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CONSERVATIVE SURGERY AND RADIATION — STAGE I AND II BREAST CARCINOMA

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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 (SN) 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 local control and equivalent survival rates comparable to those of 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 of 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, the American College of Surgeons, the College of American Pathologists, and the 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 overall and disease-free survival (DFS) rates reported for periods of 10 to over 20 years. 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

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mastectomy and BCT in the incidence of subsequent contralateral breast cancer or second nonbreast malignancies. Of note, many of these older trials were unable to differentiate recurrence of the original cancer from new primary tumors, potentially confounding their results. Later studies have attempted to make this distinction [12].

Multiple prospective clinical trials have evaluated the benefit of radiation following conservative surgery [13-19]. In all these studies RT resulted in a highly significant, approximately two-thirds reduction in local recurrence compared to lumpectomy alone. For most breast cancer patients undergoing lumpectomy, RT remains the standard of care. Its absolute benefit may not be as clinically meaningful for patients >70 years of age with node negative, estrogen receptor (ER) positive breast cancer <2 cm who will receive antiendocrine therapy for 5 years [17]. In this group of patients treated with lumpectomy a 5-year local recurrence rate of 5% was achieved when they were 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 that reports 10-year in-breast recurrence rates of 78% without RT and just 2% with RT [20]. Time to local recurrence was also prolonged with radiation (P=0.015). The overall mastectomy-free survival rates have been equivalent between the two arms. While there is a local control advantage to radiation, 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-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 [21]. 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 5.4% reduction in breast-cancer-specific mortality at 15 years with the addition of radiation, and a 4.4% improvement in overall mortality in irradiated patients [22]. 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 a 1.3% excess in non-breast-cancer deaths that were mostly from heart disease, emphasizing the importance of using careful radiation delivery methods to minimize exposure of normal tissues at risk. Promising among these methods is the use of deep-inspiration breath hold. In maximum inspiration, the heart frequently moves away from the chest wall, allowing standard tangents to largely avoid the heart. Multiple single institution series have shown favorable dosimetry when compared to free-breathing [23,24], and several commercial systems are available.

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 [25]. Arm edema, which is primarily related to the extent of axillary node dissection, is more frequent after nodal irradiation [26]. 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 [27]. More recently, two randomized trials have compared conventionally planned 2-dimensional radiation therapy with intensity-modulated radiation therapy (IMRT). Pignol et al [28] found that IMRT improved the homogeneity of the radiation dose distribution and decreased acute toxicity. In a similar study of 306 patients also randomized to conventional treatment planning versus IMRT, Donovan et al [29] found that more homogeneous treatment planning translated into an improvement in 5-year cosmetic results as well.

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. These are discussed further in the clinical evaluation section.

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.

Postoperative 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. In addition, it provides a convenient means to obtain a core biopsy of suspicious lesions.

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 [30,31]. 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). MRI can lead to a change in a planned surgical procedure (particularly from breast conservation to mastectomy) [32-34] and has not been shown to improve local control or overall survival [35]. As such, while it is commonly used at many centers, it is not presently considered a part of the standard imaging for a newly diagnosed 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 doses 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. Repeat partial breast irradiation may potentially allow patients with recurrent disease to preserve the breast, although data are too sparse to recommend this practice outside of a clinical trial.

Collagen Vascular Disease

A well-documented history of a pre-existing collagen vascular disease (CVD) is considered an absolute contraindication for BCT by some authors, and at least 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 may be at the highest risk for severe toxicities and that breast irradiation in this group should be approached with caution [36].

Multiple Lesions

The presence of two nonadjacent primaries in the same breast is considered 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. More recently, however, there is some suggestion that patients with multicentric disease may not have an inordinately high risk of local recurrence. Given the sparcity of data, however, this is most appropriately considered for patients who refuse mastectomy or are participating on a clinical trial [37]. Diffuse malignant-appearing calcifications have been classically considered a contraindication to breast conservation.

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 [38]. 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 [39].

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 [40]. Young patient age is also described as an important factor for a poorer outcome following mastectomy [41]. 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 [42] and the SEER database [43] showed a small, nonsignificant trend for increased risk of contralateral breast cancer in patients receiving RT following lumpectomy. Other registry data have not confirmed this finding [44]. 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 [6,7,9,10], but it was found to contribute to the small percentage of excess second cancers associated with RT in the EBCTG meta-analysis [22].

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 [17,21]. This option is most appropriate in the setting of other medical comorbidities that present competing mortality risks. An accelerated course of breast radiation can also be considered in this patient group. Recent data from Canada showed equivalent local control and survival with an accelerated hypofractionated whole-breast course of 42.5 Gy in 16 fractions when compared with 50 Gy in 25 fractions [45].

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 breast cancer susceptibility genes 1 and 2 (BRCA1 and BRCA2) 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 [46,47]. No decrement in overall survival has been reported, and there does not appear to be a higher risk of radiation-induced complications nor any increase in local recurrence rates of the index cancer [48]. 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 [49,50]. Patients should know that postlumpectomy RT may necessitate subsequent corrective surgery. However, the presence of breast prosthesis is not a contraindication to RT. (See Variant 1 and Variant 2.)

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. The precise width of the tumor-free distance remains under debate. Wider margins may be more important in younger patients, in those with ER negative tumors, and in situations where there is an extensive intraductal component (EIC) [51-53].

Biologic Determinants

While local control in the breast has been traditionally predicted by standard patient and pathologic characteristics, including patient age, tumor size, margin, and the use of systemic therapy, more recently there has been interest in the tumor's biologic profile. Nguyen et al [52] found that the basal subtype, as approximated by ER negative, progesterone receptor (PR) negative, and human epidermal growth factor receptor 2 (HER2) negative disease, predicted a higher risk of local recurrence in a retrospective study of 793 patients treated with breast conservation. Similarly, both Millar et al [54] and Voduc et al [55] have reported higher rates of local regional recurrence in patients with "triple negative" phenotypes than in those with ER positive disease. Mamounas et al [56] stratified patients treated on two protocols of the National Surgical Adjuvant Breast and Bowel Project (NSABP) into risk groups based on their Oncotype DX score. While preliminary, and not validated, the results suggest that Oncotype may also help predict local regional recurrence. Clearly much additional work is necessary to help determine the optimal biologic determinant of local regional recurrence, which may turn out to be very different than the markers of systemic recurrence. Hopefully this will allow for further tailoring of treatment to the individual patient, where high-risk patients can have intensification of local regional therapy, perhaps with a concurrent systemic agent, and lower-risk patients may be able to avoid treatment. (See Variant 3.)

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 SN biopsy or dissection. RT should be designed to treat the entire breast to a total dose of 44-50.4 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 10-year local recurrence-free survival rates and cosmetic results equivalent to those achieved with 5000 cGy in 25 fractions [57]. A limitation of this study is that a boost, or additional radiation delivered to the lumpectomy site, was not permitted on either arm. In addition, patients with large breasts were not eligible. Other studies, albeit with shorter follow-up, have also examined shorter whole-breast regimens with favorable early results [58,59].

Appropriate beam modification should be used (eg, wedges, compensators, multileaf collimators) 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). Adverse cosmetic results have been associated with the use of systemic therapy [27], a total dose to the breast of >50 Gy [60], and excess dose heterogeneity [29].

Randomized clinical trials have supported the use of a boost to reduce in-breast recurrences [40] when standard fractionation is used. This benefit is most pronounced in younger women. The boost dose is commonly 10-16 Gy to the lumpectomy cavity. For patients with negative resection margins, a range of 60-66 Gy cumulative dose to the boost volume is considered acceptable. 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 [61]. 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 cyclophosphamide, methotrexate, and fluorouracil (CMF) chemotherapy [62,63]. 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 [64]. Regional nodal RT is not recommended for patients with histologically negative axillary nodes as determined by SN biopsy and/or axillary node dissection [63]. The risk of nodal recurrence is low in patients with one to three positive nodes after an appropriate level I/II axillary dissection [65]. 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, lymphovascular space invasion, extranodal extension, 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 the optimal radiation technique. Radiation to the full axilla is indicated in most patients with invasive cancers in whom a SN or axillary dissection has been omitted or inadequate. Although clinical evidence of recurrence in internal mammary lymph nodes is rare [65], consideration of treatment is reasonable, particularly in patients with medial, axillary node positive tumors [66]. It is also reasonable to consider internal mammary radiation when the SN mapping shows internal mammary drainage, although internal mammary irradiation was not shown to improve survival in a prospective trial. Doses of 45-50.4 Gy delivered at 1.8-2 Gy per fraction should be used to treat regional nodes. In view of the added toxicity, careful 3-dimensional CT-based planning with attention to maximizing homogeneity 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 [67] and lymphedema [68] is increased with the addition of nodal irradiation. (See Variant 4.)

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 [69,70]. 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 rates and good to excellent cosmetic outcome rates of 1%-6% and >80%, respectively, are seen. Other methods of PBI include balloon brachytherapy and 3-dimensional conformal RT (3D-CRT). Balloon 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 the recurrence rate across all risk stratifications was <5.5% t[71]. There has also been interest in single-fraction intraoperative radiation therapy (using either electrons or low-energy photons). At present, however, there are very limited follow-up data, and this remains an experimental approach [72,73]. 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.

Trial participation is encouraged. However, in the absence of an available trial, the panel recommends following the consensus guidelines of the American Society of Therapeutic Radiology and Oncology (ASTRO) [74]. Suitable patients for treatment outside a clinical trial include those patients older than age 60 without BRCA mutations and with T1, LVI (lymphovascular invasion) negative, EIC negative, node negative, unicentric, ER positive, invasive ductal carcinoma (IDC) excised with surgical margins >2 mm.

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 [75,76]. 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 4 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 rates of local or distant failure based on sequencing [77]. In practice, patients typically complete chemotherapy after breast-conserving surgery prior to

beginning RT [78]. Tamoxifen can be given concomitantly or sequentially with RT, with no demonstrable differences in outcome [79-81]. Trastuzumab was continued during RT in those trials evaluating its efficacy [82,83]. No increased acute toxicity was seen when it was given concurrently with radiation on the North Central Cancer Treatment Group (NCCTG) trial N9831, although late toxicity, particularly cardiac in women receiving left-sided radiation, remains to be seen [84].

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 cancer recurrence is equivalent to the results in the adjuvant setting [79]. 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 thought to be appropriate candidates for lumpectomy [39]. Thorough discussion with the patient and careful pathology review are needed prior to proceeding with BCT. Moreover, because of potential discongruent patterns of shrinkage within the primary tumors, it is prudent to obtain clearly negative margins in the post-preoperative chemotherapy setting.

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; the 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.

The presence of 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 45-50.4 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, but it should be considered for select patients, including those with bulky nodes, a high nodal radio, and extracapsular extension. Hypofractionated regimens can be considered, particularly in older patients with small to modest size breasts in whom the benefit of the lumpectomy site boost is low. Altered fractionated schemes incorporating a boost, and/or regional nodal treatment are under investigation.

Summary

- Breast conservation is a safe and effective alternative to mastectomy for the majority of women with early-stage breast cancer.
- Adjuvant radiation therapy lowers the risk of recurrence within the breast and also confers a survival benefit.
- Acute side effects of radiation therapy are generally well tolerated; efforts are ongoing to minimize the long-term side effects of radiation, most prominently atherosclerotic heart disease.
- Efforts to minimize radiation therapy are underway. They include omitting treatment altogether in the elderly and using accelerated, hypofractionated whole-breast irradiation and accelerated partial-breast irradiation. Several randomized studies are underway to help determine the appropriate patients for these shorter treatments.

Supporting Documents

- ACR Appropriateness Criteria® Overview
- Evidence Table

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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

Variant 1: **Healthy 67-year-old woman, 0.5 cm well-differentiated IDC, ER/PR (+), HER2 (–), primary excised with lumpectomy, margins (–) <2 mm; anti-endocrine therapy planned.**

Treatment	Rating	Comments
Principles of Treatment		
Mastectomy + sentinel lymph node biopsy	9	If by patient choice with appropriate counseling.
Lumpectomy + sentinel lymph node biopsy + whole breast RT	9	
Lumpectomy + sentinel lymph node biopsy + accelerated PBI	8	Long-term follow-up is limited.
Lumpectomy + sentinel lymph node biopsy (no RT)	2	
RT Doses (1.8-2.0 Gy/day unless otherwise specified)		
Whole breast: 42.5 Gy (16 fractions)	9	
Whole breast: 45-50 Gy	9	
Total tumor bed dose: 42 Gy (16 fractions)	8	
Total tumor bed dose: 50 Gy	No consensus	While a lumpectomy site boost is generally well-tolerated, the benefit in women older than age 60 is small, and therefore some clinicians omit it when the surgical margin is widely negative.
Total tumor bed dose: 60 Gy	9	
Total tumor bed dose: 64-66 Gy	7	
PBI: 34-38.5 Gy over 8-10 fractions	7	Long-term follow-up is limited.

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

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

Variant 2: **Premenopausal 41-year-old woman, 1.1 cm GII IDC, upper outer quadrant (UOQ), ER/PR (+), HER2 (–), primary excised with lumpectomy, margins (–), SN biopsy negative, BRCA 1 mutation positive.**

Treatment	Rating	Comments
Principles of Treatment Whole breast irradiation	9	
Completion mastectomy	8	If by patient choice with appropriate counseling.
Completion mastectomy + contralateral mastectomy	8	If by patient choice with appropriate counseling.
Partial breast irradiation	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 3: **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 Re-excision + whole breast RT if negative margins +/- boost	9	
Completion mastectomy	8	If by patient choice with appropriate counseling.
No further surgery + RT to 66 Gy	5	If re-excision not feasible or refused.
No further surgery + RT to 60 Gy	3	Re-excision highly desirable.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

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

Variant 4: **Premenopausal 46-year-old woman, 2.6 cm UOQ IDC, primary excised with lumpectomy, margins (–), little ductal carcinoma in situ (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	Inclusion of the supraclavicular nodes in women with 1-3 positive axillary nodes remains controversial. While the risk of an isolated supraclavicular recurrence in this setting is generally low, some clinicians recommend adding nodal radiation in select cases based on pathologic and patient-related risk factors.
Completion mastectomy	2	If patient desires it and has no contraindications to breast conservation.
Nodal Radiation Volumes (assume breast RT given)		
Supraclavicular + apical (level III) axillary nodes	8	
Full axilla (level I-III)	2	
Internal mammary nodes	No consensus	Inclusion of the internal mammary nodes within the radiation fields is controversial. The risk of an isolated internal mammary recurrence is small, and radiation to the internal mammary nodes has not been proven to improve overall survival in a randomized trial. However, several randomized trials that have shown a survival benefit to adjuvant radiation have included treatment of the internal mammary nodes. This is particularly relevant in patients with medial, node-positive primary tumors in which older extended surgical series have demonstrated a significant incidence of internal mammary involvement.
RT Doses, Negative Re-excision (1.8-2.0 Gy/day unless specified otherwise)		
Whole breast: 42 Gy (2.6 Gy/day + 10 Gy boost)	4	Minimal data for hypofractionated RT in women receiving chemotherapy and in the younger patient population.
Whole breast: 42 Gy (2.6 Gy/day) (no boost)	2	Limited published experience using boost with this fractionation.
Whole breast: 45-50 Gy (no boost)	2	
Total tumor bed dose: 60-66 Gy	9	
SCL ± axillary apex: 45-50 Gy	9	
IMN: 45-50 Gy	9	As above, treatment of the internal mammary nodes is controversial. However, if treated there is uniform consensus that 45-50 Gy is an appropriate dose.

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