



## Comparison of Acute Toxicities in Conventional and Hypofractionated Radiotherapy in Post-Mastectomy Breast Cancer

(Research Article)

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### Abstract

**Background:** Breast cancer is one of the most frequently diagnosed malignancy in women worldwide. A multimodality approach is usually preferred for treatment of all the patients for local regional and systemic control of the disease. In recent times, there has been a gradual improvement in radiotherapy delivery and has shifted from conventional to hypofractionated radiotherapy with equivocal results. This article highlights the acute toxicities in conventional and hypofractionated radiotherapy.

**Aim:** To study the acute toxicity in terms of skin reaction, dysphagia and arm oedema. **Material and methods:** This prospective study was conducted at the Department of Radiation Oncology, Acharya Tulsi Regional Cancer Treatment & Research Institute, Bikaner. From Jan 2014 to Dec 2014; fifty patients of post-MRM carcinoma breast stage IIA-III A (pT1-3, pN1-2) were enrolled for the study. Informed consent patients was taken. Arm A: 50 Gy / 25fractions, over 5weeks. Arm B: 40 Gy / 15 fractions, over 3 weeks. Patients were kept supine with arm abducted to 90 degrees or higher and were treated with two field technique by using Co-60 energy source on Theratron 780C or Bhabhatron-II. Toxicity was documented according to CTCAE 3.0 version. Raw or cream Aloe-vera application to the irradiated skin was advised in every patient. P values of <0.05 were considered to be statistically significant.

**Results:** skin reactions observed at end of RT in 68% v/s 44% (P=0.023) and at 3 months, 12% v/s 4% (P=0.045). Grade 2 reactions were seen in 28% v/s 8% (P=0.0008), Grade 3 reactions were also significantly lower in study arm 4% v/s 12% (P=0.045). At the end of RT, study arm had grade 1&2 dysphagia in 32% v/s 12% patients in control arm (P=0.002). At 1 month dysphagia observed in 16% patients in study arm v/s 4% in control arm (P=0.007). No patient had grade 3 or higher dysphagia. At the end of RT, cosmetic appearance was equivocal. But at 1 month, cosmetic appearance was significantly better in study arm 80% v/s 52% (P=0.014). 32% had moderate arm edema in control arm as compared to 28% in study arm (P value = 0.28).

**Conclusion:** Present study has proved it slightly better or equivocal with conventional fractionation for post-mastectomy irradiation in terms of tolerance. Thus hypo-fractionation schedule can be adopted as a standard form of treatment in post-mastectomy patients.

**Keywords:** Breast cancer, Hypofractionation, Acute toxicities, Radiotherapy.

## Introduction

Breast cancer is the most frequently diagnosed cancer in India and worldwide and is the leading cause of cancer death among females.<sup>1,2</sup> Radiotherapy (RT) is an integral part of treatment of breast cancer and indicated in selected patients after modified radical mastectomy(MRM).<sup>3</sup> In India most of the patients undergo MRM, followed by conventional fractionation schedule which delivers a total dose of 50 Gy in 25 fractions at 2 Gy per fraction treated 5 days a week.<sup>4,5</sup> It usually takes 6-7 weeks to complete the radiotherapy treatment by conventional fractionation. Hypofractionation is now widely practiced in post-mastectomy patients. The largest studies on hypo-fractionation in breast cancer was UK standardization of Breast Radiotherapy (START A&B).<sup>6,7</sup> Long term results of these trials are now available and have encouraged radiation oncologists all-over the world to adopt hypo-fractionation in breast cancer patients.<sup>8</sup> In START trial B, hypo-fractionated schedule of 40 Gy in 15 fractions was delivered in 3 weeks.<sup>7</sup> some centers in India have started practicing this hypo-fractionated schedule in post-mastectomy patients, the data for hypo-fractionation is lacking. In this study we aim to evaluate the acute toxicities of schedule using 15 fractions of 2.66Gy compared to conventional fractionation in post-mastectomy radiotherapy.

## Aim

To study the acute toxicity in terms of skin reaction, dysphagia and arm oedema.

## Materials & Methods

This prospective study was conducted at the Department of Radiation Oncology, Acharya Tulsi Regional Cancer Treatment & Research Institute, Bikaner. From Jan 2014 to Dec 2014; fifty patients of post-MRM carcinoma breast stage IIA- IIIA (pT1-3, pN1-2) were enrolled for the study. Inclusion Criteria were patients between 18-65 years, ECOG performance score 0-2, with biopsy proven invasive carcinoma of breast that

underwent MRM and received adjuvant chemotherapy as per institute protocol and referred for adjuvant radiotherapy. Exclusion Criteria were locally advanced or metastatic carcinoma breast, severely deranged liver and kidney function tests, uncontrolled co-morbidities and previously irradiated on chest wall and/or neck region. After written informed consent patients were randomized to two arms of equal strength. Arm A: 50 Gy / 25fractions, over 5weeks. Arm B: 40 Gy / 15 fractions, over 3 weeks. Patients were kept supine with arm abducted to 90 degrees or higher and were treated with two field technique by using Co-60 energy source on Theratron 780C or Bhabhatron-II. Chest wall was treated by medial tangential and lateral tangential beams. Supraclavicular field was treated if indicated by antero-posterior beam. To reduce the incidence of radiation pneumonitis, the lung volume treated in the tangential fields was leveled by keeping central lung distance to  $\leq 3$  cm. Weekly review was done to assess compliance, toxicity and was documented according to CTCAE 3.0 version. Treatment was prescribed to all patients for prevention and treatment of radiation induced skin toxicities according to institute protocol. Raw or cream Aloe-vera application to the irradiated skin was advised in every patient. Dietary advice and treatment was prescribed for the radiation induced dysphagia according to institute protocol. Statistical Analysis was done using SPSS 20.0 software. P values of  $<0.05$  were considered to be statistically significant. 1<sup>st</sup> follow-up of patients was after 1 month of completion of radiotherapy; subsequent follow up at 3 monthly interval.

## Results

At the end of RT, 68% patients in the control arm whereas 44% in study arm had skin reactions (P=0.023). At 3 months follow-up, 12% patients in control arm whereas 4% in study arm had skin reactions (P=0.045). Grade 2 reactions were seen in 28% patients in control arm whereas only 8% patients in study arm (P=0.0008). Grade 3

reactions were also significantly lower in study arm 4% v/s 12% in control arm ( $P=0.045$ ). No patient in either arm had grade 4 or higher skin reactions. At the end of RT, study arm had grade 1&2 dysphagia in 32% cases as compared to 12% patients in control arm ( $P=0.002$ ). At 1 month follow-up 16% patients in study arm had dysphagia v/s 4% in control arm ( $P=0.007$ ). No patient had grade 3 or higher dysphagia. At the end of RT, there was non-significant difference between good to average cosmetic appearance 56% in control arm v/s 64% in study arm ( $P=0.46$ ). But at 1 month follow-up, there was significant improvement in cosmetic appearance; 52% in control arm v/s 80% in study arm ( $P=0.014$ ). From 3 months on this difference becomes non-significant. 32% had moderate arm edema in control arm as compared to 28% in study arm ( $P$  value = 0.28).

### Discussion

In this study there was a significant difference in the occurrence of acute reactions between the two arms at the end of radiotherapy. Overall rate of skin reactions was 68% in conventional fractionation as compared to 44% in the hypo-fractionation arm ( $P$  value = 0.023). Grade 2 skin reaction was observed in 28% in the control arm as compared to only 8% in study arm ( $P$  value = 0.0008). Grade 3 reactions were also significantly lower in the hypo-fractionation arm. Only about 4% patients had grade 3 reaction in the hypo-fractionation group with no grade 4 toxicity noted in any of the patients. At the completion of 6 months post radiotherapy no patient had a persisting erythema. Thus radiotherapy was very well tolerated by the Indian population with very less acute skin toxicity.<sup>9</sup>

In our study, aloe-vera application was advised in all patients for prevention and treatment of radiation induced skin reactions as per institute protocol. Aloe-vera application had reduced incidence and severity of skin reactions. This also led to earlier recovery of skin reactions. No patient had residual pigmentation at 6 months

follow-up. In this study, there was a significantly higher incidence of dysphagia among the patients of the hypo-fractionation arm as compared to conventional arm. At the end of radiotherapy 32% patients in hypo-fractionation arm had grade 1 or 2 dysphagia v/s only 12% in the conventional fractionation. There was no grade 3 or higher dysphagia in any patient. Dysphagia began to appear in the second week onward and peaked till the end of radiotherapy. At 1 month follow-up 16% patients in the hypo-fractionation arm had persistent dysphagia whereas only 4% in conventional arm. There was no persistent swallowing difficulty beyond 3 months follow-up. The dysphagia was managed appropriately with standard treatment including dietary modifications, topical anesthetics such as viscous lidocaine, proton pump inhibitors, and promotility agents. No patient required Ryle's tube feeding. Arm edema was comparable between the two arms. There was gradual increase in number of patients with mild to moderate arm edema in both the arms. 32% had moderate arm edema in control arm as compared to 28% in study arm ( $P$  value = 0.28).

To summarize, hypo-fractionation in breast cancer is an issue that can have widespread implications in breast cancer throughout the world. Overall hypo-fractionation has proved to be slightly better or equivocal with conventional fractionation for PMRT. This has an added advantage of reducing the overall treatment time by almost 2 weeks per patient which helps to reduce the machine load.

### Conclusion

Acute skin reactions were significantly lower in the hypofractionation arm. However manageable dysphagia (grade 1&2) appeared in significantly higher number of patients (about 1/3rd) in the hypo-fractionation arm. Pneumonitis and arm oedema were comparable between the two arms. Hypo-fractionation has evolved as standard treatment of post-mastectomy. Present study has proved it slightly better or equivocal with conventional fractionation for post-mastectomy

irradiation in terms of tolerance. Thus hypofractionation schedule can be adopted as a standard form of treatment in post-mastectomy patients.

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