ELSEVIER

Brachytherapy ■ (2013) ■

BRACHYTHERAPY

Brachytherapy-based partial breast irradiation is associated with low rates of complications and excellent cosmesis

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ABSTRACT

BACKGROUND: Recent retrospective, claims-based analyses have suggested a potential increased rate of toxicities associated with brachytherapy-based accelerated partial breast irradiation (APBI). The purpose of this analysis was to examine cosmesis and toxicity data from the prospective American Society of Breast Surgeons (ASBS) breast brachytherapy registry trial to compare to the findings from the claims analyses.

METHODS: The ASBS breast brachytherapy registry is a prospective nonblinded multi-institutional registry trial. Patients with Stage 0−II breast cancer undergoing breast conserving therapy were eligible. A total of 1665 patients were enrolled and 1449 treated between 2002 and 2004 with a median followup of 63 months. All patients were treated with the MammoSite (Hologic, Inc.) single-lumen device to deliver adjuvant APBI (34 Gy in 3.4 Gy fractions).

RESULTS: The rate of excellent/good cosmesis was 90.6% at 84 months. The rate of a complication (symptomatic seroma, infection, fat necrosis, telangiectasias) at 1 year/any time point was 24.2%/38.5%, whereas the rate of noninfectious complications at 1 year/any time point was 14.8%/28.9%. The rate of symptomatic seroma, fat necrosis, infection, and telangiectasia at any time was 13.4%, 2.5%, 9.6%, and 13.0%, respectively.

CONCLUSIONS: The final toxicity analysis from ASBS breast brachytherapy registry trial confirms the previously noted excellent cosmesis and toxicity profiles and fails to confirm retrospective claims analyses that have suggested higher rates of toxicity for brachytherapy-based APBI.

Keywords: Breast cancer; Radiation therapy; Partial breast irradiation; Brachytherapy; Toxicity

Introduction

Accelerated partial breast irradiation (APBI) represents an alternative to traditional whole breast irradiation (WBI) after breast conserving surgery. Recent studies have documented an increased utilization of APBI with a 10-fold increase over the past decade with up to 7% of patients currently receiving APBI (1). Although APBI can be delivered using multicatheter interstitial brachytherapy, applicator-based brachytherapy or external beam irradiation, brachytherapy represents the technique with the largest source of clinical outcomes with long-term follow-up. Currently, studies with 10 year or greater followup

Received 22 March 2013; received in revised form 4 April 2013; accepted 5 April 2013.

Conflict of interest: Martin Keisch, M.D.; consultant/advisory board: Hologic, Inc., Bedford, MA.

Financial disclosure: The American Society of Breast Surgeons breast brachytherapy registry trial was supported in part by a grant from Hologic, Inc. to the American Society for Breast Surgeons and BioStat International, Inc.

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1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2013.04.005

are only available for interstitial brachytherapy; results from a matched pair analysis and a recently updated randomized trial from Hungary found no difference in clinical outcomes between APBI and WBI with the randomized trial finding improved cosmetic outcomes for those patients undergoing APBI (2,3).

Recently, two nonrandomized, retrospective reports have been published, suggesting that brachytherapy-based APBI is associated with increased rates of infectious and noninfectious complications (4, 5). An analysis from Presley *et al.* found that brachytherapy-based APBI was associated with higher rates of complications including wound and skin complications with similar findings noted by a Medicare analysis from Smith *et al.* (4, 5). It should be noted that these reports have significant limitations including their retrospective nature, the fact that they were claims-based analyses, and failed to control for patient, pathologic, and treatment factors that may impact toxicity profiles. Based on these concerns, these analyses are more optimally suited as hypothesis generating rather than practice changing but because of increased publicity surrounding these reports, practice patterns have come into question. Moving forward, data from randomized prospective trials comparing APBI and WBI will better answer these questions; unfortunately, it will be several years before final results are available. Therefore, prospective multi-institutional trials including registry and single arm studies may provide further information in the interim. The American Society of Breast Surgeons (ASBS) MammoSite (Hologic, Inc., Bedford, Massachusetts) breast brachytherapy registry trial represents one of the largest sources of data for clinicians on the use of APBI. Previous publications from this study have documented the safety, efficacy, and toxicity profiles associated with brachytherapy-based APBI (6, 7). Therefore, the purpose of this study was to evaluate long-term cosmesis and toxicity outcomes from the final analysis of ASBS breast brachytherapy registry trial.

Methods

The ASBS breast brachytherapy registry trial was a prospective multi-institutional registry study that consisted of 97 institutions treating 1440 patients with the single lumen (SL) MammoSite Radiation Therapy System (Hologic, Inc.) between May 2002 and July 2004. The primary objective of the trial was to provide a method to collect data prospectively, objectively, and systematically on the clinical use of the brachytherapy applicator including efficacy and toxicity; no control arm was used in this study. Previous publications have discussed the design of the registry trial along with the objectives of the registry trial, data collection protocols, followup data collection, and data management; however, in summary, patients with Stage 0–II breast cancer undergoing breast conserving therapy were eligible and received 34 Gy over five days with twice daily delivery of 3.4 Gy prescribed to 1.0 cm (6, 7). With regards to enrollment, patients could be enrolled in the trial at any time during their treatment (before, during, or after), but pretreatment enrollment was encouraged. Patients were followed by either their radiation oncologist and/or surgeon and data collected include cosmetic evaluation, use of adjuvant therapy, imaging assessment, recurrence, treatment of recurrence, survival status, and toxicities. Physicians were asked to evaluate cosmesis at each followup visit using the Harvard criteria and also asked to report the presence or absence of any seromas, breast infections, telangiectasias, and fat necrosis at all time points after treatment (note: no specific criteria were given to sites to define these toxicities); patients were asked to followup at least yearly for 7 years (8). Data regarding subsequent mastectomies are unavailable. Followup for the final analysis was complete through December 2012. This represents the final toxicity analysis, as per protocol, as the study was designed to follow patients for 7 years.

Toxicity definitions and followup visit windows were provided by ASBS and its independent scientific advisory committee to Biostat International, Inc (BSI). Management and analysis of the data at BSI occurs only through in-depth discussions between statisticians at BSI and ASBS. Topics for presentation and/or publication only occur through direct discussion between ASBS-affiliated investigators and BSI. At no time does the study sponsor have access or influence on data, data analysis, or manuscript preparation or editing.

Statistical methods

All time intervals were calculated from the date of the removal of the MammoSite (Hologic, Inc.). For the evaluations and summarizations of disease characteristics, treatment parameters, and cosmesis, the unit of interest was a breast. For demographic information, adjuvant therapy, the unit of interest was a patient. In patients with bilateral breast cancers, each breast was treated independently for the purposes of cosmesis and toxicity. The first 300 and 400 cases were evaluated because of longer followup than the entire cohort. All tests were two-sided and declared statistically significant if the p-value was less than or equal to 0.05. Version 8.0 or higher of the SAS (SAS Institute, Inc., Cary, NC) statistical software package was used to provide all statistical analyses.

Results

Table 1 presents patient characteristics for the entire study population. The median age of the entire cohort was 65.5 years with a median tumor size of 10.0 mm. Thirty-eight patients (2.6%) were node positive, whereas 67.5% received some form of systemic therapy. For the entire cohort, the median followup was 63.1 months with 974 patients (67.2%), 789 patients (54.5%), and 650