

**Role of Post Mastectomy Radiotherapy in T1,T2 Lesions with 1-3 Positive Axillary Lymph Nodes - A Retrospective Study of 101 Cases.**

Dr Rajen Tankshali\*, Dr Nikhil Garg\*\*, Dr Manish Sadhwani\*\*

\*Professor head of unit, \*\*Resident, Surgical oncology, Gujarat Cancer and Research Institute, Ahmedabad

**KEY WORDS** : Breast Cancer, Mastectomy, Radiotherapy

Postmastectomy radiation (PMRT) has been shown in multiple randomized trials to reduce locoregional recurrence (LRR) rates and improve survival in women with locally advanced breast cancer.<sup>1</sup> There is international consensus to recommend PMRT for patients with tumour size more than 5 cm (T3), tumour invasion of the skin, pectoral muscle or chest wall (T4) and patients with > 4 positive lymph nodes (LN). The role of PMRT in patients with early-stage T1-2 disease with limited nodal metastasis remains a subject of ongoing debate.<sup>2</sup> Controversy surrounding the optimal locoregional management of the subset with one to three positive nodes stems from conflicting data on the benefits of PMRT in this population. The side effects of radiotherapy and its associated morbidity have to be considered in the risk benefit ratio, thus difficult to arrive at consensus in early breast cancer.<sup>3</sup> This study reports the findings from use of post operative RT (radiotherapy) on such less afflicted patients at tertiary regional cancer centre in India.

**OBJECTIVES**

1. Does RT decrease LRR (locoregional recurrence) & SR (systemic recurrence) in T1, 2 N1 disease post mastectomy?
2. Does RT decrease OR (overall recurrences) if PNE (perinodal extension) is present?
3. Does RT decrease OR in case of LVI (lymphovascular invasion)?
4. Does RT improve disease free survival?

**MATERIAL AND METHODS**

We collected data after approval from our institutional board review committee and analysed case files of patients who presented and were treated at our governmental tertiary referral centre from a period between 2014-2017. Of the 691 patients who underwent mastectomy, we short listed 101 cases for our study who fulfilled our basic inclusion criteria of T1,2 N1 on final histopathology.

**INCLUSION CRITERIA**

Female, unilateral breast cancer, M0 at initial diagnosis

Surgery - Mastectomy &amp; ALND

Postoperative pathology - T1-2 and 1-3 +ve axillary LN (T1-2N1M0) disease, at least 10 LN removed by ALND

Complete surgical resection of the tumor and negative margins

Complete (ER), (PR), (Her2) status

No neoadjuvant chemotherapy given

**Exclusion Criteria**

Patient operated outside

**Prior Radiotherapy**

In order to study the research questions, we formulated hypotheses as follows, 1. Radiotherapy does not have any impact on recurrence post mastectomy. 2. There is no influence of Perinodal extension on recurrence. The above hypotheses were tested using chi-square test, unpaired student t-test, Fisher Exact test. A p-value of less than 0.05 was considered significant.

Of the 101 patients, 60 patients who received radiotherapy and 41 who did not were selected for retrospective purposeful evaluation.

All 101 patients had received adjuvant chemotherapy and hormone receptor positive patients received endocrine therapy. Commonly used chemotherapy regimens are AC followed by Docetaxel, Dose-dense AC, TAC regimen.

RT was delivered with conventional 2D technique, dose given was 50Gy in 25 fractions at the rate of 2 Gy per fraction over a period of 5 weeks.

**Correspondence Address** : Dr. Rajen Tankshali  
88, Goyal Park Row House, Premchand Nagar Road,  
Vastrapur, Ahmedabad-380015.

## RESULTS

Radiotherapy was given in 60 patients and 41 were not given. Recurrences were obtained in 9 amongst radiotherapy and without radiotherapy in 16. When chi square was applied with 1 degree of freedom, the value was highly significant at 0.006 with 99% CI. Hence our hypothesis was rejected.

### 1. Loco-Regional Recurrence (LRR)

	LRR	No LRR
RT	2	58
No RT	9	32

Fisher's Exact probability test,  $p = 0.0065$

LRR in patients receiving radiotherapy was 3.33%, in patients whom radiotherapy was not offered LRR was 21.95%.

### 2. Systemic Recurrence (SR)

	SRR	No SRR
RT	4	56
No RT	10	31

Fisher's Exact probability test,  $p = 0.0060$

SR in patients receiving radiotherapy was 6.66%, in patients whom radiotherapy was not offered SR was 24.39%.

**3. Perinodal extension (PNE) Perinodal extension was observed in 52 patients out of 101. 35 of this patients with PNE received RT, while 17 didn't.**

	Recurrence	No Recurrence
RT + PNE	8	27
RT + No PNE	1	24
No RT + PNE	11	6
No RT + No PNE	5	19

$p$ -value of 0.0013

In patients with PNE, **Recurrence** in patients who received radiotherapy was **22.85%**, in patients who didn't recurrence was **64.70%**. Similarly in patients with No PNE, **Recurrence** in patients who received radiotherapy was **4.0%**, in patients who didn't recurrence was **20.83%**.

### 4. Lymphovascular invasion (LVI)

Lymphovascular invasion was seen in 33 of 101 patients. 23 of this patients with LVI received RT, while 10 didn't.

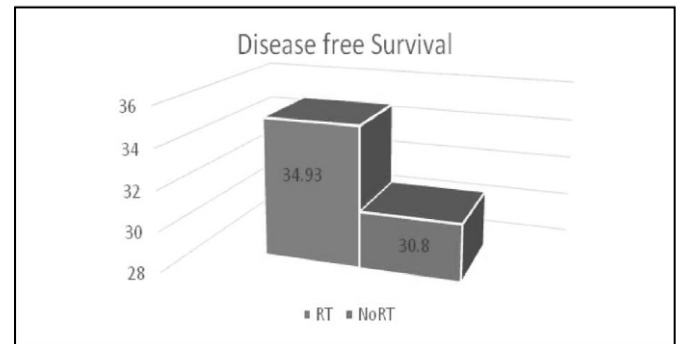
	Recurrence	No Recurrence
RT + LVI	5	18
RT + No LVI	1	36
No RT + LVI	7	3
No RT + No LVI	9	22

$p$ -value of 0.0081

In patients with LVI, **Recurrence** in patients who received radiotherapy was **21.93%**, in patients who didn't recurrence was **70%**. Similarly in patients with No PNE, **Recurrence** in patients who received radiotherapy was **2.70%**, in patients who didn't recurrence was **29.03%**.

### 5. Disease Free Survival (DFS)

Overall disease free survival in patients receiving radiotherapy was 34.93 months and those with no radiotherapy it is 30.8 months. The value of unpaired student t-test was 2.309 with a significant  $p$ -value of 0.023.



## DISCUSSION

The absolute risks of breast cancer recurrence and mortality have reduced in many countries because of advances in detection and treatment of breast cancer.<sup>4</sup>

A 2014 update of the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) metaanalysis demonstrated that patients with one to three positive lymph nodes who underwent axillary dissection and received systemic therapy had a significant reduction in 10-year isolated LRR (21.0 vs. 4.3%) and 20-year breast-cancer-specific mortality (49.4 vs. 41.5%) with PMRT<sup>5</sup>. In accordance to the findings of **EBCTCG meta-analysis**, our findings strongly suggest that Radiotherapy may be considered for T1, 2 N1 patients.

Some believe, however, that it is difficult to interpret these results in the era of modern surgical techniques and

enhanced systemic therapy, as many of the trials included in the metaanalysis were conducted in the 1970s and 1980s.

The European Organization for Research and Treatment of Cancer (EORTC) 22922 trial included patients undergoing lumpectomy or mastectomy (24%), with 43% having N1 disease and 44% having N0 disease. While an overall survival benefit was not observed in this trial, it showed improved disease-free survival (DFS) and distant DFS with regional nodal irradiation, and improved breast cancer mortality.<sup>6</sup>

In a large single-institution retrospective analysis of 1087 patients from the Memorial Sloan Kettering Cancer Center, **Moo et al.** reported 5-year LRR rates of 4.3% without PORT and 3.2% with PORT.<sup>7</sup>

**Two** ongoing randomized trials should help to provide clarity on this subject. The **Selective Use of Postoperative Radiotherapy After Mastectomy (SUPREMO)** trial, which closed to accrual in 2013, is a randomized study looking at the role of PORT in high-risk node-negative patients and those with one to three positive nodes.<sup>8</sup> The Tailor RT trial, which is sponsored by the Canadian Cancer Trials Group, is investigating the role of regional nodal irradiation after breast conservation or mastectomy in favorable patients with one to three positive axillary nodes who have estrogen-receptor-positive (ER+) tumors with low-risk Oncotype DX recurrence scores.<sup>9</sup>

### CONCLUSIONS

Radiotherapy should be strongly considered in patients with 1-3 nodes post mastectomy as it decreases the chances of recurrence and also if PNE is present chances of recurrence are increased, hence radiotherapy be considered. As this entails additional Radiotherapy regimes to this important subset of breast cancer patients in our country, one must be aware of resource constraints as this envisages provision of easier access to RT in remote areas, regular surveillance and the resulting costs.

### REFERENCES

1. Overgaard M. Danish Breast Cancer Cooperative Group 82b Trial, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. *N Engl J Med.* 1997;337(14): 94955.
2. Overgaard M, et al. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. *Lancet.* 1999;353(9165): 1641-8.
3. EBCTCG, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for

8135 women in 22 randomised trials. *Lancet.* 2014;383(9935): 2127-35.

4. Truong, P.T., Olivotto, I.A., Whelan, T.J., and Levine, M. Clinical practice guidelines for the care and treatment of breast cancer: 16. Locoregional postmastectomy radiotherapy. *CMAJ.* 2004; 170: 1263-1273
5. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials EBCTCG *Lancet* 2014; 383: 2127-35
6. Whelan TJ, et al. Regional nodal irradiation in early-stage breast cancer. *N Engl J Med.* 2015;373(4): 307-16.
7. Moo TA, et al. Selection criteria for postmastectomy radiotherapy in T1-T2 tumors with 1 to 3 positive lymph nodes. *Ann Surg Oncol.* 2013;20(10): 3169-74.
8. Kunkler IH, et al. Elucidating the role of chest wall irradiation in 'intermediate-risk' breast cancer: the MRC/EORTC SUPREMO trial. *Clin Oncol (R Coll Radiol).* 2008;20(1): 31-4.
9. Tailor RT. A randomized trial of regional radiotherapy in biomarker low risk node positive breast cancer. <https://www.ctg.queensu.ca/public/breast/breast-disease-site>. Accessed 21 Mar 2018.