5. The management of ductal carcinoma in situ (DCIS)

The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer

Abstract

Objective: To help physicians and patients arrive at the most clinically effective approach to the management of ductal carcinoma in situ (DCIS).

Options: Mastectomy, wide-excision breast-conserving surgery (BCS) plus radiotherapy and BCS alone.

Outcomes: Overall survival, local recurrence, cosmesis, complications of therapy.

Evidence: Review of English language literature published between 1976 and December 1996, identified through MEDLINE. Nonsystematic review continued to July 1997. Also reviewed were reference lists of books and relevant articles.

Recommendations:

- The first step in the diagnosis of DCIS, after history-taking and clinical examination, is a complete mammographic work-up.
- Once DCIS is suspected, either image-guided core biopsy or open surgical biopsy must be carried out.
- At surgical excision, the suspect area should be removed in 1 piece and a specimen radiograph obtained. Tissue should not be sent for frozen-section examination or hormone receptor analysis.
- The pathology report should address those features that bear on treatment choice.
- The specimen should, whenever possible, be reviewed by a pathologist experienced in breast disease.
- Treatment options for DCIS are mastectomy, wide-excision BCS plus radiotherapy or BCS alone. Treatment should aim to achieve a high degree of local control with the first treatment plan.
- Final decisions on treatment should not be made until the pathological findings have been reviewed and the specimen radiograph compared with the mammogram.
- Mastectomy is indicated when lesions are so large or diffuse that they cannot be completely removed without causing unacceptable cosmesis or when there is persistent involvement of the margins, especially with high-grade malignant lesions.
- Subcutaneous mastectomy should not be used to treat DCIS.
- Mastectomy should not be followed by adjuvant local radiotherapy or systemic therapy.
- Bilateral mastectomy is not normally indicated for patients with unilateral DCIS.
- BCS requires wide excision in patients with DCIS. It should be followed by mammography of the involved breast if the specimen radiograph does not clearly include all microcalcifications.
- BCS should normally be followed by radiotherapy. However, omission of radiotherapy may be considered when lesions are small and are low grade, and when pathological assessment shows clear margins.
- BCS should be accepted by patients only after they have received a careful explanation of the need for radiotherapy, its side effects and the associated logistic requirements.
- Axillary surgery, whether as a full or limited procedure, should not usually be performed in women with DCIS.
- Evidence is not available to support the use of tamoxifen in the treatment of women with DCIS.
- Patients should be offered the opportunity to participate in clinical trials whenever possible.

Validation: The guidelines were reviewed and revised by a writing committee, by expert primary reviewers, by secondary reviewers selected from all regions of Canada, and by the Steering Committee. The final document reflects a consensus of all these contributors. The guidelines are endorsed by the Canadian Association of Radiation Oncologists.

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Ductal carcinoma in situ (DCIS) of the breast, also known as intraductal cancer, is a malignant lesion arising from cells within the milk ducts. The term “in situ” denotes that the malignant cells have not extended through the ductal wall and are confined within the basement membrane surrounding the ducts. The clinical significance of this condition is that eventually these cells may breach the ductal basement membrane and invade the surrounding fatty tissue in the breast, thus becoming an invasive cancer.

In the past decade the frequency of diagnosis of DCIS has increased fivefold. This is attributed to the increased use and better quality of screening mammography. In the United States, almost one-third of breast neoplasms diagnosed by mammography are DCIS. In Canada, DCIS constitutes 19% of screen-detected breast cancers in women in British Columbia and 26% in Nova Scotia. As the use of screening mammography increases, the incidence of DCIS in Canada is expected to continue to rise.

The goal of treatment is to prevent invasive cancer from developing without causing unacceptable morbidity. The traditional treatment for DCIS has been mastectomy. However, since invasive breast cancer has been treated successfully with breast-conserving surgery (BCS) followed by radiotherapy (RT), this has led to the same approach being used for DCIS, even though BCS plus RT has not been evaluated against mastectomy in a randomized clinical trial for the management of DCIS.

Before screening was introduced, women with DCIS presented in the same way as those with invasive cancer: with a palpable mass, nipple discharge or Paget’s disease of the nipple. Most clinical experience is therefore based on the management of these conditions. However, experience in the treatment of screen-detected DCIS is more recent. Unfortunately, earlier experience gained with “clinical” DCIS cannot be extrapolated to guide decisions on how to manage screen-detected or subclinical disease. Thus, although the early detection and treatment of invasive breast cancer is known to be beneficial, the value of DCIS detection through screening remains to be demonstrated. Furthermore, the natural history of untreated DCIS is not known with any certainty.

As a result of this lack of information, there is wide variation in the manner in which DCIS is managed. These guidelines focus on the available evidence, and provide information and recommendations that patients and their physicians may need in order to arrive at the most effective and acceptable approach to the diagnosis and management of DCIS. For women to be able to make fully informed choices, it is essential that the physician make a clear and sympathetic presentation of the evidence and provide ample time for patients to consider the information. A more user-friendly version of this document is available for the lay person, which may be of help in achieving this task.

**Method**

A systematic search of English language articles on DCIS was carried out on MEDLINE for the period 1976 to December 1996. Guidelines were then drafted by the principal author using the best available evidence from research studies and clinical trials. Where evidence was inadequate or absent, guidelines were developed using expert opinion and accepted clinical practice. The evidence used was evaluated as shown on page S2. The guidelines were then successively reviewed and revised in the following order: by a writing committee consisting of 6 members of The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer, by 4 primary reviewers and by the Steering Committee. The prefinal draft was then submitted to 13 secondary reviewers consisting of family physicians, nurses, surgical, medical and radiation oncologists, and breast cancer survivors selected from all across Canada. The final draft was then approved by all members of the Steering Committee. This document reflects a consensus of all those involved in its preparation. The literature was reviewed and incorporated when appropriate to July 1997.

**Recommendations (including evidence and rationale)**

**Diagnosis of DCIS**

- **The first step in the diagnosis of DCIS, after history-taking and clinical examination, is a complete mammographic work-up.**

Suspicion of DCIS is initially aroused by the presence of abnormal mammographic or clinical features. Approximately 60% to 70% of patients whose diagnosis is DCIS present with abnormal features on routine mammography, and approximately 5% to 15% present with clinical features only, such as Paget’s disease, nipple discharge or a palpable lump. Both clinical and mammographic findings are found in 10% to 20% of patients, and a further 10% of cases of DCIS are found when an occult lesion is discovered coincidentally at the time of biopsy of a benign lesion. The most frequently detected mammographic abnormality (in approximately 75% of patients) is the presence of microcalcifications, the appearance of which can be linked to the subtype of DCIS.

Before embarking on any diagnostic or therapeutic intervention it is essential to obtain high-quality mammograms with spot compression or magnification views, or both. The radiologist should report the nature of and extent to which microcalcifications or architectural distortion are present in the breast.

- Once DCIS is suspected, either image-guided core biopsy or open surgical biopsy must be carried out.

For lumps that can be palpated, fine-needle aspiration (FNA) cytology is frequently used because it can be carried out easily in the clinic setting, and a positive finding assists the surgeon in planning the surgical biopsy. However, although FNA can detect malignant cells, this technique cannot distinguish between invasive cancer and DCIS. Also, nor-
The pathology report should address those features that bear on treatment choice.

These include cell morphology, clear margins, lesion size and multifocality.

Certain morphologic, cellular and nuclear features are predictive of recurrence after BCS.

The term “DCIS” refers to a heterogeneous group of lesions. These can be classified in 3 ways: according to their architectural pattern, the presence or absence of necrosis or by their cellular or nuclear characteristics. Regardless of the system of classification, however, certain features are indicative of recurrence, and these tend to be highly interrelated. Thus, the comedo architectural pattern is characterized by prominent necrosis and by cells that larger and pleomorphic, with abnormal nuclei that display frequent mitoses. Also, comedo DCIS exhibits biologic markers of high-grade malignant lesions more often than do other types. Lastly, comedo tumours are more likely to be large, associated with microinvasion and, after BCS, are more likely to recur.

In contrast, noncomedo lesions are far less commonly associated with necrosis and consist of a greater proportion of normal-sized or small cells which are rarely pleomorphic and show infrequent mitoses.

However, it is increasingly recognized that the above classification into comedo and noncomedo DCIS is an oversimplification. Contemporary classifications, using mainly nuclear grade and the presence of necrosis, now describe DCIS lesions as grade 1, 2 and 3, or as high grade, intermediate grade and low grade. When these tumours are treated by BCS without radiotherapy, the time course to local recurrence is longer with low-grade than with high-grade tumours (level III evidence). However, in 1 series, after 15 years the recurrence rates for both types of tumour had become comparable (level III evidence). Thus, the prognostic accuracy of these classifications remains to be confirmed in prospective studies with longer follow-up.

Margin involvement and close proximity of the lesion to the margins are associated with increased local recurrence.

Margin involvement describes the presence of malignant cells at the cut surface of the excision biopsy as seen on microscopic examination (often referred to as positive margins). Clear margins show only normal tissue at the cut surface. Clinical studies have shown an association between involved margins and increased local recurrence, and there is level III evidence that recurrence can be reduced by increasing the volume of tissue removed during re-excision. However, the exact width of clear margin required for a low recurrence rate in patients undergoing BCS is uncertain. Some important case series have shown residual DCIS beyond the original wide excision in 30% to 43% of cases, particularly for micropapillary and cribriform types. Also, solid DCIS is more
often excised completely than any other DCIS subtype (level III evidence).

Large lesions are more likely than small lesions to be associated with local recurrence when BCS alone is employed (level III evidence).

Small retrospective studies examining the effect of size on a spectrum of DCIS lesions have shown that lesions greater than 2.5 cm in dimension are more likely to exhibit occult invasion and are more likely to recur when treated by excision alone.\(^{16,17,40,41}\) Larger lesions are more often associated with positive margins and residual disease.\(^4\) Thus, both margin involvement and large size require extensive excision to remove residual disease, resulting in suboptimal cosmesis.

Truly multicentric tumours cannot be excised using BCS. Even multifocality, when diffuse, requires a very wide excision, resulting in poorer cosmesis or a higher probability of residual disease, or both (level IV evidence).

A multifocal tumour is one in which separate foci are close to, and in the same quadrant as, the parent tumour. In a multicentric tumour, separate foci can be found more than 5 cm from the index tumour and in more than 1 quadrant. Although multifocality is common in DCIS, true multicentricity is rare. Multifocality was present in 23% of patients who underwent mastectomy in a case series that involved careful sectioning of the whole breast. The same study showed that multicentricity was present in only 1.5% of cases.\(^2\) Previous studies reported the presence of multicentricity ranging from 15% to 78%, a variation that was probably due to lack of uniformity in the definition of multicentricity, variations in the tissue sampling techniques and differences in the amount of tissue excised.\(^{13,44–47}\)

- The specimen should, whenever possible, be reviewed by a pathologist experienced in breast disease.

The histopathological diagnosis of DCIS is often difficult. In a major multicentre clinical trial (NSABP B-17), a pathology review of specimens resulted in reclassification of 9% of the lesions originally diagnosed as DCIS. Seven percent were reclassified as atypical ductal hyperplasia and 2% as invasive breast cancer.\(^4\) Also, 21% of cases could not be assessed fully according to all the DCIS criteria because of inadequate specimens. Thus, if a major clinical trial has difficulty standardizing the interpretation of DCIS specimens, a similar or even higher rate of misinterpretation could be expected from general pathologists working in the community. Since the pathology assessment is critical not only to the diagnosis of DCIS but also to the prognosis and choice of treatment, prudence suggests that whenever the pathologist is not highly experienced, the biopsy specimen be reviewed by a pathology service with special expertise in this area (level V evidence).

**Treatment**

Treatment of DCIS is necessary because, if left untreated, a proportion of DCIS tumours will develop into invasive cancers. However, estimates of the probability of this happening are based on limited data since, in the past, most patients were treated by mastectomy. Based on a pooled analysis of 7 small case series totalling 107 patients treated by biopsy alone, the estimate of overall risk of invasive cancer developing in the same breast was 35% within 10 years.\(^2\) However, DCIS has been reported in as many as 16% of autopsies of completely asymptomatic women, and it is unlikely that all of the early lesions now being found by screening mammography would become invasive if left untreated.\(^4\) Until better data become available, it is prudent to regard all DCIS lesions as potentially invasive (level IV evidence).

- Treatment options for DCIS are mastectomy, wide excision BCS plus radiotherapy or BCS alone. Treatment should aim to achieve a high degree of local control with the first treatment plan.

Although in some ways the choice of treatment for DCIS is comparable to that for early invasive cancer (see guideline 3), there are important differences. The relevant issues to consider are survival free of breast cancer, overall survival, local recurrence, short-term morbidity and quality of life.

Survival will not differ greatly regardless of whether mastectomy or BCS is chosen (level III evidence).

There are no randomized controlled trials of mastectomy versus BCS for patients with DCIS. However, several case series have reported comparable survival rates after each of these procedures.\(^11,30–52\) The overall survival associated with both of these procedures is good. The 10-year survival after mastectomy has been reported to be 98% to 100%, and the 8-year survival after BCS plus radiotherapy has been reported to be between 95% and 100% (level III evidence).\(^31,58,52,53\)

The risk of local recurrence is greater after BCS than after mastectomy. This risk can be reduced, but not eliminated, by adjuvant radiotherapy (level I, III evidence).

Recurrence in the chest wall occurs in fewer than 2% of patients after mastectomy.\(^36,43\) With BCS alone, the risk of local recurrence can vary from 15% to 60% after 10 years.\(^26,31,32,37,41,56\) However, when radiotherapy is added to BCS, case series have indicated that recurrence rates are more than halved (level III evidence).\(^26,31,32,40,52,53,56,57\)

Only 1 randomized trial has directly addressed the effect of radiotherapy on recurrence after BCS.\(^43\) In this trial, 818 women with DCIS were randomized to receive BCS with and without radiotherapy. Most of the lesions had been mammographically detected and were less than 2 cm in diameter, and all patients were required to have pathologically negative
margins. Irradiation reduced the 5-year cumulative incidence of second cancers in the ipsilateral breast from 10.4% to 7.5% for noninvasive cancers and from 10.5% to 2.9% for invasive cancers (level I evidence).65 In patients with DCIS, approximately 50% of local recurrences after BCS alone are invasive. Thus, a goal of treatment should be to achieve a high level of local control with the first treatment plan (level IV evidence).5,11,24,31,35,56–60

**Compared to BCS, mastectomy is associated with more acute surgical morbidity, including pain, occasional delayed wound healing and seroma fluid collection. Also, the loss of the breast can have a profound and long-lasting psychosocial effect (level III evidence).**

Studies of women with invasive breast cancer show that the level of acute emotional distress is similar regardless of whether the patients are treated with mastectomy or BCS, but that after mastectomy, patients' body image and feeling of femininity are more disrupted in the long term.61–64 In a randomized controlled trial of women who underwent mastectomy or BCS, combined anxiety levels and depression were similar: 33% in the mastectomy group versus 38% in the BCS group (level II evidence). Patients who were better informed about their diagnosis and treatment experienced lower levels of subsequent anxiety and depression.62 Certain patients will have a clear preference for BCS. However, for others, the fear and uncertainty related to retaining a "dis eased" breast will lead to the choice of mastectomy or even bilateral mastectomy.67 This issue is considered in greater depth in guideline 3.

- **Final decisions on treatment should not be made until the pathological findings have been reviewed and the specimen radiograph compared with the mammogram.**

Post-biopsy mammography cannot usually be carried out for at least 4 weeks (and often longer) due to postoperative pain and tenderness. This mammogram should only be obtained when the initial mammogram is abnormal and the specimen radiograph suggests incomplete removal. The treatment options and the probable outcomes must be carefully and fully reviewed with the patient. There should be no pressure on the patient to make the choice quickly, and time must be allowed for consultation with family members, breast cancer survivors or others (level V evidence).

- **Mastectomy is indicated when lesions are so large or diffuse that they cannot be completely removed without causing unacceptable cosmesis or when there is persistent marginal involvement, especially with high-grade malignant lesions.**

The choice between BCS or mastectomy is influenced by the probability of a good cosmetic result on the one hand and the probability of ipsilateral tumour recurrence on the other. Thus, BCS is considered when tumours can be excised completely with adequate cosmetic results.

The probability of recurrence after BCS is increased when the margins of excised tissue remain positive or when lesions are diffuse or large.61,36–39,46–49 High-grade malignant features (comedo necrosis) are also independent predictors of local recurrence. In the NSABP B-17 study, when tumour-free margins were not assured, such features were associated with a small increase in recurrence rates after BCS and irradiation (level III evidence).48 However, in the same study, when tumour-free margins were obtained, the recurrence rate after BCS with radiotherapy was only 1.18% per year and was identical regardless of whether comedo necrosis was present or not (level II evidence).

- **Subcutaneous mastectomy should not be used to treat DCIS.**

A subcutaneous mastectomy removes the whole breast but spares the nipple-areolar complex. Silverstein and colleagues64 have suggested that it is a safe procedure when done carefully. This procedure has been widely used for DCIS in the past, mostly because it allows for cosmetically acceptable reconstruction.65 Unfortunately, however, this operation leaves 10% to 15% of the breast tissue, and therefore does not completely eliminate the risk of local recurrence (level IV evidence).63–66

- **Mastectomy should not be followed by adjuvant local radiotherapy or systemic therapy.**

Since the risk of recurrence in the chest wall is only 1% to 2% after mastectomy, little is gained by adding additional local therapy.44,45 No reliable data are available to guide decision-making when the deep margins of the mastectomy specimen are shown to be involved with DCIS. The use of adjuvant chemotherapy for DCIS is untried and has no demonstrated scientific basis. Hypothetically, tamoxifen might reduce the risk of DCIS in the opposite breast, but the lack of evidence of benefit in DCIS and the small risk of serious side effects (see guideline 8) militate against its use in this context (level V evidence).

- **Bilateral mastectomy is not normally indicated for patients with unilateral DCIS.**

It has been argued that prophylactic mastectomy of the uninvolved breast should be considered for patients with unilateral DCIS for several reasons: both breasts are at increased risk for disease, many DCIS lesions progress to invasive cancer, and mastectomy virtually eliminates the risk of any further breast cancer.69 In opposition to these arguments, however, is the low rate of contralateral cancer in women with unilateral DCIS.64 In a small level 3 study of women with unilateral DCIS who elected to undergo bilateral subcutaneous mastectomy, it was found that only 19% had DCIS in the opposite breast, a rate that is comparable to the 16% prevalence.
of DCIS found in autopsies of completely asymptomatic women. Thus, the benefit gained by bilateral mastectomy, if any, must be small.

The choice of bilateral mastectomy for patients presenting with synchronous bilateral DCIS rests on the same arguments as does the choice of mastectomy for DCIS in a single breast. Accordingly, bilateral BCS can be considered if the tumours are individually appropriate for such an approach.

- **BCS requires wide excision in patients with DCIS.** It should be followed by mammography of the involved breast if the specimen radiograph does not clearly include all microcalcifications.

Since residual DCIS has been shown to exist in up to 45% of patients treated with BCS (level III evidence), the surgical technique requires wide excision to ensure removal of the lesion. In a Canadian case series in which surgeons attempted to excise complete DCIS lesions based on clinical or mammographic findings, 92% of the patients required wider re-excision because of involved margins. Holland and colleagues showed that mammographically detected lesions had extended more than 2 cm beyond the known microcalcifications in 16% of patients with comedo-type DCIS and in 40% to 50% of those with cribriform/micropapillary-type DCIS. Thus, achieving good cosmesis may be difficult in some cases. The cosmetic result depends on the expertise of the surgeon as well as the size of the lesion and of the breast.

When the initially detected microcalcifications are not all clearly included in the specimen radiograph, it is advisable to carry out postoperative mammography. However, this should not be attempted for 4 weeks after surgery, and even then breast compression can be only moderate. The quality of postoperative mammograms is not as good as that of preoperative films, which should be the basis of the comparison. Nevertheless, residual microcalcifications seen on the postoperative films indicate the presence of residual DCIS.

- **BCS should normally be followed by radiotherapy.** However, omission of radiotherapy may be considered when lesions are small and low grade, and when pathological assessment shows clear margins.

From the evidence already cited it is clear that, in general, the addition of radiotherapy to BCS reduces the incidence of local recurrence of DCIS. However, as already discussed, certain features such as small tumours, cytologic findings indicating low-grade malignancy and absence of necrosis tend to identify tumours with a delayed time to recurrence in women who undergo BCS without radiation. It has been proposed, on the basis of small series, that local excision be considered as an appropriate option for treating women with noncomedo DCIS. However, the recently published results of the pathological review from the NSABP B-17 trial and the series of Solin and colleagues indicate that radiotherapy improves short-term outcome even for women with small lesions (level III evidence), although for low-grade lesions the absolute difference may be small. In the B-17 trial, recurrence rates were 1.3% per year for those who received radiotherapy versus 2.6% per year for those who did not receive radiotherapy (level II evidence). However, the applicability of these results in an era of improved pathologic classification of tumours has been disputed. Therefore, omission of radiotherapy for selected patients remains controversial outside the context of a trial. If radiotherapy is not given, the patient should be made aware that it is an option.

- **BCS should be accepted by patients only after they have received a careful explanation of the need for radiotherapy, its side effects and the associated logistic requirements.**

Some patients receiving radiotherapy to the breast will experience short-term complications (fatigue, pain and tenderness), which mostly resolve within 2 months of the end of treatment. However, in 5% to 10% of patients, breast tenderness may continue for up to 12 months after treatment. Other infrequent but lasting effects may occur, including a poorer cosmetic outcome (see guideline 6).

Radiotherapy is also associated with significant inconvenience and cost, especially to patients living outside major centres. The difficulties include interruption of work and the costs of transport and accommodation away from home. Patients from rural communities are significantly more inconvenienced by such treatment. Because of such issues, some women may prefer to avoid radiotherapy and accept the increased risk of local recurrence and the possible need for further surgery. When lesions are small and do not exhibit high nuclear grade or necrosis, and pathologically clear margins have been assured, avoidance of radiotherapy can be a reasonable option to consider as long as it is fully understood by the patient. These issues should be discussed in detail when women are presented with options regarding the management of DCIS.

- **Axillary surgery, whether as a full or limited procedure, should not usually be performed in women with DCIS.**

Axillary node metastases occur very rarely in women with DCIS, although the frequency may rise to 3% to 4% in those with microinvasion from high-grade, comedo-type larger lesions (level III evidence). Some surgeons feel that this risk justifies performing a limited axillary dissection on patients with these features, but the morbidity associated with this procedure (see guideline 4) and the low probability of lymph-node involvement in the absence of invasion suggest that axillary surgery should not be carried out, even in patients with high-grade, comedo-type large lesions.

- **Evidence is not available to support the use of tamoxifen in the treatment of women with DCIS.**

Although there is evidence to show that tamoxifen when
taken as adjuvant therapy for unilateral, invasive breast cancer can reduce the incidence of contralateral cancer, there is no direct evidence in patients with DCIS that the benefits will outweigh the risks associated with its use (see guideline 8). An NSABP study, protocol B-24, is examining this question, but the results will not be available until 1998.

• Patients should be offered the opportunity to participate in clinical trials whenever possible.

As frequently noted earlier, information in support of the therapeutic interventions used in the treatment of breast cancer often does not exist or is extremely weak. The many areas of uncertainty, indicated by level III, IV or V evidence, can only be eliminated by well-designed randomized controlled trials. Improvement in the care of future patients with breast cancer thus depends on the participation of sufficient numbers of women in such trials. Physicians treating patients with breast cancer should therefore be aware of currently available trials, and the option of participation should be offered to patients.

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