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Comparison of survival and regional failure between accelerated partial breast irradiation and whole breast irradiation

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ABSTRACT

PURPOSE: To compare rates of regional recurrence (RR) and overall survival (OS) between a pooled set of 1400 patients treated on the American Society of Breast Surgeons MammoSite (Hologic, Inc., Bedford, MA) Registry Trial to a cohort of 3600 patients treated with whole breast irradiation (WBI).

METHODS AND MATERIALS: A total of 1440 women underwent accelerated partial breast irradiation (APBI) between 2002 and 2004 as part of the American Society of Breast Surgeons Registry Trial and a total of 3593 patients who received WBI were evaluated from the Surveillance Epidemiology and End Results database with treatment received between 1980 and 2009. A matched-pair analysis was performed based on age, receipt of hormonal therapy, chemotherapy, nodal status, and tumor size (1051 patients per arm). Rates of RR and OS were then analyzed for each group.

RESULTS: After the match, no differences in patient characteristics were noted when tumor size was evaluated as a continuous variable. Rates of RR and OS were similar between the WBI and APBI groups. A Cox regression model found no difference between WBI and APBI with regard to RR; however, OS was improved in the APBI cohort (hazard ratio 0.008, $p < 0.0001$).

CONCLUSIONS: With one of the largest patient populations to date comparing WBI and APBI, no difference in RR or OS was noted between WBI and APBI treatment. Until the publication of prospective Phase III trials, these data support the continued use of APBI on protocol and off protocol in appropriately selected patients.

Keywords: Partial breast irradiation; Breast cancer; Breast conservation therapy; APBI; Whole breast irradiation

Introduction

With the publication of multiple prospective Phase III trials, breast conserving therapy with whole breast irradiation (WBI) has been found to provide equivalent outcome to mastectomy alone in terms of both local tumor control and survival. However, over the past two decades, novel strategies for delivering adjuvant radiation therapy after breast conserving surgery have emerged because of the protracted 6–7-week course of WBI required and the fact that up to 20% of patients do not receive any form of adjuvant radiotherapy (1, 2). One of the techniques that reduces the length of the radiotherapy course while delivering a biologically equivalent dose of radiation is accelerated partial breast irradiation (APBI). This technique limits the radiation target to the volume of tissue immediately surrounding the surgical cavity with a variable margin and therefore decreases treatment time to 1 week or less.

As the techniques for delivering APBI have been modified and improved, APBI has been shown not only to be feasible but associated with excellent clinical outcomes with

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5–12 years of followup (3–6). However, data are limited comparing APBI to WBI. Currently, multiple Phase III trials are underway comparing adjuvant WBI with APBI, with one of the largest being the National Surgical Adjuvant Breast and Bowel Project B-39 (7). Previously, data from William Beaumont Hospital compared outcomes between 200 patients undergoing interstitial APBI and standard WBI and showed no difference in clinical outcomes at 12 years, albeit with limited numbers and therefore, a reduced power to detect differences (4). Prospective randomized data from Polgár *et al.* (3) compared WBI and interstitial APBI or partial breast with electron fields. At 5 years, no difference in local recurrence, disease free survival, or overall survival (OS) was noted with improved cosmesis in the high-dose-rate partial breast cohort. The partial breast arm, however, was mixed as the interstitial cohort received APBI, whereas the electron cohort received partial breast treatment over a standard length of treatment. More recently, intraoperative radiation has been used to deliver APBI with the results of a prospective randomized trial comparing this technique to WBI finding no difference in outcomes at 4 years, albeit with only 18.8% of patients having followup of at least 4 years (8).

Therefore, the purpose of this analysis was to perform a comparison of APBI and WBI using the data from the American Society of Breast Surgeons (ASBS) MammoSite Registry Trial and the Surveillance Epidemiology and End Results (SEER) database and to control for differences in patient characteristics via a matched-pair analysis.

Methods and materials

ASBS patient population

The ASBS MammoSite Registry Trial consisted of 97 institutions treating 1449 patients with the original MammoSite Radiation Therapy System (Hologic, Inc., Bedford, MA) between May 4, 2002 and July 30, 2004. All centers that were provided training in the use of the MammoSite device were offered participation in the registry trial. Information on enrollment criteria, data collection, and data management has previously been published (9). Of note, patients could be enrolled in the trial at any time during their treatment (before, during, or after), but pretreatment enrollment was encouraged. Since the inception of the trial, two full-service, independent contract research organizations, Synergos, Inc. (The Woodlands, TX) and Biostat International, Inc. (Tampa, FL) have provided data management services and statistical analyses for the ASBS Registry Trial. Followup was complete through July, 2011.

SEER patient population

The Metropolitan Detroit SEER Registry was queried for patients with invasive breast cancer between 1980 and 2008. Data queried included tumor size, stage, age, nodal status, radiation treatment, hormonal therapy, chemotherapy, recurrence information, and survival. The initial query identified 25,863 patients. Only patients with primary breast tumors and initial primaries were included ($n = 22{,}801$). Only patients who had undergone postoperative radiation treatment ($n = 21{,}521$) were included with the exclusion of patients with preoperative, intraoperative, or unknown sequencing of radiation. Only patients receiving breast conserving surgery were included ($n = 16{,}130$). Patients were required to have known chemotherapy and hormonal treatment information ($n = 16{,}128$). The only histologies included in this analysis were ductal, lobular, and medullary carcinomas ($n = 16{,}053$). SEER database patients were required to have initial staging and followup data available, which yielded a final SEER database cohort size of 3593 patients available for the matching process. Local recurrence data is not consistently maintained within the SEER database and was therefore not evaluated in this study.

Statistical analyses

Patient characteristics for each cohort were analyzed including age, tumor size/stage, estrogen receptor status, margin status, lymph node status, and receipt of hormonal therapy. Clinical outcomes that were analyzed included regional recurrence (RR) and OS. RR was defined as failure within the regional lymphatics (axillary, supraclavicular, or internal mammary nodes). OS was defined as an absence of death secondary to any cause.

In matching invasive patients who received APBI to those who received WBI with respect to their baseline variables (e.g., age, chemotherapy, hormonal therapy, and nodal status), we used the propensity scoring algorithm (10). Therefore, for each patient treated with APBI or WBI, we calculated the propensity score using the logistic regression model with the baseline characteristics (age, chemotherapy, hormonal therapy, and nodal status) as explanatory variables. For each computed propensity score for patients with APBI ($n = 1440$), we selected a match from the WBI group ($n = 3593$) based on the closest absolute propensity score, that is, the ‘‘nearest neighbor’’ (11). We then conducted the selection process without replacement so that there was a 1:1 match (11, 12). After the propensity score matching, the distribution of the covariates between patients with APBI and patients with WBI were expected to be the same, leading to nonsignificant differences in the covariates across the two groups of patients (13). The matched-pair process yielded a final cohort size of 1051 women in each treatment group (WBI and APBI) with a total patient population of 2102 women in this study.

The Chi-square test was used to assess differences in baseline characteristics (age, chemotherapy, hormonal therapy, and nodal status). We compared the outcome variables (RR and OS) between APBI and WBI patients using Kaplan–Meier product–limit estimator, which calculated