 hours irrespective of whether the equipment is transferred or not. Cost is estimated as 30 minutes of Physicist's time. Note that the

Parameter	Base case	Sources and assumptions
		physicist would perform quality assurance tests on site rather than in specialised laboratory (Muradlihar and Rout 2014).
Routine maintenance	Full site: $104,075* Peripheral: $5,750*	Carl Zeiss: annual maintenance are required for sites with complete equipment and all peripheral sites with permanent components after the 2-year warranty period.
Radiation protection shields	$404 per treatment	NICE (2015): £1,041 for 5 treatments. Values are converted to New Zealand dollars using an exchange rate GBP:NZD of 1.6871.
Sterile plastic drapes	$61 per treatment	Carl Zeiss: $265 (ex GST) for a pack of 5

Note:*inclusive of 15% GST

4.1.3 Clinical service variables

A range of resources relating to planning, access to and provision of IORT and EBRT services were considered when developing the model. These variables were grouped into workforce and operating procedure development; provision of clinical services; and patient access to services (Table 4.3).

Table 4.3: Model parameter values for clinical service variables

Parameter	Base case	Sources and assumptions
Workforce and operating procedure development		
Staff training	Sites with complete package: $6,333 Sites with component: $9,333	For each purchase of a complete IORT package, Carl Zeiss provides initial training for 2 persons at TARGIT Academy in Germany and US. This includes all travel related costs. Based on NICE (2015) and consultations with informants, the model assumed that training would involve a total of 8 personnel for 2 days (2x surgeons, 2x radiation oncologists, 2x physicists and 2x nurses). The costs of training are related to the estimated time commitment and were valued according to hourly wage rates*.
Operating procedure development	$1,500 per site	NICE (2015): two days of senior staff time, valued according to radiation oncologist's salary*.
Provision of clinical services		
Standard EBRT course	$6,545	NHC (2015): estimated that a course of EBRT treatment typically has an average of 18.7 sessions, each with a cost of $350.
BCS plus EBRT	$9,828	Calculated based on WIESNZ of 0.6804 for NZDRG J07B^ and unit price of $4,824.67 (NCCP Casemix Cost Weights Project Group 2015)
BCS plus IORT	$5,995	NHC (2015) proposed a fee of $5,000 for IORT. The base case value accounted for 15.2% of IORT patients estimated to also receive EBRT, as observed in TARGIT-A (Vaidya 2014)
Transportation of shared equipment	Scenario 1: $3,300 per month Scenario 2: $2,800 per month	MoH: the shared equipment is transported among service sites on the same island on a monthly rotation. For example, for scenario 1, the single shared equipment would rotate among the four sites on the North Island on a weekly basis, while the shared equipment in the South Island would rotate on a fortnightly basis. For this scenario, there will be six shipments per month in total. The costs of transportation was obtained from one logistic company based on shipment of a case (38.7 kilogram and

Parameter	Base case	Sources and assumptions
	Scenario 3: $1,500 per month	of dimension 90.5 cm x 64 cm x 41cm). Shipment costs were estimated as $400 for short-distance transportation by road and $700 long-distance transportation by flight. Please note that only basic insurance is included in this estimate.
Annual refresher training on radiation protection	$948	Based on NICE (2015), the model assumed 1 hour annual refresher training for 15 staff
Patient access to services		
Travel costs to receive EBRT therapy	$108.26 per returned trip	A geospatial analysis by Brabyn and Skelly (2002) estimated that on average a patient would travel 89.5 minutes to a tertiary hospital in New Zealand. On this basis, the travel cost was estimated using an average travel speed of 50.4 kilometres per hour, as observed by Transport New Zealand in urban areas, and a mileage rate of $0.72 per kilometre, as estimated by Inland Revenue (2015).
Productivity losses due to attending EBRT	$133.17 on the day of treatment	It was assumed that women who receive EBRT would have the same workforce participation rate (64%) and wage rate ($27.56 per hour) (Statistics NZ 2016) as women in the general population of the same age. Lost productivity was calculated assuming that women attending EBRT would not work on the day of treatment. This assumption overestimates the potential losses because some women may continue working through the treatment period.

Note:*Hour wage rates are estimated based on annual salaries for surgeon and oncologists ($180,000, Association of Salaried Medical Specialists (2016)), and nurses and medical physicists ($100,000, CareersNZ (2015)). ^Minor procedures for non-malignant breast conditions.

4.1.4 Output variables

Output variables represent the estimated impacts from introducing IORT to the New Zealand public health system, and are a function of the data included in the model and assumptions outlined above. They include:

- capital, operational, and patient-related costs;
- net impact from a health system perspective; and
- net impact from a societal perspective where impacts on patients were incorporated.

4.2 Results

4.2.1 Base case

For the base case demand scenario, the model estimated the provision of IORT in the public health system under all three scenarios would generate cost savings from both the health system and societal perspectives (Table 4.4). From a health system perspective, the savings range from $2.22 million to $4.15 million over the 10 year period from 2017. The upfront capital expenditure in 2017 and ongoing operational costs would be offset by savings from a reduction in costs due to lower quantity of EBRT supplied ($9.95 million). Furthermore, the model estimated substantial savings for patients because of a reduced need to travel for receiving EBRT treatment ($6.04 million), and avoidance of productivity losses arising from time off work for receiving EBRT treatment ($7.43 million) (Table 4.4).

Table 4.4: Incremental costs related to the provision of IORT in 2017-2026, by scenario and perspective, base case

	Scenario 1^	Scenario 2^	Scenario 3^
Health system			
Capital			
IORT and related equipment	$4.56 m	$4.77 m	$3.59 m
Training and operating procedure development	$0.07 m	$0.07 m	$0.05 m
Operational			
Annual maintenance	$1.35 m	$1.90 m	$1.29 m
Replacement of Spherical applicators§	$0.36 m ($0.04 m ; $1.24 m)	$0.33 m ($0.04 m ; $1.24 m)	$0.36 m ($0.04 m ; $1.24 m)
Transportation, calibration and sterilisation§	$0.66 m ($0.40 m ; $1.35 m)	$0.63 m ($0.38 m ; $1.33 m)	$0.49 m ($0.24 m ; $1.18 m)
Clinical service			
Treatment with IORT, including disposables§	$27.46 m ($4.79 m ; $89.65 m)	$27.46 m ($4.79 m ; $89.65 m)	$27.46 m ($4.79 m ; $89.65 m)
Counterfactual - Treatment with EBRT§	$37.42 m ($6.52 m ; $122.15 m)	$37.42 m ($6.52 m ; $122.15 m)	$37.42 m ($6.52 m ; $122.15 m)
Incremental difference (IORT - EBRT) §	-$9.95 m (-$1.73 m ; -$32.49 m)	-$9.95 m (-$1.73 m ; -$32.49 m)	-$9.95 m (-$1.73 m; - $32.49 m)
Patient			
Travel costs§	-$6.04 m (-$1.05 m ; -$19.71 m)	-$6.04 m (-$1.05 m ; -$19.71 m)	-$6.04 m (-$1.05 m ; -$19.71 m)
Productivity losses from EBRT avoided§	-$7.43 m (-$1.20 m ; -$31.70 m)	-$7.43 m (-$1.20 m ; -$31.70 m)	-$7.43 m (-$1.20 m ; -$31.70 m)
Net impact			
Health system perspective§	-$2.91 m (+$4.72 m ; -$23.88 m)	-$2.22 m (+$5.44 m ; -$23.16 m)	-$4.15 m (+$3.49 m ; -$25.11 m)
Societal perspective§	-$16.38 m (+$4.24 m ; -$71.47 m)	-$15.69 m (+$5.49 m ; -$70.23 m)	-$17.61 m (+$2.79 m ; -$72.92 m)

Note: ^ Please refer to Table 4.1. § Numbers are presented for base case and in parenthesis low-demand and high-demand estimates

The analysis also found that the savings may not be sufficient to offset the capital and operational costs associated with IORT under the low-demand scenario. In this case, investing in IORT would incur costs to the health system under all three scenarios ($3.49 million to $5.44 million), even if the avoidance of patient travel costs and productivity losses were incorporated ($2.79 million to $5.49 million over 10 years) (Table 4.4). A further break-even analysis suggests that in order to be cost neutral from a health system perspective, demand would need to be at least 68.4% (3,939 over 10 years), 75.9% (4,365 over 10 years), and 55.1% (3,168 over 10 years) of the projected demand for scenarios 1, 2 and 3 (5,755 over 10 years) respectively.

In contrast, if the actual demand were to be higher than the base case estimates, the investment would generate considerable savings to the health system ($23.16 million to $25.11 million over 10 years) and society ($70.23 million to $72.92 million over 10 years) (Table 4.4). To realise this level of demand and savings, the system would need to be ensure a range of factors from both the demand and supply sides discussed in Section 5, which are not fully enumerated in the current model.

4.2.2 Sensitivity analysis

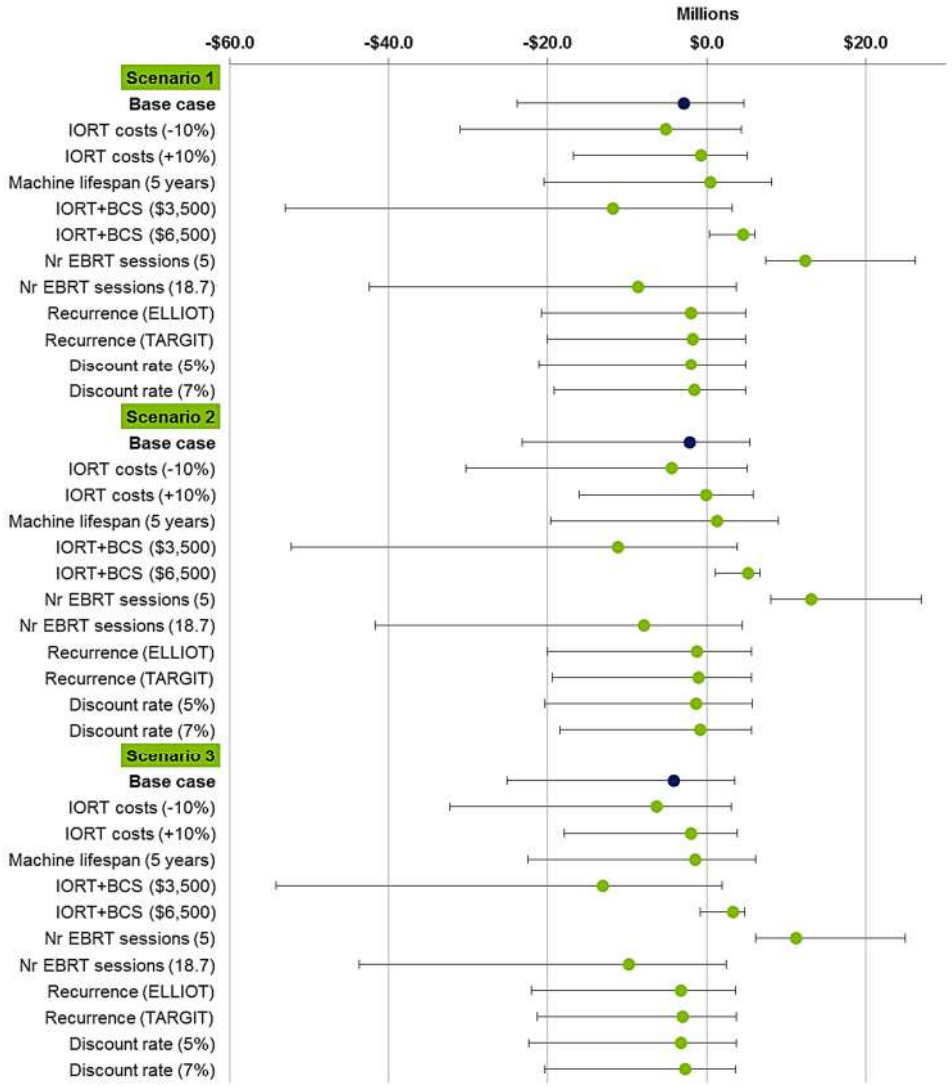
A series of one-way sensitivity analyses were undertaken to test the impact of a set of input parameters on the net costs to the health system. Table 4.5 presents the selected input parameters and values and the rationale.

Table 4.5: Parameters and values considered in one-way sensitivity analysis

Parameter	Values	Rationale
Price of IORT equipment	±10%	The base case was based on the quotation provided by Carl Zeiss with volume discount. However, the Carl Zeiss UK's price of IORT presented in NICE (2015) was substantially lower at £435,000. This is equivalent to New Zealand $843,972 at an exchange rate of 1.6871. On the other hand, depending on the timing of the purchase, the price of IORT equipment may increase.
Machine lifespan	5 years	NICE (2015) assumed in their sensitivity analysis a 5-year lifespan for the INTRABEAM machine.
Price of IORT and BCS procedure	$3,500 $6,500	In Australia, the price of IORT is AUD250 and the price of BCS for AR-DRG J07b is AUD3,017. On this basis, the analysis assumed a ±30% around the base case value of NZ5,000 for an IORT and BCS procedure.
Number of EBRT sessions	5 and 18.7	A number of shorter hypofractionated regimens may become standard of care in the future (based on FAST and START trials by Haviland et al. (2013) and FAST Trialists group (2011)).
Additional local recurrence of local breast cancer	+0.7% to +0.9% per year	While within the pre-specified equivalence margin, the local recurrence rates (LRR) of breast cancer were numerically higher in both ELIOT (LRR= 0.4% at 5.8 years for EBRT compared to 4.4%) and TARGIT trials (LRR = 1.3% over 2.33 years for EBRT compared to 3.3%). On this basis, the estimated annual probability of local recurrence was calculated and applied over the 10 year period. For a patient detected to have local recurrence, it was assumed that it would cost $7,770 for the patient to receive a mastectomy, as per recommended treatment guidelines (e.g. Cardoso et al. 2012). Patients may receive other secondary systemic treatment, depending on the characteristics of recurrence. For simplicity, this analysis has not included these potential therapies. The cost of mastectomy is calculated based on the WIESNZ for NZDRG *J06B Major Procedures for Non-Malignant Breast Conditions* (1.6104) and a unit cost of $4,824.67.
Discount rates	5% and 7%	Assumed range of real discount rates

As presented in Figure 4.1, the analysis found that varying most of the values of the parameters as specified above does not alter the overall net impact of the scenarios on the health system. That is, investing in IORT in the public sector would generate cost savings under the base case scenario, with potential net positive cost to the health system under the low-demand assumption. The exceptions are when the number of EBRT sessions is assumed to be five sessions and when the cost of IORT plus BCS is 30% greater than the base case assumption of $5,000. Specifically, if patients in New Zealand were to receive five sessions of EBRT instead of the current 15 sessions, investment in IORT equipment would result in net a cost to the health system. In contrast, savings would be more substantial if EBRT regimens are 18.7 sessions and if the costs of IORT+BCS is $3,500. The analysis did not find that the higher local recurrence rates of breast cancer in patients receiving IORT compared to EBRT, if proven to be similar to those observed in TARGIT or ELIOT, would translate into significant health system costs. However, it must be noted that the current analysis may not have captured the full impact on patient health outcomes arising from local recurrence (e.g. systemic therapies). This is discussed further in the next Section.

Figure 4.1: Net impact to the health system over 10 years, by scenario and parameters



Note: Base case values are presented as markers and values for high- and low-demand scenarios are presented as ranges.

Source: Deloitte Access Economics calculations.

5 Discussion and conclusion

The analysis presented in Section 4 compares the financial and economic impact of introducing IORT for a group of eligible patients with EBC who would have otherwise received adjuvant EBRT. The analysis indicates that IORT would present cost savings for the New Zealand health system should IORT be publicly implemented from 2017 to 2027 for all three IORT distribution scenarios if the estimated demand for IORT service is sufficiently high. From a societal perspective, the costs savings are even greater because of patient productivity gains realised through using IORT rather than EBRT. However, the interpretation of findings from the analysis requires further consideration of a number of factors, as discussed below.

5.1 Additional factors for consideration

5.1.1 Demand side factors

The number of patients who receive IORT will be heavily influenced by physician's acceptability of IORT as a replacement for EBRT. The ROWG (and the now disestablished CTAG) is the key organisation involved in the delivery of cancer services and treatments in New Zealand. In 2015, ROWG made their position against the implementation of IORT in the public system clear, pending longer-term follow-up of the TARGIT-A trial participants. CTAG endorsed ROWG's statements and additionally noted that patients should have the right to choose their treatment once they have been fully informed regarding any uncertainty around IORT's efficacy. However, in its submission to the NHC, CTAG stated that it did not believe IORT should be funded in the public health system (NHC 2015). The Faculty of Radiation Oncology of the RANZDCR, BreastSurgANZ and RACS hold a similar position. That is, the evidence for IORT in EBC as a substitute for EBRT is immature and longer follow-up data is needed.

Furthermore, there is emerging paradigm shift in the management of EBC towards reducing the duration and frequency of EBRT. For some early breast cancer cases, endocrine therapy post-BCS without other adjuvant therapy has been suggested to be the appropriate care (Shah et al 2016). The advancement in molecular biology will also influence the future management strategy for women with EBC.

For these reasons, the demand and referral of patients for IORT may be lower than predicted by this analysis, which only accounts for patients' preferences. This would in turn influence whether the capital and operational costs would be sufficiently offset by the anticipated benefits. Decision makers should consider a staged implementation to ensure that demand is not significantly lower than anticipated, and to prevent exposure to significant upfront capital investments. Additionally, lessons learned from an initial site implementation may be applied to other sites in terms of environmental preparedness, referral processes, information dissemination to the public, clinicians and other staff, and staff training.

On the other hand, the TARGIT-B trial is currently underway to assess if a tumour bed boost given intraoperatively would lead to better cancer control than a tumour bed boost given with EBRT. If a positive finding eventuates, demand for IORT would increase considerably and would present an additional financial (and may not be economic) cost to the health system in New Zealand.

5.1.2 Supply side factors

Some patients in regional areas may have their BCS in regional hospitals but travel to the closest major centre to have their EBRT. By nature of IORT, patients who opt to have IORT would need to undergo surgery at the major centres where IORT is available. This will place additional demand on services and resources at these major centres, including nurses, breast surgeons, anaesthetic services (due to longer surgical time), allied health and pharmacy. The impact on radiation oncology services may be lesser because patients receiving IORT instead of EBRT will not need to have the associated treatment planning process. Decision-makers should therefore consider providing additional resources or institute better planning processes at the major centres with IORT, in order to prevent an inadvertent increase in waiting times for elective procedures. The costs associated with this have not been considered in the analysis presented in this report because it requires data and a full assessment relating to the existing supply capacity in each centre with the proposed IORT service.

The new IORT services will also require workflow planning. Unlike the current model of care where surgery and radiation therapy are provided sequentially, IORT requires simultaneous alignment for radiation therapy, radiation oncology, medical physicist and surgical services. Given the current radiation oncologist workforce shortages discussed in section 2.2.5, this may be challenging, especially in smaller DHBs. However, stakeholders discussed the potential for IORT to release 1 to 1.5 hours of the radiation oncology workforce time as it does not require the planning process associated with EBRT.

In Section 2.2.5, this report noted that the demand for linacs in New Zealand is projected to increase because of increasing population and age and a higher intervention rate. It is estimated that an increase in supply of an additional 42 linacs by 2023 with an estimated total costs of $216 million would be needed to meet the overall demand (MoH 2016). Diverting patients with EBC requiring EBRT to IORT may reduce the demand for linacs, but the overall extent of reduction may be low because: (1) linac is used for a broad range of cancers. Patients with low-risk early breast cancer who are suitable and opting for IORT represent a relatively small proportion of the overall number of patients using linac; and (2) there is an ongoing paradigm shift where hypofractionation may become the standard of care for treatment of low-risk EBC (e.g. FAST Trialists group 2011; Hickey et al. 2016).

Since 1 October 2014, the New Zealand MoH implemented the "Faster cancer treatment" (FCT) targets to ensure that "85% of patients receive their first cancer treatment (or other management) within 62 days of being referred with a high suspicion of cancer and a need to be seen within two weeks" (MoH 2016b). BCS and EBRT can be offered to patients separately and are available at more service providers than the proposed IORT services. For this reason, the lower availability of IORT services at selected centres, together with the need to align resources, may have an unintended impact on the ability of some DHBs meeting the FCT targets and resulting in financial losses. In developing the implementation policy for IORT, decision makers may consider defining the FCT targets in view of the potential impacts on resources.

Finally, for smaller treatment centres currently offering EBRT as a core part of their scope of service, the availability of IORT may divert patients away from their service catchment and thereby have a negative impact on their ongoing financial viability. A transition plan would need to be in place to prevent vertical consolidation of services.

5.1.3 Procurement of IORT systems and ownership

The model assessed the capital and operational costs based on pricing information provided by Carl Zeiss Australia. Even with the volume discounts, the price of the INTRABEAM system and subsequent servicing quoted in the 2015 UK NICE health technology assessment (Picot et al. 2015) are lower than the prices presented in this report. During procurement process, decision makers may seek clarification regarding the differences in prices.

It is assumed that individual DHBs would own the IORT equipment and establish procurement arrangements for consumables associated with IORT equipment. However, because of the shared components across different DHBs in certain circumstances, the final procurement processes and cost-sharing arrangements may be complicated and administratively burdensome. The procurement strategy and ongoing financial arrangements would need to be carefully considered prior to commissioning of the service. For the procurement processes, management by the Pharmaceutical Management Agency (PHARMAC) on behalf of DHBs may improve value for money and reduce administrative burden on individual DHBs (PHARMAC 2016).

5.1.4 Potential impacts on mastectomy and reconstructive surgery

There is evidence that women residing in areas further away from treatment centres are more likely to have a mastectomy rather than BCS with adjuvant EBRT. For example, Goyal et al. (2015) undertook regression modelling and found that women with EBC in New Jersey in the US (n=634) were 44% and 36% more likely to have a mastectomy if their place of residence was more than 9.2 miles (14.8 kilometres) from radiation facility or if they had to travel more than 19 minutes to a radiation facility, respectively. Lautner et al. (2015) analysed the US National Cancer Data Base for women with T1 and T2 breast cancers treated in 1998 to 2011 (n=727,927) and made a similar observation: residence within 27.8 km of a treatment facility was associated with greater BCS rates than residence farther from a treatment facility (odds ratio=1.25; 1.23-1.27). On the basis of the above observations, introducing IORT in New Zealand may result in some women, particularly those residing in areas further away from treatment centres, choosing BCS and IORT over mastectomy.

However, the extent to which the introduction of IORT in New Zealand would reduce the number of mastectomies and subsequent breast reconstruction surgeries performed is not certain. There are at least two reasons for this; first, patients choosing mastectomy over BCS primarily base their decision on adverse pre-operative pathological features rather than distance from services. Shearer et al. (2016) found that a considerable proportion of women in a single treatment centre in the UK chose to undergo mastectomy despite being suitable for BCS because they felt mastectomy "gave a better long-term outcome (18 patients, 44%) and peace of mind (14 patients, 34%)". There is a possibility that women living in different geographic regions have different perception of risk, but there is insufficient evidence to confirm this. Second, patients opting to have BCS may have mastectomy as a follow-up procedure. Green et al. (2013) found that 19% and 13% of women living in rural and urban areas in Queensland in Australia who had BCS as the index surgery ultimately had a mastectomy as a follow up procedure. Finally, if shorter hypofractionated regimens were to become standard of care, more women would accept BCS, irrespective of whether IORT were introduced.

In terms of impact on subsequent breast reconstruction, women who had a mastectomy may not undergo reconstruction because of distance from plastic surgeons (Roughton et al. 2016) and the availability of service in New Zealand may be variable, as in Australia (Flitcroft et al. 2016).

5.1.5 Local recurrence, morbidity, toxicity and mortality

The base case analysis presented in this report assumed clinical equivalence for EBRT and IORT, as requested by MoH. For this reason, costs associated with additional local recurrences of breast cancer cases in patients treated with IORT were only considered in the sensitivity analysis. If IORT is proven to be clinically inferior to EBRT, a full economic analysis would need to consider differences in morbidity, mortality and quality of life outcomes arising from differences in local recurrence rates. Furthermore, depending on the stage of the disease, the analysis would need to consider costs associated not only with mastectomy, but also other surgical and pharmacological interventions.

The analysis in this report also did not consider the cost of complications in the form of local toxicity and morbidity arising from both treatments. Although most clinically significant complications have been shown to be similar in both groups, wound seroma requiring more than three aspirations has been shown to be higher in those receiving INTRABEAM. Conversely, Radiation Therapy Oncology Group (RTOG) toxicity scores of grade 3 or 4 have been shown to be more frequent in the EBRT group (Vaidya et al. 2010). The clinical impact of high RTOG scores is likely to be greater than wound seromas requiring aspiration (Picot et al. 2015). However, complication rates appeared similar in both groups after 6 months (Vaidya et al. 2010). Therefore, the impact of including these complications would likely be minimal.

5.1.6 Use for other indications

It is recognised that IORT has been considered for the treatment of a range of other cancers other than breast cancer. These include gastric, pancreatic, gynaecological, head and neck, prostate, colorectal cancers and soft tissue sarcoma. The NHC (2015) summarised the evidence regarding efficacy in each cancer finding that there may be potential benefit for adding IORT to the treatment for retroperitoneal tumours, head and neck cancers and rectal cancers. However, the overall evidence base for these indications is not well developed and in some clinical scenarios, IORT would not have adequate penetration and field size. Decision-makers should be aware that the significant start-up expenses may precipitate inappropriate uses of IORT for these other clinical conditions for which there is insufficient evidence to support its use, in order to recover costs.

5.2 Conclusion

In conclusion, on the assumption of clinical equivalence, investing in IORT in publicly funded radiation therapy centres according to the three scenarios would be likely to present cost savings for the New Zealand health system and society compared to the existing EBRT services, provided that estimated demand for IORT service is sufficiently high. In addition to the economic and financial considerations presented in this report, policy makers in New Zealand should consider other factors such as the overall policy objectives, acceptability to clinicians, impact on workforce and service capacity, the procurement arrangements, and potential indication 'creep' to other clinical conditions for which evidence remains insufficient. Furthermore, as evidence for the management of EBC continue to evolve, policy makers should anticipate and be prepared for any future changes in the treatment recommendations, including the use of IORT or radiotherapy more generally, in women with low-risk early breast cancer.

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Limitation of our work

General use restriction

This report is prepared solely for the use of the New Zealand Ministry of Health. This report is not intended to and should not be used or relied upon by anyone else and we accept no duty of care to any other person or entity. The report has been prepared for the purpose set out in Consultancy Services Order dated September 2015. You should not refer to or use our name or the advice for any other purpose.

Appendix A

Table A.1: Estimated base case demand and low-demand and high-demand in parenthesis, by year

Region	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	Total
District health board											
Northland	19 (1; 64)	20 (1; 67)	21 (1; 70)	22 (1; 73)	23 (1; 76)	25 (1; 80)	26 (1; 84)	27 (1; 89)	29 (1; 94)	30 (1; 99)	244 (12; 796)
Waitemata	54 (10; 178)	57 (10; 185)	59 (10; 194)	62 (11; 203)	65 (11; 213)	69 (12; 224)	72 (13; 235)	76 (13; 248)	80 (14; 262)	85 (15; 276)	680 (119; 2,218)
Auckland	40 (7; 129)	41 (7; 135)	43 (7; 141)	45 (8; 148)	48 (8; 155)	50 (8; 163)	53 (9; 171)	55 (9; 180)	58 (10; 190)	62 (10; 201)	495 (82; 1,614)
Counties Manukau	43 (7; 139)	45 (8; 146)	47 (8; 152)	49 (8; 160)	51 (9; 167)	54 (9; 176)	57 (10; 185)	60 (10; 195)	63 (11; 205)	67 (12; 217)	535 (93; 1,742)
Waikato	39 (7; 128)	41 (8; 133)	43 (8; 139)	45 (8; 146)	47 (9; 153)	49 (9; 161)	52 (10; 169)	55 (10; 178)	58 (11; 188)	61 (11; 199)	488 (90; 1,594)
Lakes	11 (2; 36)	11 (2; 37)	12 (2; 39)	12 (2; 41)	13 (2; 43)	14 (3; 45)	14 (3; 47)	15 (3; 50)	16 (3; 52)	17 (3; 55)	136 (25; 444)
Bay of Plenty	26 (5; 84)	27 (5; 88)	28 (5; 92)	29 (6; 96)	31 (6; 101)	32 (6; 106)	34 (7; 112)	36 (7; 117)	38 (7; 124)	40 (8; 131)	321 (62; 1,051)
Tairawhiti	5 (1; 15)	5 (1; 16)	5 (1; 17)	5 (1; 18)	6 (1; 18)	6 (1; 19)	6 (1; 20)	7 (1; 21)	7 (1; 23)	7 (1; 24)	59 (11; 192)
Taranaki	13 (2; 42)	13 (2; 44)	14 (3; 46)	15 (3; 48)	15 (3; 51)	16 (3; 53)	17 (3; 56)	18 (3; 59)	19 (3; 62)	20 (4; 66)	161 (29; 527)
Hawke's Bay	18 (3; 60)	19 (4; 62)	20 (4; 65)	21 (4; 68)	22 (4; 72)	23 (4; 75)	24 (5; 79)	26 (5; 83)	27 (5; 88)	28 (5; 93)	228 (43; 747)
Whanganui	8 (1; 25)	8 (1; 26)	8 (2; 27)	9 (2; 28)	9 (2; 30)	10 (2; 31)	10 (2; 33)	11 (2; 35)	11 (2; 37)	12 (2; 39)	95 (18; 310)
Midcentral	19 (4; 62)	20 (4; 64)	21 (4; 67)	22 (4; 70)	23 (4; 74)	24 (4; 78)	25 (5; 82)	26 (5; 86)	28 (5; 91)	29 (6; 96)	235 (44; 769)
Hutt	15 (3; 48)	15 (3; 50)	16 (3; 52)	17 (3; 55)	18 (3; 57)	18 (3; 60)	19 (3; 63)	20 (4; 67)	22 (4; 70)	23 (4; 74)	183 (32; 596)
Capital and Coast	28 (5; 90)	29 (5; 94)	30 (5; 98)	32 (5; 103)	33 (6; 108)	35 (6; 113)	37 (6; 119)	39 (7; 126)	41 (7; 133)	43 (7; 140)	345 (59; 1,124)
Wairarapa	5 (1; 18)	6 (1; 19)	6 (1; 19)	6 (1; 20)	7 (1; 21)	7 (1; 22)	7 (1; 24)	8 (1; 25)	8 (2; 26)	8 (2; 28)	68 (13; 223)

Region	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	Total
Nelson Marlborough	18 (3; 59)	19 (4; 62)	20 (4; 65)	21 (4; 68)	22 (4; 71)	23 (4; 75)	24 (5; 79)	25 (5; 83)	27 (5; 87)	28 (5; 92)	226 (44; 740)
West Coast	4 (1; 13)	4 (1; 14)	4 (1; 14)	5 (1; 15)	5 (1; 16)	5 (1; 17)	5 (1; 17)	6 (1; 18)	6 (1; 19)	6 (1; 21)	51 (09; 165)
Canterbury	55 (10; 178)	57 (10; 186)	60 (11; 195)	62 (11; 204)	65 (12; 214)	69 (12; 225)	72 (13; 236)	76 (14; 249)	80 (14; 263)	85 (15; 277)	682 (121; 2,227)
South Canterbury	8 (1; 25)	8 (2; 26)	8 (2; 27)	9 (2; 29)	9 (2; 30)	10 (2; 32)	10 (2; 33)	11 (2; 35)	11 (2; 37)	12 (2; 39)	96 (18; 313)
Southern	34 (6; 112)	36 (7; 117)	37 (7; 122)	39 (7; 128)	41 (8; 134)	43 (8; 141)	45 (8; 148)	48 (9; 156)	50 (9; 165)	53 (10; 174)	427 (78; 1,397)
Cancer centres											
Auckland	156 (24; 510)	163 (26; 532)	171 (27; 557)	179 (28; 583)	188 (29; 612)	197 (31; 643)	207 (32; 676)	218 (34; 712)	230 (36; 751)	243 (38; 793)	1,954 (306; 6,370)
Hamilton	80 (15; 263)	84 (16; 274)	88 (16; 287)	92 (17; 300)	96 (18; 315)	101 (19; 331)	107 (20; 348)	112 (21; 367)	118 (22; 387)	125 (23; 409)	1,004 (188; 3,280)
Palmerston North	58 (11; 188)	60 (11; 197)	63 (12; 206)	66 (12; 215)	69 (13; 226)	73 (14; 237)	76 (14; 250)	80 (15; 263)	85 (16; 277)	90 (17; 293)	720 (134; 2,353)
Wellington	48 (8; 156)	50 (9; 162)	52 (9; 170)	55 (10; 178)	57 (10; 187)	60 (10; 196)	63 (11; 206)	67 (12; 217)	70 (12; 229)	74 (13; 242)	596 (104; 1,943)
Christchurch	77 (14; 251)	80 (15; 262)	84 (15; 274)	88 (16; 287)	92 (17; 301)	97 (18; 316)	102 (18; 332)	107 (19; 350)	113 (21; 369)	119 (22; 390)	959 (174; 3,132)
Dunedin	42 (8; 137)	44 (8; 143)	46 (8; 149)	48 (9; 157)	50 (9; 164)	53 (10; 172)	55 (10; 181)	58 (11; 191)	62 (11; 202)	65 (12; 213)	523 (97; 1,710)
Total	461 (80; 1,504)	481 (84; 1,571)	503 (88; 1,643)	527 (92; 1,720)	553 (96; 1,805)	581 (101; 1,895)	611 (106; 1,994)	643 (112; 2,100)	679 (118; 2,215)	717 (125; 2,340)	5,755 (1,003; 18,787)

Appendix B

Table B.1: Incremental costs related to the provision of IORT under Scenario 1

Scenario 1	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	Total
Health system											
Capital											
IORT and related equipment	$4.56 m										$4.56 m
Training and operating procedure development	$0.07 m										$0.07 m
Operational											
Annual maintenance			$0.21 m	$0.19 m	$0.18 m	$0.17 m	$0.16 m	$0.15 m	$0.15 m	$0.14 m	$1.35 m
Replacement of Spherical applicators		$0.05 m ($0.00 m ; $0.23 m)	$0.05 m ($0.00 m ; $0.14 m)	$0.02 m ($0.00 m ; $0.11 m)	$0.06 m ($0.02 m ; $0.15 m)	$0.02 m ($0.00 m ; $0.12 m)	$0.06 m ($0.00 m ; $0.13 m)	$0.02 m ($0.00 m ; $0.12 m)	$0.05 m ($0.02 m ; $0.12 m)	$0.03 m ($0.00 m ; $0.13 m)	$0.36 m ($0.04 m ; $1.24 m)
Transportation, calibration and sterilisation	$0.08 m ($0.05 m ; $0.15 m)	$0.07 m ($0.05 m ; $0.15 m)	$0.07 m ($0.05 m ; $0.14 m)	$0.07 m ($0.04 m ; $0.14 m)	$0.07 m ($0.04 m ; $0.14 m)	$0.06 m ($0.04 m ; $0.13 m)	$0.06 m ($0.04 m ; $0.13 m)	$0.06 m ($0.04 m ; $0.13 m)	$0.06 m ($0.03 m ; $0.13 m)	$0.06 m ($0.03 m ; $0.12 m)	$0.66 m ($0.40 m ; $1.35 m)
Clinical service											
Treatment with IORT, including disposables	$2.89 m ($0.50 m ; $9.42 m)	$2.84 m ($0.50 m ; $9.28 m)	$2.80 m ($0.49 m ; $9.16 m)	$2.77 m ($0.48 m ; $9.05 m)	$2.74 m ($0.48 m ; $8.95 m)	$2.72 m ($0.47 m ; $8.87 m)	$2.70 m ($0.47 m ; $8.80 m)	$2.68 m ($0.47 m ; $8.75 m)	$2.67 m ($0.46 m ; $8.71 m)	$2.66 m ($0.46 m ; $8.68 m)	$27.46 m ($4.79 m ; $89.65 m)
Counterfactual - Treatment with EBRT	$3.93 m ($0.69 m ; $12.83 m)	$3.87 m ($0.67 m ; $12.64 m)	$3.82 m ($0.67 m ; $12.47 m)	$3.78 m ($0.66 m ; $12.33 m)	$3.74 m ($0.65 m ; $12.20 m)	$3.70 m ($0.65 m ; $12.09 m)	$3.67 m ($0.64 m ; $11.99 m)	$3.65 m ($0.64 m ; $11.92 m)	$3.63 m ($0.63 m ; $11.86 m)	$3.62 m ($0.63 m ; $11.82 m)	$37.42 m ($6.52 m ; $122.15 m)
Incremental difference (IORT - EBRT)	-$1.05 m (-$0.18 m ; -$3.41 m)	-$1.03 m (-$0.18 m ; -$3.36 m)	-$1.02 m (-$0.18 m ; -$3.32 m)	-$1.00 m (-$0.18 m ; -$3.28 m)	-$0.99 m (-$0.17 m ; -$3.24 m)	-$0.98 m (-$0.17 m ; -$3.21 m)	-$0.98 m (-$0.17 m ; -$3.19 m)	-$0.97 m (-$0.17 m ; -$3.17 m)	-$0.97 m (-$0.17 m ; -$3.16 m)	-$0.96 m (-$0.17 m ; -$3.14 m)	-$9.95 m (-$1.73 m ; -$32.49 m)
Patient											
Travel costs	-$0.63 m (-$0.11 m ; -$2.07 m)	-$0.62 m (-$0.11 m ; -$2.04 m)	-$0.62 m (-$0.11 m ; -$2.01 m)	-$0.61 m (-$0.11 m ; -$1.99 m)	-$0.60 m (-$0.11 m ; -$1.97 m)	-$0.60 m (-$0.10 m ; -$1.95 m)	-$0.59 m (-$0.10 m ; -$1.94 m)	-$0.59 m (-$0.10 m ; -$1.92 m)	-$0.59 m (-$0.10 m ; -$1.91 m)	-$0.58 m (-$0.10 m ; -$1.91 m)	-$6.04 m (-$1.05 m ; -$19.71 m)

Productivity losses from EBRT avoided	-$0.78 m (-$0.10 m ; -$2.54 m)	-$0.77 m (-$0.10 m ; -$2.65 m)	-$0.76 m (-$0.10 m ; -$2.77 m)	-$0.75 m (-$0.11 m ; -$2.90 m)	-$0.74 m (-$0.11 m ; -$3.04 m)	-$0.73 m (-$0.12 m ; -$3.20 m)	-$0.73 m (-$0.13 m ; -$3.36 m)	-$0.72 m (-$0.13 m ; -$3.54 m)	-$0.72 m (-$0.14 m ; -$3.74 m)	-$0.72 m (-$0.15 m ; -$3.95 m)	-$7.43 m (-$1.20 m ; -$31.70 m)
Total incremental costs											
Health system perspective	$3.67 m ($4.50 m ; $1.37 m)	-$0.90 m (-$0.13 m ; -$2.99 m)	-$0.69 m ($0.08 m ; -$2.82 m)	-$0.71 m ($0.07 m ; -$2.83 m)	-$0.68 m ($0.08 m ; -$2.77 m)	-$0.72 m ($0.04 m ; -$2.79 m)	-$0.69 m ($0.03 m ; -$2.76 m)	-$0.74 m ($0.02 m ; -$2.76 m)	-$0.71 m ($0.03 m ; -$2.76 m)	-$0.74 m (-$0.01 m ; -$2.77 m)	-$2.91 m ($4.72 m ; -$23.88 m)
Societal perspective	$2.25 m ($4.30 m ; -$3.24 m)	-$2.29 m (-$0.28 m ; -$7.30 m)	-$2.06 m ($0.12 m ; -$7.11 m)	-$2.07 m ($0.09 m ; -$7.27 m)	-$2.02 m ($0.11 m ; -$7.32 m)	-$2.06 m ($0.04 m ; -$7.51 m)	-$2.01 m ($0.01 m ; -$7.63 m)	-$2.05 m (-$0.02 m ; -$7.82 m)	-$2.02 m (-$0.01 m ; -$8.03 m)	-$2.04 m (-$0.10 m ; -$8.25 m)	-$16.38 m ($4.24 m ; -$71.47 m)

Table B.2: Incremental costs related to the provision of IORT under Scenario 2

Scenario 2	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	Total
Health system											
Capital											
IORT and related equipment	$4.77 m										$4.77 m
Training and operating procedure development	$0.07 m										$0.07 m
Operational											
Annual maintenance	$0.00 m	$0.00 m	$0.29 m	$0.27 m	$0.26 m	$0.24 m	$0.23 m	$0.22 m	$0.20 m	$0.19 m	$1.90 m
Replacement of Spherical applicators	$0.00 m ($0.00 m ; $0.00 m)	$0.03 m ($0.00 m ; $0.23 m)	$0.05 m ($0.00 m ; $0.14 m)	$0.02 m ($0.00 m ; $0.11 m)	$0.06 m ($0.02 m ; $0.15 m)	$0.02 m ($0.00 m ; $0.12 m)	$0.06 m ($0.00 m ; $0.13 m)	$0.02 m ($0.00 m ; $0.12 m)	$0.05 m ($0.02 m ; $0.12 m)	$0.03 m ($0.00 m ; $0.13 m)	$0.33 m ($0.04 m ; $1.24 m)
Transportation, calibration and sterilisation	$0.07 m ($0.05 m ; $0.15 m)	$0.07 m ($0.04 m ; $0.14 m)	$0.07 m ($0.04 m ; $0.14 m)	$0.07 m ($0.04 m ; $0.14 m)	$0.06 m ($0.04 m ; $0.13 m)	$0.06 m ($0.04 m ; $0.13 m)	$0.06 m ($0.03 m ; $0.13 m)	$0.06 m ($0.03 m ; $0.13 m)	$0.06 m ($0.03 m ; $0.12 m)	$0.05 m ($0.03 m ; $0.12 m)	$0.63 m ($0.38 m ; $1.33 m)
Clinical service											
Treatment with IORT, including disposables	$2.89 m ($0.50 m ; $9.42 m)	$2.84 m ($0.50 m ; $9.28 m)	$2.80 m ($0.49 m ; $9.16 m)	$2.77 m ($0.48 m ; $9.05 m)	$2.74 m ($0.48 m ; $8.95 m)	$2.72 m ($0.47 m ; $8.87 m)	$2.70 m ($0.47 m ; $8.80 m)	$2.68 m ($0.47 m ; $8.75 m)	$2.67 m ($0.46 m ; $8.71 m)	$2.66 m ($0.46 m ; $8.68 m)	$27.46 m ($4.79 m ; $89.65 m)
Counterfactual - Treatment with EBRT	$3.93 m ($0.69 m ; $12.83 m)	$3.87 m ($0.67 m ; $12.64 m)	$3.82 m ($0.67 m ; $12.47 m)	$3.78 m ($0.66 m ; $12.33 m)	$3.74 m ($0.65 m ; $12.20 m)	$3.70 m ($0.65 m ; $12.09 m)	$3.67 m ($0.64 m ; $11.99 m)	$3.65 m ($0.64 m ; $11.92 m)	$3.63 m ($0.63 m ; $11.86 m)	$3.62 m ($0.63 m ; $11.82 m)	$37.42 m ($6.52 m ;

											$122.15 m)
Incremental difference (IORT - EBRT)	-$1.05 m (-$0.18 m ; -$3.41 m)	-$1.03 m (-$0.18 m ; -$3.36 m)	-$1.02 m (-$0.18 m ; -$3.32 m)	-$1.00 m (-$0.18 m ; -$3.28 m)	-$0.99 m (-$0.17 m ; -$3.24 m)	-$0.98 m (-$0.17 m ; -$3.21 m)	-$0.98 m (-$0.17 m ; -$3.19 m)	-$0.97 m (-$0.17 m ; -$3.17 m)	-$0.97 m (-$0.17 m ; -$3.16 m)	-$0.96 m (-$0.17 m ; -$3.14 m)	-$9.95 m (-$1.73 m ; -$32.49 m)
Patient											
Travel costs	-$0.63 m (-$0.11 m ; -$2.07 m)	-$0.62 m (-$0.11 m ; -$2.04 m)	-$0.62 m (-$0.11 m ; -$2.01 m)	-$0.61 m (-$0.11 m ; -$1.99 m)	-$0.60 m (-$0.11 m ; -$1.97 m)	-$0.60 m (-$0.10 m ; -$1.95 m)	-$0.59 m (-$0.10 m ; -$1.94 m)	-$0.59 m (-$0.10 m ; -$1.92 m)	-$0.59 m (-$0.10 m ; -$1.91 m)	-$0.58 m (-$0.10 m ; -$1.91 m)	-$6.04 m (-$1.05 m ; -$19.71 m)
Productivity losses from EBRT avoided	-$0.78 m (-$0.10 m ; -$2.54 m)	-$0.77 m (-$0.10 m ; -$2.65 m)	-$0.76 m (-$0.10 m ; -$2.77 m)	-$0.75 m (-$0.11 m ; -$2.90 m)	-$0.74 m (-$0.11 m ; -$3.04 m)	-$0.73 m (-$0.12 m ; -$3.20 m)	-$0.73 m (-$0.13 m ; -$3.36 m)	-$0.72 m (-$0.13 m ; -$3.54 m)	-$0.72 m (-$0.14 m ; -$3.74 m)	-$0.72 m (-$0.15 m ; -$3.95 m)	-$7.43 m (-$1.20 m ; -$31.70 m)
Total incremental costs											
Health system perspective	$3.87 m ($4.70 m ; $1.57 m)	-$0.93 m (-$0.13 m ; -$2.99 m)	-$0.61 m ($0.16 m ; -$2.74 m)	-$0.64 m ($0.14 m ; -$2.76 m)	-$0.61 m ($0.15 m ; -$2.70 m)	-$0.66 m ($0.11 m ; -$2.72 m)	-$0.63 m ($0.10 m ; -$2.70 m)	-$0.68 m ($0.08 m ; -$2.70 m)	-$0.65 m ($0.09 m ; -$2.71 m)	-$0.68 m ($0.05 m ; -$2.71 m)	-$2.22 m ($5.44 m ; -$23.16 m)
Societal perspective	$2.45 m ($4.50 m ; -$3.04 m)	-$2.32 m (-$0.29 m ; -$7.31 m)	-$1.98 m ($0.28 m ; -$6.96 m)	-$2.00 m ($0.24 m ; -$7.12 m)	-$1.95 m ($0.25 m ; -$7.18 m)	-$1.99 m ($0.17 m ; -$7.37 m)	-$1.95 m ($0.13 m ; -$7.51 m)	-$1.99 m ($0.10 m ; -$7.70 m)	-$1.96 m ($0.10 m ; -$7.91 m)	-$1.99 m ($0.02 m ; -$8.13 m)	-$15.69 m ($5.49 m ; -$70.23 m)

Table B.3: Incremental costs related to the provision of IORT under Scenario 3

Scenario 3	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	Total
Health system											
Capital											
IORT and related equipment	$3.59 m										$3.59 m
Training and operating procedure development	$0.05 m										$0.05 m
Operational											
Annual maintenance	$0.00 m	$0.00 m	$0.20 m	$0.18 m	$0.17 m	$0.16 m	$0.15 m	$0.15 m	$0.14 m	$0.13 m	$1.29 m

Replacement of Spherical applicators	$0.00 m ($0.00 m ; $0.00 m)	$0.05 m ($0.00 m ; $0.23 m)	$0.05 m ($0.00 m ; $0.14 m)	$0.02 m ($0.00 m ; $0.11 m)	$0.06 m ($0.02 m ; $0.15 m)	$0.02 m ($0.00 m ; $0.12 m)	$0.06 m ($0.00 m ; $0.13 m)	$0.02 m ($0.00 m ; $0.12 m)	$0.05 m ($0.02 m ; $0.12 m)	$0.03 m ($0.00 m ; $0.13 m)	$0.36 m ($0.04 m ; $1.24 m)
Transportation, calibration and sterilisation	$0.06 m ($0.03 m ; $0.13 m)	$0.05 m ($0.03 m ; $0.13 m)	$0.05 m ($0.03 m ; $0.12 m)	$0.05 m ($0.03 m ; $0.12 m)	$0.05 m ($0.02 m ; $0.12 m)	$0.05 m ($0.02 m ; $0.12 m)	$0.05 m ($0.02 m ; $0.11 m)	$0.05 m ($0.02 m ; $0.11 m)	$0.04 m ($0.02 m ; $0.11 m)	$0.04 m ($0.02 m ; $0.11 m)	$0.49 m ($0.24 m ; $1.18 m)
Clinical service											
Treatment with IORT, including disposables	$2.89 m ($0.50 m ; $9.42 m)	$2.84 m ($0.50 m ; $9.28 m)	$2.80 m ($0.49 m ; $9.16 m)	$2.77 m ($0.48 m ; $9.05 m)	$2.74 m ($0.48 m ; $8.95 m)	$2.72 m ($0.47 m ; $8.87 m)	$2.70 m ($0.47 m ; $8.80 m)	$2.68 m ($0.47 m ; $8.75 m)	$2.67 m ($0.46 m ; $8.71 m)	$2.66 m ($0.46 m ; $8.68 m)	$27.46 m ($4.79 m ; $89.65 m)
Counterfactual - Treatment with EBRT	$3.93 m ($0.69 m ; $12.83 m)	$3.87 m ($0.67 m ; $12.64 m)	$3.82 m ($0.67 m ; $12.47 m)	$3.78 m ($0.66 m ; $12.33 m)	$3.74 m ($0.65 m ; $12.20 m)	$3.70 m ($0.65 m ; $12.09 m)	$3.67 m ($0.64 m ; $11.99 m)	$3.65 m ($0.64 m ; $11.92 m)	$3.63 m ($0.63 m ; $11.86 m)	$3.62 m ($0.63 m ; $11.82 m)	$37.42 m ($6.52 m ; $122.15 m)
Incremental difference (IORT - EBRT)	-$1.05 m (-$0.18 m ; -$3.41 m)	-$1.03 m (-$0.18 m ; -$3.36 m)	-$1.02 m (-$0.18 m ; -$3.32 m)	-$1.00 m (-$0.18 m ; -$3.28 m)	-$0.99 m (-$0.17 m ; -$3.24 m)	-$0.98 m (-$0.17 m ; -$3.21 m)	-$0.98 m (-$0.17 m ; -$3.19 m)	-$0.97 m (-$0.17 m ; -$3.17 m)	-$0.97 m (-$0.17 m ; -$3.16 m)	-$0.96 m (-$0.17 m ; -$3.14 m)	-$9.95 m (-$1.73 m ; -$32.49 m)
Patient											
Travel costs	-$0.63 m (-$0.11 m ; -$2.07 m)	-$0.62 m (-$0.11 m ; -$2.04 m)	-$0.62 m (-$0.11 m ; -$2.01 m)	-$0.61 m (-$0.11 m ; -$1.99 m)	-$0.60 m (-$0.11 m ; -$1.97 m)	-$0.60 m (-$0.10 m ; -$1.95 m)	-$0.59 m (-$0.10 m ; -$1.94 m)	-$0.59 m (-$0.10 m ; -$1.92 m)	-$0.59 m (-$0.10 m ; -$1.91 m)	-$0.58 m (-$0.10 m ; -$1.91 m)	-$6.04 m (-$1.05 m ; -$19.71 m)
Productivity losses from EBRT avoided	-$0.78 m (-$0.10 m ; -$2.54 m)	-$0.77 m (-$0.10 m ; -$2.65 m)	-$0.76 m (-$0.10 m ; -$2.77 m)	-$0.75 m (-$0.11 m ; -$2.90 m)	-$0.74 m (-$0.11 m ; -$3.04 m)	-$0.73 m (-$0.12 m ; -$3.20 m)	-$0.73 m (-$0.13 m ; -$3.36 m)	-$0.72 m (-$0.13 m ; -$3.54 m)	-$0.72 m (-$0.14 m ; -$3.74 m)	-$0.72 m (-$0.15 m ; -$3.95 m)	-$7.43 m (-$1.20 m ; -$31.70 m)
Total incremental costs											
Health system perspective	$2.66 m ($3.49 m ; $0.36 m)	-$0.92 m (-$0.15 m ; -$3.01 m)	-$0.72 m ($0.05 m ; -$2.85 m)	-$0.74 m ($0.04 m ; -$2.86 m)	-$0.70 m ($0.05 m ; -$2.80 m)	-$0.75 m ($0.02 m ; -$2.81 m)	-$0.72 m ($0.01 m ; -$2.79 m)	-$0.76 m ($0.00 m ; -$2.78 m)	-$0.73 m ($0.01 m ; -$2.79 m)	-$0.76 m (-$0.02 m ; -$2.78 m)	-$4.15 m ($3.49 m ; -$25.11 m)
Societal perspective	$1.24 m ($3.29 m ; -$4.25 m)	-$2.32 m (-$0.33 m ; -$7.34 m)	-$2.09 m ($0.06 m ; -$7.17 m)	-$2.10 m ($0.03 m ; -$7.33 m)	-$2.05 m ($0.05 m ; -$7.37 m)	-$2.08 m (-$0.02 m ; -$7.56 m)	-$2.04 m (-$0.04 m ; -$7.68 m)	-$2.07 m (-$0.07 m ; -$7.87 m)	-$2.04 m (-$0.06 m ; -$8.07 m)	-$2.06 m (-$0.13 m ; -$8.28 m)	-$17.61 m ($2.79 m ; -$72.92 m)