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CLINICAL TRIAL

Cost-efficacy of acceleration partial-breast irradiation compared with whole-breast irradiation

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Abstract The purpose of this study was to analyze the cost-efficacy of multiple accelerated partial-breast irradiation (APBI) techniques compared with whole breast irradiation (WBI) delivered utilizing 3-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiation therapy (IMRT). A previously reported matched-pair analysis consisting of 199 patients receiving WBI and 199 patients receiving interstitial APBI formed the basis of this analysis. Cost analyses included a cost minimization analysis, incremental cost- effectiveness ratio (ICER) analysis, and cost per quality adjusted life year (QALY) analysis. Per 1,000 patients treated, the cost savings with the utilization of APBI compared to WBI IMRT is $14.9 million, $10.9 million, $8.8 million, $5.0 million, and $9.7 million for APBI 3D-CRT, APBI IMRT, APBI single-lumen (SL), APBI multi-lumen (ML), and APBI interstitial, respectively. Per 1,000 patients treated, the cost savings with the utilization of APBI compared to WBI 3D-CRT is $6.0 million, $2.0 million, and $0.7 million for APBI 3D-CRT, APBI IMRT, and APBI interstitial, respectively. The cost per QALY for APBI SL, APBI ML, and APBI interstitial compared with APBI 3D-CRT are $12,273, $66,032, and $546, respectively. When incorporating non-medical costs and cost of recurrences the cost per QALY was $54,698 and $49,009 for APBI ML compared with APBI 3D-CRT. When compared to WBI IMRT, all APBI techniques are cost-effective based on cost minimization, ICER, and QALY analyses. When compared to WBI 3D-CRT, external beam APBI techniques represent a more cost-effective approach based on cost minimization with brachytherapy representing a cost-effective approach based on cost per QALY.

Keywords Accelerated partial-breast irradiation · Breast cancer · Whole breast irradiation · Breast conservation therapy · Cost-efficacy

Introduction

With over 300,000 cases diagnosed annually, breast cancer represents a large expenditure for the health care infrastructure of the United States [1]. As multiple randomized Phase III trials have demonstrated equivalence in clinical outcomes between mastectomy and breast conserving therapy (BCT), adjuvant radiation therapy represents a large component of the costs associated with early-stage breast cancer [2]. Traditionally, adjuvant radiation therapy was delivered using 2-dimensional techniques but over the past two decades has evolved to use CT-based three-dimensional techniques to deliver treatment to the whole breast. More recently, intensity-modulated radiation therapy (IMRT) has been utilized to deliver whole breast irradiation (WBI) based on prospective and retrospective data demonstrating improvements in acute and chronic toxicities with no difference in clinical outcomes including

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local/regional control noted [3–5]. A recently published study found that the use of IMRT in breast cancer increased tenfold from 2001 to 2005 with up to 25 % of patients receiving IMRT, increasing costs associated with breast cancer treatment by an average $8,000 per patient [6].

Accelerated partial-breast irradiation (APBI) represents a new modality to deliver adjuvant radiation therapy following breast conserving surgery, with recent publications documenting an over tenfold increase in the utilization of APBI over the past decade, with up to 6.6 % of patients receiving APBI [7]. Increasing data has been published documenting the clinical efficacy and excellent toxicity profiles associated with APBI, including results from a randomized trial as well as 12-year outcomes from a matched-pair analysis which compared WBI and multi-catheter interstitial APBI [8, 9]. The results of this matched-pair analysis found no difference in local control, regional control, or survival [9].

One concern regarding newer techniques such as WBI utilizing IMRT and APBI are the potential for increases in costs to the healthcare system [6, 7]. Previous cost-effectiveness analyses have found that applicator-based APBI techniques and WBI IMRT were associated with higher costs while external beam APBI techniques were associated with lower costs [10]. However, limitations of this analysis and similar cost analyses are that when comparing costs, determinations are made based on an absolute difference in costs without respect for the potential value for the more costly technique. Using such techniques as incremental cost-effectiveness ratios (ICER) and cost per quality adjust life year (QALY), cost-efficacy can be evaluated based on the key outcomes including cancer control rates, survival, and toxicity [11]. Therefore, the purpose of this analysis was to perform a cost minimization analysis based on absolute differences and an ICER/QALY cost-effectiveness analysis for APBI compared with WBI using standard 3-dimensional conformal radiotherapy (WBI 3D-CRT) and IMRT (WBI IMRT) using published clinical outcomes including local control, regional control, and overall survival.

Methods and materials

The APBI cohort for the matched-pair was derived from 221 patients with invasive early-stage breast cancer who were prospectively treated with multi-catheter interstitial APBI between October 1992 and November 2001. The WBI patients for the matched-pair were derived from a database of 1,861 women with invasive early-stage breast cancer who were treated with whole-breast irradiation (WBI) at our institution between December 1992 and November 1996. Follow-up was complete through August 2010. Institutional review board approval was given for this analysis. A total of 199 matches were made for the initial matched pair based on age, tumor size, nodal status, estrogen receptor status, and adjuvant hormonal therapy; the initial matched pair was balanced for these features but with recent updating of patient files differences did emerge which were not accounted for in the matched pair [9]. Clinical outcomes for WBI delivered via traditional techniques (2-dimensional and 3-dimensional) were extrapolated to 3D-CRT and IMRT based on previous studies, which have demonstrated differences in toxicity profiles but not clinical outcomes with IMRT; because of this extrapolation, ICERs were not calculated for toxicities [3–5]. APBI outcomes for the multi-catheter interstitial cohort were extrapolated to all APBI modalities based on the use of all three modalities on the National Surgical Adjuvant Breast and Bowel Project B-39 trial and a previous analysis which found no difference in outcomes by technique [12, 13]. APBI techniques evaluation included 3D-CRT (APBI 3D-CRT), IMRT (APBI IMRT), single-lumen applicator (APBI SL), multi-lumen applicator (APBI ML), and interstitial catheters (APBI interstitial).

Reimbursement models were generated based on 2011 Medicare schedules for each treatment technique (Tables 1, 2). WBI costs were assessed without boost incorporation; while this underestimates the cost of WBI techniques, due to heterogeneity of boost techniques utilized this was done. Reimbursement was calculated both without factoring non-medical costs and with non-medical costs incorporated based on a previous analysis from Suh et al. [10]. Assumptions included an average round-trip travel of 40 miles to the radiation center (36 cents/mile), 2 h per treatment including travel of which 30 min were spent receiving treatment ($14.78/h), and that patients receiving twice daily treatment returning to work during the interfraction interval; based on these assumptions the cost was $44.96 and $89.92 per day for once-daily and twice-daily schedules, respectively [10]. Future follow-up costs following treatment were not included in this model due to similar regimens following treatment. Costs associated with local recurrence and distant metastases were based on Stokes et al. [14] and incorporated into the model by multiplying the costs by the percentage of patients in each group having an event. All assumptions and methodology were based on and consistent with previously published manuscripts utilizing the ICER method or other cost-efficacy techniques [10, 14, 15].

Based on the absolute difference in reimbursements by technique, a cost minimization analysis was performed. Cost savings per 1,000 patients were subsequently calculated based on these absolute differences. ICERs for WBI IMRT and WBI 3D-CRT were subsequently calculated based on comparisons with the various APBI modalities; the purpose of this was to provide a relative cost-effectiveness of each WBI technique to each APBI technique based on the

Table 1 Reimbursement by common procedural terminology code for whole-breast irradiation techniques

CPT code	Description	Quantity	Facility ($)	Professional ($)	Total reimbursement ($)
WBI IMRT					
99204	New comprehensive moderate	1	0	169	169
77014	CT guidance placement	1	192	42	234
77263	Treatment planning-complex	1	0	162	162
77280	Simulation, simple	1	154	35	189
77290	Simulation, complex	1	452	78	530
77300	Dose calculation	2	77	63	140
77301	IMRT plan	1	1,687	407	2,093
77331	Special dosimetry	2	39	88	126
77334	Treatment devices, complex	1	92	62	154
77336	Weekly physicist consult	6	314	0	314
77338	MLC device for IMRT plan	1	262	218	479
77370	Special physics consult	1	117	0	117
77417	Port films	6	0	90	90
77418	IMRT delivery	28	14,556	0	14,556
77427	Weekly treatment management	6	0	1,082	1,082
77470	Special treatment in addition	1	97	105	202
			$18,037	$2,600	$20,637
WBI 3D-CRT					
99204	New comprehensive moderate	1	0	169	169
77014	CT guidance placement	1	192	42	234
77263	Treatment planning-complex	1	0	162	162
77280	Simulation, simple	1	154	35	189
77290	Simulation, complex	1	452	78	530
77295	Treatment plan 3D, reconstruction	1	335	229	565
77300	Dose calculation	2	77	63	140
77331	Special dosimetry	2	39	88	126
77334	Treatment devices, complex	3	275	186	461
77336	Weekly physicist consult	6	314	0	314
77370	Special physics consult	1	117	0	117
77414	Daily linac complex	28	7,344	0	7,344
77417	Port films	6	0	90	90
77427	Weekly treatment management	6	0	1,082	1,082
77470	Special treatment in addition	1	97	105	202
			$9,397	$2,329	$11,726

CPT current procedural terminology, *IMRT* intensity-modulated radiation therapy, *WBI* whole-breast irradiation, *3D-CRT* 3-dimensional conformal radiotherapy, *MLC* multi-leaf collimator, *CT* computed tomography

Table 2 Reimbursement by common procedural terminology code for accelerated partial-breast irradiation techniques

CPT code	Description	Quantity	Facility ($)	Professional ($)	Total reimbursement ($)
APBI 3D-CRT					
99204	New comprehensive moderate	1	0	169	169
77014	CT guidance placement	1	192	42	234
77263	Treatment planning-complex	1	0	162	162
77280	Simulation, simple	1	154	35	189
77290	Simulation, complex	1	452	78	530
77295	Treatment plan 3D, reconstruction	1	335	229	565
77300	Dose calculation	4	155	125	280
77331	Special dosimetry	4	77	175	253

Table 2 continued

CPT code	Description	Quantity	Facility ($)	Professional ($)	Total reimbursement ($)
77334	Treatment devices, complex	5	459	309	768
77336	Weekly medical physics consult	2	105	0	105
77370	Special physics consult	1	108	0	108
77414	Daily linac complex	10	2,623	0	2,623
77417	Port films	2	0	30	30
77427	Weekly treatment management	2	0	361	361
77470	Special treatment in addition	1	97	105	202
			$4,757	$1,821	$6,578
APBI IMRT					
99204	New comprehensive moderate	1	0	169	169
77014	CT guidance placement	1	192	42	234
77263	Treatment planning-complex	1	0	162	162
77280	Simulation, simple	1	154	35	189
77290	Simulation, complex	1	452	78	530
77300	Dose calculation	4	155	125	280
77301	IMRT plan	1	1,687	407	2,093
77331	Special dosimetry	4	77	175	253
77334	Treatment devices, complex	1	92	62	154
77336	Weekly medical physics consult	2	105	0	105
77338	MLC device for IMRT plan	1	262	218	479
77370	Special physics consult	1	108	0	108
77417	Port films	2	0	30	30
77418	IMRT delivery	10	5,198	0	5,198
77427	Weekly treatment management	2	0	361	361
77470	Special treatment in addition	1	97	105	202
			$8,578	$1,969	$10,547
APBI single lumen					
99204	New comprehensive moderate	1	0	169	169
19296	Device	1	3,945	0	3,945
77014	CT guidance placement	1	192	42	234
77263	Treatment planning-complex	1	0	162	162
77280	Simulation, simple	9	1,385	315	1,700
77295	Treatment plan 3D, reconstruction	1	335	229	565
77300	Central axis depth dose	10	387	313	700
77370	Special physics consult	1	117	0	117
77470	Special treatment in addition	1	97	105	202
77785	Remote HDR 1 position	10	4,094	714	4,808
			$10,553	$2,049	$12,602
APBI multi lumen					
99204	New comprehensive moderate	1	0	169	169
19296	Device	1	3,945	0	3,945
77014	CT guidance placement	1	192	42	234
77263	Treatment planning-complex	1	0	162	162
77280	Simulation, simple	9	1,385	315	1,700
77295	Treatment plan 3D, reconstruction	1	335	229	565
77300	Central axis depth dose	10	387	313	700
77370	Special physics consult	1	117	0	117
77470	Special treatment in addition	1	97	105	202

Table 2 continued

CPT code	Description	Quantity	Facility ($)	Professional ($)	Total reimbursement ($)
77786	Remote HDR 2-12 position	10	7,027	1,617	8,644
			$13,486	$2,953	$16,438
APBI interstitial					
99204	New comprehensive moderate	1	0	169	169
77014	CT guidance placement	1	192	42	234
77263	Treatment planning-complex	1	0	162	162
77280	Simulation, simple	7	1,077	245	1,322
77295	Treatment plan 3D, reconstruction	1	335	229	565
77300	Central axis depth dose	10	310	250	560
77370	Special physics consult	1	117	0	117
77470	Special treatment in addition	1	97	105	202
77787	Remote HDR >12 position	10	6,272	2,163	8,435
			$8,400	$3,365	$11,766

CPT current procedural terminology, *IMRT* intensity-modulated radiation therapy, *HDR* high dose rate, *CT* computed tomography, *3D* 3-dimensional

following equation: ($Cost_{WBI} - Cost_{APBI}/Outcome_{WBI} - Outcome_{APBI}$). The result of this equation provides the amount of increased reimbursement required to utilize WBI compared with APBI per percent improvement in the outcome evaluated. For example, if WBI costs $20,000 and APBI $5,000 and local control was 98 and 95 %, respectively, the ICER would be $5,000/percent local control ($20,000–$5,000/(98–95 %)). Outcome parameters utilized in the ICER calculations included local/regional control and overall survival; the rationale for using these parameters and in particular local control is that adjuvant radiation strategies and the value of radiation therapy following breast conserving surgery are often based on local control rates. When calculating the ICER values, the absolute difference in values for the outcome (ex. local control) was used despite no significant difference being noted in the matched pair [9]. This is based on previous ICER analyses which used similar techniques; of note, this can produce an over-estimation in the difference in outcomes between techniques [14]. Unlike QALY analyses, no definitive threshold for ICER analyses has been defined as cost-effective.

Cost per quality adjusted life year (QALY) was calculated for the APBI modalities compared with WBI IMRT and WBI 3D-CRT. In order to calculate the cost per QALY, mean utility values for the various outcome states (no recurrence = 0.92, local/regional recurrence = 0.779, distant metastases = 0.685) were utilized based on the data from Bai et al. [16]; mean utility by technique was calculated at 12 years based on the mean utility values and the time in each outcome state (taken from time to outcome).

All time intervals were calculated utilizing the date of radiation therapy (RT) completion. The rates of local control, regional control, distant metastases, disease-free survival, cause-specific survival, and overall survival were assessed utilizing the Kaplan–Meier method. The differences between the arms of the matched-pair analyses were calculated using a log-rank test. A p value of ≤ 0.05 was considered statistically significant. Statistical analyses were performed utilizing SYSTAT version 13 (SYSTAT Software, Chicago, IL) and all statistical tests were two-sided.

Results

Following the match, the WBI and interstitial APBI patients had similar patient characteristics with no differences in age (63.5 vs. 65.1, $p = 0.11$), tumor size (12.3 vs. 11.7 mm, $p = 0.31$), tumor stage ($p = 0.10$), and estrogen receptor positivity (85 vs. 86 %, $p = 0.85$) noted. WBI patients were less likely to be node positive (2.0 vs. 11.6 %, $p < 0.001$) and more likely to receive hormonal therapy (57.3 vs. 39.7 %, $p < 0.001$). No difference in the 12 year rates of local control (96.2 vs. 95.0 %, $p = 0.40$), regional control (100 vs. 98.9 %, $p = 0.15$), disease-free survival (87.0 vs. 91.0 %, $p = 0.30$), or cause-specific survival (93.0 vs. 95.0 %) were noted; however, the rate of distant metastases was significantly higher in the WBI cohort (10.1 vs. 4.5 %, $p = 0.05$) and a trend for improved overall survival (78.0 vs. 71.0 %, $p = 0.06$) was noted for WBI patients as well.

Reimbursements are presented in Table 3 including overall reimbursement and incorporation of non-medical costs as well as costs associated with recurrence. The cost minimization analysis found that per 1,000 patients treated, the cost savings with the utilization of APBI compared to WBI IMRT is $14.9 million, $10.9 million, $8.8 million,

Table 3 Reimbursements by treatment technique

Technique	Facility reimbursement	Professional reimbursement	Total reimbursement	Reimbursement including non-medical costs	Reimbursements including non-medical, recurrences
WBI 3D-CRT	$9,397	$2,329	$11,726	$12,985	$14,886
WBI IMRT	$18,037	$2,600	$20,637	$21,896	$23,797
APBI 3D-CRT	$4,757	$1,821	$6,578	$7,028	$8,522
APBI IMRT	$8,578	$1,969	$10,547	$10,997	$12,492
APBI SL	$10,553	$2,049	$12,602	$13,052	$14,547
APBI ML	$13,486	$2,953	$16,439	$16,889	$18,384
APBI interstitial	$8,400	$3,365	$11,765	$12,215	$13,710

$5.0 million, and $9.7 million for APBI 3D-CRT, APBI IMRT, APBI SL, APBI ML, and APBI interstitial, respectively, based on reimbursement alone. Per 1,000 patients treated, the cost savings with the utilization of APBI compared to WBI 3D-CRT is $6.0 million, $2.0 million, and $0.7 million for APBI 3D-CRT, APBI IMRT, and APBI interstitial, respectively with a cost decrement of $67,000 and $3.9 million for APBI SL and ABPI ML.

Incremental cost-effectiveness ratios are presented in Table 4. When examining local control, the ICERs for WBI IMRT compared with APBI 3D-CRT, APBI IMRT, APBI SL, APBI ML, and APBI interstitial are $11,716, $8,408, $6,696, $3,498, and $7,393 per percent local control improvement. When including non-medical costs and costs associated with local recurrence and distant metastases, the ICERs for WBI compared with APBI were less cost-effective (Table 4). When evaluating WBI 3D-CRT, the ICERs compared to APBI 3D-CRT and APBI IMRT were $4,290, $983 per percent local control improvement (Table 4); of note, negative ICERs were obtained for APBI SL and APBI ML due to the higher rates of reimbursement for the APBI techniques and an increase in local recurrence with essentially no difference in cost-efficacy noted for APBI interstitial (−$33). When incorporating non-medical costs, the ICERs for WBI 3D-CRT were increased compared to APBI 3D-CRT ($4,964), APBI IMRT ($1,657), and APBI interstitial ($642) reflecting increased cost-efficacy for the APBI modalities compared to WBI 3D-CRT with essentially no difference in cost-efficacy noted for APBI SL (−$56). When incorporating costs associated with local recurrences and distant metastases, the ICERs for WBI 3D-CRT favored APBI 3D-CRT ($5,303), APBI IMRT ($1,995), APBI SL ($283), and APBI interstitial ($980).

Mean utility values by recurrence status and total mean utility values are presented in Table 5. Cost per QALY was

Table 4 Incremental cost-effectiveness ratios for whole-breast irradiation delivered with intensity-modulated radiation therapy and 3-dimensional conformal radiotherapy

	Reimbursements			Reimbursement + non-medical			Reimbursement + non-medical + local recurrence/distant metastases		
	Local control	Regional control	Overall survival	Local control	Regional control	Overall survival	Local control	Regional control	Overall survival
WBI IMRT									
APBI 3-D CRT	$11,716	$12,781	$2,008	$12,390	$13,517	$2,124	$12,729	$13,886	$2,182
APBI IMRT	$8,408	$9,173	$1,441	$9,083	$9,908	$1,557	$9,421	$10,278	$1,615
APBI single-lumen	$6,696	$7,305	$1,148	$7,370	$8,040	$1,263	$7,709	$8,409	$1,321
APBI multi-lumen	$3,498	$3,816	$600	$4,173	$4,552	$715	$4,511	$4,921	$773
APBI interstitial	$7,393	$8,065	$1,267	$8,068	$8,801	$1,383	$8,406	$9,170	$1,441
WBI 3D-CRT									
APBI 3-D CRT	$4,290	$4,680	$735	$4,964	$5,416	$851	$5,303	$5,785	$909
APBI IMRT	$983	$1,072	$168	$1,657	$1,808	$284	$1,995	$2,177	$342
APBI single-lumen	−$730	−$796	−$125	−$56	−$61	−$10	$283	$308	$49
APBI multi-lumen	−$3,928	−$4,285	−$673	−$3,253	−$3,549	−$558	−$2,915	−$3,180	−$500
APBI interstitial	−$33	−$35	−$6	$642	$700	$110	$980	$1,069	$168

Table 5 Mean utility values by technique

	Mean utility value	APBI			WBI		
		Clinical outcome (%)	Mean time to recurrence (years)	Overall utility value	Clinical outcome (%)	Mean time to recurrence (years)	Overall utility value
No recurrence	0.92	89.4	–	9.87	86.1	–	9.51
Local recurrence	0.779	5.0	7.2	0.52	3.8	6.2	0.39
Regional recurrence	0.779	1.1	2.8	0.11	0	–	0
Distant metastases	0.685	4.5	4.2	0.41	10.1	4.2	0.94
Total mean utility value				10.91			10.84

Overall utility value incorporates over 12 year period the time to recurrences and the frequency of recurrence rates

WBI whole-breast irradiation, *APBI* accelerated partial-breast irradiation

not calculated for the APBI modalities compared to WBI IMRT due to the fact that WBI IMRT had higher reimbursement than all APBI techniques with a lower mean utility value leading to negative values. Similarly, cost per QALY was not calculated APBI 3D-CRT and APBI IMRT compared with WBI 3D-CRT due to the APBI modalities being reimbursed less with lower mean utility value. The cost per QALY for APBI SL, APBI ML, and APBI interstitial compared with APBI 3D-CRT are $12,273/QALY, $66,032/QALY, and $546/QALY, respectively. For APBI ML when incorporating non-medical costs and costs associated with recurrences, the cost/QALY was $54,698 and $49,009 compared with APBI 3D-CRT.

Discussion

The results of this set of analyses identified several conclusions with regards to cost-efficacy of new radiation therapy modalities; accelerated partial-breast irradiation, regardless of technique employed, represents a cost-effective treatment modality compared with whole-breast irradiation delivered using intensity-modulated radiation therapy based on cost minimization analysis and ICER analyses. However, when delivering WBI using 3D-CRT, the most cost-effective APBI options were APBI 3D-CRT or APBI IMRT based on reimbursement alone, and included APBI interstitial and APBI SL when factoring in indirect costs when using ICER analyses. When utilizing a cost per QALY assessment, brachytherapy techniques were cost-effective with a cost/QALY less than $100,000, a consistently utilized value for cost-efficacy [16]. When incorporating non-medical costs and the cost of treatment for local recurrences/distant metastases, the cost per QALY for APBI ML was less than $50,000/QALY. In summary, these results demonstrate that APBI (regardless of technique) should not be considered cost prohibitive when compared to WBI. There may be concern regarding the utilization of IMRT as a standard for comparison; however, based on recent data from Smith et al. [3–6] suggesting significant increases in the utilization of IMRT (up to 25 % of cases) and randomized trials finding a significant improvement with IMRT, we believe this technique represents a standard in the treatment of breast cancer and further, included 3D-CRT in our analyses as well.

Our results are consistent with previously published series in some aspects but divergent when examining modes of brachytherapy-based APBI. Suh et al. evaluated eight RT techniques including WBI with/without a boost, WBI with IMRT, hypofractionation, and APBI using single-lumen, interstitial, 3D-CRT, or IMRT. Costs were calculated based on sum of direct and indirect costs using the 2003 Medicare Fee Schedule for direct costs and time and travel allotments for indirect costs. Similar to our analysis, this study found that external beam techniques were the least expensive for APBI and that IMRT increased the costs for WBI; however unlike our study, this study found that brachytherapy-based APBI techniques were associated with increased costs [10]. Limitations of this study include the outdated fee schedules utilized and the failure to assess for both multi-lumen (not available at the time) and single-lumen applicators. A Markov model based analysis evaluating APBI delivered with applicator-based treatment and external beam treatment compared to traditional WBI found that external beam-based APBI techniques were cost-effective but that applicator-based techniques were not [17]. A key finding for both studies is that they did not incorporate different clinical outcomes (assumed equivalence) into their cost-effectiveness models. This analysis represents the first analysis to evaluate long-term clinical outcomes and cost-effectiveness for APBI.

Taken together, based on the cost minimization analysis, these studies show the potential for large cost savings for in the management of early-stage breast cancer. A recent study from Massachusetts General Hospital confirms these potential savings finding a potential decrease of $5.69

million per 1,000 patients treated using a cost-minimization strategy [18]. Our cost minimization analysis confirmed the potential for significant cost containment with a savings of $5.01–$14.87 million per 1,000 patients treated using APBI techniques compared with WBI IMRT and a savings $1.99–$5.96 million per 1,000 patients treated with external beam APBI techniques compared with WBI 3D-CRT. Currently, the annual incidence of breast cancer is 300,000 cases per year in the United States with 39 % of cases being early-stage, node-negative and 77.5 % of these cases pursuing breast conserving therapy. Based on these numbers and a 25 % of WBI IMRT utilization, approximately 22,669 patients would receive WBI IMRT following breast conserving surgery and the cost savings with switching to APBI would be between $113 and $325 million. Based on the above estimates, 68,006 patients would receive WBI 3D-CRT for a savings of $135–$408 million for external beam APBI techniques compared to WBI 3D-CRT [1, 6, 19, 20]. These represent overestimations as not all early-stage, node-negative patients would be eligible for APBI, and alternative treatments may be used, but do suggest a large potential cost savings when appropriately selected patients are offered APBI; furthermore, such cost savings depend significantly on the proportion of patients eligible for APBI which may vary significantly in different countries as well as regions within the United States.

There are limitations to this analysis. Clinical data for WBI IMRT was extrapolated from WBI data delivered using traditional techniques; however, it is unlikely that IMRT would alter clinical outcomes beyond toxicity profiles. Furthermore, the interstitial APBI dataset was extrapolated to all other APBI techniques; as with the WBI data, it is unlikely that clinical outcomes beyond toxicity would differ by technique. Because of the limitations noted above, cost-effectiveness based on toxicities was not evaluated at this time. However, future studies should address the cost-effectiveness of APBI and IMRT based on acute and chronic toxicities as significant differences in toxicity profiles would be expected with these newer techniques [5]. Also, future studies will need to incorporate alternate fractionation schedules including Canadian fractionation which our study did not include due to a lack of clinical data with this technique from our institution. Significant differences did exist with respect to nodal status and hormonal therapy due to updates in patient data from the initial match which may explain the higher rates of distant metastases noted in the WBI cohort.

Our analysis did not include post-treatment indirect costs outside of costs associated with recurrence; however, follow-up physician visits and mammogram protocols are the same in our clinic regardless of RT technique. When calculating costs and reimbursements, boost costs were not included in the WBI cost figures. If the reimbursement for lumpectomy bed boost had been included, WBI treatment cost would have been significantly higher and the benefit of using APBI would be even more substaintial. Finally, when calculating the ICERs, the absolute value of differences in clinical outcomes were used despite a lack of clinical significance; while this technique has been used in the past it is a limitation as it overestimates the efficacy of WBI. However, this would underestimate the magnitude of benefit providing a more cautious estimate of cost-efficacy for APBI. Despite these limitations, this study represents one of the only analyses to examine the cost-effectiveness of these novel RT techniques based on clinical outcomes.

Conclusions

Accelerated partial-breast irradiation represents a cost-effective method, compared with whole-breast irradiation delivered using intensity-modulated radiation therapy, to deliver adjuvant radiation therapy following breast conserving surgery, regardless of the APBI technique employed. Based on cost per QALY, accelerated partial-breast irradiation performed using brachytherapy is cost-effective compared with whole breast delivered using 3-dimensional conformal radiotherapy.

Conflict of interest All authors have no conflicts of interest.

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