Clinical practice guidelines for the care and treatment of breast cancer:

5. Management of ductal carcinoma in situ (DCIS) (2001 update)

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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 or BCS alone.

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

Evidence: Review of English-language literature published between 1976 and April 2001, identified through MEDLINE and CANCERLIT. Nonsystematic review continued to June 2001.

Recommendations:

Diagnosis and pathologic assessment

- 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 one piece and a specimen radiograph obtained.
- The pathology report should address those features that bear on treatment choice, including as a minimum tumour size, morphology and grade,

presence of necrosis, and width of margins.

- To obtain sufficient pathology information for treatment planning, attention should be paid to tissue processing and analysis.
- The specimen should, whenever possible, be reviewed by a pathologist experienced in breast disease.

Management

- Treatment options for DCIS are mastectomy, BCS plus radiotherapy or BCS alone. The treatment should aim to achieve a high degree of local control. The optimal treatment for an individual woman should take into consideration the extent and type of disease, the ability of a cosmetically acceptable excision to achieve clear margins, and the woman's preference for breast conservation or avoidance of further treatment or breast cancer recurrence risk. The choice of local therapy does not significantly affect survival if local control is achieved.
- Compared with BCS, mastectomy is associated with more acute surgical morbidity, including pain, occasional delayed wound healing and seroma collection. In addition, the loss of the breast can have a profound and long-lasting psychosocial effect.
- Patients with DCIS treated by BCS should have a wide excision to remove all mammographically and pathologically evident DCIS. Mammographic imaging of the involved breast is required if the radiograph of the specimen does not clearly show all microcalcifications.
- The risk of local recurrence is greater after BCS than after mastectomy. This risk can be reduced, but not eliminated, by patient selection and the use of adjuvant radiotherapy.
- BCS should usually be followed by radiotherapy. Patients with a sufficiently low risk of local recurrence with BCS alone are difficult to identify. However, BCS alone may be considered after a careful discussion with the patient, if detailed pathologic assessment confirms that the lesion is small and does not have high-grade nuclei or comedo-type necrosis and the surgical margins are clear of disease. In addition, in such circumstances the surgical excision should be cosmetically acceptable.

- Patients should be informed of the role of radiotherapy, its side effects and the associated logistic requirements before they are expected to make the decision for BCS or mastectomy.
- Mastectomy is an option for all women with DCIS. Mastectomy should be recommended when lesions are so large or diffuse that they cannot be completely removed without causing an unacceptable cosmetic effect or when there is persistent margin involvement after 2 or more attempts at excision. If mastectomy is undertaken, breast reconstruction is an option.
- Mastectomy should not be followed by adjuvant local radiotherapy or systemic therapy.
- Bilateral mastectomy is not normally indicated for patients with unilateral DCIS.
- Axillary surgery, whether a full or limited procedure, should not be performed in women with DCIS.
- The role of tamoxifen in the management of patients with DCIS continues to evolve. The potential benefits and risks should be discussed with patients.
- Patients should be offered participation in clinical trials whenever possible.

Validation: The authors' original text was revised by a writing committee, primary and secondary reviewers, and the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. The final document reflects a consensus of all these contributors. The current update did not undergo an external review. A writing committee updated the original guideline and then submitted it for further review, revision and approval by the steering committee.

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Completion date: July 2001.

This guideline refers to the classification and management of ductal carcinoma in situ (DCIS or intraductal carcinoma) of the breast.[1,2] DCIS is a proliferation of malignant-appearing cells of the ducts and terminal lobular units of the breast that have not breached the ductal basement membrane. DCIS (TNM stage T_{is}) [3] must be distinguished pathologically from atypical ductal hyperplasia[1,4] and microinvasive breast cancer (TNM stage $T1_{mic}$).[1–3,5] The occurrence of DCIS has increased over 5-fold since the mid-1980s in association with the increasing use of screening mammography.[6,7]

Methods

This guideline is based on a systematic review of the English-language literature published from 1976 to April 2001, identified primarily through MEDLINE and CANCERLIT. Key words combined in the search were: "breast neoplasms," "carcinoma in situ," and "carcinoma, intraductal, non-infiltrating" as subject headings; and "duct," "dcis" and "ductal carcinoma" as text words. The search was restricted to controlled clinical trials, meta-analyses, practice guidelines and literature reviews on the topic. References in review articles and textbooks were also used. A nonsystematic review of the literature was continued to June 2001. The quality of the evidence on which conclusions were based was categorized into 5 levels (see Levels of Evidence).[8] The iterative process used to develop this guideline has been described previously.[9] A writing committee updated the original guideline and then submitted it for further review, revision and approval by the steering committee.

Diagnosis and pathologic assessment

Diagnosis of DCIS

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

DCIS most commonly presents as clustered or irregular calcifications on a screening mammogram in an otherwise asymptomatic woman. DCIS may present as nipple discharge or a palpable mass, usually also associated with mammographic

calcifications. DCIS may also present as an incidental finding in a biopsy of a benign lesion.

Detailed breast imaging is required before biopsy in any woman with suspected DCIS because the DCIS may be extensive and may grow as discontinuous areas of calcification.[10] As a minimum, each woman should have high-quality, bilateral, 2-view mammograms with magnification or other special views of all areas that contain calcifications, masses or architectural distortion. The purpose of this pre-biopsy imaging evaluation is to accurately map areas of potential involvement by DCIS and determine the location(s) for biopsy.

- **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 one piece and a specimen radiograph obtained.**

Where facilities exist, an imaging-directed core biopsy to establish a diagnosis and plan an appropriate volume of excision is recommended.[11–16]

Although a stereotactic core biopsy can establish the presence or absence of DCIS, pathologic examination of the entire surgically excised lesion is necessary to exclude the possibility of invasive cancer and to determine the lesion size and margin status. When possible, the suspicious mammographic area should be excised in a single specimen. The excised specimen should be oriented by the surgeon, and a specimen radiograph, with areas of radiologic suspicion noted, should be obtained to confirm removal of the entire lesion.[11,17,18] Tissue should not normally be sent for frozen-section examination or hormone-receptor analysis.

Pathologic prognostic factors

- **The pathology report should address those features that bear on treatment choice, including as a minimum tumour size, morphology, grade, presence of necrosis and width of margins.**

A thorough pathologic assessment is crucial to manage DCIS appropriately. The presence of microscopic or frank invasion should be sought. If present, the patient's stage should be recorded as $T1_{mic}$ or $T1_{a/b/c}$ depending on the maximum size of the invasive component, and the case should not be reported or managed as DCIS.[3] One series, with short follow-up, suggested that the outcomes of DCIS cases were equivalent with or without microinvasion (level V evidence).[19]

Multiple pathologic factors have been investigated in an effort to find potential predictors of local recurrence in patients who have had DCIS excised.[2,20–41] Approximately 50% of local recurrences are invasive. Investigators have tried to identify a subset of women whose risk of breast cancer recurrence is sufficiently low to justify breast-conserving surgery (BCS) alone.

An international consensus conference has made recommendations for the classification and pathologic processing of DCIS.[17] The most clinically useful factors are: nuclear grade, necrosis, margin width and lesion size.[17,28,42–47] Nuclear grade, necrosis and margin width have been combined in various prognostic indices.[28,42–47]

Tumour morphology: Historically, the architectural type of DCIS (solid, cribriform, comedo, papillary, micropapillary) was used for classification. This classification may be recorded, but it has not been associated with the risk of local recurrence as reliably as the presence of necrosis, nuclear grade and margin width.[46,48] The comedo pattern is characterized by prominent necrosis and by the presence of large, pleomorphic cells with abnormal nuclei that display frequent mitoses. These lesions are more likely to be associated with microinvasion and to recur after BCS alone.[22,29–32]

Nuclear grade and necrosis: Nuclear grade (low, intermediate, high) and necrosis (present or absent and quantified as comedo-type or punctate) have been investigated individually and in combination. There is an association between high nuclear grade and comedo-type necrosis. This type of necrosis may be associated less commonly with

intermediate and, occasionally, low nuclear grade. Prognostic schema that include both necrosis and grade have been more predictive of local recurrence than grade or necrosis alone.[28,29,36,44,47] In one series of patients treated with BCS plus radiotherapy, high nuclear grade was associated with higher rates of recurrence at 5 and 10 years than was low nuclear grade. However, there was no difference in the rates of recurrence at 15 years between patients with low and high nuclear grade lesions.[33]

Margin width: Clinical studies have shown an association between involved or close margins and an increased rate of local recurrence (level I evidence).[36,45,49] There is level IV and V evidence that increasing the volume of tissue removed during re-excision is associated with a lower recurrence risk.[2,21,45,50–52] A margin of 1 cm or more of noninvolved breast tissue would be considered a wide margin by all authors. The *minimum* width of clear margins required in patients undergoing BCS alone is uncertain. Pure micropapillary DCIS may be quite extensive within the breast, and obtaining clear margins of excision may be difficult without mastectomy.[53] A detailed pathologic assessment with extensive sampling of margins showed that a margin width of 10 mm or more was associated with an 8-year rate of ipsilateral breast cancer recurrence of 3%–4% after BCS with or without radiotherapy (level IV evidence).[45]

Lesion size: The extent of DCIS is often underestimated on the basis of its mammographic appearance.[10] Lesions less than 2.5 cm,[5,31] or in some studies 1.5 cm,[28,47] in dimension have been associated with lower rates of breast cancer recurrence than larger lesions. More diffuse growth is associated with a lower likelihood of acheiving widely clear margins. In one series, in which patients frequently had repeat excisions and margins were assessed with detailed sampling to confirm a clearance of at least 10 mm, lesion size was not predictive of recurrence (level IV evidence).[45] Achieving very wide margins of excision around a large area of DCIS is often limited by the potential for a poor cosmetic outcome.

Other factors: Biologic markers and growth factors such as estrogen receptor, HER2, p53, ploidy and S-phase fraction have been investigated and incorporated in prognostic indices (level V evidence).[27] These factors have not been reliably associated with breast cancer recurrence risks and are not currently useful for treatment selection. They may be useful in a research context.

Multifocal and multicentric DCIS: Past descriptions of the multifocality and multicentricity of DCIS have been confusing. Multifocal tumours arise at different points along a single duct system and present as diffuse foci of disease in the same breast quadrant, often with discontinuous areas of mammographic calcification. Multicentric tumours arise from different duct systems in different segments of the breast and present as separate foci of DCIS separated by more than 5 cm of intervening normal breast tissue. Multifocality is common. True multicentricity is rare.[10] From careful, serial sectioning and radiologic–pathologic correlation of mastectomy specimens, Holland and colleagues demonstrated that multifocality was present in 23% and multicentricity in 1.5% of cases.[10] Previous studies reported the presence of multicentricity in 15% to 78% of cases; this wide range is due to a lack of uniformity in the definition of multicentricity, variations in tissue sampling techniques and differences in the amount of tissue excised.[32,34,35,54–56] Truly multicentric tumours cannot be completely excised with BCS. Multifocal tumours, when diffuse, require a very wide excision, which may adversely affect cosmetic outcome, and they are likely to be associated with a higher risk of residual disease following BCS.

Tissue processing

- **To obtain sufficient pathology information for treatment planning, attention should be paid to tissue processing and analysis.**

To obtain sufficient pathology information for treatment planning if BCS is contemplated, thoughtful attention should be paid to tissue processing and analysis.[17] The specimen margins should be marked before sectioning. The entire specimen should be thoroughly sampled by “bread-loafing” at 3-mm to 5-mm intervals and labelling the slices sequentially (e.g., from medial to lateral). The same process should be followed for re-excision specimens. Processing the specimen methodically permits better characterization and examination of the margin width and lesion size than does random sectioning or partial tissue processing. Lesion size is determined by recording the number of sequential sections containing DCIS and multiplying by the average section width. For example, in a 2.5-cm biopsy specimen, sectioned at 3-mm intervals, there would be 8

sections labelled A to H. If DCIS was seen in sections C to G, the estimated size would be 15 mm (3 mm × 5 sections). Random sectioning of the excision specimen and sampling of areas with calcifications alone is discouraged.

A specific comment should be made in the pathology report regarding the presence of calcifications and their association with DCIS, benign disease or both, the presence and type of necrosis, the nuclear grade and how the pathologic findings correlate with the radiologic appearance.[17]

Margin assessment requires quantification of the distance between malignant ducts and the inked surface of the excision on microscopic examination. Margin width should be reported as the closest margin in millimeters, and if margin involvement is present it should be specified as focal or diffuse.

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

The histopathological diagnosis of DCIS is often difficult. In a multicentre clinical trial, 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 (level III evidence).[36] In addition, 21% of cases could not be assessed fully according to all the DCIS criteria because of inadequate specimens. Since a detailed pathologic assessment is critical for accurate classification of DCIS for prognosis and treatment choices, prudence suggests that the specimen be reviewed by a pathology service with special expertise in this area if the pathologist does not have a large experience in breast cancer pathology.

Management

- **Treatment options for DCIS are mastectomy, BCS plus radiotherapy or BCS alone. The treatment should aim to achieve a high degree of local control. The optimal treatment for an individual woman should take into consideration the extent of disease, the ability of a cosmetically acceptable excision to achieve clear margins, and the woman's preference for breast conservation or avoidance of**

further treatment or breast cancer recurrence risk. The choice of local therapy does not significantly affect survival if local control is achieved.

Treatment of DCIS is necessary because, if left untreated, invasive cancer will develop in a proportion of patients. There are limited data on the rate of development of invasive cancers from untreated DCIS because most patients were treated by mastectomy in the past. A report of 7 small case series totalling 107 patients treated by biopsy alone estimated the risk of invasive cancer to be 35% within 10 years (level V evidence).[20] Patients included in those series had low-grade DCIS, initially thought to be benign disease. The risk of recurrence with high-grade DCIS will be higher. DCIS has been reported in as many as 16% of autopsies of asymptomatic women.[57] Randomized controlled trials and multiple case series of women with DCIS treated by BCS have shown that approximately 50% of recurrences will be invasive disease (level I, IV and V evidence).[21,30,37–41,43,45,51,58–63] Therefore, although it is possible that a proportion of the early lesions detected by screening mammography may not progress to invasive cancer if left untreated, the goal of treatment should be to achieve a high level of control in the breast.

There are no randomized clinical trials comparing mastectomy and BCS for the treatment of DCIS. However, several case series have reported comparable survival rates after either procedure (level V evidence).[21,59,62,64,65] The 10-year survival rates among patients treated by mastectomy were 98%–100%, and after BCS plus radiotherapy 95%–100% (level V evidence).[30,59,60,64] Comparable overall survival rates were found among selected patients treated with BCS alone with clear margins (level I and IV evidence).[37,45,63]

- **Compared with BCS, mastectomy is associated with more acute surgical morbidity, including pain, occasional delayed wound healing and seroma collection. In addition, the loss of the breast can have a profound and long-lasting psychosocial effect.**

Women with invasive breast cancer report similar levels of acute emotional distress whether treated with mastectomy or BCS. However, patient satisfaction, psychological distress (anxiety, depression), body image and feelings of femininity

are more disrupted after mastectomy (level V evidence). [66–70] In a randomized trial comparing mastectomy with BCS plus radiotherapy, the proportions of women reporting significant anxiety or depression were similar: 33% in the mastectomy group and 38% in the BCS group (level II evidence).[67] Patients who were better informed about their diagnosis and given choices about their treatment options experienced lower levels of subsequent anxiety and depression than patients who were not well informed or given treatment choices.[67] Long-term psychosocial distress was shown to be worst after mastectomy, intermediate after mastectomy with reconstruction and lowest after BCS.[70] Certain patients will have a clear preference for BCS. However, other women may prefer a mastectomy or even bilateral mastectomy because of fear and uncertainty related to retaining a "diseased" breast (level V evidence).[71] This issue is considered in greater depth in guideline 3.

- **Patients with DCIS treated by BCS should have a wide excision to remove all mammographically and pathologically evident DCIS. Mammographic imaging of the involved breast is required if the radiograph of the specimen does not clearly show all microcalcifications.**

Since residual DCIS has been shown to exist in up to 45% of patients treated with BCS, the surgical technique requires wide excision to ensure removal of all mammographically and pathologically evident disease (level V evidence). [51,72,73] Holland and colleagues[10] (level V evidence) showed that the pathologic extent of DCIS may extend more than 2 cm beyond the known microcalcifications in 16% of patients with high-grade, comedo-type DCIS, and in 40%–50% of those with lower grade, cribriform and micropapillary DCIS. The cosmetic result of BCS depends on the expertise of the surgeon and on the size of the lesion and the breast. Achieving good cosmesis may be difficult in some cases of diffuse DCIS, and mastectomy may be preferred.

When the DCIS is associated with microcalcifications and the radiograph of the specimen does not clearly show that all calcifications have been removed, postoperative mammography of the ipsilateral breast should be performed. However, this should not be attempted for 4 to 6 weeks after surgery, and even then the quality

of mammography may be compromised by breast tenderness, limiting the patient's tolerance of breast compression. Residual microcalcifications may indicate the presence of residual DCIS and the need for further surgery (level V evidence).[59,73]

- **The risk of local recurrence is greater after BCS than after mastectomy. This risk can be reduced, but not eliminated, by patient selection and the use of adjuvant radiotherapy.**

Recurrence in the chest wall occurs in less than 1% of patients after mastectomy.[74–76] With BCS alone, the risk of local recurrence varies from 4% to 60% after 10 years depending on patient selection, pathologic characteristics and the extent of breast surgery.[19,28,30,32,38,45,50] Randomized trials and case series have shown that recurrence rates are approximately halved with the addition of adjuvant radiotherapy to the breast after BCS (level I evidence).[28,30,37–39,57,59,60,63,77] Two multicentre randomized clinical trials have directly addressed the effect of radiotherapy on recurrence after BCS in women with DCIS.[37,40,63]

The National Surgical Adjuvant Breast and Bowel Project (NSABP) protocol B-17 randomly assigned 818 women with DCIS in Canada and the United States to receive BCS with or without radiotherapy between 1985 and 1990.[37] Most lesions were mammographically detected and less than 2 cm in diameter. All patients were required to have pathologically negative margins, defined as no DCIS seen at the surgical margin, as assessed by the local pathologist. With a mean follow-up of 90 months, radiotherapy was found to reduce the risk of noninvasive ipsilateral breast cancer recurrence from 13.4% to 8.2% ($p = 0.007$) and the risk of invasive ipsilateral breast cancer recurrence from 13.4% to 3.9% ($p < 0.0001$) (level I evidence).[37] Radiotherapy seemed to be more effective at preventing invasive than noninvasive recurrences.

From 1986 to 1996 the European Organization for Research and Treatment of Cancer (EORTC) protocol 10853 randomly assigned 1010 women with DCIS from 46 institutions in 13 countries in Europe and South Africa to receive either BCS alone or BCS followed by radiotherapy. [63] Seventy-one percent of the cases were mammographically detected. The mean diameter of the DCIS was 2 cm. All cases

were required to have pathologically clear margins of excision. The width of margins was not quantified, but 34% of the patients had a re-excision. With a median follow-up of 4.25 years, local recurrence was reduced by radiotherapy from 16% to 9% (p = 0.005) (level I evidence). The 4-year overall survival was identical between the 2 arms, at 99%. The 4-year distant metastasis-free rate was 98% with BCS alone, and 99% with BCS plus radiotherapy (difference not significant). Radiotherapy had a similar effect on the prevention of invasive and noninvasive recurrences.

- **BCS should usually be followed by radiotherapy. Patients with a sufficiently low risk of local recurrence with BCS alone are difficult to identify. However, BCS alone may be considered after a careful discussion with the patient, if detailed pathologic assessment confirms that the lesion is small and does not have high-grade nuclei or comedo-type necrosis and the surgical margins are clear of disease. In addition, in such circumstances the surgical excision should be cosmetically acceptable.**

Randomized clinical trials have demonstrated that radiotherapy reduces the risk of ipsilateral invasive and noninvasive breast cancer recurrence even for patients with clear margins of excision.[37,63] However, as already discussed, certain pathologic features such as small lesion size (< 2 cm), widely clear margins (≥ 1 cm), low nuclear grade and the absence of necrosis tend to identify patients with a lower risk of recurrence when treated with BCS without radiotherapy.[33,45,52,78] A woman with *all* of these favourable risk factors may have a 4%–10% risk of breast cancer recurrence with BCS alone after 10 years. In these women, radiotherapy will reduce the risk of breast cancer recurrence further, but the absolute benefit for an individual woman will be very small. Omission of radiotherapy in selected patients remains controversial outside the context of a clinical trial. If radiotherapy is not given, the patient should be made aware that it is an option.

- **Patients should be informed of the role of radiotherapy, its side effects and the associated logistic requirements before they are expected to make the decision for BCS or mastectomy.**

Radiotherapy after BCS requires 3 to 6 weeks of daily visits to a radiation therapy centre. This may cause significant inconvenience and cost, especially to patients living some distance from the centres. Most patients receiving radiotherapy will experience short-term side-effects such as fatigue, tenderness, redness and itchiness of the skin, which mostly resolve within several months after the end of treatment. However, in 5%– 10% of patients, breast tenderness may continue for 12 months or longer after treatment. Other infrequent but lasting effects may occur, including a poorer cosmetic outcome (see guideline 6).

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 with BCS alone or elect to have a mastectomy. These issues should be discussed in detail when women are presented with options regarding the management of DCIS.

- **Mastectomy is an option for all women with DCIS. Mastectomy should be recommended when lesions are so large or diffuse that they cannot be completely removed without causing an unacceptable cosmetic effect or when there is persistent margin involvement after 2 or more attempts at excision. If mastectomy is undertaken, reconstruction is an option.**

The risk of recurrence after BCS is increased when the excision margins are involved or when the lesion is diffuse or large (level V evidence).[2,5,19,21,45,50,51,79] If a lesion is large and clear margins cannot be obtained, the risk of breast cancer recurrence exceeds 30% within 10 years even when radiotherapy is added to BCS. In this case, mastectomy is the preferred treatment option.[45,62]

If a mastectomy is to be done, it should be a complete procedure. Immediate reconstruction is an option.[70]

Subcutaneous mastectomy is a procedure that has been used to treat DCIS in the past, because it allows for a cosmetically acceptable reconstruction.[80] Silverstein and colleagues[51] have suggested that it is safe when done carefully. However, DCIS may involve the lactiferous sinuses, and although subcutaneous mastectomy attempts to remove the whole breast, the nipple–areolar complex and 10%–15% of the breast

tissue are not removed. Subcutaneous mastectomy therefore does not completely eliminate the risk of local recurrence (level V evidence).[64,81]

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

Since the risk of recurrence in the chest wall is at most 1% after a mastectomy, little is gained by adding further local therapy (level V evidence).[74,75] No reliable data are available to guide decision-making when the deep margins of the mastectomy specimen are shown to be close to or involved with DCIS. There are no data on the use of tamoxifen specifically in women with DCIS who have undergone mastectomy. Tamoxifen will likely reduce the risk of DCIS and invasive cancer in the opposite breast (level I evidence),[77,82,83] but in this case its use should be considered in the context of prevention of breast cancer. The role of tamoxifen and other agents for the chemoprevention of breast cancer, including the reduction in risk of contralateral disease, is the subject of a separate guideline (see guideline 12).

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

Prophylactic contralateral mastectomy has been considered for patients with unilateral DCIS because of concern about bilateral disease. The rate of developing contralateral breast cancer is comparable to the approximately 0.5% annual risk among women with unilateral invasive breast cancer (level I evidence).[37,63,83] Tamoxifen reduces the rate of contralateral disease (level I evidence).[77,82,83]

Bilateral mastectomies may be appropriate for patients presenting with synchronous bilateral DCIS. However, the risks of recurrence and choice of local therapy including mastectomy should be considered individually for each breast and be based on the same rationale as the choice of local therapy for DCIS in a single breast. Bilateral BCS with or without radiotherapy or mastectomy may be considered if the tumours are individually suitable for such an approach.

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

Axillary nodal metastases occur very rarely in women with DCIS. The frequency of nodal metastases rises to 3%–5% among patients with microinvasive breast cancer, but DCIS with invasion is not considered to be DCIS (level IV and V evidence).[19,22,34,59,84,85] The low probability of lymph node involvement in the absence of invasion suggests that axillary surgery should not be performed, even in patients with high-grade, comedo-type large lesions. The role of lymphatic mapping and sentinel lymph node biopsy is considered experimental (see guideline 13).

- **The role of tamoxifen in the management of patients with DCIS continues to evolve. The potential benefits and risks should be discussed with patients.**

In the NSABP B-24 trial, 1804 women with DCIS from Canada and the United States who were treated with BCS plus radiotherapy between 1991 and 1994 were randomly assigned to receive tamoxifen, 20 mg daily, or placebo for 5 years. Tamoxifen reduced the risk of both ipsilateral and contralateral breast cancer. At 5 years the cumulative risk of breast cancer events was 13.4% and 8.2% ($p = 0.0009$) among patients receiving placebo and tamoxifen respectively. The risk of an invasive event was reduced from 7.2% to 4.1% ($p = 0.004$), and the risk of an in situ event was reduced from 6.2% to 4.2% ($p = 0.08$) (level I evidence).[77] The proportional reduction of breast cancer events was 38%, which is comparable to the rates observed in the NSABP breast cancer prevention trial [82] and in the meta-analysis of randomized trials assessing the value of tamoxifen in patients with invasive breast cancer.[83] However, the absolute number of women who benefited in terms of avoiding an ipsilateral breast cancer recurrence was small, 3% at 5 years.[77]

Tamoxifen is associated with a small but significant risk of side-effects that may impair quality of life, including hot flushes, vaginal dryness, vaginal discharge and depression. Tamoxifen is also associated with potentially life-threatening complications, including a 1% excess risk of venous thrombosis or pulmonary embolism and a less than 1% excess risk of endometrial carcinoma (see guideline 12).[77,82,86] The risk of

complications is higher among older women and lower among women who have had a hysterectomy.

A clear recommendation that all, or even most, women with unilateral DCIS should receive tamoxifen cannot be made at this time.[87] The potential benefits and risks of tamoxifen in the context of DCIS should be discussed with the patient. Tamoxifen may be a reasonable option for a woman motivated to do everything possible to avoid breast cancer recurrence but who declines mastectomy, especially if she has a higher risk of contralateral breast cancer and a lower than average risk of tamoxifen complications.

- **Patients should be offered participation in clinical trials whenever possible.**

The many areas of uncertainty can only be eliminated by well-designed randomized clinical trials. Physicians treating patients with breast cancer should be aware of currently available trials, and the option of participation should be offered to patients.

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