The Diagnosis and Management of Ductal Carcinoma In-Situ of the Breast

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Abstract
The widespread utilization of screening mammography has produced a shift in the stage of breast cancer at diagnosis in the US: Currently, 12% to 15% of newly diagnosed breast cancer cases annually are ductal carcinoma in-situ (DCIS). The diagnosis is made, in at least 90% of patients, with mammography. Only about 10% of patients will have a palpable mass.

The accurate characterization and visualization of calcifications typically requires magnification of mammographic imaging. The morphology of the calcifications is generally considered to be the most important factor in differentiating benign from malignant formations. Round and uniform shapes are more likely to be benign, while linear and heterogeneous morphologies are associated with DCIS.

Following a complete mammographic work-up, most suspicious lesions are potential candidates for a stereotactic core needle biopsy. Ten percent to 50% of patients initially diagnosed with atypical ductal hyperplasia by needle biopsy have subsequently been surgically diagnosed with cancer near the biopsy site. Due to this relatively high incidence of co-existent carcinoma, a needle biopsy diagnosis of atypical ductal hyperplasia necessitates subsequent surgical excision.

The most important change in our thinking about DCIS was from a monolithic view, conceiving of DCIS as a single disease highly likely to invade if left untreated, to the realization that DCIS represents a non-obligate precursor with a variable risk of progression, depending on a combination of factors, such as histology, lesion, size, and margin status.

In discussing treatment options, patients should understand that local recurrence following total mastectomy is rare and that this is the procedure of choice for disease that cannot be adequately encompassed with a breast-conserving approach. If the patient and her surgeon are in agreement about proceeding with a breast-conserving approach, there needs to be a clear understanding of the incidence and implications of local recurrence. In all such discussions with newly diagnosed patients, however, it is essential to emphasize the excellent prognosis with this disease, irrespective of the surgical approach. (CA Cancer J Clin 2000;50:184-200.)

Introduction
Prior to the introduction of dedicated mammography equipment in 1969, xeroradiography in 1971, and screen-film systems in 1972, ductal carcinoma in-situ (DCIS) was termed intraductal carcinoma and was categorized and treated by most clinicians as breast cancer, without differentiating invasive from non-invasive disease. In fact, DCIS most com-
monly presented as a palpable mass because it was associated with invasive cancer. Today, however, only about 10% of patients with pure DCIS present with a mammographic mass unassociated with microcalcifications.

The hallmark study that elevated public and professional awareness of the value of mammography and stimulated technical developments was conducted by the Health Insurance Program of Greater New York. Reports from this study in the late 1960s and early 1970s demonstrated a 30% decrease in breast cancer mortality in the group randomized to receive screening mammography versus the group not undergoing screening mammography. These findings, in turn, led to the initiation of the Breast Cancer Detection Demonstration Project (BCDDP) supported by the American Cancer Society and the National Cancer Institute.

Recently, a 20-year update of the 283,222 women enrolled in that early study demonstrated that the adjusted survival rates for women with invasive breast cancers were 90.2% for cancers smaller than 1 cm, 80.5% for cancers between 1.0 and 2.0 cm, 70.5% for cancers between 2.0 and 4.9 cm, and 60.6% for cancers larger than 5 cm. It is noteworthy that 11.5% of the women originally enrolled in the BCDDP study were diagnosed with DCIS and had a long-term adjusted survival rate of 97.2%, figures strikingly similar to those seen in contemporary reports.

With this history in mind, it is not surprising that prior to the advent of mammography, DCIS of the breast as a pure entity was a rather unusual finding. Since it most commonly co-existed with invasive cancer, it was treated by radical mastectomy followed by progressively more conservative procedures.

Data from the National Cancer Data Base estimate that 12% to 15% of newly diagnosed breast cancer in the US today is DCIS. Thus, approximately 25,000 to 30,000 women each year, the vast majority of whom will be diagnosed with a screening mammogram, will present to their physicians with several key questions, such as: 1) Does my breast need to be removed? 2) If my breast is not removed, do I need radiation therapy? 3) Should my lymph nodes be removed? 4) What is my prognosis if my breast is removed versus preserved? 5) How often do I need to be seen and to have mammograms? 6) Is there anything I can do to prevent recurrence of breast cancer?

Although the state of our present

Figure 1

Heterogeneous, faint, and linearly oriented calcifications representing DCIS.
knowledge about DCIS is incomplete, there is sufficient information available to allow clinicians to guide their patients through a difficult decision-making process. This review embodies the contemporary knowledge base. Despite remaining questions, optimal understanding of the diagnosis and management of this disease entity enhances the physician’s ability to communicate with the patient and her family.

**Mammographic Diagnosis**

Although microcalcifications are the most common mammographic manifestation of DCIS, numerous benign entities also present as microcalcifications. Accurate mammographic characterization is, therefore, essential to the diagnosis. Analysis of microcalcifications includes an assessment of their number, morphology, distribution, and size.

The accurate characterization and visualization of calcifications typically requires magnification of mammographic imaging. Faint calcifications not appreciated on standard mammographic images are frequently revealed on magnification views. Magnification images, therefore, are extremely important to accurately assess the extent of disease and determine the appropriateness of breast-conserving surgical treatment.

Morphology of the calcifications is generally considered to be the most important factor in differentiating benign formations from malignant ones. Basically, round and uniform shapes are more likely to be benign while linear and heterogeneous morphologies are associated with carcinoma. Malignant calcifications typically form in the intraductal spaces of the cancer resulting in faint, irregular, linear and often branching distribution patterns. Heterogeneous clustered calcifications, fine linear branching calcifications, or calcifications in a segmental distribution are suggestive of malignancy (Fig.1).

In contrast, random calcifications scattered throughout large volumes of breast tissue are almost always benign. The appearance of calcium sediment layering in cysts (milk of calcium), lucent-centered calcifications of fat necrosis, dermal calcifications, and solid, large rod-shaped secretory calcifications are indicative of a benign diagnosis (Fig. 2).

Sonography has no utility in the analysis of calcifications. Infrequently, DCIS can present as a mammographic and sonographic mass.
Despite careful mammographic analysis of calcifications, a definitive diagnosis cannot always be established. Calcifications frequently have an indeterminate appearance that implies a definable probability of malignancy. These indeterminate calcifications fall into the “suspicious category” in accordance with the American College of Radiology Breast Imaging Reporting and Data System (BIRADS), and warrant tissue sampling. Image-directed procedures are necessary for the definitive diagnosis of microcalcifications.

**Stereotactic Needle Core Biopsy**

**PATIENT SELECTION**

Following a complete mammographic work-up, most suspicious lesions or lesions highly suggestive of malignancy are potential candidates for a stereotactic needle core biopsy. Patient factors, together with technical advances and differences in equipment, will determine the limitations of and patient eligibility for this procedure.

Significant bleeding diathesis is a general contraindication to a stereotactic needle core biopsy procedure when hemostasis could be better controlled intraoperatively. Those patients with small breast size or deeply positioned calcifications may not be candidates for a stereotactic procedure, as adequate patient positioning may not be possible. Likewise, thinly compressed breasts may not allow the necessary deployment of the automated biopsy device.

Recent technical advances in the stereotactic prone table may allow for needle sampling of very thin breasts when a lateral arm device is available. Very faint calcifications diagnosed by film screen mammography may not be visible on the digital stereotactic monitors. Patients unable to cooperate with the stereotactic positioning requirements are also not appropriate candidates for stereotactic needle core biopsy. When the patient or available equipment does not allow for the stereotactic biopsy approach, an image-directed open surgical biopsy is required.

**STEREOTACTIC TECHNIQUES**

Depending on the available equipment, the stereotactic needle core biopsy of the breast is performed using a 14 gauge or 11 gauge needle with the patient in a prone position or sitting upright. Either a vacuum-assisted device or spring-activated...
needle core biopsy device is utilized. The basis of stereotactic imaging lies in the ability to visualize calcifications on 15 degree oblique images of the breast and computerized calculations to approximate the three dimensional coordinates of the calcifications. Once the location is established, the needle is inserted for sample acquisition (Fig. 3). Specimen radiography is necessary to confirm the presence of calcifications within the excised biopsy samples.

**Utilization of Stereotactic Needle Core Biopsy**

Clustered calcifications with an indeterminate appearance are ideal lesions for the minimally invasive stereotactically guided needle core biopsy procedure. Use of the stereotactic needle core biopsy can help distinguish patients who require surgical management from those who can be followed with routine clinical and mammographic follow-up.

A 50% reduction in biopsy costs with the use of stereotactic needle core biopsies has been reported. Moreover, the reliability of percutaneous needle core biopsy has been well established with a multi-institutionally reported “cancer-miss” rate of less than 2%. Stereotactic needle core biopsy of calcifications in the BI-RADS category “highly suggestive of malignancy” enables preoperative confirmation of the diagnosis and expedites surgical treatment and planning.

It must be realized, however, that a needle biopsy diagnosis of DCIS may underestimate the presence of invasive disease due to sampling error. Studies report that 16% to 20% of patients with DCIS diagnosed by needle biopsy were subsequently diagnosed with invasive disease upon surgical excision.

**Complications**

Complications are generally limited to bruising and mild tenderness that may limit activities for approximately one day. In a multi-institutional study, fewer than 1% of women undergoing stereotactic needle core biopsy reportedly developed an infection requiring antibiotics or a hematoma requiring surgical drainage. Inadequate sampling and an inability to demonstrate calcifications within the excised tissue may occur, particularly when patient motion becomes a factor during the needle biopsy procedure. Small clusters of malignant calcifications may be completely excised during the stereotactic needle core biopsy procedure. If no adjacent landmarks remain, a subsequent surgical excision may require the removal of a large volume of tissue. When using an 11-gauge vacuum-assisted biopsy device, a small micro-clip can be inserted into the biopsy cavity at the time of the stereotactic procedure to guide future localization efforts (Fig. 4).

**Lesions Requiring Surgical Excision**

Ten to 50% of patients initially diagnosed with atypical ductal hyperplasia by needle biopsy have subsequently been surgically diagnosed with cancer near the biopsy site. Due to this relatively high incidence of coexistent carcinoma, a needle biopsy diagnosis of atypical ductal hyperplasia necessitates a subsequent surgical excision. Discordance between...
the mammographic appearance and the pathologic diagnosis suggests that the lesion was not successfully biopsied and repeat biopsy is required.

**THE SURGICAL APPROACH**

The surgical approach to non-palpable, mammographically detected DCIS requires imaging guidance. At the time of pre-surgical localization, the patient will be placed in mammographic compression using a perforated or open plate compression paddle. Typically, one or more needles/wires are inserted by the radiologist into the patient’s breast at the appropriate location. Additional mammographic images confirm needle/wire placement and direct the surgeon to the region of concern.

**Pathologic Considerations in DCIS**

Since DCIS is, by definition, an atypical proliferation of cells confined to the ductolobular system of the breast by an intact basement membrane, it cannot cause serious morbidity unless and until it becomes invasive. Thus, the major goal of any pathologic evaluation of a patient with DCIS should be to determine the level of risk of subsequent invasion so that optimal treatment can be offered and possible over- or undertreatment is avoided.

In the pre-mammographic era, pure DCIS was most often seen as a high-grade, comedo-type mass lesion associated with invasive cancer and usually treated with mastectomy. In the current clinical setting, however, the vast majority of DCIS cases present as a mammographic abnormality that may be entirely incidental to the lesion seen on x-ray. As the pattern of the disease has shifted over the years from a bulky mass with a high risk of invasion to minute foci of questionable clinical significance, numerous studies have been undertaken to identify prognostic factors and thus optimize therapy for individual patients.

The most important change in our thinking about DCIS was from a monolithic view, conceiving of DCIS as a single disease highly likely to invade if left untreated, to the realization that DCIS represents a non-obligate precursor with a variable risk of progression, depending on a combination of factors. These factors include histologic pattern—and by extension, histologic grade—lesion size, margin status, and results of ancillary studies such as proliferation markers and HER 2/neu.

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**Figure 5**

A: Comedo DCIS with solid proliferation of cells surrounding central necrosis (original magnification, 20x).  
B: High nuclear grade qualifies this as high-grade DCIS (original magnification, 40x).
Classification of DCIS

Although the traditional classification of DCIS based on architectural pattern is now recognized to be limited in terms of prognostic value, it remains in use by many pathologists and merits review for that reason. In addition, before prognosis can be assessed, the pathologist must establish a diagnosis by applying criteria to distinguish DCIS from other atypical or non-atypical proliferations. These criteria are almost purely architectural and include the solid, cribriform, micropapillary, papillary, and intraductal comedocarcinoma variants.

**COMEDO DCIS**

Comedo DCIS is the only type likely to present as a palpable mass and accounts for the majority of cases of DCIS diagnosed before the advent of mammography. It is also the most likely to be high-grade and as such, the most likely DCIS type to be associated with concurrent or subsequent invasion. The histologic features of comedo DCIS are solid growth with central necrosis, often with calcification (Fig. 5A,B). Marked nuclear atypia is often seen, but a recent consensus conference on the classification of DCIS\textsuperscript{11} allows use of the comedo designation in the absence of high nuclear grade. Marked fibrosis and elastosis of the surrounding stroma are frequently present, as is an associated periductal lymphocytic infiltrate. Not infrequently, a question of possible microinvasion arises, as small nests of tumor cells are trapped in the fibroinflammatory reaction encircling the affected ducts. Diagnostic criteria for microinvasion are not well established, nor is its clinical significance, but at present, it is probably best to limit such a diagnosis to those cases where single tumor cells are clearly evident outside of an affected duct.

**MICROPAPILLARY DCIS**

Micropapillary DCIS, which is sometimes referred to as “clinging carcinoma,” may vary in appearance from a relatively flat proliferation with short projections to a pattern of long, slender epithelial fronds lacking fibrovascular cores (Fig. 6A,B). Peripheral spaces formed by so-called “Roman bridges” are common and lead some pathologists to group micropapillary and cribriform lesions together. Key features of micropapillary carcinoma distinguishing it from similar-appearing but benign proliferations are monomorphism.
and lack of polarity. Myoepithelial cells should be absent from their usual peripheral location, and the atypical cells should be homogeneous in appearance. Micropapillary carcinoma is usually composed of cells with low-grade nuclei, although cases with high nuclear grade are not rare. Centrally located necrotic debris and microcalcification may be present, especially in cases with high-grade nuclei. There is some evidence that micropapillary DCIS may be more likely to involve multiple quadrants than other forms of DCIS. Further studies will be necessary to establish the clinical significance of this finding in terms of risk of future invasion from residual disease.

**Cribriform DCIS**

Cribriform DCIS is a lesion characterized by the formation of secondary microlumens. These lumens tend to be round and uniformly distributed, although some variability is acceptable. The classic term used to describe the monomorphous nature of the cells outlining the spaces is “rigid bridges,” referring to the lack of stretched or elongated cells separating glandular spaces (Fig. 7A). Nuclear morphology is typically low-grade, although high-grade variants exist. Likewise, necrosis is commonly encountered in cribriform DCIS and may be so prominent as to mimic comedo DCIS (Fig. 7B). Fortunately, as will be seen in the discussion on grading, this distinction is obviated in current classification systems.

**Solid DCIS**

As the name implies, solid DCIS consists of a solid proliferation of neoplastic cells filling a ductal structure (Fig. 8A,B). Nuclear grade may vary widely, and spotty necrosis may be encountered. As in the other forms of DCIS, the monomorphous nature of the cell population is the hallmark of the process.

**Papillary DCIS**

Papillary DCIS is the least common of the well-described variants and exhibits prominent papillary features with fibrovascular cores but no myoepithelial cell layer (Fig. 9A,B). As in other variants, a monomorphous cytologic appearance is essential to the diagnosis.

**Grading of DCIS**

As previously alluded to, DCIS grade has
largely supplanted pattern as the most important guide to clinical behavior and treatment. A variety of different systems have been proposed but all include some assessment of nuclear features combined with other factors, typically necrosis or cell polarity, with classification of cases into either two or three grades.

Two recent studies\textsuperscript{13, 14} have compared a number of different grading systems for their interobserver reproducibility. While none of the systems demonstrated a very high degree of agreement among reviewing pathologists, both studies found the Van Nuys system of Silverstein and Lagios\textsuperscript{15} to be the most reproducible. This scheme relies on differentiating among the three nuclear grades on the basis of size, texture, and nucleoli, and on the presence or absence of comedo-type necrosis. Using these parameters, tumors can be divided into three groups. Group 1 (low-grade) includes those tumors with either low- or

\textbf{Figure 8}

A: Solid variant of DCIS with no necrosis (original magnification, 20x). \textbf{B}: Non-high grade nuclei and lack of necrosis make this lesion low grade (original magnification, 40x).

\textbf{Figure 9}

A: Papillary DCIS composed of long, slender papillary projections with fibrovascular cores (original magnification, 10x). \textbf{B}: Higher power demonstrates the atypia and lack of a myoepithelial layer (original magnification, 20x).
intermediate-grade nuclei and no necrosis. Group 2 (intermediate-grade) covers those tumors with low- or intermediate-grade nuclei and comedo necrosis, while group 3 (high-grade) encompasses all tumors with high-grade nuclei regardless of necrosis.

While tumor grade has emerged as a significant prognostic factor for risk of recurrence, other pathologic features may also be of importance. The Van Nuys grading scheme is part of a prognostic index for DCIS that includes tumor grade, tumor size, and margin width. In DCIS, however, evaluation of the latter two factors can be problematical. Since DCIS only rarely forms a grossly visible mass, measurement of lesion size is typically done from the microscopic slides. If, as is often the case, tumor is present on more than one slide, the pathologist must be able to reconstruct the specimen to estimate size. This obviously requires that the sections be submitted in some orderly fashion to permit such reconstruction. Even so, it is sometimes difficult to know how to report lesion size when small foci of DCIS are scattered throughout a lumpectomy specimen, and such data are not readily available in existing clinical studies.

If tumor size assessment is occasionally a problem, margin width determination is even more so. The most common approach involves the application of colored ink(s) to the surface of a specimen that has been oriented by the surgeon. The specimen is then submitted for microscopic examination in serial transverse section and the shortest distance between tumor and ink is then reported as the margin width. As this method can only examine a tiny fraction of the actual surface area of the specimen, it is a crude measurement at best. Some recommend an alternate method in which sections are shaved tangentially from the surface of the specimen to permit wider sampling of the margins. Yet another technique advocated by some surgeons is the separate removal of shaved margins from the biopsy cavity after the specimen has been resected. Ultimately, selection of a method of margin examination will depend on the experience and preference of the pathologist and surgeon, at least until better clinical studies are available.

As most “recurrences” of DCIS probably represent persistence following incomplete removal, the issue of margins is not trivial. Routine specimen mammography is often helpful in guiding the pathologic sampling by identifying areas of suspicious calcification near resection margins.

Given all of these considerations, the pathology report in cases of DCIS must include a large amount of data. Many institutions have found that use of a template form ensures that all vital data are gathered and reported. Such a form would typically include features such as nuclear grade, pattern, presence of necrosis, distance to margin, lesion size, presence of calcifications, and any other parameters deemed to be of importance. This type of systematic reporting scheme has the added advantage of making any retrospective clinical studies much easier to perform.

Newly diagnosed patients with DCIS of the breast need to be reassured of their excellent prognosis, irrespective of the surgical approach.
Newly diagnosed patients with DCIS of the breast need to be reassured of their excellent prognosis, irrespective of the surgical approach. Patients should understand that local recurrence following a well performed total mastectomy is rare and that this is the procedure of choice for disease that cannot be adequately encompassed with a breast-conserving approach. If, based on mammographic and pathologic evaluation of the lesion, the surgeon believes that breast-conserving surgery can be accomplished with an acceptable cosmetic result, then that option becomes an attractive choice for the patient. Nonetheless, long-term follow-up of patients treated optimally with complete surgical excision and radiation therapy shows that as many as 19% or more experience a local recurrence, with up to half of these local recurrences being invasive.16

If the patient and her surgeon are in agreement regarding a breast-conserving approach, the implications of local recurrence need to be fully and clearly explained. It is often useful to present easily understandable numbers: If 100 properly selected patients have margin-negative surgery and standard postoperative radiation therapy, at least 80 will achieve long-term local control. Assuming that with long-term follow-up, 20 patients experience local recurrences, 10 will have non-invasive recurrence and 10 will have invasive recurrence. The 10 patients with non-invasive recurrence will achieve virtually 100% local control and cure with completion total mastectomy. The 10 patients with invasive local recurrence will experience a 75% five-year survival rate with completion modified radical mastectomy.2 Thus, from the original 100 patients with DCIS managed with breast-conserving treatment, two or three will succumb to the disease. Given these numbers, most patients will opt for a breast-conserving approach, although some will prefer total mastectomy. During this treatment decision process, it is imperative that the surgeon counsel the patient with particular focus on the risks for local recurrence.

Predictive Factors for Local Recurrence after Breast-Conserving Treatment

Predictive factors for local recurrence can be conveniently categorized into clinical, pathologic, and biologic.

Clinical Factors

The relationship of age to local recurrence is controversial. Many surgeons believe that age younger than 40 is an a priori indication for mastectomy. Unfortunately, the literature on this subject provides no clear guidance. Four reports failed to demonstrate a relationship, but three others reported a breast tumor recurrence of approximately 25% in young women compared with only 10% in older women.2

Another unanswered question with respect to local recurrence is a positive family history. Two reports in the literature indicate a significantly higher local recurrence rate among women with a positive family history for breast cancer whereas an additional study does not corroborate these findings.2

Bloody nipple discharge as the presenting symptom leading to the diagnosis of DCIS intuitively suggests the possibility for a higher local recurrence, but a major collaborative study reported by Solin et al failed to identify an increased risk in this subset of patients.16

One clear-cut predictor of local recurrence is failure to remove all of the suspicious microcalcifications. Two reports confirm an extraordinarily high rate of local recurrence in this setting.2

In summary, as the only consistent predictor of local recurrence with breast-conserving surgery is a residual positive margin, young age and positive family
history should not be considered absolute contraindications.

**PATHOLOGIC FACTORS**

Pathologic predictive factors include histologic subtype, nuclear grade, size, necrosis, and margin status.

It is commonly believed that comedo-type lesions, especially with necrosis, are more likely to recur locally after conservative surgery than are non-comedo types. While this is probably true for larger lesions, overall, Solin’s collaborative study reported a 10-year actuarial breast recurrence rate of 18% with comedo-type and high-nuclear grade compared with 15% for DCIS lacking these factors (p=0.15). An important observation made in this study was that comedo, high-grade lesions tend to recur locally in a shorter time interval (3.1 years) than non-comedo DCIS (6.5 years). This emphasizes the importance of long-term follow-up in assessing local recurrence with relation to histologic subtype.

Other pathologic predictive factors have been conveniently grouped by Silverstein and colleagues into the Van Nuys Prognostic Index (VNPI). Size, margin width, and pathologic classification are assigned a score of 1 to 3, with the smallest, non-high grade lesions and the broadest margin widths assigned 1, and those with the highest grade, largest, and narrowest margin width on excision being assigned 3.

Silverstein and Lagios have suggested that a VNPI score of 3 or 4 may indicate a need for excision only without radiation therapy; a score of 5, 6, or 7, excision plus radiation therapy; and 8 or 9, total mastectomy. The widespread adoption of this index is limited by the variability in uniformly assessing size, margin status, and grade, but has value if consistent criteria are applied in individual institutions.

**BIOLOGIC FACTORS**

Biologic factors that have been implicated as predictors for local recurrence include absent estrogen receptor, HER-2-neu overexpression, P-53 alterations, aneuploidy, and increased angiogenesis. Further study of these factors, or a combination of these factors, with logistic regression analysis or neural network technology, may prove useful in the future.

In summary, there are many factors considered predictive of local recurrence in women with DCIS who elect breast-conserving treatment, some well studied and others controversial. If wide surgical excision with negative margins can be achieved and radiotherapy delivered postoperatively, results from a large collaborative study indicate a high degree of success with a median follow up of 9.3 years. The crude local recurrence rate was 29% for patients with close or positive margins compared with 7% for those with negative margins.

**Treatment Options**

Representatives from the American College of Radiology, the American College of Surgeons, the College of American Pathologists (also known as “the colleges”), and the Society of Surgical Oncology recently agreed upon standards for the management of DCIS.

**INDICATIONS FOR MASTECTOMY**

Although many women with DCIS are candidates for breast-conserving treatment with or without irradiation, mastectomy is clearly indicated in some patients. Such patients include women with two or more primary tumors in the breast or with diffuse malignant-appearing microcalcifications, as well as in those with persistent positive margins after reasonable surgical attempts.

In addition, for some women the risk:benefit ratio of breast conservation must be carefully assessed and consideration must be given to mastectomy as a treatment alternative.
Neither tumor size nor histologic type of DCIS is an absolute indication for mastectomy. However, a relative indication for mastectomy is the presence of extensive DCIS that can be removed with only a small negative margin. This is particularly true in a patient with a small breast in which an adequate resection would result in a significant cosmetic alteration that is unacceptable to the patient.

If mastectomy is the treatment of choice, a skin-sparing approach, removing only the skin of the nipple-areola complex and biopsy scar, facilitates breast reconstruction and should not compromise local control.

INDICATIONS FOR BREAST-CONSERVING SURGERY AND RADIATION THERAPY

Indications for breast-conserving surgery and radiation therapy include DCIS, detected mammographically or by physical examination, that is localized (without evidence of gross multi-centricity or diffuse malignant calcifications). The extent of DCIS should be less than 4 cm because few data exist to support the effectiveness of breast conservation for larger lesions. The difficulty in measuring the size of DCIS makes definitive recommendations difficult.

For mammographically detected DCIS presenting as microcalcifications, all malignant calcifications must be removed before radiation is initiated. Negative margins of resection are important to minimize ipsilateral breast tumor recurrences.

Certain factors preclude the use of radiation in the treatment of patients with DCIS and are unrelated to the extent of the disease. These include a history of collagen vascular disease (especially scleroderma and lupus erythematosus), previous therapeutic radiation to the breast or chest, and pregnancy. The first two factors are related to the potential for significant morbidity and the last is related to radiation exposure to the fetus.

INDICATIONS FOR BREAST-CONSERVING SURGERY ALONE

Individual centers have suggested a low local recurrence rate for low-grade tumors of small volume excised with clear margins, but the maximum size of DCIS for which radiation therapy could be safely omitted is not known. The precise indications for breast-conserving surgery alone will be best determined by prospective clinical trials still in progress.

ROLE OF RADIATION THERAPY

A study (B-17) by the National Surgical Adjuvant Breast and Bowel Project (NS-ABP), initiated in 1985 and closed in 1990 has been recently updated. All 814 patients have been followed for more than five years with about a third followed for more than eight years. About a quarter (25.8%) of patients treated with lumpectomy alone were reported to have ipsilateral breast tumor recurrence. For patients receiving radiation therapy after lumpectomy, local recurrence was significantly reduced to 11.4%. Approximately half of the local recurrences in the non-irradiated group were invasive. Invasive local recurrences were less frequently observed in the patients treated with lumpectomy and radiation therapy. Thirty (8.2%) ipsilateral breast tumor recurrences were non-invasive, and 17 (3.9%) were invasive. The conclusions of this update, namely that ipsilateral breast tumor recurrence of both invasive and non-invasive breast cancer is significantly reduced by post-lumpectomy radiation therapy, did not differ from those of the original reports.

ROLE OF MARGIN WIDTH

Silverstein and colleagues have recently described the influence of margin width on local control of DCIS. Although radiation therapy improved local control in patients with margin widths less than 1 mm, 21 out of 73 patients in this group experienced local recurrence. A logical conclusion would be to re-excise margins.
The Role of Tamoxifen

Two randomized clinical trials, NSABP B-24 and the Cooperative Study of the United Kingdom, New Zealand, and Australia, are examining the role of tamoxifen as an adjunct to reduce local recurrence of DCIS. In B-24, all patients are irradiated whereas in the Cooperative Study, a two-by-two factorial design is used in which patients may be randomized to receive or not to receive radiotherapy and to receive or not to receive tamoxifen.

The standards agreed upon by the three “colleges” and the Society of Surgical Oncology concluded, “until more data become available, the use of tamoxifen outside a clinical trial is not appropriate.” That statement must now be reconsidered in light of updated NSABP B-24 results in which Wolmark reported a 34% decrease in breast cancer events in the tamoxifen group compared with the placebo group. In addition, the findings from the NSABP Breast Cancer Prevention Trial (P-1) revealed a 49% reduction in breast cancer development among high-risk patients (defined as age older than 60, previous biopsy, lobular carcinoma in situ, and positive family history) treated with tamoxifen relative to those in the placebo group. Patients with DCIS were not part of that study but are clearly at increased risk relative to women without DCIS and at a comparable or greater risk than the subjects enrolled in P-1.

Patterns of Care in the US

Information from the National Cancer Data Base summarized in Fig. 10 indicates that the utilization of breast conservation has increased from 31.3% in 1985 to 61.2% in 1996. As of 1996, 27.8% of women with pure DCIS underwent axillary lymph node removal despite abundant evidence over the last three decades...
that pure DCIS is rarely associated with axillary lymph node metastases. There may well be a role for sentinel lymph node biopsy in patients with large high-grade lesions where the risk of microinvasion is significantly elevated.

Fig. 11 indicates that, as of 1985, only 40% of patients were receiving radiation therapy following conservative surgery for DCIS, whereas in 1996, 53.7% were receiving this modality. Clinical trial data are lacking to support this approach but retrospective series with highly selective patients demonstrate its efficacy.

The fundamental elements that must be included when excising DCIS without postoperative therapy are a complete radiologic evaluation preoperatively, intraoperatively, and postoperatively; rigorous selection criteria taking into account the size of the lesion and its histologic features; and wide excision with meticulous margin evaluation. Surgeons should be cautioned, however, regarding a need for long-term follow up for favorable cases, avoidance of compromising the cosmetic result with overzealous excision, and informed consent, preferably with a formalized institutional protocol.

Management of Local Recurrence

If local recurrence is observed in a patient who has previously undergone excision only, re-excision with clear margins and postoperative radiation therapy is an option, providing the previously described criteria for this approach are met. If, on the other hand, local recurrence is observed in a patient who has undergone conservative surgery and radiation therapy and the local recurrence is non-invasive, completion total mastectomy is the standard of care. If breast reconstruction is chosen, irradiated skin may not tolerate the extensive flap dissection used with skin-sparing mastectomy.

If the local recurrence is invasive, completion total mastectomy with sentinel lymph node biopsy or axillary dissection is indicated. In centers experienced with sentinel lymph node biopsy, histologically negative sentinel lymph...
nodes preclude the need for a full axillary dissection.

**Follow-up Surveillance**

Patients with DCIS who required total mastectomy should have a clinical evaluation every six months for the remainder of their lives, with particular attention to the contralateral breast. Annual screening mammography should be performed.

For patients managed with breast conservation, the same periodicity of clinical examination is recommended. There is no clear-cut consensus with respect to the frequency of mammographic evaluation of the treated breast. At our institution, annual mammography is generally performed for both breasts. This has been our policy because most centers performing more frequent mammography do so in the first year or two, a period of time during which local recurrence is rare and the evolving surgical scar may present interpretive problems and lead to unnecessary biopsy. A pre-radiation therapy mammogram should be done to confirm excision of microlcalkifications.

**Conclusions**

1. The widespread use of screening mammography has resulted in an increase in the diagnosis of DCIS to a level of 12% to 15% of all newly diagnosed breast cancer in the US. These percentages seem to be leveling off.
2. A complete imaging work-up should be conducted in patients found to have suspicious microlcalkifications. Magnification views are critical to determine the morphology and extent of microlcalkifications.
3. Vital pathologic data include nuclear grade, pattern, necrosis, distance to margins, lesion size, and presence of calcifications.
4. The sensitivity and specificity of stereotactic core needle biopsy for diagnosing DCIS are comparable to needle localization and open surgical biopsy. It is the diagnostic procedure of choice unless there are specific contraindications to the stereotactic approach.
5. The selection of treatment for DCIS must be thoughtfully undertaken with input from the patient, surgeon, radiologist, and pathologist.
6. The treatment selection process must focus on the risk of local recurrence. Clear surgical margins are critical.
7. Optimal surgery and radiation therapy can conserve the patient’s breast and decrease local recurrence in properly selected patients.
8. It is probable that a subset of patients treated with breast-conserving surgery will not require radiation therapy, but selection criteria need further refinement.

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