

Clinical Investigation

High-Dose-Rate Brachytherapy Boost Effect on Local Tumor Control in Young Women With Breast Cancer



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Summary

We performed a prospective study to evaluate the effect of a single 7-Gy fraction of high-dose-rate brachytherapy boost on local tumor control in 167 women, 45 years of age and younger, after breast-conserving therapy with pathology-free margin status. The 10-year local relapse rate was 4.3%, and breast relapse rate was 4.9%, with breast preservation in 93.4%, improving local control based on previously published data.

Purpose: To evaluate the local control rate and complications of a single fraction of high-dose-rate brachytherapy (HDR BT) boost in women aged 45 years and younger after breast-conserving therapy.

Methods and Materials: Between 1999 and 2007, 167 patients between the ages of 26 and 45 years old (72 were 40 years old or younger), with stages T1 to T2 invasive breast cancer with disease-free margin status of at least 5 mm after breast-conserving surgery received 46 to 50 Gy whole-breast irradiation plus a 7-Gy HDR-BT boost (“fast boost”). An axillary dissection was performed in 72.5% of the patients and sentinel lymph node biopsy in 27.5%. A supraclavicular area was irradiated in 19% of the patients. Chemotherapy was used in 86% of the patients and hormone treatment in 77%. Clinical nodes were present in 18% and pathological nodes in 29%. The pathological stage was pT0: 5%, pTis: 3%, pT1: 69% and pT2: 23%. Intraductal component was present in 40% and 28% were G3.

Results: At a median follow-up of 92 months, 9 patients relapsed on the margin of the implant, and 1 patient in another quadrant, resulting in a 10-year local relapse rate of 4.3% and a breast relapse rate of 4.9%, with breast preservation in 93.4%; no case of mastectomy due to poor cosmesis arose. Actuarial 5- and 10-year disease-free, cause-specific, and overall survival rates were 87.9% and 85.8%, and 92.1% and 88.4%, and 92.1% and 87.3%, respectively. In a univariate analysis, triple-negative cases and negative hormone receptors did worse, but in a multivariate analysis, only the last factor was significant for local and breast control. Asymptomatic fibrosis G2 was

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recorded in 3 cases, and there were no other late complications. Cosmetic results were good to excellent in 97% of cases.

Conclusions: A single dose of 7 Gy using the fast-boost technique is well tolerated, with a low rate of late complications and improved local tumor control in women aged 45 and younger, compared to published data. This approach is recommended in breast-preserving treatment. © 2015 Elsevier Inc.

Introduction

Breast-conserving therapy is as effective as mastectomy in breast carcinoma, with good cosmetic results. Radiation is able to control microscopic disease after excision of the gross tumor. However, in high-risk patients, a boost in addition to the standard 45- to 50-Gy whole-breast irradiation (WBI) is required for optimal local control. The largest clinical trial performed in invasive breast carcinoma patients with disease-free margin status has clearly shown that a boost of 16 Gy reduces local relapse (LR) by one half (1). The relapse rate is dose-dependent, that is, the higher the dose the lower the failure but with an increased rate of fibrosis.

Younger women have an increased risk of LR compared to older women. In the boost-no boost trial, age was the main prognostic factor for relapse (2). A boost is always useful, but it is especially recommended in women under 50. In women aged 41 to 50, breast relapse at 10 years dropped from 12.5% to 8.7%, and in women aged 40 or younger, relapse declined from 24% to 13.5% with the use of a boost. Multiple studies have confirmed that younger age is associated with a higher number of relapses, and therefore, in some centers, a mastectomy is recommended.

The optimal dose and radiation technique to deliver the boost have yet to be determined. Interstitial brachytherapy (BT) has conventionally been used when higher doses are required, and the effectiveness of a single dose of high-dose-rate (HDR) BT has been proven in several publications. One prospective study delivering a single fraction of 7-Gy HDR BT boost in 84 women with disease-free surgical margins showed, at a median 10-year follow-up (FU), an LR rate of 4.4% (3).

We performed a prospective study in women aged 45 years and younger treated with breast-conserving surgery (BCS), WBI, and a single fraction of HDR BT boost. The primary objective was to optimize local tumor control in this high-risk group of young women, with an easy method to give the boost and with a low rate of late complications. Secondary aims were to determine breast control rate, development of metastasis, and cause-specific survival (CSS) rates.

Methods and Materials

After BCS, WBI was given to all women. In 1999, we started a prospective study using a boost with a single

fraction of HDR BT rather than electrons, which was our previous practice. Inclusion criteria were invasive breast carcinoma, conserving surgery with a disease-free surgical margin status of at least 5 mm, either an invasive or associated intraductal component, stages T1 to T2 disease, and WBI with 46 to 50 Gy. Exclusion criteria were medical problems that precluded anesthesia, a small volume of residual breast tissue after BCS, close or positive surgical margins, and clinical T3 to T4 tumors. All patients gave written informed consent form.

WBI was performed with 6-MV photons, using tangential conformal fields; 2 Gy was delivered to the reference point daily, 5 days per week, to a total dose of 46 to 50 Gy. The supra- and infraclavicular areas were included in 19% of patients, and the internal mammary chain with a separate direct field was included in 2% of patients. Chemotherapy was used in 86% of patients (19% received neoadjuvant therapy, and 67% received adjuvant therapy). Hormone treatment was given to 77% of patients. Some HER-2-positive patients received trastuzumab during the last year of the study. Treatment details are summarized in Table 1.

Brachytherapy was performed for no longer than 2 weeks following WBI, using intravenous sedation, analgesia, and local anesthesia, on an outpatient basis. The tumor bed was defined by clinical assessment, taking into account initial mammograms, surgical description, and physical examination. No computed tomography or x-ray guidance images were used. The tumor bed plus 1 cm was drawn on the skin to define the projection of the clinical tumor volume. The implantation technique has been described elsewhere (3). Needles were fixed with an external template forming triangles with 1.6-cm sides. The median number of needles inserted was 7 on 2 planes, (minimum of 5 on a single plane; maximum of 12 on 3 planes). Dosimetric calculations were based on the active length of each needle as measured clinically on the skin.

Table 1 Treatment modality

	No. of patients (%)
External beam radiation therapy	
46 Gy whole-breast	28 (17%)
50 Gy whole-breast	139 (83%)
Chemotherapy	142 (85%)
Adjuvant	110 (66%)
Neo-adjuvant	32 (19%)
Hormone therapy	129 (77%)

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