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Original article

Prospective evaluation of concomitant tumour bed boost with whole breast irradiation in patients with locally advanced breast cancer undergoing breast-conserving therapy

Rakesh Jalali*, Rohit Malde, Ritu Bhutani, Ashwini Budrukkar, Rajendra Badwe, Rajiv Sarin

Department of Radiation Oncology and Surgical Oncology, Tata Memorial Hospital, 125, Parel, Mumbai 400 012, India

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Abstract

Background and purpose: To evaluate prospectively the feasibility of concomitant weekly tumour bed electron boost along with whole breast radiotherapy (RT) following breast-conserving therapy (BCT) in patients with locally advanced breast cancer (LABC) with the aim of reducing overall treatment time.
Materials and methods: Thirty patients with LABC suitable for BCT following neoadjuvant chemotherapy (CAF/CEF) were accrued in the study. Conventional RT (CRT) to the whole breast was delivered 5 days a week to a dose of 50 Gy using 6–10 MV photons. In addition, an electron boost to the tumour bed was delivered every Saturday, eventually delivering 5 such weekly fractions to a boost dose of 12.5 Gy. Patients were evaluated for acute reactions during the treatment and cosmetic evaluation was done before, at the end of radiation therapy and at follow up by 2 independent observers blinded to each other. The study population (concomitant boost (CB) group) was compared with a similar cohort of 32 patients treated conventionally with tumour bed boost of 15 Gy in 6 fractions delivered after the completion of whole breast irradiation (CRT group).
Results: All patients completed RT within the stipulated time with no grade IV skin toxicity in either group. At conclusion of RT, in the CB group, confluent moist desquamation (grade III) developed within the tumour bed region in 1 patient (3.3%) and outside tumour bed region in 3 patients (10%). In the CRT group, 3 and 4 patients (9.4% and 12%) developed moist desquamation within and outside the tumour bed regions, respectively. CB did not affect the global cosmesis as compared with CRT group ($p = 0.23$) at the end of 3 years.
Conclusion: Concomitant tumour bed boost along with whole breast RT appears to be safe and feasible in a select group of patients. As the treatment is completed earlier by 6–10 days than conventional practice, it has favourable time and resource implications, particularly attractive for patients travelling long distances for treatment. Based on these encouraging results, we are planning to confirm the results in an appropriately designed and powered randomised trial.

Keywords: Breast cancer; Locally advanced; Breast-conserving therapy; Concomitant boost

Introduction

Breast cancer is the commonest cancer among women in the western world accounting for 18% of all cancer in women and is also showing a rising trend in developing countries. In India, it is the second most common cancer in females with 75,000 new cases occurring every year.[1] Management of such cancers involves a multimodality approach employing surgery, radiotherapy (RT), chemotherapy and hormonal therapy, and therefore requiring considerable health care resources. The equivalence of breast conservation treatment (BCT) to modified radical mastectomy in early breast cancer has been proven in several randomised trials,[2–6] meta-analysis[7,8] and our own experience.[9] BCT is being increasingly employed in patients with locally advanced breast cancer (LABC) after the tumours have been downsized by neoadjuvant chemotherapy. Radiation protocols for such patients have been modelled along the lines of early breast cancer.

*Corresponding author. Tel.: +91 22 24177153; fax: +91 22 24146937.
E-mail address: rjalali@tmc.gov.in (R. Jalali).

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The advantage of tumour bed boost after whole breast RT has been proven by European Organization for Research and Treatment of Cancer (EORTC) study, which showed a significant reduction in the 5-year actuarial rate of local recurrence (7.3% vs. 4.3%, $p<0.001$) by addition of tumour bed boost as compared with no additional boost after 50 Gy irradiation to the whole breast.[10] Conventional RT (CRT) regimen therefore typically spans 6–7 weeks of daily treatment in most institutes from Monday to Friday, 5 days a week. Lately, there has been an increasing interest in modifying RT regimens, with equivalent local control and a decrease in overall treatment time thereby reducing the time and cost burden to patient and health resources. Concomitant boost (CB) regimens have led to improvement in disease-free survival in head and neck cancers and being evaluated in other sites as well.[11]

To shorten the relatively long duration of treatment, a prospective study of delivering a CB to the tumour bed on Saturdays, thus completing the whole course of treatment in 5 weeks was conducted at our centre.[12] The aim of the study was to test the feasibility in terms of patient tolerance and cosmesis.

Materials and Methods

Study design and eligibility

Between March 2002 and December 2003, 62 patients with locally advanced breast cancer, who following neoadjuvant chemotherapy were found suitable for BCT and had undergone breast-conserving surgery were screened for participating in the study. Patients older than 60 years of age, an Eastern Cooperative Oncology Group (ECOG) performance score higher than 2, history of any previous cancer, multiple tumour foci in more than 1 quadrant, a positive cut margin on histopathology and patients with very large pendulous breasts or with tumours in the axillary tail in whom a brisk skin reaction were expected were ineligible. Depending upon the slots available on the RT machine for delivering boost treatments on Saturday, eligible patients were invited for the study and given an informed consent form in 2 vernacular languages as per the local ethics committee requirements. Out of 36 such patients invited, 30 patients agreed to participate and constitute the CB group. Patients, who declined to take part in the study along with other eligible patients (32 patients) but not accrued in view of the limited slots availability during the study period intervals, constitute the 'CRT' group and received standard treatment of sequential boost after the conclusion of whole breast radiation.

Treatment

Patients with LABC had been treated with neoadjuvant chemotherapy to downstage the tumour, as per standard unit guidelines. About 2–6 cycles of standard chemotherapy regimens such as 5-Fluorouracil, Doxorubicin/Epirubicin and Cyclophosphamide (FAC/FEC) were employed in all patients. After maximal response to chemotherapy, patients were assessed for surgery. Suitable patients showing good response and eligible for BCT underwent breast-conserving surgery (primary tumour with a 1 cm margin of macroscopically normal tissue) and a complete axillary dissection. After surgery the remaining chemotherapy cycles were completed followed by adjuvant RT.

Radiotherapy details

Patients were simulated and planned as per standard guidelines of the unit. A contour through the breast was taken and a computer plan generated. Plan with appropriate energy and wedges was selected ensuring optimal coverage of the target volume and sparing of the heart and lungs. Care was taken to deliver adequate dose to the skin and subcutaneous tissue in view of a high risk of local recurrences in these patients. The tumour bed was determined from clinical notes, mammograms, biopsy scar and surgical clips and typically involved pre-chemotherapy volumes with a 1–2 cm margin. A computerized tomography planning scan was done to determine the optimum electron energy (typically between 9 and 20 MeV). Conventional bilateral tangential photon fields to the whole breast (6–10 MV photons) and a direct supraclavicular field (6 MV) was delivered every day from Monday to Friday for 25 fractions to a dose of 50 Gy. In addition, an electron boost to the tumour bed was also delivered every Saturday, eventually delivering 5 such weekly fractions to a boost dose of 12.5 Gy.

Evaluations

During RT, patients were evaluated every week and skin reactions recorded as per the Radiation Therapy Oncology Group (RTOG) common toxicity criteria. Skin reactions were recorded at 3 different locations namely, the tumour bed boost region, the whole breast region excluding the tumour bed region and the supraclavicular region. In addition, the cosmesis of the breast was recorded as per the 6-point EORTC breast cosmetic score before radiation,[13] at 6, 12 and 36 months of follow up. Breast cosmesis was documented by 2 investigators (physicians) independently, blinded to each other during the out patient clinic assessments.

Comparison with conventional group

Patients accrued in the CB group were compared with the CRT group, as discussed above. For comparative purposes, cosmetic scores of 1 (experienced and constant observer) were taken for patients in the CRT group.