PRACTICE GUIDELINE FOR THE MANAGEMENT OF DUCTAL CARCINOMA IN-SITU OF THE BREAST (DCIS)

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

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American College of Surgeons
College of American Pathologists
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I.   INTRODUCTION

It is recognized that 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 there was a sufficient body of knowledge on ductal carcinoma in-situ of the breast to publish a guideline. The guideline was updated in 1997 and 2001 to reflect changes in clinical practice which occurred in response to new data.

Prior to 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, there is a limited amount of information on the natural history of DCIS on which to base treatment decisions. In addition, the majority of DCIS seen today is identified mammographically, due to the presence of microcalcifications, and it is uncertain 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 all been advocated as management strategies for DCIS. The acceptance of breast-conserving therapy for invasive carcinoma has stimulated great interest in its use for managing DCIS.

The direct extrapolation of data from randomized trials comparing mastectomy to lumpectomy and irradiation in invasive carcinoma to the patient with DCIS is inappropriate. In the patient with invasive carcinoma, the risk of metastatic disease is present at the time of diagnosis, and many distant failures occur without evidence of 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 possibility of breast cancer mortality. The goal of the therapy of DCIS is the prevention of the recurrence of either invasive or noninvasive cancer. The appropriateness of breast-conserving approaches in DCIS should be guided by the incidence of 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 and differences in the extent of mammographic and pathologic evaluation over time, as well as the long natural history of the disease.

Treatment selection for the individual patient with DCIS requires a clinical, imaging, and pathological evaluation. The term DCIS encompasses a heterogeneous group of lesions, and prior to the determination of a patient's suitability for breast conservation with or without irradiation or the necessity of mastectomy, a thorough evaluation to characterize the extent and character of the patient's disease is necessary.

II.   PATIENT EVALUATION

An adequate history and physical examination will 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 breast cancer's specific history and physical examination are listed in Tables 1 and 2 and represent information that may affect the selection of local therapy.

III.   IMAGING EVALUATION

The most common mammographic presentation of DCIS is microcalcifications. In 54 patients with DCIS undergoing needle localization, 53 of the 54 (98%) had calcifications on mammography as reported by Dershaw et al [1]. Similarly, Stomper, et al reported that 90% of their DCIS cases presented with microcalcifications [2]. Calcifications in DCIS typically are pleomorphic, varying in size, form, and density and grouped in a cluster, frequently manifesting linear or segmental arrangements, reflecting their presence in the duct. In contrast, calcifications associated with benign disease tend to be more rounded, more uniform in density, and scattered or distributed in groups [3].

Approximately 10% of mammographically evident DCIS will be without calcifications. On occasion, DCIS will be diagnosed without mammographic findings. In a retrospective, consecutive series of 190 DCIS cases, calcifications were the most common finding of malignancy (117/190, 62%), soft tissue changes other than calcifications were less common (43/190, 22%), and even fewer patients had negative mammograms (30/190, 16%). Atypical mammographic findings of DCIS included a mass (16/190, 8%), nodules or prominent ducts (16/190, 8%), or other soft tissue changes (12/190, 6%) [4].

Recent mammographic evaluation (usually within 3 months) prior to biopsy or definitive surgery is needed to establish the appropriateness of breast conservation treatment by defining the extent of a patient's disease. In addition to mediolateral oblique and craniocaudal views, if calcifications are present, magnification views should be obtained routinely. Magnifications or spot-compression magnification views increase imaging resolution for better depiction of shapes of calcifications and their number and extent [6-8].

The preoperative diagnosis of DCIS can be suggested by mammography, but a definitive diagnosis depends on pathologic evaluation of the specimen. Imaging techniques are not reliable to determine whether or not the basement membrane has been violated, and peritumoral inflammation and/or fibrosis can cause a mass to be present along with microcalcifications in the absence of invasion. The subtypes of DCIS, nuclear grade, and extent of necrosis can be suggested on the basis of characteristic patterns of calcifications, but these patterns are not diagnostic, and the definitive diagnosis depends on the analysis of tissue by the pathologist [16-17].

The mammogram may underestimate the extent of DCIS. Underestimation is increasingly likely with increasing lesion size. However, an effort should be made to determine the extent of tumoral calcifications preoperatively in all cases, and the maximal span of the calcifications should be reported. If a mass is present it should be measured. The size of low- and intermediate-grade DCIS is underestimated by 2 cm in as many as 50% of cases when only two-view mammography is performed [18,19]. The routine use of magnification views, as well as other special views as required, will significantly reduce the likelihood of this problem. The entire breast should be carefully examined to determine if areas of tumor are present elsewhere in the breast, thereby influencing a decision about breast-conserving treatment.

The contralateral breast should also be evaluated, and bilateral mammography is required. Bilateral DCIS was found in 7 (19%) of 36 women with DCIS who underwent contralateral subcutaneous mastectomy [9]. However, in a population-based study which included 18,895 patients initially diagnosed with DCIS, the incidence of contralateral breast carcinoma was only 6% at 10 years [20].

The role of other images modalities, especially MRI, has yet to be established in DCIS. Contrast-enhanced MRI is very sensitive for invasive cancers, but DCIS has nonspecific appearances and kinetic enhancement curves that can mimic fibrocystic changes and other benign findings [10-14].

Berg found that MRI was more sensitive than mammography and sonography in detecting DCIS; however, disease extent was overestimated in 50% of involved breasts [21]. Therefore, because of the lack of specificity of MRI, suspicious enhancing lesion(s) should undergo image-guided core biopsy or needle localized excisional biopsy prior to definitive surgery. The impact of MRI on clinical outcomes such as local recurrence in the preserved breast remains to be demonstrated.

Improvements in ultrasound (US) transducers have resulted in utilization of US to evaluate DCIS, especially when the presenting symptom is a palpable abnormality. Moon found that a microlobulated mass with mild hypoechogenicity, ductal extension, and normal acoustic transmission was the most common US findings in DCIS. One advantage of demonstrating DCIS on US is the ease of percutaneous biopsy [22].

IV.   SURGICAL CONSIDERATIONS

A.   Introductory Comments

When breast conservation treatment is appropriate, the goals of any surgical procedure on the breast are total removal of the suspicious or known malignant tissue 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 presenting as a palpable mass can occur but is unusual. The surgical techniques described for the evaluation and excision of palpable invasive disease apply to palpable DCIS. The most common presentation of DCIS is microcalcifications. Thus, image-directed procedures will be necessary for diagnosis and treatment.

B.   Image-Directed Biopsy

1.   Stereotactic core needle biopsy

Stereotactic core needle biopsy of the breast, performed by qualified radiologists, surgeons, or other physicians, should be utilized as the initial approach for biopsying suspicious nonpalpable mammographic abnormalities not visualized with ultrasound [15]. Ultrasound-guided biopsy is useful for nonpalpable masses and microcalcifications that can be imaged sonographically.

Not all patients with microcalcifications are ideal candidates for stereotactic biopsy. Some patients' breasts may be too small to accommodate the biopsy probe. The thickness of the breast must be adequate to allow the full throw of the device. Abnormalities just under the skin and those in extremely posterior locations may pose technical problems in some cases. Recent improvements in core needle design include shorter throw needles with smaller tissue acquisition aperture to facilitate biopsy procedures in smaller or thinner breasts and superficial lesions. Widely separated calcifications may pose difficulties with generating accurate stereotactic coordinates to guide needle biopsy. When microcalcifications are not tightly clustered or when the sensitivity or resolution of the stereotactic imaging system is such that individual microcalcifications are not well-visualized, accurate localization and retrieval of microcalcifications within core biopsy specimens may be difficult. The difficulty of the procedure will be increased with an uncooperative patient.

Other medical issues such as bleeding related to coagulation defects, patients considered at high-risk for stopping anticoagulation, inability to lie prone due to obesity, respiratory disease, or heart failure are contraindications to stereotactic core needle biopsy. Some patients with collagen vascular disorders are felt to be poor candidates

for this procedure as well. Anticoagulation has been considered a contraindication to stereotactic core biopsy, but the procedure has been safely performed on anticoagulated patients [23]. In the anticoagulated patient the choice of biopsy techniques should be made after consultation between the radiologist, the surgeon, and the physician responsible for the anticoagulation. However, for the majority of patients' image guided needle biopsy is the diagnostic procedure of choice. It is particularly useful to avoid open biopsy for calcifications too diffuse to allow breast-conserving surgery to facilitate skin sparing mastectomy [15].

For lesions amenable to stereotactic breast biopsy, multiple cores should be taken and specimen radiography performed to confirm an adequate sampling of the microcalcifications. A marker should be placed at the site of the biopsy and its location accurately validated. This is essential for guiding the surgeon and radiologist for needle localization and excision if the final diagnostic core biopsies reveal DCIS.

If a presurgical diagnosis of DCIS is made by percutaneous core needle biopsy, physicians should be aware that areas of invasive carcinoma will be found in about 10%-20% of cases at the time of surgical excision [24,25]. The risk of invasive carcinoma varies with the features of the lesion being biopsied, the type and gauge of biopsy needle used, and the number of cores obtained. Studies have shown that a preoperative core biopsy diagnosis of DCIS does not facilitate achieving negative margins compared to a diagnostic needle localization performed by experienced surgeons [26,27].

2. Wire-guided open biopsy

When surgical excision of a nonpalpable mammographically or sonographically visible lesion is required, it is conducted with presurgical localization with a guide, such as a hookwire. Any suspicious lesion detected by mammography requires presurgical localization to assure accurate removal of the abnormal area and to avoid excess sacrifice of breast tissue. Methods of localization can be by needle-hookwire, dye injection, or a combination of both. The localization should be precise and may require positioning of more than one wire. Labeled craniocaudal and 90-degree lateral films or other orthogonal views that show the hookwire should be sent to the operating room for the surgeon's orientation. Availability of 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 wires, and place the incision closest to the area of pathology to achieve the best cosmetic result (Figure 1). Placement of a radiopaque skin marker at the point of entry of the wire into the breast prior to obtaining the final radiographs of the wire position will facilitate incision placement. Tunneling should be avoided, and the skin incision should be made as close to the lesion as possible. The length of the incision should be sufficient to permit the removal of the specimen in one piece. Morcellation of the specimen should be avoided. Removal of the lesion in multiple fragments precludes margin assessment and size determination.
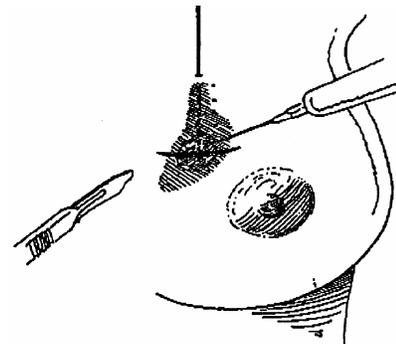
Figure 1A. Incision placement for needle localization biopsy should be over the lesion, not at the point of entry of the wire into the breast.
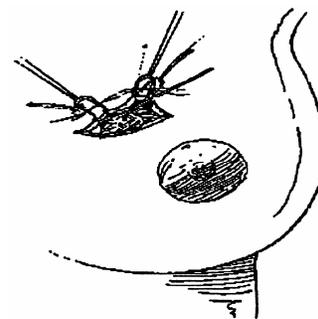
Figure 1B. The breast tissue is dissected until the wire is identified within the parenchyma, and then the wire is stabilized distally and brought into the field. Traction on the wire should be avoided at all times. *(Reprinted with the permission from Silen W, Matory EJ Jr., Love S. Atlas of Techniques in Breast Surgery. Philadelphia, PA: Lippincott-Raven; 1996:53-54.)*

Curvilinear skin incisions are preferable, but for tumors at 3 o'clock, 9 o'clock, or in the inferior breast, radial incisions may provide the best cosmesis (Figure 2). The surgeon should always place the location of the incision so that it can be easily incorporated within the mastectomy specimen if negative margins cannot be achieved with breast conservation surgery. Periareolar incisions are not appropriate for lesions in the periphery of the breast. The procedure can be readily accomplished under local anesthesia with or without intravenous sedation.
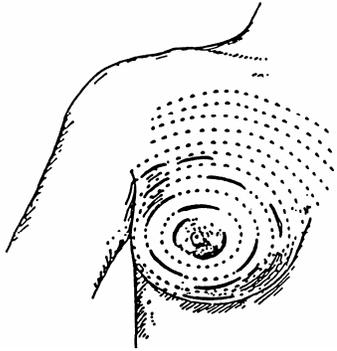
Figure 2. Recommended locations of incisions for performing breast biopsy. For larger lesions in the lower breast, a radial incision may result in better cosmesis. *(Reprinted with permission from Bland KI, Copeland EM. Indications and techniques for biopsy. In: Bland KI, Copeland EM, eds. The Breast: Comprehensive Management of Benign and Malignant Disease. Philadelphia, PA: WB Saunders; 1998:802-816.)*

Meticulous hemostasis is of critical importance. Hematoma formation produces changes that are difficult to interpret by physical examination. These changes may be long lasting and lead to unnecessary biopsy because of the difficulty in evaluation. A better cosmetic result can be expected by leaving 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. In addition, clips outlining the excision cavity may be placed to aid in the planning and executing of radiation therapy and to demarcate the tumor bed for future imaging studies.

Skin incisions should be closed with a subcuticular technique.

Intraoperative specimen radiography should be performed 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 will increase the resolution of the radiograph, and may be necessary to visualize the lesion. However these may make measurement of the distance of DCIS from the anterior and posterior margins inaccurate due to the increased compressibility of the fat relative to the tumor, rather than to any alteration of the tumor. 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, extensions of calcification (or mass) to the margin of the specimen suggest that a residual tumor might be present in the breast and that further resection along that margin may be indicated.

In cases where no lesion remains on mammography and the only guide to accurate excision is a marker previously placed at the time of core biopsy, the radiologist should confirm that the clip has not migrated. Specimen radiography should confirm inclusion of the marker in the specimen. If migration has occurred it is incumbent upon the radiologist to place the guidewire as accurately as possible into the original biopsy site. When the clip is inaccurately placed or has migrated, excision of the clip is not mandatory. This should be determined prior to surgery after consultation between the surgeon and the radiologist.

The specimen radiograph is not adequate to determine the completeness of excision. Histologically negative margins also do not guarantee complete lesion removal since DCIS may grow in a discontinuous fashion. A postoperative mammogram should be obtained to document complete removal of calcifications unless specimen radiography clearly documents complete removal of all calcifications. This postoperative mammogram can be performed as soon as the patient can tolerate compression. However, a large seroma may obscure small residual calcifications. Magnification views may show calcifications not evident on nonmagnified views. Margin status and the postoperative mammogram are complementary means of assessing the completeness of excision. If re-excision is performed for residual calcifications, specimen radiography and a postexcision mammogram should again be obtained to reassess the tumorectomy site.

C. Re-Excision of Biopsy Site

Re-excision of the previous biopsy site must be performed carefully to assure negative margins of resection, avoid

excess breast tissue removal, and achieve good cosmesis. If microcalcifications are the indication for re-excision, needle localization should be considered. Proper orientation of the original biopsy specimen will allow identification of the individual margin surfaces involved with tumor. Re-excision can be limited to these areas. When the specimen has not been oriented, removal of a rim of tissue around the previous biopsy is necessary.

D.   Management of the Axilla

By definition, DCIS is confined to the ducts. Metastases to the axillary nodes may occur when unrecognized invasive carcinoma is present. Up to 20% of patients who have DCIS diagnosed by image-guided biopsy will have invasive carcinoma identified when the entire lesion is removed [24,32], but after complete excision of the DCIS lesion unrecognized invasive carcinoma appears to be rare. This is supported by several clinical observations. Long-term survival rates of 97-99% [28-30] for DCIS patients treated by surgery alone are not compatible with a significant incidence of invasive carcinoma with nodal metastases, and in patients with DCIS who undergo an axillary lymph node dissection with conventional hematoxylin and eosin pathologic analysis, the rate of axillary metastasis is < 1% [31,76].

Axillary lymph node assessment in patients who have a diagnosis of DCIS is not routinely undertaken except in patients undergoing mastectomy. Some factors that may be associated with the presence of invasive disease include: age 55 or younger; diagnosis made with core biopsy; mammographic primary tumor size greater than 4 cm; and high-grade DCIS [34]. However, the most important factors that indicate the need for axillary lymph node assessment are the presence of a mass in association with the DCIS or a large volume of DCIS. Since sentinel node biopsy is not possible after mastectomy, its routine use is justified in patients undergoing the procedure. In patients having breast-conserving surgery, the need for axillary staging can be assessed after the DCIS is completely excised, or sentinel node biopsy can be selectively used in those felt to be at high risk for invasive carcinoma.

Sentinel lymph node biopsy should be used for assessing the axilla. This procedure can be undertaken using an injection of vital blue dye (isosulfan blue), of a radioactively labeled sulfur colloid, or both. Some reports have indicated that the identification rate is somewhat higher when both are used [35], but these rates seem to be more closely related to the experience level of practitioners with a particular modality. Thus, some institutions report excellent identification rates using blue dye alone. Nonetheless, the use of radioactively-labeled colloid can provide helpful information. If sentinel nodes are not visible on lymphoscintigraphy after injection of

the colloid, there is an increased probability that the sentinel node will not be identified [36]. While the identification rate will still be around 85%, it may be prudent to advise the patient of the possibility that an axillary lymph node dissection may be needed. On the other hand, if there are good counts detected using a percutaneous hand-held probe immediately prior to surgery, it may be possible to avoid the use of the blue dye, which has a small but significant probability of inducing anaphylactic shock or allergic skin reactions [37,38]. The disadvantages of using a radioactive colloid injection are that it is expensive and can be difficult to schedule on the same day as the surgery. It has recently been demonstrated, however, that injection of radioactive colloid can be done successfully a day prior to surgery, with no difference detected by lymphoscintigraphy in the patterns of distribution of the radionuclide in the lymph nodes [39]. An important technical detail related to success rate in sentinel node mapping is the selection of injection site. While original protocols called for intraparenchymal injections in the peritumoral area, later reports indicate that identification rates increase (significantly, in the case of radioactive colloid) when the injections are made intradermally [35,40].

Axillary node dissection is not recommended as an initial staging procedure for patients with DCIS.

V.   PATHOLOGIC EVALUATION

A.   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 to the pathologist for review while examining the specimen.

Gross examination should document the type of surgical specimen when this information is provided to the pathologists (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 them with India ink or with a multicolored inking system if the specimen has been oriented by the surgeon. In general, 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 [42,43].

Frozen section examination of image-guided needle biopsies of nonpalpable lesions or mammographically directed biopsies done for microcalcifications is strongly discouraged [44]. 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. In general, frozen sections should be prepared only when there is sufficient tissue that the final diagnosis will not be compromised (i.e., grossly visible tumors larger than 1.0 cm) and when the information is necessary for immediate therapeutic decisions.

B.   Pathologic Features Influencing Treatment Choice

DCIS has traditionally been classified primarily by architectural pattern. In this system, DCIS is divided into comedo, cribriform, micropapillary, papillary, and solid subtypes. However, this classification was developed at a time when all patients with DCIS were treated by mastectomy, and the histologic subclassification of DCIS was largely an academic exercise. With the increasing use of breast-conserving therapy for DCIS, there is a need to identify those lesions more likely to recur or progress to invasive cancer. To address this need, several classification systems have been proposed, based primarily on nuclear grade and/or necrosis [45-50]. Several studies have supported the clinical relevance of this approach, showing that high nuclear grade and/or necrosis (particularly extensive comedo necrosis) are associated with a higher risk of early local recurrence following breast conservation therapy [51,52]. Although the architectural pattern of DCIS does not correlate well with the risk of local recurrence [52], studies have shown that micropapillary subtypes tend to be more extensive [53,54]. No classification system to date, however, has been useful in predicting whether local disease is likely to recur as in-situ or invasive carcinoma.

A consensus conference on the classification of DCIS was convened in 1997. Although a single classification system for DCIS was not endorsed at this meeting, it was recommended that the pathologist should clearly report the nuclear grade of the lesion and the presence or absence of necrosis and cell polarization. Because of the recognition of the importance of nuclear grade, this was defined in detail in the consensus document [55]. If a specific grading system for DCIS is used, it should be stated in the pathology report. The report also should include the architectural patterns present, since this may have clinical relevance (e.g., the micropapillary pattern may be more prone to multiple quadrant involvement, independent of nuclear grade) [53,54].

A few recent studies have addressed the issue of consistency among pathologists in categorizing DCIS using the newer classification systems [51,56-59]. In general, greatest consistency is achieved using classification systems based primarily on nuclear grade.

Knowledge of the extent (size) of DCIS is important in deciding treatment, but in contrast to most invasive cancers, measuring the size of DCIS is difficult because it is usually nonpalpable and cannot be identified grossly. While a precise measurement of size 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: 1) directly measuring the size of the lesion when 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 (2-3 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 in the pathologic evaluation of breast tumor excisions in patients with DCIS 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 from the nearest margin.

In contrast to DCIS, lobular carcinoma in situ (LCIS, lobular neoplasia) is an incidental histologic finding that is considered a marker of increased risk for subsequent breast cancer rather than a malignant lesion requiring surgical excision. This increase in risk applies to both breasts and is probably lifelong. The relation between LCIS and surgical margins is not important. The management of patients with recently recognized histological variants of LCIS (such as pleomorphic LCIS) has not been defined due to lack of information about the natural history of such lesions.

Data from the NSABP B24 trial indicate that the addition of tamoxifen to local excision and radiation decreases the risk of local recurrence [60]. Furthermore, a recent analysis of DCIS lesions from a subgroup of patients in that trial suggested that the benefit of tamoxifen in reducing the local recurrence risk in this setting is limited to patients in whom the DCIS is estrogen receptor positive [61]. Therefore, some clinicians now routinely request that estrogen receptor assays be performed on newly diagnosed cases of DCIS. At the present time, there is no clinically documented role for the routine assessment of progesterone receptor, HER2 protein, or any other biomarker in DCIS.

C. The Pathology Report

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

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 or 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.

The use of a synoptic report summarizing key features such as tumor size, grade, and margin status in a list is highly recommended [55].

VI.   SELECTION OF TREATMENT OPTIONS

A. Introduction

It is the collective responsibility of the surgeon, pathologist, radiation oncologist, and radiologist to integrate all available data in order to clearly articulate treatment options and recommendations to the patient. The treatment team must decide, on the basis of imaging studies, the physical exam, and the pathology report, whether the patient is a candidate for a breast-conserving approach. If so, further discussion regarding the issue of local recurrence must be conducted. 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 small. Finally, patients need to understand the excellent prognosis for this disease with either surgical approach**.**

B. Supporting Literature

1. Mastectomy

There have been no prospective randomized trials comparing the treatment of DCIS by mastectomy versus breast conservation. Studies from single institutions, including patients with both clinically evident and mammographic

DCIS, indicate that 1% to 2% of patients treated by mastectomy will relapse, either regionally or systemically, presumably due to the presence of unrecognized foci of invasive tumor in the breast (see Table 3). Thus, while mastectomy results in cure rates approaching 100%, this may be overtreatment for many patients with DCIS, particularly those with small, mammographically detected lesions.

2. Breast-conserving surgery and radiation therapy

a. Prospective randomized clinical trial data

In 1985, the National Surgical Adjuvant Breast Project (NSABP) began protocol B-17, a prospective randomized study to evaluate the worth of postoperative radiation therapy following lumpectomy for patients with DCIS. The initial clinical and pathologic results were published in 1993 and 1995 [62,63].

In 2001, the results on the 813 patients in NSABP B-17 were updated [64]. Eighty percent of patients had lesions detected by mammographic screening. Negative margins, defined as tumor-filled ducts not touching ink, were required. For this 12-year analysis, the median follow-up time was 129 months.

The 12-year cumulative incidence of ipsilateral breast tumor recurrences (IBTR) was reduced by 58% with the use of breast irradiation. The 12-year cumulative incidence of invasive recurrence was 17% in the nonirradiated group compared to 8% in the irradiated group (p<0.01). The 12-year cumulative incidence of recurrent DCIS was also significantly reduced, from 15% in the group with no radiation compared to 8% in the irradiated group (p<0.01). The overall 12-year survival rate did not differ between groups: 86% for patients treated by lumpectomy alone and 87% for lumpectomy and radiation therapy (RT).

The impact of pathologic features on IBTR was reported for a subset of 623 patients in NSABP B-17 with 8-year follow-up [65]. The cumulative frequency of IBTR was 137 (22%) for all 623 patients. Ninety-four of 303 (31%) occurred in the lumpectomy-only group and 43 of 320 (13%) in those receiving RT. This represented a 61%

relative reduction in IBTR for patients receiving RT (log rank test, p<0.0001).

Nine pathologic features were examined for prognostic significance, and only moderate to marked comedonecrosis was an independent predictor for IBTR in both irradiated and nonirradiated patients. RT reduced the 8-year risk of recurrence in the breast from 40% to 14% in patients with moderate or marked comedonecrosis. Patients with absent or slight comedonecrosis experienced a decrease in local recurrence from 23% to 13% with RT. Of note, in irradiated patients comedonecrosis was not a predictor of an increased risk of breast recurrence. Margin status was not found to be a significant predictor of recurrence in this study, but it is likely that the definition of a negative margin which was used (tumor-filled ducts not touching ink) and the lack of postexcision mammograms resulted in some patients with significant residual DCIS being included in the "negative" margin group. For the "most favorable" group in the study, those with negative margins and absent or slight comedonecrosis, the addition of RT to excision resulted in a 7% absolute reduction in local failure at 8 years [65].

Of the 818 patients in the B17 trial [66], only 14 had died of breast cancer with a mean follow-up of 90 months. Three deaths occurred after IBTR, 3 in patients who developed regional failure without recurrent breast tumor, 2 in patients who developed invasive contralateral breast cancer, and 6 in patients who developed distant metastases without locoregional failure. These findings indicate that even the most meticulous local control in the breast will not eliminate all breast cancer mortality in patients diagnosed with DCIS.

Two additional prospective randomized trials have examined the role of RT in DCIS. The European Organization for Research and Treatment of Cancer (EORTC) trial enrolled 1,002 patients between 1986 and 1996 [68]. Mammographic lesions were present in 71% of the study population. The U.K. Coordinating Committee on Cancer Research trial included 1,701 patients who were entered into a 2x2 factorial designed trial testing both RT and tamoxifen. Individual institutions were allowed to select which of the randomizations they would participate in (RT versus no RT, tamoxifen vs. none), introducing potential imbalances in the treatment arms [67]. Both trials showed that the use of RT reduces ipsilateral breast tumor recurrence by approximately 50%, with both invasive and DCIS recurrences being reduced by a similar proportion. In irradiated patients, the risk of an invasive recurrence is 0.5% to 1.0% per year. In the EORTC trial, the impact of the grade of the DCIS lesion on the risk of invasive recurrence was examined, and there was no evidence that high-grade DCIS was more likely to recur as invasive carcinoma [78] than low-grade DCIS. No survival benefit was seen for RT.

b. Retrospective series data

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

The long-term results of conservative surgery and radiation for ductal carcinoma in situ were reported by Solin et al [69]. This collaborative study of 10 institutions in the United States and Europe analyzed outcome in 259 patients. Seventy-eight percent of the tumors were detected solely by mammography. The 10-year actuarial risk of breast recurrence was 16%, and the 10-year actuarial cause specific survival was 97% [69]. 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 [70].

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 whom mastectomy may be recommended. One factor for which there appears to be agreement in terms of its association with a high risk of recurrence is the presence of residual malignant-appearing calcifications on a postbiopsy mammogram. Failure to remove these calcifications prior to radiation has resulted in a 100% recurrence rate in the few patients reported [73,74]. DCIS presenting as a bloody nipple discharge was noted in earlier series to be associated with a

higher risk of recurrence. However, in the collaborative study, there appeared to be no increased risk in this group of patients [76].

Young age (<40 years) appears to be associated with an increased risk of local recurrence after breast- conserving surgery. In the EORTC study, age less than 40 years was associated with a hazard ratio of 2.14 (95% CI 1.17-3.91) for local recurrence in multivariate analysis [78] The effect of age on local failure was analyzed in NSABP B24, a prospective randomized study of 1,804 women with DCIS. All patients received radiotherapy and were randomized to tamoxifen 20 mg daily for 5 years or placebo [60]. Negative margins were not required. The rate of ipsilateral breast recurrence in women age 49 or less in the placebo arm was 33.3 per 1,000 per year, compared to 13.03 per 1,000 per year for those ages 50 and older. For those taking tamoxifen, recurrence rates were 20.77 per 1,000 per year for those ages 49 and under, and 10.19 per 1,000 per year for those in the older age group. These studies do not mean that young age is a contraindication to breast- conserving therapy, but they do indicate the need for careful attention to the completeness of the surgical excision. RT and tamoxifen will have greater benefit in very young women due to the higher baseline risk of local recurrence.

Controversy exists regarding the impact of a positive family history of breast cancer on the risk of local recurrence. Two series [73,80] have reported a higher breast recurrence rate (approximately 40%) in women with a positive family history when compared with those with no such history (approximately 10%). However, a third series found no such association [77]. The impact of 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 initially suggested that high-grade or comedo DCIS was associated with a higher breast recurrence rate [69,80]. 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=.15) [69]. The median interval to recurrence for comedo DCIS was 3.1 years versus 6.5 years for the noncomedo DCIS. Therefore, series with shorter follow-up tend to underestimate the number of recurrences in low-grade or noncomedo DCIS, and recurrences in the high-grade or comedo DCIS predominate. As previously discussed, NSABP B17 found that the presence of comedonecrosis was not a predictor of breast recurrence when RT was given [24].

The majority of breast recurrences in patients undergoing conservative surgery and radiation for DCIS occur in the vicinity of the primary tumor, and approximately 50% are invasive cancers [69,70,74, 80,84,85]. Invasive recurrences appear at later intervals than noninvasive ones and may occur in a separate quadrant [60,76,87]. Virtually all patients who develop a noninvasive recurrence, and approximately 75% of those with an invasive recurrence, are long-term survivors after mastectomy [73,74,80,84-88].

Over the last 15 years, there has been a significant change in the method of detecting DCIS. Approximately 85% of all DCIS is now detected solely as a mammographic finding, which is most often characterized by the presence of microcalcifications. The earlier reports of conservative surgery and radiation for DCIS do not accurately reflect outcome for mammographically detected DCIS since 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 used for comparisons with those of conservative surgery alone for mammographically detected DCIS and not infrequently claimed to be equal. The NSABP B24 trial [60] prospectively documented that the risk of local failure for clinically evident DCIS was approximately twice that of mammographically detected DCIS, as did the EORTC study [78].

The results of conservative surgery and radiation for mammographically detected DCIS are presented in Table 5. The 10-year

actuarial breast recurrence rate ranges from 6% to 23%, with a 10-year cause-specific survival of 96%-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. There is increasing evidence that wide surgical excision [74] and negative margins of resection diminish the risk of a breast recurrence in patients with mammographically detected DCIS treated with conservative surgery and radiation [60,74,76]. In the collaborative study with a median follow-up of 9.3 years, the crude breast recurrence rate was 29% for patients with a close or positive margin compared with 7% for those with negative margins [76]. In NSABP B24 [60], patients with positive margins had a significantly higher rate of breast recurrence than those with negative margins, regardless of whether tamoxifen was given (RR 1.68, 95% CI 1.20-2.34).

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, < 2.5 cm negative margins, and negative post-biopsy mammogram) [76,77]. In these two studies, there have been no breast recurrences in the 37 patients reported to date (median follow-up 4.9 and 9.3 years). In comparison, Lagios reported a 17% breast recurrence rate in 78 such patients treated by excision alone with a follow-up of 10.3 years [89].

3. Accelerated partial breast irradiation

Accelerated partial breast irradiation (APBI) is an alternative RT treatment option that has been utilized in highly selected patients treated with breast conservation therapy (BCT) for nearly a decade. The primary advantage of this treatment approach is the reduced time required to deliver post-lumpectomy RT (generally from 6.5 weeks to 5 days or less). The most commonly utilized techniques to deliver APBI include catheter based interstitial brachytherapy, balloon brachytherapy catheter, or 3D conformal external beam irradiation [90-93]. Regardless of which technique is employed, the scientific justification for APBI is that the vast majority of recurrences after standard BCT occur in the vicinity of the tumor bed. As a result, it is believed that limiting

RT to a 1-2 cm rim of breast tissue around the lumpectomy cavity may be adequate to eliminate residual disease in the breast after surgery in certain patients. Since the volume of breast tissue that receives a tumoricidal dose of RT is significantly reduced when APBI is utilized, it is possible (radiobiologically) to safely increase the dose per fraction and, as a result, complete adjuvant RT in a significantly shorter period of time.

To date, most of the experience with APBI has been limited to those patients with invasive breast cancer and highly selected tumors. Although 5-year results with APBI have generally been quite good, data are limited and longer-term follow-up is minimal [90]. The most commonly utilized technique of APBI with the longest follow-up has been catheter-based interstitial brachytherapy. More recently, newer techniques that are more patient and physician friendly have been developed and the interest in APBI has as a result increased dramatically [91]. Several phase III trials exploring the efficacy of APBI have recently been started in both the United States and Europe. At the present time, patients with invasive or noninvasive breast cancer undergoing BCT and interested in APBI should be made aware of the status of data exploring this treatment approach and given the option of participation in these important phase III studies. Recently, the NSABP and RTOF opened a phase III trial (NSABP B-39/RTOG 0413) comparing the efficacy of APBI with standard whole breast RT. Data from this trial will be critical in helping to determine the long-term efficacy of APBI and the patients most suitable for its application.

4. Breast-conserving surgery alone

Results of breast-conserving surgery (BCS) alone for DCIS are available from prospective randomized clinical trials, prospective single-arm studies, and retrospective, single-institution analyses (Table 6). The results from the randomized clinical trials [64,66,68,94] and from retrospective studies in relatively unselected patients [78,95-102] indicate an ipsilateral breast tumor recurrence rate of 2-3% per year or about 10-15% at 5 years and 20-30% at 10 years.

Attempts have been made to incorporate various clinical or pathologic factors into a prognostic index to identify patients who could be managed by BCS alone. One such index is the Van Nuys Prognostic Index (VNPI), which assigns a score of 1, 2, or 3 for histologic type, width of the

surgical margin, and size of the lesion [100]. DCIS with low VNPI scores are said to be suitable for excision alone; those with intermediate scores (5 to 7) require the addition of radiation therapy; and those with high scores require mastectomy. Although such a simplification of the decision-making process is attractive, this index has a number of limitations. It was developed using retrospective data on 254 patients and was "validated" using retrospective data on a small series of 79 patients from another institution. The use of any classification system is dependent on the reproducibility of the individual components. However, the histologic classification scheme and method of tumor measurement used in this score are not universal, or even in routine use. The potential problems in duplicating these elements have been discussed in detail by Schnitt et al [104]. Also important is the fact that the patients used to develop this index were treated over a large time span from 1972 to 1995 with treatment by excision alone used in more recent years and treatment with excision and irradiation used more commonly in the prior years. Therefore, it is likely that the low rate of local recurrence seen after excision alone may be due to improvements in mammographic and pathologic evaluation as well as in surgical approach. For example, Hiramatsu et al [80] reported that incidence of local recurrence 6.5 years after excision and irradiation decreased from 12% to 2% when patients treated between 1976 and 1985 were compared to those between 1985 and 1995, although radiation technique did not change. Independent attempts to validate the VNPI have not been successful [106,107]. The VNPI has subsequently been modified to include patient age, with age cutoffs of less than 40 (score 3), 40 to 60 (score 2), and greater than 60 (score 1). In a retrospective analysis of 538 patients treated with breast-conserving therapy, those with the lowest VNPI score (4, 5, or 6) were not found to benefit from breast irradiation [107]. Like the original VNPI, this classification system has not been prospectively validated by another group. For all these reasons, the VNPI is not an appropriate substitute for an individualized assessment of the risks and benefits of the available treatment options for DCIS.

Most recently, Silverstein et al have suggested that when DCIS is excised with a margin width of 1 cm or greater, local recurrence is very low, even without irradiation [108]. All of the concerns about generalizability of the VNPI system to other centers also apply to this hypothesis, and two prospective studies have failed to validate this hypothesis [109,110].

There are two observations after the use of BCS alone for DCIS. One is that the addition of radiation therapy has not been found to result in an improvement in survival, and any large improvement in survival is unlikely. Secondly, while tamoxifen has been found to further improve the results when added to excision and irradiation [60], it has not been found to improve results when added to BCS alone [64].

A detailed discussion of the pros and cons of the various options is needed to allow each woman with DCIS to make an informed treatment choice. BCS alone may be an appropriate treatment for selected older women with small (less than 1 cm), low-grade DCIS with clearly negative margins; however, the efficacy of this approach has not been fully established (Table 6).

5. The role of tamoxifen in DCIS

The role of tamoxifen was addressed in the NSABP B24 trial [60] in which 1,804 women with DCIS were treated with excision and radiation and randomized to tamoxifen 20 mg daily for 5 years or placebo. Neither negative margins nor estrogen receptor (ER) determination were required for study entry. After a median follow-up of 82 months, tamoxifen reduced the total number of breast cancer events by 37% (p=.1). This included a 47% reduction in invasive breast cancer events (p=.001) and a 31% reduction in any ipsilateral breast cancer events (p=.02). As anticipated from other studies of tamoxifen, there was a 47% reduction in contralateral breast cancer events. This translates into an absolute reduction in breast cancer events from 17% to 10%. Tamoxifen was found to reduce the risk of recurrence in patients with both positive and negative margins. However, even with tamoxifen there were fewer local failures (12.5 per 1,000 per year) in the group with negative margins than in the group with positive margins (17.4 per 1,000 per year), emphasizing the importance of complete surgical excision [60].

The well-documented side effects of tamoxifen were again observed in this study. These included an increase in endometrial carcinoma from 0.45 to 1.53 per 1,000 per year in the tamoxifen group and an increase in deep-vein thrombosis from 0.2% to 1.0%. No pulmonary

emboli were reported. Hot flashes were noted in 69.6% of tamoxifen patients and 59% of the placebo group. In this study, the reductions in ipsilateral breast tumor recurrence were less than those observed for invasive cancer. This may in part be due to the inclusion of patients with both ER positive and ER negative DCIS in the NSABP B24 study. A subset analysis in 626 of the 1,840 trial participants in whom ER could be assessed has been conducted [61]. In the 77% of patients who were ER positive, a 59% reduction in all breast cancer events was observed compared with the 37% reduction seen in the group as a whole. No benefit for tamoxifen was seen in the small group of ER negative patients. A second trial performed by the UK Coordinating Committee on Cancer Research [67] has examined the effect of tamoxifen with and without radiotherapy in women with DCIS.

Overall, the incidence of new breast cancer events in women receiving tamoxifen was 14% compared to 18% in those who did not take the drug. (Hazard ratio 0.83, 95% confidence interval 0.64-1.06, p=0.13.) In the subset of 1,053 patients not receiving radiotherapy, the incidence of breast cancer events was 12% in the tamoxifen arm and 15% in the no tamoxifen arm. This trial did not require ER measurement for entry, and the 2X2 factorial design which allowed patients and physicians to choose which randomizations in which to participate may have resulted in imbalances in the treatment arms. Taken together, these studies indicate that tamoxifen provides a modest reduction in the risk of both ipsilateral and contralateral breast cancer events in women with DCIS, and that the reduction appears to be limited to those with ER positive DCIS. It is not a mandatory part of treatment, but the risk/benefit ratio should be considered for each patient. Women undergoing breast-conserving therapy, premenopausal women, and postmenopausal women without a uterus are likely to achieve the greatest benefit from tamoxifen, as are women felt to be at high risk of local failure. Tamoxifen appears to have little impact in preventing recurrence following lumpectomy without RT.

C. Treatment Options

1. Indications for mastectomy
   Although many women with DCIS are candidates for breast-conserving treatment with or without irradiation, there are some patients for whom mastectomy is clearly indicated. These include:

   a. Women with two or more primary tumors in the breast or with diffuse malignant-appearing microcalcifications.
   b. Women with persistent positive margins after reasonable surgical attempts.

   In addition, there are some women for whom the risk/benefit ratio of breast conservation must be carefully assessed and consideration 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, particularly in a young patient. This is especially true in the patient with a small breast in which an adequate resection would result in a significant cosmetic alteration unacceptable to the patient.

2. Indications for breast-conserving surgery and radiation therapy

   DCIS detected mammographically or by physical exam that is localized (without evidence of gross multicentricity or diffuse malignant calcifications) is an indication for breast-conserving surgery and radiation therapy. The size of the DCIS lesion does not constitute an absolute contraindication to breast-conserving therapy, especially in view of the difficulties in measuring DCIS and the absence of a uniform technique of measurement. However, a relative contraindication is the presence of a large area of DCIS in a small breast in which an adequate resection would result in significant cosmetic alteration.

   For mammographically detected DCIS presenting as microcalcifications, all malignant calcifications must be removed prior to the initiation of radiation. Negative margins of resection are important to minimize the ipsilateral breast recurrence rate in patients with DCIS.

   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), prior therapeutic radiation to the breast and/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. However, pregnancy does not mandate mastectomy for all women with

DCIS. The long natural history of DCIS suggests that for some women, excision during pregnancy with radiation delayed until after delivery is an appropriate approach. In the absence of definitive data, these decisions must be undertaken on a case-by-case basis, taking into account the extent and grade of DCIS, the time interval until delivery, and the patient's wishes.

3. 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 unknown. Three randomized trials have demonstrated risk reduction with radiation for all subgroups of DCIS patients studied, but for some groups the absolute benefit of radiation is very small. The patient's attitude toward risks and benefit should play a major factor in the decision to omit radiation in these cases. Ongoing studies will further clarify this issue, and patients desiring excision alone should be encouraged to participate.

D. 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 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. A number of factors should be considered:

1. Long-term survival.
2. The possibility and consequences of local recurrence.
3. Psychological adjustment (including the fear of cancer recurrence and attitudes toward radiation), cosmetic outcome, sexual adaptation, and functional competence.

For most patients, the choice of mastectomy with or without reconstruction or breast conservation treatment does not impact on the likelihood of survival, but it may have a differential effect on the quality of life. Psychological research comparing patient adaptation following mastectomy and 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 and 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.

Psychological research also indicates that many women with DCIS greatly overestimate their risk of breast cancer recurrence and death and experience levels of anxiety similar to those of women with Stage 1 and 2 invasive carcinoma. A recent study of the patient's role in the treatment decision making process in DCIS found that mastectomy was recommended to only 15% of women with DCIS, approximately half of whom had contraindications to breast-conserving surgery. However, a significant number of women chose to undergo mastectomy because of concerns about recurrence or radiotherapy [72]. An important part of the counseling process in DCIS is to emphasize that regardless of the type of local therapy chosen, the risk of breast cancer death is small.

VII. 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.

A. Elements in the Technique of Irradiation

There is a general consensus 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 and has been able to undergo mammography with magnification views to exclude the presence of residual calcifications when indicated, radiation therapy should begin. Therefore, irradiation usually can begin within 2 to 4 weeks of uncomplicated breast-conserving surgery.

The radiation oncologist should use measures to assure reproducibility of patient set-up, treatment simulation, treatment planning, and choice of supervoltage equipment to assure dose homogeneity. The tumor bed, surrounding tissue, and most of the ipsilateral breast are encompassed in paired tangential photon fields. Higher energy photons ($\geq$10 MV) may be indicated for very large-breasted

women or patients with significant dose inhomogeneity of ≥10 % on treatment planning using lower energy photons.

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.

Each field should be treated on a daily basis, Monday through Friday. Bolus should not be used. In order to minimize the risk of radiation pneumonitis, not more than 3-3.5 cm of lung (as projected on the radiograph at isocenter) should ordinarily be treated, and a minimum of 1-1.5 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 4,500-5,000 cGy at 180-200 cGy per fraction.

Controversy exists concerning the need for delivering an additional boost dose to the primary site. Several considerations may be involved in the decision to use a boost: histological studies show that residual cancer following resection of the primary usually is in the vicinity of the primary site; recurrences following 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 6,000-6,600 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.

B. Techniques to be Avoided

There is agreement on the need to avoid certain radiation therapy techniques that either have no demonstrated benefit or expose the patient to excessive risk.

1. Nodal irradiation is unnecessary for patients with DCIS.
2. Excess dose to the heart or lungs through tangential irradiation of the breast must be avoided.

VIII. 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 guideline, 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 where 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 scans, chest X-ray, CT scans, and liver function tests are not indicated for asymptomatic patients treated for DCIS.

The following evaluations should be performed by the physician at the cited intervals following the completion of treatment:

A. Examinations and Mammography

1. History and physical examination

Examination frequency is directed toward identifying local recurrence and new second primary tumors.

a. 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.)
b. Annually thereafter. Annual follow-up after surgical recovery may also be appropriate for patients treated by mastectomy due to the extremely low risk of local recurrence.
c. Many patients with DCIS are treated by a team of physicians. It is not necessary for each physician to see the patient at 6 month intervals provided that good communication between providers is maintained.

2. 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.

Postsurgical and radiation edema, skin thickening, and postoperative fluid collections will be most marked in the first 6 months. For most patients, radiographic changes will slowly diminish after the first 6-12 months and will demonstrate stability within 2 years [111-115].

In order to interpret the mammograms accurately and assess the direction of change, the current mammogram must be compared in sequence with the preceding studies. 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 will facilitate more confident radiographic interpretations.

3. Schedule of imaging of the treated breast

A postoperative mammogram should be obtained to document complete removal of calcifications unless specimen radiography clearly documents complete removal of all calcifications. 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 should be performed during the first 6-12 months following breast conservation treatment. A mammogram should be performed at least annually thereafter, or at

more frequent intervals as warranted by clinical or radiographic findings.

4. Schedule of imaging of the contralateral breast

A mammogram should be performed 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 untreated breast.)

B. 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:

1. Assessment of the overall cosmetic result. A four-point scoring system is recommended for assessing the cosmetic result (Appendix A).
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.

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APPENDIX A

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FOUR-POINT SCORING SYSTEM OF BREAST COSMESIS

Excellent
Treated breast almost identical to untreated breast.

Good
Minimal difference between the treated and untreated breasts.

Fair
Obvious difference between the treated and untreated breasts.

Poor
Major functional and esthetic sequelae in the treated breast.

TABLE 1: Elements of the Breast Cancer Specific History

- Family history – Relatives with breast cancer, age at diagnosis, bilaterality, ovarian carcinoma, and other malignancies.
- History of prior therapeutic irradiation involving breast region.
- History of collagen vascular disease – type, documentation of diagnosis.
- Presence of breast implants – submammary or sub-pectoral.
- Date of last menstrual period, possibility of pregnancy, use of hormone replacement therapy, oral contraceptives, or fertility and gynecologic surgeries.

TABLE 2: Elements of the Breast Physical Exam

- Tumor size (measured) and location, if palpable
- Nipple discharge – Discharging duct, guaiac positive or negative
- Nipple appearance – eczema, discoloration
- Ratio of breast size to tumor size
- Axillary node status – size, mobility
- Supraclavicular nodes
- Opposite breast and axilla
- Nipple discharge – spontaneous versus induced, color.

TABLE 3:   Results of Treatment of DCIS with Mastectomy

Author	No. of Patients	Follow Up	% Nonpalpable	No. of Recurrences
Ashikari et al [116]	92	11 yrs (max)	0	0
Sunshine et al [117]	68	10 yrs (min)	0	0
Farrow [118]	181	5-20 yrs	0	2
Silverstein et al [119]	228	7 yrs (median)	80	2
Von Rueden & Wilson [120]	45	Not stated	7	0
Lagios [51]	42	Not stated	60	0
Kinne et al [28]	101	11.5 yrs (median)	59	1
Schuh et al [121]	51	5.5 yrs (mean)	33	1
Arnesson et al [122]	28	77 months	100	0

TABLE 4: Results of Conservative Surgery and Radiation for Clinically and Mammographically Detected DCIS

	Number of Patients	% Crude Breast Recurrence	5-yr Cause Specific Survival	Median Follow-up Years
McCormick et al [73]	54	18	100	3
Haffty et al [82]	60	7	100	3.6
Kurtz et al [83]	47	4	100	5
Ray et al [84]	56	9		5
Solin et al [87]	51	10		5.7
Van Zee et al [75]	65	10		6.2
Hiramatsu et al [81]	76	9	100	6.2
Sneige et al [74]	49	10		7.2
Fourquet et al [85]	153	16		9
Collaborative Group [69,70]	268	17	97	10.3
Amichetti et al [124]	139	9	100	6.8
Beron et al [125]	185	16	99	7.5
Mirza et al [126]	87	13	99	11.0

TABLE 5:   Results of Conservative Surgery and Radiation for Mammographically Detected DCIS

	No. of Pts.	Actuarial Breast Recurrence %			Cause-specific Specific Survival %			Median Follow-Up Years
		5 yr	8 yr	10 yr	5 yr	8 yr	10 yr	
NSABP B17 [63,65]	411	10	12.1			96		7.5 mean
Kuske et al [80]	44	7						4
Fowble et al [77]	110	1		15	100		100	5.3
Kestin et al [79]	146	8.0		9.2	100		99.2	7.2
Hiramatsu et al [81]	54	2		23			96	6.2
Sniege et al [74]	31	0		8				7.2
Silverstein et al [86]	33*	7		19			97	7.8
Collaborative Group [69,70]	110	7		14	100		96	9.3

*89 mammo detected

Table 6: Results of BCS Alone by Study Type

	Study Type	# Pts	Median FU	Margin Width	IBTR	Invasive IBTR	DCIS IBTR
NSABP B-17 [64,66)	RCT	403	129 mos	No DCIS on Ink	32% a 12 yrs	17%	15%
EORTC 10853 [68]	RCT	500	51 mos	'complete excision'	16% at 4 yrs	8%	8%
UK/ANZ [67]	RCT	508	53 mos	No DCIS on ink	14% at 5 yrs	6%	7%
Dana-Faerber/ Harvard	PROS	157 (grade 1,2)	40 mos	1 cm	12.5% at 5 yrs	31% of Total	69% of Total
Nottingham	PROS	256	86 mos	1 cm	11% (crude)	64% of Total	35% of Total
Silverstein et al	RETRO	93	72 mos	1 cm	3% at 8 yrs	NA	NA

IBTR = Ipsilateral breast tumor recurrence;   NA = not available; RCT = randomized clinical trial; PROS = prospective trial; RETRO = retrospective study

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