

Clinical Investigation: Breast Cancer

Factors Associated With Optimal Long-Term Cosmetic Results in Patients Treated With Accelerated Partial Breast Irradiation Using Balloon-Based Brachytherapy

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Received Feb 3, 2011, and in revised form May 20, 2011. Accepted for publication Jul 6, 2011

Summary

This study analyzed cosmetic outcomes for the American Society of Breast Surgeons (ASBS) MammoSite Registry with 6 years of follow-up. At 36 and 72 months, the rate of excellent/good cosmesis was 93.3% and 90.4% respectively. Best outcomes were associated with larger skin spacing and smaller tumors (less than 2 cm).

Purpose: To evaluate factors associated with optimal cosmetic results at 72 months for early-stage breast cancer patients treated with Mammosite balloon-based accelerated partial breast irradiation (APBI).

Methods and Materials: A total of 1,440 patients (1,449 cases) with early-stage breast cancer undergoing breast-conserving therapy were treated with balloon-based brachytherapy to deliver APBI (34 Gy in 3.4-Gy fractions). Cosmetic outcome was evaluated at each follow-up visit and dichotomized as excellent/good (E/G) or fair/poor (F/P). Follow-up was evaluated at 36 and 72 months to establish long-term cosmesis, stability of cosmesis, and factors associated with optimal results.

Results: The percentage of evaluable patients with excellent/good (E/G) cosmetic results at 36 months and more than 72 months were 93.3% ($n = 708/759$) and 90.4% ($n = 235/260$). Factors associated with optimal cosmetic results at 72 months included: larger skin spacing ($p = 0.04$) and T1 tumors ($p = 0.02$). Using multiple regression analysis, the only factors predictive of worse cosmetic outcome at 72 months were smaller skin spacing (odds ratio [OR], 0.89; confidence interval [CI], 0.80–0.99) and tumors greater than 2 cm (OR, 4.96, CI, 1.53–16.07). In all, 227 patients had both a 36-month and a 72-month cosmetic evaluation. The number of patients with E/G cosmetic results decreased only slightly from 93.4% at 3 years to 90.8% ($p = 0.13$) at 6 years, respectively.

Conclusions: APBI delivered with balloon-based brachytherapy produced E/G cosmetic results in 90.4% of cases at 6 years. Larger tumors (T2) and smaller skin spacing were found to be the two most important independent predictors of cosmesis. © 2012 Elsevier Inc.

Keywords: Accelerated partial breast irradiation, MammoSite, Cosmesis, Brachytherapy, Breast cancer

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Conflict of interest: Dr. Keisch is a paid consultant to Hologic, Inc. All other authors report no conflicts of interest.

The MammoSite Breast Brachytherapy Registry Trial is supported in part by an unrestricted educational grant from Hologic Inc. to the American Society of Breast Surgeons and BioStat International, Inc.

Introduction

Accelerated partial breast irradiation (APBI) continues to be investigated as an alternative option to deliver adjuvant radiation therapy (RT) after lumpectomy in selected patients with early-stage breast cancer treated with breast-conserving therapy (BCT). The goal of APBI is to deliver a homogenous dose of RT in a shorter period of time (5 days or less as opposed to 6–7 weeks) to the tumor bed region. In addition to convenience, APBI may potentially reduce fatigue, while improving cosmesis and the quality of life of some patients.

APBI can be delivered using one of several techniques including multi-catheter interstitial brachytherapy (MIB), balloon-catheter brachytherapy, three-dimensional conformal radiotherapy (3D-CRT), and single-fraction intra-operative radiotherapy (IORT). Each technique delivers a relatively homogenous dose of RT to the target area, which is designed to be radiobiologically equivalent to traditional, protracted whole-breast irradiation (WBI) with respect to tumor control and associated acute and late toxicities. The MammoSite breast brachytherapy catheter (Hologic, Bedford, MA) was developed as an APBI technique to provide a logistically simpler, technically more reproducible, and patient-friendly method to perform APBI (1). After clearance of the device by the FDA for clinical use in 2002, a registry trial was initiated by the manufacturer to provide a method to prospectively, objectively, and systematically collect data on the clinical use of the brachytherapy applicator. In November of 2003, the American Society of Breast Surgeons (ASBS) assumed primary management of the trial.

The purpose of the present analysis is to evaluate factors related to long-term cosmetic outcome from the ASBS registry trial at 72 months in an effort to determine which patients are at a higher risk of a negative cosmetic outcome and to potentially provide clinicians with recommendations for achieving more idealized cosmetic results.

Methods and Materials

Between May 4, 2002 and July 30, 2004, a total of 97 institutions participated in this registry trial, which was designed to collect data on the clinical use of the MammoSite radiation therapy system (RTS) as a modality for the delivery of APBI or as boost irradiation as previously published (2). A total of 1,449 cases (1,440 patients) were enrolled on the trial. Patients received 34 Gy, given as 3.4-Gy fractions, twice daily, for ten total fractions at a point 1.0 cm from the surface of the balloon over 5 to 7 days using a remote HDR after-loader. For boost patients, the recommended dose was 10 Gy at a point 1 cm from the surface of the balloon in 5-Gy fractions (twice daily), preferably over 1 day (interfraction separation was a minimum of 6 h). Detailed outcomes of these 1,449 cases, including assessment of cosmetic outcome, local control, and toxicity, have been previously reported at various follow-up intervals (2–5). A detailed description of the use of chemotherapy in these patients has been previously reported (6).

Patient eligibility criteria and technical guidelines

Recommended criteria for patient enrollment have been published (2–5). Final determination of suitability for high-dose-rate

brachytherapy treatment was recommended after device placement using computed tomography (CT). The parameters measured included the applicator to skin distance (recommended minimum of 5 mm, preferably greater than 7 mm), conformance of the applicator to the target area 1 cm around the lumpectomy cavity, and symmetry of the center catheter shaft. Skin spacing was defined on as the distance from the balloon to the skin surface. CT and fluoroscopic simulation were advised for treatment planning, both to determine the dwell position in the center of the balloon and for daily confirmation of balloon diameter.

Data collection and quality assurance

Information on patient demographics, technical reproducibility, cosmesis, toxicity, and overall efficacy were collected on the registry trial data forms supplied to investigators. All data forms were collected and reviewed for inaccuracies, omissions, and conflicting information by an independent contract research organization. When the ASBS assumed management of the trial, additional follow-up to verify and collect more complete information about cosmetic results, adjuvant therapy, adverse events, radiation recall reactions, disease recurrence, and patient survival were collected. Enrollment was closed in July 2004. However, as mandated by the protocol, all treated patients are required to return for annual follow-up visits for 7 years. The ASBS and the independent contract research organization (BioStat International Inc [BSI]) continue to query sites for follow-up information on all treated patients. Patients are followed by either their radiation oncologist or surgeon. Data collected include cosmetic evaluation, use of adjuvant therapy, imaging assessment, recurrence and treatment of recurrence, survival status, radiation recall, and toxicities.

Cosmesis

Cosmesis was evaluated at each follow-up visit by the treating radiation oncologist or surgeon according to the Harvard criteria (provided in the registry trial data forms). An excellent cosmetic result score was assigned when the treated breast looked essentially the same as the contralateral breast (as it relates to radiation effects). A good cosmetic score was assigned for minimal but identifiable radiation effects of the treated breast. A fair score meant that significant radiation effects were readily observable. A poor score was used for severe sequelae of breast tissue secondary to radiation effects; these included severe scarring or thickening of the breast induced by radiation effects. Investigators were also asked to report the presence or absence of any seromas and/or fat necrosis at all time points after treatment.

Statistical methods

Definitions of recurrence and toxicity categories, and follow-up visit windows, were provided by the ASBS and its independent scientific advisory committee to BSI. Management and analysis of the data at BSI occurs only through in-depth discussions between statisticians at BSI and the ASBS. (It should be noted that topics for presentation and/or publication and rules for authorship and data analysis, including the entire preparation of this article manuscript, remain under the complete control of the scientific advisory committee of the ASBS.) All time intervals were

Table 1 Patient, tumor, and treatment-related characteristics

Characteristic	All cases	Invasive	DCIS
No. of cases	1,449	1,255	194
Age (y)			
Median (range)	65.5 (31.8–93.5)	65.9 (31.8–93.5)	62.1 (40.7–88.0)
Tumor Size (mm)			
Median (range)	10.0 (1.0–45.0)	10.0 (1.0–42.0)	8.0 (1.0–45.0)
Chemotherapy alone	83 (5.8%)	83 (6.6%)	0 (0.0)
Hormonal therapy alone	772 (53.6%)	674 (54.0%)	98 (50.5%)
Chemotherapy and hormones	83 (5.8%)	83 (6.6%)	0 (0.0%)
Breast infections	138 (9.5%)	122 (9.7%)	16 (8.2%)
Breast seromas	405 (28.0%)	359 (28.6%)	46 (23.7%)
Clinical follow-up* (mo)			
Median	59	59.1	58.3
Mean	53.3	53.2	54
Range	0.0–98.9	0.0–98.9	0.4–92.5
>2 Years	1,119 (77.2%)	962 (76.7%)	157 (80.9%)
>3 Years	1,022 (70.5%)	881 (70.2%)	141 (72.7%)
>4 Years	889 (61.4%)	768 (61.2%)	121 (62.4%)
>5 Years	645 (44.5%)	557 (44.4%)	88 (45.4%)
>6 Years	370 (25.5%)	310 (24.7%)	60 (30.9%)

* Surviving patients.

calculated from the date of MammoSite removal. Cosmetic outcome was evaluated at each follow-up visit and dichotomized as excellent/good or fair/poor. In addition a greater than or equal to 72 month cosmesis result was defined as the last evaluation of cosmesis on or after 71 months from device removal. This 72-month result was defined as the response variable in all univariate and multivariate analyses. Associations between baseline and treatment characteristics and 36- or 72-month cosmetic outcomes as the response variable were analyzed using univariate analysis. Multiple logistic regression analyses with the 36- or 72-month cosmetic outcome as the response variable and baseline and treatment characteristics as covariates were performed. In addition, the best predictive models using backward elimination procedures were derived to obtain the best predictive probabilities for fair/poor cosmetic outcome at 36 or 72 months. The stability of cosmetic results was investigated by testing for agreement between 36- and 72-month responses within the same cohort where both evaluations were present. A McNemar test for agreement was performed. All tests were declared statistically significant if the calculated p value was less than or equal to 0.05. Version 8.0 or higher of the SAS statistical software package (SAS, Cary, NC) was used to provide all statistical analyses.

Results

Table 1 presents selected clinical, pathologic, and treatment-related characteristics of the study population. Of the 1,449 patients, 1,255 (87%) had invasive breast cancer (93% T1, 3% N1, median size 10 mm) and 194 (13%) had DCIS (median size 8 mm). Overall, 1119 (77.2%) cases have been followed for greater than 24 months, 1022 (70.5%) for greater than 36 months, 889 (61.4%) for greater than 48 months, 645 (44.5%) for greater than 60 months, and 370 (25.5%) for greater than 72 months. Median follow-up for surviving patients was 59 months (range, 0–98.9 months). The 5-year actuarial rate of local recurrence in the breast was 3.6%.

For the entire population, the percentage of patients with good/excellent cosmetic results at 12, 24, 36, 48, 60, and 72 months were as follows: 94.6% (958/1013), 93.8% ($n = 801/854$), 93.3% ($n = 708/759$), 90.8% ($n = 600/661$), 91.2% ($n = 405/444$), and 89.0% ($n = 210/236$), respectively. It should be noted that on some follow-up visits, cosmesis was not always reported. Therefore, the number of breasts evaluable for cosmesis is not necessarily consistent with the number of patients evaluable for other variables (*i.e.*, local recurrence, etc). Univariate analysis of variables associated with cosmesis at 72 months found skin spacing (as a continuous variable) and tumors greater than 2 cm were both associated with cosmetic outcomes at 72 months on univariate analysis ($p = 0.04$, and 0.02, respectively) (Table 2).

Best predictive models were fit via backward elimination methods on 36- and 72-month outcomes. The best predictive model at 36 months included skin spacing and breast infection as predictive factors for worse cosmetic outcome (Table 3). Factors associated with a worse cosmetic outcomes at 72 months (using multiple regression analysis) included smaller skin spacing (odds ratio [OR], 0.89; confidence interval [CI], 0.80–0.99) and tumors 2 cm or larger (OR, 5.16, CI, 1.41–18.87) (Table 3). The finding of tumors greater than 2 cm was a new finding and therefore, a correlation analysis was performed to determine whether tumor size was correlated with skin spacing; however, no correlation was noted ($p = 0.91$). To examine the stability of cosmetic results with time, the same group of patients was evaluated at different time intervals. A total of 227 patients had both a 36- and 72-month cosmetic evaluation. The percentage of patients with good/excellent results at 36 months was 93.4% vs. 90.8% at 72 months, which was not statistically significant ($p = 0.13$).

Acute toxicities (<180 days from removal) are presented in Table 4. Skin spacing ($p < 0.001$), receipt of chemotherapy ($p = 0.003$) and hormonal therapy ($p = 0.005$), breast infection ($p < 0.001$), seroma ($p = 0.004$), telangiectasia formation ($p = 0.001$), and bra size ($p = 0.01$) were significantly associated with comparable findings for the invasive and DCIS subsets (Table 4).

Table 2 Univariate analysis of variables associated with cosmetic results at 72 months

Variable No. of breasts	Last visit > 72 months		<i>p</i> Value
	Excellent/Good <i>n</i> (%)	Fair/Poor <i>n</i> (%)	
	235 (90.4)	25 (9.6)	
Skin spacing, mm			
Mean (SD)	12.9 (6.82)	9.9 (3.15)	0.04*
Skin spacing (<7 vs. ≥7 mm)	21 (87.5) vs. 212 (90.6)	3 (12.5) vs. 22 (9.4)	0.71
Chemotherapy use (yes vs. no)	28 (93.3) vs. 207 (90.0)	2 (6.7) vs. 23 (10.0)	0.75
Hormone therapy use (yes vs. no)	162 (90.5) vs. 73 (90.1)	17 (9.5) vs. 8 (9.9)	1.0
Infection (yes vs. no)	26 (89.7) vs. 209 (90.5)	3 (10.3) vs. 22 (9.5)	0.74
Seroma (yes vs. no)	77 (85.6) vs. 158 (92.9)	13 (14.4) vs. 12 (7.1)	0.08
Axillary node sampling	177 (89.4) vs. 58 (93.5)	21 (10.6) vs. 4 (6.5)	0.46
Re-excision (yes vs. no)	49 (89.1) vs. 185 (90.7)	6 (10.9) vs. 19 (9.3)	0.80
Tumor size >2 cm (yes vs. no)	13 (72.2) vs. 222 (91.7)	5 (27.8) vs. 20 (8.3)	0.02*
Bra size (A and B vs. C and D)	63 (87.5) vs. 70 (87.5)	9 (12.5) vs. 10 (12.5)	1.0
Balloon fill (≤50 cc vs. >50 cc)	96 (92.3) vs. 139 (89.1)	8 (7.7) vs. 17 (10.9)	0.52

* Statistically significant.

Cox multivariate analysis found skin spacing ($p < 0.001$; hazard ratio [HR], 2.89), breast infection ($p < 0.001$; HR, 3.59), telangiectasias ($p = 0.01$; HR, 2.1), and tumor size greater than 2 cm ($p = 0.03$; HR, 2.2) to be associated with acute toxicity for all patients and invasive patients. DCIS patients had similar findings for skin spacing and breast infection but hormonal therapy and re-excision were also associated (Table 5). Chronic toxicities (>180 days from removal) are also presented in Table 4, with skin spacing ($p < 0.001$), receipt of chemotherapy ($p = 0.004$), breast infection ($p < 0.001$), seroma ($p < 0.001$), telangiectasia formation ($p < 0.001$), and tumor size greater than 2 cm ($p = 0.003$) as significant factors (Table 4). Multivariate analysis of chronic toxicities found skin spacing ($p < 0.001$; HR, 2.65), breast infection ($p = 0.003$; HR, 2.34), seroma ($p = 0.03$; HR, 1.56), telangiectasia ($p < 0.001$, $p < 5.24$), and tumor size greater than 2 cm ($p = 0.01$, HR, 2.19) to be associated with similar findings for invasive and DCIS patients.

Toxicities over time

A total 28% of patients developed seromas at any time after treatment, of which 13% were symptomatic. The overall rate of breast infections at 72 months was 9.5%. The vast majority (>95%) of these infections occurred within the first 12 months after treatment completion. Finally, the incidence of fat necrosis

within the first 12 months and after 12 months was 0.9% and 1.4%, respectively, for an overall incidence of 2.3%.

Discussion

The current study was conducted to evaluate factors associated with optimal long-term cosmetic results at 72 months for early-stage breast cancer patients treated with balloon-based adjuvant APBI using the original single-lumen MammaSite device. The percentage of evaluable patients with E/G cosmetic results at 36 and at greater than 72 months was 93.4% and 90.8%, respectively. Factors associated with optimal cosmetic results at 72 months included: tumors less than 2 cm and larger skin spacing. These results compare favorably with other forms of APBI or WBI with similar lengths of follow-up. In addition, cosmetic results appear to be relatively stable with time. Evaluation of acute and chronic toxicities demonstrated similar findings with a few notable exceptions, namely the loss of association of with chemotherapy receipt and the increased association with tumor size.

Historical perspective

For APBI to be considered an acceptable option for women with early-stage breast cancer treated with BCT, it must meet the

Table 3 Multiple logistic regression of factors associated with worse cosmetic outcome at 36 months and 72 months

Factor	36 Months			72 Months		
	Odds ratio	Confidence interval	<i>p</i> Value	Odds ratio	Confidence interval	<i>p</i> Values
Tumor size >2 cm	1.57	(0.54–4.62)	0.41	5.16	(1.41–18.87)	0.01*
Axillary node sampling	1.04	(0.55–2.00)	0.90	1.57	(0.49–5.07)	0.45
Balloon fill (>50)	0.69	(0.38–1.28)	0.24	1.23	(0.46–3.32)	0.68
Bra size (C and D)	0.65	(0.35–1.18)	0.16	1.07	(0.43–2.68)	0.88
Skin spacing (continuous)	0.92	(0.87–0.99)	0.02*	0.89	(0.80–0.99)	0.03*
Seroma	1.52	(0.81–2.86)	0.19	2.11	(0.84–5.31)	0.11
Chemotherapy use	1.77	(0.80–3.91)	0.16	0.45	(0.09–2.31)	0.34
Breast infection	2.70	(1.27–5.74)	0.01*	0.68	(0.16–2.99)	0.61

* Statistically significant.

Table 4 Univariate analysis of acute and chronic toxicity

	Acute toxicity			Chronic toxicity		
	All patients	Invasive	DCIS	All patients	Invasive	DCIS
Skin spacing (<7 mm)	<0.001*	0.001*	<0.001*	<0.001*	<0.001*	<0.001*
Chemotherapy (yes vs. no)	0.003*	0.005*	—	0.004*	0.002*	—
Hormonal therapy (yes vs. no)	0.005*	0.008*	0.22	0.51	0.46	0.84
Breast infection (yes vs. no)	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	0.006*
Seroma (yes vs. no)	0.004*	0.02*	0.05*	<0.001*	0.005*	0.008*
Telangiectasia (yes vs. no)	0.001*	<0.001*	0.85	<0.001*	<0.001*	<0.001*
Axillary node sampling (yes vs. no)	0.59	0.80	0.53	0.59	0.31	0.76
Re-excision (yes vs. no)	0.59	0.94	0.09	0.10	0.51	0.05
Tumor size >2 cm	0.21	0.25	—	0.0034*	0.003*	—
Bra size (A and B vs. C and D)	0.01*	0.02*	0.15	0.10	0.17	0.44
Balloon fill (<50 cc vs. >50 cc)	0.72	0.88	0.62	0.64	0.38	0.48

* Statistically significant.

excellent standards set by WBI with respect to long-term local tumor control, toxicities, and cosmetic outcome. Only through large randomized trials with long-term follow-up will it be determined conclusively whether APBI is equivalent to WBI. Although multiple Phase III trials are currently being conducted in the United States and Europe to address this issue, data from these studies will not be available for many years. Until then, the ASBS MammoSite registry trial offers one of the largest databases to assess all aspects of efficacy (at the present time) and possibly to alert clinicians to concerns related to the application of this technique and/or the patients most suitable for its application. The cosmetic results in this analysis compare favorably with other published reports of APBI using multi-catheter interstitial brachytherapy (the only technique with longer follow-up than the MammoSite) or with other experiences using the MammoSite device (3, 7–15) (Table 6). Wazer *et al.* reported on a series of 75 women with early stage breast cancer treated with HDR MIB. With a median follow-up of 6 years, 91% of patients had good/excellent cosmetic results (16). In a separate study from the National Institute of Oncology in Budapest, Hungary (again using HDR MIB as the APBI technique), 84% of patients had good/excellent cosmetic results at 7 years (17). Studies using WBI are also important to establish objective baseline standards for cosmetic result comparisons for APBI. In a study of 458 patients who received WBI, Taylor *et al.* reported E/G cosmetic results in 87% of breasts with a median follow-up of 4.4 years (18). Variables affecting cosmetic outcome included the number of fields used (tangents vs. three or more), whole breast dose greater than 50 Gy, total tumor bed dose greater than 65 Gy, and the use of compensating filters. Further, an additional study by Beadle *et al.*

reported on 239 patients treated with adjuvant WBI and found an 86% rate of E/G cosmetic results at 5 years (19).

In the current analysis, skin spacing continues to remain one of the most important variables associated with cosmetic results. This has been noted in several previous studies addressing this issue when using balloon-based brachytherapy (1, 15). Fortunately, this technical limitation can now be potentially overcome by using newer versions of balloon-based brachytherapy using multiple-lumen catheters (MLC) (20). Unfortunately, the rate and extent of telangiectasias was not a consistently reported cosmetic endpoint in this analysis and therefore, variables associated with the development of telangiectasias could not be determined. It is hoped that by reducing the skin dose to approximately 100% of the prescribed dose (as is easily accomplished with these newer MLC devices), cosmetic results should continue to improve and the rates of telangiectasia decrease to baseline levels seen with WBI.

One new variable that was found to be associated with long-term cosmetic results in this analysis was the tumor stage. Larger tumors (T2) were associated with worse cosmetic results at 72 months. To our knowledge, this is the first study of balloon-based brachytherapy to demonstrate this finding. We believe this may be secondary (in part) to the larger surgeries performed in these patients at lumpectomy. In studies of WBI, the extent of surgery has consistently been demonstrated as one of the most critical variables negatively affecting cosmesis. It is interesting that, with longer follow-up in these patients treated with APBI, the impact of surgery on cosmesis is now evident. Nonetheless, it will be important to continue to monitor these patients and to determine whether this observation is real or merely a transient statistical

Table 5 Multivariate analysis of acute and chronic toxicity

	Acute toxicity			Chronic		
	All patients	Invasive	DCIS	All patients	Invasive	DCIS
Skin spacing <7 mm	<0.001	0.003	<0.001	<0.001	<0.001	0.003
Breast infection	<0.001	<0.001	<0.001	0.003	0.007	0.005
Telangiectasia	0.01	0.006	—	<0.001	<0.001	0.01
Tumor size >2 cm	0.03	0.04	—	0.01	0.006	—
Seroma	—	—	—	0.03	—	—
Hormonal therapy	—	—	0.03	—	—	—
Re-excision	—	—	0.02	—	—	—

Table 6 Published studies addressing the use of the MammoSite catheter

Trial or first author (Ref)	No. of cases	Follow-up	Local control	Cosmesis (good/excellent)	Findings
ASBS Registry Trial (3)	1,449	50	96% (5-year)	92% (5-year)	Original ASBS MammoSite Registry Trial (previous study)
Benitez <i>et al.</i> (7)	43	60	100% (5-year)	84% (5-year)	Original FDA trial (last follow-up); excellent patient tolerance
Wilder <i>et al.</i> (8)	137	33	100%	NS	Dosimetry similar between MS and IB
Zauls <i>et al.</i> (9)	183	45	4.4% (5-year)	NS	Patients with DCIS had slightly higher failure rates
Ko <i>et al.</i> (10)	100	21	97% (3-year)	NS	Less acute toxicity than WBI treatment
Cutino <i>et al.</i> (11)	483	24	98.8% (2-year)	91% (2-year)	Similar outcome to ASBS Registry Trial Data
Ravi <i>et al.</i> (12)	57	—	100%	NS	Open cavity placement did not increase chronic seromas
Harper <i>et al.</i> (13)	111	46	95% (4-year)	NS	Excellent overall findings at 6 years of follow-up
Haley <i>et al.</i> (14)	92	24	100%	98%	Open cavity placement resulted in increased chronic seroma rate
Chao <i>et al.</i> (15)	80	22.1	97.1 (3-year)	88.2 (3-year)	Stable early cosmetic results noted

Abbreviations: DCIS = ductal carcinoma *in situ*; IB = interstitial brachytherapy; MS = MammoSite; NS = not stated; Ref = reference; WBI = whole breast irradiation.

association that is not reproducible with further follow-up or in other series.

Study limitations

Although data for APBI use of the MammoSite catheter in this registry trial compare favorably with WBI data, given the relative large fraction sizes used, additional follow-up is still mandatory to establish the long-term cosmetic stability associated with use of this APBI technique. It is important to note that these results are based on a voluntary registry study and therefore are subject to certain limitations. Because this was not a prospective trial and patients could be enrolled at any time before or after treatment, results should be interpreted carefully. As we have stated in the past, selection bias in patient enrollment cannot be ruled out; and, as a result, cosmetic results, toxicities, and local recurrence rates must be viewed with this in mind. As with any type of retrospective analysis, results must be considered carefully. Data from other, more controlled, prospective trials with longer follow-up and better defined criteria for objectively assessing many of these endpoints must be obtained to validate these preliminary observations. Nonetheless, this large, prospective registry trial affords the opportunity to evaluate cosmetic outcomes as a function of patient-related and balloon catheter-associated techniques and variables. Although breast infections were no longer noted to be a long-term predictor of a poor/fair cosmetic outcome, efforts to minimize the likelihood of these infections may ultimately prove useful in improving early cosmesis.

Conclusion

In conclusion, with a follow-up of 6 years, APBI with balloon-based brachytherapy resulted in E/G cosmesis in more than 90% of cases. Tumors greater than 2 cm and technique-specific treatment parameters such as skin spacing are important long-term

predictors of cosmetic outcome. Although we found no statistically significant deterioration in the rate of E/G cosmetic results with time, additional follow-up is still necessary to draw definitive conclusions regarding the durability of cosmetic outcomes with balloon-based brachytherapy.

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