ELSEVIER

Brachytherapy 11 (2012) 97−104

BRACHYTHERAPY

Four-year results using balloon-based brachytherapy to deliver accelerated partial breast irradiation with a 2-day dose fractionation schedule

J. Ben Wilkinson[1], Alvaro A. Martinez[1], Peter Y. Chen[1], Mihai I. Ghilezan[1], Michelle F. Wallace[1], Inga S. Grills[1], Chirag S. Shah[1], Christina K. Mitchell[1], Evelyn Sebastian[1], Amy S. Limbacher[1], Pamela R. Benitez[2], Eric A. Brown[2], Frank A. Vicini[1,*]

[1]*Department of Radiation Oncology, Beaumont Cancer Institute, Oakland University William Beaumont School of Medicine, Royal Oak, MI*
[2]*Department of Surgery, Beaumont Cancer Institute, Oakland University William Beaumont School of Medicine, Royal Oak, MI*

ABSTRACT

PURPOSE: We present 4-year results from a Phase I/II trial using balloon-based brachytherapy to deliver accelerated partial breast irradiation in 2 days.

MATERIALS/METHODS: Forty-five patients received breast-conserving surgery followed by adjuvant radiation therapy using a balloon-based brachytherapy applicator delivering 2800 cGy in four fractions over 2 days. Outcomes analyzed include toxicities scored using the NCI Common Toxicity Criteria v3.0 scale, ipsilateral breast tumor recurrence, regional nodal failure, distant metastasis, disease-free survival, cause-specific survival, and overall survival.

RESULTS: Median age was 66 years (range, 48−83 years) and median tumor size was 0.6 cm (range, 0.2−2.3 cm). Five percent of patients were node positive ($n = 2$), whereas 73% was estrogen receptor positive ($n = 33$). Median followup was 3.7 years (2.4−7.0 years) with greater than 2 years of followup for all patients. Only Grades 1 and 2 chronic toxicities were noted with fat necrosis (18%) and asymptomatic seromas (42%) being the most common toxicities. Seven percent of patients developed ipsilateral rib fractures ($n = 3$), although this was not statistically associated with maximum rib dose ($p = 0.31$). Ninety-eight percent of patients had a good or excellent radiation-related cosmetic outcome at the time of last followup. There were no ipsilateral breast tumor recurrences or regional nodal failures; however, 2 patients developed distant metastases. Four-year actuarial disease-free survival, cause-specific survival, and overall survival were 96%, 100%, and 93%, respectively.

CONCLUSIONS: Treatment of early-stage breast cancer patients with breast-conserving therapy using a 2-day radiation dose schedule resulted in acceptable chronic toxicity and similar clinical outcomes as standard 5-day fractionation.

Keywords: APBI; Hypofractionation; Partial breast irradiation; IORT; Breast cancer

Introduction

Adjuvant radiation to the whole breast after breast-conserving surgery has been established as a standard of care in the treatment of early-stage breast cancer in multiple prospective randomized trials (1, 2). Beginning in the early 1990s, an accelerated schedule of radiation delivery to the portion of the breast at highest risk for local failure (e.g., accelerated partial breast irradiation [APBI]) was developed to improve the option for breast conservation by reducing the overall treatment time and potentially improving the quality of life of patients (3, 4). Gradually, this technique has been made available to larger groups

Received 1 April 2011; received in revised form 24 May 2011; accepted 26 May 2011.

Prior Presentation(s): Presented (Poster Discussion Session) at the 2011 Annual Meeting of the American Brachytherapy Society.

Disclosures: Eric Brown, M.D., has received honoraria to speak at education sessions for Ethicon, Inc. (no commerical relationship with Hologic, Inc.)

* Corresponding author. Department of Radiation Oncology, Beaumont Cancer Institute, Oakland University William Beaumont School of Medicine, 3601 W. 13 Mile Road, Royal Oak, MI 48073. Tel.: +1-248-551-1219; fax: +1-248-551-0089.

E-mail address: fvicini@beaumont.edu (F.A. Vicini).

1538-4721/$ - see front matter
doi:10.1016/j.brachy.2011.05.012

of carefully selected women with low-risk disease. Phase I/II studies with 5- and 10-year followup using interstitial brachytherapy techniques to deliver APBI have documented acceptable rates of cosmesis, toxicity, and local control (4–6). Balloon- or applicator-based brachytherapy and three-dimensional conformal radiation therapy have become the most common methods for APBI in the United States (7, 8). Several groups (including a national registry trial) (9–13) have published results using the MammoSite Radiation Therapy System (RTS) (Hologic, Inc., Bedford, MA, USA) showing excellent rates of local control with adequate early and late toxicity.

Although varied radiation fractionation schedules exist in the literature to deliver APBI, the radiation dose schedule used in the United States has been fairly uniform. Patients who receive interstitial brachytherapy or applicator-based brachytherapy traditionally receive a total dose of 34 Gy divided into 10, twice-daily fractions with a minimum interfraction interval of 6 hours. Patients who are treated with the three-dimensional conformal radiation therapy technique of APBI typically receive 38.5 Gy also divided into 10 fractions using a twice-a-day dose–delivery schedule.

Over the past 5 years, there has been increasing interest in further shortening the treatment length for patients receiving APBI. Hypofractionated APBI can vary from one to four fractions and has been studied using a variety of delivery techniques (14–17). We present an update of our previously published results of a Phase I/II trial using a balloon-based catheter to deliver APBI in four fractions over 2 days.

Materials and methods

Investigational review board approval was granted in 2004 for this Phase I/II, nonrandomized, prospective pilot trial using a balloon-based brachytherapy device (the MammoSite RTS) to deliver adjuvant radiation after lumpectomy in 2 days (investigational review board #2004-007).

Study participants

Between March 2004 and August 2007, 45 patients with early-stage breast cancer were enrolled onto a Phase I/II clinical trial and received breast-conserving surgery followed by adjuvant radiation therapy using a single-lumen balloon-based brachytherapy applicator. Eligibility for this trial included age >40, ≤ 3.0 cm tumor size, ≤ 3 pathologically positive lymph nodes, and negative margins (per National Surgical Adjuvant Breast and Bowel Project [NSABP] criteria).

Prescribed radiation dose and placement techniques

An equivalent dose to standard whole breast irradiation (45 Gy in 25 fractions) with lumpectomy cavity boost (16 Gy in 8 fractions and 61 Gy in total) was estimated using the linear quadratic model. An alpha/beta ratio for tumor control of 4.0 was used to calculate a dose and fractionation pattern of four fractions of 700 cGy to a total dose of 28 Gy delivered over 2 days. This calculated dose was prescribed to a distance of 1.0 cm beyond the surface of the balloon. Minimum interfraction time for all patients was 6 hours. Our device placement and treatment-planning techniques using the MammoSite RTS have been previously described (9, 15). All patients met dosimetric criteria specified by the NSABP B-39/Radiation Therapy Oncology Group 0413 Phase III trial. Acceptable balloon fill volumes were 35–125 mL corresponding to device diameters between 4 and 6 cm. The prescription dose was delivered by connecting the applicator's central port to an afterloader equipped with an iridium-192 source. After completion of the fourth fraction, the radiation oncologist removed the brachytherapy applicator.

Outcome measures and toxicity analysis

Our primary objective was to measure both clinical effectiveness and rates of toxicity using our 2-day fraction schedule. Toxicities were evaluated using the National Cancer Institute Common Toxicity Criteria for Adverse Events v3.0 scale. Methods of analysis for both acute and late toxicity for this trial have also been previously described (15). Patients were followed every 3 months for the first 2 years by the radiation oncologist or the breast surgeon and then every 6 months thereafter. Cosmesis was scored by the physician using the Harvard Criteria (18) at each followup encounter beginning with the 6-month visit. Mammograms were obtained annually, and additional imaging studies were ordered at the discretion of the radiologist, radiation oncologist, or surgeon. Clinical outcomes evaluated include ipsilateral breast tumor recurrence (IBTR), regional nodal failure (RNF), distant metastasis (DM), disease-free survival (DFS), cause-specific survival (CSS), and overall survival (OS).

Statistical analysis

The estimated likelihood for IBTR, RNF, DM, DFS, CSS, and OS were calculated using the Kaplan–Meier method. Microsoft Excel was used to calculate data counts, mean, median, and ranges for patient characteristics and toxicity rates. Statistical significance of toxicity levels as compared with radiation dose and clinical outcomes were established using linear regression, a Pearson chi-square test, and two sample T tests. Statistical analyses were performed using Systat version 11.0 (Systat Software, Inc., Chicago, IL), and all statistical tests were two sided.

Results

Clinical and treatment-related characteristics

Patient characteristics are summarized in Table 1. Of the 45 women treated, the median age was 66 years (range, 48–83 years) with a median tumor size of 0.6 cm (range,