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Original research article

Hypofractionation with concomitant boost using intensity-modulated radiation therapy in early-stage breast cancer in Mexico

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ABSTRACT

Aim: To evaluate whether hypofractionation with integrated boost to the tumour bed using intensity-modulated radiation therapy is an acceptable option and to determine whether this treatment compromises local control, toxicity and cosmesis.

Background: Retrospective studies have demonstrated that patients who are treated with HF and integrated boost experience adequate local control, a dosimetric benefit, decreased toxicity and acceptable cosmesis compared with conventional fractionation.

Materials and methods: A retrospective, observational and longitudinal study was conducted from January 2008 to June 2015 and included 34 patients with breast cancer (stage 0–II) who were undergoing conservative surgery.

The prescribed doses were 45 Gy in 20 fractions (2.25 Gy/fraction) to the breast and 56 Gy in 20 fractions (2.8 Gy/fraction) to the tumour bed.

Results: Thirty-four patients were included. The mean follow-up was 49.29 months, and the mean age was 52 years. The mean percentage of PTV from the mammary region that received 100% of the prescribed dose was 97.89% (range 95–100), and the mean PTV percentage of the tumour bed that received 100% of the dose was 98% (95–100).

The local control and the overall survival were 100%, and the cosmesis was good in 82% of the patients. Grade 1 acute toxicity was present in 16 patients (47%), and grade 1 chronic toxicity occurred in 6 cases (18%).

Conclusion: The results of the present study demonstrate that hypofractionation with integrated boost using intensity-modulated radiation therapy is an acceptable option that provides excellent local control and low toxicity.

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1. Background

In patients with early-stage breast cancer, the finding that treatment with conservative surgery and adjuvant radiotherapy (RT) has greater efficacy in local control (LC, i.e., a decreased risk of recurrence of up to 70% within 5 years) and overall survival (OS, i.e., 5% absolute improvement over 15 years) has been established for several decades with the support of several randomized studies.[1–4]

The boost to the surgical area was initially questioned, but 2 randomizphase III studies have confirmed that the increase to the tumour bed reduces local recurrence (LR) without deteriorating the cosmesis.[4–9] In the beginning of 2015, the results of the NCT0229033 study were reported[10]; this study was a 20-year follow-up in which the OS rates were similar in both arms, and the cumulative recurrences were 16.4% without boost vs. 12% with boost with an hazard ratio (HR) of 0.95 [99% CI (0.52–0.81), $p < 0.0001$].

Regarding conventional RT to the breast and concomitant boost to the tumour bed, there are few studies, and most of these are institutional[11–15]; these studies used fractions of 1.6–1.8 Gy with total doses of 45–51 Gy to the mammary gland and doses of 2.3–2.4 Gy per fraction (Fx) to the tumour bed for total doses of 60–73 Gy.

Hypofractionation (HF) plus sequential boost is a treatment that was proposed many years ago. The LRs over 5 years were similar in the Royal Marsden Hospital and START (A, B) studies and ranged from 9 to 14% and 2–5% to 10 years, respectively.[16,17]

HF has expanded as an option and does not involve differences from the conventional schedule regarding LC, locoregional control (LRC) or OS.[4,18–20]

There is not much phase III evidence regarding HF with concomitant boost to the tumour bed.[21–24] Few phase I—II studies have been published, and the available studies have heterogeneous numbers of patients and involve doses to the breast ranging from 2.5 to 2.7 Gy/Fx with totals of 15–20 Fx and doses to the tumour bed of 2.75–3.5 Gy/Fx.[25–30] Regarding patients over 70 years of age who have been treated with this schedule, the evidence is scarce, but the results have proven this approach to be an option for this population group.[20,31–35]

The 2018 management guides of the National Comprehensive Cancer Network (NCCN) indicate that boost to the tumour bed is indicated for those who are <50 years of age and have high-grade or focally positive margins. The boost to positive margins requires an increase of the dose to the tumour bed and may increase fibrosis. Therefore, caution is required for an indication for an additional dose to this site.[1]

The present study utilized HF to the breast with concomitant boost to the tumour bed using intensity-modulated radiation therapy (IMRT) based on the schedule proposed by Freedman et al. in which the dose is maintained, while the boost energy is modified.

2. Aim

- Evaluate whether HF with concomitant boost applied through IMRT is an acceptable technique.
- Determine whether this radiation technique compromises local control, toxicity or cosmesis.

3. Materials and methods

This is a retrospective, observational and longitudinal study that was conducted from January 2008 to June 2015 in the Radiotherapy Unit of the Hospital General de Mexico. Thirty-nine cases were reviewed, and 5 were excluded because they did not meet the inclusion criteria. Therefore, 34 patients were included in the study. The inclusion criteria were as follows: patients who had been subjected to conservative surgery with a histopathological diagnosis of breast cancer in the initial stage (pTis-T2) according to the American Joint Committee on Cancer (AJCC, 6th edition), tumours < 3 cm, negative lymph nodes (N0), and older than 40 years of age. The exclusion criteria were as follows: patients younger than 40 years, multifocal disease, positive lymph nodes, synchronous or metachronous disease, collagen disease, second primary disease, surgery outside the hospital, and previous radiation therapy (Fig. 1).

The included patients received an HF schedule with concomitant boost to the tumour bed using IMRT. The dose to the mammary area was 45 Gy in 20 Fx, and the dose to the tumour bed was 56 Gy in the same number of fractions.

3.1. *Simulation, volume definition and planning*

The patients were placed in the supine position with both arms above the head level, and a ramp was used under the breast. In cases of patients with voluminous breasts, prone ramps were used. The patients were aligned, and we defined the origin using lasers. Radiopaque marks were placed on the surgical scar and on the drainage sites. Planning was performed using axial images from tomography with 5-mm cuts from the lower border of the jaw extending to 2–3 cm below the inframammary border.

The computed tomography (CT) scans were sent to the Eclipse planning system version 7.3.10 from 2004 to 2014 and to the Eclipse 13 version beginning in 2015. The volume definitions were based on the International Commission on Radiation Units and Measurements (ICRU) 50, and the volumes were defined for the mammary region and the tumour bed. The clinical target volume (CTV) of the breast was defined to include all mammary tissue, and the planning target volume (PTV) was created by allowing a 3-mm margin from the mammary CTV. The tumour bed was outlined from the surgical clips that were placed during surgery, a 3–5-mm margin was given to create the CTV from the site, and the PTV of the tumour bed was created by allowing a 5-mm margin from the CTV of the site. The mammary PTV was maintained 3 mm under the skin in all cases.

The risk organs were outlined and included the ipsilateral lung, heart (including the pericardium), pulmonary trunk and contralateral breast. The contralateral lung was outlined but was not included as a risk organ.

The treatment plan was executed in all patients with the forward IMRT technique with multiple beams (7–9 fields) using a step-and-shoot approach with a photon energy of 6 MV (MV). Fields with a perpendicular entrance to the breast were