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Magnetic Resonance Image-guided Brachytherapy for Cervical Cancer: Budget Impact Analysis

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Cancer Care Ontario

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2DBT	Two-dimensional Brachytherapy
ALR	Activity Level Reporting
BT	Brachytherapy
CCO	Cancer Care Ontario
CT	Computed Tomography
CTBT	Computed Tomography Brachytherapy
CUA	Cost-Utility Analysis
FIGO	International Federation of Gynecology and Obstetrics
GynCoP	Gynecological Community of Practice
HDR	High-Dose-Rate
ICIS	Intracavitary and Interstitial
LACC	Locally Advanced Cervical Cancer
MOHLTC	Ministry of Health and Long-Term Care
MR	Magnetic Resonance
MRgBT	Magnetic Resonance image-guided Brachytherapy
OCR	Ontario Cancer Registry
PEBC	Program in Evidence-Based Care
QALY	Quality-Adjusted Life Year
RCC	Regional Cancer Centre

EXECUTIVE SUMMARY

In Ontario, over 500 women were newly diagnosed with cervical cancer annually between 2012 and 2016. The standard management of locally advanced cervical cancer (LACC) consists of external beam radiotherapy with concurrent chemotherapy followed by brachytherapy (BT). BT may be delivered using 2D imaging technology, i.e., two-dimensional brachytherapy (2DBT) or computed tomography brachytherapy (CTBT), or using 3D imaging technology, i.e., magnetic resonance guided brachytherapy (MRgBT). Clinical effectiveness studies have shown that MRgBT is associated with lower rates of cancer recurrence, better overall survival, and fewer complications than 2DBT or CTBT (1-4). Furthermore, the Program in Evidence-Based Care (PEBC) guidelines recommend MRgBT over 2DBT and CTBT for LACC (5). A cost-utility analysis (CUA) was undertaken to estimate the cost-effectiveness of MRgBT in comparison to 2DBT and CTBT. The results showed MRgBT to be an economically attractive option from the public healthcare payer perspective (6, 7). In particular, over a five-year time horizon, MRgBT was found to have lower costs and greater benefits, measured as quality-adjusted life years (QALYs), compared to 2DBT and CTBT. The CUA results found that the larger upfront costs of providing MRgBT were offset by reduced costs later on due to fewer recurrences and treatment complications. Despite mounting favourable evidence of this now mature treatment technology, current public healthcare funding does not cover the investment required to provide MRgBT to all Ontarian women with LACC. The objective of this study was to estimate the investment required to implement a new treatment scenario in which all Ontarian women have access to MRgBT from a public healthcare payer perspective over a five-year time horizon.

A budget impact analysis (BIA) was conducted to estimate the incremental cost of a proposed new scenario. Currently, 10 of the 14 regional cancer centres (RCCs) provide a mix of 2DBT, CTBT, or MRgBT to treat LACC. In the proposed new scenario, six RCCs provide only MRgBT to all Ontarian women. Data to support the analyses were provided by the RCCs and provincial cancer registries. Deterministic sensitivity analyses were used to explore uncertainty.

The investment required to provide MRgBT to all Ontarian women with LACC was estimated to be $4.8 million in the first year, half of which was to provide training for an interdisciplinary team, including a radiation oncologist, medical physicist, and radiation therapist, at 6 RCCs. In subsequent years, an investment of$2.5 million annually was required. Sensitivity analyses found training costs to have the largest impact.

This BIA estimated the investment needed for a potential patient treatment pathway towards the implementation of MRgBT. The estimated investment would provide the personnel time, equipment, MR imaging time, and training required to treat all Ontarian women with LACC with evidence-based best practice care.

BACKGROUND

Cervical cancer affects women of all ages, including those in the prime of life with young families, making it particularly devastating (8). Human papilloma virus vaccination programs are predicted to reduce the incidence of cervical cancer in the long-term but progress is likely to be slow. A recent Canadian Cancer Society report indicated that the annual number of new cases in Canada is likely to decline by less than 9% over the next 20 years even with high vaccination rates, reinforcing the importance of continuing to build treatment capacity for women with established disease (9).

Many of the women with cervical cancer have locally advanced cervical cancer (LACC), a diagnosis which cannot be treated surgically. The standard management of these women consists of external beam radiotherapy and concurrent chemotherapy followed by brachytherapy (BT). BT is acknowledged to be an essential component of cervical cancer treatment, with large population-based studies demonstrating substantially lower survival among women who are deprived of BT during treatment (10, 11). In Ontario, either two-dimensional brachytherapy (2DBT) or computed tomography brachytherapy (CTBT) are most commonly used (12). However, new BT techniques that exploit the superior properties of high-resolution magnetic resonance imaging and the use of interstitial needles (MRgBT) have shown to have increased treatment precision and the ability to escalate doses with minimal damage to normal surrounding tissue (1, 2, 13, 14). Clinical effectiveness studies have shown MRgBT to be associated with lower rates of cancer recurrence, better overall survival, and fewer treatment complications than 2DBT or CTBT (1-4).

The Program in Evidence-Based Care (PEBC) develops internationally recognized guidelines and in November 2018, released guidelines on MRgBT for cervical cancer (5). The guidelines compare MRgBT to 2DBT and CTBT in women with non-operable LACC. There are three key recommendations in the guidelines: 1) In Ontario, MRgBT is the preferred treatment for cervical cancer patients over 2DBT; 2) MRgBT is preferred over CTBT; and 3) intracavitary and interstitial (ICIS) BT with interstitial needles should be considered for patients with tumor shape and size such that ICIS could reduce toxicity (5).

We evaluated the cost-effectiveness of implementing MRgBT, now considered a mature treatment approach, as a new model of care for the treatment of LACC in Ontario and compared it to 2DBT and CTBT. Using a decision analytic model, the cost-effectiveness of MRgBT was examined from the perspective of the Ontario Ministry of Health and Long-Term Care (MOHLTC) over a five-year time horizon (6, 7, 15). Results indicated that, compared to both 2DBT and CTBT, MRgBT improved treatment effectiveness, expressed as quality-adjusted life years (QALYs), and was less costly when considering all eligible patients (6, 7). The findings showed that although the initial costs to provide MRgBT are more costly than 2D procedures, those costs were offset by lower costs for recurrences, complications, and palliative care (6, 7).

Although MRgBT has been shown to be a clinically and an economically attractive option at the system level, the implementation of MRgBT in Ontario has been slow, possibly due to province-wide variation in expertise, equipment, and patient volumes. The optimal approach to implementing this new model of care and making it available to all women with LACC in the province is unclear. This gap speaks to the need for a budget impact analysis (BIA) as the next logical step in evaluating the implementation of MRgBT, focusing on the upfront resource requirements, the optimal distribution of resources, and ongoing operating costs from the perspective of the MOHLTC.

Objective

The objective of this study was to estimate the budget impact of funding MRgBT for locally advanced cervical cancer (LACC) compared to the currently funded 2DBT and CTBT from the perspective of the MOHLTC over five years. Specifically, we aimed to estimate the investment required rather than the overall budget impact including potential savings due to reduced toxicities and recurrences.

METHODS

Using guidelines for conducting BIAs set out by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force, we conducted a BIA with a five-year time horizon from the MOHLTC perspective (16).

Target Population

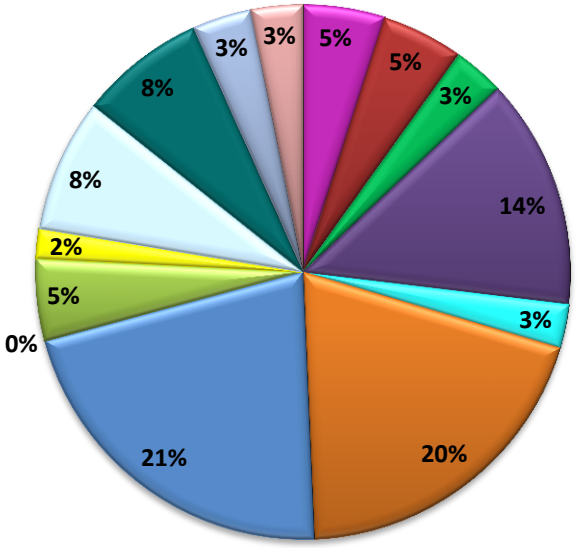
The target population of this analysis was women aged 18 years and older who had LACC (using the International Federation of Gynecology and Obstetrics (FIGO) Stages from IB to IV) who are treated with external beam radiation followed by BT.

Scenarios

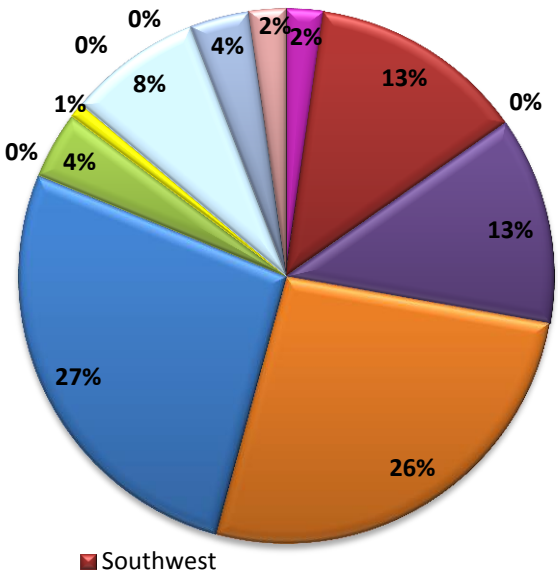
Currently, there are 14 Regional Cancer Centres (RCC) in Ontario (Appendix A). RCCs provided data on the number of patients treated with external beam radiation therapy and BT in fiscal year 2016-2017 (Figure 1). This data informed the current scenario, in which 10 of the 14 RCCs have active cervical cancer BT programs and use a combination of 2DBT, CTBT, and MRgBT to treat LACC. However, the RCCs that use MRgBT are financing MRgBT using non-MOHLTC funding such as research grant dollars and philanthropic donations.

Figure 1 Distribution of Treatment across Regional Cancer Centres in Current Scenario

a. External beam radiation therapy



b. Brachytherapy



- Erie St. Clair
- Waterloo Wellington
- Central West/Mississauga Halton
- Toronto Central South
- Central East
- Champlain
- North East
- Southwest
- Hamilton Niagara Haldimand Brant
- Toronto Central North
- Central
- South East
- North Simcoe Muskoka
- North West

MRgBT is a highly skilled procedure and requires a minimum patient volume to ensure quality. There are no guidelines on the number of procedures required. However, a panel of Canadian radiation oncologists believed that a radiation therapy program should treat at least 10 new cervical cancer patients annually for 2D procedures (17). In the absence of guidelines, members of the current Radiation Treatment Program Gynecological Community of Practice (GynCoP) feel that the number of procedures required to ensure quality for 3D procedures is likely well in excess of 10 unique patients per RCC. In the current scenario not all sites meet even the 2D threshold, and as a result, the proposed new scenario would make use of centralized sites to ensure that minimum patient volumes are met. To achieve the goal of providing access to MRgBT for all Ontarian women with LACC, we propose using six centralized RCCs. There are two patient pathways. In the first pathway, patients receive both external beam radiation therapy and MRgBT at the same RCC, while in the second; the patient receives external beam radiation therapy and MRgBT at different RCCs. If a patient's home site is not a centralized RCC then the patient would be referred to a centralized RCC (Appendix B). As demonstrated in the current scenario (Figure 1), it is clear from comparing Figures 1a and 1b that there are some patterns of referral already established. Proposed referral patterns were informed by members of the Radiation Treatment Program GynCoP and centralized sites chosen were based on clinical expert opinion, current referral patterns,

RCCs that are already Gynecological Oncology Centres (GOCs), those already doing MRgBT for cervical cancer, current capacity and ability to increase patient load, and geographic regions.

In the proposed new scenario, six of the RCCs would provide MRgBT to all patients in Ontario. An additional analysis was run in which the proposed new scenario consisted of five centralized RCCs. The details of that analysis can be found in Appendix C.

New Scenario: For modeling purposes, the six centralized RCCs are Southwest, Hamilton Niagara Haldimand Brant, Toronto Central North, Toronto Central South, Champlain, and Central East, all of which are Gynecologic Oncology Centres. The proposed referral patterns are as follows:

- Southwest takes Erie St. Clair, Waterloo Wellington, and North East's patients
- Hamilton Niagara Haldimand Brant takes no additional patients
- Toronto Central North takes South East's patients
- Toronto Central South takes Central West/Mississauga Halton, Central, North Simcoe, and North West's patients
- Champlain takes no additional patients
- Central East takes no additional patients

Perspectives

This budget impact analysis took the perspective of the MOHLTC.

Time Horizon

The budget impact was estimated annually over a 5-year time horizon from 2019 to 2023.

Model Parameters and Data Sources

Incident Cases

Members of the Surveillance, Analytics and Informatics team at Cancer Care Ontario (CCO) provided the annual number of projected incident cases of cervical cancer in Ontario between 2019 and 2023 (Table 1). Two projection methods were used which provided an upper (projection method A) and lower bound (projection method B) on the number of projected incident cases of cervical cancer in Ontario from 2019 to 2023. Both projection methods used data from the Ontario Cancer Registry (OCR), a database containing all Ontario provincial data on cancer incidence and mortality (18). The mean of the two methods was used in the base case analysis and a sensitivity analysis was done using the upper and lower bounds for the high and low estimates, respectively.

Table 1 Annual Number of Projected Incident Cases of Cervical Cancer in Ontario

Projection Method	Number of annual incident cases of cervical cancer				
	2019	2020	2021	2022	2023
A	676	686	697	708	719
B	569	575	582	588	594
Mean of A and B	622	631	640	648	657

Note. The mean value was calculated prior to rounding and may differ from the mean calculated from the rounded values.

A systematic review and meta-analysis by Hanna and colleagues (19) found that 53% of all cervical cancer patients had indications for radiotherapy. This value was used to narrow down the number of projected incident cases of cervical cancer to only those that would require BT. Data on the actual proportion of patients who received BT were provided by the Cancer Analytics team at CCO using the OCR and Cancer Activity Level Reporting (ALR). The ALR database contains information of patient level activity reported by RCCs and partial data from the 2017 calendar year indicated that 50% of patients were treated with radiation therapy, consistent with literature.

Representatives from the RCCs and members of the GynCoP provided the number of patients who initiated treatment for LACC (e.g., received external beam radiotherapy) at their RCC. This information was used as the current distribution of LACC patients across RCCs. GynCoP members further provided where patients received BT and which type of BT they received. This informed the referral patterns used in the new scenario of the BIA model. Currently, some of the RCCs do provide MRgBT; however, as mentioned earlier, they use research grants and philanthropic donations to finance it. To estimate the budget impact from the MOHLTC perspective, we assumed that, without external funding, RCCs could only provide 2DBT and CTBT. The current scenario in the BIA model, from the perspective of the MOHLTC, therefore assumed all RCCs provide only 2DBT and CTBT. A full list of model assumptions is provided in Appendix D.

Costs

The cost of equipment, magnetic resonance (MR) imaging time, personnel time, and training were estimated for both the current scenario and the new scenario. We assumed that each type of BT was delivered as an outpatient procedure using four intracavitary insertions with supplementary needles and high-dose-rate (HDR) treatment. All patients received external beam radiotherapy whether or not they received MRgBT; therefore, we have excluded the costs associated with external beam radiotherapy in the current and new scenarios. While there are additional costs due to toxicities and recurrences occurring with 2DBT and CTBT, MRgBT has been shown to offset the additional costs of MRgBT (6, 7) – and for this reason, we chose to exclude the costs of toxicities and recurrences as the focus of this analysis is on the investment required to provide MRgBT to all Ontarian women with LACC.

Equipment Costs

We used three categories of equipment costs. BT equipment comprised the first two categories and was separated into consumable and reusable equipment. Anesthesia consumable equipment made up the third category. All costs are presented in Table 2 as per patient costs. To estimate per patient costs of reusable equipment, we assumed that each RCC treated 100 patients annually. At $150,000 each for MR-compatible intracavitary applicator sets, this cost comprised the majority of the reusable equipment costs. Further, we also assumed RCCs would purchase four intracavitary applicator sets to assure redundancy and replace them every three years, as per manufacturer recommendations. Transfer tubes and obturators accounted for the remainder of the reusable equipment costs. Only MRgBT required consumable BT equipment consisting of interstitial needles and guide tubes. In keeping with the GEC-ESTRO EMBRACE II planning projections (20), we assumed that an average of two interstitial needles and two guide tubes were used in 50% of patients for intracavitary MRgBT with supplemental needles, and were replaced after each insertion.

Table 2 Equipment Costs per Patient

Equipment	Costs		
	2DBT/CTBT	**MRgBT**	**Incremental**
Total brachytherapy consumables cost per patient	$-	$1,020	$1,020
Total brachytherapy reusable equipment cost per patient	$1,160	$2,009	849
Anesthesia consumables cost per patient	$2,000	$2,000	0
Total equipment cost per patient	**$3,160**	**$5,029**	**$1,869**

Note. 2DBT = Two-dimensional Brachytherapy; CTBT = Computed Tomography Brachytherapy; MRgBT = Magnetic Resonance image-guided Brachytherapy.

MR Imaging Costs

Basic radiation treatment and BT infrastructure, such as a C-arm x-ray machine or x-ray simulator, CT simulator, and HDR BT afterloader, was assumed to be available for cervical cancer BT at no additional cost. We assumed that MR imaging time was purchased from the radiation treatment program for centres with an MR simulator or from diagnostic radiology for RCCs without an MR simulator. A cost of $1,000/hour was used based on the estimated cost provided by the Joint Department of Medical Imaging at Princess Margaret Hospital in Toronto, Ontario. It was assumed that 30 minutes was required to acquire basic axial, sagittal, and coronal T2 imaging without contrast or special MR pulse sequences. The costs of MR installation, maintenance, and the cost of the MR technologist were accounted for in the MR imaging costs. This approach in which MR time is purchased rather than purchasing new MR machines was taken because this target population does not require full time use of an MR machine, RCCs are able to access MR machines through their associated hospitals' radiation treatment program, and using existing infrastructure will not postpone implementation.

Personnel Costs

Treatment with BT requires an interdisciplinary team with an anesthesiologist, a radiation oncologist, a medical physicist, a radiation therapist, and a nurse. The costs for personnel time are provided in Table 3. When estimating the personnel costs for treatment, a clinical expert estimated the time required from the induction of anesthesia to the completion of treatment and patient recovery. 2DBT and CTBT treatments were assumed to require 1.5 hours and MRgBT was assumed to require 5.25 hours. The costs for anesthesiologists and radiation oncologists were derived from the Ontario Health Insurance Plan Schedule of Benefits (21). The costs for the medical physicist, radiation therapist, and nurse were derived from hourly pay scales at Princess Margaret Cancer Centre, Toronto, Ontario.

Table 3 Cost of Personnel Time for Brachytherapy per Patient

Personnel	Costs	
	2DBT/CTBT	**MRgBT**
Anesthesiologist	$600	$600
Radiation oncologist	$3,400	$4,000
Medical physicist	$300	$1,320
Radiation therapist	$360	$1,000
Nurse	$360	$900
Total cost for personnel time per patient	**$5,020**	**$7,820**

Note. 2DBT = Two-dimensional Brachytherapy; CTBT = Computed Tomography Brachytherapy; MRgBT = Magnetic Resonance image-guided Brachytherapy.

Training Costs

We estimated the cost of training personnel to provide MRgBT (Table 4). The costs for the medical physicist and radiation therapist were again derived from hourly pay scales at Princess Margaret Cancer Centre, Toronto, Ontario. For training costs, we assumed that a radiation oncologist fellow rather than a staff physician would be trained. The salary of a postgraduate year six radiation oncologist fellow was taken from the Professional Association of Residents of Ontario (22). In total, two radiation oncology fellows, two medical physicists, and two radiation therapists would require six months of training to practice MRgBT, based on the clinical expert opinion of professionals currently practicing MRgBT in Ontario. Although training may occur prior to the first year of implementing the new scenarios, the training costs were applied in the first year of the model. It was also assumed that training costs in subsequent years would be 10% of the initial cost of training to cover ongoing training needs, such as learning new techniques, training with new equipment, and staff turnover.

Table 4 Cost of MRgBT Training per Regional Cancer Centre

Personnel/professional	Annual Salary	Number of months of training required	Number of staff required	Total calculated cost
Radiation oncologist (fellow)	$98,000*	6	2	$98,000
Medical physicist	$234,000	6	2	$234,000
Radiation therapist	$97,500	6	2	$97,500
Total initial training cost				**$429,500**

*This cost will increase if using a staff physician.

Analysis

Using the projected number of incident cervical cancer patients for 2019 to 2023 and the estimated proportion of cervical cancer patients who require BT, we estimated the number of treated patients from 2019 to 2023. In both scenarios 1 and 2, we assumed that the distribution of patients across RCCs remained constant. In the current scenario, we assumed that patients were treated using 2DBT or CTBT at any of the RCCs. The cost of treating these patients included equipment (Table 2) and personnel costs (Table 3). These patients were not provided MRgBT and therefore did not incur costs for MR imaging or MRgBT training of personnel. In the new scenario we assumed that all patients received MRgBT and the total cost included the resources needed for equipment, personnel, MR imaging time, and personnel training in MRgBT. It was assumed that the referral patterns provided by members of the GynCoP remained consistent from 2019 to 2023 in order to estimate the number of patients treated with MRgBT and the costs incurred for each RCC.

Sensitivity Analysis

A sensitivity analysis was performed for each variable. The ranges used in the sensitivity analysis are outlined in Table 5. All cost variables were ranged ±10% of their base case value. The uptake rate (proportion of referred patients who can travel to a new RCC) was assumed to be 100% in the base case. For the sensitivity analysis, a lower limit of 80% was used and assumed that 20% of patients may not be able to travel due to socioeconomic reasons. This value is consistent with the mean value of responses to the question, "*What is your best estimate of the percentage (%) of LACC patients your centre sees on an annual basis that can't afford to travel for socioeconomic reasons (i.e., in centres without an active brachytherapy program for cervix cancer, where patients may receive treatment at both a local and a centre offering brachytherapy for cervical cancer, what percentage of LACC patients can't afford to travel)?*" Responses to this question from members of the GynCoP ranged from 0 to 80%. The value for the proportion of LACC patients who require BT was taken from a study by Hanna and colleagues (19) and was confirmed by data reported in the OCR and ALR. We allowed the value to range from 40% to 60% in the sensitivity analysis. The upper limit of this value may also provide an estimate of the cost to provide MRgBT to patients who have other types of gynecological cancers that are best treated with

MRgBT such as endometrial or vaginal cancers. The cost of intracavitary applicators was also estimated and it was assumed that each RCC treated 50 patients annually rather than 100. As a result, programs would only require two applicators rather than four, and this equated to the same cost per patient – leaving the results unchanged.

Table 5 Values for Sensitivity Analysis

Variable	Base case	Lower Limit	Upper Limit
Uptake rate (proportion of patients who can travel)	100%	80%	100%
Proportion of LACC that requires BT	53%	40%	60%
Number of women with cervical cancer	varies by year Mean of projection methods A and B	varies by year Projection method B	varies by year Projection method A
Cost for personnel for 2DBT/CTBT	$5,020	$4,518	$5,522
Cost for personnel for MRgBT	$7,820	$7,038	$8,602
Cost of MR imaging time for MRgBT	$2,000	$1,800	$2,200
Cost of brachytherapy consumable equipment for MRgBT	$1,020	$918	$1,122
Cost of anesthesia consumable equipment for 2DBT/CTBT	$2,000	$1,800	$2,200
Cost of anesthesia consumable equipment for MRgBT	$2,000	$1,800	$2,200
Cost of reusable equipment for 2DBT/CTBT	$1,160	$1,044	$1,276
Cost of reusable equipment for MRgBT	$2,009	$1,808	$2,210
Annual salary of radiation oncologist	$98,000	$88,200	$107,800
Annual salary of medical physicist	$234,000	$210,600	$257,400
Annual salary of radiation therapist	$97,500	$87,750	$107,250
Number of months of training for radiation oncologist	6	3	9
Number of months of training for medical physicist	6	3	9
Number of months of training for radiation therapist	6	3	9
Everyone's training duration changes	6	3	9
Number of radiation oncologists trained	2	2	3
Number of medical physicists trained	2	2	3
Number of radiation therapists trained	2	2	3
Number of all staff trained changes	2	2	3
Percentage of total training cost in years 2 to 5	10	5	15

Note. 2DBT = Two-dimensional Brachytherapy; CTBT = Computed Tomography Brachytherapy; LACC = Locally Advanced Cervical Cancer; MRgBT = Magnetic Resonance image-guided Brachytherapy; BT = Brachytherapy.

RESULTS

From 2019 to 2023, over 300 patients are projected to be treated annually with MRgBT. The number of patients treated at each RCC in the new scenario is presented in Table 6. In the new scenario, the minimum number of patients treated at any one RCC was greater than 10, which is in line with Canadian and other national recommendations for the minimum number of patients treated using less complex treatment techniques of 2DBT or CTBT (17, 23, 24).

Table 6 Number and Distribution of Patients Treated with MRgBT across Regional Cancer Centres in New Scenario

Regional Cancer Centre	2019 (N=330)		2020 (N=334)		2021 (N=339)		2022 (N=343)		2023 (N=348)	
	n	%	n	%	n	%	n	%	n	%
Southwest	63	19	63	19	64	19	65	19	66	19
Hamilton Niagara Haldimand Brant	46	14	47	14	47	14	48	14	49	14
Toronto Central North	73	22	73	22	76	22	76	22	76	22
Toronto Central South	102	31	104	31	105	31	106	31	108	31
Central East	20	6	20	6	20	6	21	6	21	6
Champlain	26	8	27	8	27	8	27	8	28	8

Note. N = total annual number of patients; n = RCC's number of patients.

Base Case Analysis

The upfront investment required to provide MRgBT to all Ontarian women with LACC was estimated to be approximately $4.8 million in the first year. The upfront investment in subsequent years was estimated to be approximately $2.5 million annually for both scenarios. Detailed results are shown in Table 7. The 2D procedures have a total annual cost of approximately $2.7 million which is comprised of only personnel and equipment costs. MRgBT has a total cost of approximately $7.5 million in the first year, $2.6 million of which comes from training for an interdisciplinary team, including a radiation oncologist, medical physicist, and radiation therapist, at 6 RCCs. In subsequent years, the total annual cost for MRgBT is approximately $5.3 million which is comprised of costs from personnel, MR imaging time, equipment, and ongoing training. The higher personnel costs for MRgBT, approximately $2.6 million annually, compared to 2D procedures, approximately $1.7 million annually, were a result of the additional personnel time required for the planning and quality assurance of the more complex MRgBT procedure. MRgBT also required MR imaging time to exploit the enhanced 3D imaging abilities which are not provided in 2D procedures and resulted in just under $700,000 in additional costs annually.

Finally, the equipment for MRgBT cost approximately $1.7 million annually whereas 2D procedures equipment cost about $1 million annually. The additional equipment costs included an MR-compatible applicator and equipment necessary to deliver intracavitary/interstitial brachytherapy in accordance with GEC-ESTRO EMBRACE II planning projections (20).

Table 7 Results of Budget Impact Analysis

Cost outcomes	2019 (N = 330)	2020 (N = 334)	2021 (N = 339)	2022 (N = 343)	2023 (N = 348)
Current Scenario					
Personnel	$1,654,893	$1,678,839	$1,702,784	$1,724,069	$1,748,014
MR imaging time*	$-	$-	$-	$-	$-
Equipment	$1,041,726	$1,056,799	$1,071,872	$1,085,270	$1,100,344
MRgBT Training¶	$-	$-	$-	$-	$-
Total cost for current scenario	$2,696,619	$2,735,637	$2,774,656	$2,809,339	$2,848,358
6-site Scenario					
Personnel	$2,577,941	$2,615,243	$2,652,544	$2,685,701	$2,723,002
MR imaging time	$659,320	$668,860	$678,400	$686,880	$696,420
Equipment	$1,657,750	$1,681,737	$1,705,724	$1,727,045	$1,751,032
MRgBT Training	$2,577,011	$257,701	$257,701	$257,701	$257,701
Total cost for 6-site scenario	$7,472,023	$5,223,541	$5,294,369	$5,357,327	$5,428,155
TOTAL INCREMENTAL COST	**$4,775,404**	**$2,487,903**	**$2,519,713**	**$2,547,988**	**$2,579,798**

Note. 2DBT = Two-dimensional Brachytherapy; CTBT = Computed Tomography Brachytherapy; MR = Magnetic Resonance; MRgBT = Magnetic Resonance image-guided Brachytherapy; N = total annual number of patients; *Not applicable since all patients were treated with 2DBT or CTBT; ¶ Not applicable because no patients received MRgBT.

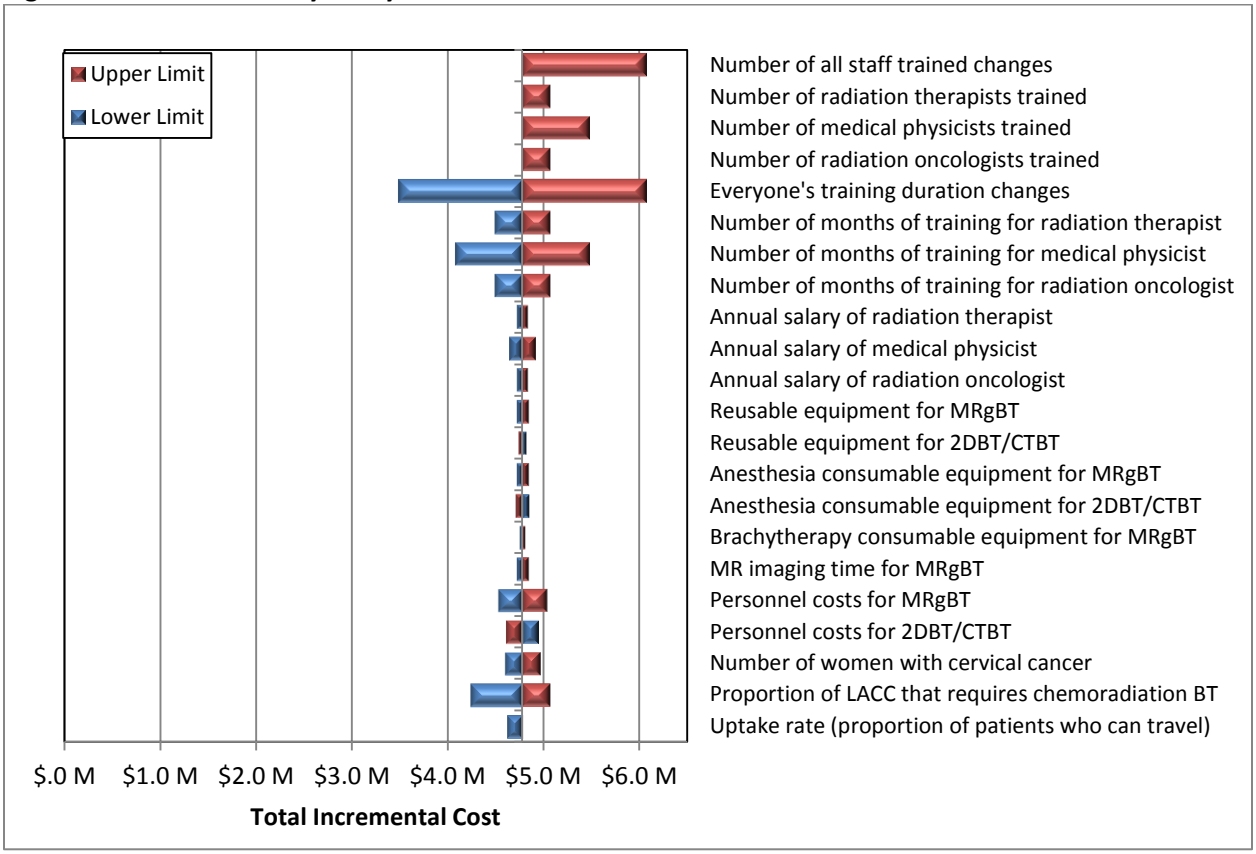
Sensitivity Analysis

The results of the sensitivity analysis are presented as tornado diagrams in years 1 and 5 (Figures 2 and 3, respectively). The horizontal blue and red bars are centered on the budget impact in the base case, $4.8 million in year 1 and approximately $2.5 million annually in subsequent years. Each variable in the sensitivity analysis was ranged between a lower and upper limit (Table 5). The upper limit is shown in red. When the upper limit (red bar) falls on the right side of the vertical budget impact, it means that an increase in that variable results in an increased budget impact, and similarly a decrease in the variable results in a decreased budget impact. For example, the variable “Everyone’s training duration changes” represent the number of months all personnel are trained in the MRgBT procedure. In the base case, each professional receives 6 months of training; however, if the training duration increased to 9 months the results of the sensitivity analysis show us that the budget impact would also increase from $4.8

million to approximately $6.0 million in year 1 (Figure 2). On the other hand, if the duration of training were reduced to 3 months, as represented by the blue bar, the budget impact would decrease to approximately $3.5 million in the first year (Figure 2).
When the lower limit (blue bar) falls on the right side on the vertical budget impact, it means that a decrease in that variable results in an increased budget impact, and similarly an increase in the variable results in a decreased budget impact. For example, the variable "Personnel costs for 2DBT/CTBT" represents the per patient cost of personnel time to perform 2D procedures. In the base case this cost is $5,020. We've allowed for a 10% increase and decrease in this variable from $5,522 to $4,518. When the personnel cost for 2D procedures decreases to $4,518 per patient, the budget impact increases from $4.8 million to approximately $4.9 million in the first year (Figure 2). However, when the personnel cost for 2D procedures increases to $5,522, the budget impact decreases to approximately $4.6 million in the first year (Figure 2).

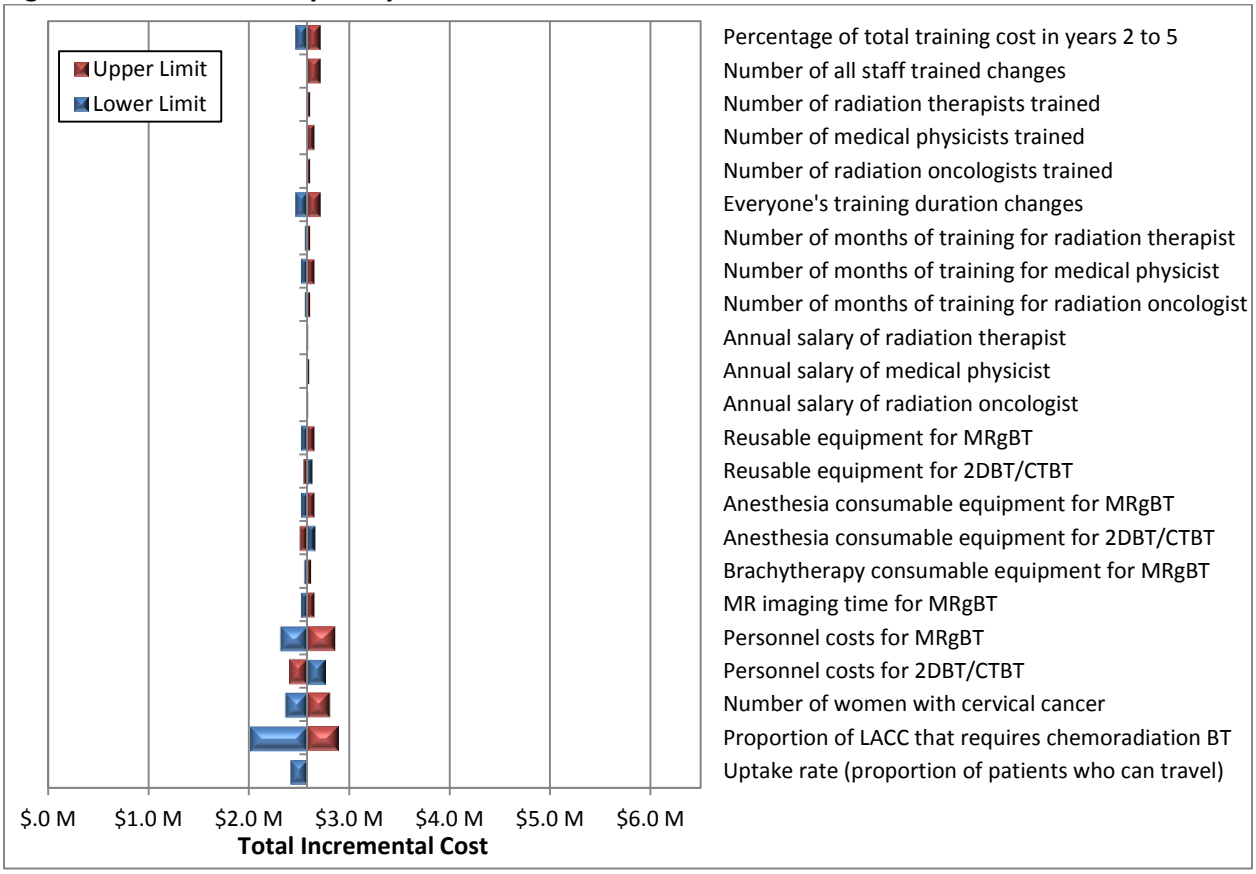
The results of the sensitivity analysis in the first year are different from subsequent years because of the bulk of training costs that occur in year 1. Sensitivity analyses results were similar across years 2 to 5 and as a result, only year 5 is shown here (Figure 3).

Figure 2 Sensitivity Analysis for Year 1



Note. 2DBT = Two-dimensional Brachytherapy; CTBT = Computed Tomography Brachytherapy; LACC = Locally Advanced Cervical Cancer; MRgBT = Magnetic Resonance image-guided Brachytherapy; BT = brachytherapy.

Figure 3 Sensitivity Analysis for Year 5



Note. 2DBT = Two-dimensional Brachytherapy; CTBT = Computed Tomography Brachytherapy; LACC = Locally Advanced Cervical Cancer; MRgBT = Magnetic Resonance image-guided Brachytherapy; BT = Brachytherapy.

DISCUSSION

All Ontarian women with non-operable LACC should be treated using MRgBT, a mature treatment method that has been shown to be safer and more effective than what is currently provided in the province. For this treatment to become available, an investment of approximately $4.8 million in the first year and $2.5 million in subsequent years would be needed. In the new scenario there is a substantial cost of training in the first year, and as a result, the first year budget impact was higher than subsequent years.

Strengths and Limitations

There are some limitations in this study that should be considered with the results of this analysis. First is the exclusion of the costs of toxicities and recurrences. Although we did not include the costs that would offset the additional cost to provide MRgBT instead of 2DBT or CTBT, we concluded from our previous cost-utility analysis that this intervention could be an economically attractive option from the MOHLTC perspective. Thus, this study built on the previous CUA and focused on the initial investment

required to provide MRgBT. As this analysis takes the perspective of the MOHLTC, patient travel costs were not considered. Data from the 2016-2017 fiscal year was used to inform the distribution of LACC patients across RCCs and it was assumed that this distribution would remain constant between 2019 and 2023. It is unlikely that the distribution of LACC across Ontario would change over the next five years – and even if it did, such a change would not affect the overall budget impact from the MOHLTC perspective – suggesting that our estimates are realistic. Another assumption made was that referral patterns would not change over the next five years. The likelihood that these established referral patterns would change over the next five years is expected to be minimal based on the experience of and reporting by RCCs. Additionally, referral pattern changes would not influence the budget impact from the perspective of the MOHLTC.

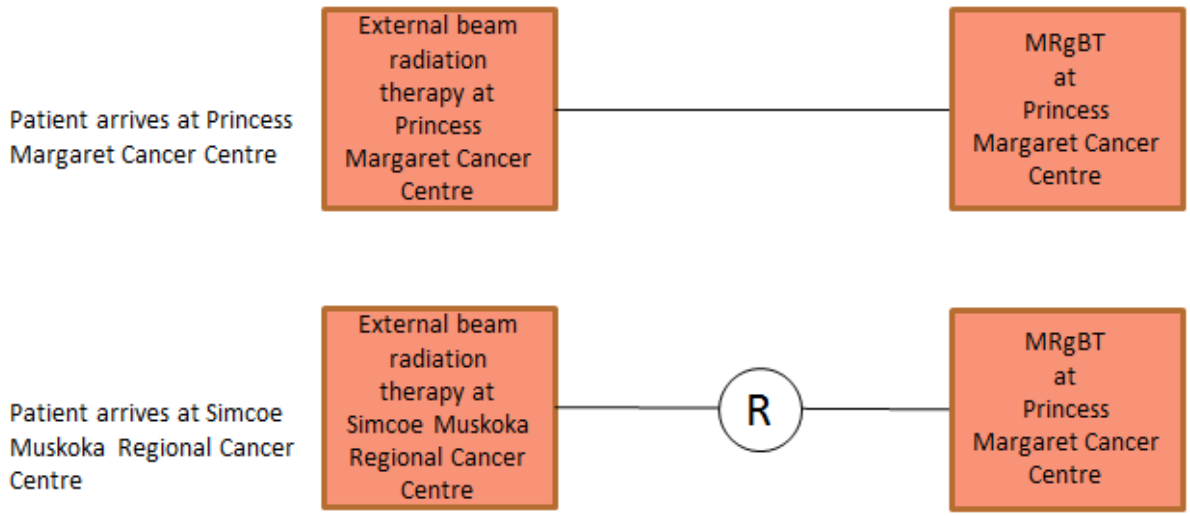
In terms of strengths, this BIA of MRgBT is built upon existing evidence of the effectiveness and cost-effectiveness of MRgBT compared to 2DBT or CTBT (1-4, 6, 7). This study was also strengthened by support from the members of the GynCoP who provided site-level data to inform the current scenario and referral patterns for both new scenarios. Additionally, using information on the individual RCCs, two proposed scenarios were considered, one in which six Ontario RCCs provide MRgBT and a second in which there were five Ontario RCCs providing MRgBT. Information on the cost of equipment, personnel time, and training were also provided by clinical experts currently practicing MRgBT. Lastly, the results of this analysis were reported following recommended BIA reporting guidelines (16).

APPENDICES

Appendix A Regional Cancer Centres

Regional Cancer Centre	Regional Cancer Program	Host Hospital	City
Windsor Regional Cancer Centre	Erie St. Clair	Windsor Regional Hospital	Windsor
London Regional Cancer Program	Southwest	London Health Sciences Centre	London
Grand River Regional Cancer Centre	Waterloo Wellington	Grand River Hospital	Kitchener
Juravinski Cancer Centre	Hamilton Niagara Haldimand Brant	Hamilton Health Sciences	Hamilton
Carlo Fidani Regional Cancer Centre	Central West	Trillium Health Partners-Credit Valley Site	Mississauga
Odette Cancer Centre	Toronto Central North	Sunnybrook Health Sciences Centre	Toronto
Princess Margaret Cancer Centre	Toronto Central South	University Health Network	Toronto
Stronach Regional Cancer Centre at Southlake	Central	Southlake Regional Health Centre	Newmarket
R.S. McLaughlin Durham Regional Cancer Centre	Central East	Lakeridge Health	Oshawa
Cancer Centre of Southeastern Ontario	South East	Kingston General Hospital	Kingston
The Ottawa Hospital Cancer Centre	Champlain	The Ottawa Hospital	Ottawa
Simcoe Muskoka Regional Cancer Centre	North Simcoe Muskoka	Royal Victoria Hospital	Barrie
Northeast Cancer Centre	North East	Health Sciences North/Horizon Santé-Nord	Sudbury
Regional Cancer Care Northwest	North West	Thunder Bay Regional Health Sciences Centre	Thunder Bay

Appendix B Sample Patient Pathways



Appendix C Referral Patterns of cervical cancer brachytherapy patients reported by GynCoP members

Regional Cancer Centre	Regional Cancer Centre to which they refer
Windsor Regional Cancer Centre	London Regional Cancer Program
London Regional Cancer Program	Not applicable
Grand River Regional Cancer Centre	Not available
Juravinski Cancer Centre	London Regional Cancer Program
Carlo Fidani Regional Cancer Centre	Princess Margaret Cancer Centre or Odette Cancer Centre
Odette Cancer Centre	Not applicable
Princess Margaret Cancer Centre	Not applicable
Stronach Regional Cancer Centre at Southlake	Not available
R.S. McLaughlin Durham Regional Cancer Centre	Not available
Cancer Centre of Southeastern Ontario	Odette Cancer Centre
The Ottawa Hospital Cancer Centre	Not available
Simcoe Muskoka Regional Cancer Centre	Princess Margaret Cancer Centre
Northeast Cancer Centre	London Regional Cancer Program
Regional Cancer Care Northwest	London Regional Cancer Program Princess Margaret Cancer Centre Odette Cancer Centre

Note. Question asked of sites on May 11, 2018 was "*If your cancer centre does not offer MR guided brachytherapy, which cancer centre are patients typically referred to? (Note: MRgBT is referring to use of MR immediately before and during brachytherapy to facilitate adaptive brachytherapy treatment planning (including the use of interstitial needles when necessary) with optimization of tumor and normal tissue dosimetry.). Not available means either the question wasn't answered or the RCC did not have representation at May 11, 2018 meeting. Not applicable means as of May 11, 2018, the RCC offered MR guided brachytherapy. GynCoP = Gynecological Community of Practice; RCC = Regional Cancer Centre.*

Appendix D 5-site Scenario

For modeling purposes, the five RCCs are Southwest, Hamilton Niagara Haldimand Brant, Toronto Central North, Toronto Central South, and Champlain.

- Southwest takes Erie St. Clair, Waterloo Wellington, and North East's patients
- Hamilton Niagara Haldimand Brant takes no additional patients
- Toronto Central North takes South East's patients
- Toronto Central South takes Central West/Mississauga Halton, Central, North Simcoe, and North West's patients
- Champlain takes Central East's patients

Number and Distribution of Patients Treated with MRgBT across Regional Cancer Centres 5-site Scenario

Regional Cancer Centre	2019 (N=330)		2020 (N=334)		2021 (N=339)		2022 (N=343)		2023 (N=348)	
	n	%	n	%	n	%	n	%	n	%
Southwest	63	19	63	19	64	19	65	19	66	19
Hamilton Niagara Haldimand Brant	46	14	47	14	47	14	48	14	49	14
Toronto Central North	73	22	73	22	76	22	76	22	76	22
Toronto Central South	102	31	104	31	105	31	106	31	108	31
Central East	0	0	0	0	0	0	0	0	0	0
Champlain	46	14	47	14	47	14	48	14	49	14

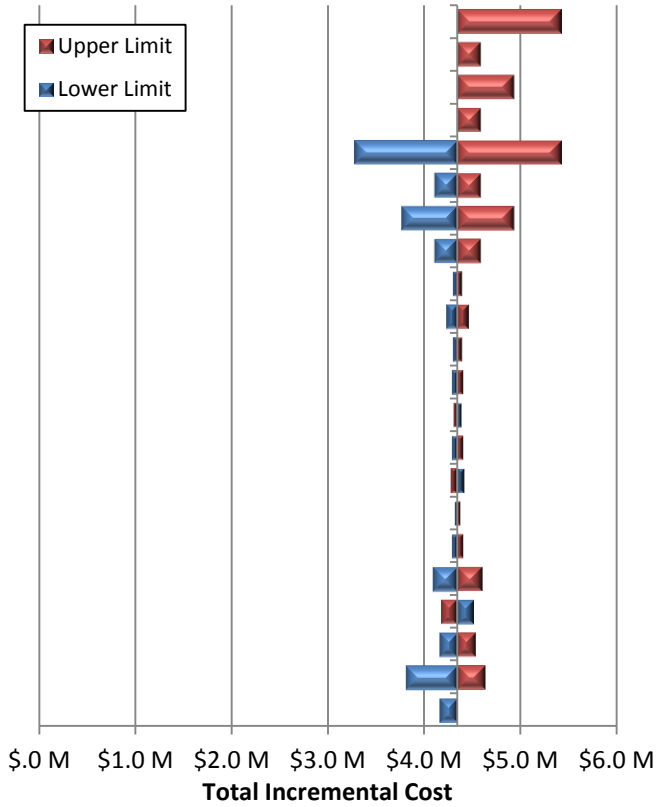
Note. N = total annual number of patients; n = RCC's number of patients.

Results of the Budget Impact Analysis for the 5-site Scenario

Cost Outcomes	2019 (N = 330)	2020 (N = 334)	2021 (N = 339)	2022 (N = 343)	2023 (N = 348)
Current Scenario					
Personnel	$1,654,893	$1,678,839	$1,702,784	$1,724,069	$1,748,014
MR imaging time*	$-	$-	$-	$-	$-
Equipment	$1,041,726	$1,056,799	$1,071,872	$1,085,270	$1,100,344
MRgBT Training¶	$-	$-	$-	$-	$-
Total cost for current scenario	$2,696,619	$2,735,637	$2,774,656	$2,809,339	$2,848,358
5-site Scenario					
Personnel	$2,577,941	$2,615,243	$2,652,544	$2,685,701	$2,723,002
MR imaging time	$659,320	$668,860	$678,400	$686,880	$696,420
Equipment	$1,657,750	$1,681,737	$1,705,724	$1,727,045	$1,751,032
MRgBT Training	$2,147,509	$214,751	$214,751	$214,751	$214,751
Total cost for 5-site scenario	$7,042,521	$5,180,591	$5,251,419	$5,314,377	$5,385,205
TOTAL INCREMENTAL COST	**$4,345,902**	**$2,444,953**	**$2,476,763**	**$2,505,038**	**$2,536,847**

Note. MR = Magnetic Resonance; MRgBT = Magnetic Resonance image-guided Brachytherapy; *Not applicable since all patients were treated with 2DBT or CTBT; ¶ Not applicable because no patients received MRgBT.

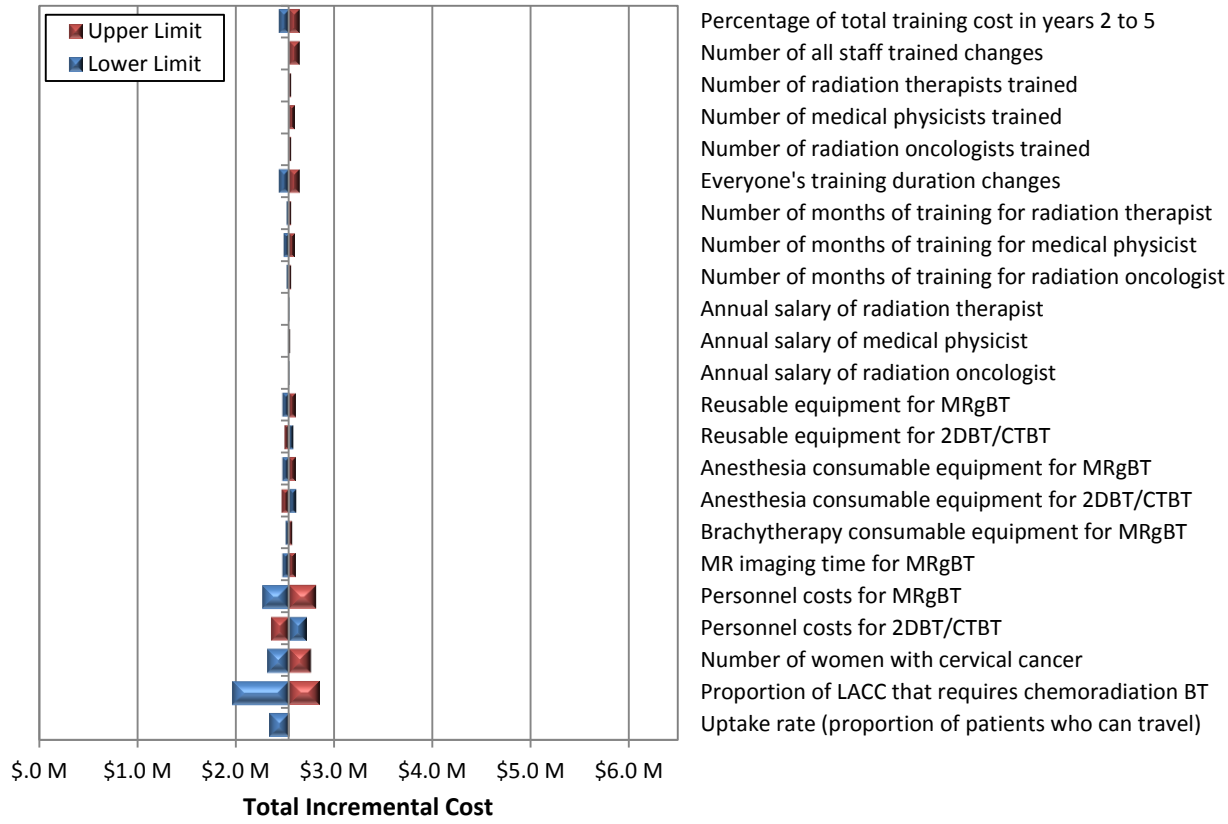
Sensitivity Analysis for the 5-site Scenario in Year 1



Number of all staff trained changes
Number of radiation therapists trained
Number of medical physicists trained
Number of radiation oncologists trained
Everyone's training duration changes
Number of months of training for radiation therapist
Number of months of training for medical physicist
Number of months of training for radiation oncologist
Annual salary of radiation therapist
Annual salary of medical physicist
Annual salary of radiation oncologist
Reusable equipment for MRgBT
Reusable equipment for 2DBT/CTBT
Anesthesia consumable equipment for MRgBT
Anesthesia consumable equipment for 2DBT/CTBT
Brachytherapy consumable equipment for MRgBT
MR imaging time for MRgBT
Personnel costs for MRgBT
Personnel costs for 2DBT/CTBT
Number of women with cervical cancer
Proportion of LACC that requires chemoradiation BT
Uptake rate (proportion of patients who can travel)

Note. 2DBT = Two-dimensional Brachytherapy; CTBT = Computed Tomography Brachytherapy; LACC = Locally Advanced Cervical Cancer; MRgBT = Magnetic Resonance image-guided Brachytherapy; BT = Brachytherapy.

Sensitivity Analysis for the 5-site Scenario in Year 5



Note. 2DBT = Two-dimensional Brachytherapy; CTBT = Computed Tomography Brachytherapy; LACC = Locally Advanced Cervical Cancer; MRgBT = Magnetic Resonance image-guided Brachytherapy; BT = Brachytherapy.

Appendix E Assumptions

Population Assumptions
• The number of patients with cervical cancer is reported for FIGO stages IA to IV; we assume that when we reduce the population to those who are treated with brachytherapy, we have identified all LACC patients (FIGO stages IB to IV)
• The distribution of patients across RCCs remains constant from years 2019 to 2023.
• Referral patterns among RCCs do not change between 2019 and 2023.
Clinical Assumptions
• There is no maximum to the number of patients that an RCC can treat annually.
• Each type of brachytherapy is delivered as an outpatient procedure using 4 intracavitary insertions and HDR treatment.
• 2DBT and CTBT treatment each take 1.5 hours from the induction of anesthesia to completion of treatment and patient recovery, while MRgBT takes 5.25 hours.
• On average 2 interstitial needles are used in 50% of patients for intracavitary MRgBT with supplemental needles, in keeping with the GEC-ESTRO EMBRACE II planning projections.
Cost Assumptions
• External beam costs are excluded because they are the same in each group.
• Costs of toxicities and recurrences are excluded.
• An interdisciplinary team is required to deliver brachytherapy. This includes an anesthesiologist (present for 1h during the procedure), a radiation oncologist (100% of the procedure), a medical physicist (50% of the procedure), a radiation therapist (100% of the procedure) and a nurse (100% of the procedure).
• Training costs apply in year 1 followed by 10% of year 1 costs in years 2 to 5.
• Intracavitary MRgBT applicator costs are based on high volume centres which require 4 applicators to treat 100 patients annually.
• Programs will purchase four intracavitary MRgBT applicator sets to assure redundancy and replace them every three years, as per manufacturer recommendations.
• Additional intracavitary brachytherapy devices (such a source transfer tubes) are also assumed to be replaced every three years.
• Basic radiation treatment and brachytherapy infrastructure, such as a C-arm x-ray machine or x-ray simulator, CT simulator, and HDR brachytherapy afterloader, is assumed to be available for cervical cancer brachytherapy at no additional cost.
• MR imaging time is assumed to be purchased from the radiation treatment program (centres with an MR simulator) or diagnostic radiology (centres without an MR simulator) at a cost of $1,000/hour.
• It is assumed that 30 minutes will be required to acquire basic axial, sagittal, and coronal T2 imaging without contrast or special MR pulse sequences.
• The cost of MR installation and maintenance and the MR technologist are included in the costs of the MR imaging time.

Note. 2DBT = Two-dimensional Brachytherapy; CT = Computed Tomography; CTBT = Computed Tomography Brachytherapy; FIGO = International Federation of Gynecology and Obstetrics; HDR = High-dose-rate; LACC = Locally Advanced Cervical Cancer; MR = Magnetic Resonance; MRgBT = Magnetic Resonance image-guided Brachytherapy; RCC = Regional Cancer Centre.

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