Standards for Diagnosis and Management of Ductal Carcinoma in Situ (DCIS) of the Breast

David P. Winchester, MD
Eric A. Strom, MD

Introduction

Standards of care in the diagnosis and management of any disease should be based on the best available scientific information. Such information is derived from prospective, randomized clinical trials through the cooperative group or intergroup mechanism, single or multi-institutional prospective trials, prospective nonrandomized trials, retrospective studies, and personal experience.

A collaborative effort of the American College of Radiology, the American College of Surgeons, the College of American Pathologists, and the Society of Surgical Oncology in 1992 culminated in a publication entitled “Standards for Breast-Conservation Treatment.” Both invasive and noninvasive diseases were considered in that document, although the focus was on invasive breast cancer. A task force of the same four national organizations decided that a sufficient body of knowledge had developed about ductal carcinoma in situ of the breast for a separate standard to be published.

Before the widespread use of screening mammography, ductal carcinoma in situ (DCIS) was an infrequently encountered problem that was routinely treated by mastectomy. As a result, a limited amount of information exists about the natural history of DCIS to act as a basis for treatment decisions. In addition, most DCIS seen today is identified mammographically because of the presence of microcalcifications, and it is unclear whether the biologic potential of this subclinical DCIS is the same as that of clinically evident DCIS.

Total mastectomy, excision, and irradiation, and excision alone have been advocated as management strategies for DCIS. The acceptance of breast-conserving therapy for invasive carcinoma has stimulated great interest in the use of this technique for the management of DCIS. However, data from randomized trials comparing mastectomy with lumpectomy and irradiation in patients with invasive carcinoma cannot be directly extrapolated to patients with DCIS. In the patient with invasive carcinoma, the risk of metastatic disease is present at the time of diagnosis and is not altered by local recurrence in the breast. In DCIS, the risk of metastases at the time of diagnosis is negligible, so an invasive local recurrence carries with it the risk of increased breast cancer mortality.

The appropriateness of breast-
conserving approaches in DCIS should be determined by the incidence of invasive recurrence in the breast and the results of salvage therapy. The evaluation of the results of different local therapies in DCIS is complicated by changes in the presentation of DCIS, differences in the extent of mammographic and pathologic evaluation over time, and the long natural history of the disease.

Treatment selection for the individual patient with DCIS requires a clinical, mammographic, and pathologic evaluation. The term “ductal carcinoma in situ” encompasses a heterogeneous group of lesions. Before a patient’s suitability for breast conservation with or without irradiation or the necessity of mastectomy can be determined, the extent and character of the patient’s disease must be identified by a thorough evaluation.

History and Physical Examination
An adequate history and physical examination include a complete assessment of the patient’s overall health status. Much of the information needed to determine a patient’s suitability for breast-conservation therapy can be obtained from a directed history and physical examination. The elements of the history and physical examination specific for breast cancer, which are listed in Table 1 of this article and Table 8 of “Standards for Diagnosis and Management of Invasive Breast Carcinoma” (page 90), represent information that may influence the selection of local therapy.

Mammographic Evaluation
DCIS most commonly presents mammographically as microcalcifications. How-
ever, about 10% of mammographically evident DCIS is an uncalcified mass. Occasionally, DCIS is diagnosed without mammographic findings.

Recent mammographic evaluation (usually within 3 months) before biopsy or definitive surgery is needed to establish the appropriateness of breast-conservation treatment by defining the extent of the patient’s disease. Because the contralateral breast should be evaluated, bilateral mammography is required.

Preoperatively, the diagnosis of DCIS can be suggested by mammography, but a definitive diagnosis depends on pathologic evaluation of the specimen. Because imaging techniques cannot determine whether the basement membrane has been violated, mammography cannot determine whether a tumor is invasive. Additionally, because peritumoral inflammation or fibrosis (or both) can cause a mass to be present along with microcalcifications, the diagnosis of DCIS requires histopathologic examination. The subtypes of DCIS can be suggested on the basis of characteristic patterns of calcifications, but these patterns are not diagnostic; the definitive diagnosis depends on the analysis of tissue by the pathologist.

The mammogram may underestimate the extent of DCIS. This may be true with increasing lesion size. However, in all cases an effort should be made to determine the extent of tumoral calcifications preoperatively. In addition to routine mediolateral oblique and craniocaudal views, magnification views and any other special views that may be required should be obtained in an attempt to identify areas of calcified tumor that otherwise might not be apparent. The entire breast should be carefully examined to determine if areas of tumor are present elsewhere in it, which would influence a decision about breast-conserving treatment. The role of other imaging modalities, especially magnetic resonance (MR) imaging, in staging the extent of tumor within the breast has yet to be established.

**Surgical Considerations**

When breast-conservation treatment is appropriate, the goals of any surgical procedure on the breast are total removal of the tissue suspected or known to be malignant and minimal cosmetic deformity. These goals apply to both diagnostic biopsy and definitive local excision. Failure to consider them at all stages may jeopardize conservation of the breast.

DCIS can present as a palpable mass, but this presentation is unusual.

---

### Table 1

**Elements of Physical Examination of the Breast**

| Element                              |
|--------------------------------------|
| Tumor size (measured) and location, if palpable |
| Nipple discharge, including whether discharge is from duct and whether guaiac positive or negative |
| Nipple appearance, including presence of eczema or discoloration |
| Ratio of breast size to tumor size |
| Axillary node status, including size and mobility |
| Presence of supraclavicular nodes |
| Appearance of opposite breast and axilla |

---

**Diagnosis and Management Standards for DCIS**

- Tumor size (measured) and location, if palpable
- Nipple discharge, including whether discharge is from duct and whether guaiac positive or negative
- Nipple appearance, including presence of eczema or discoloration
- Ratio of breast size to tumor size
- Axillary node status, including size and mobility
- Presence of supraclavicular nodes
- Appearance of opposite breast and axilla
The standards described for palpable invasive disease apply to palpable DCIS. Because DCIS most commonly presents as microcalcifications, image-directed procedures are necessary for diagnosis and treatment.

**IMAGE-DIRECTED BIOPSY**

**Stereotactic Core-Needle Biopsy**

Stereotactic core-needle biopsy of the breast—performed by qualified radiologists, surgeons, or other physicians—can be the initial approach for sampling suspicious nonpalpable mammographic abnormalities. Ultrasound-guided biopsy is useful for nonpalpable masses but usually cannot be relied upon for biopsy of microcalcifications.

Not all patients with microcalcifications are ideal candidates for stereotactic biopsy. Some patients’ breasts may be too small to be accommodated by the stereotactic system. The thickness of the breast must be adequate to allow the full throw of the automated biopsy device when such a device is used. Abnormalities just under the skin may pose technical problems in some cases.

If calcifications are widely separated, generating useful stereotactic coordinates to guide needle biopsy may be difficult. When microcalcifications are not tightly clustered or when the sensitivity or resolution of the stereotactic imaging system is hampered so that individual microcalcifications are not well visualized, accurate localization and retrieval of microcalcifications within core biopsy specimens may be difficult.

Finally, the difficulty of the procedure increases with an uncooperative patient. If any one or a combination of these adverse factors exists, image-directed open surgical biopsy is the preferred approach.

For lesions amenable to stereotactic breast biopsy, multiple cores should be obtained, and the specimen should be radiographed to confirm an adequate sampling of the microcalcifications. Leaving some microcalcifications at the site is desirable because if DCIS is diagnosed, they can accurately image-direct the surgeon to definitive excision. If all microcalcifications or the entire mass has been removed, a marker can be left at the biopsy site so that the area can be localized.

If a presurgical diagnosis of DCIS is made by percutaneous core-needle biopsy, physicians should be aware that areas of invasive carcinoma are found in about 20% of cases at the time of surgical excision.

**Guided Wire Open Biopsy**

Nonpalpable, mammographically evident lesions that are excised surgically should be localized presurgically with a guide, such as a guide wire. Any suspicious lesion detected by mammography requires presurgical localization to ensure accurate removal of the abnormal area and to avoid excess sacrifice of breast tissue. The localization method can be needle-hook wire, dye injection, or a combination of both. Localization should be precise and may require positioning of more than one wire.

Labeled craniocaudal and lateral films that show the hook wire should be sent to the operating room for the surgeon’s orientation. The current diagnostic films may be of additional value to the surgeon.

The surgeon should assess the exact location by triangulation (based on the position, depth of penetration, and angle of the wire) and place the incision closest to the tip of the wire to achieve the best cosmetic result (see Fig. 2 of “Standards for Diagnosis and Management of Invasive Breast Carcinoma,” page 97). Tunneling should be avoided, and the skin incision should be made as close to the lesion as possible. The incision should be long enough to permit the removal of the specimen in one piece. Removal of the lesion in numerous fragments should be avoided because doing so precludes margin assessment and size determination.
Curvilinear skin incisions are preferable (see Fig. 1 of “Standards for Diagnosis and Management of Invasive Breast Carcinoma,” page 96). Periareolar incisions are not appropriate for lesions in the periphery of the breast. The procedure can be done readily with the patient under local anesthesia with or without intravenous sedation.

Meticulous hemostasis is critically important. Hematoma formation produces changes that are difficult to interpret by physical examination. In addition, the evolving scar from a hematoma may make interpretation of mammography difficult. These changes may be long lasting and lead to unnecessary biopsy because of the difficulty in evaluation. A better cosmetic result can be achieved by allowing the biopsy cavity to fill with serum, although reapproximation of the biopsy cavity may be appropriate under some circumstances. Drains in the breast should be avoided.

Skin incisions should be closed with a subcuticular technique.

The specimen should be radiographed intraoperatively to determine that the mammographic lesion has been excised and to direct pathologic analysis to the site in question in the removed tissue. Magnification and compression of the specimen increase the resolution of the radiograph.

The specimen film should be correlated with a preoperative mammogram and interpreted without delay. Absence of the mammographic abnormality on the specimen radiograph usually indicates that it has not been removed. If the diagnosis is DCIS, extension of calcification (or mass) to the margin of the specimen suggests that a residual tumor might be present in the breast and that further resection along that margin may be indicated.

The specimen radiograph is not adequate to determine the completeness of excision. Histologically negative margins also do not guarantee complete removal of the lesion because DCIS may grow in a discontinuous fashion.

A postoperative mammogram should be obtained to document complete removal of the mammographic abnormality. It can be done as soon as the patient can tolerate compression. Magnification views may be helpful. Margin status and the postoperative mammogram are complementary means of assessing the completeness of excision. If re-excision is done, another postexcision mammogram should be obtained to reassess the tumorectomy site.

**Reexcision of Biopsy Site**

The previous biopsy site must be reexcised carefully to ensure negative margins of resection, avoid excess removal of breast tissue, and achieve good cosmesis. If the presence of microcalcifications is the indication for reexcision, needle localization should be considered. Proper orientation of the original biopsy specimen avoids removal of an already adequate margin. When the site of inadequate margins is not known, a rim of tissue must be removed around the previous biopsy site.

**Management of the Axilla**

Axillary node metastases are uncommon in DCIS. Axillary dissection is not necessary for the management of most patients with DCIS.

Unsuspected invasive or microinvasive carcinoma occurs more frequently in association with extensive DCIS of high nuclear grade. Most of these patients need mastectomy to encompass the disease. Therefore, a low axillary sampling or level I dissection performed when the mastectomy is done avoids a second operative procedure if invasive carcinoma is found in the mastectomy specimen. If a clinically suspicious node is found during surgery, a frozen section should be done, and if the node is positive, a level I and II axillary node dissection should be performed.
Pathologic Evaluation

Tissue Handling

The excised tissue should be submitted for pathology examination with appropriate clinical history and anatomic site specifications, including laterality (right or left breast) and quadrant. For wide excisions or segmental breast resections, the surgeon should orient the specimen (e.g., superior, medial, lateral) for the pathologist with sutures or other markers. The specimen radiograph should be available for the pathologist to review while examining the specimen.

The pathologist’s gross examination should document the type of surgical specimen when this information is provided (e.g., excisional biopsy, quadrantectomy), the size of the specimen, and the proximity of the tumor (if visible) or biopsy site to the margins of excision.

The presence or absence of tumor at the margins of excision is determined by marking the margins with India ink or using another suitable technique. The entire mammographic lesion, and as much of the remaining specimen as practical, should be submitted for histologic examination. Additionally, the margins of the specimen must be thoroughly evaluated, particularly those closest to the lesion.

Frozen-section examination of image-guided needle biopsies of nonpalpable lesions or mammographically directed biopsy done for microcalcifications is strongly discouraged. Distinguishing between atypical ductal hyperplasia and DCIS may be impossible in frozen-section preparations, and small foci of microinvasion may be lost or rendered uninterpretable by freezing artifact.

Frozen sections should be prepared only when enough tissue is present that the final diagnosis will not be compromised (i.e., grossly visible tumors larger than 1.0 cm) and when the information is needed for immediate therapeutic decisions.

Pathologic Features Influencing Treatment Choice

DCIS traditionally has been classified primarily by architectural pattern. In this system, DCIS is divided into comedo, cribriform, micropapillary, papillary, and solid subtypes. This classification was developed at a time when all patients with DCIS were treated by mastectomy, however, and the histologic subclassification of DCIS was largely an academic exercise.

With the increasing use of breast-conserving therapy for DCIS, lesions more likely to recur or progress to invasive cancer must be identified. Several new classification systems have been proposed, based primarily on nuclear grade, necrosis, or both. Many studies have supported the clinical relevance of this approach, showing that high nuclear grade or necrosis is associated with a higher risk of early local recurrence after breast-conservation therapy.

Although a single classification system for DCIS has not yet been uniformly accepted, the pathologist should clearly report the nuclear grade of the lesion and the presence or absence of necrosis. If a specific grading system for DCIS is used, this should be stated in the pathology report. The report also should include the architectural patterns present because they may have clinical relevance (e.g., the micropapillary pattern may be more prone to involvement of multiple quadrants, independent of nuclear grade).

The extent (size) of DCIS is an important factor in treatment decisions. In contrast to most invasive cancers, however, DCIS is difficult to measure because it is usually nonpalpable and cannot be identified grossly. Although precise measurement may not be possible, the pathologist may be able to estimate the extent of DCIS, and this information should be included in the pathology report.

Several methods for estimating the extent (size) of DCIS have been suggested, including (1) directly measuring the size of the lesion if it is confined to a
single slide; (2) determining the size after submitting the entire specimen for microscopic examination in sequence and in sections of uniform thickness (2 to 3 mm); (3) estimating the percentage of breast tissue involved by DCIS in relation to the total specimen; and (4) reporting the total number of slides examined and the number with DCIS.

The assessment of surgical margins is arguably the most important aspect of the pathologic evaluation of breast tumor excisions in patients being considered for breast conservation. Although the definitions of “positive” and “negative” margins vary among institutions, microscopic extension of DCIS to surgical margins usually results in further surgery. The pathologist should clearly specify in the pathology report whether DCIS is transected at the surgical margin, and if not, how close the lesion is to the nearest margin.

Determinations of estrogen and progesterone receptors, DNA content (ploidy), S-phase, and oncogene amplification are not necessary for noninvasive breast carcinomas.

**PATHOLOGY REPORT**

Certain pathologic features should be included in the surgical pathology consultation report because they help determine the most appropriate therapy. These features include the following:

1. How the specimen was received (e.g., number of pieces, fixative, orientation)
2. The laterality and quadrant of the excised tissue and the type of procedure, as specified by the surgeon
3. Size of the specimen in three dimensions
4. Whether the entire specimen was submitted for histologic examination
5. The histologic features of DCIS (e.g., nuclear grade, necrosis, architectural pattern)
6. An estimate of the extent (size) of DCIS (if possible)
7. The location of microcalcifications (e.g., in DCIS, in benign breast tissue, or both)
8. The presence or absence of DCIS at the margins of excision. If possible, the distance of the lesion or biopsy site from the margin should be stated.

**Selection of Treatment**

Without mature data from clinical trials, it is the collective responsibility of the surgeon, pathologist, radiation oncologist, and radiologist to integrate all available data so that treatment options and recommendations can be articulated clearly to the patient.

The surgeon must decide, based on imaging studies and the pathology consultation report, whether the patient is a candidate for a breast-conserving approach. If so, local recurrence must be further discussed. Local recurrence with total mastectomy is rare. Local recurrence is observed at a higher rate in patients treated with breast conservation, but the impact of these local recurrences on overall survival is probably small. Finally, patients need to understand the excellent prognosis for this disease with either surgical approach.

**PATTERNS OF CARE**

Information on 39,010 patients with DCIS of the breast diagnosed between 1985 and 1993 was collected through the National Cancer Data Base. During the 8 years of analysis, the use of breast-conservation therapy increased from 31% to 54%. Tumors with favorable sizes and grades were associated with increased rates of breast preservation and lower rates of axillary dissection and use of radiotherapy. In the early years of the study, radiotherapy was administered to only 38% of patients postoperatively, but by 1993 it was used in 54%. The axilla was dissected in 49% of the patients initially and in 37% by the end of the study.

The inappropriately high rate of
axillary dissection and the low rate of postoperative radiation therapy should improve through dissemination of clinical trial results and professional education.

Supporting Literature

Mastectomy

No prospective randomized trials have compared the treatment of DCIS by mastectomy with treatment by breast conservation. Studies from single institutions, including patients with both clinically evident and mammographically detected DCIS, indicate that 1% to 2% of patients treated by mastectomy will relapse, either regionally or systemically (Table 2). Presumably, relapse is caused by unrecognized foci of invasive tumor present in the breast. Thus, although mastectomy results in cure rates approaching 100%, it may be overtreatment for many patients with DCIS, particularly those with small, mammographically detected lesions.

Breast-Conserving Surgery and Radiation Therapy

Data from Prospective Randomized Clinical Trials

In 1985, the National Surgical Adjuvant Breast and Bowel Project (NSABP) began protocol B-17, a prospective randomized study to evaluate the worth of postoperative radiation therapy after lumpectomy for patients with DCIS. The initial results, with an average follow-up of 43 months, were published in 1993.2 Additional details of the pathology were published in 1995.3

In 1997, the results were updated.4 For this analysis, 814 patients were eligible for evaluation, with a mean time in the study of 90 months (range, 67 to 130 months). All patients had been followed for more than 5 years, and 35% had been followed for more than 8 years. Thirty-eight percent of these patients had axillary dissections, all of which were negative. The total number of ipsilateral breast tumor recurrences was 151, and 70 (46.4%) recurrences were invasive. Most of the ipsilateral breast tumor recurrences were at or near the original lesion.

Analysis by treatment arm showed 104 ipsilateral breast tumor recurrences among 403 patients treated with lumpectomy only (25.8%) (Table 3). The cumulative rate of ipsilateral breast tumor recurrence at 8 years was only slightly higher, 26.8%. (For comparison, the cumulative ipsilateral breast tumor recurrence rate at 5 years reported in 1993 was 20.9%.2) Fifty-one ipsilateral breast

| Reference                  | No. Patients | Follow-Up          | Nonpalpable (%) | No. Recurrences |
|----------------------------|--------------|--------------------|-----------------|-----------------|
| Ashikari et al21           | 92           | 11 yrs (maximum)   | 0               | 0               |
| Sunshine et al32           | 68           | 10 yrs (minimum)   | 0               | 0               |
| Farrow23                   | 181          | 5–20 yrs           | 0               | 2               |
| Silverstein et al34        | 228          | 7 yrs (median)     | 80              | 2               |
| Von Rueden & Wilson45      | 45           | Not stated         | 7               | 0               |
| Lagios et al24             | 42           | Not stated         | 60              | 0               |
| Kinne et al36              | 101          | 11.5 yrs (median)  | 59              | 1               |
| Schuh et al37              | 51           | 5.5 yrs (mean)     | 33              | 1               |
| Arnesson et al38           | 28           | 77 months          | 100             | 0               |

Table 2 Results of Treatment of Ductal Carcinoma in Situ with Mastectomy
tumor recurrences were noninvasive (13.4%) and 53 were invasive (13.4%).

The rate of ipsilateral breast tumor recurrence was markedly reduced for patients who received radiation therapy in addition to lumpectomy. Only 47 ipsilateral breast tumor recurrences occurred in 411 patients treated with lumpectomy plus radiation therapy (11.4%). The cumulative ipsilateral breast tumor recurrence rate at 8 years was only slightly higher, 12.1%. (Again for comparison, the cumulative ipsilateral breast tumor recurrence rate at 5 years for patients treated with lumpectomy and radiation therapy as reported in 1993 was 10.4%.2)

Thirty ipsilateral breast tumor recurrences were noninvasive (8.2%), and 17 were invasive (3.9%) (Table 3). The P values were significantly different when patients who received radiation therapy were compared with patients who did not.

The update confirmed the original conclusions of NSABP protocol B-17 that ipsilateral breast tumor recurrence of both invasive and noninvasive breast cancer is significantly reduced by post-lumpectomy radiation therapy.

In the original analysis, margin status and the presence of comedonecrosis were independent predictors of ipsilateral breast tumor recurrence.

Other randomized trials that have been started in North America and Europe (Table 4) compare the results achieved using breast-conserving surgery alone with those of breast-conserving surgery plus radiation therapy. All of them (except the Swedish trial) require histologically “negative” margins as an entry criterion. (Attempts by national cooperative groups in Germany and Denmark to perform randomized trials comparing surgery alone with surgery and radiotherapy had to be abandoned because of poor accrual.) As yet, no data are available from these trials.

### Retrospective Series

The results of conservative surgery and radiation for DCIS from retrospective series are presented in Table 5. The crude incidence of breast tumor recurrence ranges from 4% to 18%. Deaths caused by breast cancer have been reported in up to 4% of patients treated in studies with a median follow-up of 10 years or fewer.

The long-term results of conservative surgery and radiation for DCIS were reported by Solin et al.5,6 This collaborative study of 10 institutions in the United States and Europe analyzed outcome in 268 patients. Seventy-eight percent of the tumors were detected by mammography alone. The 10-year actuarial risk of breast

---

**Table 3**

| Type of Recurrence | Lumpectomy plus Radiation Therapy | P Value |
|--------------------|-----------------------------------|---------|
|                    | No. | Cumulative IBTR | No. | Cumulative IBTR | |
| Noninvasive        | 51  | 13.4%           | 30  | 8.2%            | 0.007   |
| Invasive           | 53  | 13.4%           | 17  | 3.9%            | < 0.000005 |
| Total              | 104 | 26.8%           | 47  | 12.1%           | < 0.000005 |

IBTR = ipsilateral breast tumor recurrence (local recurrence). Data from Mamounas et al.4
recurrence was 16%, and the 10-year actuarial cause-specific survival was 97%. The 15-year actuarial breast recurrence was 19%, and the 15-year actuarial cause-specific survival was 96%. Median follow-up was 10.3 years.6

Various clinical, pathologic, and treatment-related factors have been assessed for their ability to identify patients with a substantial risk of recurrence in the treated breast. For these patients, mastectomy may be recommended. One factor that appears to be associated with a high risk of recurrence is the presence of residual malignant-appearing calcifications on a postbiopsy mammogram. Failure to remove these calcifications before radiation has resulted in a 100% recurrence rate in the few patients reported.7,8 DCIS presenting as a bloody nipple discharge was

**Table 4**

| Study                  | Dates            | Actual or Planned Accrual | Coexisting LCIS Allowed? | Nonpalpable Tumors | Size Limits |
|------------------------|------------------|----------------------------|--------------------------|---------------------|-------------|
| NSABP B-17,2,3         | 1985–1990        | 790                        | Yes                      | 83%                 | None        |
| EORTC 108539           | 1986–1996        | 1,010                      | No                       | NS                  | ≤5 cm       |
| Swedish National DCIS Trial40 | 1989–ongoing | 1,000                      | NS                       | NS                  | <1 quadrant |
| UK-Australian-New Zealand Trial29,30 | 1990–ongoing | 1,000                      | Yes                      | NS                  | None        |

DCIS = ductal carcinoma in situ; EORTC = European Organization for Research and Treatment of Cancer; LCIS = lobular carcinoma in situ; NS = not stated; NSABP = National Surgical Adjuvant Breast and Bowel Project.

**Table 5**

| Reference                | No. Patients | Breast Recurrence Crude Incidence (%) | Median Follow-up (Yrs) |
|--------------------------|--------------|--------------------------------------|------------------------|
| McCormick et al7         | 54           | 18                                   | 3.0                    |
| Haffty et al20           | 60           | 7                                    | 3.6                    |
| Kurtz et al17            | 47           | 4                                    | 5.0                    |
| Ray et al18              | 56           | 9                                    | 5.0                    |
| Solin et al40a           | 51           | 10                                   | 5.7                    |
| Van Zee et al11          | 63           | 10                                   | 6.2                    |
| Hiramatsu et al12*       | 76           | 9                                    | 6.2                    |
| Sneige et al8            | 49           | 10                                   | 7.2                    |
| Fourquet et al16         | 153          | 16                                   | 9.0                    |
| Solin et al5,6†          | 268          | 17                                   | 10.3                   |

*Ten-year cause-specific survival 96%.
†Ten-year cause-specific survival 97%.
noted in earlier series to be associated with a higher risk of recurrence. In the collaborative study, however, no increased risk appeared to exist in this group of patients.6

The significance of young age (less than 40 years) is controversial. Three studies have observed an increased risk of breast tumor recurrence (approximately 25%) in young women who have DCIS treated with conservative surgery and radiation compared with older women (approximately 10%).9-11 However, four additional studies have found no correlation between young age and breast recurrence rates.6,8,12,13

A similar controversy exists regarding a positive family history of breast cancer. Two series7,12 have reported a higher breast tumor recurrence rate (approximately 40%) in women with a positive family history compared with those who do not have such a history (approximately 10%). However, a third series found no such association.10 The impact of young age and a positive family history of breast cancer on treatment options in women with DCIS requires further evaluation.

The contribution of various pathologic factors (histologic subtype, nuclear grade, necrosis) to the risk of breast recurrence in patients treated with conservative surgery and radiation is controversial.

It was suggested initially that high-grade or comedo DCIS was associated with a higher rate of breast tumor recurrence.5,14 However, in the collaborative study, the 10-year actuarial breast recurrence rate was 18% for tumors with the combination of both comedo pattern and a high nuclear grade versus 15% for DCIS in which these factors were absent (P = 0.15).6 The median interval to recurrence for comedo DCIS was 3.1 years versus 6.5 years for non-comedo DCIS. Therefore, series with shorter follow-up tend to underestimate the number of recurrences in low-grade or non-comedo DCIS, and recurrences in high-grade or comedo DCIS predominate. The influence of necrosis on breast recurrence rates remains to be determined.

Silverstein and colleagues15 have designed the Van Nuys Prognostic Index. This is a quantitative algorithm that uses tumor size, margin width, and a pathologic classification based on nuclear grade and comedo-type necrosis to predict the likelihood of local recurrence with breast-conservation treatment for patients with DCIS. Scores range from a low of 3 (best prognosis) to a high of 9 (worst prognosis). Their results suggest that patients who score 3 or 4 generally have small, well-excised, low-grade lesions that can be treated successfully with excision alone. The Van Nuys Prognostic Index must be confirmed by others before it is accepted for widespread use.

Most breast tumor recurrences in patients undergoing conservative surgery and radiation for DCIS occur near the primary tumor, and approximately 50% are invasive cancers.6-8,12,14,16-20 Invasive recurrences appear at later intervals (5 years) than do noninvasive recurrences (4 years) and may occur in a separate quadrant.9,17 Nearly all patients who develop a noninvasive recurrence are salvaged with mastectomy, and approximately 75% of those with an invasive recurrence are salvaged.7,8,12,16,18-21

Over the last 10 years, the method of detection of DCIS has changed significantly. Approximately 85% of all DCIS is now detected solely as a mammographic finding, which is most often characterized by the presence of microcalcifications. Earlier reports of conservative surgery and radiation for DCIS do not accurately reflect outcome for mammographically detected DCIS because many included clinically evident DCIS (palpable mass or bloody nipple discharge), and detailed mammographic and pathologic correlation was frequently lacking. Unfortunately, the results of these earlier series were compared with those of conservative surgery alone for mammographically detected DCIS and often
The results of conservative surgery and radiation for mammographically detected DCIS are shown in Table 6. The 10-year actuarial breast tumor recurrence rate ranges from 6% to 23%, with a 10-year cause-specific survival of 96% to 100%. The variation in the results reported reflects differences in patient selection, the extent of surgical resection, and the degree of mammographic and pathologic correlation.

Increasing evidence exists that wide surgical excision and negative margins of resection diminish the risk of breast tumor recurrence in patients with mammographically detected DCIS treated with conservative surgery and radiation. In the collaborative study (which had a median follow-up of 9.3 years), the crude breast tumor recurrence rate was 29% for patients with close or positive margins compared with 7% for those with negative margins.

Two series have reported the results of conservative surgery and radiation for mammographically detected DCIS in patients who would meet Lagios’ criteria for observation (presence of calcifications only, size less than 2.5 cm, negative margins, and negative postbiopsy mammogram). In the 37 patients reported to date (median follow-up 4.9 and 9.3 years, respectively), Lagios reported a 17% breast tumor recurrence rate in 78 such patients with a follow-up of 10.3 years.

Breast-Conserving Surgery Alone
More than 15 years ago, Lagios and associates first suggested excision only without postoperative radiation therapy as treatment for selected patients with DCIS. Their criteria for excision only were strict: a lesion had to be nonpalpable and discovered by the presence of mammographic microcalcifications. In addition, the lesion had to be 25 mm or less in maximum size and free of microcalcifications on postoperative mammography, and specimen margins had to be clear of DCIS by 1 mm or more.

| Reference | Total No. Patients | Actuarial Breast Recurrence (%) 5 Years | Actuarial Breast Recurrence (%) 10 Years | Cause-Specific Survival (%) 5 Years | Cause-Specific Survival (%) 10 Years | Median Follow-up (Yrs) |
|-----------|--------------------|-----------------------------------------|-----------------------------------------|-----------------------------------|-----------------------------------|-------------------------|
| NSABP B-17 | 399*               | 10                                      | —                                       | —                                 | —                                 | 3.6 (mean)              |
| Kuske et al | 44                 | 7                                       | —                                       | —                                 | —                                 | 4.0                     |
| Fowlie et al | 110               | 1                                       | 15                                      | 100                               | 100                               | 5.3                     |
| Vicini et al | 102               | 4                                       | 6                                       | —                                 | 99                                | 6.1                     |
| Hiramatsu et al | 54          | 2                                       | 23                                      | —                                 | 96                                | 6.2                     |
| Sneige et al | 31                 | 0                                       | 8                                       | —                                 | —                                 | 7.2                     |
| Silverstein et al  | 33†               | 7                                       | 19                                      | —                                 | 97                                | 7.8                     |
| Solin et al | 110               | 7                                       | 14                                      | 100                               | 96                                | 9.3                     |

*81% detected by mammography.
†89% detected by mammography.
— = data not available.
NSABP = National Surgical Adjuvant Breast and Bowel Project.
Recently, Lagios updated his series of 79 patients, reporting an 18% actuarial local recurrence rate at 15 years. Subdivision of these patients by nuclear grade revealed that high-grade lesions were much more likely to recur than low- or intermediate-grade lesions. The rate of local recurrence was 33% for high-grade lesions, 10% for intermediate-grade lesions, and 6% for low-grade lesions. No breast cancer–related deaths occurred, and no patients have developed distant metastases.

The seminal work of Lagios and colleagues led many others to study the role of excision only as the treatment for selected patients with DCIS. The results of several of these series are shown in Table 7.

Table 7
Results of Treatment of Ductal Carcinoma in Situ by Excision Alone

| Reference          | No. Patients | Follow-up (Months) | Recurrence (%) | Invasive (%) |
|--------------------|--------------|--------------------|----------------|--------------|
| Arnesson et al     | 169          | 80*                | 16/22†         | 36           |
| Baird et al        | 30           | 43†                | 13             | 25           |
| Carpenter et al    | 28           | 38†                | 18             | 20           |
| Cataliotti et al   | 99           | 79†                | 8/23‡          | 38           |
| Eusebi et al       | 80           | 210                | 20             | 69           |
| NSABP B-17         | 403          | 90‡                | 27§            | 50           |
| NSABP B-06         | 21           | 83‡                | 43             | 55           |
| Lagios et al       | 79           | 130*               | 18¶            | 56           |
| Salvadori et al    | 74           | 31†                | 14             | 60           |
| Schreer            | 102          | 56‡                | 24             | 42           |
| Schwartz et al     | 194          | 53*                | 14/25‡         | 18           |
| Sibbering & Blamey | 48           | 58*                | 6              | 33           |
| Silverstein        | 130          | 45*                | 21§            | 33           |
| Silverstein et al  | 85           | 45*                | 14§            | 33           |

*Median.
†5-year actuarial/10-year actuarial.
‡Mean.
§8-year actuarial.
¶15-year actuarial.
NSABP = National Surgical Adjuvant Breast and Bowel Project.

Role of Tamoxifen in DCIS
Two trials have been designed to examine the value of tamoxifen for patients with DCIS. The NSABP B-24 study was conducted from 1991 to 1995, with an accrual goal of 1,800 patients. Unlike the B-17 trial, in which patients were randomly assigned to receive radiation, in the B-24 study all patients were irradiated. Patients were not required to have histologically negative margins for entry. Indeed, patients with multicentric disease or unbiopsied suspicious calcifications (even in multiple quadrants) were eligible.

In 1990, cooperative groups in the United Kingdom began a trial that has also been open in New Zealand and Australia since 1992. This study has a 2 by 2 factorial design in which patients may
be randomized to receive or not receive radiotherapy and to receive or not receive tamoxifen. However, clinicians are allowed to elect whether their patients enter only one of these randomizations (and which one) or both randomizations. Histologically negative margins (defined as no tumor seen directly at an inked surface) are required for entry. Tamoxifen is given in the same dosage and duration as in the NSABP B-24 trial. A total of 1,000 patients are to be accrued over all the study arms; 458 had been entered by the end of March 1995.30

Until more data become available, the use of tamoxifen outside a clinical trial is not appropriate.

TREATMENT OPTIONS

Indications for Mastectomy

Although many women with DCIS are candidates for breast-conserving treatment with or without irradiation, in some patients mastectomy is clearly indicated. Such patients include women with two or more primary tumors in the breast or with diffuse, malignant-appearing microcalcifications and 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.

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 multicentricity or diffuse malignant calcifications). The extent of DCIS should be less than 4 cm because few data exist to support breast conservation’s effectiveness in 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 the ipsilateral breast tumor recurrence rate.

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.

PATIENT CHOICE ISSUES

Perhaps the most difficult aspect of patient evaluation is the assessment of the patient’s needs and expectations regarding breast preservation. The patient and her physician must discuss the benefits and risks of mastectomy compared with breast-conservation treatment in her in-
individual case, with thoughtful consideration of each.

Each woman must evaluate how her choice of treatment is likely to affect her sense of disease control, self-esteem, sexuality, physical functioning, and overall quality of life. Several factors should be considered, including (1) long-term survival; (2) the possibility and consequences of local recurrence; and (3) psychological adjustment (including the fear of cancer recurrence), cosmetic outcome, sexual adaptation, and functional competence.

For most patients, the choice of mastectomy (with or without reconstruction) or breast-conservation treatment does not influence the likelihood of survival. Nevertheless, it may affect the quality of life.

Psychological research comparing patient adaptation after mastectomy with that after breast-conservation treatment shows no significant differences in global measures of emotional distress. Research also does not reveal significant changes in sexual behavior and erotic feelings in the treated breast or nipple-areolar complex. However, women whose breasts are preserved have more positive attitudes about their body image and experience fewer changes in their frequency of breast stimulation and feelings of sexual desirability.

**Radiation Therapy Considerations**

Radiation therapy should be delivered only after evaluation of the mammography findings, the pathology findings, and the surgical procedures performed on the patient. The optimal combination of surgery and irradiation to achieve the dual objectives of local tumor control and preservation of cosmetic appearance varies from patient to patient. The optimal combination is determined by the extent, nature, and location of the tumor; the patient’s breast size; and the patient’s relative concerns about local recurrence and preservation of cosmetic appearance.

**TECHNIQUES**

A consensus exists regarding some, but not all, of the elements in the technique of irradiation. As soon as the patient has healed adequately from the surgical procedure, radiation therapy should begin. Therefore, irradiation usually can begin within 2 to 4 weeks after uncomplicated breast-conserving surgery.

The radiation oncologist should use measures to ensure reproducibility of patient set-up, treatment simulation, treatment planning, and choice of supervoltage equipment for dose homogeneity. Higher energy photons (10 MV or more) may be indicated for large-breasted women or patients with significant dose inhomogeneity (10% or more) when lower energy photons are used.

The radiation oncologist can use sophisticated treatment planning that involves three-dimensional rather than two-dimensional dose distributions and accounts for the lower density of lung tissue in the treatment field. (In standard treatment planning, the lung is considered to have unit density.) However, the impact of this recent development on patient outcomes has not been demonstrated. Currently, three-dimensional dose distributions are not considered standard.

Each field should be treated on a daily basis, Monday through Friday. A bolus should not be used. To minimize the risk of radiation pneumonitis, not more than 3.0 to 3.5 cm of lung (as projected on the radiograph at isocenter) should be treated, and a minimum of 1.0 to 1.5 cm of lung is required. For left-sided lesions, efforts should be made to minimize the amount of heart in tangential fields. Whole-breast radiation therapy is delivered using opposed tangential fields to a dose of 4,500 to 5,000 cGy at 180 to 200 cGy per fraction.

Controversy exists about the need for delivering an additional boost dose to the primary site. Several considerations may be involved in the decision to use a boost: histologic studies show that resid-
ual cancer after resection of the primary usually is near the primary site, recurrences after treatment usually are seen at or near the primary site, and boost treatment can be delivered without significant morbidity. Although boost irradiation often is used, the precise indications for its use are not well defined.

When used, boost irradiation usually is delivered using electron beam or interstitial implantation. The total dose to the primary tumor site is increased to approximately 6,000 to 6,600 cGy.

A boost may not be required for patients who have been treated with more extensive breast resections and have margins of resection that are clearly negative. If the breast boost is omitted in these patients, the only available data indicate that the standard whole-breast radiation therapy dose is 5,000 cGy at 200 cGy per fraction.

**Techniques to Avoid**

Agreement exists about the need to avoid certain radiation therapy techniques that either have no demonstrated benefit or expose the patient to excessive risk. Nodal irradiation is unnecessary, and excess dose to the heart or lungs through tangential irradiation of the breast must be avoided.

**Follow-up Care Recommendations**

Follow-up assessment of the results of breast-conservation treatment should be provided by surgeons and oncologists experienced in that treatment as outlined in this standard, and it should also evaluate the cosmetic outcome as well as the functional consequences. The goals of a regular follow-up examination include the following:

1. Early detection of recurrent or new cancer, allowing timely intervention
2. Identification of any treatment sequelae and appropriate interventions when indicated
3. Provision of the individual practice with the database necessary to optimize treatment and compare outcomes against national standards.

Regular history and physical examination in conjunction with breast imaging are the cornerstones of effective follow-up care. Unfortunately, many patients perceive history and physical examination to be less important as reliable follow-up measures than sophisticated medical testing. Routine tests such as bone scanning, chest radiography, computerized tomography (CT) scanning, and liver function tests are not indicated for asymptomatic patients treated for DCIS. A public education effort is needed to address this problem.

The evaluations outlined in the following sections should be done by the physician at the cited intervals after treatment is completed.

**History and Physical Examination**

The frequency of examination, which is based on optimal timing for identification of local recurrence and second primary tumors, is as follows:

1. Every 6 months, years 1 to 5 (some oncologists prefer every 6 months until after year 8, when the risk of local recurrence with breast-conservation treatment begins to approach the risk of contralateral breast cancer)
2. Annually thereafter

**Mammography**

A goal of follow-up imaging of the treated breast is the early recognition of tumor recurrence. To prevent unnecessary biopsy, it is important to know that postoperative and irradiation changes overlap with signs of malignancy on a mammogram. The changes include masses (postoperative fluid collections and scarring), edema, skin thickening, and calcifications.

At times, these changes may be impossible to distinguish. Postsurgical and radiation edema, skin thickening, and postoperative fluid collections are most marked in the first 6 months. For most
patients, radiographic changes slowly resolve after the first 6 to 12 months and show stability within 2 years.

The current mammogram must be compared in sequence with the preceding studies so that it can be accurately interpreted and the direction of change can be assessed accurately. The diagnostic radiologist should carefully tailor mammographic studies of the treated breast to the surgical site by using special mammographic views in addition to routine mediolateral oblique and craniocaudal views. Magnification and spot compression can be used with any view to increase detailed visualization of the site of tumor excision and other areas. Magnification radiography is useful for classifying calcifications morphologically and quantitating them. Other special views may be useful in the assessment of the breast after conservation.

As postoperative masses resolve and scars form, a spiculated mass that mimics tumor may be seen on the mammogram. Additional radiographic projections of the site of tumor removal facilitate more confident radiographic interpretations.

Schedule of Imaging of the Treated Breast
A postoperative mammogram is essential to ensure that microcalcifications have been removed in patients having breast-conservation treatment with or without irradiation. The site of the excision may be optimally evaluated with magnification radiography for residual microcalcifications if none are seen on routine views.

A baseline mammogram is done during the first year after breast-conservation treatment and at least annually thereafter or at more frequent intervals as warranted by clinical or radiographic findings.

Schedule of Imaging of the Contralateral Breast
The contralateral breast should undergo mammography annually, according to the guidelines endorsed by both the American College of Radiology and the American Cancer Society. More frequent intervals may be warranted by clinical or radiographic findings. (The risk of cancer is approximately the same for both the treated and the untreated breast.)

Evaluation of Sequelae
At the time of the first follow-up examination and serially thereafter, the physician should evaluate the patient for any treatment-related toxicities. This evaluation should include the following:

1. Assessment of the overall cosmetic result. A four-point scoring system is recommended for assessing the cosmetic result (see Table 10 of “Standards for Diagnosis and Management of Invasive Breast Carcinoma,” page 101).

2. Patient evaluation of results. The patient’s evaluation of treatment outcomes in terms of psychological, functional, and cosmetic consequences should be taken into account in the follow-up process.

Research Questions
Although great progress has been made in the treatment of early-stage breast cancer, several important questions remain unresolved. Clinical and laboratory investigations will address many of these questions in the coming years, including the following:

1. For which patients can radiation therapy safely be omitted?

2. What is the effect of age and family history on the risk of local recurrence and the risk of invasive local recurrence?

3. What new methods can be developed to determine the extent of the lesion and assess the adequacy of excision?

4. What role do biologic markers and genetic analysis play in predicting recurrence and progression to invasion?

5. What is the optimal width of mar-
gins with and without radiation therapy after surgery?
6. What is the role for tamoxifen and other chemopreventive agents?
7. Should an irradiation boost be used for patients with negative margins?
8. How best can the pathologic features of lesions be classified? Should pathologic criteria be standardized?
9. What are the interactions among various histologic factors?
10. How will stereotactic, thermal, or laser ablation affect the treatment of occult DCIS?

References
1. Winchester DP, Cox JD: Standards for breast-conservation treatment. CA Cancer J Clin 1992;42:134-162.
2. Fisher B, Costantino J, Redmond C, et al: Lumpectomy compared with lumpectomy and radiation therapy for the treatment of intraductal breast cancer. N Engl J Med 1993;328:1581-1586.
3. Fisher ER, Costantino J, Fisher B, et al: Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) Protocol B-17. Intraductal carcinoma (ductal carcinoma in situ). Cancer 1995;75:1310-1319.
4. Mamounas E, Fisher B, Dingam J, et al: Effects of breast irradiation following lumpectomy in intraductal carcinoma (DCIS): Updated results from NSABP B-17. Proc Soc Surg Oncol 1997;50:7.
5. Solin LJ, Recht A, Fourquet A, et al: Ten-year results of breast-conserving surgery and definitive irradiation for intraductal carcinoma (ductal carcinoma in situ) of the breast. Cancer 1991;68:2337-2344.
6. Solin LJ, Kurtz J, Fourquet A, et al: Fifteen-year results of breast-conserving surgery and definitive breast irradiation for the treatment of ductal carcinoma in situ of the breast. J Clin Oncol 1996;14:754-763.
7. McCormick B, Rosen PP, Kinne D, et al: Duct carcinoma in situ of the breast: An analysis of local control after conservation surgery and radiotherapy. Int J Radiat Oncol Biol Phys 1991;21:289-292.
8. Sneige N, McNeese MD, Atkinson EN, et al: Ductal carcinoma in situ: Pathologic findings from the National Surgical Adjuvant Breast Project (Protocol 6): II. Relation of local recurrence to multicentricity. Cancer 1994;30:3-9.
9. Kurtz JM, Sass R, Fisher B, et al: Pathologic, and treatment related factors affecting local recurrence following breast-conserving therapy. CA Cancer J Clin 1992;42:134-162.
10. How will stereotactic, thermal, or laser ablation affect the treatment of occult DCIS?
multicentricity, lymph node metastases, and short-term treatment failures. Cancer 1982;50:1309-1314.
25. Lagios MD: Ductal carcinoma in situ: Controversies in diagnosis, biology, and treatment. Breast J 1995;1:68-78.
26. Lagios MD: Lagios experience, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 361-365.
27. Lagios MD, Margolin FR, Westdahl PR, et al: Mammographically detected duct carcinoma in situ: Frequency of local recurrence following tylectomy and prognostic effect of nuclear grade on local recurrence. Cancer 1989;63:618-624.
28. Lagios MD: Duct carcinoma in situ: Pathology and treatment. Surg Clin North Am 1990;70:853-871.
29. Fentiman IS: Treatment of screen detected ductal carcinoma in situ: A silver lining within a grey cloud? Br J Cancer 1990;61:795-796. Editorial.
30. Spittle M, Stewart HJ: Non-surgical management of early breast cancer in the United Kingdom: Ductal carcinoma in situ. Clin Oncol 1995;7:217-218.
31. Ashikari R, Huvos AG, Synder RE: Prospective study of non-infiltrating carcinoma of the breast. Cancer 1977;39:435-439.
32. Sunshine JA, Moseley HS, Fletcher WS, et al: Breast carcinoma in situ: A retrospective review of 112 cases with a minimum 10 year follow-up. Am J Surg 1985;150:44-51.
33. Farrow JH: Current concepts in the detection and treatment, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 367-372.
34. Silverstein MJ, Cohlan BF, Gierson ED, et al: Duct carcinoma in situ: 227 cases without microinvasion. Eur J Cancer 1995;30A(Suppl 2):S33. Abstract.
35. Solin LJ, Fowble BL, Schultz DJ, et al: Definitive irradiation for intraductal carcinoma of the breast. Int J Radiat Oncol Biol Phys 1990;19:843-850.
36. Arnesson LG, Olsen K: Linkoping experience, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 373-378.
37. Fentiman IS, Julien JP, van Dongen JA, et al: Management of screen detected ductal carcinoma in situ of the female breast. Br J Surg 1989;76:564-567.
38. Cataliotti L, Distante V, Pacini P, et al: Florencce experience, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 449-454.
39. Eusebi V, Feudale E, Foschini MP, et al: Long-term follow-up of in situ carcinoma of the breast. Semin Diagn Pathol 1994;11:223-235.
40. Fisher ER, Leeming R, Anderson S, et al: Conservative management of intraductal carcinoma (DCIS) of the breast. J Surg Oncol 1991;47:139-147.
41. Salvadori B, Delledonne V, Rovini D: National Cancer Institute-Milan experience, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 427-432.
42. Shreer I: Conservative therapy of DCIS without radiation. Breast Dis 1996;9:27-36.
43. Schwartz GF, Finkel GC, Garcia JC, et al: Subclinical ductal carcinoma in situ of the breast: Treatment by local excision and surveillance alone. Cancer 1992;70:2468-2474.
44. Schwartz GF: Treatment of subclinical ductal carcinoma in situ by excision and local surveillance, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 353-360.
45. Silverstein MJ, Poller DN, Waisman JR, et al: Frequency of local recurrence following tylectomy for comedo-type intraductal carcinoma of the breast. Eur J Cancer 1994;30A(Suppl 2):S33. Abstract.
46. Solin LJ, Fowble BL, Schultz DJ, et al: Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 373-378.
47. Schnitt SJ, Harris JR, Smith BL: Developing a prognostic index for ductal carcinoma in situ of the breast. Are we there yet? Cancer 1996;77:2189-2192. Editorial.
48. Stomper PC, Margolin FR: Ductal carcinoma in situ: The mammographer’s perspective. AJR Am J Roentgenol 1994;162:585-591.

Selected Bibliography

MAMMOGRAPHIC EVALUATION

1. Dershaw DD, Abramson A, Kinne DW: Ductal carcinoma in situ: Mammographic findings and clinical implications. Radiology 1989;170:411-415.
2. Schnitt SJ, Harris JR, Smith BL: Developing a
Surgical Considerations

1. Dershaw DD, Giess CS, McCormick B, et al: Patterns of mammographically detected calcifications after breast-conserving therapy associated with tumor recurrence. Cancer 1997;79:1355-1361.
2. Fisher ER, Leeming R, Anderson S, et al: Conservative management of intraductal carcinoma (DCIS) of the breast. J Surg Oncol 1991;47:139-147.
3. Gluck BS, Dershaw DD, Liberman L, et al: Microcalkifications on postoperative mammograms as an indicator of adequacy of tumor excision. Radiology 1993;188:469-472.
4. Holland R, Hendriks JH, Veerbeek AL, et al: Extent, distribution, and mammographic/histological correlations of breast ductal carcinoma in situ. Lancet 1990;335:519-522.
5. Lee CH, Carter D: Detecting residual tumor after excisional biopsy of impalpable breast carcinoma: Efficacy of comparing preoperative mammograms with radiographs of the biopsy specimen. AJR Am J Roentgenol 1995;164:81-86.
6. Solin LJ, Fourquet A, McCormick B, et al: Salvage treatment for local recurrence following breast conserving surgery and definitive irradiation for ductal carcinoma in situ (intraductal carcinoma) of the breast. Int J Radiat Oncol Biol Phys 1994;30:3-9.

Pathologic Evaluation

1. Fleming ID, Cooper JS, Henson DE, et al (eds): Manual for Staging of Cancer, ed 5. Philadelphia, JB Lippincott, 1997.
2. Association of Directors of Anatomic and Surgical Pathology: Immediate management of mammographically detected breast lesions. Hum Pathol 1993;24:689-690.
3. Association of Directors of Anatomic and Surgical Pathology: Recommendations for the reporting of breast carcinoma. Mod Pathol 1996;9:77-81.
4. Holland R, Petere J, Millis RR, et al: Ductal carcinoma in situ: A proposal for a new classification. Semin Diagn Pathol 1994;11:167-180.
5. Patchefsky AS, Schwartz GF, Finkelstein SD, et al: Heterogeneity of intraductal carcinoma of the breast. Cancer 1989;63:731-741.
6. Poller DN, Silverstein MJ, Galea M, et al: Ductal carcinoma in situ of the breast: A proposal for a new simplified histological classification association between cellular proliferation and c-erbB-2 protein expression. Mod Pathol 1994;7:257-262.
7. Schnitt SJ, Connolly JL: Processing and evaluation of breast excision specimens: A clinically oriented approach. Am J Clin Pathol 1992;98:125-137.
8. Schnitt SJ, Silen W, Sadowsky NL, et al: Ductal carcinoma in situ (intraductal carcinoma) of the breast. New Engl J Med 1988;318:898-903.
9. Schuh ME, Nemoto T, Penetrante RB, et al: Intraductal carcinoma: Analysis of presentation, pathologic findings, and outcome of disease. Arch Surg 1986;121:1303-1307.
10. Stomper PC, Connolly JL: Ductal carcinoma in situ of the breast: Correlation between mammographic calcification and tumor subtype. AJR Am J Roentgenol 1992;159:483-485.

Selection of Treatment

1. Ernster VL, Barclay J, Kerlikowske K, et al: Incidence of and treatment for ductal carcinoma in situ of the breast. JAMA 1996;275:913-918.
2. Winchester DJ, Menck HR, Winchester DP: National treatment trends for ductal carcinoma in situ of the breast. Presented at the Annual Scientific Session of the Western Surgical Association; November 20, 1996: Portland, OR.
3. Bellamy CO, McDonald C, Salter DM, et al: Noninvasive ductal carcinoma of the breast: The relevance of histologic categorization. Hum Pathol 1993;24:16-23.
4. Farrow JH: Current concepts in the detection and treatment of the earliest of the early breast cancers. Cancer 1970;25:468-477.
5. Kinne DW, Petrek JA, Osborne MP, et al: Breast carcinoma in situ. Arch Surg 1989;124:33-36.
6. Osteen RT, Karmell LH: The National Cancer Data Base report on breast cancer. Cancer 1994;73:1994-2000.
7. Rosen PP, Senie R, Schottenfeld D, et al: Noninvasive breast carcinoma: Frequency of unsuspected invasion and implications for treatment. Ann Surg 1979;189:377-382.
8. Silverstein MJ, Cohan BF, Gierson ED, et al: Duct carcinoma in situ: 227 cases without microinvasion. Eur J Cancer 1992;28:630-634.
9. Von Rueden DG, Wilson RE: Intraductal carcinoma of the breast. Surg Gynecol Obstet 1984;158:105-111.
10. Stotter AT, McNeece M, Oswald MJ, et al: The role of limited surgery with irradiation in primary treatment of ductal in situ breast cancer. Int J Radiat Oncol Biol Phys 1990;18:283-287.
11. Winchester DP, Menck HR, Osteen RT, et al: Treatment trends for ductal carcinoma in situ of the breast. Ann Surg Oncol 1995;2:207-213.
12. Fisher ER, Costantino J, Fisher B, et al: Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) protocol B-17: Intraductal carcinoma (ductal carcinoma in situ). Cancer 1995;76:2386-2387. Letter.
13. Arnesson LG, Smeds S, Fagerberg G, et al: Follow-up of two treatment modalities for ductal carcinoma in situ of the breast. Br J Surg 1989;76:672-675.
14. Ashikari R, Huvos AG, Synder RE: Prospective study of non-infiltrating carcinoma of the breast. Cancer 1977;39:435-439.
15. Fisher ER, Sarr R, Fisher B, et al: Pathologic findings from the National Surgical Adjuvant Breast Project (Protocol 6): II. Relation of local breast recurrence to multicentricity. Cancer 1986;57:1717-1724.
16. Fourquet A, Zafra B, Campana F: Breast conserving treatment of ductal carcinoma in situ. Semin Radiat Oncol 1992;2:116-124.
17. Fowble B, Hanlon AL, Fein DA, et al: Results of conservative surgery and radiation for mammographically detected ductal carcinoma in situ (DCIS). Int J Radiat Oncol Biol Phys 1997;38:949-957.
18. Hiramatsu H, Bornstein BA, Recht A, et al: Local recurrence after conservative surgery and radiation therapy for ductal carcinoma in situ: Possible importance of family history. Cancer J Sci Am 1995;1:55-61.
19. Silverstein MJ, Barth A, Poller DN, et al: Ten-year results comparing mastectomy to excision and radiation therapy for ductal carcinoma in situ of the breast. Eur J Cancer 1995;31:1425-1427.
20. Snejö N, McNeese MD, Atkinson EN, et al: Ductal carcinoma in situ treated with lumpectomy and irradiation: Histopathological analysis of 49 specimens with emphasis on risk factors and long term results. Hum Pathol 1995;26:642-649.
21. Solin LJ, Kurtz J, Fourquet A, et al: Fifteen-year results of breast-conserving surgery and definitive breast irradiation for the treatment of ductal carcinoma in situ of the breast. J Clin Oncol 1996;14:754-763.
22. Solin LJ, McCormick B, Recht A, et al: Mammographically detected, clinically occult ductal carcinoma in situ (intraductal carcinoma) treated with breast conserving surgery and definitive breast irradiation. Cancer J Sci Am 1996;2:158-165.
23. Sunshine JA, Moseley HS, Fletcher WS, et al: Breast carcinoma in situ: A retrospective review of 112 cases with a minimum 10 year follow-up. Am J Surg 1985;150:44.
24. Zafrani B, Fourquet A, Vilcoq JR, et al: Conservative management of intraductal breast cancer with tumorectomy and radiation therapy. Cancer 1986;57:1299-1301.
25. Arnesson LG, Olsen K: Linkoping experience, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 373-378.
26. Baird RM, Worth A, Hislop G: Recurrence after lumpectomy for comedo-type intraductal carcinoma of the breast. Am J Surg 1990;159:479-481.
27. Carpenter R, Boulter PS, Cooke T, et al: Management of screen detected ductal carcinoma in situ of the female breast. Br J Surg 1989;76:564-567.
28. Cataliotti L, Distante V, Pacini P, et al: Florence experience, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 449-454.
29. Eusebi V, Feudale E, Foschini MP, et al: Long-term follow-up of in situ carcinoma of the breast. Semin Diagn Pathol 1994;11:223-235.
30. Fisher B, Costantino J, Redmond C, et al: Lumpectomy compared with lumpectomy and radiation therapy for the treatment of intraductal breast cancer. New Engl J Med 1993;328:1581-1586.
31. Fisher ER, Leeming R, Anderson S, et al: Conservative management of intraductal carcinoma (DCIS) of the breast. J Surg Oncol 1991;47:139-147.
32. Mamounas E, Fisher B, Dingam J, et al: Effects of breast irradiation following lumpectomy in intraductal carcinoma (DCIS): Updated results from NSABP B-17. Proc Soc Surg Oncol 1997;50:7.
33. Salvadori B, Delledonne V, Rovini D: National Cancer Institute-Milan experience, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 427-432.
34. Shreer I: Conservation therapy of DCIS without radiation. Breast Dis 1996;9:27-36.
35. Schwartz GF, Finkel GC, Garcia JC, et al: Subclinical ductal carcinoma in situ of the breast: Treatment by local excision and surveillance alone. Cancer 1992;70:2468-2474.
36. Schwartz GF: Treatment of subclinical ductal carcinoma in situ by excision and local surveillance, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 353-360.
37. Sibbering DM, Blamey RW: Nottingham experience, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 367-372.
38. Silverstein MJ: Van Nuys experience by treatment, in Silverstein MJ (ed): Ductal Carcinoma in Situ of the Breast. Baltimore, Williams & Wilkins, 1997, pp 443-448.
39. Silverstein MJ, Poller DN, Waisman J, et al: Prognostic classification of ductal breast carcinoma-in-situ. Lancet 1995;345:1154-1157.

**FOLLOW-UP RECOMMENDATIONS**
1. Dershaw DD, McCormick B, Osborne MP: Detection of local recurrence after conservative therapy for breast carcinoma. Cancer 1992;70:493-496.
2. Dershaw DD, Shank B, Reisinger S: Mammographic findings after breast cancer treatment with local excision and definitive irradiation. Radiology 1987;164:455-461.
3. Dershaw DD: Mammography in patients with breast cancer treated by breast conservation (lumpectomy with or without radiation). AJR Am J Roentgenol 1995;509-316.
4. Gallagher WJ, Koerner FC, Wood WC: Treatment of intraductal carcinoma with limited surgery: Long-term follow-up. J Clin Oncol 1989;7:376-380.
5. Stomper PC, Recht A, Berenberg AL, et al: Mammographic detection of recurrent cancer in the irradiated breast. AJR Am J Roentgenol 1987;148:39-43.