

Breast Conservation Surgery Using Nipple-Areolar Resection for Central Breast Cancers

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Hypothesis: Resection of the nipple-areolar complex (NAC) for central breast cancers that involve the nipple or areola, with postoperative radiation therapy, adheres to the oncologic principles established for breast conservation surgery of other breast cancers. Good or excellent cosmetic results can be achieved. The rate of ipsilateral breast recurrence will be similar to that seen with peripheral breast cancers. The indications for breast conservation surgery can be safely extended to include patients with breast cancers that involve the NAC.

Design: Retrospective medical record review; follow-up patient questionnaire.

Setting: Community teaching hospital.

Patients: Fifteen patients, aged 46 to 88 years, whose central breast cancers involved the NAC precluding preservation of the NAC.

Interventions: Nipple-areolar complex resection, postoperative radiation therapy.

Main Outcome Measures: Ipsilateral breast recurrence, survival, cosmesis.

Results: Ten patients had subareolar cancers that directly involved the nipple or areola; 5 patients had Paget disease of the nipple. Average tumor size was 1.6 cm (range, 0.2-3.5 cm). With a mean follow-up of 32 months (range, 4-109 months), there has been only 1 recurrence (7%), which was treated successfully by modified radical mastectomy. All 15 patients are alive and free of disease. Cosmetic results are satisfactory to excellent, as judged by both the patients and the surgeons.

Conclusions: Nipple-areolar complex resection for central subareolar cancers that directly involve the NAC, as well as for Paget disease of the nipple, extends the indications for breast conservation in other areas of the breast, and with acceptable cosmesis.

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BREAST-CONSERVING SURGERY combined with radiation is now well established as the preferred local-regional treatment for a majority of patients with early stage (American Joint Committee on Cancer stage 0, stage I, and stage II) breast cancers. Properly selected patients can expect equivalent long-term survival from the disease, yet avoid mastectomy with all the negative physical and psychological aspects of that more radical, ablative procedure. Not all patients, however, are considered appropriate candidates for a breast-conserving approach. One such group, patients whose breast cancers directly involve the nipple or areola (including those with Paget disease of the nipple), is usually excluded from breast-conservation therapy and continues to be treated with mastectomy. Breast-conserving surgery for this group of patients requires resection of some or

all of the nipple-areolar complex (NAC) for complete tumor excision. Resection of the NAC has been rejected by many surgeons because of a purported higher incidence of multifocality and multicentricity associated with central breast cancers, both intraductal and invasive cancers.¹⁻⁸ In

See Invited Critique at end of article

addition, many feel that resection of the NAC will lead to unacceptable cosmesis (historically, most often judged by the surgeon).⁹ As a result of these concerns, women with central breast cancers were ineligible, and thus excluded from the large prospective randomized studies of breast-conserving surgery that definitively established breast conservation as an equivalent option (in terms of survival) in the 1980s and 1990s. Foremost among these studies in the United States was the

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National Surgical Adjuvant Breast and Bowel Project B-06 study, which specifically did not include patients with central tumors that involved the NAC for study of breast conservation.¹⁰ Consequently, reliable long-term results of breast-conserving surgery and radiation as compared with mastectomy in large numbers of patients with central breast cancers do not exist. A number of small, non-randomized series have subsequently addressed the issue of breast-conserving surgery in women with central breast cancers and have suggested that resection of the NAC is an acceptable technique for some of these women. However, resection of the NAC to expand indications for and to extend the option of breast-conserving surgery to more women with central breast cancers has still not been widely accepted.

The principal requirement for successful breast-conserving surgery is resection of the primary tumor with a circumferentially uninvolved margin of benign breast tissue. This basic principle of breast-conserving surgery, which we have learned from follow-up of large prospective randomized studies, should not be compromised to use breast-conservation therapy in patients with central breast cancer. Direct involvement of the NAC by breast cancer would, by definition, preclude a margin-free resection without resection of the involved nipple or areola. However, resection of the central portion of the breast, including resection of the NAC, can allow a wide excision of the malignant process with uninvolved margins of resection, consistent with the established principles of successful breast-conserving surgery. Postoperative radiation therapy to the remainder of the breast is then delivered to treat the theoretical subclinical microscopic disease that may exist in remaining areas of the breast, exactly as it is used for other noncentral breast cancers. Cosmetically, the patient preserves a sensate, intact breast mound with normal peripheral contours. Extensive breast reconstruction procedures, which lack sensation and can be associated with a variety of short- and long-term complications, can be avoided. Nipple-areolar reconstruction can be performed easily with a minor office-based procedure, after adjuvant therapy has been completed, if elected by the patient.

We report our 10-year experience with breast conservation using resection of the NAC and postoperative radiation as treatment for stage 0, stage I, and stage II central breast cancers that involve the NAC.

METHODS

Between 1989 and 1999, select patients with central breast cancers that involved the nipple or areola were offered breast conservation by resection of the central aspect of the breast, including resection of the NAC. Central breast cancer was defined as in situ or invasive carcinomas that involved or were in very close proximity to the NAC, precluding complete tumor resection without removal of the NAC. Patients with Paget disease of the nipple were included. In all cases, the only surgical alternative to resection of the NAC and central aspect of the breast would have been total mastectomy.

Surgery was performed using a transverse, elliptical skin incision large enough to include the entire NAC. Dissection extended into the central breast tissue to allow a 1- to 2-cm gross margin of normal-appearing breast tissue around the known

tumor. Local anesthesia with intravenous sedation was preferred; general anesthesia was used if axillary dissection was also performed. The resulting wound was closed with absorbable sutures, without a drain, and avoiding deep parenchymal sutures. All patients with invasive disease underwent either level I or level II axillary dissection or axillary radiation if axillary surgery was not performed. Sentinel lymph node biopsy was not used in this group of patients.

Postoperative radiation consisted of 0.46 rad (46 Gy) to the entire breast and an additional 0.14 rad (14 Gy) to the primary site, similar to that used after breast-conserving surgery in other areas of the breast. In addition, patients with proven axillary lymph node metastasis received systemic chemotherapy. Adjuvant hormonal therapy with tamoxifen citrate was used for patients with invasive cancers and positive hormone receptors. All patients with invasive cancer underwent a distant metastatic workup that included a chest x-ray, a bone scan, and a computed tomography scan of the abdomen.

Follow-up consisted of an annual mammography and at least biannual office visits with a symptom-based history obtained and a complete breast examination. Breast recurrence was treated by mastectomy. The medical records of all patients who underwent NAC resection for central breast cancers in 2 surgeons' practices (C.M.P. and J.S.K.) were reviewed retrospectively for patient demographics; clinical presentation; tumor type, location, and size; operative margins; adjuvant treatment; and follow-up information. A questionnaire was sent to all patients to elicit their opinion and evaluation concerning the cosmetic result of the procedure, as well as the perceived psychological impact of this breast-conserving approach.

RESULTS

During the 10-year study period, 15 female patients underwent breast-conserving surgery using resection of the NAC as described earlier. Patients ranged in age from 46 to 88 years, with a median age of 80 years. Four of the 15 patients were premenopausal.

Five patients presented with a palpable mass; 5 with visible changes involving the NAC; and 5 with both a palpable mass and visible changes that affected the NAC. Visible NAC changes included retraction (4 patients), excoriation (3 patients), and ulceration (3 patients). Of those with visible change involving the NAC, 5 patients presented with findings typical of Paget disease of the nipple. All patients had an initial biopsy of the breast abnormality that established the diagnosis of primary breast cancer. Five patients were found to have noninvasive ductal carcinoma in situ (DCIS) only, and the remaining 10 patients had invasive breast carcinoma, with or without associated DCIS. Of the patients with Paget disease of the nipple, 4 had purely DCIS without invasion, and 1 had invasive disease. All 10 patients with invasive disease presented with a palpable mass, 5 of whom also had visible changes involving the NAC. All patients underwent complete resection of the NAC as previously described.

Negative surgical margins were achieved with initial resection of the NAC in 13 (87%) of the 15 patients and 2 patients (13%) were judged to have inadequate excision margins. One patient with an initial margin of less than 1 mm and an invasive cancer subsequently underwent reexcision with negative margins. The other patient had Paget disease, DCIS only, and positive margins; she refused reexcision or further surgery. Thus 14 of 15 patients ultimately achieved negative surgical mar-



Figure 1. A 46-year-old patient with invasive breast cancer who had a 1.8-cm tumor and negative axillary lymph node dissection on the right. Nipple-areolar reconstruction 14 months postoperatively produced excellent results.

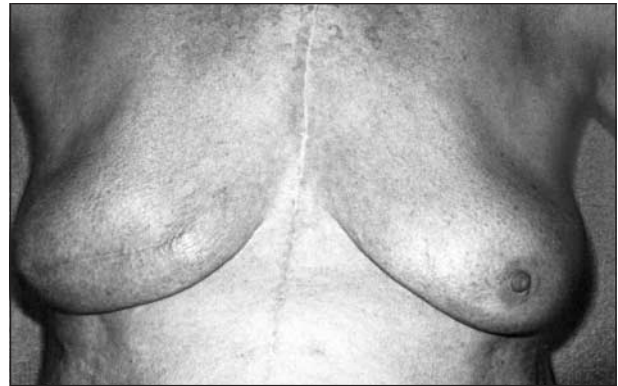


Figure 3. An 80-year-old patient who had Paget disease and a 1.2-cm focus of ductal carcinoma in situ. She had a previous sternotomy, and, despite her lumpectomy, her breasts are nearly symmetrical.



Figure 2. A 48-year-old patient with invasive breast cancer who had a 2.5-cm tumor and 5 of 19 positive axillary lymph nodes. Although the breast is smaller, its contour and natural shape have been preserved.

gins of excision, with 1 patient left with noninvasive disease at the microscopic margin.

Tumor size ranged from 0.2 cm to 3.5 cm, with similar ranges for pure DCIS and the invasive carcinomas. Of the 5 patients with pure DCIS, the tumor was less than 1 cm in 1 patient, 1 cm to 2 cm in 2 patients, and between 2 cm and 4 cm in 2 patients. The 10 invasive tumors were less than 1 cm in 3 patients, 1 cm to 2 cm in 6 patients, and between 2 cm and 4 cm in 1 patient.

Axillary dissection was performed at the time of resection of the NAC for 5 patients with invasive disease. Three of the 5 patients were found to have axillary lymph node metastasis, with more than 4 lymph nodes involved in 2 of these 3 patients. Two patients had negative axillary dissection. Axillary radiation was used for the remaining 5 patients with invasive disease (0.46 rad [46 Gy] to the ipsilateral axilla) who did not undergo axillary dissection. Axillary radiation was chosen for 4 elderly patients to avoid general anesthesia risks and for whom adjuvant therapy decisions were unaffected by axillary nodal status, as well as for 1 patient who refused axillary dissection. The distant metastatic workup was negative in all cases. The tumors were staged according to the American Joint Committee on Cancer.¹¹ Five patients had stage 0 disease; 7 patients, stage I; and 3 patients, stage II.

Adjuvant chemotherapy was administered to 4 patients. All 3 of the patients with axillary lymph metastasis

found at axillary dissection received adjuvant chemotherapy, along with one 46-year-old premenopausal patient with negative axillary nodes. All postmenopausal patients with invasive cancer (n=9) received postoperative adjuvant hormonal therapy with tamoxifen.

Mean follow-up was 32 months, with a median of 25 months (range, 4-109 months). Fourteen (93%) of the 15 patients are alive and well at the time of last follow-up, never experiencing evidence of recurrent disease. There was one ipsilateral breast recurrence (7%) at 53 months after operation in a patient who had Paget disease and a 1.5-cm area of DCIS. The recurrent neoplasm was a 4-cm infiltrating ductal carcinoma located deep and lateral to the original incision margin. The patient underwent modified radical mastectomy with no evidence of further disease and had 0 of 16 lymph nodes positive. She remains disease free 16 months later and 69 months from the original diagnosis. There have been no nodal or distant recurrences in the 15 patients during the follow-up period. Thus, all 15 patients are presently alive and disease free.

Cosmetic results were first assessed in the office setting by the surgeons in follow-up. In all 15 patients, the surgeon rated the cosmetic result as acceptable or better. Seven (47%) of the 15 patients, who represented the younger half of the study group, returned the patients' questionnaire by mail. The respondents rated their cosmetic results with and without clothing on a scale of 1 (unsatisfactory) to 5 (very satisfied). Median score with clothing was 5 and without clothing was 3. All respondents were more concerned with the preservation of the breast mound and contour than the loss of the NAC. All respondents stated that, in retrospect, they would choose the same treatment. None of the patients had reconstructive surgery to alter the size of the breast mound, and 1 had NAC reconstruction by areolar tattoo and nipple reconstruction with excellent results as evaluated by the surgeon and the patient (**Figures 1, 2, and 3**).

COMMENT

Breast-conserving therapy is well established as an appropriate treatment option for patients with early stage breast cancer (stages 0 to II), as numerous prospective randomized studies in North America and Europe have

shown long-term survival rates equivalent to mastectomy. The basic hypothesis—that removal of the primary cancer with enough adjacent normal breast tissue to ensure removal of the entire gross tumor along with any microscopic extension, resulting in a microscopically negative surgical margin and followed by radiation therapy to the remainder of the breast, will lead to equal long-term survival compared with mastectomy—has been tested and confirmed by these studies. Despite initial concerns about a significant risk of clinically undetectable microscopic foci of multifocal or multicentric breast cancer that is not surgically removed with breast conservation, no difference in the incidence of distant metastatic disease or in overall survival has been seen.

Not all breast cancer patients, however, have been considered appropriate candidates for breast-conserving therapy, and therefore not all patients are offered this option by their surgeons. Historically, one such subgroup of patients are those with a central breast cancer that directly involves the NAC. This includes patients with Paget disease of the nipple, with or without an underlying mass, and patients with subareolar breast cancers that invade the nipple or areola, or so closely approximate these structures that resection that preserves these structures and still achieves a negative microscopic margin is not possible. Breast-conservation therapy in this situation, to adhere to the basic principles established by the prospective randomized studies mentioned earlier, would mandate resection of some or all of the NAC to achieve a negative surgical margin.

The principal reasons that patients with breast cancers involving the NAC have not been often considered appropriate candidates for breast-conserving surgery surround the perceived unacceptable cosmetic effect that would result from resection of the NAC, as well as oncologic concerns about multicentricity or multifocality associated with these tumors that might lead to unacceptably high rates of ipsilateral breast recurrence and the lack of significant experience or published data treating this particular group of patients other than by mastectomy.

Based on anecdotal clinical experience with resection of the NAC, we hypothesized that the cosmetic result that could be achieved would be, contrary to traditional thinking, at least satisfactory and superior to mastectomy, with or without breast reconstruction. The majority of the breast tissue can be preserved, sensation to the skin is maintained (in contrast to mastectomy and breast reconstruction), the contour of the breast can be preserved, and plastic and reconstructive surgical techniques could be used to reconstruct the NAC if desired. Wide and clear surgical margins can be obtained, adhering to the accepted and proven principles of breast reconstruction used for breast cancers in other portions of the breast. Adjuvant radiation, exactly as used for breast conservation in other patients, would then be used to control the significant likelihood of clinically undetectable microscopic multifocal or multicentric breast cancer in the remainder of the breast.

Fowble et al¹² reported 70 patients with subareolar breast cancers treated with breast-conserving therapy and adjuvant breast irradiation (**Table**). Most of these patients did not have direct involvement of NAC, however,

Breast Conservation for Central/Subareolar Cancers and Resection of the Nipple-Areolar Complex

Source	Total No. of Patients	Patients With Complete NAC Resection	Ipsilateral Breast Recurrence, %	Median Follow-up, y
Paone and Baker ¹⁶ (1981)	5	5	0	10
Fowble et al ¹² (1992)	70	3	8.6	5
Haffty et al ¹⁴ (1995)	98	10	6.1	9.03
Bussieres et al ¹⁵ (1996)	37	20	0	4.08
Dale and Giuliano ¹³ (1996)	25	0	4.8	4
Iino et al ¹⁷ (1996)	4	4	0	0.08-1.41
Lajos et al ¹⁹ (1984)*†	5	4	0	4.2
Fourquet et al ²⁰ (1987)*	20	3	15	7.5
Dixon et al ¹⁸ (1991)*†	10	10	40	4.7
Pierce et al ²⁴ (1997)*	30	22	14	5.2
Kollmorgen et al ²⁵ (1998)*	10	5	20	5.08
Bijker et al ²⁶ (2001)*	61	61	5.2	6.4
Present study (2003)	15	15	7	2.7

Abbreviation: NAC, nipple-areolar complex.

*Included patients with Paget disease only.

†Patients received no radiation therapy.

and so only 3 required excision of the NAC. They found that the incidence of multicentricity, margin involvement with the initial excision, lymph node metastasis, and most importantly 5-year recurrence rates were similar to breast cancers originating in other regions of the breast.

Similarly, Dale and Giuliano¹³ performed breast-conserving therapy with preservation of the NAC in 25 patients with central breast cancers and reported a 4.8% 4-year local recurrence rate. Haffty et al¹⁴ reported a 6% local recurrence rate in 98 patients with central breast cancers treated with breast-conserving therapy, including 10 who underwent NAC excision. These authors have concluded that the NAC, as well as the breast itself, can be preserved in patients with small tumors within 2 cm of the NAC if clear surgical margins can be obtained. In the present study, it is in patients in whom clear surgical margins cannot be obtained and still preserve the NAC, because of direct involvement of the NAC by tumor, that resection of the NAC was used to extend the alternative of breast conservation.

Bussieres et al¹⁵ described 37 patients with central breast cancers, 12 of whom had direct infiltration of the NAC. The remaining 25 patients had nipple retraction from subareolar tumors (n=24) or a subareolar tumor within 1 cm of the NAC (n=1). In this study, 20 patients underwent complete resection of the NAC, 9 underwent a partial resection of the NAC, and 8 had the NAC preserved. With median follow-up of 49 months,

only 1 patient in the entire group developed an ipsilateral breast recurrence. The recurrence was noninvasive and located in the inferior quadrants in a patient who underwent partial NAC resection.

Paone and Baker¹⁶ reported resection of the NAC in 5 patients with Paget disease of the nipple, not followed by adjuvant breast irradiation. There was no recurrence after 10 years. Iino et al¹⁷ described their results with resection of the NAC in 4 patients with subareolar breast cancers, combined with radiation therapy, and saw no recurrences during follow-up ranging from 1 to 17 months.

Other small studies have specifically examined combinations of limited, breast-conserving surgery or radiotherapy in patients with Paget disease of the nipple,^{16,18-25} but the largest experience with breast-conserving surgery and radiation specifically for patients with Paget disease of the nipple was reported by Bijker et al.²⁶ Sixty-one patients with Paget disease of the nipple, all DCIS alone (stage 0), were treated by simple excision of the NAC followed by external irradiation to the entire breast (0.50 rad [50 Gy] in 25 fractions). With a median follow-up of 6.4 years, only 4 of 61 patients had developed recurrence in the treated breast, for a 5.2% 5-year local recurrence rate. They concluded breast-conserving therapy is a feasible alternative for patients with Paget disease and a limited extent of underlying DCIS. They were not, however, able to evaluate the cosmetic results.

The issue of multicentricity or multifocality, and the concern that it, at least in theory, will lead to unacceptably high ipsilateral breast failure rates in these patients, is based largely on older pathologic studies that carefully examined the incidence of clinically occult multicentric or multifocal disease in patients with breast cancer. In a study of 203 mastectomy specimens, Rosen et al³ found an 80% incidence of multicentricity with subareolar breast cancers vs 25% in other breast cancers. More recent studies, although relatively smaller in sample size, have found no evidence of a significantly greater incidence of multicentricity in subareolar cancers, and more importantly, equal recurrence rates for subareolar and other breast cancers when adjuvant radiation therapy was included in the therapeutic regimen. Gajdos et al²⁷ described 60 patients with subareolar breast cancers, 11 of whom underwent resection of the NAC, and, not surprisingly, found that postoperative adjuvant radiation therapy played a critical role in lowering the ipsilateral breast recurrence rate.

The pathologic studies of Rosen et al³ demonstrated that occult foci of multicentricity and multifocality are relatively common occurrences in patients with breast cancer regardless of the specific location of the primary tumor within the breast. It is concern for this significant incidence of microscopic unresected disease and the risk of recurrence that might result from it that leads to the routine addition of adjuvant radiation therapy to the remainder of the breast after breast-conserving therapy, regardless of the primary tumor site within the breast. Radiation therapy has been proven to be effective in significantly reducing the incidence of ipsilateral breast recurrence, and therefore must have a meaningful therapeutic effect on microscopic residual disease, which is known to be present in a significant number of patients

with breast cancer treated with less than total mastectomy.¹⁰ Follow-up data from our study, along with the other studies discussed, suggests that a theoretical concern about multicentricity and multifocality, which was also raised in the early days of breast-conservation surgery for peripherally located breast cancers, can be largely rendered clinically insignificant, as is the case for breast conservation in other areas of the breast, with the addition of adjuvant radiation therapy to the breast. Our breast recurrence rate of 6% (1 of 15 patients) suggests that multifocality and multicentricity do not become clinically significant in most patients after adequate excision followed by radiation therapy, even in tumors that directly involve the NAC. Larger studies and longer follow-up, however, are needed for more definitive conclusions.

Published data concerning the cosmetic results and psychological impact of breast-conserving therapy for this group of patients is even more limited than data concerning the oncologic outcomes of breast preservation and survival. The loss of the NAC has been proposed by several authors to be cosmetically unacceptable and disfiguring,^{9,13,15} but few studies elicited the patients' opinions. Galimberti et al²⁸ stated that simple resection of the NAC as described herein gives a poor cosmetic outcome, and therefore many surgeons prefer mastectomy with breast reconstruction. He describes a more extensive procedure combining resection of the NAC and central breast tissue with "remodeling" of the breast using a skin-glandular flap for better cosmetic results and breast conservation in these cases.

Haffty et al¹⁴ and Dale and Giuliano¹³ recommended preservation of the NAC but did note that their patients who had NAC resection were satisfied with the cosmetic result. Iino et al¹⁷ reported excellent cosmetic results, as judged by patient and physician, in 4 patients who had NAC resection. Bussieres et al¹⁵ suggested that the NAC should be spared in younger women who are sexually active but not in older women. Of their patients to whom they suggested breast enlargement and NAC reconstruction after breast-conserving surgery and NAC resection, all but one refused the reconstructive procedure. Interestingly, their patients, including younger women, were apparently not dissatisfied with the loss of the NAC. Dale and Giuliano¹³ did assess the postoperative cosmetic results using a scale, but it was the physician—not the patient—who provided the evaluation. The current study is the first to attempt to quantitate patients' evaluations concerning the cosmetic result, as well as their opinions about the decision to undergo breast conservation with resection of the NAC as opposed to mastectomy. Our patients judged their cosmetic results to be far better than they had expected, and, interestingly, they judged the cosmetic results to be better than their surgeons had judged them. Current plastic and reconstructive surgical techniques allow for the option of excellent NAC reconstruction, as demonstrated in 1 of our patients (Figure 1), but the responses from our patient questionnaire indicate that preservation of breast mound and contour seems to be of greater importance than the loss of the NAC.

We believe that these data, in the context of similar studies with small groups of treated patients, will fur-

ther validate breast conservation as an acceptable and preferable alternative to mastectomy for patients with early stage central breast cancers that directly involve the NAC or are located in such close proximity to the NAC that they cannot be excised with a negative surgical margin and preserve the NAC. By adhering to the important principles of breast-conserving surgery—complete resection of the primary tumor with a negative surgical margin, adjuvant radiation therapy to the remainder of the breast to treat subclinical microscopic disease that may remain elsewhere in the breast—acceptable cosmetic results are possible.

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