

American College of Radiology ACR Appropriateness Criteria®

DUCTAL CARCINOMA IN SITU

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Summary of Literature Review

Introduction

Ductal carcinoma in situ (DCIS; intraductal carcinoma) is a noninvasive breast cancer originating from the cells that line the mammary ducts. The term encompasses a broad range of diseases ranging from low-grade, indolent lesions to high-grade aggressive tumors that can be a precursor to invasive disease. Patients with DCIS can be asymptomatic at the time of presentation (radiographic findings or mammogram) or present with symptoms such as a palpable mass or nipple discharge. The incidence of DCIS has markedly increased in the past decade, primarily due to improved screening utilization and imaging techniques. This has led to a shift in disease presentation from years past where patients with DCIS had symptomatic findings to the current era in which these lesions are most commonly detected solely by abnormal mammographic findings.

Pathologically, DCIS is defined by the presence of malignant epithelial cells within the well-defined breast ducts. The malignant cells are, by definition, bound by an intact basement membrane without any basal myoepithelial layer invasion. There are several architectural subtypes of DCIS: solid, comedo, micropapillary, papillary, cribriform. Furthermore, DCIS is classified qualitatively by grade (reported as high, intermediate, and low based on cytologic/structural features) and the presence or absence of necrosis [1,2]. Often, patients with DCIS have lesions that contain at

least two architectural subtypes. Although pathologic criteria have been established to classify DCIS in comparison to normal hyperplasia and atypical ductal hyperplasia (ADH), the diagnosis can still be very challenging for pathologists, as these entities represent a continuum of cellular and architectural atypia. Distinguishing between ADH and DCIS can particularly be difficult, as demonstrated by significant differences in diagnosis on expert pathology review [3].

There are three general treatment approaches for women with DCIS: 1) mastectomy 2) breast conserving surgery (BCS) alone, encompassing wide local excision, lumpectomy, quadrantectomy, and partial mastectomy; and 3) BCS followed by radiation therapy, classically defined as breast conservation therapy (BCT). Historically, mastectomy was the standard treatment for this disease. Over the last two decades, the treatment has shifted to a breast-conserving approach (ie, lumpectomy with or without definitive breast irradiation) for patients with DCIS localized to one quadrant, if the disease is resectable with acceptable cosmesis. The standard radiation treatment has used conventionally fractionated, whole-breast radiation, delivered daily over 5-7 weeks, but in more recent years, there has been a resurgence of accelerated partial-breast irradiation (PBI), delivering biologically equivalent doses of radiation to only a portion of the breast for a shorter period (typically ≤ 5 days) for both DCIS and invasive breast cancers.

The management of DCIS remains controversial for several reasons. While there are no randomized trials comparing BCT to mastectomy for DCIS, comparisons of BCT to historic mastectomy controls suggest no difference in overall survival. In terms of breast conservation, there are four published randomized trials for DCIS evaluating the benefit of adjuvant whole-breast radiotherapy after local excision: the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-17 [4-6], the European Organization for Research and Treatment of Cancer (EORTC) 10853 [7,8], the UK/Australia/New Zealand (UK/ANZ) cooperative trial [9], and the Swedish trial [10]. All suggest a benefit in local control with the addition of whole-breast radiation compared with lumpectomy alone (with or without tamoxifen).

Because of the heterogeneity of DCIS, it is unclear whether all patients with DCIS uniformly benefit from treatment. While it appears, based on retrospective series, that there is an increased propensity for local recurrence after breast conservation treatment for comedo histologies, high-grade lesions, close/positive surgical margins, and younger patients, there is a paucity of complete data on these prognostic factors. The limited existing randomized DCIS studies do not adequately address the relative impact of these various factors in a prospective manner, and thus it is unclear how to factor

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them into the decision-making process. Thus, additional prospective studies incorporating these variables into the therapeutic interventions are required before they can routinely be used to guide treatment decisions. Furthermore, the randomized data assess the benefit of adjuvant, whole-breast radiation after local excision, but a more recent trend toward PBI has not been adequately studied. The existing body of literature on PBI for DCIS consists mainly of retrospective analyses with relatively short follow-up.

Additionally confounding the data, the proportion of patients with DCIS detected by physical findings and symptoms has decreased significantly with the increased use of screening mammography. Thus the earlier literature reporting on clinically symptomatic DCIS patients is not directly applicable to and cannot be used to guide decision-making for patients diagnosed in the current era, in which the vast majority of patients have subclinical disease at presentation that is subsequently detected, mainly by mammography. Furthermore, it is now more apparent that the variations in clinical and pathologic presentations of DCIS subtypes and the differences in their natural histories suggest that DCIS is not one entity, but rather a spectrum of diseases which ultimately may require different management approaches. Unfortunately, there are insufficient long-term data assessing the efficacies of the various treatment modalities for the different subtypes of DCIS. Lastly, there is a paucity of data on the natural history of DCIS in the untreated patient.

More recently, the addition of tamoxifen has been shown to help prevent recurrence of ipsilateral breast cancer in some groups of DCIS patients. The use of tamoxifen as a therapeutic option after BCS (with or without radiation) has added to the complexity of therapeutic decision-making, but must also be considered in hormone-receptor-positive DCIS patients as a means of decreasing in-breast recurrence. Complicating treatment considerations further, tamoxifen is also beneficial in reducing contralateral breast cancers. Since the focus of this document is on local treatment management and prevention of local relapse, tamoxifen and other antiendocrine agents will be discussed below as they relate to or affect local treatment choices.

Several ongoing randomized trials are attempting to address many important local and systemic therapies for DCIS: Radiation Therapy Oncology Group® (RTOG®) 98-04, NSABP B-35, International Breast Intervention Study (IBIS) II, and NSABP B-39/RTOG® 0413.

Local Treatment Variables

Mastectomy

Many reasons have been cited to justify the use of mastectomy as initial treatment of intraductal carcinoma. First, the rate of occult multicentricity found in mastectomy specimens is approximately 20%-30%. This rate, however, may be decreasing, as tumors are being detected earlier with wider use of screening mammography. Second, the rate of occult invasive

disease found in mastectomy specimens is approximately 10%. Third, residual normal breast tissue left in the patient after BCS might undergo malignant transformation over time. Mastectomy essentially eliminates this possibility, with local relapse rates approaching 0%. Fourth, there is a significant risk of invasive recurrence after BCT, and invasive cancers are theoretically more life-threatening than DCIS. Lastly, mastectomy series consistently provide the highest relapse-free survival rates of any treatment approach.

The reported outcome after treatment with mastectomy shows survival rates of 96%-100%. Local-regional control rates are also reported as 96%-100% [3,11,12]. However, survival and local-regional results are virtually always reported using crude outcome calculations. The lack of actuarial outcome analyses for mastectomy series is a serious impediment to comparison with breast-conservation series, which have typically been reported with actuarial outcome calculations. While the recent emphasis on the treatment of DCIS has focused on BCT instead of mastectomy, no prospective, randomized trials have included a mastectomy arm to date (mainly due to the number of patients that would be required to test for a potential survival advantage of 1%-3% over breast-conservation treatment, which would be so large that accruing patient would not be feasible). Furthermore, it would be difficult, if not impossible, to convince the needed number of women to agree to randomization between two such drastically different local therapies in contemporary practice. Therefore, the absence of a mastectomy arm in current prospective, randomized trials will preclude the definitive comparison of mastectomy with breast-conservation treatment.

While breast-conserving approaches have replaced mastectomy for DCIS in most cases, there are a few instances in which a mastectomy may be indicated. These include multicentric DCIS, unattainable negative margins, patient choice, large tumor size relative to small breast size, and diffuse microcalcifications on imaging studies. (See [Variant 1](#) and [Variant 2](#).)

Breast-Conservation Approaches

The components of treatment that need to be considered in a DCIS patient motivated to receive breast conservation can be divided into three major categories:

1. BCS to remove all disease and suspicious calcifications, and achieve a negative surgical margin.
2. Adjuvant radiation therapy, used to further decrease local relapse after BCS. Can be divided into three delivery methods:
 - Standard, conventionally fractionated, whole-breast radiation (delivered daily over 5 weeks with or without boost).
 - Accelerated, partial breast radiation (APBI), where a limited portion of the breast at highest risk for local recurrence is radiated in a shorter course, typically ≤ 5 days.

- Accelerated, hypofractionated whole-breast radiation, in which the whole-breast is radiated with higher daily fraction size for a shorter overall treatment time of approximately 3-4 weeks.

The following will review data on the radiation delivered with conventionally fractionated, whole-breast treatment for DCIS. The data on APBI and accelerated, hypofractionated whole-breast radiation therapy as it pertains to DCIS will be discussed in a separate section in this guideline.

3. Tamoxifen for 5 years in hormone-receptor-positive DCIS (used in a few of the randomized trials) to further reduce in-breast recurrence rates.

While both the addition of radiotherapy and tamoxifen have been shown to independently improve local control in randomized, prospective studies, the question remains whether sub-sets of DCIS patients have limited benefit and can forego these adjuvant treatments since neither confers a survival benefit.

Breast-Conserving Surgery Followed by Radiotherapy

Single-institution data on patients treated with surgical excision followed by radiation therapy demonstrate breast failure rates of 6%-10% [12-14], although generally with relatively short follow-up. Solin et al [13] recently updated the largest multi-institutional experience of DCIS, and reported a 15-year actuarial local failure rate of 19%. Subset analyses demonstrated local failure rates of $\leq 8\%$ for patients with negative margins or age ≥ 50 years. The cause-specific survival rate for these conservatively managed patients was an excellent 98% at 15 years, which is comparable to the results of mastectomy series.

Re-evaluation of the pathologic material from NSABP B-06 (a randomized trial evaluating postlumpectomy breast radiation for invasive breast cancer) revealed that 76 patients had in-situ rather than invasive breast cancer [3]. Local failure rates for the patients treated with excision versus excision followed by radiation therapy were 43% and 7%, respectively, at a mean follow-up interval of 83 months [3].

As mentioned above, four prospective, randomized trials have been published to date comparing excision alone with excision followed by radiation therapy (with or without tamoxifen). All trials treated the whole-breast to 50 Gy in 5 weeks without the use of a boost. The first trial, NSABP B-17, has the longest follow-up of 20 years. It randomized patients after lumpectomy to radiation versus no radiation (tamoxifen was not used) and demonstrated that local failure was reduced from a crude rate of 31.7% without radiation to 15.7% with radiation [5]. The inclusion criteria for this study were localized DCIS of any histology detected either clinically or mammographically, with negative margins following excision (defined as no tumor cells on the inked resection margin). The 12-year data revealed that radiation therapy has a greater impact on reducing the incidence of invasive recurrences, the potentially life-threatening form of recurrence (relative risk [RR] = 0.38, $P=0.00001$), but

also significantly reduces noninvasive recurrences (RR=0.49, $P=0.001$). Local failure was significantly increased for patients with questionable or positive surgical margins and for those with marked to moderate comedo necrosis [6].

The EORTC 10853 trial for DCIS randomized patients after lumpectomy to radiation versus no radiation without use of tamoxifen. With a median follow-up of 51 months, local failure was 16% in patients who were only observed versus 9% in patients who were radiated [8]. In the 10-year update, local relapse increased to 26% of patients without radiation versus 15% of those with radiation (log-rank $P<0.0001$; hazard ratio [HR] = 0.53) [15].

Similar to the long-term outcomes in the B-17 trial, radiation significantly reduced invasive and DCIS recurrences in this trial. Factors that predicted an increased local recurrence on multivariate analysis included age 40 years or younger, palpable DCIS lesions, involved surgical margins, cribriform and solid histologic subtypes, and treatment with lumpectomy only [7].

The UK/ANZ DCIS randomized trial had a more complex design in which patients were entered into a modified 2x2 randomization design after study enrollment of with or without radiation therapy and with or without tamoxifen, or elect randomization to only with or without radiation therapy or with or without tamoxifen [9]. Notwithstanding the complexity of the study design, the published results (median follow-up of 52.6 months) demonstrated a reduction in ipsilateral breast cancer recurrence rates with the addition of radiotherapy (14% vs 6%, $P<0.0001$).

A phase III trial originating from Sweden (the SweDCIS Trial) [10] also demonstrated a benefit to adjuvant radiation with a cumulative incidence of recurrence of 0.07 (95% confidence interval [CI] 0.050–0.10) in the radiation arm compared with 0.22 (95% CI 0.18–0.26) in the observation arm with a corresponding overall HR of 0.33 (95% CI 0.24–0.47, $P<0.0001$) at a median follow-up of 5.2 years. A notable difference in this protocol from the above aforementioned trials was that this study did not require microscopically negative margins prior to radiation; 10% of the patients had positive surgical margins in this study.

In summary, all four of these randomized, prospective trials have consistently demonstrated a significant improvement in local control with the use of adjuvant radiation, with a risk reduction of both invasive and in-situ ipsilateral breast recurrence rates of $>50\%$ with the addition of postlumpectomy whole-breast radiotherapy, with no difference in overall survival (these studies were not powered to detect a survival difference).

Excision Alone

The primary criticism of the currently published randomized DCIS trials is the lack of stratification before randomization by tumor grade, histology, or size because such stratification might have identified a subset of patients that may be adequately treated with excision alone. Selected patients have been managed with excision alone in retrospective studies [16]. The criteria for

consideration of excision alone in these studies were similar: lesions detected mammographically, without a palpable component, measuring ≤ 25 mm, and with negative margins following excision; with local failure rates of reported to be 10%-15%, comparable to single-institution reports of surgical excision followed by radiation therapy in less rigorously selected patients. These series also note that most of the breast failures were in patients with tumors of the comedo subtype, or inadequate margins, and young patients. For patients treated with lumpectomy alone, Silverstein et al [16] reported that the risk of local recurrence was reduced with increasingly wide negative margins of resection.

The Van Nuys Prognostic Index, adopted from a review in which a risk category was developed based on margin status, histologic subtype, tumor size, and patient age using a cohort of DCIS patients treated from two institutions [17], continues to be used by some practitioners as part of their decision-making process for adjuvant radiation after local excision. It is important to note that the data from this “scoring system” were derived from retrospective data, and that all randomized prospective data published to date have consistently demonstrated an improvement in local control in all patients.

Other groups have attempted to identify subgroups of DCIS patients who may have minimal benefit from radiotherapy, using a prospective study design. A notable single-arm prospective protocol of highly selected small, low-grade DCIS patients treated with breast-conserving surgery with widely negative margins of ≥ 1 cm was initiated in Boston but was closed early due to the high number of local recurrences with observation alone [18]. Unfortunately, the RTOG® 98-04, which was designed to assess the outcomes of observed versus radiated low-risk DCIS patients after BCS, was also closed prematurely due to lack of accrual.

And lastly, the Eastern Cooperative Oncology Group (ECOG) initiated a prospective, single-arm trial (E5194) of observation for low- and intermediate-risk DCIS [19]. The stratification of the two cohorts in this study included the low-risk group, defined as low- or intermediate-grade DCIS measuring ≤ 2.5 cm; and intermediate-risk group, defined as high-grade DCIS measuring ≤ 1 cm with negative margin widths of ≥ 3 mm. It is notable that the average tumor sizes for the low- and intermediate-risk cohorts were only 6 mm and 5 mm (when enrollment guidelines allowed for ≤ 25 mm and ≤ 10 mm, respectively), suggesting that the patients enrolled in this trial were highly selected with tumors significantly smaller than permitted by the protocol eligibility. With a median follow-up of 6.7 years for the low-risk group and 6.2 years for the intermediate-risk group, the ipsilateral breast relapse rates were 6% and 15%, respectively. Given the long natural history of DCIS, often with late recurrences (>10 years), particularly in low- and intermediate-grade DCIS, these data are considered early results, and longer follow-up is required. (See [Variant 3](#) and [Variant 4](#).)

Systemic Therapy

Because DCIS is a process confined within the ductal system of the breast, it has no potential to spread to distant body sites. Thus, there is no need to deliver any therapy that would treat the patient “systemically” (ie, with chemotherapy or antiendocrine therapy to treat organs beyond the breast). However, BCT has been improved (yet made more complex) by the recent appreciation that antiendocrine therapy (using tamoxifen) impacts local control in the breast conservation setting. Results of the NSABP B-24 trial demonstrated that the addition of tamoxifen to postlumpectomy breast radiotherapy for DCIS significantly reduced ipsilateral breast tumor recurrences (RR=0.60, 95% CI=0.38-0.96) but did not have an impact on survival [20]. Further progress was made when Allred et al [21] analyzed subsets of patients treated in the NSABP B-24 trial and found that the benefit in local control with tamoxifen was associated with patients with estrogen-receptor (ER)-positive only. As a result, all DCIS lesions should routinely undergo hormone receptor status assessment prior to consideration of eligibility for tamoxifen. The role of tamoxifen in the setting of DCIS treated with mastectomy has not been determined to date.

Wapnir et al [22] analyzed data from 2,615 women with primary DCIS who participated in the NSABP B-17 and B-24 trials for ipsilateral breast tumor recurrence; patients were followed for a median of >12 years. Ipsilateral breast tumor recurrence was a first failure in 465 patients (243 invasive, 222 noninvasive). The 12-year cumulative incidence of all such recurrences was 32.9% for lumpectomy only, 15.8% for lumpectomy with whole-breast irradiation, and 12.5% for lumpectomy with whole-breast irradiation plus tamoxifen.

Currently there are no published phase III data on the use of aromatase inhibitors for DCIS. Both NSABP B-35 (http://www.nsabp.pitt.edu/NSABP_Protocol_Chart.pdf) and IBIS-II (<http://www.ibis-trials.org/about/dcis2.php>) are currently accruing patients and comparing anastrozole to tamoxifen as adjuvant therapy for DCIS. Because DCIS expresses human epidermal growth factor receptor 2 (HER2/neu) more often than invasive cancers [23], the benefit of trastuzumab for HER2/neu-positive DCIS is being evaluated in a phase III trial of adjuvant trastuzumab in the NSABP B-43 trial (<http://clinicaltrials.gov/ct2/show/NCT00769379>), in which patients will receive 6 weeks of whole-breast irradiation and be randomized to 2 cycles of trastuzumab delivered concurrently with radiation versus no systemic therapy.

The Role of Surgical Assessment of the Axilla in DCIS

There is currently no role for axillary dissection in the management of DCIS, even for high-grade or comedo lesions, because in theory, pure DCIS is preinvasive and should not metastasize. While the risk of axillary involvement for pure DCIS approaches 0% in contemporary studies [14], the preoperative diagnosis of DCIS by core-needle biopsy is upstaged after the definitive procedure in as many as 9%-15% of patients

[24,25], requiring these patients to subsequently undergo a separate second surgical procedure to evaluate the axilla. Furthermore, contemporary series suggest that there is a difference in lymph node involvement for patients with DCIS diagnosed at biopsy (10% node positive) versus pure DCIS after definitive surgery (5% node positive) [26,27] as well as DCIS with microinvasion (9% node positive) versus pure DCIS (5% node positive) [28,29].

These contemporary series use the sentinel lymph node biopsy (SLNB) procedure to assess the axillary nodal status in lieu of a full axillary dissection, thus diminishing the morbidity of surgical evaluation of the axilla while preserving the accuracy of surgical nodal evaluation. As a consequence, there is renewed discussion as to the appropriateness of surgical evaluation of the axilla for DCIS using SLNB to identify patients at increased risk for nodal involvement, in order to prevent an additional delayed procedure after the definitive local surgery.

From the more detailed histopathologic evaluation of lymph nodes removed from SLNB compared to axillary dissection, reports of positive SLNBs have been described in up to 12% of cases of DCIS [30,31], but the clinical relevance of a positive SLNB in the setting of pure DCIS has yet to be demonstrated [32]. Currently, the few studies reporting the impact of SLNB on DCIS patients is limited mainly to single institutional series, and it remains particularly unclear how micrometastasis or isolated tumor cells in lymph nodes affect outcomes or should influence management [33].

As a result, while SLNB is not a routine component of breast-conserving surgical management of most patients with DCIS, it is used in specific situations. For example, in patients undergoing mastectomy with the preoperative diagnosis of DCIS, an SLNB is often advocated, due to the greater than 10% risk of occult invasive disease in the mastectomy specimen and the greater than 10% sentinel node positivity [34]. If SLNB is not performed at the time of mastectomy, the ability to perform an SLNB procedure subsequent to mastectomy is precluded, with delayed complete axillary dissection as the only option for surgical evaluation of the axilla. In DCIS patients with radiographic evidence of extensive disease or tumor size measuring >2.5 cm, SLNB may also be considered, as the risk of nodal involvement appears to rise with increased size of DCIS [25].

Microinvasive Disease (DCIS with Microinvasion)

Microinvasive carcinoma (DCIS with microinvasion) is pathologically defined by the presence of early and minimal penetration of the duct wall by cancer cells beyond the basement membrane as seen by conventional light microscopic evaluation [39]. While special staining can be used to demonstrate the absence of a myoepithelial layer surrounding the tumor cells to define a tumor that has invaded beyond the confines of a duct, there remains some controversy as to the exact definition of microinvasion for DCIS, due to variations in the quantitative definitions. Many publications use the criteria of ≤ 2 mm of invasion [35], while the AJCC staging

system specifically defines microinvasion as ≤ 0.1 cm (T1mic). The presence of unequivocal invasion is required for the diagnosis; cases with equivocal invasion should not be considered microinvasion. Cases with >2 mm of invasion are sometimes considered as having “minimal invasion” but should be distinguished from microinvasion (T1mic) as an invasive cancer (T1a).

Limited information has been reported regarding treatment outcome for microinvasive carcinoma of the breast as a separate entity. Typically, DCIS with microinvasion cases are included with early-stage invasive disease (eg, T1a lesions) [35]. Thus there are limited data on DCIS with microinvasion, although the actual diagnosis of microinvasive carcinoma is increasing due to improved early detection. The number of reported cases, especially with long-term follow-up information, is small, and there are no randomized trials that evaluate therapy for microinvasive disease.

For regional nodal management, microinvasive carcinoma carries a small but real risk of axillary lymph node metastasis, with nodal involvement ranging from 3%-10%, although higher and lower risks have been reported [35]. With the development of SLNB techniques, the decision to evaluate the axilla surgically is a less difficult one, given the reduced morbidity of the procedure compared with axillary node dissection and the large impact a positive lymph node would potentially have on systemic management of a patient with a microinvasive primary. Most clinicians now include pathologic axillary staging (for example, with an SLNB) as a standard part of surgical management of this disease [31].

The major difference in the local management of DCIS with microinvasion compared with pure DCIS is that lumpectomy alone is not considered a standard management option for microinvasive carcinoma of the breast. The possible exception to this caveat would be in the setting of an ER-positive microinvasive tumor in a postmenopausal “elderly” woman following lumpectomy who will be receiving adjuvant hormonal therapy. In the Cancer and Leukemia Group B (CALGB) randomized trial of lumpectomy followed by tamoxifen alone versus tamoxifen and radiation for women 70 years of age and older with T1 tumors (which presumably included but was not specifically evaluating microinvasive disease), the recent update showed only a modest benefit with the use of radiation (breast relapse-free survival rates of 98% vs 92% at 10.5 year follow-up) [36]. While the existing data on DCIS with microinvasion are retrospective with small numbers of patients [37,38], a recent relatively large, single institutional series reported their long-term outcomes of pure DCIS compared to microinvasive DCIS with microinvasion treated with BCS and radiation therapy, and found no significant differences in local relapse, disease-free survival or overall survival [39]. While somewhat conflicting, these studies collectively suggest that the microinvasion in and of itself may not confer a worse prognosis; the clinical behavior may be related to the pathologic features of the underlying DCIS (eg, comedo necrosis, high-grade disease). (See [Variant 5.](#))

Use of Magnetic Resonance Imaging in DCIS

The use of breast magnetic resonance imaging (MRI) is increasingly prevalent in the preoperative management of invasive breast cancers and, more recently, for DCIS. Early in the era of breast MRI, this mode of imaging was felt to be less sensitive than mammography for pure intraductal cancers [40], and thus its use in the workup of DCIS was discouraged. More recently, it has become apparent that the diagnostic criteria for MRI assessment of DCIS differ from those of invasive cancers [41], and that MRI does allow for more effective diagnosis of DCIS [42-44]. Several studies indicate that breast MRI is more sensitive in detecting multicentric disease for DCIS compared with mammography [43,44]. For estimating the size of DCIS lesions using MRI, conflicting results have been published [44-46]. Generally it is felt that MRI provides an overall improvement of size estimation for DCIS compared with mammography but with both over- and under-estimation of tumor size compared with pathologic analysis. Breast MRI has been found to be more sensitive for detecting intermediate and high-grade DCIS [45,46]. Lastly, recent reports suggest that the varied morphology of DCIS seen on breast MRI is a reflection of the heterogeneous differences of DCIS pathology [47]. For example, clumped enhancement patterns are more associated with high-grade lesions than more heterogeneous patterns, and small focal masses are associated with ER-positive DCIS. There are several advantages in using an MRI in the preoperative setting, including its high sensitivity for DCIS that ranges from 72%-84% [48]; the possibility of detecting DCIS without microcalcifications that are mammography occult; its ability to better assess for multicentricity than mammography; its ability to outperform mammography in dense breasts; and lastly, its ability to improve on the size estimation for guiding local treatment decisions. These pluses have to be weighed against the disadvantages, including high false positive rates potentially requiring unnecessary further workup and additional invasive procedures, delay of definitive treatment for the known malignancy, and increased anxiety for the patient. It is important to note that while no studies to date demonstrate a benefit in **outcomes** with the use of MRI for DCIS, the use of breast MRI in DCIS has been shown to decrease the need for re-excisions secondary to incomplete surgical removal and positive margins [45].

Accelerated Partial Breast Radiation

Though APBI is being increasingly used for breast cancer, there are no randomized, prospective studies published to date reporting its long-term efficacy compared with standard, conventionally fractionated, whole-breast radiation. While some well-controlled, prospective, single-arm studies exist for invasive cancers and for DCIS specifically, there is a paucity of such data. While not a traditionally “prospective” study, the most notable experience of APBI for DCIS comes from the American Society of Breast Surgeons’ (ASBS) Mammosite® registry trial, an analysis of patient data collected from 97 institutions that allowed for treating

physicians to enter patient information at any time before, during, or after Mammosite® treatment for future analysis and study. In the most recent update, at 5 years, of the 194 (13%) patients in the registry who had DCIS, the 5-year actuarial local relapse was 3.34% with the use of Mammosite®, comparable to historic controls of conventionally fractionated, whole-breast radiation [49]. Due to the limited data using the various APBI modalities for DCIS, the American Society for Radiology Oncology (ASTRO) recently published a consensus statement regarding the use of APBI, where three categories of appropriateness for APBI were generated (“suitable,” “cautionary,” and “unsuitable”) based on the level of prospective data and follow-up [50]. Due to the limited prospective data on APBI for DCIS, this disease entity was categorized in the “cautionary” group. Similarly, the Breast Cancer Working Group of the Groupe European de Curiotherapie and the European Society of Therapeutic Radiology (GEC-ESTRO) recently published guidelines of three categories for patient selection for APBI [51] where DCIS was placed in the “intermediate risk group.”

A randomized phase III trial is currently accruing patients (with DCIS or invasive tumors ≤ 3 cm) to determine the relative efficacy and toxicity of APBI compared to whole-breast radiotherapy (NSABP B-39/RTOG® 0413) (<http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0413>). Patients randomized to PBI can receive either luminal-based brachytherapy, interstitial brachytherapy, or 3D conformal external beam radiation. This trial will provide very important information regarding the long-term outcomes, cosmetic results, and toxicities of APBI for DCIS delivered via these APBI techniques. (See [Variant 6](#) and [Variant 7](#).)

Hypofractionated Whole-Breast Radiation

There has been a recent resurgence of hypofractionated whole-breast radiation for women with early-stage breast cancer. There are now four prospective, randomized trials confirming that treatment with accelerated, hypofractionated radiation with doses of 39-43 Gy in 13-16 fractions provides local tumor control comparable to that provided by standard fractionation of 50 Gy in 25 fractions, with equivalent acute and late effects of treatment in patients with early-stage invasive breast cancers. While these trials did not specifically assess hypofractionated radiation in DCIS patients, long-term data suggest no difference in hypofractionated, whole-breast radiation compared to the standard fractionation in terms of local control, cosmesis, and other long-term effects in the setting of breast conservation. Although patients in these trials had invasive disease, the cosmetic and long-term effects would not be expected to be different in DCIS. While the presumption is that local control rates for DCIS using hypofractionated whole-breast radiation would be comparable to the standard fractionation schemes, patients with DCIS were excluded from the randomized hypofractionation whole-breast trials. Based on the lack of available prospective randomized data, a recent ASTRO task force concluded that at this time there are insufficient data to allow an evidence-based recommendation for or against

hypofractionated whole-breast radiation for women with DCIS [52]. An ongoing, randomized phase III study, TROG 07.01/BIG 03-07/IBCSG Trial 38-10 (<http://www.clinicaltrials.gov/ct2/show/NCT00470236?term=TROG%20DCIS&rank=1>), is studying radiation doses and fractionations specifically for DCIS of the breast.

Management Guidelines

DCIS

Patients with DCIS are eligible for breast conservation when the area of involvement is amenable to complete surgical excision without compromise of ultimate cosmetic outcome. In general, this is defined as tumors ≤ 4 -5 cm, but requires consideration of tumor size and location relative to breast size and patient preference for breast conservation with joint input from the surgeon and radiation oncologist. Patients with extensive microcalcifications, large tumor size relative to small breast size, involvement of more than one quadrant, or multicentric disease should be considered for mastectomy. When undergoing mastectomy, an SLNB is a reasonable staging intervention.

There is no consensus on the definition of negative margins. In general, trials using lumpectomy alone have required greater negative margin clearance (generally ≥ 5 -10 mm) than those using definitive breast irradiation (ranging from no tumor on ink to 1-3 mm). It is clear that there is a correlation between the degree of margin clearance and local control.

Breast irradiation requires treatment to the whole-breast to a total dose of 4,500-5,040 cGy in standard fractionation (180-200 cGy/day); with the option for a tumor bed boost to ensure that the total dose ranges between 5,000-6,600 cGy, depending on pathologic findings.

It remains unclear which patients are appropriate candidates for excision alone, but early results of observation in selected DCIS patients are promising [19]. The addition of tamoxifen in a hormone-receptor-positive DCIS patient should be considered and weighed against the side effects of the medication.

At the time of this writing, the only phase III trials open to accrual pertaining to treatment management of DCIS are NSABP B-39/RTOG[®] 0413 (<http://clinicaltrials.gov/ct2/show/NCT00103181>) for whole-breast versus PBI, NSABP B-43 (<http://clinicaltrials.gov/ct2/archive/NCT00769379>) assessing the use of adjuvant herceptin in HER2+ DCIS patients, and IBIS-II DCIS/BIG 5-02 (<http://clinicaltrials.gov/ct2/show/NCT00072462>), assessing tamoxifen versus anastrozole in the adjuvant setting, are all open to accrual.

DCIS with Microinvasion

Eligibility for breast conservation in patients with DCIS and microinvasion requires the same clinical and pathologic considerations as those for DCIS patients with regard to tumor size, tumor location, breast size, and the feasibility of complete excision. This scenario differs,

however, in the distinctly increased but low possibility of axillary node involvement and occult systemic metastatic disease. If knowledge of positive axillary nodes would prompt a recommendation for systemic therapy, an SLNB (by a surgeon experienced in this technique) may be performed, or irradiation of the axilla may be done, depending on the clinical situation.

Breast irradiation involves treatment to the whole-breast to a total dose of 4,500-5,040 cGy in standard fractionation, with the option for a tumor bed boost to ensure that the total dose ranges between 5,000-6,600 cGy, depending on pathologic findings. Treatment with lumpectomy and tamoxifen without breast radiotherapy in elderly women with ER positive microinvasive tumors following lumpectomy and negative margins may be considered.

Tamoxifen should be considered for hormone-receptor-positive patients. Aromatase inhibitors are also an option for postmenopausal patients in whom anti-endocrine therapy is being considered, and they are currently being studied as adjuvant therapy for DCIS in the phase III setting (IBIS II DCIS/BIG 5-02).

Summary

- Breast conservation therapy (consists of breast-conserving surgery to achieve negative margins followed by adjuvant radiation therapy to the whole-breast) is an acceptable treatment alternative to mastectomy for women with localized DCIS wishing to conserve their breast.
- In selected older patients with fully excised, low-grade disease, observation may be considered after conservative surgery.
- When a mastectomy is desired or required, most surgeons will simultaneously perform a sentinel node biopsy.
- Conventionally fractionated, whole-breast radiation for DCIS consists of 45-50.4 Gy in 25-28 fractions, with or without a boost to the tumor bed.
- While there are currently no phase III data to support the use of a boost in DCIS, most radiation oncologists will deliver a boost dose of 10-16 Gy depending on age and margin status.
- PBI may be used in appropriately selected patients, but should be delivered on protocol.
- Tamoxifen should be considered in ER-positive patients with DCIS.
- DCIS with microinvasion is managed similarly to DCIS, except that SLNB is often used and axillary RT may be considered in selected cases.
- Hypofractionated whole-breast radiation for DCIS is being investigated in ongoing phase III studies, but it may be considered in appropriately selected elderly patients.
- The use of MRI for DCIS remains unclear but may be considered in selected patients in whom there are

concerns regarding additional disease that would alter the planned management.

Supporting Document(s)

- [ACR Appropriateness Criteria® Overview](#)
- [Evidence Table](#)

References

1. Consensus Conference on the classification of ductal carcinoma in situ. The Consensus Conference Committee. *Cancer* 1997; 80(9):1798-1802.
2. Solin LJ, Yeh IT, Kurtz J, et al. Ductal carcinoma in situ (intraductal carcinoma) of the breast treated with breast-conserving surgery and definitive irradiation. Correlation of pathologic parameters with outcome of treatment. *Cancer* 1993; 71(8):2532-2542.
3. Fisher ER, Leeming R, Anderson S, Redmond C, Fisher B. Conservative management of intraductal carcinoma (DCIS) of the breast. Collaborating NSABP investigators. *J Surg Oncol* 1991; 47(3):139-147.
4. Fisher B, Dignam J, Wolmark N, et al. Lumpectomy and radiation therapy for the treatment of intraductal breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-17. *J Clin Oncol* 1998; 16(2):441-452.
5. Fisher B, Land S, Mamounas E, Dignam J, Fisher ER, Wolmark N. Prevention of invasive breast cancer in women with ductal carcinoma in situ: an update of the national surgical adjuvant breast and bowel project experience. *Semin Oncol* 2001; 28(4):400-418.
6. Fisher ER, Costantino J, Fisher B, Palekar AS, Redmond C, Mamounas E. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) Protocol B-17. Intraductal carcinoma (ductal carcinoma in situ). The National Surgical Adjuvant Breast and Bowel Project Collaborating Investigators. *Cancer* 1995; 75(6):1310-1319.
7. Bijker N, Peterse JL, Duchateau L, et al. Risk factors for recurrence and metastasis after breast-conserving therapy for ductal carcinoma-in-situ: analysis of European Organization for Research and Treatment of Cancer Trial 10853. *J Clin Oncol* 2001; 19(8):2263-2271.
8. Julien JP, Bijker N, Fentiman IS, et al. Radiotherapy in breast-conserving treatment for ductal carcinoma in situ: first results of the EORTC randomised phase III trial 10853. EORTC Breast Cancer Cooperative Group and EORTC Radiotherapy Group. *Lancet* 2000; 355(9203):528-533.
9. Houghton J, George WD, Cuzick J, Duggan C, Fentiman IS, Spittle M. Radiotherapy and tamoxifen in women with completely excised ductal carcinoma in situ of the breast in the UK, Australia, and New Zealand: randomised controlled trial. *Lancet* 2003; 362(9378):95-102.
10. Emdin SO, Granstrand B, Ringberg A, et al. SweDCIS: Radiotherapy after sector resection for ductal carcinoma in situ of the breast. Results of a randomised trial in a population offered mammography screening. *Acta Oncol* 2006; 45(5):536-543.
11. Cutuli B, Teissier E, Piat JM, et al. Radical surgery and conservative treatment of ductal carcinoma in situ of the breast. *Eur J Cancer* 1992; 28(2-3):649-654.
12. Silverstein MJ, Cohlan BF, Gierson ED, et al. Duct carcinoma in situ: 227 cases without microinvasion. *Eur J Cancer* 1992; 28(2-3):630-634.
13. Solin LJ, Fourquet A, Vicini FA, et al. Long-term outcome after breast-conservation treatment with radiation for mammographically detected ductal carcinoma in situ of the breast. *Cancer* 2005; 103(6):1137-1146.
14. Solin LJ, Kurtz J, Fourquet A, et al. Fifteen-year results of breast-conserving surgery and definitive breast irradiation for the treatment of ductal carcinoma in situ of the breast. *J Clin Oncol* 1996; 14(3):754-763.
15. Bijker N, Meijnen P, Peterse JL, et al. Breast-conserving treatment with or without radiotherapy in ductal carcinoma-in-situ: ten-year results of European Organisation for Research and Treatment of Cancer randomized phase III trial 10853--a study by the EORTC Breast Cancer Cooperative Group and EORTC Radiotherapy Group. *J Clin Oncol* 2006; 24(21):3381-3387.
16. Silverstein MJ, Lagios MD, Groshen S, et al. The influence of margin width on local control of ductal carcinoma in situ of the breast. *N Engl J Med* 1999; 340(19):1455-1461.
17. Silverstein MJ. The University of Southern California/Van Nuys prognostic index for ductal carcinoma in situ of the breast. *Am J Surg* 2003; 186(4):337-343.
18. Wong JS, Kaelin CM, Troyan SL, et al. Prospective study of wide excision alone for ductal carcinoma in situ of the breast. *J Clin Oncol* 2006; 24(7):1031-1036.
19. Hughes LL, Wang M, Page DL, et al. Local excision alone without irradiation for ductal carcinoma in situ of the breast: a trial of the Eastern Cooperative Oncology Group. *J Clin Oncol* 2009; 27(32):5319-5324.
20. Fisher B, Dignam J, Wolmark N, et al. Tamoxifen in treatment of intraductal breast cancer: National Surgical Adjuvant Breast and Bowel Project B-24 randomised controlled trial. *Lancet* 1999; 353(9169):1993-2000.
21. Allred DC, Bryant J, Land S, et al. Estrogen receptor expression as a predictive marker of effectiveness of tamoxifen in the treatment of DCIS: findings from NSABP Protocol B-24. *Breast Cancer Res Treat* 2002; 76(Suppl 1):S36. abstract.
22. Wapnir I, Dignam J, Julian TB, et al. Long-term outcomes after invasive breast tumor recurrence (IBTR) in women with DCIS in NSABP B-17 and B-24. *J Clin Oncol* 2007; 25 No. 18S (June 20 Supplement) 2007:520.
23. Allred DC, Clark GM, Molina R, et al. Overexpression of HER-2/neu and its relationship with other prognostic factors change during the progression of in situ to invasive breast cancer. *Hum Pathol* 1992; 23(9):974-979.
24. Bruening W, Fontanarosa J, Tipton K, Treadwell JR, Launders J, Schoelles K. Systematic review: comparative effectiveness of core-needle and open surgical biopsy to diagnose breast lesions. *Ann Intern Med* 2010; 152(4):238-246.
25. Moran CJ, Kell MR, Flanagan FL, Kennedy M, Gorey TF, Kerin MJ. Role of sentinel lymph node biopsy in high-risk ductal carcinoma in situ patients. *Am J Surg* 2007; 194(2):172-175.
26. Meijnen P, Oldenburg HS, Loo CE, Nieweg OE, Peterse JL, Rutgers EJ. Risk of invasion and axillary lymph node metastasis in ductal carcinoma in situ diagnosed by core-needle biopsy. *Br J Surg* 2007; 94(8):952-956.
27. Yi M, Krishnamurthy S, Kuerer HM, et al. Role of primary tumor characteristics in predicting positive sentinel lymph nodes in patients with ductal carcinoma in situ or microinvasive breast cancer. *Am J Surg* 2008; 196(1):81-87.
28. Katz A, Gage I, Evans S, et al. Sentinel lymph node positivity of patients with ductal carcinoma in situ or microinvasive breast cancer. *Am J Surg* 2006; 191(6):761-766.
29. Sakr R, Bezu C, Raoust I, et al. The sentinel lymph node procedure for patients with preoperative diagnosis of ductal carcinoma in situ: risk factors for unsuspected invasive disease and for metastatic sentinel lymph nodes. *Int J Clin Pract* 2008; 62(11):1730-1735.
30. Farkas EA, Stolier AJ, Teng SC, Bolton JS, Fuhrman GM. An argument against routine sentinel node mapping for DCIS. *Am Surg* 2004; 70(1):13-17; discussion 17-18.
31. Intra M, Veronesi P, Mazzarol G, et al. Axillary sentinel lymph node biopsy in patients with pure ductal carcinoma in situ of the breast. *Arch Surg* 2003; 138(3):309-313.
32. Lara JF, Young SM, Velilla RE, Santoro EJ, Templeton SF. The relevance of occult axillary micrometastasis in ductal carcinoma in situ: a clinicopathologic study with long-term follow-up. *Cancer* 2003; 98(10):2105-2113.
33. Moore KH, Sweeney KJ, Wilson ME, et al. Outcomes for women with ductal carcinoma-in-situ and a positive sentinel node: a multi-institutional audit. *Ann Surg Oncol* 2007; 14(10):2911-2917.
34. Dominguez FJ, Golshan M, Black DM, et al. Sentinel node biopsy is important in mastectomy for ductal carcinoma in situ. *Ann Surg Oncol* 2008; 15(1):268-273.
35. Solin LJ, Fowble BL, Yeh IT, et al. Microinvasive ductal carcinoma of the breast treated with breast-conserving surgery and definitive irradiation. *Int J Radiat Oncol Biol Phys* 1992; 23(5):961-968.
36. Hughes KS, Schnaper LA, Cirrincione C, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 or older with early breast cancer. *J Clin Oncol* 2010; 28: 15s, 2010 (suppl; abstr 507).

37. Cavaliere A, Scheibel M, Bellezza G, et al. Ductal carcinoma in situ with microinvasion: clinicopathologic study and biopathologic profile. *Pathol Res Pract* 2006; 202(3):131-135.
38. Vieira CC, Mercado CL, Cangiarella JF, Moy L, Toth HK, Guth AA. Microinvasive ductal carcinoma in situ: clinical presentation, imaging features, pathologic findings, and outcome. *Eur J Radiol* 2010; 73(1):102-107.
39. Parikh RR, Haffty BG, Lannin D, Moran MS. Ductal Carcinoma In Situ with Microinvasion: Prognostic Implications, Long-Term Outcomes, and Role of Axillary Evaluation. *Int J Radiat Oncol Biol Phys* 2010; [Epub ahead of print].
40. Bazzocchi M, Zuiani C, Panizza P, et al. Contrast-enhanced breast MRI in patients with suspicious microcalcifications on mammography: results of a multicenter trial. *AJR* 2006; 186(6):1723-1732.
41. Raza S, Vallejo M, Chikarmane SA, Birdwell RL. Pure ductal carcinoma in situ: a range of MRI features. *AJR* 2008; 191(3):689-699.
42. Kuhl CK, Schrading S, Bieling HB, et al. MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study. *Lancet* 2007; 370(9586):485-492.
43. Menell JH, Morris EA, Dershaw DD, Abramson AF, Brogi E, Liberman L. Determination of the presence and extent of pure ductal carcinoma in situ by mammography and magnetic resonance imaging. *Breast J* 2005; 11(6):382-390.
44. Santamaria G, Velasco M, Farrus B, Zanon G, Fernandez PL. Preoperative MRI of pure intraductal breast carcinoma--a valuable adjunct to mammography in assessing cancer extent. *Breast* 2008; 17(2):186-194.
45. Schouten van der Velden AP, Boetes C, Bult P, Wobbes T. The value of magnetic resonance imaging in diagnosis and size assessment of in situ and small invasive breast carcinoma. *Am J Surg* 2006; 192(2):172-178.
46. Shiraishi A, Kurosaki Y, Maehara T, Suzuki M, Kurosumi M. Extension of ductal carcinoma in situ: histopathological association with MR imaging and mammography. *Magn Reson Med Sci* 2003; 2(4):159-163.
47. Esserman LJ, Kumar AS, Herrera AF, et al. Magnetic resonance imaging captures the biology of ductal carcinoma in situ. *J Clin Oncol* 2006; 24(28):4603-4610.
48. Estevez LG, Alvarez I, Segui MA, et al. Current perspectives of treatment of ductal carcinoma in situ. *Cancer Treat Rev* 2010; 36(7):507-517.
49. Vicini F, Beitsch P, Quiet C, et al. Five-year analysis of treatment efficacy and cosmesis by the American Society of Breast Surgeons MammoSite Breast Brachytherapy Registry Trial in patients treated with accelerated partial breast irradiation. *Int J Radiat Oncol Biol Phys* 2011; 79(3):808-817.
50. Smith BD, Arthur DW, Buchholz TA, et al. Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). *Int J Radiat Oncol Biol Phys* 2009; 74(4):987-1001.
51. Polgar C, Van Limbergen E, Potter R, et al. Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: recommendations of the Groupe Europeen de Curietherapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009). *Radiother Oncol* 2010; 94(3):264-273.
52. Smith BD, Bentzen SM, Correa CR, et al. Fractionation for Whole Breast Irradiation: An American Society for Radiation Oncology (ASTRO) Evidence-Based Guideline. *Int J Radiat Oncol Biol Phys* 2011; 81(1):59-68.

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:**Ductal Carcinoma in Situ****Variant 1:**

55-year-old woman with mammographically detected 2.0 cm comedo, high nuclear grade DCIS, ER-positive. Surgically excised, multiple foci of DCIS in lateral and medial specimen close to excision margin (≤ 1.0 mm).

Treatment	Rating	Comments
Principles of Treatment		
Mastectomy without LN staging	7	Most surgeons would do a sentinel lymph node biopsy (SNLB).
Mastectomy with LN staging	8	
Re-excision lumpectomy and RT if margins negative	9	
Re-excision lumpectomy alone, no RT	2	
RT alone, no re-excision	2	
Breast MRI prior to additional surgery	4	
RT Volumes (Assuming re-excision with widely negative margins)		
Whole-breast	9	
Boost to tumor bed	8	
PBI: only on protocol	8	
PBI: off protocol	2	
RT Doses (180-200 cGy/daily fractions unless otherwise specified)		
Whole-breast: 4250 cGy/16 fractions	2	Without boost.
Whole-breast: 4500-4680 cGy/23-26 fractions	8	With or without boost.
Whole-breast: 5000-5040 cGy/25-28 fractions	9	With or without boost.
Total cumulative dose: 4000 cGy	3	
Boost dose 10 Gy in 2 Gy fractions after WBRT dose of 50 Gy (assume < 1 mm margins, no re-excision)	3	Higher boost needed.
Boost dose 16 Gy in 2 Gy fractions after WBRT dose of 50 Gy (assume < 1 mm margins, no re-excision)	7	While there are no phase III data for DCIS, most radiation oncologists would boost.
Boost dose 10 Gy in 2 Gy fractions (assume re-excision, widely negative margin of > 1.0 cm)	7	While there are no phase III data for DCIS, most radiation oncologists would boost.
Boost dose 16 Gy in 2 Gy fractions (assume re-excision, widely negative margin of > 1.0 cm)	6	Boost dose of 16 Gy may be higher than necessary with widely negative margins.
Systemic Therapy		
Tamoxifen (5 years) after lumpectomy + RT	8	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition:

Ductal Carcinoma in Situ

Variant 2:

50-year-old woman with extensive pleomorphic microcalcifications in more than one quadrant on mammography. Area too large to excise with cosmetically acceptable outcome. Core biopsies demonstrate DCIS involving more than one quadrant.

Treatment	Rating	Comments
Principles of Treatment		
Mastectomy without LN staging	4	Most surgeons would do SNLB with mastectomy.
Mastectomy with LN staging	9	
Attempt at lumpectomy with adjuvant RT	2	More than one quadrant.
Attempt at lumpectomy, LN staging, adjuvant RT	2	
Breast MRI prior to definitive surgery	2	Provides no additional information if microcalcifications and biopsy suggest disease is in more than one quadrant and patient will have mastectomy.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 3:

78-year-old woman with mammographically detected 1 cm, low nuclear grade DCIS, ER-positive. Surgically excised with 5 mm negative margins. Excellent performance status, no comorbidities. Plans to take tamoxifen for 5 years.

Treatment	Rating	Comments
Principles of Treatment		
Adjuvant RT	7	
No RT (observation)	7	Can consider observation for elderly patients or those with low-grade or negative margins.
RT Volumes		
Whole-breast +/- boost	8	
Axilla	1	
Supraclavicular fossa	1	
PBI: only on protocol	8	
PBI: off protocol	5	
RT Doses (180-200 cGy/daily fractions unless otherwise specified) (Assuming widely negative margins)		
Whole-breast: 4250 cGy/16 fractions	8	Data supporting hypofractionated RT from invasive cancer treatment, reasonable in this elderly patient with good prognostic features.
Whole-breast: 4500-4900 cGy	7	
Whole-breast: 5000-5040 cGy	8	
Total cumulative dose, including any boost: 4000 cGy	2	Dose too low.
Total cumulative dose, including any boost: 5000-5040 cGy	8	
Boost dose 10 Gy in 2 Gy fractions after WBRT dose of 50 Gy	5	Can use boost, but benefit is questionable.
Boost dose 16 Gy in 2 Gy fractions after WBRT dose of 50 Gy	3	Boost dose too high.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition:**Ductal Carcinoma in Situ****Variant 4:**

41-year-old woman with mammographically detected 0.9 cm, intermediate nuclear grade, comedo DCIS, ER negative. Surgically excised with widely negative margins.

Treatment	Rating	Comments
Principles of Treatment		
LN staging and RT	2	LN staging not necessary.
RT but no further surgery	9	
No further surgery or RT (observation)	2	Young, high-grade tumor, observation contraindicated.
Breast MRI (after DCIS on biopsy and prior to definitive surgery)	4	Unclear, but may detect additional disease in ipsilateral or contralateral breast, particularly in high grade DCIS.
RT Volumes		
Whole-breast alone	7	Most radiation oncologists would boost, given the high-risk features of young age and high-grade disease despite phase III data.
Whole-breast + boost	8	
PBI: only on protocol	7	
PBI: off protocol	2	
RT Doses (180-200 cGy/daily fractions unless otherwise specified) (Assuming negative margins)		
Whole-breast: 4250 cGy/16 fractions (without boost)	2	Young patient with high-grade disease, no phase III data on DCIS and hypofractionation.
Whole-breast: 4500 cGy	8	
Whole-breast: 5000-5040 cGy	9	
Total cumulative dose, including any boost: 4000 cGy	2	Dose too low.
Boost dose 10 Gy in 2 Gy fractions (in addition to whole-breast 50 Gy)	8	Most radiation oncologists would boost.
Boost dose 16 Gy in 2 Gy fractions (in addition to whole-breast 50 Gy)	6	May be higher than necessary.
Systemic Therapy		
Tamoxifen (5 years)	3	ER negative disease.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition:**Ductal Carcinoma in Situ****Variant 5:**

49-year-old woman with mammographically detected 1 cm high-grade, comedo DCIS with single focus microinvasion, ER-positive. Surgically excised with widely negative margins (>5 mm).

Treatment	Rating	Comments
Principles of Treatment		
Mastectomy with LN staging	7	If patient chooses mastectomy over BCT.
Mastectomy without LN staging	3	Most surgeons would do SNLB.
LN staging + adjuvant RT	9	
No LN staging required, proceed with adjuvant RT alone	5	Most surgeons would assess axilla surgically. Can be treated with radiation.
No LN staging, no adjuvant RT (observation)	1	Young patient, high grade, microinvasion, no role for observation.
RT Volumes (Assuming negative margins)		
Whole-breast + axilla and supraclavicular fossa (s/p ALND, 1/7 LN+)	5	Benefit of regional nodal radiation is unclear.
Whole-breast + axilla and supraclavicular fossa (s/p ALND, 1/12 LN+, no ECE)	3	Benefit of regional nodal radiation is unclear.
Whole-breast + supraclavicular fossa (s/p SLNB, 1/12 LN+, no ECE)	5	Benefit of regional nodal radiation is unclear.
PBI: only on protocol	7	
PBI: off protocol	1	
RT Doses (180-200 cGy/daily fractions unless otherwise specified) (Assuming negative margins)		
Whole-breast: 4250 cGy/16 fractions	4	Young patient with high grade disease and microinvasion, no phase III data on DCIS with microinvasion using hypofractionation.
Whole-breast: 5000-5040 cGy	8	
Total cumulative dose, including any boost: 4000 cGy	2	Dose too low.
Whole-breast 50 Gy + boost 10 Gy	8	
Whole-breast 50 Gy + boost 16 Gy	6	May be higher than necessary with widely negative margins, but not inappropriate.
Systemic Therapy		
Tamoxifen (5 years)	8	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition:**Ductal Carcinoma in Situ****Variant 6:****41-year-old woman with mammographically detected 0.9 cm, high nuclear grade DCIS, plus comedo necrosis, ER-negative. Surgically excised. Assume final margins >1cm, patient wants partial breast irradiation.**

Treatment	Rating	Comments
PBI: only on protocol	9	
PBI: off protocol	1	Should be considered on protocol.
Systemic Therapy		
Tamoxifen (5 years, in addition to PBI)	2	
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 7:**58-year-old woman with mammographically detected 1.9 cm, intermediate nuclear grade solid DCIS, ER-positive. Surgically excised. Assume final margins >1cm, patient wants partial breast irradiation.**

Treatment	Rating	Comments
PBI: only on protocol	9	
PBI: off protocol	5	Should be considered on protocol.
Systemic Therapy		
Tamoxifen (5 years, in addition to PBI)	8	
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		