Original Article

Eur J Breast Health 2019; 15(2): 71-75
DOI: 10.5152/ejbh.2019.4481

Post Mastectomy Radiation for Stage II Breast Cancer Patients with T1/T2 Lesions

Shai Libson[1], Eduardo Perez[1], Christiane Takita[2], Eli Avisar[1]
[1]Department of General Surgery, Miami University School of Medicine, Miami, USA
[2]Department of Radiation Oncology, Miami University School of Medicine, Miami, USA

ABSTRACT

Objective: Post mastectomy radiation (PMR) is usually recommended for T3 or N2 breast cancer (BC). The role of PMR for stage II BC with T1/T2 lesions remains controversial. The aim of this study was to assess the role of PMR in this subgroup of patients.

Materials and Methods: A retrospective analysis of a prospectively collected database of all stage II BC patients treated with mastectomy at our institution between the years 2005-2008 was performed. Demographics, disease-free survival rates were compared between the patients receiving radiation vs. those who were not irradiated.

Results: Eighty-two patients underwent mastectomies for stage II disease with a T1/T2 lesion. Twenty-two of those (27%) received PMR. Loco regional recurrence (LRR) occurred only in the non -irradiated (NR) group. A Kaplan Meier analysis of time to LRR in the NR group was performed. Mean time to local failure was 78.9 months, 6% at 3 years and 13% at 5 years. The time to LRR was significantly lower in the estrogen receptor (ER) negative group compared to the ER positive group (64 vs. 82 months, p=0.029). LRR free rate at 5 years was 100% in low grade tumors vs. 53% in high grade tumors, (p=0.001). In a Cox regression multivariate analysis none of those factors maintained significance.

Conclusion: ER negative status, high grade and node negativity were associated with LRR. A prospective trial randomizing stage II BC patients with T1/T2 lesions, negative hormone receptors and high-grade tumors to PMR following mastectomy arm vs. no radiation arm is recommended.

Keywords: Breast cancer, mastectomy, radiation

Cite this article as: Libson S, Perez E, Takita C, Avisar E. Post Mastectomy Radiation for Stage II Breast Cancer Patients with T1/T2 Lesions. Eur J Breast Health 2019; 15(2): 71-75.

Introduction

Adjuvant radiation therapy after partial mastectomy is associated with 15.7% reduction in any first recurrence for absolute 10 years and a 3.8% absolute reduction in the 15-year mortality rate, avoiding 1 death by the year 15 for every 4 recurrences avoided by the year 10 (1). Adjuvant post-mastectomy radiation (PMR) reduces not only locoregional recurrence (LRR) but improves overall survival, as well (2). There is a general agreement that PMR is indicated in locally advanced disease with a tumor size of >5 cm or presence of more than three lymph nodes (LN) (3). Controversy exists in the intermediate risk group where only one to three nodes are involved. One school of thought limits PMR to high risk patients, mainly N2 patient group where the LRR rate may reach a level of 25% or more (3). While others claim that the absolute reduction is similar to the high-risk group although the overall risk is smaller in the intermediate group (4). The ASCO-ASTRO-SSO guidelines agree that PMR reduces the LRR in the intermediate risk group; however, in a subset of patients, the benefit is outweighed by potential toxicities and therefore the decision requires clinical judgment (5). The BIG 2-04 SUPREMO is a phase 3 randomized trial evaluating PMR for intermediate risk BC. 1688 patients were enrolled from 16 countries between 2006 and 2013 but the results are not available yet (6). The aim of this study was to compare clinical outcomes of early breast cancer (BC) treated by mastectomy with or without radiation therapy and identify risk factors leading to LRR in this group.

Materials and Methods

A retrospective analysis of a prospectively collected database of all stage II BC patients treated with mastectomy at our institution between the years 2005-2008 was performed. Eighty-two BC patients with pathologically stage II excluding T3, N0 who were treated by mastectomy and axillary staging were identified. In 22 patients PMR was administered and in 60 patients no form of radiation therapy was given. Decision about radiation therapy was based on physician's choice. The prescribe dose was 50 Gy/25fractions, five fractions per

Corresponding Author:
Shai Libson; libson@bgu.ac.il

Submitted: 14.11.2018
Accepted: 21.02.2019

week. Radiation was generally administered to the chest wall omitting a full axillary field when axillary dissection was performed, with an individualized approach to the internal mammary chain taking into account the risk of internal node involvement. The systemic treatment was at the medical oncologist discretion but usually was anthracycline based with the addition of anti Her-2 agents when appropriate.

Patient characteristics (age, menopausal status), pathological data (tumor size, LN staging, grade, receptor status), systemic treatment (hormonal, chemotherapy), and clinical outcome (chest wall recurrence, regional recurrence and distal metastatic progression) were analyzed.

The distribution pattern of the clinic-pathological characteristic of the PMR group and the non-irradiated (NR) group were compared by Chi square test. Kaplan-Meier curves of the clinical outcome rates were computed. Multivariate analysis of prognostic factors for LRR was performed using the Cox proportional hazard recurrence regression analysis. The statistical significance was defined as $p<0.05$. All statistical analysis was performed using Statistical Packages for the Social Sciences software version 18 (SPSS Inc., Chicago, IL, USA).

Results

Eighty-two patients underwent mastectomies for stage II disease with a T1/T2 lesion, 22 (27%) received PMR and 60 (73%) were not irradiated. The median follow up time was 47 months (range, 32-86 months). The clinical and pathological characteristics are summarized in Table 1. The patients in the PMR group had significantly larger tumors (90% vs. 64%, p=0.01), more advanced stages (55% vs. 17%, p=0.03) and higher-grade histology (59% vs. 32% p=0.04). Menopausal status, nodal disease, histology, multifocality rate and receptors status did not differ significantly between the groups.

During the follow up interval 3 patients in the NR group had a distant recurrence, one with metastatic disease to the bones at 12 months of follow up, the second had liver metastasis at 30 months of follow up and the third had multi organ metastasis with contra lateral breast cancer at 72 months of follow up interval. An additional patient had a contra lateral recurrence at 24 months of follow up. Two patients in PMR group had distal failure one with metastatic disease to the lungs and bones at 45 months of follow up and the second had a large mass in the mediastinum at 13 months of follow. No difference was found in terms of disease-free survival between the 2 groups. In terms of LRR 4/60 (6.7%) patients had a chest wall recurrence in the NR group vs. 0/22 in the PMR group. However, this was not statistically significant. Kaplan Meier analysis of time to LRR in the NR group was performed. Mean time to LRR was 78.9 months, 4% had chest wall recurrence at 1 year, 6% at 3 years and 13% at 5 years. In a univariate analysis of prognostic factors for LRR, the time to LRR was significantly lower in the estrogen receptor (ER) negative group compared to the ER positive group 64 vs. 82 months, p=0.029, (Figure 1). LRR free rate at 5 years was 100% in low or moderate grade tumors vs. 53% in high grade tumors, p=0.001, (Figure 2). There was a trend for higher LRR rate in the T2 lesions vs.T1 lesions that did not reach statistical significance, p=0.07. Surprisingly all LRR occurred in the node negative group, p=0.003. In terms of treatment variables only hormonal treatment was found significant with a mean time to recurrence of 64.9 months in the non-hormonal treated group vs. 82.3 months in the hormonal treated group, p=0.038. In a Cox regression multivariate analysis, none of those factors maintained their significance.

Table 1. Clinical and pathological characteristics

	No radiation	Radiation	
Characteristic	**n=60 (%)**	**n=22 (%)**	**p**
Age	53.5 (33-82)	49.9 (38-69)	Non-significant (NG)
Axillary surgery			
Axillary dissection	52 (87)	21 (95)	NG
Sentinel node	8 (13)	1 (5)	
Menopausal status			
Postmenopausal	41 (68)	12 (55)	NG
premenopausal	19 (32)	10 (45)	
Tumor size			
T1	T1 22 (36)	2 (10)	0.015
T2	T2 38 (64)	20 (90%)	
Lymph node status			
N1	N1 38 (58.3)	15 (68)	NG
N0	N0 22 (41.7)	7 (32)	
Stage	IIA 44 (73.3) IIB 16 (16.7)	IIA 10 (45.4) IIB 12 (54.6)	0.03
Receptor status			
Estrogen positive	45 (75)	14 (63.6)	NG
Her2 positive	5 (8.3)	3 (13.6)	
Triple negative	10 (16.7)	5 (22.7)	
Histology			
Ductal	57 (95)	20 (91)	NG
lobular	3 (5)	2 (9)	
Focality			
Multifocal	9 (15)	6 (27)	NG
Unifocal	51 (85	16 (73)	
Grade			
High grade	19 (31.7)	13 (59.1)	0.04
Low or Moderate grade	41 (68.3)	9 (40.9)	

Discussion and Conclusion

Radiation therapy in general is not an innocuous treatment. Multiple short and long terms side effects such as contra lateral breast cancer and an excess of none breast cancer mortality that mainly involves heart disease and lung cancer has been recognized (2, 7, 8). Due to these concerns many centers avoided radiation to the internal mammary nodes. The Radiation Oncology and Breast Cancer Groups investigated the effect of extended radiation including internal mammary and supraclavicular nodes, concluding that at median follow up of 10.9 years extended irradiation was associated with improved rates of disease-free survival with reduced rates of breast cancer but without improvement in overall survival (9). These results are consistent with the MA 20 trial results showing that regional nodal irradiation including internal mammary,

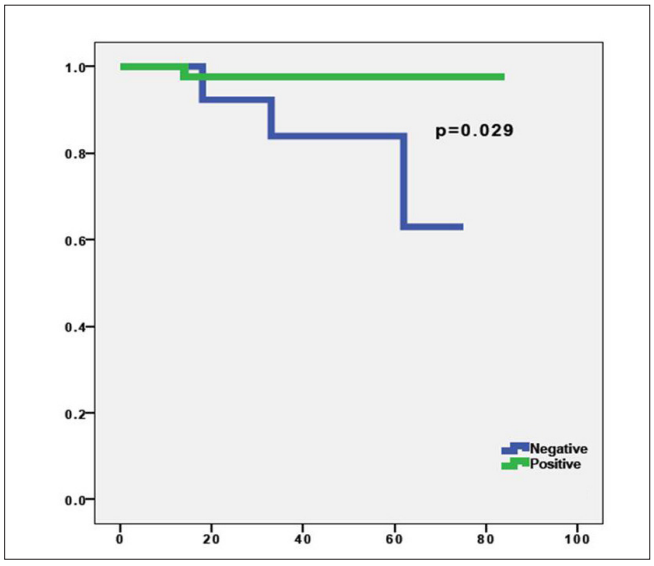

Figure 1. Association between receptor status and LRR in the NR group

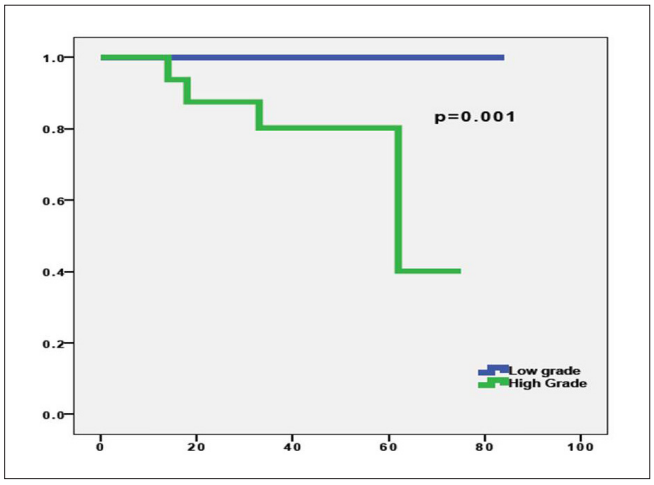

Figure 2. Association between grade and LRR in the NR group

supraclavicular and axillary lymph nodes increased relative disease-free survival by 24% without improvement of overall survival (10). PMR to the chest wall is associated with additional risks compared to post breast conservation radiation, this additional risk is reflected by the gap found between the reduction in the all-cause mortality (4.4%) and the BC mortality (5.4%), this gap is attributed most probably to PMR since no such gap exists in post breast conserving radiation (2).

Two seminal studies have solidified the indication for PMR for N2 disease (11-13). Those same trials reported over 20% decrease in the absolute LRR rate for the 1-3 involved nodes as well; more than 50% of failures were in the chest wall. The extent of the axillary dissection was limited in those two trials with a median of only 7 nodes removed in the Danish (11-12) trials and 11 in the British Colombia trial (13). Marks, however, in an editorial article disagrees with the argument that a more complete dissection would have had an impact on the N staging, showing according to mathematical models that close to 70% of patients will remain in the same N staging even if more nodes would have been removed (4).

In the EBCTG 20-year meta-analysis, the absolute recurrence gain by radiation was 11.5% (45.7% vs. 34.2%) in the N1 group compared to 8.8% (75.1% vs. 66.3%) in the N2 lymph node group. Reduction in the 20-year breast cancer mortality was noted as well, 7.9% gain (50.2% vs. 42.3%) in the N1 group compared to 9.3% gain (80% vs. 70.7%) in the N2 group (14). Voordeckers demonstrated a survival benefit of more than 6% in a retrospective series of low risk node negative post mastectomy irradiated patients vs. SEER data patients were the only significant difference between the groups was the use of post mastectomy radiation (15). In a series from MD Anderson Cancer Center evaluating more than a thousand patients who were treated with modern chemotherapy, a 10-year LRR rate of 10% was reported in the 1-3 involved nodes group (16). Recht evaluated a series of over 2000 patients and reported a 10-year failure rate of only 12% in the groups with 1-3 nodes involved (17). Taghian examined 5758 patients enrolled from 5 NSABP trials and reported a 10-year LRR of 10.6% and 15.3% in T1N1 and T2N1 respectively (18). This lower rate which is partly attributed to superior adjuvant systemic therapy in modern trails reduces the absolute benefit in the intermediate group which is the critical component guiding treatment decisions.

Despite the lower rate of LRR reported in the more recent trials, there seems to be a subgroup of patients in the intermediate group who are at a higher risk and therefore will benefit from PMR as well. In the IBCSG overview, a stratification of patients into risk of LRR was performed. A high risk of LRR (>24%) in the 1-3 involved LN group was identified in the presence of high grade or vascular invasion in premenopausal patients or in the presence of high grade and size >2 cm in postmenopausal patients (19). In a recent update, the numbers of uninvolved nodes were found to have a significant role as well (20). In the NSABP overview, age as well the number of involved nodes constituted a risk factor for LRR; patients <50 had a 10-year LRR rate of 19% vs. 12% in the older age group (18). Another important risk factor was identified in the M.D Anderson series, patients with a ratio ≤20% involved lymph nodes had 10.4% LRR vs. 25.2% in ratio >20% group. In a subgroup analysis in the latter, patients with tumor ≤3.5 cm had 17.5% LRR rate vs. 36.3% in tumors >3.5cm (21). This additional factor may standardize results obtained from series with small number of LN removed. For example, a patient with 2/7 involved nodes, although belonging to the intermediate group according to the N staging would have a high risk (25%) of LRR utilizing the LN ratio factor, this rate is closer to the rates reported in the Danish trials. Indeed, Truong was able to show similar LRR rates between the M.D Anderson series and the Canadian trial using the LN ratio factor.

In the ASCO guidelines the panel agreed that certain factors should be taken into account before reaching a decision to radiate in the intermediate risk group these include: triple negative, lymphovascular invasion, Her2 positive or age <40 (5).

A number of recently retrospective studies reported lower LRR in irradiated treated patients. Hounag compared 163 PMR patients to 155 non-irradiated patients and found 3.1% vs. 11% LRR rate, respectively (22). Macdonald et al. (23) compared 73 radiated patients vs. 165 non-irradiated patients and found a 5-year LRR of 6% in the non-irradiated group vs. none in the radiated group. Both studies included only T1/T2, N1 patients. These rates are similar to the findings in our cohort 6.7% in the NR group vs. none in the irradiated group, bearing in mind that our follow up period was shorter.

There were no specific guidelines for PMR in our cohort and the decision was made at the discretion of the treating physician. Size and grade influenced the decision to radiate patients, thus explaining the

higher rate of these factors in the radiated treated patients. For that reason, a true comparative statistical analysis between the PMR and the NR groups is not possible. In fact, the lack of statistically significant difference in LRR between the groups might be explained by the more aggressive tumors included in the PMR group and the relatively small sample size. Nevertheless, a univariate and multivariate analysis of the NR group was possible in an effort to identify specific prognostic factors of local failure. High grade and negative receptor status were associated with chest wall recurrence in the NR group. Size, T2 vs. T1, showed a trend that did not reach statistical significance. Surprisingly, all four LRR occurred in node negative patients, this unexpected finding is partly explained by the selection criteria of our cohort that included only T1N1, T2N0 and T2N1 patients. For that reason, the tumors were larger (all T2) in the node negative group compared to only 40% T2 tumors in the node positive group. In contrast to our study which defined the intermediate group as all stage II patients excluding T3 N0, other have (15, 16) identified the intermediate group as T1-2, N1 but excluded T2N0 patients. Excluding those patients from the intermediate group may not be obvious, as can be seen in our cohort where all local failures occurred in T2, N0 patients.

The overall LRR rate in the post mastectomy setting is low and the absolute benefit rate is even smaller. The rate of LRR reported in our trial is 6.7% which in the same range as reported by others (15, 16). Administering radiation where the overall risk is <10% does not seem to be justified and it is therefore important to define a profile of high-risk patients for LRR within the stage II group. Our study is retrospective in nature and was limited by the small number of patients, even with this limitation we can conclude that hormone receptors negative status, high grade and T2 patients constitute a subgroup of higher risk patients. Further prospective trials randomizing stage II BC patients with T1/T2 lesions, negative hormone receptors and high-grade tumors to PMR following mastectomy *vs*. no radiation is recommend.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Jackson Memorial Hospital.

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.A.; Design - E.A., S.L.; Supervision - E.A., E.P.; Resources - E.A., S.L., C.T.; Data Collection and/or Processing - E.P., E.A., S.L.; Analysis and/or Interpretation - S.L., E.P.; Literature Search - S.L., E.A.; Writing Manuscript - S.L., E.A.; Critical Review - E.P., C.T.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Darby S, McGale P, Correa C, Taylor C, Arriagada R, Clarke M, Cutter D, Davies C, Ewertz M, Godwin J, Gray R, Pierce L, Whelan T, Wang Y, Peto R. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomized trials. Lancet 2011; 378: 1707-16. (PMID: 22019144) [CrossRef]
2. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans V, Godwin J, Gray R, Hicks C, James S, MacKinnon E, McGale P, McHugh T, Peto R, Taylor C, Wang Y. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomized trials. Lancet 2005; 366: 2087-2106. (PMID: 16360786) [CrossRef]
3. Olivotto IA, Truong PT, Chua B. Postmastectomy radiation therapy: who needs it? J Clin Oncol 2004; 22: 4237-4239. (PMID: 15452185) [CrossRef]
4. Marks LB, Zeng J, Prosnitz LR. One to three versus four or more positive nodes and postmastectomy radiotherapy: time to end the debate. J Clin Oncol 2008; 26: 2075-2077. (PMID: 18445836) [CrossRef]
5. Recht A, Somerfield MR, Edge SB Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update Summary. J Oncol Pract 2016; 12: 1258-1261. (PMID: 27650832) [CrossRef]
6. Kunkler IH, Canney P, van Tienhoven G, Russell NS. Elucidating the role of chest wall irradiation in 'intermediate-risk' breast cancer: the MRC/EORTC SUPREMO trial. Clin Oncol (R Coll Radiol) 2008; 20: 31-34. (PMID: 18345543) [CrossRef]
7. Darby SC, Ewertz M, McGale P, Bennet AM, Blom-Goldman U, Brønnum D, Correa C, Cutter D, Gagliardi G, Gigante B, Jensen MB, Nisbet A, Peto R, Rahimi K, Taylor C, Hall P. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med 2013; 368: 987-998. (PMID: 23484825) [CrossRef]
8. Kaplan HG, Malmgren JA, Atwood MK. Increased incidence of myelodysplastic syndrome and acute myeloid leukemia following breast cancer treatment with radiation alone or combined with chemotherapy: a registry cohort analysis 1990-2005. BMC Cancer 2011; 11: 260. (PMID: 21693006) [CrossRef]
9. Poortmans PM, Collette S, Kirkove C, Van Limbergen E, Budach V, Struikmans H, Collette L, Fourquet A, Maingon P, Valli M, De Winter K, Marnitz S, Barillot I, Scandolaro L, Vonk E, Rodenhuis C, Marsiglia H, Weidner N, van Tienhoven G, Glanzmann C, Kuten A, Arriagada R, Bartelink H, Van den Bogaert W. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. N Engl J Med 2015; 373: 317-327. (PMID: 26200978) [CrossRef]
10. Whelan TJ, Olivotto IA, Levine MN. Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med 2015; 373: 1878-1879. (PMID: 26535517) [CrossRef]
11. Overgaard M, Hansen PS, Overgaard J, Rose C, Andersson M, Bach F, Kjaer M, Gadeberg CC, Mouridsen HT, Jensen MB, Zedeler K. Postoperative Radiotherapy in High-Risk Premenopausal Women with Breast Cancer Who Receive Adjuvant Chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. N Engl J Med 1997; 337: 949-955. (PMID: 9395428) [CrossRef]
12. Overgaard M, Jensen MB, Overgaard J, Hansen PS, Rose C, Andersson M, Kamby C, Kjaer M, Gadeberg CC, Rasmussen BB, Blichert-Toft M, Mouridsen HT. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomized trial. Lancet 1999; 353: 1641-1648. (PMID: 10335782) [CrossRef]
13. Ragaz J, Jackson SM, Le N, Plenderleith IH, Spinelli JJ, Basco VE, Wilson KS, Knowling MA, Coppin CM, Paradis M, Coldman AJ, Olivotto IA. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. N Engl J Med 1997; 337: 956-962. (PMID: 9309100) [CrossRef]
14. McGale P, Taylor C, Correa C, Cutter D, Duane F, Ewertz M, Gray R, Mannu G, Peto R, Whelan T, Wang Y, Wang Z, Darby S. 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: 2127-2135. (PMID: 24656685) [CrossRef]
15. Voordeckers M1, Van de Steene J, Vinh-Hung V, Storme G. Adjuvant radiotherapy after mastectomy for pT1-pT2 node negative (pN0) breast cancer: is it worth the effort?. Radiother Oncol 2003; 68: 227-231. [CrossRef]
16. Katz A, Strom EA, Buchholz TA, Thames HD, Smith CD, Jhingran A, Hortobagyi G, Buzdar AU, Theriault R, Singletary SE, McNeese MD. Locoregional recurrence patterns after mastectomy and doxorubicin-based chemotherapy: implications for postoperative irradiation J Clin Oncol 2000; 18: 2817-2827. (PMID: 10920129) [CrossRef]
17. Recht A, Gray R, Davidson NE, Fowble BL, Solin LJ, Cummings FJ, Falkson G, Falkson HC, Taylor SG 4th, Tormey DC. Locoregional failure 10 years

after mastectomy and adjuvant chemotherapy with or without tamoxifen without irradiation: experience of the Eastern Cooperative Oncology Group. J Clin Oncol 1999; 17: 1689-1700. (PMID: 10561205) [CrossRef]

18. Taghian A, Jeong JH, Mamounas E, Anderson S, Bryant J, Deutsch M, Wolmark N. Patterns of locoregional failure in patients with operable breast cancer treated by mastectomy and adjuvant chemotherapy with or without tamoxifen and without radiotherapy: results from five National Surgical Adjuvant Breast and Bowel Project randomized clinical trials. J Clin Oncol 2004; 22: 4247-4254. (PMID: 15452182) [CrossRef]
19 Wallgren A, Bonetti M, Gelber RD, Goldhirsch A, Castiglione-Gertsch M, Holmberg SB, Lindtner J, Thürlimann B, Fey M, Werner ID, Forbes JF, Price K, Coates AS, Collins J. Risk factors for locoregional recurrence among breast cancer patients: results from International Breast Cancer Study Group Trials I through VII. J Clin Oncol 2003; 21: 1205-1213. (PMID: 12663706) [CrossRef]
20. Karlsson P, Cole BF, Price KN, Coates AS, Castiglione-Gertsch M, Gusterson BA, Murray E, Lindtner J, Collins JP, Holmberg SB, Fey MF, Thürlimann B, Crivellari D, Forbes JF, Gelber RD, Goldhirsch A, Wallgren A. The role of the number of uninvolved lymph nodes in predicting locoregional recurrence in breast cancer. J Clin Oncol 2007; 25: 2019-2026. (PMID: 17420511) [CrossRef]
21. Katz A, Buchholz TA, Thames H, Smith CD, McNeese MD, Theriault R, Singletary SE, Strom EA. Recursive partitioning analysis of locoregional recurrence patterns following mastectomy: implications for adjuvant irradiation. Int J Radiat Oncol Biol Phys 2001; 50: 397-403. (PMID: 11380226) [CrossRef]
22. Huang CJ, Hou MF, Chuang HY, Lian SL, Huang MY, Chen FM, Fu OY, Lin SF. Comparison of clinical outcome of breast cancer patients with T1-2 tumor and one to three positive nodes with or without postmastectomy radiation therapy. Jpn J Clin Oncol 2012; 42: 711-720. (PMID: 22645150) [CrossRef]
23. Macdonald SM, Abi-Raad RF, Alm El-Din MA, Niemierko A, Kobayashi W, McGrath JJ, Goldberg SI, Powell S, Smith B, Taghian AG. Chest wall radiotherapy: middle ground for treatment of patients with one to three positive lymph nodes after mastectomy. Int J Radiat Oncol Biol Phys 2009; 75: 1297-1303. (PMID: 19327896) [CrossRef]