Date of origin: 1996
Last review date: 2012

American College of Radiology
ACR Appropriateness Criteria®

POSTMASTECTOMY RADIOTHERAPY

Expert Panel on Radiation Oncology–Breast: Kathleen C. Horst, MD[1]; Bruce G. Haffty, MD[2]; Eleanor E. R. Harris, MD[3]; Lisa Bailey, MD[4]; Jennifer R. Bellon, MD[5]; Lisa Carey, MD[6]; Gary M. Freedman, MD[7]; Sharad Goyal, MD[8]; Michele Y. Halyard, MD[9]; Shannon M. MacDonald, MD[10]; Meena S. Moran, MD[11]; W. Warren Suh, MD.[12]

Summary of Literature Review

This summary focuses on the role of postoperative radiation therapy in patients treated with modified radical mastectomy for invasive breast cancer, particularly in patients receiving systemic therapy. Treatment of patients with locally advanced breast cancer, including large tumors or those involving the skin or chest wall, and breast cancers with extensive lymphadenopathy, is addressed in the ACR Appropriateness Criteria® on "Locally Advanced Breast Cancer."

Patterns of Locoregional Failure after Mastectomy Alone

Older randomized studies have demonstrated that in the absence of radiotherapy (RT), locoregional failure can occur in approximately 25%-40% of node-positive patients, and up to 15%-20% of node-negative patients, who do not receive systemic therapy [1,2]. The most frequent site of locoregional recurrence (LRR) is the chest wall [3,4], followed by axillary and supraclavicular nodal regions. Clinical detection of internal mammary (IM) nodal recurrences is rare, as they are primarily detected by imaging [3].

The overall risk of LRR, including the chest wall and nodal sites, is influenced by tumor size, tumor grade, the presence or absence of lymphovascular space invasion, surgical margin status, involvement of the fascia or skin, the number of involved lymph nodes (LNs), and the percentage of nodal involvement (or nodal ratio) [4-9]. Several reports confirm the interaction of these pathologic features, as well as patient age, as compounding factors that determine the risk of LRR [4-10]. In some series, the presence of extracapsular nodal extension has not been associated with an increased risk of local-regional failure when the total number of LNs is taken into account [11,12]. Axillary or supraclavicular recurrences are rare following removal of Level I and II LNs when they are negative or when there are only one to three positive LNs. However, such failures are more common in patients with four or more positive LNs [4,6,13,14]. With the increasing understanding of the importance of biologic subtypes in breast cancer, retrospective data suggest that estrogen receptor (ER)/progesterone receptor (PR) negative and HER2-positive tumors have higher rates of LRR compared with receptor-positive or HER2-negative subtypes [15,16].

More recent trials have demonstrated that the addition of systemic therapy improves LRR rates [9,16,17], which has raised the question of whether RT in the setting of modern systemic therapy can further improve outcomes.

Locoregional Risk Reduction and Impact on Survival with Postmastectomy Radiotherapy

Multiple trials over the last several decades have demonstrated that adjuvant postmastectomy radiotherapy (PMRT) reduces the risk of LRR. However, prior to the publication of the relatively recent randomized trials from the British Columbia Cancer Agency and the Danish Breast Cancer Cooperative Group, the use of PMRT was thought to improve local control only, without a significant effect on survival. These large prospective randomized trials, initially published in 1997 and 1999 and subsequently updated in 2005 and 2006 [3,18-21], were the first trials using modern radiation techniques to demonstrate not only an improvement in local recurrence with the use of PMRT, but also an improvement in survival.

[1]Principal Author, Stanford University School of Medicine, Stanford, California. [2]Panel Chair, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, New Jersey. [3]Panel Vice-chair, Moffitt Cancer Center, Tampa, Florida. [4]Alta Bates Summit Medical Center, Oakland, California, American College of Surgeons. [5]Dana Farber Cancer Institute, Boston, Massachusetts. [6]University of North Carolina Health Care System, Chapel Hill, North Carolina, American Society of Clinical Oncology. [7]University of Pennsylvania, Philadelphia, Pennsylvania. [8]UMDNJ-Robert Wood Johnson Medical School, New Brunswick, New Jersey. [9]Mayo Clinic, Scottsdale, Arizona. [10]Massachusetts General Hospital, Boston, Massachusetts. [11]Yale University School of Medicine, New Haven, Connecticut. [12]Cancer Center of Santa Barbara, Santa Barbara, California.

Reprint requests to: Department of Quality & Safety, American College of Radiology, 1891 Preston White Drive, Reston, VA 20191-4397.

In premenopausal patients, the Danish Trial 82b initially reported a statistically significant improvement in rates of local recurrence (32% vs 9%, P<.0001), disease-free survival (DFS) (34% vs 48%, P<.001), and overall survival (OS) (45% vs 54%, P<.001) in favor of chest wall and regional lymphatic irradiation plus cyclophosphamide, methotrexate, 5-flourouacil (CMF) chemotherapy compared with CMF alone [18]. This study included stage II and III patients and had a median follow-up of 10 years at the time of initial publication. Most of these patients had node-positive disease, but node-negative patients with tumors >5 cm and/or skin or pectoralis fascia involvement were also eligible. Multivariate analysis confirmed that irradiation after mastectomy was a statistically significant factor in improving DFS and OS rates. This finding was consistent regardless of tumor size, number of positive LNs, or tumor grade, and was upheld with longer follow-up [3].

The Canadian Trial [19] also examined outcomes for node-positive premenopausal patients randomized to CMF alone versus CMF plus locoregional irradiation. Updated results at 20 years demonstrated statistically significant improvements in event-free survival (25% vs 38% P=.009), survival free of isolated local failure (74% vs 90%, P=.002), breast-cancer-free survival (30% vs 48%, P=.001), and OS (37% vs 47%, P=.03) with the use of PMRT. These results are similar to the findings reported by the Danish Trial 82b. This analysis was stratified by the number of positive LNs, and no difference in risk reduction with PMRT was identified between patients with one to three positive LNs and those with four or more positive LNs [20].

The value of PMRT in node-positive postmenopausal patients was prospectively evaluated in the Danish Trial 82c [3,21]. The study design included randomization to tamoxifen for 1 year only versus tamoxifen plus chest wall and regional lymphatic irradiation after mastectomy. Ten-year analysis showed statistically significant improvement in local recurrence rate (35% vs 8%, P<0.001), DFS rate (24% vs 36%, P<0.001), and OS rate (36% vs 45%, P=.03). An updated publication [22] from the Danish 82b and 82c [18,21] trials showed continued benefit from PMRT at a median potential follow-up time of 18 years. The 18-year probability of any breast cancer event was 73% without RT and 59% with RT (P<.001, relative risk [RR] 0.68, 95% confidence interval [CI], 0.63 to 0.75). The 18-year probability of LRR, with or without distant metastases (DM), was 49% without RT and 14% with RT (P<.001, RR 0.23, 95% CI, 0.19 to 0.27). The 18-year probability of DM after LRR was 35% with no RT and 6% with RT (P<.001, 95% CI, 0.11 to 0.20). The 18-year probability of any DM was 64% without RT and 53% with RT (P<.001, RR 0.78, 95% CI, 0.71 to 0.86) [3].

Furthermore, a subset analysis of the Danish 82b and 82c trials suggested that the survival benefit after PMRT was restricted to the more favorable biologic profiles (hormone receptor positive and HER2-negative), while those with the poorest prognostic biologic features (hormone receptor negative and HER2-positive) had no significant OS improvement after PMRT [23]. Questions therefore remain as to whether biologic features, in addition to nodal status, should be considered when evaluating the role of PMRT and its impact on survival.

The impact of PMRT on local control and OS has been further supported by the results of the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis of 78 prospective randomized clinical trials [24]. In those trials investigating mastectomy with and without RT, the addition of PMRT provided similar proportional reductions in local recurrence regardless of patient age, tumor characteristics, use of systemic therapy, or treatment era, although the absolute risk reduction was larger in the higher-risk populations The 5-year local recurrence risks in LN-negative patients with and without PMRT were 2% and 6%, respectively, with a 3.6% decrement in 15-year breast cancer mortality. In LN-positive patients, the 5-year local recurrence risks were 6% and 23%, respectively, which translated into a 5.4% benefit in 15-year breast cancer mortality.

This meta-analysis demonstrated the relationship between the absolute reduction in 5-year local recurrence risk and breast cancer mortality. In those trials where the absolute reduction in LRR was <10% (mean 1%), the 15-year breast cancer mortality rates was improved by only 1%. A 10%-20% absolute risk reduction in LRR (mean 17%) corresponded to a 4.5% absolute reduction in 15-year breast cancer mortality. The greatest benefit in breast cancer mortality was identified in those with >20% absolute reduction in 5-year local recurrence risk. If PMRT reduced the 5-year local recurrence risk by 20%, the 15-year breast cancer mortality rate would be reduced by 5.2%, suggesting that the addition of PMRT would eliminate one breast cancer death at 15 years for every four local recurrences prevented. Therefore, the baseline risk of LRR is directly related not only to the magnitude of the LRR risk reduction after PMRT but also to the potential survival benefit. (See Variant 1 and Variant 2.)

Postmastectomy Radiotherapy for Intermediate-Risk Patients

After the initial publication of the Danish and Canadian studies, the benefit of PMRT was readily accepted for women at high risk of LRR. However, some uncertainty remained as to the role of PMRT in patients with one to

three involved LNs or high-risk node-negative disease [25]. This controversy is due in part to the discrepancy in local recurrence rates among patients with one to three positive LNs who did not receive PMRT in the Danish and Canadian trials compared to the U.S. cooperative group trials. The LRR rates in these patients were substantially higher in the Danish and Canadian trials (30%-33%) than those reported in the retrospective analyses of prospective chemotherapy trials by the Eastern Cooperative Oncology Group (ECOG) and National Surgical Adjuvant Breast and Bowel Project (NSABP) chemotherapy trials, which both reported 10-year LRR rates of 13% [4,6]. Variations in the extent of axillary surgery may account for the higher LRR rates noted in the Danish and Canadian trials, where the median numbers of LNs removed were seven and 11, respectively, compared to 15 and 16 in the ECOG and NSABP trials, respectively. With fewer LNs resected, the true number of involved LNs may be underestimated in those trials, leading to a potential underestimation of risk due to nodal involvement and an overestimation of PMRT benefit in the intermediate-risk population.

In an attempt to address this question, investigators from the Danish Breast Cancer Group reanalyzed their data to exclude patients who had fewer than eight LNs resected [22]. In patients with one to three positive LNs, the 15-year loco-regional failure rates with and without PMRT were 4% and 27% ($P<0.001$), respectively, compared to 10% and 51% ($P<0.001$) in patients with four or more involved LNs. The 15-year OS rates in patients with one to three positive LNs were 57% with PMRT and 48% without ($P=0.03$), compared to 21% and 12% ($P=0.03$) in patients with four or more positive LNs. Interestingly, the number of patients needed to treat to avoid a LRR or to avoid a death was similar between the two groups. The needed to treat to avoid a LRR was four in the group with our or more positive LNs and five in those with one to three positive LNs, while the needed to treat to avoid a death was 10 and 11, respectively. These results addressed initial criticism regarding the extent of axillary surgery and demonstrate that PMRT is as beneficial in patients with one to three involved LNs as it is in higher-risk patients.

Further contributing to the uncertainty of survival benefit of PMRT in patients at intermediate risk, an analysis of women with T1-2 LN-positive breast cancer from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program demonstrated a 8% improvement in 10-year OS for patients with seven or more positive LNs but was not associated with reduced mortality in patients with one to six positive LNs [26].

Given the ongoing controversy regarding PMRT in patients with one to three positive LNs or high-risk LN-negative disease, several retrospective studies have identified factors other than the number of involved LNs that may be associated with a higher risk of LRR after mastectomy alone. Such factors include young age, premenopausal status, tumor size, tumor grade, lymphovascular invasion (LVI), margin status, nodal ratio (number of positive LNs/total LNs resected), ER status, tumor subtype, 21-gene recurrence score, and the genomic predictive index [6,9,23,27-33]. When more than one of these adverse risk factors is present in the setting of nodal involvement, more aggressive locoregional management may be warranted.

Additional prospective data evaluating the role of PMRT in intermediate risk patients are expected from an ongoing study in the UK (Selective Use of Postoperative Radiotherapy after Mastectomy); however, it will be several years before the results are available [34]. A phase III trial in North America, in which women with one to three positive LNs after mastectomy were randomized to PMRT versus observation, closed prematurely due to poor accrual. (See Variant 3, Variant 4, Variant 5, and Variant 6.)

Postmastectomy Radiotherapy for pT3N0

Only approximately 1% of breast cancer patients present with pathological stage T3N0 disease [35]. With this presentation, failure in the chest wall along the surgical scar is the most common site of LRR, followed by supraclavicular failures and, rarely, IM or axillary failures.

An older prospective trial by Klefstrom et al [36] reported LRR in five of 13 pT3N0 patients (38%) not randomized to postoperative irradiation compared with none of 27 patients treated with postoperative irradiation ($P=.002$). Similarly, the prospective Danish 82b study included women with T3N0 tumors (n=135) and demonstrated a reduction in LRR with PMRT (17% vs 3%) as well as an improvement in 10-year actuarial OS in this subgroup (70% vs 82%) [37]. The prospective Danish 82c study in postmenopausal women (n=132) found a similar reduction in the 10-year risk of LRR (23% vs 6%); however, the 10-year OS rates were not significantly different (55% vs 56%). These results support consideration of treatment to the chest wall in patients with pT3N0 breast carcinoma.

Despite the prospective evidence in support of PMRT for patients with pT3N0 disease, more recent retrospective data has challenged its routine use in this group of patients. Although an older retrospective series by Helinto et al [38] reported results in accordance with previously published prospective data (LRR in three of five patients (60%) treated without PMRT as compared to LRR in three of 33 patients (9%) who received PMRT [P=0.0003]), Floyd et al analyzed 70 patients with pT3N0 disease and demonstrated a 5-year rate of LRR without PMRT of only 7.6% [39]. Of note, patients with lymphovascular space invasion were at significantly higher risk of local-regional failure. An analysis of 330 pT3N0 patients selected from various NSABP studies similarly reported a low LRR rate, with a 10-year isolated locoregional failure rate of 7.1% [40]. The median number of LNs removed in both of these studies was 16, and 56% and 74% of patients, respectively, received systemic therapy. Mignano et al reported a 10-year and 15-year rate of local recurrence of 12% and 13% in 101 patients with T3N0 breast cancer treated with mastectomy without PMRT [41]. From the British Columbia Cancer Agency, Goulart et al [42] reported a 10-year cumulative LRR rate of 8.9% in 56 LN-negative patients with tumors ≥5 cm treated with mastectomy without PMRT compared to 2.3% in the 44 patients who received PMRT (P=.02). All six patients who recurred had grade 3 tumors and had not received systemic therapy. The curves for breast-cancer-specific survival diverged over time between the PMRT and no-PMRT cohorts; however, this difference was not statistically significant.

Finally, Yu et al [43] reported an analysis of the NCI SEER database consisting of 1,777 patients with pT3N0 disease treated with mastectomy, 32% of whom received PMRT. In this analysis, PMRT was not a significant predictor of OS or cause-specific survival. Due to limitations of the SEER database, analysis of LRR rates was not possible.

Given the conflicting prospective and retrospective data, treatment of pT3N0 patients should continue to be highly individualized, taking into consideration the extent of nodal dissection, the use of systemic therapy, the pathologic margin status, the presence of LVI, and the biologic subtype. (See Variant 7.)

Postmastectomy Radiotherapy following Neoadjuvant Chemotherapy

The NSABP B-18 trial [44] and a meta-analysis of nine randomized trials [45] found no differences in DFS or OS when systemic therapy was given in the neoadjuvant or adjuvant setting. The parameters suggesting the need for PMRT may be different, however, with neoadjuvant therapies compared to adjuvant therapies. As there are no randomized data evaluating the role of PMRT after neoadjuvant chemotherapy, the best available data to assess its benefit are from retrospective studies of prospective neoadjuvant chemotherapy trials.

The M.D. Anderson Cancer Center has compared LRR rates after mastectomy without RT in patients treated with neoadjuvant (n=150) or adjuvant (n=1031) chemotherapy [46]. The analysis was made from pooled findings of prospective trials involving patients with clinical stage I-IIIB disease treated with doxorubicin-based therapy. The 5-year actuarial LRR was 27% in the neoadjuvant group versus 15% in the adjuvant group (P=.001), representing primarily the imbalance in disease stage between the two groups. Both the initial clinical extent of disease and the pathologic residual disease were found to be important predictors of LRR. The authors concluded that PMRT should be offered to patients with four or more positive LNs, pathologic tumor >5 cm, or clinical stage III disease regardless of whether they receive neoadjuvant or adjuvant chemotherapy. In a further analysis of the 150 patients treated with neoadjuvant chemotherapy, an additional risk factor associated with LRR was no tamoxifen use [47]. For patients with clinical stage II disease treated with neoadjuvant chemotherapy without irradiation, clinical and pathologic features associated with LRR include clinical T3N0 disease, four or more positive LNs after chemotherapy, age <40 years at diagnosis, and no use of tamoxifen with ER-positive disease [48].

After identifying those patients at risk for LRR after mastectomy in the setting of neoadjuvant chemotherapy, the investigators at MD Anderson evaluated outcomes in patients treated with and without PMRT [37]. All patients received doxorubicin-based chemotherapy and a standard axillary dissection, with a median of 15 LNs removed. RT was delivered to the chest wall, supraclavicular, and IM areas, with inclusion of the axilla if insufficient numbers of axillary LNs were sampled. Ten-year LRR rates were 11% with PMRT versus 22% without (P=.0001). PMRT statistically significantly reduced LRR rates in patients with clinical T3 or T4 tumors, clinical N2-3, pT >2 cm, and four or more positive LNs. In addition, cause-specific survival was significantly improved with PMRT in patients who had clinical stage ≥IIIB, clinical T4 or N2/N3 disease, and four or more positive residual LNs. Upon multivariate analysis no radiation, ≥20% nodal ratio, stage ≥IIIB, no tamoxifen, ER-negative tumors, or minimal response to chemotherapy were associated with higher rates of LRR. Additional studies found

that those patients presenting with clinical T3N0 disease or patients <35 years of age had high rates of LRR after neoadjuvant chemotherapy and mastectomy if RT was omitted [49,50].

Another area of uncertainty is the role of PMRT in patients who achieve a pathologic complete response (pCR) after chemotherapy. An additional analysis by the MD Anderson group evaluated 106 patients who achieved a pCR (72 received PMRT and 34 did not) [51]. The 10-year LRR rates in stage III patients with and without PMRT were 7.3% and 33.3% (P=.04). The use of PMRT was also associated with improved disease-specific and OS. Of the 30 clinical stage II patients, there were no local recurrences in either group, limiting any definitive conclusions about the potential benefit of PMRT in this subset of patients. In contrast, Le Scodan et al [52] reported no differences in LRR or survival with or without PMRT in 134 patients with stage II-III breast cancer who achieved pathologically negative LNs after neoadjuvant chemotherapy. Additional data from the NSABP B-18/B-27 trials showed that patients with clinical stage II disease who have negative LNs after preoperative chemotherapy have an 8-year risk of LRR after mastectomy that is less than 10% [53].

In 2007, the National Cancer Institute convened a multidisciplinary expert panel to discuss the locoregional management of breast cancer after neoadjuvant chemotherapy. Based on the limited prospective data and the retrospective data from primarily a single institution, the NCI conference report recommends PMRT after neoadjuvant chemotherapy for patients presenting with clinical stage III disease or those with positive LNs after neoadjuvant therapy. There are limited data to recommend the routine use of PMRT in patients with clinical stage II disease prior to neoadjuvant therapy who achieve a pCR [53]. (See Variant 8 and Variant 9.)

Postmastectomy Radiotherapy for Ductal Carcinoma in Situ

There are no prospective randomized data evaluating the role of PMRT for patients undergoing mastectomy for ductal carcinoma in situ (DCIS). Retrospective data most commonly address the question of PMRT in the setting of close or positive surgical margins.

Rashtian et al [54] reported that PMRT may be of benefit for patients with very close (<3 mm) or positive margins, particularly in the setting of high-grade disease. Local recurrences in patients with >3 mm margins were rare. With a median follow-up of 49 months, six of 81 patients (7.4%) had LRRs. Chest wall recurrences were noted in 4 patients, with the remaining two patients having axillary recurrences. The recurrence rates in patients with close, very close, or positive surgical margins were 2%, 11%, and 33% respectively. Patients with high-grade lesions had an 11% LRR rate, whereas low- to intermediate-grade lesions had a 3% recurrence rate. In the subgroup of patients with very close or positive surgical margins who had high-grade disease, a recurrence rate of 24% was observed.

In contrast, other series report low risks of LRR such that PMRT may not be warranted. Carlson et al reported LR in two of 19 (10.5%) patients treated with skin-sparing mastectomy with margins ≤1 mm, yet the overall recurrence rate of 5.1% at a mean follow-up of 82.3 months was thought to be similar to that seen after conventional mastectomy, suggesting that skin-sparing mastectomy for DCIS does not necessarily lead to excessively high rates of local recurrence compared to conventional mastectomy if margins are negative [55]. Similarly, Chan et al [56] reported a 1.7% risk of chest wall recurrence in 59 patients with DCIS treated with mastectomy alone with close (<5 mm) or positive margins with a median follow-up of 8 years, and 3.3% in the patients with high-grade DCIS. They conclude that even in patients with close margins, recurrences are low enough that PMRT may not be warranted, although re-excision is recommended if feasible.

In a review of 10 cases of patients with DCIS treated with mastectomy who subsequently developed a chest wall recurrence, Kim et al [57] noted common features among the chest wall relapse cases: young patient age, multiquadrant disease, and the presence of residual normal breast tissue after the mastectomy. Outcome following salvage radiation for the chest wall recurrences was excellent, with nine of the 10 patients alive without evidence of disease.

With these limited retrospective data, the use of PMRT for DCIS needs to be highly individualized, with consideration of age of the patient, extent of disease, amount of residual breast tissue, and margin status. (See Variant 10.)

Treatment Volumes, Techniques, Toxicity

Volumes

In the three randomized trials demonstrating a benefit in local control as well as OS with the use of PMRT, RT was delivered to the chest wall and surgical scar, as well as to the regional LNs, including the supraclavicular,

infraclavicular, axillary and IM LNs. Based on these results, it is generally accepted that the entire chest wall and mastectomy scar should be included. However, there is much more controversy as to which nodal regions to include. For most LN-positive patients, the ipsilateral supraclavicular fossa is usually included in the treatment volume, with much more variation as to when the IM LNs are included [6]. This variation arises in part due to the potential increase in toxicity with the addition of IM nodal irradiation, particularly for left-sided cancers, and the uncertain additional benefit of nodal irradiation to chest wall RT alone. In early 1996 the European Organization for Research and Treatment of Cancer (EORTC) began a trial (protocol 22922/10925) examining the value of IM and medial supraclavicular chain irradiation for patients with positive axillary LNs or central/medial tumors treated with either breast-conserving surgery or mastectomy. The results of this trial are still pending. Preliminary data from a French study, in which 1,334 women treated with mastectomy with positive LNs or central tumors were randomized to chest wall and supraclavicular irradiation with or without IM RT, demonstrated no difference in OS between the two treatment groups [58]. The recently presented MA-20 National Cancer Institute of Canada clinical trial demonstrated an improvement in DFS with the use of regional nodal irradiation, including IM LNs, in node-positive or high-risk node-negative patients treated with breast-conserving surgery followed by whole-breast RT [59]. With approximately 85% of patients in this trial having one to three positive LNs, these results challenge what was otherwise thought to be a lower risk group than those with four or more involved LNs. A retrospective study from the MGH demonstrated similar rates of LRR, DFS, and OS in, patients with one to three positive LNs treated with chest wall RT only as compared to those treated with chest wall and nodal irradiation, suggesting that PMRT to the chest wall only may be appropriate for women with tumors <5 cm and one to three positive LNs [60]. The results from the EORTC 22922/10925 trial as well as longer follow-up of the MA-20 trial will help further elucidate the role of nodal irradiation in addition to chest wall RT in node-positive and high-risk node-negative patients.

Techniques

For patients receiving PMRT, the use of a computed tomography (CT) simulator and 3-dimensional treatment planning is preferable in order to allow visualization of the target and normal tissues. Given the variability of target and normal structure delineation for breast cancer [61], an expert panel developed a breast cancer contouring atlas for RT treatment planning [62].

Several techniques have been described to treat the chest wall after mastectomy, including tangential photon beams or en face electrons [63]. The dose delivered to the chest wall is usually 50-50.4 Gy in 1.8-2 Gy fractions. The use of bolus is recommended to ensure that the dose to the skin is adequate. Occasionally a 10-16 Gy boost to the mastectomy scar is added, particularly in patients with a positive margin.

When targeting the supraclavicular fossa and axillary apex, an oblique anterior-posterior field is matched to the chest wall fields. CT-based treatment planning is important as the depth of the supraclavicular and level III LNs can vary based on patient anatomy. The exact depth can be determined from the CT and may influence the photon energy necessary or whether an anterior-posterior or posterior-anterior field may need to be considered. The dose to the supraclavicular/axillary apical field is usually 45-50.4 Gy in 25-28 fractions.

When targeting the IM LNs, CT simulation is helpful for visualizing the IM vessels. A separate electron field or a combination of low-energy photons and electrons can be used to treat the first three intercostal spaces. Another technique described is the use of partially wide tangential fields with blocking of the heart and inferior lung [64]. Deep tangents may be considered; however, excessive dose to the lung and heart should be avoided. Doses of 45-50 Gy in 1.8-2 Gy fractions are usually used.

Institutions in Europe and Canada have often used hypofractionated schedules for breast cancer treatment [65-67]. Most of the experience has been with whole-breast RT after breast-conserving surgery. However, 15% and 8% of the patients enrolled in the UK Standardisation of Breast Radiotherapy (START) trials A and B, respectively, were treated with mastectomy. Only 14% and 7% of all the patients received regional nodal treatment. The START A and B trials have reported acceptable late tissue effects and tumor control with treatment schedules of 13-15 fractions at 250-320 cGy per fraction [67]. In the British Columbia randomized trial [20] 37.5 Gy was delivered in 16 fractions to the chest wall, while the supraclavicular/axillary field received 35 Gy in 16 fractions. Although hypofractionated treatment has been used in these trials in the postmastectomy setting, the risk of potential additional toxicity, particularly to the brachial plexus and the lymphatics, should be considered.

Toxicity

The EBCTCG meta-analysis demonstrated that the addition of PMRT improved breast-cancer-specific survival at the cost of increased risks of contralateral breast cancer (1.18, P=.02) and non-breast-cancer-related deaths (1.12, P=.001). Most non-breast-cancer deaths were attributed to cardiac causes and, to a lesser extent, lung cancer. Both of these results were seen at 5 years and continued to be evident at the 15-year analysis [24].

An analysis using SEER data found that the cardiac mortality ratio for patients treated with PMRT for left ventricle versus right-sided has improved over time, with 10-year cardiac mortality ratios of 1.2, 1.04, and 0.96 for patients treated between 1973-1982, 1983-1992, and 1993-2001, respectively [68]. This is likely a reflection of the use of more modern treatment techniques, and it emphasizes the importance of 3-dimensional treatment planning to minimize dose to the left ventricle and left anterior descending coronary artery, particularly with the use of cardiotoxic systemic agents such as anthracyclines and trastuzumab. The mortality ratio for lung cancer increased with longer follow-up, so long-term follow-up of patients treated with modern techniques will still be important, particularly in smokers.

The addition of a supraclavicular field increases the risk of lymphedema. The frequency of edema varies according to the extent of lymph node resection and body mass index. Conventional fractionation may be preferred to minimize risk of lymphedema as well as brachial plexopathy.

Summary

- PMRT is recommended for patients with T3N1, T4N1, and T4N2 primary tumors as well as T1-2 disease with 4 or more positive LNs.
- Some controversy remains regarding the benefit of PMRT in patients with T1-2 disease and with one to three positive LNs.
- Patients with pT3N0 tumors may benefit from PMRT in terms of locoregional control, though there are conflicting data regarding its impact on survival.
- Patients undergoing neoadjuvant chemotherapy followed by mastectomy should receive PMRT if they present with clinical stage III disease or have residual nodal involvement.
- There are limited data supporting the routine use of PMRT in patients presenting with clinical stage II disease who achieve a pCR after neoadjuvant chemotherapy.
- The role of IM irradiation in addition to the chest wall and supraclavicular/axillary apex region is unclear, and long-term results from several trials will be important in defining which patients should receive treatment to the IM LNs. Treatment should be considered for patients at risk of IM involvement, such as those with medial or centrally located tumors and positive axillary LNs.
- Three-dimensional treatment planning is important to minimize dose to the lung and heart, particularly the left ventricle and left-anterior descending artery, in order to assure that improvements in breast-cancer-specific survival are not offset by non-breast-cancer mortality.

Supporting Documents

- ACR Appropriateness Criteria® Overview
- Evidence Table

References

1. Arriagada R, Rutqvist LE, Mattsson A, Kramar A, Rotstein S. Adequate locoregional treatment for early breast cancer may prevent secondary dissemination. *J Clin Oncol.* 1995;13(12):2869-2878.
2. Arriagada R, Rutqvist LE, Le MG. Postmastectomy radiotherapy: randomized trials. *Semin Radiat Oncol.* 1999;9(3):275-286.
3. Nielsen HM, Overgaard M, Grau C, Jensen AR, Overgaard J. Study of failure pattern among high-risk breast cancer patients with or without postmastectomy radiotherapy in addition to adjuvant systemic therapy: long-term results from the Danish Breast Cancer Cooperative Group DBCG 82 b and c randomized studies. *J Clin Oncol.* 2006;24(15):2268-2275.
4. Recht A, Gray R, Davidson NE, et al. 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(6):1689-1700.

5. Cheng JC, Chen CM, Liu MC, et al. Locoregional failure of postmastectomy patients with 1-3 positive axillary lymph nodes without adjuvant radiotherapy. *Int J Radiat Oncol Biol Phys.* 2002;52(4):980-988.
6. Taghian A, Jeong JH, Mamounas E, et al. 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(21):4247-4254.
7. Truong PT, Lee J, Kader HA, Speers CH, Olivotto IA. Locoregional recurrence risks in elderly breast cancer patients treated with mastectomy without adjuvant radiotherapy. *Eur J Cancer.* 2005;41(9):1267-1277.
8. Truong PT, Yong CM, Abnousi F, et al. Lymphovascular invasion is associated with reduced locoregional control and survival in women with node-negative breast cancer treated with mastectomy and systemic therapy. *J Am Coll Surg.* 2005;200(6):912-921.
9. Abi-Raad R, Boutrus R, Wang R, et al. Patterns and risk factors of locoregional recurrence in T1-T2 node negative breast cancer patients treated with mastectomy: implications for postmastectomy radiotherapy. *Int J Radiat Oncol Biol Phys.* 2011;81(3):e151-157.
10. Truong PT, Olivotto IA, Speers CH, Wai ES, Berthelet E, Kader HA. A positive margin is not always an indication for radiotherapy after mastectomy in early breast cancer. *Int J Radiat Oncol Biol Phys.* 2004;58(3):797-804.
11. Hetelekidis S, Schnitt SJ, Silver B, et al. The significance of extracapsular extension of axillary lymph node metastases in early-stage breast cancer. *Int J Radiat Oncol Biol Phys.* 2000;46(1):31-34.
12. Gruber G, Cole BF, Castiglione-Gertsch M, et al. Extracapsular tumor spread and the risk of local, axillary and supraclavicular recurrence in node-positive, premenopausal patients with breast cancer. *Ann Oncol.* 2008;19(8):1393-1401.
13. Recht A, Pierce SM, Abner A, et al. Regional nodal failure after conservative surgery and radiotherapy for early-stage breast carcinoma. *J Clin Oncol.* 1991;9(6):988-996.
14. Strom EA, Woodward WA, Katz A, et al. Clinical investigation: regional nodal failure patterns in breast cancer patients treated with mastectomy without radiotherapy. *Int J Radiat Oncol Biol Phys.* 2005;63(5):1508-1513.
15. Albert JM, Gonzalez-Angulo AM, Guray M, et al. Patients with only 1 positive hormone receptor have increased locoregional recurrence compared with patients with estrogen receptor-positive progesterone receptor-positive disease in very early stage breast cancer. *Cancer.* 2011;117(8):1595-1601.
16. Wang SL, Li YX, Song YW, et al. Triple-negative or HER2-positive status predicts higher rates of locoregional recurrence in node-positive breast cancer patients after mastectomy. *Int J Radiat Oncol Biol Phys.* 2011;80(4):1095-1101.
17. Abdulkarim BS, Cuartero J, Hanson J, Deschenes J, Lesniak D, Sabri S. Increased risk of locoregional recurrence for women with T1-2N0 triple-negative breast cancer treated with modified radical mastectomy without adjuvant radiation therapy compared with breast-conserving therapy. *J Clin Oncol.* 2011;29(21):2852-2858.
18. Overgaard M, Hansen PS, Overgaard J, et al. 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(14):949-955.
19. Ragaz J, Jackson SM, Le N, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. *N Engl J Med.* 1997;337(14):956-962.
20. Ragaz J, Olivotto IA, Spinelli JJ, et al. Locoregional radiation therapy in patients with high-risk breast cancer receiving adjuvant chemotherapy: 20-year results of the British Columbia randomized trial. *J Natl Cancer Inst.* 2005;97(2):116-126.
21. Overgaard M, Jensen MB, Overgaard J, 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):1641-1648.
22. Overgaard M, Nielsen HM, Overgaard J. Is the benefit of postmastectomy irradiation limited to patients with four or more positive nodes, as recommended in international consensus reports? A subgroup analysis of the DBCG 82 b&c randomized trials. *Radiother Oncol.* 2007;82(3):247-253.
23. Kyndi M, Sorensen FB, Knudsen H, Overgaard M, Nielsen HM, Overgaard J. Estrogen receptor, progesterone receptor, HER-2, and response to postmastectomy radiotherapy in high-risk breast cancer: the Danish Breast Cancer Cooperative Group. *J Clin Oncol.* 2008;26(9):1419-1426.

24. Clarke M, Collins R, Darby S, et al. 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 randomised trials. *Lancet.* 2005;366(9503):2087-2106.
25. The NCCN Clinical Practice Guidelines in Oncology™ Breast Cancer Version 2.2011 © 2011 National Comprehensive Cancer Network, Inc. 2010; Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
26. Smith BD, Smith GL, Haffty BG. Postmastectomy radiation and mortality in women with T1-2 node-positive breast cancer. *J Clin Oncol.* 2005;23(7):1409-1419.
27. Cheng SH, Horng CF, West M, et al. Genomic prediction of locoregional recurrence after mastectomy in breast cancer. *J Clin Oncol.* 2006;24(28):4594-4602.
28. Jagsi R, Raad RA, Goldberg S, et al. Locoregional recurrence rates and prognostic factors for failure in node-negative patients treated with mastectomy: implications for postmastectomy radiation. *Int J Radiat Oncol Biol Phys.* 2005;62(4):1035-1039.
29. Mamounas EP, Tang G, Fisher B, et al. Association between the 21-gene recurrence score assay and risk of locoregional recurrence in node-negative, estrogen receptor-positive breast cancer: results from NSABP B-14 and NSABP B-20. *J Clin Oncol.* 2010;28(10):1677-1683.
30. Sharma R, Bedrosian I, Lucci A, et al. Present-day locoregional control in patients with t1 or t2 breast cancer with 0 and 1 to 3 positive lymph nodes after mastectomy without radiotherapy. *Ann Surg Oncol.* 2010;17(11):2899-2908.
31. Wallgren A, Bonetti M, Gelber RD, et al. 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(7):1205-1213.
32. Yang PS, Chen CM, Liu MC, et al. Radiotherapy can decrease locoregional recurrence and increase survival in mastectomy patients with T1 to T2 breast cancer and one to three positive nodes with negative estrogen receptor and positive lymphovascular invasion status. *Int J Radiat Oncol Biol Phys.* 2010;77(2):516-522.
33. Truong PT, Woodward WA, Thames HD, Ragaz J, Olivotto IA, Buchholz TA. The ratio of positive to excised nodes identifies high-risk subsets and reduces inter-institutional differences in locoregional recurrence risk estimates in breast cancer patients with 1-3 positive nodes: an analysis of prospective data from British Columbia and the M. D. Anderson Cancer Center. *Int J Radiat Oncol Biol Phys.* 2007;68(1):59-65.
34. 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(1):31-34.
35. Ahmann DL, O'Fallon JR, Scanlon PW, et al. A preliminary assessment of factors associated with recurrent disease in a surgical adjuvant clinical trial for patients with breast cancer with special emphasis on the aggressiveness of therapy. *Am J Clin Oncol.* 1982;5(4):371-381.
36. Klefstrom P, Grohn P, Heinonen E, Holsti L, Holsti P. Adjuvant postoperative radiotherapy, chemotherapy, and immunotherapy in stage III breast cancer. II. 5-year results and influence of levamisole. *Cancer.* 1987;60(5):936-942.
37. Huang EH, Tucker SL, Strom EA, et al. Postmastectomy radiation improves local-regional control and survival for selected patients with locally advanced breast cancer treated with neoadjuvant chemotherapy and mastectomy. *J Clin Oncol.* 2004;22(23):4691-4699.
38. Helinto M, Blomqvist C, Heikkila P, Joensuu H. Post-mastectomy radiotherapy in pT3N0M0 breast cancer: is it needed? *Radiother Oncol.* 1999;52(3):213-217.
39. Floyd SR, Buchholz TA, Haffty BG, et al. Low local recurrence rate without postmastectomy radiation in node-negative breast cancer patients with tumors 5 cm and larger. *Int J Radiat Oncol Biol Phys.* 2006;66(2):358-364.
40. Taghian AG, Jeong JH, Mamounas EP, et al. Low locoregional recurrence rate among node-negative breast cancer patients with tumors 5 cm or larger treated by mastectomy, with or without adjuvant systemic therapy and without radiotherapy: results from five national surgical adjuvant breast and bowel project randomized clinical trials. *J Clin Oncol.* 2006;24(24):3927-3932.
41. Mignano JE, Gage I, Piantadosi S, Ye X, Henderson G, Dooley WC. Local recurrence after mastectomy in patients with T3pN0 breast carcinoma treated without postoperative radiation therapy. *Am J Clin Oncol.* 2007;30(5):466-472.

42. Goulart J, Truong P, Woods R, Speers CH, Kennecke H, Nichol A. Outcomes of node-negative breast cancer 5 centimeters and larger treated with and without postmastectomy radiotherapy. *Int J Radiat Oncol Biol Phys.* 2011;80(3):758-764.
43. Yu JB, Wilson LD, Dasgupta T, Castrucci WA, Weidhaas JB. Postmastectomy radiation therapy for lymph node-negative, locally advanced breast cancer after modified radical mastectomy: analysis of the NCI Surveillance, Epidemiology, and End Results database. *Cancer.* 2008;113(1):38-47.
44. Fisher B, Bryant J, Wolmark N, et al. Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. *J Clin Oncol.* 1998;16(8):2672-2685.
45. Mauri D, Pavlidis N, Ioannidis JP. Neoadjuvant versus adjuvant systemic treatment in breast cancer: a meta-analysis. *J Natl Cancer Inst.* 2005;97(3):188-194.
46. Buchholz TA, Katz A, Strom EA, et al. Pathologic tumor size and lymph node status predict for different rates of locoregional recurrence after mastectomy for breast cancer patients treated with neoadjuvant versus adjuvant chemotherapy. *Int J Radiat Oncol Biol Phys.* 2002;53(4):880-888.
47. Buchholz TA, Tucker SL, Masullo L, et al. Predictors of local-regional recurrence after neoadjuvant chemotherapy and mastectomy without radiation. *J Clin Oncol.* 2002;20(1):17-23.
48. Garg AK, Strom EA, McNeese MD, et al. T3 disease at presentation or pathologic involvement of four or more lymph nodes predict for locoregional recurrence in stage II breast cancer treated with neoadjuvant chemotherapy and mastectomy without radiotherapy. *Int J Radiat Oncol Biol Phys.* 2004;59(1):138-145.
49. Nagar H, Mittendorf EA, Strom EA, et al. Local-regional recurrence with and without radiation therapy after neoadjuvant chemotherapy and mastectomy for clinically staged T3N0 breast cancer. *Int J Radiat Oncol Biol Phys.* 2011;81(3):782-787.
50. Garg AK, Oh JL, Oswald MJ, et al. Effect of postmastectomy radiotherapy in patients <35 years old with stage II-III breast cancer treated with doxorubicin-based neoadjuvant chemotherapy and mastectomy. *Int J Radiat Oncol Biol Phys.* 2007;69(5):1478-1483.
51. McGuire SE, Gonzalez-Angulo AM, Huang EH, et al. Postmastectomy radiation improves the outcome of patients with locally advanced breast cancer who achieve a pathologic complete response to neoadjuvant chemotherapy. *Int J Radiat Oncol Biol Phys.* 2007;68(4):1004-1009.
52. Le Scodan R, Selz J, Stevens D, et al. Radiotherapy for stage II and stage III breast cancer patients with negative lymph nodes after preoperative chemotherapy and mastectomy. *Int J Radiat Oncol Biol Phys.* 2012;82(1):e1-7.
53. Buchholz TA, Lehman CD, Harris JR, et al. Statement of the science concerning locoregional treatments after preoperative chemotherapy for breast cancer: a National Cancer Institute conference. *J Clin Oncol.* 2008;26(5):791-797.
54. Rashtian A, Iganej S. 195 Close or Positive Margins Following Mastectomy for Ductal Carcinoma in Situ (DCIS): Patterns of Relapse and Potential Indications for Radiotherapy. *Int J Radiat Oncol Biol Phys.* 2006;66(3 Suppl 1):S108-S109.
55. Carlson GW, Page A, Johnson E, Nicholson K, Styblo TM, Wood WC. Local recurrence of ductal carcinoma in situ after skin-sparing mastectomy. *J Am Coll Surg.* 2007;204(5):1074-1078; discussion 1078-1080.
56. Chan LW, Rabban J, Hwang ES, et al. Is radiation indicated in patients with ductal carcinoma in situ and close or positive mastectomy margins? *Int J Radiat Oncol Biol Phys.* 2011;80(1):25-30.
57. Kim JH, Tavassoli F, Haffty BG. Chest wall relapse after mastectomy for ductal carcinoma in situ: a report of 10 cases with a review of the literature. *Cancer J.* 2006;12(2):92-101.
58. Romestaing P, Belot A, Hennequin C, et al. Ten-year Results of a Randomized Trial of Internal Mammary Chain Irradiation after Mastectomy. *International Journal of Radiation Oncology*Biology*Physics.* 2009;75(3, Supplement 1):S1-S1.
59. Whelan TJ, Olivotto I, Ackerman I, et al. NCIC-CTG MA.20: An intergroup trial of regional nodal irradiation in early breast cancer. *ASCO Meeting Abstracts.* 2011;29(18_suppl):LBA1003.
60. Macdonald SM, Abi-Raad RF, Alm El-Din MA, et al. 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(5):1297-1303.
61. Li XA, Tai A, Arthur DW, et al. Variability of target and normal structure delineation for breast cancer radiotherapy: an RTOG Multi-Institutional and Multiobserver Study. *Int J Radiat Oncol Biol Phys.* 2009;73(3):944-951.
62. Radiation Therapy Oncology Group. Breast cancer atlas for radiation therapy planning: consensus definitions. http://www.rtog.org/LinkClick.aspx?fileticket=vzJFhPaBipE%3D&tabid=236. Accessed 5 December 2011.

63. Moran MS, Haffty BG. Radiation techniques and toxicities for locally advanced breast cancer. *Semin Radiat Oncol.* 2009;19(4):244-255.
64. Pierce LJ, Butler JB, Martel MK, et al. Postmastectomy radiotherapy of the chest wall: dosimetric comparison of common techniques. *Int J Radiat Oncol Biol Phys.* 2002;52(5):1220-1230.
65. Shelley W, Brundage M, Hayter C, Paszat L, Zhou S, Mackillop W. A shorter fractionation schedule for postlumpectomy breast cancer patients. *Int J Radiat Oncol Biol Phys.* 2000;47(5):1219-1228.
66. Whelan TJ, Pignol JP, Levine MN, et al. Long-term results of hypofractionated radiation therapy for breast cancer. *N Engl J Med.* 2010;362(6):513-520.
67. Bentzen SM, Agrawal RK, Aird EG, et al. The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. *Lancet.* 2008;371(9618):1098-1107.
68. Darby SC, McGale P, Taylor CW, Peto R. Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: prospective cohort study of about 300,000 women in US SEER cancer registries. *Lancet Oncol.* 2005;6(8):557-565.

Clinical Condition: **Postmastectomy Radiotherapy**

Variant 1: **50-year-old woman, infiltrating ductal carcinoma, status post (S/P) modified radical mastectomy, 1.5 cm upper outer quadrant (UOQ), margins (–), 4/15 LNs (+). No blood vessel invasion or LVI, no metastasis, systemic treatment planned (type undecided). ER/PR (+), Her2 not overexpressed.**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	9	
Supraclavicular fossa/level III axilla RT	9	
Supraclavicular fossa and level I-III axilla RT	3	
Internal mammary node RT	7	
Central chest wall boost	8	Boost may be appropriate, as indicated by risk of residual microscopic disease relative to the radiation dose achieved with comprehensive chest wall irradiation.
Chest Wall RT Doses		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	6	In selected cases may be appropriate.
Supraclavicular Fossa/Axillary RT Doses		
45-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
IMN Chain RT Doses (if treating)		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
Chest Wall Boost RT Doses (if treating)		
10 Gy in 5 fractions	9	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**

Clinical Condition: **Postmastectomy Radiotherapy**

Variant 2: **50-year-old postmenopausal woman, infiltrating ductal carcinoma, S/P modified radical mastectomy, 6.5 cm UOQ, margins (–), 2/15 LNs (+), ER/PR (+), Her2 (–). No blood vessel invasion or LVI, no metastasis, systemic treatment planned (type undecided).**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	9	
Supraclavicular fossa/level III axilla RT	9	
Supraclavicular fossa and level I-III axilla RT	3	
Internal mammary node RT	8	
Central chest wall boost	8	Boost may be appropriate, as indicated by risk of residual microscopic disease relative to the radiation dose achieved with comprehensive chest wall irradiation.
Chest Wall RT Doses		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	6	In selected cases may be appropriate.
Supraclavicular Fossa/Axillary RT Doses		
45-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
IMN Chain RT Doses (if treating)		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
Chest Wall Boost RT Doses (if treating)		
10 Gy in 5 fractions	9	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**

Clinical Condition: **Postmastectomy Radiotherapy**

Variant 3: **54-year-old postmenopausal woman, infiltrating ductal carcinoma, S/P modified radical mastectomy, 1.5 cm UOQ, margins (–), 2/15 LNs (+), ER/PR (+), Her2 (–). No blood vessel invasion or LVI, no metastasis, systemic treatment planned (type undecided).**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	7	
Supraclavicular fossa/level III axilla RT	7	
Supraclavicular fossa and level I-III axilla RT	3	
Internal mammary node RT	7	
Central chest wall boost	7	Boost may be appropriate, as indicated by risk of residual microscopic disease relative to the radiation dose achieved with comprehensive chest wall irradiation.
Chest Wall RT Doses		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	6	In selected cases may be appropriate.
Supraclavicular Fossa/Axillary RT Doses		
45-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
IMN Chain RT Doses (if treating)		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
Chest Wall Boost RT Doses (if treating)		
10 Gy in 5 fractions	9	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 4: **40-year-old woman, S/P mastectomy and sentinel node biopsy for multifocal invasive breast cancer, no focus greater than 1.0 cm. Sentinel node frozen section was negative, but the permanent section shows a focus of metastasis (<2 mm). Completion level I/II axillary dissection demonstrates no further tumor in nine lymph nodes. Cytotoxic chemotherapy is planned. ER/PR (–), immunohistochemistry only (+).**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	1	
Supraclavicular fossa/level III axilla RT	1	
Supraclavicular fossa and level I-III axilla RT	1	
Internal mammary node RT	1	
Central chest wall boost	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Postmastectomy Radiotherapy**

Variant 5: **50-year-old woman, grade 3 infiltrating ductal carcinoma, S/P modified radical mastectomy, tumor is 3.5 cm UOQ, margins (–), 0/15 LNs (+). No blood vessel invasion or LVI, no metastasis, systemic treatment planned (type undecided). ER/PR, Her2, and menopause status will not alter treatment options.**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	1	
Supraclavicular fossa/level III axilla RT	1	
Supraclavicular fossa and level I-III axilla RT	1	
Internal mammary node RT	1	
Central chest wall boost	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 6: **40-year-old premenopausal woman, with infiltrating ductal carcinoma, S/P modified radical mastectomy, 3.5 cm UOQ, positive deep margins (tumor at ink), 0/15 LNs (+). No blood vessel invasion or LVI, no metastasis, systemic treatment planned (type undecided).**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	9	
Supraclavicular fossa/level III axilla RT	2	
Supraclavicular fossa and level I-III axilla RT	1	
Internal mammary node RT	2	
Central chest wall boost	9	
Chest Wall RT Doses		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	6	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Postmastectomy Radiotherapy**

Variant 7: **50-year-old postmenopausal woman with infiltrating ductal carcinoma, S/P modified radical mastectomy, 6.5 cm UOQ, margins (–), 0/15 LNs (+), ER/PR (+), Her2 (–). No blood vessel invasion or LVI, no metastasis, systemic treatment planned (type undecided).**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	7	Recommendation to treat is individualized and based on patient age, tumor grade, margin status and +/- LVI.
Supraclavicular fossa/level III axilla RT	5	
Supraclavicular fossa and level I-III axilla RT	1	
Internal mammary node RT	5	There may be circumstances where nodal radiation is appropriate, depending on optimal chest wall coverage relative to the primary tumor position.
Central chest wall boost	7	Boost may be appropriate, as indicated by risk of residual microscopic disease relative to the radiation dose achieved with comprehensive chest wall irradiation.
Chest Wall RT Doses		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	6	In selected cases may be appropriate.
Supraclavicular Fossa/Axillary RT Doses		
45-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
IMN Chain RT Doses (if treating)		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
Chest Wall Boost RT Doses (if treating)		
10 Gy in 5 fractions	9	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**

Clinical Condition: **Postmastectomy Radiotherapy**

Variant 8: **50-year-old postmenopausal woman with clinical stage III (T3N1) infiltrating ductal carcinoma, ER/PR (–), Her2 (–); treated with neoadjuvant chemotherapy followed by mastectomy and sentinel lymph node biopsy. Final pathology demonstrates no residual tumor in the breast and 0/2 SLN. Margins (–), no LVI.**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	8	
Supraclavicular fossa/level III axilla RT	7	
Supraclavicular fossa and level I-III axilla RT	7	
Internal mammary node RT	5	
Central chest wall boost	4	
Chest Wall RT Doses		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
Supraclavicular Fossa/Axillary RT Doses		
45-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
IMN Chain RT Doses (if treating)		
50-50.4 Gy in 25-28 fractions	8	
37.5-42.5 Gy in 16 fractions	3	
Chest Wall Boost RT Doses (if treating)		
10 Gy in 5 fractions	8	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**

Clinical Condition: **Postmastectomy Radiotherapy**

Variant 9: **50-year-old postmenopausal woman with clinical stage IIB (T2N1) infiltrating ductal carcinoma, ER/PR (+), Her2 (+); Prechemotherapy FNA of axillary LN was positive. Treated with neoadjuvant chemotherapy followed by mastectomy and lymph node dissection. Final pathology demonstrates no residual tumor in the breast and 0/15 LN. Margins (–), no LVI.**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	7	
Supraclavicular fossa/level III axilla RT	7	
Supraclavicular fossa and level I-III axilla RT	3	
Internal mammary node RT	4	
Central chest wall boost	4	
Chest Wall RT Doses		
50-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	2	
Supraclavicular Fossa/Axillary RT Doses		
45-50.4 Gy in 25-28 fractions	9	
37.5-42.5 Gy in 16 fractions	3	
IMN Chain RT Doses (if treating)		
50 Gy in 25 fractions	8	
37.5-42.5 Gy in 16 fractions	3	
Chest Wall Boost RT Doses (if treating)		
10 Gy in 5 fractions	8	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 10: **45-year-old woman, with diffuse suspicious calcifications, positive for DCIS, S/P simple mastectomy, no invasive carcinoma, but diffuse high-grade comedo DCIS with a positive deep margin (tumor at ink). Sentinel node at the time of mastectomy was negative.**

Treatment	Rating	Comments
Principles of Treatment (Volumes)		
Chest wall RT	7	Chest wall irradiation may be indicated, depending on tumor grade, histology and the patient's age.
Supraclavicular fossa/level III axilla RT	1	
Supraclavicular fossa and level I-III axilla RT	1	
Internal mammary node RT	1	
Central chest wall boost	7	Boost is considered appropriate if a decision to treat is made and site of margin can be identified at simulation by surgical clips.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		