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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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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.

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

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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