American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Conservative Surgery and Radiation — Stage I and II Breast Carcinoma**

Variant 1: **Premenopausal 45-year-old woman, left breast 1.9 cm UIQ, primary with lumpectomy, margins (–), GIII IDC, ER/PR (–), Her2 (–), SN 1/3 (+) micro metastases; chemotherapy planned.**

Treatment	Rating	Comments
Principles of Treatment		
Modified radical mastectomy	9	If by patient choice.
LND + RT	9	
No LND + breast and nodal RT	7	
No LND + breast RT	5	LND is standard of care.
Simple mastectomy	2	LND is standard of care.
LND + accelerated partial breast irradiation (PBI)	No consensus	No consensus for standard of care outside of protocol participation.
Radiation Volumes (assume LND done, 10 additional negative nodes)		
Whole breast ± boost	9	
Supraclavicular + apical axillary nodes (level III) (assumes breast RT given)	6	
IMN (assumes breast RT given)	6	
Full axilla (level I-III) (assumes breast RT given)	2	
RT Doses (180-200 cGy/day unless specified otherwise), assume LND done, 10 additional negative nodes		
Whole breast: 42 Gy (16 fractions) no boost	4	No published experience using boost with this fractionation.
Whole breast: 45-50 Gy	9	
Total tumor bed dose: 45-49 Gy	1	
Total tumor bed dose: 50 Gy	3	
Total tumor bed dose: 60-66 Gy	9	
SCL ± axillary apex: 45-50 Gy	6	If treated.
IMN: 45-50 Gy	6	If treated.
Radiation Volumes (assume NO LND done and breast RT planned)		
SCL + full axilla	8	
Level 1-2 axilla (without SCL)	8	
IMN	7	
SCL + apical nodes (without axilla)	3	

RT Doses (180-200 cGy/day unless specified otherwise), assume No LND done Full axilla: 45-50 Gy	9	
Whole breast: 42 Gy (16 fractions) no boost	4	No published experience using boost with this fractionation.
Whole breast: 45-50 Gy	9	
Total tumor bed dose: 45-49 Gy	1	
Total tumor bed dose: 50 Gy	3	
Total tumor bed dose: 60-66 Gy	9	
SCL: 45-50 Gy	6	If treated.
IMN: 45-50 Gy	6	If treated.
Other Treatment Factors CT based multiplane or 3D treatment planning with dose homogeneity compensation	9	
Lung inhomogeneity correction	9	
Fluoroscopic 2D planning with single-slice homogeneity corrections	4	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Clinical Condition: **Conservative Surgery and Radiation — Stage I and II Breast Carcinoma**

Variant 2: **74-year-old woman, 1.2 cm well differentiated IDC, ER/PR (+) Her2 (–) UOQ, primary excised with lumpectomy, margins (–), clinically negative axilla; anti-endocrine therapy planned; KPS=90.**

Treatment	Rating	Comments
Principles of Treatment		
Modified radical mastectomy	9	If by patient choice.
Sentinel lymph node biopsy (SN) + RT breast	9	
Breast RT, no further surgery	8	
SN biopsy, no RT	7	
No further surgery or RT	7	
Breast RT + low axilla RT, no further surgery	7	
SN biopsy + accelerated PBI	6	Long term follow-up is limited.
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Variant 3: **Postmenopausal 56-year-old woman, 1.7 cm UOQ primary excised with lumpectomy–infiltrating lobular carcinoma associated with scattered LCIS, LCIS at margins, SN biopsy (–); ER/PR (+), Her2 (–); chemotherapy and anti-endocrine therapy planned.**

Treatment	Rating	Comments
Principles of Treatment		
Completion mastectomy	9	If by patient choice.
Whole breast RT, ± boost	9	
Reexcision + RT if negative LCIS margin	3	Re-excision of LCIS generally not necessary but pleomorphic LCIS needs special consideration.
Accelerated PBI	No consensus	No consensus for standard of care outside of protocol participation.
RT Doses (180-200 cGy/day unless otherwise stated)		
Whole breast: 42 Gy (16 fractions) no boost	4	No published experience using boost with this fractionation.
Whole breast: 45-50 Gy	8	
Total tumor bed dose: 45-49 Gy	1	
Total tumor bed dose: 50 Gy	3	
Total tumor bed dose: 60-66 Gy	9	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Clinical Condition: **Conservative Surgery and Radiation — Stage I and II Breast Carcinoma**

Variant 4: **Premenopausal 42-year-old women, 1.8 cm UOQ, IDC, no DCIS, SN biopsy negative, primary excised with lumpectomy, 1 focus of microscopic margin involvement, ER/PR (+), Her2 (–); chemotherapy and anti-endocrine therapy planned.**

Treatment	Rating	Comments
Principles of Treatment		
Completion mastectomy	9	If by patient choice.
Reexcision + whole breast RT if negative margins	9	
No further surgery, breast RT	7	Reexcision is highly desirable, but no further surgery is acceptable.
Reexcision + accelerated PBI if negative margins	No consensus	No consensus for standard of care outside of protocol participation.
RT Doses - Assume no Re-excision, (1.8-2.0 Gy/day- unless noted otherwise)		
Whole breast: 42 Gy (16 fractions)	4	
Whole breast: 45-50 Gy	9	
Total tumor bed dose: 42 Gy (16 fractions)	1	
Total tumor bed dose: 45-50 Gy	1	
Total tumor bed dose: 60-62 Gy	7	
Total tumor bed dose: 64-66 Gy	9	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Variant 5: **Premenopausal 41-year-old woman, 1.1 cm GII IDC, UOQ, ER/PR (+), Her2 (–), primary excised with lumpectomy, margins (–), SN biopsy negative, BRCA 1 mutation positive.**

Treatment	Rating	Comments
Principles of Treatment		
Completion mastectomy	9	If by patient choice with appropriate counseling.
Completion mastectomy + contralateral mastectomy	9	If by patient choice with appropriate counseling.
Breast RT	9	If by patient choice with appropriate counseling.
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Clinical Condition: **Conservative Surgery and Radiation — Stage I and II Breast Carcinoma**

Variant 6: **Postmenopausal 56-year-old woman, 2.5 cm UOQ moderately differentiated, EIC present, SN (–), ER/PR (+), Her2 (–), primary excised with lumpectomy, 1 focus of margin involvement; chemotherapy and anti-endocrine therapy planned.**

Treatment	Rating	Comments
Principles of Treatment		
Completion mastectomy	9	If by patient choice.
Reexcision + whole breast RT if negative margins	9	
No reexcision + RT	4	Re-excision highly desirable.
Reexcision + accelerated PBI if negative margins	No consensus	No consensus for standard of care outside of protocol participation.
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Variant 7: **Premenopausal 46-year-old women, 2.6 cm UOQ IDC, primary excised with lumpectomy, margins (–), little DCIS, 2/10 LNs (+), level I-II axillary node dissection, ER/PR (–), Her2 (–), chemotherapy planned, patient desires breast conservation.**

Treatment	Rating	Comments
Principles of Treatment		
Whole breast RT + nodal RT	8	
Whole breast RT alone	7	
Completion mastectomy	1	Patient desires breast conservation.
Nodal Radiation Volumes (assume breast RT given)		
Supraclavicular + apical (level III) axillary nodes	8	
Internal mammary nodes	8	
Full axilla (level 1-3)	3	
RT Doses, Negative Re-excision (1.8-2.0 Gy/day unless specified otherwise)		
Whole breast: 42 Gy (2.6 Gy/ day) (no boost)	4	Limited published experience using boost with this fractionation.
Whole breast: 45-50 Gy	9	
Total tumor bed dose: 42 Gy (16 fractions)	1	
Total tumor bed dose: 45-50 Gy	1	
Total tumor bed dose: 60-66 Gy	9	
SCL ± axillary apex: 45-50 Gy	8	
IMN: 45-50 Gy	8	
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Clinical Condition: **Conservative Surgery and Radiation — Stage I and II Breast Carcinoma**

Variant 8: **Healthy 67-year-old woman, 0.5 cm well-differentiated IDC, ER/PR (+), Her2 (–), primary excised with lumpectomy, margins (–); anti-endocrine therapy planned.**

Treatment	Rating	Comments
Principles of Treatment		
Mastectomy + sentinel LN biopsy	9	If by patient choice.
Sentinel LN biopsy alone	3	Needs RT.
Sentinel lymph node biopsy + whole breast RT	9	
Sentinel lymph node biopsy + accelerated PBI	6	Long-term follow-up is limited.
RT Doses (1.8-2.0 Gy/day unless otherwise specified)		
Whole breast: 42 Gy (16 fractions)	8	
Whole breast: 45-50 Gy	9	
Total tumor bed dose: 42 Gy (16 fractions)	8	
Total tumor bed dose: 45-49 Gy	1	
Total tumor bed dose: 50 Gy	8	
Total tumor bed dose: 60 Gy	9	
Total tumor bed dose: 64-66 Gy	5	
PBI: 34-38.5 Gy over 8-10 fractions	6	Long-term follow-up is limited.
Rating Scale: 1=Least appropriate, 9=Most appropriate		

Clinical Condition: **Conservative Surgery and Radiation — Stage I and II Breast Carcinoma**

Variant 9: **Postmenopausal 55-year-old woman, clinical T2N1, core biopsy shows poorly differentiated IDC, palpable LN FNA (+), ER (–), Her2 (3+), treated with neoadjuvant chemotherapy with excellent clinical response; primary excised with lumpectomy, 1.0 cm pathologic residual, margins (–), 1/20 LNs (+), planning trastuzumab (Herceptin) for 12 months; patient desires breast conservation.**

Treatment	Rating	Comments
Principles of Treatment		
Radiation therapy breast and nodes	9	
Radiation therapy breast only	3	
Completion mastectomy	1	Patient desires breast conservation.
Radiation Volumes (assume breast RT given)		
Supraclavicular + apical axillary nodes	9	
Internal mammary nodes	5	
Full axilla (level I-III)	3	
RT Doses (1.8-2.0 Gy/day unless specified otherwise)		
Whole breast: 42 Gy (16 fractions)	1	
Whole breast: 45-50 Gy	9	
Total tumor bed dose: 45-59 Gy	1	
Total tumor bed dose: 50 Gy	3	
Total tumor bed dose: 60-66 Gy	9	
SCL ± axillary apex: 45-50 Gy	9	
IMN: 45-50 Gy	9	Cardiac irradiation should be especially avoided with concurrent Herceptin.
Rating Scale: **1=Least appropriate, 9=Most appropriate**		

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

Summary of Literature Review

Invasive breast cancer is the most common malignancy in women in the United States [1]. Breast-conserving therapy (BCT) has become firmly established as a standard therapeutic approach for eligible women with early-stage breast cancer over the past two decades, replacing mastectomy as the predominant treatment. BCT is defined as excision of the primary breast tumor with a rim of adjacent normal breast tissue sufficient to achieve negative resection margins, with or without axillary sentinel node biopsy or dissection, followed by irradiation. In the United States, between 38%-65% of patients with early-stage breast cancer undergo BCT, although closer to 80% of patients are appropriate candidates [2,3]. The goals of BCT are to: 1) use moderate doses of radiation to eradicate microscopic foci of cancer that may remain in the breast after limited surgery to remove the primary tumor; 2) provide comparable local control and equivalent survival rates to mastectomy; and 3) maximize quality of life while minimizing complications and achieving an acceptable cosmetic result.

The following issues related to conservative surgery and radiation for stage I and II breast cancer are addressed below: the NIH (National Institutes of Health) Consensus Conference statement, results of prospective randomized clinical trials, patient selection and evaluation, radiation therapy (RT) following conservative surgery, treatment technique, the role for accelerated partial breast irradiation, the integration of radiation and adjuvant systemic therapy, and follow-up care.

NIH Consensus Conference

The Office of Medical Applications of Research of the NIH and the National Cancer Institute convened a consensus development conference on the treatment of early-stage breast cancer in June 1990. The panel concluded that "breast conservation treatment is an appropriate method of primary therapy for the majority of women with stage I and II breast cancer and is preferable to mastectomy because it provides survival rates equivalent to those of total mastectomy and axillary dissection while preserving the breast" [4]. The validity of this statement has been upheld by long-term data from prospective randomized trials. The rate of BCT for eligible breast cancer patients has risen steadily since the consensus conference statement.

Since 1991 representatives from the American College of Radiology, American College of Surgeons, College of American Pathologists, and Society of Surgical Oncology have met to develop practice guidelines for BCT to promote better and more consistent patient care. The Practice Guideline for Breast Conservation Therapy in the Management of Invasive Breast Carcinoma was most recently updated in 2006 [5].

Results of Prospective Randomized Clinical Trials

Six modern prospective randomized trials have compared mastectomy and BCT for stage I and II invasive breast cancer [6-11]. These data are very mature, with 10-20 year overall and disease-free survival (DFS) rates reported. They all have demonstrated no significant differences in distant metastases, cause-specific survival, or overall survival between the two treatment approaches. Three of these trials reported equivalent local regional control when BCT was compared to mastectomy. In all these trials, there was no difference between mastectomy and BCT in the incidence of subsequent contralateral breast cancer or second nonbreast malignancies.

Multiple prospective clinical trials have evaluated the benefit of radiation following conservative surgery [12-18]. In all these studies RT resulted in a highly significant, approximately two-thirds reduction in local recurrence compared to lumpectomy alone. For the majority of breast cancer patients undergoing lumpectomy, RT remains the standard of care. Its absolute benefit may not be as clinically meaningful for patients >70 years with node negative, estrogen receptor positive breast cancer <2 cm who will receive antiendocrine therapy for 5 years [16]. In this group of patients treated with lumpectomy a 5-year local recurrence rate of 5% was achieved when treated with tamoxifen alone versus 0.6% with the addition of breast irradiation. Follow-up for this trial has been presented in an abstract and reveals 8-year local recurrence rates of 7% versus 1% without and with radiation, respectively [19]. So far, the overall mastectomy-free survival rates have been equivalent between the two arms. Consideration of treatment without RT following lumpectomy for elderly patients should be individualized based on clinical determination of competing medical risks from pre-existing comorbidities and overall performance status.

In each of the individual trials overall, survival was not improved by the addition of RT following breast-

[1]Principal Author, Medical College of Wisconsin, Milwaukee, Wisconsin.
[2]Co-Author, Marin Cancer Institute, Greenbrae, Calif.[3]Panel Chair, University of Colorado Cancer Center, Denver, Colorado.
[4]Mount Sinai Medical Center, New York, New York.
[5]UMDNJ-Robert Wood Johnson Medical School, New Brunswick, New Jersey.
[6]Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.
[7]University of Texas, M.D. Anderson Cancer Center, Houston, Texas.
[8]Washington University, Saint Louis, Missouri.
[9]Roswell Park Cancer Institute, Buffalo, New York, American College of Surgeons.

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

conserving surgery. However, a pooled analysis of 15 randomized clinical trials that evaluated radiation after lumpectomy demonstrated a small but significant increase in survival with the addition of RT [20]. The Early Breast Cancer Trialist's Group (EBCTG) meta-analysis of 10 randomized trials that evaluated breast-conserving surgery alone versus the same followed by RT demonstrated a statistically significant 5.2% reduction in breast cancer at 15 years with the addition of radiation, and a similar reduction in overall mortality in irradiated patients [21]. However, at 15 years in irradiated cases there was a 1.8% excess of second cancers that were primarily contralateral breast and lung cancers, and 1.3% excess non-breast-cancer deaths that were mostly from heart disease and lung cancer, emphasizing the importance of using careful radiation delivery methods to minimize exposure of normal tissues at risk.

Complications from breast irradiation have been better evaluated in retrospective series. The risk of symptomatic pneumonitis, rib fracture, pericarditis, brachial plexopathy, severe breast fibrosis, or soft-tissue necrosis is less than 1%-4% when the breast alone is irradiated [22]. Arm edema, which is primarily related to the extent of axillary node dissection, is more frequent after nodal irradiation. Good to excellent cosmetic results are achieved in 85%-90% of patients and are influenced by surgical and radiotherapy techniques as well as the addition of adjuvant systemic therapy.

Patient Selection

BCT is now accepted as standard treatment for the vast majority of women with stage I or II breast cancer. The rate of medical contraindications to BCT has been estimated to be low — approximately 10% for stage I and-30% for stage II [23], although more women with stage II breast cancer might be good candidates for BCT after neoadjuvant chemotherapy.

Only about 50% of women with stage I and II breast carcinoma have BCT in spite of the aforementioned prospective randomized clinical trials. A joint study of the American College of Radiology and the American College of Surgeons found that high mastectomy rates in the United States are the result of inappropriate use of medical selection factors (eg, tumor size, grade, node status) and a function of demographics (eg, age, geographical location) [2]. Contraindications to breast conserving treatment are few and easily identified.

Breast Imaging

Preoperative mammographic evaluation is necessary to determine a patient's eligibility for BCT. Mammography aids in defining the extent of a lesion, and in determining whether the lesion is a unifocal or a multicentric process; it also evaluates the contralateral breast. If the mass is associated with microcalcifications, the extent of microcalcifications, both within and outside of any tumor mass, should be noted. Magnification views and spot compressions should be performed to better delineate tumor extension and define the full extent of microcalcifications.

Postbiopsy mammograms should be obtained to assess the completeness of resection of tumors with microcalcifications (see the Pathologic Factors section).

Ultrasound (US) can be important for further characterizing masses seen on mammography. It can better evaluate the size of the lesion in some cases and is helpful in determining the extent of a mass in breasts that are dense on mammography.

Magnetic resonance imaging (MRI) is increasingly being used as an adjunct to mammography to help select patients for BCT by defining the extent of disease within the breast [24,25]. In particular, MRI can be beneficial in patients whose disease is not demarcated well on mammography, (eg, those with very dense breast tissue on mammography or lobular histology). So far, MRI is not considered a part of the standard imaging for a breast cancer patient.

Clinical Evaluation

Pregnancy

Pregnancy, unless terminated, is an absolute contraindication to treatment with RT. Late in the third trimester, it may be possible to perform breast-conserving surgery and treat the patient with irradiation after delivery.

Prior Radiation Therapy

A history of prior RT (eg, for the treatment of Hodgkin's disease or lung cancer) that delivered significant dose to the breast and for which retreatment would result in an excessively high total radiation dose to the breast tissue is a contraindication for a breast-conserving approach. High radiation doses to the breast result in unacceptable long-term toxicity and poor cosmesis rates.

Collagen Vascular Disease

A well-documented history of a pre-existing collagen vascular disease (CVD) (eg, lupus, scleroderma) is considered an absolute contraindication for BCT by some authors, and a relative contraindication by most. Breast cancer patients with CVD should be made aware of the potential for exaggerated acute and late toxicity related to RT. From retrospective studies so far, it appears that patients with scleroderma and other nonrheumatoid arthritis CVD may be at the highest risk for severe toxicities such that breast irradiation in this group should be approached with caution [26].

Multiple Lesions

The presence of two nonadjacent primaries in the same breast is a relative contraindication for a breast-conserving approach, for two reasons. First, the cosmetic results of multiple wide local excisions and RT boosts are likely to be poor, unless both primaries are very small. Second, these patients may have a larger residual tumor burden after breast-conserving surgery, placing them at risk for higher rates of local failure. Multicentricity, such as seen by very extensive malignant-appearing microcalcifications on mammograms, is a contraindication to BCT.

Breast Size
The treatment of women with very large breasts is technically more challenging and may require the use of higher energy photons and specialized radiation techniques to minimize dose heterogeneity. Prone breast RT may be useful in this population. Large pendulous breasts can have greater retraction and poorer cosmetic results after BCT than smaller breasts if careful radiation techniques are not used.

Tumor Size
One major patient selection criterion is the ability to completely resect the primary tumor without causing unacceptable cosmetic deformity. There is no difference in recurrence rates based on the size of the tumor itself. Hence, tumor size is only a factor as it relates to the expected cosmetic result, although there are few published reports on tumors larger than 4 to 5 cm. Larger unifocal tumors that are considered borderline for breast conservation may be candidates for neoadjuvant chemotherapy to reduce the tumor size and improve the successful completion of BCT. Retraction of skin or nipple is not a contraindication for BCT**.**

Subareolar Location
Subareolar tumors may require resection of the nipple areola complex for complete excision, but this is not a contraindication to a breast-conserving approach. Although the appearance of the breast may then be unacceptable to some patients, it is likely to be preferable to a reconstructed breast mound after mastectomy to many. Reconstruction of a nipple areola complex is feasible in this BCT setting.

Patient Age
Many series have suggested that young patients (younger than age 30-40) may have a higher risk of breast cancer recurrence than older patients. This risk may be explained at least in part by differences in the pathologic features of tumors in very young patients. Overall, very young patients have an increased risk of local recurrence compared with older patients. Young patient age is also described as an important factor for a worse outcome following mastectomy. It is not clear that the risk is greater in patients treated with a breast-conserving approach than with mastectomy.

In women younger than age 45, the Connecticut Tumor Registry [27] and the SEER database [28] showed a small, non-significant trend for increased risk of contralateral breast cancer in patients receiving RT following lumpectomy. Other registry data have not confirmed this finding [29]. RT did not increase the risk for development of contralateral breast cancer in any of the individual randomized trials comparing RT after lumpectomy to mastectomy [6-10], but it was found to contribute to the small percentage of excess second cancers associated with RT in the EBCTG meta-analysis [21].

Older patients are also good candidates for RT. Transportation problems can often be overcome, and treatment is well tolerated. For women older than age 70 with receptor positive breast cancer <2 cm who will be treated with antiendocrine therapy, omission of RT after lumpectomy may be reasonable[16,20]. This option is most appropriate in the setting of other medical comorbidities that present in competing mortality risks. An accelerated course of breast radiation is also a consideration in this patient group [30].

Family History
Family history of breast cancer is not considered a contraindication to BCT or use of breast RT.

Hereditary Breast Cancer
The use of BCT in stage I and II breast cancer patients with germline mutations in BRCA 1 or 2 is a complex issue. There may be higher rates of late breast cancer events in mutation carriers compared to sporadic cases. All studies have reported significantly higher rates of contralateral breast cancer, ranging from 14%-42% at 10 years [31,32]. No decrement in overall survival has been reported. Patients require detailed discussions, and informed patients desiring BCT should receive counseling on subsequent risk reduction for contralateral breast cancer by using antiendocrine therapy if appropriate and undergoing prophylactic salpingo–oopherectomy. Bilateral mastectomy for treatment of the affected breast and for risk reduction on the contralateral side is an option that should be considered.

Prosthetically Augmented or Reconstructed Breasts
The development of significant capsular contracture may be increased after RT. The reported incidence varies widely, but capsular contracture has been reported to occur in 35%-65% of cases [33,34]. Patients should know that postlumpectomy RT may necessitate subsequent corrective surgery. However, the presence of breast prosthesis is not a contraindication to RT.

Pathologic Factors

Margins
The pathologic specimen must be appropriately sampled to document the presence or absence of gross or microscopic carcinoma in the margins of excision. Microscopic status of the resection margins is the most commonly used method for estimating the residual tumor burden in the breast remaining after conservative surgery. The goal of breast-conserving surgery is to achieve negative margins of excision. When margins are microscopically involved, a re-excision should be performed. Re-excisions may not be necessary for select patients when there is only focal involvement of a margin and no extensive intraductal component (EIC) is identified [35,36].

Presence of an Extensive Intraductal Component in Infiltrating Ductal Carcinoma
EIC is defined as intraductal carcinoma comprising a prominent portion of the primary tumor mass and clearly extending beyond the infiltrating portion of the tumor, or in grossly normal adjacent breast tissue, or both. (Intraductal carcinoma with microinvasion is addressed in other ACR Appropriateness Criteria® topics.) Patients with EIC may have a more widespread process within the

breast than patients with EIC-negative tumors. Patients with EIC-positive tumors with positive or unknown resection margins who undergo BCT have unacceptably high rates of ipsilateral in-breast cancer recurrence. These patients should undergo a re-excision to obtain negative margins. If negative margins of excision are obtained around the infiltrating and in-situ tumor, the increased risk of recurrence is eliminated and these patients are excellent candidates for BCT. As opposed to DCIS lobular CIS at margins does not typically require re-excision.

No other pathologic prognostic factors, including histologic subtype of infiltrating cancer, axillary lymph node status, or other molecular factors, have been consistently shown to clearly divide patients into groups at significantly higher risk of breast recurrence.

Patient Preference

Each patient must have a thorough discussion of options, addressing their fears and expectations. For patients who meet the selection criteria, choosing mastectomy does not increase survival. Psychological adaptation is equivalent for women who choose mastectomy or BCT. Patients who undergo BCT, however, have a more positive body image.

Radiation Therapy Techniques

Computed tomography (CT)-based treatment planning for megavoltage beam irradiation is recommended by consensus of the panel for optimal RT following excision of the primary tumor and axillary sentinel node biopsy or dissection. RT should be designed to treat the entire breast to a total dose of 45-50 Gy in 1.8-2 Gy fractions for 4.5 to 5.5 weeks. In one randomized trial of 1,234 patients with stage I breast cancer, a shorter course of breast radiation delivering 4250 cGy in 16 fractions over 22 days proved to have equivalent 5-year local recurrence-free survival rates and cosmetic results as 5000 cGy in 25 fractions [30].

Appropriate beam modification should be used (eg, wedges, compensators, multileaf collimators, etc.) to minimize dose heterogeneity throughout the treated breast. The use of dynamic wedges or multileaf collimators instead of physical wedges for beam modification will reduce scatter — particularly to the opposite breast from the medial tangent field(s). RT technique can affect the risk of breast recurrence. Prolongation of the overall treatment time, eg, with less than 8 Gy per week, increases the recurrence rate. RT technique also affects cosmetic results. Adverse cosmetic results have been associated with the use of daily fractions of >2.5 Gy, a total dose to the breast of >50 Gy, excess dose heterogeneity, the use of a large volume boost, and the use of lower photon beam energy (cobalt 60 or 4 MV photons when compared with 6 MV or 8 MV photons).

Randomized clinical trials have supported the use of a boost to reduce in-breast recurrences [37]. The boost dose is commonly 10-16 Gy to the lumpectomy cavity plus a margin. For patients with negative resection margins, a range of 60-66 Gy cumulative dose to the boost volume is considered acceptable. For patients who do not undergo re-excision for a focal area of microscopic margin involvement, a final dose of approximately 64-66 Gy to the boost volume is most appropriate. Because normalization conventions and prescription points differ from institution to institution, and there is no consensus on which convention to use, all doses given are approximate. Multiple studies have demonstrated the inadequacy of clinically directed boost fields and have emphasized the importance of careful treatment planning to ensure the boost dose covers the targeted at-risk breast tissue [38]. There is no correlation between the type of boost used and the risk of breast recurrence [39]. In those cases where no boost is given, a breast dose of 50 Gy is most appropriate.

Postmastectomy chest wall and regional nodal irradiation has been documented to improve survival in node-positive breast cancer patients in randomized trials evaluating its efficacy after surgery and CMF chemotherapy [40,41]. The role of regional node irradiation in patients with early-stage breast cancer and positive nodes receiving BCT remains controversial. The results of clinical trials evaluating its role are pending [42]. Regional nodal RT is not recommended for patients with histologically negative axillary nodes as determined by sentinel node biopsy and/or axillary node dissection [41]. The risk of nodal recurrence is low in patients with one to three positive nodes after an appropriate level I/II axillary dissection [43]. Therefore the role of regional node irradiation in patients with one to three positive nodes is uncertain. The panel determined that consideration for treatment is appropriate and that a thorough discussion of the potential benefits and risks with the patient is warranted. Clinical factors that can influence the decision to irradiate the regional nodes in patients with one to three positive lymph nodes include the primary tumor size, the nodal ratio, and the extent of axillary dissection. Regional nodal irradiation is recommended for women with four or more positive nodes.

Regional nodal irradiation volumes typically include the supraclavicular fossa and axillary apical or level III lymph nodes. There was no consensus on the indications to irradiate all levels of the axilla or optimal radiation technique. Radiation to the full axilla is indicated in most patients with invasive cancers in whom a sentinel node or axillary dissection has been omitted or inadequate. Although clinical evidence of recurrence in internal mammary lymph nodes is rare, consideration of treatment is appropriate. Doses of 45-50 Gy delivered 1.8-2 Gy per fraction should be used to treat regional nodes. In view of the added toxicity, careful planning is necessary to minimize exposure to normal tissue while adequately covering the breast and/or chest wall and regional nodes. The incidence of symptomatic pneumonitis, lymphedema, and fibrosis is increased with the addition of nodal irradiation.

Accelerated Partial Breast Irradiation

Accelerated partial-breast irradiation (PBI) delivers hypofractionated radiation to the 1-2 cm of breast tissue around the lumpectomy cavity where the vast majority of in-breast recurrences occur. It is commonly delivered in twice-daily treatments (minimal 6-hour interfraction time interval) over 5-8 days. The smaller target volume allows for hypofractionated radiation. A growing body of data has demonstrated that PBI with multicatheter brachytherapy following lumpectomy in selected cases yields local control and cosmetic results similar to historical outcomes with whole-breast irradiation [44-46]. In these studies, radiation doses between 30-38 Gy of high-dose radiation was delivered in 7-10 fractions over 5-8 days or 45-50 Gy (0.4-.05 Gy/hour) of low-dose radiation. With median follow-up times between 30-80 months, in-breast recurrence and good to excellent cosmetic outcome rates of 1%-6% and >80%, respectively, are seen. Other methods of PBI include MammoSite® brachytherapy and 3-dimensional conformal RT (3D-CRT). MammoSite® brachytherapy was approved by the FDA in May 2002, and prospective data are primarily from the initial 43 patients studied in a multi-institutional trial evaluating the safety of the device. At 5 years of follow-up there have not been any in-breast recurrences [47]. Accrual is ongoing to a phase III trial cosponsored by the National Surgical Bowel and Breast Program and the Radiation Therapy Oncology Group (RTOG®) randomizing patients with stage 0-II cancer who have undergone lumpectomy to either whole-breast irradiation or PBI. There are other randomized trials ongoing in Canada and Europe examining this question, but their results are several years away. To date, there is no consensus for standard of care for the use of PBI outside of protocol participation.

The vast majority of patients treated to date with PBI in published results have had relatively low-risk breast cancer: older than 60 years with T-1a or b invasive ductal cancer, negative resection margins, negative nodes, no EIC, and positive receptors receiving antiendocrine therapy [42-45]. In these select cases of breast cancer, the panel determined that consideration of PBI is appropriate, but a discussion with the patient regarding the short outcome data relative to standard whole-breast irradiation is warranted. There are limited published data so far from the use of 3D-CRT PBI, and its use should be confined to a clinical trial [48].

Integration of Radiation Therapy and Adjuvant Systemic Therapy

In most series, the addition of adjuvant chemotherapy to RT results in a decreased incidence of breast recurrence when compared with conservative surgery and RT alone. Early adjuvant systemic chemotherapy in patients at substantial risk of metastases is believed to be important. Concurrent regimens have the theoretical advantage of initiating both local and regional treatments with systemic therapy at the same time without delay in either modality, although there is concern about potential toxicity [49,50]. Given the lack of demonstrated benefit and higher toxicity rates from concurrent therapy, sequential therapy is considered standard. Some retrospective series had demonstrated that delaying the initiation of RT by at least four months results in an increased risk of breast recurrence. A randomized trial evaluating sequencing chemotherapy first versus RT first had initially demonstrated a trend toward increased local recurrence in the chemo-first arm and increased distant metastases in the RT-first arm. However, at 10 years there was no difference in the rate of local or distant failure based on sequencing [51]. In practice, patients typically complete chemotherapy after breast-conserving surgery prior to beginning RT [52]. Tamoxifen can be given concomitantly or sequentially with RT [53]. Trastuzumab was continued during RT in those trials evaluating its efficacy. No irradiation of the internal mammary nodes was allowed in those patients receiving regional nodal irradiation and Trastuzumab [54].

Neoadjuvant Chemotherapy

Patients with large tumors relative to their breast size, in whom resection would result in a cosmetically unacceptable breast appearance, should be considered for neoadjuvant chemotherapy to reduce the tumor size. An approximately 20% relative increase in BCT is achieved with neoadjuvant chemotherapy and overall breast recurrence is equivalent to the adjuvant setting [53]. There is equivalent overall survival from neoadjuvant compared to adjuvant chemotherapy. However, a small but not statistically significant increased rate of breast recurrence has been noted in downstaged patients who were initially ineligible for lumpectomy, compared to patients who were initially good candidates for lumpectomy [55]. Thorough discussion with the patient and careful pathology review are needed prior to proceeding with BCT.

Follow-up

Women treated for breast cancer should have a history and physical examination performed every 3-6 months for the first 3 years after treatment, then every 6-12 months; examination should be coordinated among specialties. A new baseline mammogram should be obtained approximately 6 months after completion of RT, when postsurgical and radiation changes have peaked. Annual mammograms should be obtained after mammographic stability. There are insufficient data to recommend the routine use of other studies.

Management Guidelines

The vast majority of women with stage I or II breast cancer are good candidates for BCT. Whole-breast irradiation with or without boost is the standard of care following lumpectomy. Contraindications to BCT include patients with *very* extensive malignant-appearing calcifications on the mammogram. Postbiopsy mammograms should be obtained to assess the completeness of resection in patients whose tumors demonstrate microcalcifications on mammograms.

Two nonadjacent primary tumors in the same breast is a relative contraindication to RT. Pregnancy is an absolute contraindication. A history of well-documented collagen

vascular disease and a history of prior RT to a high total dose, or significant volume, or both are considered relative contraindications to a breast-conserving approach. Any other patient who desires a breast-conserving approach and in whom negative margins of excision around the primary tumor can be obtained, (eg, in patients with EIC-positive tumors), is a good candidate for BCT.

RT to the entire breast, to a total dose of 45-50 Gy in 1.8-2 Gy fractions for 4.5-5.5 weeks, generally followed by a supplemental boost dose of radiation to the surgical tumor bed, is recommended. Regional nodal irradiation is not recommended for patients with negative axillary nodes. The role of regional nodal irradiation in patients with one to three positive nodes is uncertain.

Supporting Document(s)

- ACR Appropriateness Criteria® Overview
- Evidence table under review

References

1. Greene FL, Page DL, Fleming ID, et al, eds, for the American Joint Committee on Cancer. *AJCC Cancer Staging Manual.* New York, NY: Springer-Verlag; 2002.
2. Morrow M, White J, Moughan J, et al. Factors predicting the use of breast-conserving therapy in stage I and II breast carcinoma. *J Clin Oncol* 2001; 19(8):2254-2262.
3. Parviz M, Cassel JB, Kaplan BJ, et al. Breast conservation therapy rates are no different in medically indigent versus insured patients with early stage breast cancer. *J Surg Oncol* 2003; 84(2):57-62.
4. NIH consensus conference. Treatment of early-stage breast cancer. *Jama* 1991; 265(3):391-395.
5. Practice guideline for breast conservation therapy in the management of invasive breast carcinoma. *Practice Guidelines and Technical Standards*. Reston, Va: American College of Radiology; 2006:443-468.
6. Arriagada R, Le MG, Rochard F, Contesso G. Conservative treatment versus mastectomy in early breast cancer: patterns of failure with 15 years of follow-up data. Institut Gustave-Roussy Breast Cancer Group. *J Clin Oncol* 1996; 14(5):1558-1564.
7. Blichert-Toft M, Rose C, Andersen JA, et al. Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. Danish Breast Cancer Cooperative Group. *J Natl Cancer Inst Monogr* 1992; (11):19-25.
8. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002; 347(16):1233-1241.
9. Jacobson JA, Danforth DN, Cowan KH, et al. Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. *N Engl J Med* 1995; 332(14):907-911.
10. van Dongen JA, Voogd AC, Fentiman IS, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. *J Natl Cancer Inst* 2000; 92(14):1143-1150.
11. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002; 347(16):1227-1232.
12. Clark RM, Whelan T, Levine M, et al. Randomized clinical trial of breast irradiation following lumpectomy and axillary dissection for node-negative breast cancer: an update. Ontario Clinical Oncology Group. *J Natl Cancer Inst* 1996; 88(22):1659-1664.
13. Fisher B, Bryant J, Dignam JJ, et al. Tamoxifen, radiation therapy, or both for prevention of ipsilateral breast tumor recurrence after lumpectomy in women with invasive breast cancers of one centimeter or less. *J Clin Oncol* 2002; 20(20):4141-4149.
14. Forrest AP, Stewart HJ, Everington D, et al. Randomised controlled trial of conservation therapy for breast cancer: 6-year analysis of the Scottish trial. Scottish Cancer Trials Breast Group. *Lancet* 1996; 348(9029):708-713.
15. Fyles AW, McCready DR, Manchul LA, et al. Tamoxifen with or without breast irradiation in women 50 years of age or older with early breast cancer. *N Engl J Med* 2004; 351(10):963-970.
16. Hughes KS, Schnaper LA, Berry D, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. *N Engl J Med* 2004; 351(10):971-977.
17. Liljegren G, Holmberg L, Bergh J, et al. 10-Year results after sector resection with or without postoperative radiotherapy for stage I breast cancer: a randomized trial. *J Clin Oncol* 1999; 17(8):2326-2333.
18. Veronesi U, Marubini E, Mariani L, et al. Radiotherapy after breast-conserving surgery in small breast carcinoma: long-term results of a randomized trial. *Ann Oncol* 2001; 12(7):997-1003.
19. Hughes KS, Schnaper LA, Berry D, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer: a report of further follow-up. San Antonio Breast Cancer Symposium. 2006:Abstract 11.
20. Vinh-Hung V, Verschraegen C. Breast-conserving surgery with or without radiotherapy: pooled-analysis for risks of ipsilateral breast tumor recurrence and mortality. *J Natl Cancer Inst* 2004; 96(2):115-121.
21. 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.
22. Meric F, Buchholz TA, Mirza NQ, et al. Long-term complications associated with breast-conservation surgery and radiotherapy. *Ann Surg Oncol* 2002; 9(6):543-549.
23. Morrow M, Bucci C, Rademaker A. Medical contraindications are not a major factor in the underutilization of breast conserving therapy. *J Am Coll Surg* 1998; 186(3):269-274.
24. Hylton N. Magnetic resonance imaging of the breast: opportunities to improve breast cancer management. *J Clin Oncol* 2005; 23(8):1678-1684.
25. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin* 2007; 57(2):75-89.
26. Chen AM, Obedian E, Haffty BG. Breast-conserving therapy in the setting of collagen vascular disease. *Cancer J* 2001; 7(6):480-491.
27. Boice JD, Jr., Harvey EB, Blettner M, Stovall M, Flannery JT. Cancer in the contralateral breast after radiotherapy for breast cancer. *N Engl J Med* 1992; 326(12):781-785.
28. Gao X, Fisher SG, Emami B. Risk of second primary cancer in the contralateral breast in women treated for early-stage breast cancer: a population-based study. *Int J Radiat Oncol Biol Phys* 2003; 56(4):1038-1045.
29. Storm HH, Andersson M, Boice JD, Jr., et al. Adjuvant radiotherapy and risk of contralateral breast cancer. *J Natl Cancer Inst* 1992; 84(16):1245-1250.
30. Whelan T, MacKenzie R, Julian J, et al. Randomized trial of breast irradiation schedules after lumpectomy for women with lymph node-negative breast cancer. *J Natl Cancer Inst* 2002; 94(15):1143-1150.
31. Haffty BG, Harrold E, Khan AJ, et al. Outcome of conservatively managed early-onset breast cancer by BRCA1/2 status. *Lancet* 2002; 359(9316):1471-1477.
32. Robson M, Svahn T, McCormick B, et al. Appropriateness of breast-conserving treatment of breast carcinoma in women with germline mutations in BRCA1 or BRCA2: a clinic-based series. *Cancer* 2005; 103(1):44-51.
33. Gray RJ, Forstner-Barthell AW, Pockaj BA, Schild SE, Halyard MY. Breast-conserving therapy and sentinel lymph node biopsy are feasible in cancer patients with previous implant breast augmentation. *Am J Surg* 2004; 188(2):122-125.
34. Mark RJ, Zimmerman RP, Greif JM. Capsular contracture after lumpectomy and radiation therapy in patients who have undergone uncomplicated bilateral augmentation mammoplasty. *Radiology* 1996; 200(3):621-625.
35. Park CC, Mitsumori M, Nixon A, et al. Outcome at 8 years after breast-conserving surgery and radiation therapy for invasive breast cancer: influence of margin status and systemic therapy on local recurrence. *J Clin Oncol* 2000; 18(8):1668-1675.
36. Peterson ME, Schultz DJ, Reynolds C, Solin LJ. Outcomes in breast cancer patients relative to margin status after treatment with breast-conserving surgery and radiation therapy: the University of

Pennsylvania experience. *Int J Radiat Oncol Biol Phys* 1999; 43(5):1029-1035.
37. Bartelink H, Horiot JC, Poortmans PM, et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. *J Clin Oncol* 2007; 25(22):3259-3265.
38. Benda RK, Yasuda G, Sethi A, Gabram SG, Hinerman RW, Mendenhall NP. Breast boost: are we missing the target? *Cancer* 2003; 97(4):905-909.
39. Poortmans P, Bartelink H, Horiot JC, et al. The influence of the boost technique on local control in breast conserving treatment in the EORTC 'boost versus no boost' randomised trial. *Radiother Oncol* 2004; 72(1):25-33.
40. 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.
41. 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.
42. Olivotto IA, Chua B, Elliott EA, et al. A clinical trial of breast radiation therapy versus breast plus regional radiation therapy in early-stage breast cancer: the MA20 trial. *Clin Breast Cancer* 2003; 4(5):361-363.
43. 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.
44. King TA, Bolton JS, Kuske RR, Fuhrman GM, Scroggins TG, Jiang XZ. Long-term results of wide-field brachytherapy as the sole method of radiation therapy after segmental mastectomy for T(is,1,2) breast cancer. *Am J Surg* 2000; 180(4):299-304.
45. Kuske RR, Winter K, Arthur W, et al. A phase II trial of brachytherapy alone following lumpectomy for stage I or II breast cancer: Initial outcomes of RTOG 9517. *Journal of Clinical Oncology, 2004 ASCO Annual Meeting Proceedings (Post-Meeting Edition)* 2004; 22(14S):565.
46. Vicini FA, Kestin L, Chen P, Benitez P, Goldstein NS, Martinez A. Limited-field radiation therapy in the management of early-stage breast cancer. *J Natl Cancer Inst* 2003; 95(16):1205-1210.
47. Benitez PR, Keisch ME, Vicini F, et al. Five-year results: the initial clinical trial of MammoSite balloon brachytherapy for partial breast irradiation in early-stage breast cancer. *Am J Surg* 2007; 194(4):456-462.
48. Vicini F, Winter K, Straube W, et al. A phase I/II trial to evaluate three-dimensional conformal radiation therapy confined to the region of the lumpectomy cavity for Stage I/II breast carcinoma: initial report of feasibility and reproducibility of Radiation Therapy Oncology Group (RTOG) Study 0319. *Int J Radiat Oncol Biol Phys* 2005; 63(5):1531-1537.
49. Formenti SC, Volm M, Skinner KA, et al. Preoperative twice-weekly paclitaxel with concurrent radiation therapy followed by surgery and postoperative doxorubicin-based chemotherapy in locally advanced breast cancer: a phase I/II trial. *J Clin Oncol* 2003; 21(5):864-870.
50. Hanna YM, Baglan KL, Stromberg JS, Vicini FA, D AD. Acute and subacute toxicity associated with concurrent adjuvant radiation therapy and paclitaxel in primary breast cancer therapy. *Breast J* 2002; 8(3):149-153.
51. Bellon JR, Come SE, Gelman RS, et al. Sequencing of chemotherapy and radiation therapy in early-stage breast cancer: updated results of a prospective randomized trial. *J Clin Oncol* 2005; 23(9):1934-1940.
52. Pierce LJ, Moughan J, White J, Winchester DP, Owen J, Wilson JF. 1998-1999 patterns of care study process survey of national practice patterns using breast-conserving surgery and radiotherapy in the management of stage I-II breast cancer. *Int J Radiat Oncol Biol Phys* 2005; 62(1):183-192.
53. Pierce LJ, Hutchins LF, Green SR, et al. Sequencing of tamoxifen and radiotherapy after breast-conserving surgery in early-stage breast cancer. *J Clin Oncol* 2005; 23(1):24-29.
54. Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med* 2005; 353(16):1673-1684.
55. Wolmark N, Wang J, Mamounas E, Bryant J, Fisher B. Preoperative chemotherapy in patients with operable breast cancer: nine-year results from National Surgical Adjuvant Breast and Bowel Project B-18. *J Natl Cancer Inst Monogr* 2001; (30):96-102.