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Five fraction accelerated partial breast irradiation using noninvasive image-guided breast brachytherapy: Feasibility and acute toxicity

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ABSTRACT

PURPOSE: To improve efficiency, convenience, and cost, a prospective phase II trial was initiated to evaluate accelerated partial breast irradiation delivered with noninvasive image-guided breast brachytherapy (NIBB) via five once-daily fractions.

METHODS AND MATERIALS: Women ≥50 years old with early-stage breast cancer undergoing breast conserving surgery were enrolled. Eligibility criteria included invasive carcinoma ≤2.0 cm or ductal carcinoma in situ ≤3.0 cm, ER positive (if invasive), lymph node negative, LVI absent, and margins negative by 2 mm. Patients received a total dose of 28.5 Gy in five daily fractions. NIBB was delivered using two orthogonal axes for each fraction. Applicators were selected to encompass the lumpectomy cavity with a 1.0 cm clinical target volume margin and 0 to 0.5 cm planning target volume margin. Acute and late toxicity was assessed based on CTCAE v3.0.

RESULTS: Forty patients with a mean age of 67 years underwent protocol treatment. Mean tumor size was 1.0 cm (0.3−2.0 cm). Eighty percent had invasive carcinoma and the remainder had ductal carcinoma in situ. Mean tumor bed volume was 21 cc (5−79 cc) and mean breast volume was 1319 cc (499−3044 cc). Mean breast separation with compression was 6.7 cm (3.5−8.9 cm). All patients tolerated well. Median discomfort with compression was 1 (range: 0−7) on a 10-point pain scale. Acute skin reaction was Grade 0−1 in 70%, Grade 2 in 28%, and Grade 3 in 3%. Acute skin toxicity was not associated with breast size but was associated with larger breast separation with compression ($p < 0.01$) and larger applicator size ($p < 0.01$). No Grade 3+ late toxicity or local recurrences have been observed at a median followup of 14 months.

CONCLUSIONS: Accelerated partial breast irradiation delivered using NIBB over five daily fractions is a convenient treatment option that is feasible and well tolerated.

Keywords: Breast cancer; Accelerated partial breast irradiation; APBI; Noninvasive image-guided breast brachytherapy; NIBB; Brachytherapy

Introduction

Breast irradiation has been shown to be an essential component of breast conserving therapy for most women, improving both local control and overall survival (1). Accelerated partial breast irradiation (APBI) is an attractive alternative to whole breast irradiation whereby both the volume of normal breast tissue irradiated and the overall treatment time is reduced. This approach has been shown to be

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noninferior for appropriately selected women (2). However, the most commonly used techniques for delivery of APBI are not ideal for all patients (3). Interstitial and intracavitary brachytherapy are invasive requiring placement of percutaneous catheters. Three-dimensional conformal radiation therapy (3D-CRT) is noninvasive but requires larger treatment margins to account for target motion that have been associated with a high rate of late toxicity and suboptimal cosmetic outcomes (4–7). Noninvasive image-guided breast brachytherapy (NIBB) is a novel technique to deliver APBI (8). Initial data using a commonly used fractionation schedule of 34 Gy in 10 fractions have shown encouraging results (9). To further improve patient convenience, increase access to care, and reduce costs of therapy, shorter irradiation schedules are desirable. Therefore, a prospective phase II trial evaluating short course NIBB APBI to a dose of 28.5 Gy delivered in five fractions was initiated. This report presents the initial feasibility and acute toxicity.

Methods

This prospective phase II trial underwent review and approval by the institutional review boards of all participating centers (NCT01961531) and was monitored by the Brown University Oncology Research Group data safety monitoring board. There were three participating centers, and patients were recruited between 2014 and 2016 with an accrual goal of 40 patients.

Patient eligibility

Patients were eligible for enrollment based on criteria similar to the APBI patient selection guidelines from the American Society of Brachytherapy and the American Society of Radiation Oncology (10, 11). Specifically, patients had to be 50 years or older with a confirmed histological diagnosis of invasive breast carcinoma or ductal carcinoma in situ (DCIS) and treated with breast-conserving surgery. Invasive tumors had to be ≤2 cm in size and estrogen receptor positive. DCIS had to be ≤3 cm in size. Final resection margins had to be negative by at least 2 mm unless at the pectoralis fascia or skin. Patients had to be lymph node negative. Pathologic nodal assessment was required except for patients with a very low risk of sentinel node involvement including patients with pure DCIS, microinvasion, tubular or mucinous histology, or age ≥70 years. Multicentric disease and lymphovascular invasion were exclusion criteria. Patients with poor performance status (Eastern Cooperative Oncology Group >2), limited life expectancy, breast augmentation, systemic lupus erythematosus, or scleroderma were not eligible.

NIBB technique

NIBB was delivered using the AccuBoost Applicators (Advanced Radiation Therapy, Inc., Tyngsborough, MA). The NIBB technique and dosimetry has previously been described (8, 12, 13). Briefly, the patient's breast is placed between a pair of compression plates and immobilized with gentle compression (Fig. 1). A mammography-like, kV image is obtained to identify and target the tumor bed. A pair of appropriately shaped and sized applicators is selected to encompass the target volume. The treatment is delivered using a high-dose-rate Ir-192 source via remote afterloader. The process is then repeated at an orthogonal angle. The use of two orthogonal treatment angles results in conformal coverage of the tumor bed with relative sparing of skin and nontarget breast tissue. To be an appropriate candidate for the NIBB technique on this trial, the entire tumor bed had to be identifiable on AccuBoost imaging, the planning target volume (PTV) had to be encompassed by one of the available applicators, and breast immobilization had to be achieved with a resulting breast separation of ≤8 cm. Factors influencing eligibility for the NIBB technique have previously been evaluated (14). A separation of ≤8 cm was restricted as skin dose increases with increased separation for Ir-192, and therefore wider separation could result in unacceptable skin toxicity.

A dose of 28.5 Gy in five fractions delivered daily over 1 week was prescribed to encompass the PTV. For this trial,

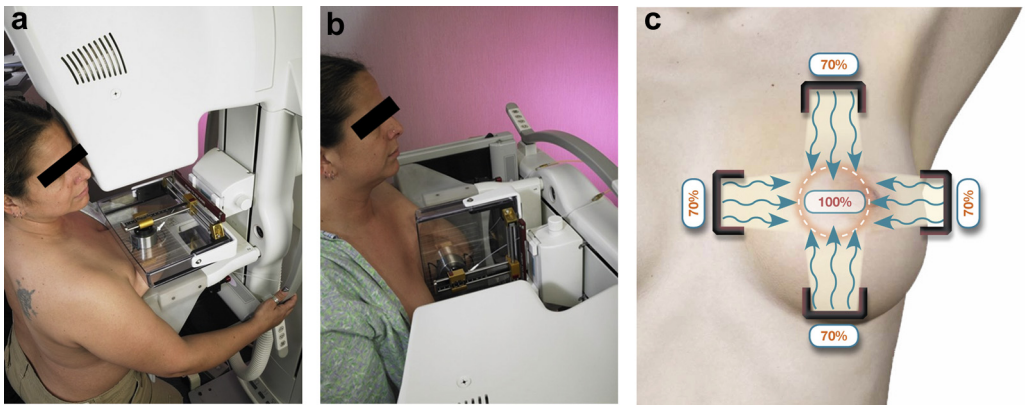

Fig. 1. Noninvasive image-guided breast brachytherapy technique using the AccuBoost applicators with cranial-caudal breast compression (a) followed by medial-lateral breast compression (b) resulting in conformal coverage of the target volume with relative sparing of superficial tissues (c).