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Full Length Article

An accelerated hypofractionated schedule with a daily concomitant boost after breast conservation surgery: the feasibility and toxicity

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Abstract *Aims and background:* Reduction of overall treatment time of postoperative irradiation and evaluation of the feasibility and preliminary toxicity of an accelerated hypofractionated whole breast irradiation with an addition of a concomitant daily boost in patients with early breast cancer submitted to conservation surgery.

Materials: Between June 2010 and September 2011, 122 patients underwent accelerated hypofractionated adjuvant radiation after conservation surgery (pT1 or pT2, pN0-N1). Radiotherapy consisted of 45 Gy, to the whole breast in 20 fractions with 2.25 Gy/fraction; an additional daily boost dose of 0.25 Gy was concomitantly delivered to the lumpectomy cavity, total dose 5 Gy. Toxicity was assessed at the end of radiation therapy and at 3, 6, and 12 months using the RTOG/EORTC toxicity scale. Cosmetic results were assessed in agreement with the Harvard criteria.

Results: Median follow-up was 31 months, 74% showed grade 0–1 skin toxicity, 20% grade 2, and 6% grade 3. At 3 months of follow-up, grade 0 skin toxicity was observed in 51% of cases; grade 1 in 36%, and grade 2 in 13%. At 6 months, late skin and subcutaneous tissue toxicities were scored as grade 0 in 71%, grade 1 in 18%, and grade 2 in 11% of patients.

At 1 year almost all the patients showed grade 0–1 skin toxicity. 97% of patients showed excellent or good cosmetic results.

Conclusions: Accelerated hypofractionated radiotherapy for early breast cancer with concomitant electron boost seems to be feasible providing consistent clinical results with acceptable toxicity profile.

Introduction

Worldwide, breast cancer is the most common cancer among females. The American Cancer Society estimates that 234,190 Americans will be diagnosed with invasive breast cancer and 10,730 will die of the disease in the United States in 2015 [1].

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Breast conservation surgery (BCS) followed by adjuvant whole breast irradiation (AWBI) remains the standard of care for early stage breast cancer. In a large metaanalysis, BCS was associated with a proven local control benefit and a gain in overall survival [2].

In addition, randomized clinical trials showed that a boost after whole-breast irradiation further improved local control. Consequently, boost RT is a widely accepted practice in patients at a higher risk of local recurrence, particularly younger patients, and those with close surgical margins. The updated results of the European Organization for Research and Treatment of Cancer (EORTC) 22,881 study, with a median follow-up of 10.8 years, demonstrated a highly significant reduction in local recurrence rates for patients randomized to a sequential boost of 16 Gy in 8 fractions, compared to those receiving no boost (6.2% vs. 10.2%, $p < 0.0001$) [3]. However, the rate of severe fibrosis in those receiving a boost was increased (4.4% vs. 1.6%, $p < 0.0001$).

Similarly, Romestaing et al. reported that an additional 10 Gy boost in five fractions was associated with decreased five-year local recurrence rates (3.6% vs. 4.5%, $p = 0.044$), however, this was associated with an increased rate of grades 1 and 2 telangiectasias (12.4% vs. 5.9%) [4].

The optimal dose, fractionation schedule, methods of delivery, and timing of the boost, remains as yet undefined. Although many centers have adopted hypofractionated breast radiotherapy as the standard for whole breast irradiation (WBI), it is still unclear how best to incorporate a boost into this hypofractionated schema, particularly from a radiobiological perspective. Three of four large randomized trials allowed a sequential boost, which typically consisted of five conventional fractions of 2 Gy each delivered with en face electrons [5–8].

In our study, we present the preliminary results in feasibility, toxicity, and cosmesis obtained from 122 patients treated with hypofractionated WBI with a daily concomitant boost (CB) regimen.

Patients and methods

One hundred and twenty-two consecutive patients with operable early-stage invasive breast cancer were treated at Tanta University hospital with hypofractionated External Beam Radiation Therapy (EBRT) as part of their breast conservation treatment (BCT) between June 2010 and September 2011.

Eligibility criteria for this protocol were histologically proved adenocarcinoma of the breast; prior BCS (namely lumpectomy or quadrantectomy); pathological stage, pT1 or pT2, pN0–1 according to America Joint Committee on Cancer (AJCC) (seventh edition) [9]; no clinical evidence of distant metastases at diagnosis.

Exclusion criteria included carcinoma in situ, locally advanced or metastatic disease, prior radiation to the thoracic region, active connective tissue disease, age >80 years, the synchronous finding of a second primary tumor, pregnancy or the presence of a concomitant psychiatric disorder precluding an aware informed consent. Patients with large breasts (separation is greater than 25 cm, that is, the breast measured more than 25 cm left to right at its widest part) were also excluded [7,10]. All patients provided written informed consent before starting treatment.

Radiation therapy was planned immediately after BCS in low-risk patients or sequentially after chemotherapy (CT) in those at higher risk of failure. Prognostic classes were assigned according to the St. Gallen Consensus Conference [11].

This protocol has been submitted and approved by our institutional ethics committee.

Volumes of interest and treatment planning

A planning CT scan was carried out for each patient from the level of the larynx to the upper abdomen including the bases of both lungs with the patient in the supine position on a ''wingboard'' with both arms raised above the head. Scan thickness was 5 mm. Radiopaque wires and markers were used to locate palpable breast tissue and visible surgical scars. Three tattoos were made on the thoracic skin to enable patient repositioning during treatment.

The CT data were transferred to the Eclipse Treatment Planning System (Varian, Palo Alto, CA, USA). The Whole Breast Clinical Target Volume (WB-CTV) included glandular breast tissue but exclude the pectoralis major, the ribs and the skin. The Whole Breast Planning Target Volume (WB-PTV) was generated by adding a 3-D 5 mm margin around the WB-CTV while a 10 mm margin was used for the cranial and caudal directions. The definition of the lumpectomy cavity was guided by the presence of surgical clips, seroma, hematoma, or other surgery-induced changes considered to be part of the cavity. The concomitant boost CTV (CB-CTV) was generated by adding at least a 10 mm margin around the lumpectomy cavity and the corresponding concomitant boost PTV (CB-PTV) was created by adding a further 5 mm 3 D margin around CB-CTV. The heart and ipsilateral lung were considered organs at risks (OARs). The ipsilateral lung was contoured in all its extension. The heart was contoured from the pulmonary trunks superiorly to its base and included the pericardium. The major blood vessels were excluded.

Treatment planning

The WB-PTV was covered by two opposing tangential beams. A multi-leaf collimator (MLC) was used to spare OARs. The appropriate gantry angles were determined in order to achieve maximal avoidance of the heart, ipsilateral lung and contralateral breast. A boost plan was created conformal to the CB-PTV, using an electron field. Wedge and MLC shielding were selected in order to obtain a 95% isodose encompassing the boost PTV. A cumulative dose-volume histogram was created to evaluate dose distribution to WB-PTV, CB-PTV, and OARs and accept the proposed plan.

Radiation fractionation and treatment

The basic course for adjuvant whole breast irradiation concomitant boost (AWBI-CB) consisted of 45 Gy, prescribed to the ICRU reference point dose delivered to the whole breast in 20 fractions with 2.25 Gy/fraction with two opposing 6 MV tangential field; an additional electron dose boost of 0.25 Gy was concomitantly delivered, on a daily basis, to the lumpectomy cavity (CB-PTV), for a total additional dose of 5 Gy. The cumulative nominal dose was 50 Gy delivered in four weeks with a daily dose of 2.5 Gy. Finally, the isocenter