American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Local Regional Recurrence (LR) and Salvage Surgery — Breast Cancer**

Variant 1: **37-year-old, 1.2 cm LR in breast 2.5 years after BCT with lumpectomy and axillary node dissection + RT for T1bN0 lesion. ER/PR (–). EOD workup negative.**

Treatment	Rating	Comments
Principles of Treatment		
Chemotherapy	8	Consider clinical trial.
Simple mastectomy (SM)	8	
SM + sentinel lymph node biopsy (SLNB)	3	
SM + LND or modified radical mastectomy	2	
Lumpectomy	2	Only in a clinical trial.
Quadrantectomy	2	
Lumpectomy + RT	1	Only in a clinical trial.
Hormone therapy	1	
RT Volumes		
Whole breast +/- boost	1	
Chest wall (after mastectomy)	1	
Supraclavicular (adequate LND)	1	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Variant 2: **52-year-old, 0.5 cm LR in breast 15 years after BCT with lumpectomy and axillary node dissection + RT for T1bN0 lesion. ER/PR (+). EOD workup negative.**

Treatment	Rating	Comments
Principles of Treatment		
Simple mastectomy (SM)	8	
SM + sentinel lymph node biopsy (SLNB)	3	
SM + LND or modified radical mastectomy	2	
Lumpectomy	3	Only in a clinical trial.
Quadrantectomy	3	
Lumpectomy + RT	1	Only in a clinical trial.
RT Volumes		
Whole breast +/- boost	1	
Chest wall (after mastectomy)	1	
Supraclavicular (adequate LND)	1	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Clinical Condition: **Local Regional Recurrence (LR) and Salvage Surgery — Breast Cancer**

Variant 3: **60-year-old, simultaneous breast skin + SCL recurrence 3 years after BCT with lumpectomy + RT for T1bN0 lesion. ER/PR (–). EOD workup negative.**

Treatment	Rating	Comments
Principles of Treatment		
Chemotherapy	9	
Simple mastectomy (SM)	2	
SM + LND or modified radical mastectomy	2	
Lumpectomy	2	
Quadrantectomy	2	
Lumpectomy + RT	2	
Hormone therapy	2	
RT Volumes		
Supraclavicular (adequate LND)	8	
Whole breast +/- boost	2	
Chest wall (after mastectomy)	2	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Variant 4: **42-year-old, 3.0 cm LR in breast 6 years after BCT + chemo for T1cN0 lesion. ER/PR (–). EOD workup positive: liver and multiple bone metastases.**

Treatment	Rating	Comments
Principles of Treatment		
Chemotherapy	9	
Simple mastectomy (SM)	2	
SM + LND or modified radical mastectomy	2	
Lumpectomy	2	
Quadrantectomy	2	
Lumpectomy + RT	2	
Hormone therapy	2	
RT Volumes		
Whole breast +/- boost	2	
Chest wall (after mastectomy)	2	
Supraclavicular (adequate LND)	2	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Clinical Condition: **Local Regional Recurrence (LR) and Salvage Surgery — Breast Cancer**

Variant 5: **55-year-old, 1.5 cm LR in breast 7 years after BCT with lumpectomy only + RT for original diagnosis of DCIS, not otherwise specified. Biopsy: invasive ductal carcinoma. ER/PR (–). EOD workup negative.**

Treatment	Rating	Comments
Principles of Treatment		
Chemotherapy	8	
SM + LND or modified radical mastectomy	8	
SM + sentinel lymph node biopsy (SLNB)	8	
Simple mastectomy (SM)	2	
Lumpectomy	2	
Quadrantectomy	2	
Lumpectomy + RT	2	
Hormone therapy	2	
RT Volumes		
Whole breast +/- boost	2	
Chest wall (after mastectomy)	2	
Supraclavicular (adequate LND)	2	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Variant 6: **55-year-old, 7 nodules (1-2 cm diameter) along MRM scar 3 years after MRM + chemo + adjuvant chest wall/SCL RT (50 Gy). Primary and LR both ER/PR (–).**

Treatment	Rating	Comments
Complete excision of recurrence	8	If technically possible with primary closure with or without simple advancement flap.
Chemotherapy	7	Consider for study.
Radiation therapy	7	Use judgment on RT volume.
Hyperthermia + RT	6	
Hormone therapy	1	
Hyperthermia alone	1	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Clinical Condition: **Local Regional Recurrence (LR) and Salvage Surgery — Breast Cancer**

Variant 7: **60-year-old, 2 cm nodule on MRM scar 4 years after MRM + chemo for T1N1 [3 LNs (+)]. FNA (+). Primary ER/PR (+): PR (+): Nodule ER/PR (+) by immunohist. Asymptomatic EOD workup negative.**

Treatment	Rating	Comments
Principles of Treatment		
Complete excision of recurrence	8	
Radiation therapy	8	
Hormone therapy	8	
Chemotherapy	5	
Hyperthermia	2	
RT Volumes		
Chest wall	9	
Supraclavicular fossa	8	
Axilla	2	
Internal mammary nodes (IMN)	2	
RT Doses		
Chest Wall: 4000 cGy/16-20 fractions	2	
Chest Wall: 4500-4680 cGy/23-26 fractions	2	
Chest Wall: 5000-5040 cGy/25-28 fractions	8	
Supraclavicular: 4000 cGy/16-20 fractions	2	
Supraclavicular: 4500-4680 cGy/23-26 fractions	8	
Supraclavicular: 5000-5040 cGy/25-28 fractions	8	
IMN (excluding gross disease): 4500-4680 cGy/23-26 fractions	2	
IMN (excluding gross disease): 5000-5040 cGy/25-28 fractions	2	
Total dose including boost: 5000 cGy	2	
Total dose including boost: 5100-5900 cGy	8	
Total dose including boost: 6000-7000 cGy	8	
Total dose including boost: >7000 cGy	2	
Modality/Other Factors		
Wedge filters (chest wall photons)	8	
Computer planning	8	
Photons with bolus (chest wall)	8	
Electrons	8	

Rating Scale: **1=Least appropriate, 9=Most appropriate**

Clinical Condition: **Local Regional Recurrence (LR) and Salvage Surgery — Breast Cancer**

Variant 8: **42-year-old, 2 cm parasternal lump (2nd interspace) + 1 cm medial SCL Node 9 months after MRM + chemo for T2N1 [4 LNs (+)]. Primary ER/PR (+): PR (+). Lump ER/PR (+) by immunohist. EOD workup negative.**

Treatment	Rating	Comments
Principles of Treatment		
Chemotherapy	9	
Radiation therapy	9	
Hormone therapy	8	
Complete excision of recurrence	2	
Hyperthermia	2	
RT Volumes		
Chest wall	9	
Supraclavicular fossa	9	
Internal mammary nodes (IMN)	9	
Axilla	3	
RT Doses		
Chest Wall: 4000 cGy/16-20 fractions	2	
Chest Wall: 4500-4680 cGy/23-26 fractions	2	
Chest Wall: 5000-5040 cGy/25-28 fractions	8	
Supraclavicular: 4000 cGy/16-20 fractions	2	
Supraclavicular: 4500-4680 cGy/23-26 fractions	2	
Supraclavicular: 5000-5040 cGy/25-28 fractions	8	
IMN(excluding gross disease): 4500-4680 cGy/23-26 fractions	5	
IMN (excluding gross disease): 5000-5040 cGy/25-28 fractions	8	
Total dose including gross disease site boost: 5000 cGy	2	
Total dose including gross disease site boost: 5100-5900 cGy	3	
Total dose including gross disease site boost: 6000-7000 cGy	8	
Total dose including gross disease site boost: >7000 cGy	3	
Modality/Other Factors		
Wedge filters (chest wall photons)	8	
Computer planning	8	
Photons with bolus (chest wall)	8	
Electrons	8	

Rating Scale: **1=Least appropriate, 9=Most appropriate**

Clinical Condition: **Local Regional Recurrence (LR) and Salvage Surgery — Breast Cancer**

Variant 9: **42-year-old, 2.0 cm nodule on MRM scar 6 years after MRM for T1bN0 lesion. FNA (+). ER/PR (+) nodule. Asymptomatic EOD workup negative.**

Treatment	Rating	Comments
Principles of Treatment		
Complete excision of recurrence	8	
Radiation therapy	8	
Chemotherapy	8	
Hormone therapy	8	
Hyperthermia	2	
RT Volumes		
Chest wall	9	
Supraclavicular fossa	8	
Internal mammary nodes (IMN)	5	
Axilla	2	
RT Doses		
Chest Wall: 4000 cGy/16-20 fractions	2	
Chest Wall: 4500-4680 cGy/23-26 fractions	2	
Chest Wall: 5000-5040 cGy/25-28 fractions	8	
Supraclavicular: 4000 cGy/16-20 fractions	2	
Supraclavicular: 4500-4680 cGy/23-26 fractions	8	
Supraclavicular: 5000-5040 cGy/25-28 fractions	8	
IMN (if treated): 4500-4680 cGy/23-26 fractions	8	
IMN (if treated): 5000-5040 cGy/25-28 fractions	8	
Total dose including gross disease site boost: 5000 cGy	2	
Total dose including gross disease site boost: 5100- 5900 cGy	3	
Total dose including gross disease site boost: 6000-7000 cGy	8	
Total dose including gross disease site boost: >7000 cGy	2	
Modality/Other Factors		
Wedge filters (chest wall photons)	8	
Computer planning	8	
Photons with bolus (chest wall)	8	
Electrons	8	

Rating Scale: **1=Least appropriate, 9=Most appropriate**

Clinical Condition: **Local Regional Recurrence (LR) and Salvage Surgery — Breast Cancer**

Variant 10: **55-year-old, 1.5 cm LR in breast 7 years after BCT with lumpectomy only for 1.2 cm tubular CA. Biopsy: tubular CA. ER/PR (–). EOD workup negative.**

Treatment	Rating	Comments
Principles of Treatment		
Simple mastectomy (SM) + lymph node dissection (LND)	8	
Modified radical mastectomy	8	
Lumpectomy + RT	8	
Lumpectomy + LN staging + RT	8	
Simple mastectomy (SM)	2	
Lumpectomy	2	
Quadrantectomy	2	
RT Volumes		
Whole breast +/- boost	8	
Chest wall (after mastectomy)	2	
Supraclavicular (adequate LND)	2	
Rating Scale: **1=Least appropriate, 9=Most appropriate**		

Expert Panel on Radiation Oncology–Breast: Sheryl Green, MB, ChB[1]; Brenda M. Shank, MD, PhD[2]; Bruce G. Haffty, MD[3]; Francine E. Halberg, MD[4]; Sandra E. Mitchell, MD[5]; Rachel Rabinovitch, MD[6]; Lawrence J. Solin, MD[7]; Eric A. Strom, MD[8]; Marie E. Taylor, MD[9]; Julia R. White, MD[10]; Melody A. Cobleigh, MD[11]; Stephen B. Edge, MD.[12]

Summary of Literature Review

Introduction

For almost two decades, the major focus of radiation oncologists specializing in the management of breast cancer has been on performing both randomized and nonrandomized trials comparing breast-conserving surgery and radiation with the more traditional modified radical mastectomy. With the gradual acceptance of these two local regional therapies as equivalent in the management of early-stage invasive breast cancer by the late 1980s, attention was then refocused on identifying factors (pathologic, patient, or therapy-oriented), that predicted for the success or failure of the treatment locally.

Accompanying these very real clinical goals was a philosophical discussion on the relationship of a local recurrence to the development of distant failure and eventually death from the disease. Early on, it was noted that the survival rate from salvage surgery for failures in the conserved breast was 50% or higher at five years, and local failures following breast-conserving surgery and radiation were somehow classified as "different" from local regional failures following mastectomy, which were readily linked with the development of distant disease and thought incurable [1-5].

The success story of systemic chemotherapy and hormone therapy in the management of breast cancer needs to be emphasized as well. The survival and disease-free survival patterns of patients have changed. Women who decades ago would have died rapidly from distant disease may now survive long enough to exhibit a local regional failure. Thus, our thoughts on the consequences of these failures without distant disease must change as well. A prospective randomized trial from the European Organization for Research and Treatment of Cancer (EORTC) group comparing mastectomy with breast-conserving surgery and radiation in patients of similar stages with similar systemic therapy surprisingly showed almost identical 5-year survival rates following salvage procedures for local-only failures in both the breast-conserved arm and the mastectomy arm [6].

The relationship between local failure and distant failure must be reanalyzed in both groups of patients, ie, those treated with mastectomy and those treated with breast-conserving surgery and radiation. Conversely, the importance of obtaining local control with initial treatment must remain important not only for the goal of preventing either the loss of the breast in the conserved patients or painful and difficult-to-control local failure in the mastectomy patients, but also to potentially decrease subsequent distant metastases that may be associated with these local failures. As chemotherapeutic regimens for the risk of distant disease become more effective, this goal of ensuring local control takes on a potentially greater importance. Although Fisher et al [7] have hypothesized that local failure in the conserved breast is a predictor of distant failure as well, others have challenged this concept and concluded that a recurrence in the breast causes distant metastases. Data from the Early Breast Cancer Trialists Collaborative Group (EBCTCG) demonstrate that treatments resulting in improved local control may lead to decrease in breast cancer mortality [8]. The overview analysis also suggests that avoidance of local recurrence in a conserved breast (after breast-conserving surgery and radiation) and avoidance of a local recurrence elsewhere (ie, the chest wall or regional nodes) after mastectomy are of comparable relevance to 15-year breast cancer mortality.

Recurrence after Breast-Conserving Surgery and Radiation

Predictors for local regional failure after both breast-conserving surgery and radiation can be divided into three broad categories. The first involves factors related to the patient herself. Very young age at the time of diagnosis, defined as either younger than age 30 or 40, appears to be a strong predictor [7,9-11].

The second category consists of tumor factors that have been analyzed after breast-conserving surgery. Most studies have found that positive microscopic margins, gross multifocality, and an extensive intraductal component (EIC) are associated with a higher risk of recurrence in the conserved breast. Some series have noted larger size and lymphatic vessel invasion as risk factors [6,7,9,11-18].

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The third category consists of therapeutic factors, the most important of which is the omission of breast radiation, for predicting local recurrence. Numerous studies have demonstrated that radiation therapy dramatically reduces the risk of recurrence in the breast [7,19,20]. Patients receiving systemic chemotherapy or hormone therapy appear to have higher local control rates, all else being equal, than those who do not [15,21]. The size of the surgical procedure affects local control in many series, which can also be related to the margin status [9,16]. The addition of a radiation boost to the lumpectomy cavity may decrease the incidence of a recurrence in the conserved breast, particularly in women (younger than age 40.) [21].

The generally recommended treatment for locally recurrent breast cancer after breast conservation is salvage mastectomy [22]. This results in local control in 85%-95% of patients with an ipsilateral breast tumor recurrence (IBTR) [1,3-5,23-27]. Following an IBTR, overall survival rates range from 45%-80% at 5 years and 40%-65% at 10 years [1,3-5,23-27].

In patients who are operable after local recurrence only, involvement of the skin or multiple positive lymph nodes appears to be associated with a larger risk of subsequent failure than recurrence in breast tissue only [23,27,28]. The incidence of nodal recurrence in breast-conserving series is low and has not been a major management problem [29-31]. However, involvement of the nodes would have significant impact on outcome; therefore, assessment of the axillary status for an invasive local recurrence of the breast should be considered. The role of sentinel lymph node biopsy (SLNB) in this scenario remains to be defined. Preliminary data indicate that SLNB may be performed at the time of salvage surgery, as previous breast or axillary surgery may not be a contraindication to SLNB [32,33].

Because of the relationship between local recurrence and distant failure, systemic therapy must also be considered in the treatment program of this patient group. To date, no published series has shown a statistically significant improvement in subsequent outcome with the administration of salvage chemotherapy or hormonal intervention at the time of local recurrence. Factors to be considered in this clinical decision include prior systemic therapy, if any; extent of recurrence; time interval from initial treatment to recurrence; tumor hormone receptor status, patient age, and general medical condition [1,23,34]. The National Surgical Adjuvant Breast and Bowel Project (NSABP) are evaluating the benefit of adjuvant chemotherapy following radical resection of locoregionally recurrent breast cancer. This prospective randomized trial is currently open to accrual.

Some patients who present with an IBTR following conservative surgery and radiation therapy may have a new primary tumor as opposed to a true local recurrence [35,36]. The second breast tumor has been defined as a new primary if it is distinctly different from the original tumor with respect to histology subtype, if it presents in a different location in the breast, or if flow cytometry has changed from aneuploid to diploid. The time interval between the original primary and the second tumor is generally considerably greater for new primaries compared to true recurrences (7.3 vs 3.7 years) [36]. Ten-year overall survival rates (75% vs 55%) and distant disease-free survival rates (85% vs 41%) tend to be much better for patients with new primaries compared to those with true recurrences [36]. Thus the diagnosis of a new primary as opposed to a true recurrence implies a different natural history and prognosis, and has different implications for therapeutic management. Unfortunately, most series addressing breast tumor recurrences do not adequately distinguish between the two entities. This may be of particular importance to breast cancer management in young women with BRCA 1/2 mutations, who are at increased risk for breast tumor recurrences due to new primaries.

Patients with DCIS who undergo breast-conserving therapy and subsequently sustain a recurrence in the treated breast appear to have an excellent outcome following salvage therapy [37]. In most series, about half of the recurrences are invasive, with the other half recurring as DCIS. Nevertheless, almost all these patients can be cured by mastectomy. Solin et al reported an overall survival rate of 92% and a distant metastasis-free survival rate of 89% at 8 years, following salvage therapy [37,38].

Recurrence after Mastectomy

Risk factors for local regional failure following mastectomy can also be divided into clinical, pathological, and treatment-related categories. Young age (defined as younger than 35 or 40 years) has been associated with an increased risk of locoregional recurrence after mastectomy [24,26]. Patients with certain pathological risk factors, principally four or more involved nodes, T3 or T4 tumors, lymphatic vessel invasion, or involvement of the overlying skin or underlying muscle, are at increased risk for local regional recurrence. Patients whose mastectomy specimens yield a positive deep margin are also at increased risk for such failure. Elective postmastectomy irradiation reduces this risk. There is controversy regarding the risk of chest wall recurrence in the subgroup of patients with one to three positive nodes and their need for postmastectomy radiation therapy (See the Appropriateness Criteria® topic on "Postmastectomy Radiotherapy").

Systemic therapy appears to have an impact on locoregional control. In the most recent meta-analysis of systemic therapy from the EBCTG, five years of tamoxifen reduced the local recurrence rate by about one-half in women with hormone receptor-positive disease (local recurrence ratio of 0.47), while, irrespective of hormone receptor status, polychemotherapy reduced it by about one-third (ratios 0.63-0.70 depending on patient age) [39].

In contrast to local recurrence in the breast following breast-conserving therapy (BCT), local chest wall or

regional recurrence of breast cancer, or both, following mastectomy carries a worse prognosis. Five year survival rates range from 35%-75% and 10 year survival rates range from 25%-55%. Long-term control of the local regional disease is achieved in only 45%-70% of patients. Most patients develop distant metastases [2,4,40]. Prognostic factors include the extent of disease initially and at recurrence, the disease-free interval, and the ER status as well as the use of surgical excision, radiation, and hormonal therapy. Aggressive attempts at controlling the local-regional recurrence are warranted, however, because patients with uncontrolled local-regional disease are usually symptomatic, are more likely to develop distant metastases, and die sooner than patients whose local-regional recurrences are controlled.

A multidisciplinary approach is required for the management of a chest wall recurrence after mastectomy. Surgical resection should be performed if the size and location of the recurrence permit. In patients who have not received prior radiation therapy, local-regional recurrences are managed with high-dose irradiation [41]. Local-regional recurrence after mastectomy is a harbinger of distant metastases, so systemic treatment should also be considered. If the patient is ER positive, tamoxifen, an aromatase inhibitor (depending on menopausal status) or ovarian ablation may be used. If the patient is ER negative, then chemotherapy may be given [2].

Treatment Guidelines after Breast Conserving Therapy

For patients failing BCT that included standard whole-breast radiation and an axillary node dissection, simple mastectomy is recommended as the local treatment of choice when the failure is confined to the breast parenchyma and is operable.

In the clinical situation involving recurrence in the treated breast, along with a supraclavicular nodal failure, the recommendation is for radiation to the untreated supraclavicular area, and chemotherapy. Although this pattern of recurrence is not common, it is viewed as systemic failure based on existing evidence. Similarly, for patients with clear distant metastases as well as local failure, primary systemic management is recommended rather than mastectomy.

In the rare clinical situation of a local recurrence for a patient whose initial treatment consisted only of a wide local excision without radiation or axillary dissection, treatment options include either modified radical mastectomy or lumpectomy, axillary nodal evaluation, and radiation therapy, in other words, the decision tree open to a patient with newly diagnosed breast cancer, provided the systemic workup was negative.

Given the situation of a patient who had had lumpectomy plus radiation therapy only, for a diagnosis of DCIS initially, with recurrence of operable invasive cancer, modified radical mastectomy is recommended, as well as consideration of systemic therapy.

Supporting Document(s)

- ACR Appropriateness Criteria® Overview
- Evidence table under review

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