Three-Year Analysis of Treatment Efficacy, Cosmesis, and Toxicity by the American Society of Breast Surgeons MammoSite Breast Brachytherapy Registry Trial in Patients Treated With Accelerated Partial Breast Irradiation (APBI)

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BACKGROUND. This report presents 3 years of data on treatment efficacy, cosmetic results, and toxicities for patients enrolled on the American Society of Breast Surgeons MammoSite (Cytyc, Bedford, Mass) Breast Brachytherapy Registry Trial.

METHODS. A total of 1440 patients (1449 cases) with early stage breast cancer who were undergoing breast-conserving therapy were treated with the MammoSite device to deliver accelerated partial breast irradiation (APBI) (34 Gy in 3.4 Gy fractions). Of these, 1255 (87%) cases had invasive breast cancer (IBC; median size = 10 mm), and 194 (13%) cases had ductal carcinoma in situ (DCIS; median size = 8 mm). Median follow-up was 30.1 months.

RESULTS. Twenty-three (1.6%) cases developed an ipsilateral breast tumor recurrence (IBTR) for a 2-year actuarial rate of 1.04% (1.11% for IBC and 0.59% for DCIS). No variables were associated with IBTR. Six (0.4%) patients developed an axillary failure. The percentages of breasts with good to excellent cosmetic results at 12 (n = 980), 24 (n = 752), 36 (n = 403), and 48 months (n = 67 cases) were 95%, 94%, 93%, and 93%, respectively. Breast seromas were reported in 23.9% of cases (30% in open-cavity implants and 19% in closed-cavity implants). Symptomatic seromas occurred in 10.6% of cases, and 1.5% of cases developed fat necrosis. A subset analysis of the first 400 consecutive cases enrolled was performed (352 with IBC, 48 DCIS). With a median follow-up of 37.5 months, the 3-year actuarial rate of IBTR was 1.79%.

CONCLUSIONS. Treatment efficacy, cosmesis, and toxicity 3 years after treatment with APBI using the MammoSite device are good and similar to those reported with other forms of APBI with similar follow-up. Cancer 2008;112:758–66. © 2008 American Cancer Society.

KEYWORDS: breast-conserving therapy, brachytherapy, radiation, partial breast irradiation, MammoSite.

Victor J. Zannis has received honoraria from Cytyc.

Maureen Lyden receives support from and is the lead researcher for MammoSite, manufactured by Cytyc.

Presented at the American Society for Therapeutic Radiology and Oncology 49th Annual Meeting, October 28-November 1, 2007, Los Angeles, California.

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Received July 31, 2007; revision received August 31, 2007; accepted September 6, 2007.
Accelerated partial breast irradiation (APBI) is currently being explored 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). Although there are several different types of RT that can be used to deliver APBI, techniques using brachytherapy have been the most frequently used modality. The reported 5-year and 10-year rates of local tumor control have been excellent, but interstitial brachytherapy can be a difficult technique to teach and learn. In addition, because interstitial brachytherapy requires the use of multiple catheters, widespread patient acceptance has been limited. In recognition of these problems, a logistically simpler, technically more reproducible, and patient “friendly” device (the MammoSite breast brachytherapy catheter manufactured by Cytyc, Bedford, Mass) was developed to deliver APBI. After clearance of the device by the US Food and Drug Administration (FDA) for clinical use in May 2002, a registry trial was initiated concurrently by the manufacturer. The goals and objectives of the trial were to provide a method to prospectively, objectively, and systematically collect data on the clinical use of the brachytherapy applicator. In November 2003, the American Society of Breast Surgeons assumed primary management of the trial. This article presents data on treatment efficacy, cosmesis, and toxicity at the 3-year follow-up for patients treated on the trial.

**MATERIALS AND METHODS**

Between May 4, 2002 and July 30, 2004, 97 institutions participated in a Registry Trial designed to collect data on the clinical use of the MammoSite device as a modality for the delivery of APBI or as boost irradiation. The trial was initiated concurrently by the manufacturer with the clearance of the brachytherapy device by the FDA for clinical use in May 2002. The goals and objectives of the trial were to provide a method to prospectively, objectively, and systematically collect data on the clinical use of the brachytherapy applicator. Data on the technical reproducibility of the device on a large scale, acute toxicity, cosmesis, efficacy, and adherence to placement in appropriate patients were sought. A previous trial in 43 patients used to obtain FDA clearance and to establish the safety of the device as a breast brachytherapy catheter has been previously reported. On November 17, 2003, the American Society of Breast Surgeons (ASBS) assumed primary management of the trial. A total of 951 patients had been enrolled on the trial when the ASBS assumed its management. Since assumption of the trial, an additional 714 patients have been enrolled by the ASBS.

Since assuming management of the Registry trial, the ASBS has attempted to collect additional information than originally intended at the start of the trial. Recognizing the importance of these data in helping to establish the efficacy of APBI, the ASBS has continuously expanded the type, quality, and nature of the data collected.

Synergos Inc (The Woodlands, Tex), an independent full-service Contract Research Organization (CRO) not affiliated with the ASBS, the manufacturer, or any of the institutions participating in this trial, was initially hired to provide services to collect, manage, and analyze data for the ASBS. This CRO provides regulatory, clinical trial management, monitoring, data management, statistical analysis, and report-writing services for numerous pharmaceutical and medical device companies. After assuming management of the Registry Trial, the ASBS asked Synergos to initiate an additional follow-up protocol to verify and collect more complete information about cosmetic results, adjuvant therapy, adverse events, radiation recall reactions, disease recurrence, and patient survival. The additional data collection began in July 2004 for the 1051 patients with at least 1 follow-up visit as of that time and has been completed for 881 (84%) of these patients.

In June 2006, a new independent full-service CRO (BioStat International Inc [BSI] Tampa, Fla) assumed responsibility of the independent management and statistical analysis of the Registry Trial data for the ASBS. Since that time, extensive review and cleaning of database records have been performed with emphasis on obtaining clean and correct cosmesis, recurrence, survival, and toxicity information. All paper records were verified to be entered in the database, site verification of recurrence information was obtained, and a cleaning of adverse event records for terminology and missing descriptive information such as grading and timing of onset was completed. The consistent and ongoing practice of timely data cleaning and site communication has reduced incomplete and missing information and provided quality data records for summary and analysis.

**Registry Trial Design/Patient Enrollment**

All centers that were trained and were using the MammoSite device clinically were offered and encouraged to participate in the Registry Trial. The Registry Trial Program was incorporated into the regional training programs for the device. The
recruitment goals for the program were to incorporate as many institutions as feasible to provide for a large database of patients in various clinical settings (ie, academic, private practice, and hospital). No site with adequate resources to complete the required data forms was denied participation in the study. It should be noted that patients could be enrolled in the trial at anytime (before, during, and after treatment) although enrollment before treatment was strongly encouraged.

Because data entry and processing were a continuous process for this program, a data cutoff date was chosen for the current article to allow for auditing and analysis (May 15, 2007). A total of 1449 breasts treated with APBI (1440 treated subjects) were submitted for analysis from a total of 97 participating institutions. These 1449 patients treated with APBI are the subjects of this analysis; no boost patients are included.

**Patient/Technical Eligibility Criteria**
Recommended criteria for patient enrollment in the protocol using the device were based upon previous publications on the use of APBI by the American Brachytherapy Society (ABS).7,8 Recommended technical guidelines were established in the protocol to exclude the treatment of patients with inadequate balloon-to-skin distances, excessive cavity size, or poor balloon-cavity conformance.

**Data Collection/Quality Assurance**
Information on patient demographics, technical reproducibility, cosmesis, toxicity, and overall efficacy were collected on the Registry Trial data forms supplied to investigators. After the American Society of Breast Surgeons assumed management of the trial, additional data were collected. This consisted of 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.

All data forms were collected and reviewed for inaccuracies, omissions, and conflicting information by Synergos. Upon receipt of the data forms, a medical review was performed to ensure that no pertinent data were omitted or contained conflicting information. Patients were not included in the Registry Trial until all of the information that was deemed critical was provided. In addition, an audit (random) of 10% of these patients was performed (at the request of the American Society of Breast Surgeons) to verify the accuracy of the data that was collected. During the course of the audit, source documents (when available) were used to verify as much of the data as possible. (Note: The accuracy of data entered into the registry database was verified through the use of actual source documents in >10% of cases).

In addition, the new CRO (BSI) has performed checking of the database for completeness against paper records and systematically reviewed 100% of the critical database elements. BSI identified and corrected information not entered or entered inconsistently and reviewed all adverse events for duplications and incomplete descriptive information. Changes were made in adverse-event recording practices, such as the discontinuation of over-reporting of ongoing events, to minimize errors and to obtain consistent reporting across sites. Before data summary, definitions of recurrence and toxicity categories, and follow-up visit windows, were provided by the American Society of Breast Surgeons to BSI, thus enabling BSI to perform consistent reporting. As the data continues to be collected, review rules remain consistent and querying of sites for additional or missing information is timely so the database can be current. The ongoing emphasis on completeness and consistency in the management of the data at BSI and in-depth discussions between statisticians at BSI and the American Society of Breast Surgeons has greatly improved the quality and usability of the Registry Trial database.

Institutional review board (IRB) approval was not required for participation in the Registry Trial but was recommended by the sponsor. Eighty percent of the clinical sites were affiliated with an IRB and obtained IRB approval to participate in the study. All patients enrolled in the study were required to sign an informed consent, and patients who were treated on or after April 14, 2003 were required to sign a Notice of Privacy Practices in accordance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA agreement) allowing the release of their data. All clinical sites were provided with a sample informed consent and HIPAA agreement that contained all of the required elements necessary for informed consent. Patient data submitted without an informed consent and/or HIPAA, if applicable, are not part of this analysis.

Enrollment was closed in July of 2004. However, as required by the protocol, all treated patients are required to return for an annual follow-up visit for 7 years. The American Society of Breast Surgeons and BSI continue to query sites for follow-up information on all treated patients. Patients are followed by either their radiation oncologist or surgeon and data collected include cosmetic evaluation (Harvard Scale), use of adjuvant therapy, imaging assessment, recurrence and treatment of recurrence, survival status, radiation recall, and toxicities.
Local, Regional, and Distant Disease Recurrence
For the purposes of this analysis, an ipsilateral breast tumor recurrence (IBTR) was defined as the reappearance of cancer in the treated breast (before the development of distant metastases) and was confirmed pathologically. Investigators were asked to classify IBTRs by their clinical location in relation to the lumpectomy cavity according to the criteria described by Recht et al. A true recurrence/marginal miss (TR/MM) was defined as a recurrence of the treated cancer within or immediately adjacent to the primary tumor site. An elsewhere failure (E failure) was defined as an IBTR several centimeters from the primary site and was generally felt to be a new primary cancer. Investigators were also asked to classify regional failures as an axillary, supraclavicular, or internal mammary lymph-node recurrence. For the purposes of this analysis, overall survival reflected all deaths, cancer-related or otherwise. Cause-specific survival was based upon deaths attributed to breast cancer.

Cosmesis/Toxicities
Investigators (radiation oncologist or surgeon) were asked to evaluate cosmesis at each follow-up visit using 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 significant radiation effects were readily observable. A poor score was used for severe sequelae of breast tissue secondary to radiation effects.

Investigators were also asked to report the presence or absence of any seromas and fat necrosis at all time points after treatment (Note: No specific criteria were given to sites to define these toxicities.) In addition, whether or not these toxicities produced symptoms or required some type of intervention was also reported.

Statistical Methods
All time intervals were calculated from the date of MammoSite removal. For the evaluations and summarizations of disease characteristics, which were MammoSite treatment parameters, cosmesis, and local recurrence, the unit of interest was a breast. For demographic information, adjuvant therapy, distant disease, and survival, the unit of interest was a patient. Nonparametric estimates of the survival or recurrence-free distributions or recurrence (failure) distribution were obtained by life table methods. Associations between clinical, pathologic, and treatment-related variables and recurrence or survival event rates were analyzed by fitting parametric models to the failure-time data and examining the significance of the parameter estimates. Associations between dichotomous cosmetic outcomes (Excellent/Good vs Fair/Poor) and treatment-related variables were analyzed by Fisher exact tests for categorical measurements and Wilcoxon rank sum tests for continuous measurements. All tests were declared statistically significant if the calculated P-value was ≤.05. All tests appear as 2-sided P-values. Descriptive statistics consist of numbers and percentages of responses in each category for discrete measures and of medians, minimum, and maximum values for continuous measures. Version 8.0 or higher of the SAS statistical software package (SAS, Cary, NC) was used to provide all statistical analyses.

RESULTS

Study Populations
Table 1 presents selected clinical, pathologic, and treatment-related characteristics of the study population. In 1249 patients, 1255 (87%) cases had invasive breast cancer (IBC; 93% T1, 3% N1, median size = 10 mm), and 194 (13%) cases had DCIS (median size 8 mm). For follow-up, 1236 (85%) breasts have been followed ≥12 months, 964 (67%) ≥24 months, 490 (34%) ≥36 months, and 79 (6%) ≥48 months. Median follow-up for surviving patients was 30.1 months (range, 0 to 58.6 months).

A subset analysis of the first 400 consecutive cases enrolled on the study was performed. A total of 352 (88%) of these cases in 351 patients had IBC (median tumor size = 10 mm), and 48 (12%) cases had DCIS (median size = 9 mm). Median follow-up for surviving patients was 37.5 months (range, 0.2 to 58.6 months) in this subset of patients. The frequency of all clinical, pathologic, and treatment-related characteristics of these 400 cases was similar to the overall population.

Failure Patterns
Ipsilateral breast tumor recurrences (IBTRs); all patients (N = 1449)
A total of 23 (1.6 %) cases developed an IBTR as some component of their initial failure (before distant metastases) for a 2-year actuarial rate of 1.04% (1.11% for IBC and 0.59% for DCIS; Table 2). The median time to IBTR was 23.5 months (range, 4.9–36.8 months). In 17 (74%) breasts, the IBTR was felt to be a new primary breast cancer unrelated to the index lesion (E failure) by the investigator and in 6 (26%) breasts, it was thought to represent a recurrence of...
the primary cancer (TR/MM failure). The 2-year actuarial rate of TR/MM failure was 0.33% and the 2-year actuarial rate of E failure was 0.71%.

Several variables were analyzed for an association with the development of an IBTR in all patients and in those treated for IBC or DCIS. These variables included margin status (positive vs negative), nodal status, tumor size and location, an extensive intraductal component (EIC), age at diagnosis (<45 vs ≥45 years), bra size, method of placement (open vs closed), tamoxifen use, or chemotherapy use. The only variable associated with the development of an IBTR included an extensive intraductal carcinoma (EIC) of marginal significance (P = .0844) in IBC cases.

Subset analysis (first 400 cases enrolled)
A total of 6 (1.5%) cases developed an IBTR as some component of their initial failure (before distant metastases) for a 3-year actuarial rate of 1.79% (2.04% for IBC, 0.0% for DCIS; Table 3). The median time to IBTR was 23.6 months (range, 12.7–36.8 months). In 5 (83%) breasts, the IBTR was felt to be a new primary breast cancer unrelated to the index lesion (E failure), and in 1 (17%) breast, it was thought to represent a recurrence of the primary cancer (TR/MM failure). The 3-year actuarial rate of TR/MM failure was 0.34%, and the 3-year actuarial rate of E failure was 1.45%.

Several variables were analyzed for an association with the development of an IBTR in all patients and in those treated for IBC or DCIS. The only variable associated with the development of an IBTR included an extensive intraductal component (marginal significance of P = .0549 in IBC cases).

Cosmetic Results
The percentage of breasts with good and/or excellent cosmetic results at 12, 24, 36, and 48 months were as follows: 95% (n = 980), 94% (n = 752), 93% (n = 403), and 93% (n = 67), respectively (Table 4).

Variables associated with optimal cosmetic results
Multiple variables were analyzed for their association with the development of a good and/or excellent cosmetic result at 2 years and at 3 years. At 24 months (n = 708 evaluable breasts), factors associated with good and/or excellent cosmetic results included increased balloon-to-skin distance (as a continuous variable, P = .0007), increasing skin spacing as a categorical variable (95.4% vs 83.5%; P = .0003), no infection (94.8% vs 77.8%; P = .0033), and no systemic chemotherapy treatment (94.9% vs 88.4%; P = .0249). At 3 years, only breast infection occurrence had a statistically significant association with cosmetic outcome (P = .0063).

Toxicity
Table 5 displays the rates of seroma reporting overall and at 12, 24, and 36 months after treatment. Most seromas were reported in the first year after MammSite removal. In addition, seromas were reported more frequently in open versus closed implants.

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**Table 1: Patient, Tumor and Treatment-related Characteristics (All Cases)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All cases</th>
<th>Invasive</th>
<th>DCIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>1440*</td>
<td>1249</td>
<td>194</td>
</tr>
<tr>
<td>Breasts</td>
<td>1440</td>
<td>1255</td>
<td>194</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Med [range], y</td>
<td>65.5 [31.8-93.5]</td>
<td>65.9 [31.8-93.5]</td>
<td>62.1 [40.7-88.0]</td>
</tr>
<tr>
<td>&lt;60</td>
<td>929 (64.5)</td>
<td>815 (65.3)</td>
<td>117 (60.3)</td>
</tr>
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<td>50-60</td>
<td>380 (26.4)</td>
<td>324 (25.9)</td>
<td>56 (28.9)</td>
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<tr>
<td>40-50</td>
<td>126 (8.8)</td>
<td>105 (8.4)</td>
<td>21 (10.8)</td>
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<td>&lt;40</td>
<td>5 (0.3)</td>
<td>5 (0.4)</td>
<td>0 (0.0)</td>
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<td>Tumor size, mm</td>
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<td></td>
<td></td>
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<tr>
<td>Med [range]</td>
<td>10.0 [1.0-45.0]</td>
<td>10.0 [1.0-42.0]</td>
<td>8.0 [1.0-45.0]</td>
</tr>
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<td>&lt;5</td>
<td>130 (9.0)</td>
<td>89 (7.1)</td>
<td>41 (21.1)</td>
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<td>431 (34.3)</td>
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<td>652 (52.0)</td>
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<td>≥20</td>
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<td>79 (6.3)</td>
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<td>4 (0.3)</td>
<td>37 (19.1)</td>
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<tr>
<td>No</td>
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<td>1152 (91.8)</td>
<td>53 (27.3)</td>
</tr>
<tr>
<td>N+</td>
<td>206 (14.2)</td>
<td>65 (5.2)</td>
<td>141 (72.7)</td>
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<td>84 (5.8)</td>
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<td>53 (27.3)</td>
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<tr>
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<td>1155 (92.0)</td>
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<tr>
<td>Close</td>
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<td>89 (7.1)</td>
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<td>86 (6.9)</td>
<td>1 (0.5)</td>
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<td>752 (52.2)</td>
<td>654 (53.4)</td>
<td>98 (50.9)</td>
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<tr>
<td>Both chemotherapy</td>
<td>80 (5.6)</td>
<td>80 (6.4)</td>
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<td>Follow-up, mo</td>
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<td></td>
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<tr>
<td>Med [range]</td>
<td>30.1 [0.0-58.6]</td>
<td>30.3 [0.0-58.6]</td>
<td>28.6 [0.2-54.0]</td>
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<tr>
<td>&lt;1 y (% of total cases)</td>
<td>1184 (81.7)</td>
<td>1021 (81.4)</td>
<td>163 (84.0)</td>
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<tr>
<td>≥2 y (% of total cases)</td>
<td>931 (64.3)</td>
<td>805 (64.1)</td>
<td>126 (64.9)</td>
</tr>
<tr>
<td>≥3 y (% of total cases)</td>
<td>476 (32.9)</td>
<td>417 (33.2)</td>
<td>59 (30.4)</td>
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<tr>
<td>≥4 y (% of total cases)</td>
<td>79 (5.5)</td>
<td>72 (5.7)</td>
<td>7 (3.6)</td>
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</table>

DCIS indicates ductal carcinoma in situ; not applicable.
* Nine patients were treated for bilateral disease.
1 Close ≤2 mm.
2 Surviving patients.

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(Continued...
(29.6% vs 19.2%) and with the use of larger (5–6 cm vs 4–5 cm) brachytherapy balloons (30.3% vs 23.2%; data not presented).

**DISCUSSION**

Data on the clinical use of the MammoSite breast brachytherapy applicator to deliver APBI were collected in a registry trial managed by the American Society of Breast Surgeons to determine 2-year and 3-year cosmetic results and toxicities associated with its use and short-term efficacy. With a median follow-up of 37.5 months in the first 400 enrolled cases, 6 (1.5%) breasts developed an IBTR for a 3-year actuarial rate of 1.79% (2.04% for IBC, 0.0% for DCIS). Two patients developed an axillary failure...
(AF) for a 3-year actuarial rate of 0.61% (0.3% for a 3-year actuarial rate of isolated AF). The percentages of patients with good and/or excellent cosmetic results at 24 (n = 214), 36, (n = 178), and 48 months (n = 67 cases) were 93%, 89%, and 93%, respectively. Finally, breast seromas were reported in 23.9% of patients overall (29.6% in open-cavity and 19.2% in closed-cavity implants). A total of 10.6% of cases developed symptomatic seromas. Fat necrosis was observed in 1.5% of all patients. These results demonstrate that treatment efficacy, cosmesis, and toxicities 2-years and 3-years after treatment with APBI using the MammoSite device in this registry trial are similar to those reported with other forms of APBI with similar follow-up.

Ipsilateral Breast Tumor Recurrence
One of the potential advantages of APBI is the reduced time required for the delivery of adjuvant RT. In order for this treatment approach to be considered an acceptable alternative to whole-breast RT, treatment efficacy (local tumor control) must be shown to be equivalent. Although 3-year results are insufficient to establish long-term efficacy, they do provide some indication of the adequacy of this treatment approach to control the index lesion in comparison to other forms of APBI with similar follow-up. The reported 3-year actuarial rate of local failure (1.79%) is comparable to failure rates observed with interstitial brachytherapy to deliver APBI in the RTOG 95–17 trial and in multiple single-institution experiences from several other centers. These trials demonstrate 3-year to 5-year rates of IBTR ranging from 0% to 6%. Certainly, longer follow-up will be needed to confirm the stability of these early control rates. Furthermore, additional follow-up will be useful in helping to establish clinical, pathologic, and technical factors associated with optimal control rates and patients most suitable for the use of APBI in general, and the MammoSite in particular. Nevertheless, these early findings are encouraging, and patients will continue to be closely followed to further document treatment efficacy.

Regional Failure
One of the additional concerns expressed with the use of APBI is the possibility of higher rates of regional failure (primarily axillary failure). This concern is based upon the observation that the lower axilla is not generally included in the radiotherapy target volume with APBI as it many times can be with whole breast RT. However, no recent APBI study has yet to report a significantly higher rate of regional nodal recurrence, and the low axillary failure rate observed in this trial (3-year actuarial rate of 0.61%) does not suggest this should become a significant problem with longer follow-up. Only additional follow-up (and mature phase 3 trial data; see below) will conclusively establish the impact of APBI or whole-breast RT on the rate of AF.

Although no variable was associated with the development of an AF (data not presented), the number of events was quite small. Further follow-up and additional failures will be needed to determine whether any clinical, pathologic, or treatment-related factor should be avoided for a patient not to be considered an optimal candidate for APBI.

Cosmetic Results
The results of this trial confirm prior observations by Keisch et al. that early cosmesis is strongly related to
balloon-to-skin spacing.4 At 24 months (n = 752 breasts), increasing skin spacing was associated with good and/or excellent cosmetic results both as a numeric (P = .0007) and as a categorical variable (83.5% vs 95.4%, P = .0003). As observed in numerous studies of standard whole-breast irradiation, no infection (94.8% vs 77.8%; P = .0033) and no systemic chemotherapy treatment (94.9% vs 88.4%; P = .0249) were also associated with good and/or excellent cosmetic results with the use of the device. Certainly, additional follow-up will be needed to confirm these observations (further stability of cosmesis over time) because cosmetic results after standard BCT generally stabilize after 3 years. However, data from Benitez et al. and Chen et al. show that cosmetic results actually improved over time (after 2 years) in patients treated with similar fractionation schedules using interstitial brachytherapy to deliver APBI.12,13 This occurred despite the finding that other endpoints, such as telangiectasia and fat necrosis, increased with longer follow-up. As these data continue to mature, further analyses by the American Society of Breast Surgeons will be conducted to help establish the stability of these observations and the factors associated with optimal long-term cosmetic results.

Toxicities
The monitoring of specific toxicities (seromas and fat necrosis) potentially related to the use of this form of APBI is important to assess its overall efficacy. Breast seromas were reported in 23.9% of patients overall (10.6% of cases had symptomatic seromas). Although this rate appears to be high, it should be noted that this is very similar to the overall rates reported after standard BCT (range, 10% to 30%).14 In addition, the rate of symptomatic seroma formation is quite low and, again, similar to rates observed with standard BCT. Unfortunately, specific criteria that have been used to consistently define the presence and/or severity of seromas after BCT are lacking, making it difficult to objectively compare rates between various types of treatment. Fat necrosis was observed in 1.5% of all patients. These toxicities will continue to be monitored carefully to determine any changes in their incidence over time and factors associated with their development.

Treatment of Ductal Carcinoma In Situ With APBI
The treatment of DCIS has evolved significantly over the past decade. Recommendations have ranged from simple mastectomy to lumpectomy alone or lumpectomy followed by whole-breast RT.15 Because most patients with DCIS now present with small, mammographically detected lesions, many investigators have attempted to define subsets of patients who are adequately treated with excision alone. Unfortunately, results with this approach have been inconsistent, and many institutions continue to recommend postlumpectomy RT for most patients.

Accelerated partial breast irradiation is now being explored as a possible treatment alternative in these low-risk patients with the goal of providing similar local control to whole breast RT but with reduced morbidity. To our knowledge, the current study represents the largest compilation of patients with DCIS treated with APBI (Note: These patients were enrolled on the Registry trial despite the finding that it was designed for patients with invasive cancer.) These early results (3-year actuarial local control rate of 100% in the first 48 cases enrolled) are encouraging and support the continued exploration of this approach for these local-risk patients.

Study Limitations and Future Considerations
It is important to note that the data presented in this article are based upon results compiled in a voluntary registry study and, therefore, subject to the limitations of this type of investigation. Because this was not a prospective trial and patients could be enrolled at various times, results should be interpreted with caution. Selection bias in patient enrollment cannot be ruled out, and, as a result, rates of cosmesis, some toxicities, and local recurrence must be viewed with this in mind. However, previous subset analyses of the 51% of patients enrolled in the trial before treatment demonstrated no statistically significant differences in any of these measures of efficacy (local control and cosmesis). Also, the growing body of published data on the clinical use of the device parallels the early observations in this trial.

It also must be pointed out that much of this information was collected retrospectively and that sites were not asked to record some toxicity information at the initiation of the trial. As a result, under-reporting of some toxicities must be seriously considered, and the data must be viewed cautiously (as with any type of retrospective analysis). 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.

Although these early results on outcome using the MammoSite to deliver APBI are good, continued follow-up of these patients and results from other prospective studies and randomized trials will be needed to help validate the long-term efficacy of APBI and the applicability of each APBI technique.
for certain clinical settings. Fortunately, the device is being studied as 1 of 3 possible APBI techniques in the multi-institutional, prospective, randomized trial of the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-39/Radition Therapy Oncology Group (RTOG) 0413. Enrollment of patients (using the MammoSite) in this trial is strongly encouraged to objectively address the critical endpoints of treatment efficacy, cosmesis, and toxicity.

REFERENCES