

The Conservative Management of Paget's Disease of the Breast with Radiotherapy

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BACKGROUND. The purpose of this study was to evaluate the feasibility of breast-conserving therapy involving limited surgery and definitive radiotherapy as a treatment for Paget's disease, and to determine the disease free and overall survival associated with this approach.

METHODS. The authors retrospectively reviewed the charts of all patients treated during the period 1980-1994 for Paget's disease of the breast who did not present with a palpable mass or mammographic density. Through a collaborative review, 30 cases were identified. A biopsy confirming the presence of typical Paget's cells was performed on all patients. All patients received external beam radiotherapy to the breast, with a median dose of 50 gray (Gy). Ninety-seven percent received a boost to the remaining nipple or tumor bed, with a median dose to the tumor bed of 61.5 Gy.

RESULTS. The median follow-up for surviving patients was 62 months. Three patients (10%) developed a recurrence in the breast as the only site of first failure, and 2 additional patients (7%) experienced failure in the breast as a component of first failure. The median time to local failure was 69 months. The 5- and 8-year actuarial estimates of local failure as the only site of first failure were 9% (95% confidence interval [CI], 0-20%) and 16% (95% CI, 0-31%), respectively. Of the 5 patients with local failures, 3 were among 22 patients (14%) who underwent complete resection of the nipple or nipple-areola complex, compared with 2 failures among 6 patients (33%) after partial resection ($P = 0.29$). There were no failures among 2 patients who had a biopsy only. Four of 5 local failures were salvaged by mastectomy, and 3 of these patients were free of disease after a median follow-up of 52 months. The 5- and 8-year estimates of disease free survival for the overall series were both 95% (95% CI, 87-100%); cause specific overall survival was 100% at 8 years.

CONCLUSIONS. Breast-conserving therapy involving complete resection of the nipple-areola complex followed by definitive radiotherapy is a viable alternative to mastectomy in the treatment of Paget's disease. High rates of disease free and cause specific survival, in addition to adequate local control, justify consideration of a conservative approach. *Cancer* 1997;80:1065-72.

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Since the original association between skin changes of the nipple and the subsequent development of breast carcinoma was re-

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ported by Sir James Paget in 1874, the condition later termed Paget's disease of the nipple has been a well documented clinical entity.¹ The description of clinical changes of the nipple and areola described by Sir Paget as having the ". . . appearance of a florid intensely red raw surface; very finely granular, as if the whole thickness of the epidermis were removed; like the surface of very acute diffuse eczema . . . (with) cancer of the mammary gland (following) within at the most two years and usually within one year . . ." remains as accurate a description today as when initially described.

Paget's disease of the breast occurs in approximately 1–3% of all primary breast carcinoma series^{2–4} and most often presents clinically as eczematous changes of the nipple, associated with bleeding, itching, and ulceration.^{2,5} Although approximately 50% of patients also present with an associated palpable mass elsewhere in the breast, 40–50% of patients are diagnosed with Paget's disease without a clinically detectable breast lesion.^{2,3,6} In recent studies in which mammographic findings have been correlated with clinical findings, the majority of women presenting with nipple changes in the absence of a palpable mass have had negative mammographic findings as well,⁷ with negative mammograms reported in 63% of women presenting only with nipple changes in 1 series.⁷

Pathologically, all patients with Paget's disease have characteristic round intraepidermal cells of the nipple. However, variable pathologic findings have been reported in the remainder of the breast, dependent primarily on the presence or absence of a breast mass. An underlying breast malignancy has been documented in 96–100% of cases when breast specimens have been analyzed after mastectomy.^{3,4,8} Among those patients presenting with a palpable mass, approximately 90–94% are found to have invasive disease, whereas patients presenting without a clinical mass often have noninvasive disease, with 66–86% of patients having ductal carcinoma in situ (DCIS) exclusively.^{2,3} Survival has varied by clinical and pathologic findings, with patients presenting without a mass and predominantly noninvasive disease having 5-year cause specific survivals of 90–100% after mastectomy^{2,3,4} versus 37–43% for women with palpable masses and invasive disease.^{2,3}

Historically, the standard local therapy for Paget's disease has been mastectomy.^{2,3,5} However, with the highly favorable prognosis of Paget's disease in the absence of a breast mass, and the increasing reports of the successful use of conservative surgery and radiotherapy in the treatment of DCIS of the breast,^{9,10} interest in a breast-conserving option has been generated. However, limited data exist concerning the outcome

of Paget's disease treated in this manner.^{11,12} Therefore, the authors collectively reviewed their experience using definitive radiotherapy in the management of Paget's disease presenting as nipple changes in the absence of a palpable mass or a mammographic density, and report the local control and disease specific survival achieved with a breast-conserving approach.

MATERIALS AND METHODS

Patient Eligibility

To generate a series of patients treated with limited surgery and breast radiotherapy for Paget's disease, clinical cases were combined from seven institutions into a single data base at the University of Michigan. Thirty cases of Paget's disease of the nipple without a palpable mass or mammographic density treated with definitive radiotherapy were identified from the following institutions: six cases each from the University of Michigan and Yale University, five cases from the University of Pennsylvania, four cases each from Memorial Sloan-Kettering Cancer Center and William Beaumont Hospital, three cases from Tufts University, and two cases from the Joint Center for Radiation Therapy. All patients were treated with breast conservation based on patient preference. No patients were referred for radiotherapy due to medical contraindications to surgery.

Twenty-nine women were diagnosed with AJCC clinical Tis N0 M0, Stage 0 Paget's disease of the breast; one patient with Paget's disease of the nipple was diagnosed with clinical T1N0M0, Stage I disease due to a focus of microinvasion.¹³ All patients were treated between 1980–1994. Each patient had a nipple biopsy demonstrating large, pale, rounded, or ovoid intraepidermal cells with extensive cytoplasm and enlarged nuclei and nucleoli, characteristic of Paget's cells. All pathology slides were reviewed at diagnosis by the originating institution for histologic confirmation. A central pathology review was not performed.

Surgical Therapy

Surgery was comprised of complete or partial nipple excision, or complete or partial excision of the nipple and areola with associated retroareolar breast tissue. No patient required an excision elsewhere in the breast. Ten percent of patients (3 of 30) underwent total nipple excision, 13% (4 of 30) underwent partial nipple excision, and 63% (19 of 30) and 7% (2 of 30) underwent total and partial nipple-areolar excision, respectively. Two patients (7%) underwent biopsy only without resection of the nipple. Fourteen patients (47%) had a reexcision performed and 15 (50%) were not reexcised; the use of reexcision was unknown in 1 patient (3%). Final margins were negative in 16 cases

(53%), positive in 2 (7%), and unknown in 12 (40%). Eleven women (37%) had an axillary lymph node dissection, with a median of 13 lymph nodes removed (range, 8–24 lymph nodes). All lymph nodes were pathologically negative for metastatic disease.

Radiotherapy

All patients received external beam radiotherapy to the breast using tangential irradiation. The median dose to the entire breast was 50 grays (Gy) (range, 45–54 Gy). The median fraction size was 2 Gy (range, 1.8–2 Gy). Dose distributions were reviewed for intentional underwedging at the nipple-areolar region. Six plans were intentionally underwedged to generate an area of increased dose in the nipple-areolar area. The median isodose of these plans was 110% (range, 106–110%). A boost was delivered to the remaining nipple or tumor bed in 97% of cases (29 of 30) to a median dose of 14 Gy (range, 9–20 Gy). The median total dose to the tumor bed was 61.5 Gy (range, 50.4–70 Gy). Of the 29 patients receiving a boost, 86% (25 of 29) were treated with electrons, and 3% (1 of 29) each were treated using 100-kilovolt photons, cobalt, or a double-plane iridium implant. One patient was treated with a boost of unknown type. Bolus was used in the photon and/or electron portion of treatment in 33% of cases (10 of 30), not used in 60% (18 of 30) of cases, and unknown in 7% of cases. Of the ten patients who were treated with bolus, bolus was applied to the remaining nipple-areolar complex daily in six, two were bolused to the remaining scar, and two received bolus to the entire breast for a portion of the external beam treatment. In addition to breast irradiation, 1 patient received supraclavicular radiotherapy to a dose of 46 Gy and a second patient was treated comprehensively to the supraclavicular, axillary, and internal mammary lymph nodes to a total dose of 50 Gy. One patient received systemic treatment with tamoxifen.

Data Analysis

Patient records were reviewed for the following characteristics: age, menopausal status, presenting symptoms, duration of symptoms, mammographic findings, extent of surgical excision, final margin status, pathologic findings, dissection of the axillary lymph nodes, and the results of the dissection if performed. Actuarial curves for local control, survival free of disease, and overall survival were generated using the Kaplan–Meier method, measured from the completion of radiotherapy.¹⁴ A local failure as only first failure was defined as a patient who recurred in the breast without preceding or simultaneous regional or distant disease. A local failure as a component of first failure included all patients who developed a breast failure

whether it was isolated or concurrent with regional and/or distant failure. Patients were scored as being without evidence of disease (NED) at last observation if they had been continuously free of disease from the completion of radiotherapy to the last follow-up visit or had developed local and/or regional failure that was successfully salvaged at the last observation period. For the calculation of cause specific survival, only deaths secondary to breast carcinoma were scored as events. For the calculation of overall survival, all deaths were scored as events.

Univariate analyses were performed using Fisher's exact test to evaluate the strength of association between clinical characteristics and local control. The small sample sizes and number of events in this series precluded performing a meaningful multivariate analysis.

RESULTS

Clinical, Mammographic, and Pathologic Findings

The median age at diagnosis was 50 years (range, 35–79 years). Thirteen patients (43%) were premenopausal, 16 (53%) were postmenopausal, and 1 patient (3%) was perimenopausal when diagnosed. The presenting symptoms at the nipple-areolar complex were as follows: 67% of patients (20 of 30) presented with nipple pain, itching and/or scaling; 37% (11 of 30) presented with nipple discharge; 20% (6 of 30) presented with nipple erythema; and 17% (5 of 30) presented with nipple ulceration. No patients were asymptomatic at presentation. The median duration of symptoms was 8.5 months (range, 1–36 months).

Twenty-nine of 30 patients (97%) underwent a mammogram at presentation. Twenty-four of 29 mammograms were read as negative for malignancy. Of the remaining five studies in which mammographic changes were noted, findings included two with retro-areolar calcifications, two with nonspecific calcifications, and one with suspicious calcifications elsewhere in the breast. Three of these mammograms also included results suggestive of nipple thickening. There were no mammographic findings suspicious for a breast mass.

Two patients underwent an incisional biopsy of the nipple only; the remaining 28 patients underwent either partial or complete excision of the nipple or nipple-areolar complex, as outlined earlier. Pathologic review revealed Paget's cells of the nipple in all 30 cases. In addition to the presence of the Paget's cells, DCIS was identified in 23 of the biopsy specimens (77%), and DCIS with a single focus of microinvasion was found in 1 specimen (3%). The remaining 6 cases (20%) either had no underlying breast parenchyma

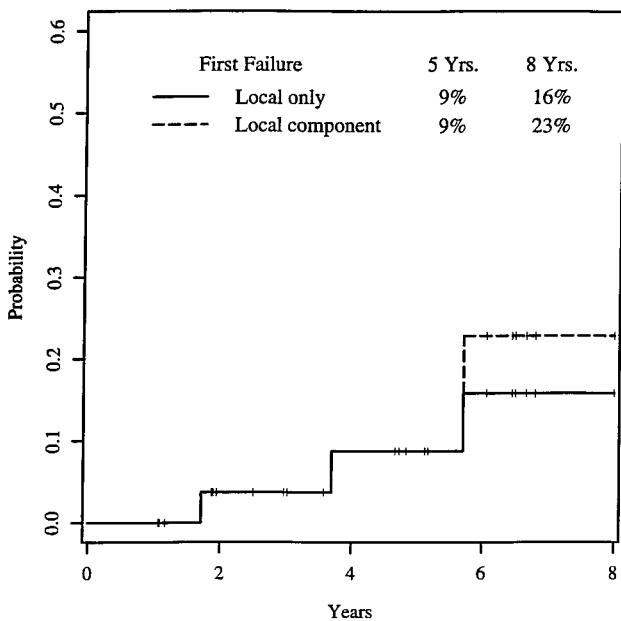


FIGURE 1. Five- and 8-year estimates of local failure as only site of first failure and component of first failure.

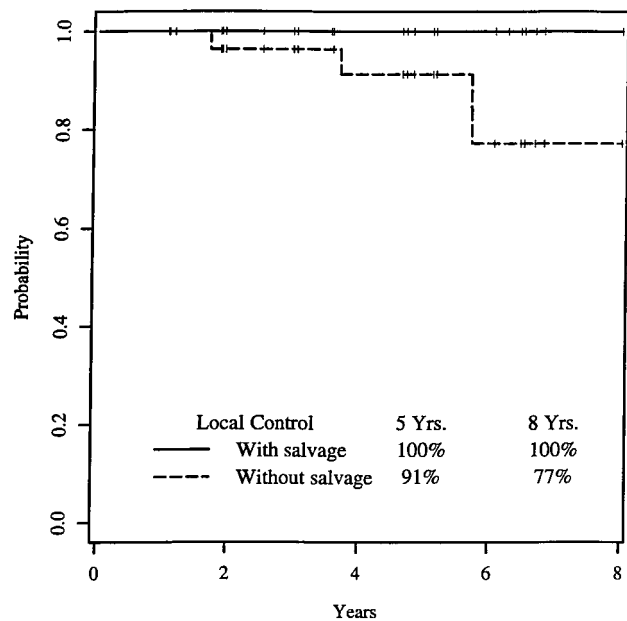


FIGURE 2. Five- and 8-year estimates of local control with and without surgical salvage.

for pathologic assessment or had no DCIS or invasion present.

Locoregional Control

With a median follow-up of 62 months for surviving patients (range, 13–176 months), 3 patients (10%) had developed a recurrence in the breast as the only site of first failure (Fig. 1). The 5- and 8-year actuarial local control rates for a breast failure as the only site of first failure were 91% (95% confidence interval [CI] 80–100%) and 84% (95% CI, 69–100%), respectively. Two additional patients developed a breast failure simultaneously with regional or distant failure; the cumulative 5- and 8-year actuarial control rates for a breast recurrence as component of first failure were 91% (95% CI, 80–100%) and 77% (95% CI, 59–100%), respectively. For those who experienced a breast recurrence, the median time to local failure was 69 months (range, 21–122 months). Despite treatment to the axilla in only 12 of 30 patients (40%) (i.e., 11 with axillary lymph node dissection and 1 with comprehensive regional irradiation) only 1 patient developed a clinical ipsilateral axillary lymph node failure (3%), which was surgically salvaged. She had not undergone previous axillary surgery or radiotherapy.

All three recurrences in patients with breast-only failures as first failure were detected by mammogram only and successfully salvaged by mastectomy. One of these three patients had residual microcalcifications on a postbiopsy mammogram that were not excised

prior to radiotherapy. Persistent calcifications led to a subsequent biopsy 4 years later that confirmed residual DCIS. She had focal intraductal carcinoma only in the mastectomy specimen. Another patient had multifocal DCIS in the mastectomy specimen, and the third had both invasive and noninvasive disease.

Of the two additional patients with a local recurrence as a component of first failure, one experienced a simultaneous breast and axillary lymph node failure, and the second had a breast and distant (contralateral axillary) lymph node failure. Both local recurrences were detected by both physical examination and mammogram and pathologically contained invasive and intraductal disease. The former patient was treated by mastectomy; 6 of 19 lymph nodes were found to contain metastatic disease. The patient subsequently received 6 cycles of cyclophosphamide, doxorubicin, and 5-fluorouracil, followed by tamoxifen, and at last follow-up was free of disease 64 months after recurrence. The patient with simultaneous local and distant failure recurred 10 years and 6 months after therapy to the breast. At the time of recurrence, only a biopsy was performed of the treated breast; no attempt was made to perform a mastectomy. Thus, 29 of 30 patients (97%) were ultimately locally controlled by either primary treatment or salvage surgery at last follow-up. The actuarial rates of local control including surgical salvage at 5 and 8 years were 100% and 100%, respectively, as shown in Figure 2. (The single

TABLE 1
Univariate Analysis for Local Failure

Clinical factor	No.	Local failure	P-value ^a
Mammographic findings			
Negative	24	16.7%	>0.99
Calcifications	5	20.0%	
Not done	1	0%	
Extent of nipple-areolar excision			
Complete nipple/nipple-areolar	22	14.0%	0.29
Partial nipple/nipple-areolar	6	33.3%	
Final margin status			
Negative	16	12.5%	0.74
Positive	2	0%	
Unknown	12	25%	
Pathology of lumpectomy specimen			
Paget's disease only	6	0%	0.55
Paget's disease with DCIS ± invasion	24	20.8%	
Breast dose (Gy)			
< 50	12	8.3%	0.62
≥ 50	18	22.2%	
Dose to tumor bed with boost (Gy)			
< 60	4	0%	>0.99
≥ 60	26	19.2%	
Use of bolus			
No	18	11.1%	0.32
Yes	10	30.0%	
Unknown	2	0%	

DCIS: ductal carcinoma in situ; Gy: grays.

^a Calculated using Fisher's exact test.

local recurrence for which salvage was not attempted occurred beyond the last point of actuarial analysis.)

Univariate analysis for local failure as component of first failure was performed for the following factors: mammographic findings, extent of nipple/nipple-areolar complex resection (complete nipple/nipple-areolar excision vs. partial nipple/nipple-areolar excision), pathologic results in the lumpectomy specimen (Paget's cells only vs. DCIS with or without microinvasion), final margin status, whole breast dose (< 50 Gy vs. ≥ 50 Gy), total tumor bed dose (< 60 Gy vs. ≥ 60 Gy), and the use of bolus. No factors emerged as statistically significant predictors of local failure at the conventional level ($P \leq 0.05$), Table 1. However, there was a trend toward improved local control in patients treated with total nipple/nipple-areolar excision (3 failures in 22 patients; 14%) compared with partial nipple/nipple-areolar excision (2 failures in 6 patients; 33%) ($P = 0.29$).

NED Survival and Overall Survival

At last follow-up, two patients were alive with distant disease. The NED survival rate at 5 and 8 years was

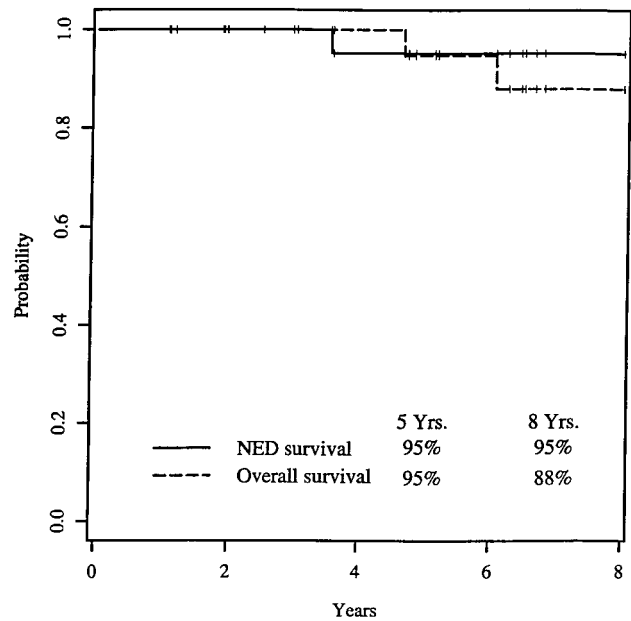


FIGURE 3. Five- and 8-year estimates of survival with no evidence of disease (NED) and overall survival.

95% (95% CI, 87–100%) (Fig. 3). At last follow-up, two patients had died, both without evidence of disease, resulting in overall survival rates at 5 years of 95% (95% CI, 85–100%) and of 88% at 8 years (95% CI, 73–100%). The cause specific survival rate at both 5 and 8 years was 100%.

Cosmesis and Complications

The cosmetic result was assessed by the treating radiation oncologist in 24 patients using the criteria previously suggested by Harris et al.¹⁵ Nine of 24 patients (38%) were believed to have an excellent result, 13 (54%) a good result, and 2 (8%) a fair result. The cosmetic result did not vary significantly by the extent of the resection (data not shown); however, three of the patients with good to excellent results underwent nipple reconstruction after complete nipple-areolar resection.

The incidence of complications was assessed in 27 of 30 cases. No complications were reported in 89% of the patients reviewed (24 women). One patient each developed protracted chest wall pain (4%), chronic breast infection treated with antibiotics (4%), and a questionable radiation dermatitis treated with steroids (4%).

DISCUSSION

The purpose of this study was to present the local control and survival rates for a consecutive series of patients treated with conservative surgery and radio-

therapy for Paget's disease of the nipple, and to contrast these results with historic controls treated with mastectomy. The clinical characteristics of the patients in the current study are comparable to those described in mastectomy series. The median age at diagnosis was 50 years, consistent with surgical series,^{3,5,16} and all patients presented with clinical changes at the nipple typical of Paget's disease, including pruritis, erythema, and mild ulceration. The median duration of symptoms prior to diagnosis was 8.5 months, which is also in agreement with mastectomy series, in which the diagnosis often has been delayed secondary to the presumption of benign skin disease.

In general, the prognosis after mastectomy in the absence of a palpable mass has been very favorable, with some series reporting no deaths secondary to carcinoma at 5 years.² However, others have reported invasive recurrences after mastectomy. In a series of 37 patients with Paget's disease of the nipple without a palpable mass treated with simple mastectomy, Dixon et al. reported a 5% incidence of invasive recurrence with a 40-month median follow-up.⁴ Thus, although distant disease free survival exceeds 90–95% in patients with Paget's disease without a palpable mass treated with ablative surgery, mastectomy does not uniformly result in survival free of disease.

Limited experiences using breast-conserving surgery followed by definitive radiotherapy have produced results similar to those reported after mastectomy. Fourquet et al. from the Institut Curie retrospectively examined 20 patients with Paget's disease without a detectable mass treated at a single institution.¹¹ Seventeen patients underwent biopsy only, whereas 3 underwent excision of the nipple or nipple and areola prior to radiotherapy. The median dose delivered to the breast was 57 Gy, with a boost given to 90% of patients to a median total dose of 72 Gy to the tumor site (range, 55–83 Gy). With a median follow-up of 90 months, 15% of failures recurred in the breast only, and were successfully salvaged by mastectomy. All three failures were in patients who did not undergo complete excision of the lesion. There were no deaths due to breast carcinoma. Bulens et al. reported a series of 13 patients treated conservatively in Leuven, Belgium.¹² Disease was limited to the nipple or skin without evidence of an underlying tumor. Patients underwent biopsy without an attempt at complete excision. The entire breast received 30 to 65 Gy, with a boost to the tumor bed for a total dose of 60–70 Gy. At a median follow-up of 52 months, there were no local or distant failures. A series from Guildford, England included patients treated over a long period with varying presentations and therapy.¹⁶ There was 1 local failure at 38 months among the 8 patients who

were treated with supervoltage techniques with a follow-up ranging from 11 months to nearly 14 years (median, 66 months). Of note, these patients usually were treated with biopsy alone, followed by irradiation limited to the central portion of the breast. In the current series, 2 patients have developed distant disease, resulting in 5- and 8-year distant disease free survivals of 95%. Therefore, although the results of breast-conserving therapy using radiotherapy cannot be definitively compared with those obtained using mastectomy in the absence of a randomized trial, these retrospective analyses suggest similar distant disease free results for the two treatment modalities and encourage consideration of a conservative approach for selected patients with Paget's disease of the nipple.

Although the presence of the intraepidermal Paget's cell is the pathologic hallmark of the disease, the histogenesis of the Paget's cell is controversial. Two theories have been proposed to account for the pathogenesis of the disease.¹⁷ The first theory, the epidermotropic theory, suggests that Paget's cells are derived from ductal epithelium and are essentially DCIS cells that have migrated to the epidermis by way of the lactiferous ducts. The second theory, the transformation theory, proposes that Paget's cells are transformed in situ keratinocytes of the epidermis of the nipple and represent a malignant process independent of the underlying breast parenchyma. Light microscopy studies have produced evidence supporting both theories, but immunohistochemical studies have favored a mammary origin for Paget's cells.^{18–20} Studies using different monoclonal antibodies against low molecular weight epithelial keratins, such as keratins 8, 18, and 19 have demonstrated their presence in large amounts in Paget's cells and their absence in surrounding keratinocytes, characteristic of cells of normal luminal mammary epithelium.⁸ More recent studies have demonstrated concordance of immunoreactivity in the Paget's cells and the underlying carcinoma, including almost identical immunohistochemical staining profiles with antibody 21N, which was raised against a peptide from the C-terminus of the predicted sequence of the *c-erb* B-2 product.^{19,20} Thus, most evidence strongly supports the epidermotropic theory of an underlying carcinoma; however, rare cases of Paget's disease in which an underlying carcinoma cannot be detected histologically still prompt consideration of the in situ transformation theory.

The origin of the Paget's cell has implications for treatment. If the Paget's cell originated de novo in the nipple epithelium, simple resection of the nipple-areolar complex followed by no additional therapy to the remaining breast parenchyma might be an appro-

appropriate therapeutic alternative. However, the presence of an underlying breast malignancy would necessitate treatment to the residual breast tissue. Attempts of nipple-only excision, as suggested by the transformation theory, have produced varying results. In a small series reported by Lagios et al. from San Francisco, 1 of 5 patients treated with complete or partial nipple-areolar excision in the absence of a palpable mass or any suspicious mammographic finding recurred locally at 12 months.²¹ This patient (initially treated with partial nipple-areolar excision) recurred in the residual areolar skin. She was salvaged with reexcision, and all patients remained free of disease with an average of 50 months of follow-up (range, 30–69 months). Paone and Baker at the Johns Hopkins Hospital reported that none of the five patients with Paget's disease presenting in the absence of a palpable mass recurred after nipple excision and wedge resection of underlying breast tissue⁵; however, the length of follow-up was not specified. Dixon et al. in Nottingham, United Kingdom presented the outcome of ten patients with Paget's disease presenting in the absence of a palpable mass with mammographic changes suggesting in situ changes only immediately adjacent to the nipple who were treated with excision of the nipple-areolar complex with a cone of underlying breast tissue.⁴ Despite all patients having negative microscopic deep resection margins, 40% (4 of 10) developed a local failure at 8–19 months after surgery. Three of the four patients recurred with invasive disease; two developed distant metastases, with one death from disease. A recent abstract from Memorial Sloan-Kettering Cancer Center described five patients with Paget's disease with no evidence of invasion treated with a central quadrantectomy including removal of the nipple, and microscopically negative margins; three recurred locally.²² Although the first two series may be consistent with the in situ transformation theory of the histopathogenesis of the Paget's cell, the latter two series strongly support the epidermotropic theory and demonstrate the importance of treatment to the underlying breast in patients with Paget's presenting with in situ disease even in the presence of negative margins.

The current study reports the 5- and 8-year actuarial breast recurrence rates to be 9% and 16%, respectively, when local failure as only site of first failure is calculated. These estimates of breast failure are consistent with those reported for DCIS treated definitively with radiotherapy. The National Surgical Adjuvant Breast Project B-17 trial reported a 5-year breast recurrence rate of 7% with 43-month mean follow-up.⁹ Solin et al. presented the collaborative results from nine institutions using breast-conserving surgery and radiotherapy for DCIS of the breast.²³ The 5- and 10-

year actuarial rates of local failure were 6% and 16%, respectively. Rates of surgical salvage were similar between the series reported by Solin et al.²³ and the current series, with 86% and 80% (4 of 5) of the local recurrences, respectively, salvaged by additional treatment. In addition, the long term rates of survival free from distant metastases were comparable between the two series, with the study by Solin et al.²³ reporting a 10-year actuarial rate of freedom from distant failure of 96% versus 95% at 8 years in the current study. Because DCIS represents the predominant underlying malignancy in the breast of patients with Paget's disease without a palpable mass, it is understandable that the local control rate and distant disease free survival for conservatively managed Paget's disease treated with radiotherapy would parallel the results achieved for DCIS.

The authors believe treatment of Paget's disease should include excision of the entire nipple-areolar complex with negative microscopic margins, and all suspicious microcalcifications demonstrated on a pretreatment mammogram, as confirmed by a negative postbiopsy mammogram.²⁴ Although the current series does not have the statistical power to detect a significant impact of complete excision of the nipple-areolar complex or margin status on local control, improved control with complete excision and negative margins is consistent with treatment guidelines for DCIS, in which all areas of potential disease are excised prior to definitive radiotherapy.

Although, to the authors' knowledge, this series is the largest report of patients with Paget's disease of the nipple treated with breast-conserving surgery and radiotherapy, the number of patients and the number of events in the current collective series is small. Other limitations include the lack of a central pathologic and imaging review due to the unavailability of all pathologic and mammographic studies. Thus, additional series are needed to confirm the findings of the current study. However, this study demonstrates the successful results using breast-conserving treatment as an alternative to mastectomy. High rates of disease free and overall survival, in addition to adequate local control, justify consideration of a conservative approach when presenting management options to women with Paget's disease of the nipple presenting in the absence of a palpable mass or mammographic density.

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