

# 5 Years Local Recurrence Rates Following Post-Operative 2D Radiotherapy Treatment Planning Patients – An Institutional Experience

Maitrik J. Mehta, Dhal Shikha, Suryanarayan U

Department of Radiation Oncology, The Gujarat Cancer & Research Institute, New Civil Hospital Campus, Asarwa, Ahmedabad-380016, Gujarat, India

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Maitrik J. Mehta

## ABSTRACT

**Introduction:** In India, almost 150,000 women are diagnosed with breast cancer every year and almost half of patients expected to die of the disease. In India most of patients with breast cancer diagnosed with advanced stage of the disease. As breast cancer treatment is multimodality approach Radiation therapy has significant impact on prevention of local recurrence. So, purpose of the study is to assess 5 year rates of local recurrence following post-operative 2D Radiotherapy treatment planning.

**Methods and Materials:** We have selected 198 patients treated for post-operative 2D Radiotherapy treatment planning from September 2009-September 2010. All patients had undergone surgery in form of mastectomy or modified radical mastectomy. None of the patients with breast conservation surgery had been selected. All patients underwent chemotherapy either Induction chemotherapy following surgery or chemotherapy after surgery. All patients had been treated with 2D conventional Radiotherapy treatment plan with tangential fields and supraclavicular and axillary fields according to histopathology report. Patients were first taken on simulator machine and planning was done with breast wedge in position and fully abducted arm of the patient. Radiotherapy treatment dose was – 45Gy/20#, 2.25Gy/#, 5 days/week, total 4 weeks of treatment. Patients were assessed for acute toxicity every week. Patients were followed every monthly for 2 years, 2 monthly for 3<sup>rd</sup> year, 4 monthly for 4<sup>th</sup> year up to 5 year. Patients were assessed for Local recurrence up to 5 years.

**Results:** 152 (77%) patients had undergone upfront Surgery. 46 (23%) patients were diagnosed with LABC, and had undergone chemotherapy first for downstage of the disease. After a median follow up of 34 months (range: 9-67 months), out of total 198 patients, 8.6% patients developed local recurrence. In which 6.5% (10 patients out of 152) in upfront surgery group and 15.2% (7 patients out of 46) in LABC group developed local recurrence. So, total 5% (10 patients) in upfront surgery group and 3.5% (7 patients) in LABC group out of 198 total patients developed local recurrence.

**Conclusion:** Local recurrence after treatment of breast cancer with mastectomy+radiotherapy+/-systemic therapy is associated with a significantly higher risk of distant metastasis and death. So, in this retrospective study we have shown comparable results after 2D Conventional Radiotherapy Treatment Planning for prevention of local recurrence. Approach is safe, easy, and feasible, less time consuming and in Indian scenario where patients come in advanced stage of the disease and most of the time death is due to disease itself it is quite suitable approach at our centre. Also, we use hypofractionation regimen of 45Gy/20#, which is also feasible to reduce total treatment time and it has also shown equivalent results.

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## INTRODUCTION

In India, almost 150000 women are suffering from Breast cancer every year. Nearly half of them die due to the disease.<sup>1</sup> Breast cancer management is multimodality approach including Chemotherapy, Surgery, and Radiotherapy and Hormonal treatment<sup>2-4</sup> Breast cancer

## Corresponding Author:

Dr. Maitrik J. Mehta, Associate Professor, Department of Radiation Oncology, The Gujarat Cancer & Research Institute, New Civil Hospital Campus, Asarwa, Ahmedabad-380016, Gujarat, India, Mobile: +919825947472 E-mail: dr\_maitrik@yahoo.co.in

is considered as systemic disease from initial presentation.<sup>5-7</sup> Radiotherapy has been considered as local treatment after mastectomy/modified radical mastectomy/breast conservation surgery to prevent local recurrence in breast cancer.<sup>8-10</sup> It can also be used as local treatment to palliate symptoms of metastatic disease. Local recurrence after surgery is significantly worse prognostic factor for survival of breast cancer patients. So, Radiotherapy has a major role after surgery as a local treatment to prevent local recurrence.<sup>11,12</sup>

From long time 2D Conventional Radiotherapy Treatment Planning is used for breast cancer patients to prevent local recurrence. At our Regional Cancer Centre, we have almost 300 new breast cancer patients for local post-operative Radiotherapy Treatment. In most of the patients, we use 2D Conventional Radiotherapy Treatment Planning as local treatment.

In this article, we did retrospective analysis to assess effect of 2D Conventional Radiotherapy Treatment planning for prevention of local recurrence.

Intensity Modulated Radiotherapy treatment planning is also used to prevent late side effects in form of cardiac and lung toxicity.<sup>13,14</sup> But, we have very high number of patients for treatment, and also acceptable local recurrence results, so we use 2D Conventional Radiotherapy Treatment in most of our patients.

From long time conventional fractionation 50Gy/25# has been used as standard fractionation regimen.

We use hypofractionation regimen that lasts 4 weeks of treatment.<sup>15</sup> Dose we use is 45Gy/20#. 2D Conventional Radiotherapy Treatment technique is simple, safe, less time consuming and most feasible approach.

In India, most of patients come with initial presentation of advanced stage of the disease and where more than half of patients die due to disease itself and also in most number of patients surgery is done mostly either mastectomy/modified radical mastectomy, 2D Conventional Radiotherapy Treatment approach is quite appropriate. So, we have shown local recurrence rates due to 2D Conventional Radiotherapy approach as it is significant worse prognostic factor for distant metastasis and death.

## METHODS AND MATERIALS

From September 2009- September 2010, 238 patients were referred for post-operative Radiotherapy treatment to our Radiotherapy department. Out of them, 198 patients were eligible for this retrospective analysis of Post-operative 2D Conventional Radiotherapy Treatment Planning. In all

patients written consent was taken. All patients underwent mastectomy/modified radical mastectomy. Patients age was >20 years and <75 years.

The initial evaluation included chest x-ray, ultrasonography of abdomen and pelvis region, bone scan in selected patients, blood count, renal and liver function tests. All patients were assigned for 2D Conventional Radiotherapy Treatment Planning with dose of 45Gy/20#, 2.25Gy/#, total 4 weeks of treatment.

## Radiation Technique

All patients were planned using 2D system, with two tangential portals for chest wall with breast wedge in position using simulator-based planning. Direct anterior field to the supraclavicular and axillary areas were planned where lower border of supraclavicular field matches upper border of tangential field.<sup>16</sup>

Patients were treated in supine position with use of breast wedge. (Figure 1) Patients were treated using 6-MV linear accelerator. The Superior border at 2nd Intercoastal space and inferior border at 2cm below the contralateral infra-mammary fold. The medial border of target volume was at mid-sternal line, lateral border at mid-axillary line. (Figure 2) The medial border at mid-sternal line and lateral border at mid-axillary lines are marked to include the chest wall and to limit the lung volume at the central plane to less than 2-2.5 cm. (Figure 3).

We did not use bolus as tangential fields have self-bolusing effect.



Figures 1: Patient in supine position with Breast Wedge on simulator machine

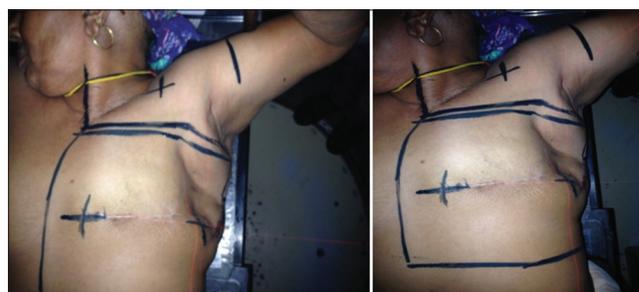


Figure 2: Tangential breast planning with Superior border at 2<sup>nd</sup> Intercoastal space, Inferior border at 2 cm below opposite inframammary line, Medial border midsternal line, and Lateral border midaxillary line. Also, Supraclavicular field drawn



**Figure 3:** To limit the lung volume at the central plane to less than 2-2.5 cm

In patients with skin positivity from initial presentation or after surgery in histopathologic examination we gave 10Gy/5# electron boost to whole local area with 6-8 MeV electrons.<sup>17</sup>

### Assessment for Local Recurrence

The primary endpoint was local recurrence in all patients. We assess patients for loco-regional recurrence as it is significant worse prognostic factor for distant metastasis and death.

## RESULTS

198 patients were eligible for 2D Radiotherapy Treatment Planning. 152 patients were initially treated by Mastectomy/ Modified Radical Mastectomy and 46 patients who were in initial presentation with locally advanced breast cancer (LABC), they were initially assigned to receive neo-adjuvant chemotherapy<sup>18-21</sup> followed by surgery was done. In patients with upfront surgery chemotherapy was given afterwards. In locally advanced breast cancer also who were not completed full chemotherapy cycles presurgery were given chemotherapy after surgery. Average age was 48.5 years (range 22-75 years). Most of the patients were with performance status I.

We have depicted all data in Table 1.

### Disease Characteristics

Tumor size:

- In patients with Up front surgery group – 52% patients were PT2 tumor size, 22.3% with PT3 and 18.4% with PT4 disease.
- In patients with LABC where chemotherapy was given first – 26.1% patients were PT2 tumor size, 17.4% with PT3 and 50% patients with PT4 disease.
- In combined analysis – 46% patients with PT2, 21.2% with PT3, 25.8% with PT4 disease.

Nodal status:

- From above chart, it can be clearly seen that in Upfront

surgery group most of the patients are in PN1 status and in LABC group most of the patients are in PN3 status.

### Treatment Characteristics

- In one patient, initially surgery was done and HPE was P3N2MO and no adjuvant Rx was given. Then patient developed local recurrence after 9 months. Then 4 cycles of chemotherapy was given and local clinical examination showed pigmentation over chest wall and local RT Rx was given.
- Another patient, Lumpectomy was done followed by surgery was done then patient received 6 cycles of chemotherapy. Then patient developed recurrent nodule – Wide local excision was done then local RT Rx was given
- In 2 patients chemotherapy was not given

In rest all patients, treatment was regular and on time.

In all patients radiotherapy treatment was started within 6 months post-surgery period.

All patients completed treatment without break. For all patients, tolerance was good and patients completed 4 weeks of Radiotherapy treatment without treatment break.

### Local Recurrence Data Analysis

After a median follow up of 34 months (range: 9-67 months), out of total 198 patients, 8.6% patients developed local recurrence.

In which 6.5% (10 patients out of 152) in upfront surgery group and 15.2% (7 patients out of 46) in LABC group developed local recurrence.

So, total 5% (10 patients) in upfront surgery group and 3.5% (7 patients) in LABC group out of 198 total patients developed local recurrence.

Here, it can also be seen that axillary lymph node involvement is most important risk for local recurrence.

## DISCUSSION

Adjuvant irradiation in high risk patients reduces risk of locoregional recurrences to  $\leq 10\%$ . In multivariate analysis, it was proven that the greatest benefit is obtained in patients who have tumor size more than 7.5 cm and/or axillary node positive status.<sup>22,23</sup>

In the Eastern Cooperative Oncology Group (ECOG) study, node positive patients who received adjuvant chemotherapy alone without irradiation, the loco-regional recurrences remained high. Thus systemic chemotherapy in these high

**Table 1: Demographic characteristics, T-stage, N-staging and chemotherapy regimens given for patients**

	Upfront surgery 152	LABC 46	Total 198
Age			
20-29	2	2	4
30-39	29	14	43
40-49	51	10	61
50-59	41	12	53
60-69	25	7	32
70-79	4	1	5
Site of breast			
Right	87	24	111
Left	65	22	87
Tumor size (%)			
pT1	11 (7.2)	3 (6.5)	14 (7.1)
PT2	79 (51.9)	12 (26.1)	91 (46)
PT3	34 (22.3)	8 (17.4)	42 (21.2)
PT4	28 (18.4)	23 (50)	51 (25.8)
Nodal status (%)			
PNO	17 (25.8)	10 (21.7)	27 (12.1)
PN1	58 (88.2)	13 (28.2)	71 (35.8)
PN2	46 (69.9)	10 (21.7)	56 (28.2)
PN3	31 (47.1)	14 (30.4)	45 (22.7)
Chemotherapy Rx	11 4 AC 4 paclitaxel	3 3 FEC - Sx - 3 docetaxel	
	3 3 FAC	6 3 TAC - Sx - 3 TAC	
	61 6 FAC	3 6 FAC - Sx	
	2 6 AC	4 4 FAC - Sx - 4 taxol	
	3 3 FEC	5 3 FAC - Sx	
	1 4 AC F- 12 wk pacli	1 3 pacli+carbo - Sx - 3 pacli+carbo	
	7 4 AC	3 3 FAC - Sx - 3 taxol	
	1 3 TAC	2 3 FAC - Sx - 4 docetaxel	
	2 6 docetaxel	1 3 FAC - 3 docetaxel - Sx	
	6 6 FEC	1 6 AC - Sx	
	1 4 docetaxel	1 3 AC - Sx - 4 paclitaxel	
	1 6 CMF	5 3 FAC - Sx - 3 FAC	
	2 3 FAC 4 docetaxel	1 3 FAC - Sx - 3 FEC	
	3 3 FAC 3 Pacli	1 4 FAC - Sx - 2 FAC	
	6 3 FAC 3 docetaxel	1 3 FAC - Sx - 4 FAC	
	4 3 FEC 3 docetaxel	1 6 TAC - Sx	
	1 3 FAC 3 TAC	1 3 FEC - Sx	
	2 3 AC	1 3 FEC - Sx - 3 pacli+carbo	
	2 4 FAC 4 docetaxel	1 5 CMF - Sx	
	1 4 AC 2 paclitaxel		
	1 6 pacli+epirubicin		
	2 6 TAC		
	1 4 EC 12 wkly pacli		

risk patients does not influence the loco-regional control and addition of postoperative RT is strongly recommended.<sup>23</sup>

Joint analysis of long-term results from the Oslo and Stockholm trials statistical analysis showed a significant reduction in distant metastasis and improvement in the overall survival for the irradiated patients.

The Danish Breast Cancer cooperative group randomized trial was done to involve 1708 pathological stage II or III breast cancer cases. High risk factors defined as one or more

of following: involvement of axillary lymph nodes,  $\geq 5$  cm tumor size, infiltration of skin or pectoral fascia. 852 women assigned to receive 8 cycles if CMF plus irradiation of the chest wall and regional lymph nodes. 856 women assigned to receive 9 cycles of CMF alone. Loco regional recurrence alone or distant metastasis was 9% among women who received radiotherapy plus CMF and 32% among those who received CMF alone ( $p < 0.001$ ). The probability of disease free survival after 10 years was 48% among women assigned to radiotherapy plus CMF and 34% among those treated by CMF alone ( $p < 0.001$ ).

Multivariate analysis demonstrated that irradiation after mastectomy significantly improved disease-free survival and overall survival, irrespective of tumor size, the number of positive nodes or the histopathological grade.<sup>24</sup>

It has also been proved that local recurrence increase the risk of death by a factor of 1.7 and in a Cox regression model, axillary lymph node status, T-category and local recurrence were significant prognostic factors for overall survival.

The current study is retrospective and single large arm. With two groups we have divided for better understanding of recurrence pattern of disease. (Table 1). It confirms feasibility of 2D Conventional Radiotherapy Treatment Planning as most of the patients are in loco-regionally advanced stage of the disease. Most of the patients are  $\geq 30$  years of age.

After a median follow up of 34 months (range: 2-67 months), out of total 198 patients, 8.6% patients developed local recurrence.

In which 6.5% (10 patients out of 152) in upfront surgery group and 15.2% (7 patients out of 46) in LABC group developed local recurrence.

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Here, it can also be seen that axillary lymph node involvement is most important risk for local recurrence.

Dunst J et al<sup>25</sup> did a retrospective study to analyze impact of local recurrence in patients with adjuvant radiation therapy after mastectomy for breast cancer. They analyzed 959 patients for the study. All patients were irradiated after mastectomy. The Median follow up of 3.1 years (0.3-12.2 years). 35% had T3-T4 tumors, 62% had axillary lymph node involvement and 66% received systemic hormonal and/or cytotoxic therapy. They used dose of 50Gy in 2Gy/#.

- In our study 46% had PT3-T4 tumor. And 88% had axillary nodal involvement.

In their study overall survival was 70.5% after 5 years and 59.8% after 10 years. 5.5% developed loco regional recurrence 2-96 months after treatment (median 26 months). The local control rate was 92.7% after 5 and 86.4% after 10 years.

- In our study too, after a median follow up of 34 months (range: 9-67 months), out of total 198 patients, 8.6% patients developed local recurrence.

The study contains small number of patients and comparatively short period of follow up that represent major limitations for the conclusion. Finally, this study shows equivalent results with other trials and it also shows efficacy of 2D Conventional Radiotherapy Treatment Planning to prevent local recurrence rates.

Another point to note that, In India, and at our cancer centre, most of the patients comes with advanced stage of the disease and it can also be seen in this data. It is also clear to state that most of the patients in India die due to disease itself.

2D Conventional Radiotherapy Treatment Planning is safe, efficacious, less time consuming and gives svery good results to prevent local recurrence which is significantly important prognostic factor for distant metastasis and death.

We also use hypofractionation 45Gy/20#, so we are reducing time to total treatment also. We are reducing time to 4 weeks instead of 5-6 weeks on conventional fractionation base. This fractionation regimen also gives equivalent results. And we can enroll more patients for treatment planning. This would result in substantial economic benefit as breast cancer patients represent majority of patients treated in radiotherapy departments.

In this article, we did not assess for overall survival or assessment for toxicities because our prime importance was on assessment for local recurrence only. As 2D Conventional Radiotherapy Treatment Planning is most common approach in our setup and Local recurrence is significantly worse prognostic factor for distant metastasis and death.

## CONCLUSION

Local recurrence after treatment of breast cancer with mastectomy+radiotherapy+/-systemic therapy is associated with a significantly higher risk of distant metastasis and death.

So, in this retrospective study we have shown comparable results after 2D Conventional Radiotherapy Treatment Planning for prevention of local recurrence. Approach is safe, easy, feasible, less time consuming and in Indian scenario where patients come in advanced stage of the disease and most of the time death is due to disease itself it is quite suitable approach at our centre.

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