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Long-Term Results of Breast Conservation Therapy for Breast Cancer

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Objective

This study was done to determine the long-term outcome of breast conservation therapy (BCT) for patients with early-stage breast cancer during a period of treatment evolution at a single institution.

Summary Background Data

Breast cancer treatment has evolved from extensive surgical extirpation of the breast to treatment options that conserve the breast. Prospective and retrospective studies have confirmed the efficacy of BCT and justify its use for many patients with early breast cancer, but there is no universally accepted consensus as to who benefits from more aggressive application of surgery or radiotherapy in BCT. Prognostic variables for breast cancer and information on factors that contribute to local recurrence help predict BCT results. Continued analysis of BCT still is necessary to improve patient outcome.

Methods

Eighty-five patients treated with BCT (lumpectomy with adjuvant radiation therapy) at the Medical College of Virginia from 1980 to 1990 were identified. Clinicopathologic parameters and treatment details were analyzed for relationship to development of local recurrence, distant metastasis, and survival. Fisher's exact test was used for comparisons. Actuarial survival curves were plotted. The earlier treatment period (1980–1985) was compared with the later treatment period (1985–1990).

Results

Median follow-up was 5 years. Actuarial overall survival was 83% at 5 years (69% at 10 years), and 5-year distant metastasis-free survival was 79%. The 5-year actuarial local recurrence rate was 6.6% (crude rate 10.6%, 9/85). Young patients (age <40 years) were found to be at increased risk for local recurrence (24% < 40 years *vs.* 6% ≥ 40 years, $p < 0.05$). Tumor margins ≤ 3 mm were more frequently found, and lumpectomy site radiation boost was used increasingly from 1986 to 1990. Almost half of all local recurrences occurred after 5 years.

Conclusions

Survival and local recurrence rates were comparable to other series. Young patients were found to be at increased risk for local recurrence. Negative microscopic margins, even when close, can provide low local recurrence rates when adjuvant radiation therapy is administered.

Lumpectomy and axillary lymph node dissection plus radiation therapy—breast conservation therapy (BCT)—has become an accepted method of primary treatment for the majority of women with stage I and stage II breast cancer.[1] In this country, prospective BCT trials began in the late 1970s with National Surgical Adjuvant Breast and Bowel Project (NSABP) B06.[2,3] Results from the NSABP trial, as well as other prospective randomized studies, have demonstrated 5-year overall survival rates from 79% to 93% for BCT, equivalent to those for modified radical mastectomy. Five-year local recurrence rates for BCT reported in prospective studies range from 2% to 13%.[2-5] Retrospective studies of BCT have assessed various risk factors for local recurrence to identify patients who may benefit from more aggressive treatment, *e.g.*, a wider breast resection or higher dose radiation, or even mastectomy.[6] This study was done to determine the long-term results of BCT in a single institution and to assess for the effect of prognostic variables in patients with early-stage breast cancer.

MATERIALS AND METHODS

Clinicopathologic parameters and treatment details were retrospectively reviewed for patients undergoing BCT over a 10-year period (1980–1990). A list of patients who underwent lumpectomy or axillary lymph node dissection at the Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia, was obtained by reviewing the operating room master log. Records from inpatient charts, surgical and radiation oncology clinic charts, NSAPB study charts (when applicable), and the Virginia Cancer Registry were reviewed.

Patient history and physical examination findings were reviewed, including risk factors and the method of breast lesion detection (mammogram or palpable abnormality). Clinical TNM stage was recorded. Diagnosis of breast cancer was by fine-needle aspiration cytology or open surgical biopsy, with the latter procedure considered a lumpectomy if margins were histologically negative. Surgical treatment followed NSABP guidelines, with lumpectomy performed to remove the tumor and sufficient surrounding normal tissue to ensure tumor-free margins. Margins were considered negative if no tumor was in contact with the inked edges of the resected specimen. Throughout the 10-year period, surgical re-excision was used liberally to achieve negative histologic margins. At least a level I and II axillary lymph node dissection was performed as a standard part of BCT. Surgical complications were analyzed.

Histologic evaluation of the specimen included initial biopsy diagnosis and final pathologic diagnosis (biopsy diagnosis was used as final pathologic diagnosis if re-excision was negative for residual tumor). Pathologic findings were re-evaluated in detail in three fourths of cases for the purposes of this study, with the remainder not having sufficient material available for re-evaluation (biopsy slides from outside hospitals or inadequate slides from our institution). Specimen assessment also included distance in millimeters to the surgical margin, as measured from either tumor edge or biopsy cavity (if re-excision was performed). Complete pathologic analysis was recorded, including the histologic type of the neoplasm (ductal, lobular, medullary, etc.), histologic features (intraductal component, extensive intraductal component [EIC], lymphatic or vascular invasion, and grade), tumor size and node involvement (pathologic TNM stage), surgical specimen size, and hormone receptor status.

After surgery, all 85 patients were treated to the entire breast with opposed tangential photon fields, and 56 of these patients received additional dose to the tumor bed by either electron beam, photons, or brachytherapy. Typically, 45 to 50 Gy in 1.8 to 2.0 Gy fraction was delivered to the entire breast, using either a 4- or 6-megavolt linear accelerator. Cobalt 60 was used for some of the earlier cases. Boosting of the tumor bed before 1988 was at the discretion of the treating radiation oncologist, and its use became more frequent after 1985. This consisted of an additional 10 to 15 Gy, usually delivered as electrons. In 1988, a treatment policy was initiated to standardize the method and amount of additional dose delivered to the tumor bed based on pathologic margin status.[6] A measurement from the edge of tumor to the surgical margin was requested in each case. If the closest margin was >5 mm, an additional 10 Gy was delivered to the tumor bed with electrons. A margin of 2 to 5 mm was considered close and 14 to 16 Gy were given. If a margin of <2 mm or a focally positive margin was encountered, an additional 20 Gy to the tumor bed was indicated, and a brachytherapy implant with iridium 192 was preferably used. Total dose delivered, therefore, ranged from 45 to 50 Gy to the entire breast and from 45 to 70 Gy to the tumor bed, depending on whether a boost dose was used. The use of adjuvant chemotherapy and hormonal therapy was variable in regard to type or combination. Many of the patients were enrolled in NSABP studies and received adjuvant therapy according to protocol guidelines.

Patient follow-up was by both the surgical and radia-

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Table 1. OPERATING ROOM MASTER LOG: 1980–1990

	Number
"Segmental mastectomy/lumpectomy"	135
Completed BCT	85
No radiation	25
Randomization (NSABP B06)	7
Favorable pathology (DCIS, LCIS, colloid, phyllodes)	7
Reason not documented	4
Extreme age (> 80 yrs old)	3
Noncompliance	3
Distant metastatic disease discovered	1
Excluded from analysis	25
Insufficient information	10
Mastectomy (6 for positive margins, 2 patient preference)	8
Biopsy (6 benign, 1 known stage IV disease)	7

BCT = breast conservation therapy; NSABP = National Surgical Adjuvant Breast and Bowel Project; DCIS = ductal carcinoma *in situ*; LCIS = lobular carcinoma *in situ*.

tion oncologists, initially every 3 months for at least 2 years, and subsequently at 6-month intervals. Mammograms were obtained every year for follow-up of both the treated and contralateral breast. Additional workup was done as clinically indicated. Details of follow-up, specifically whether recurrent or metastatic disease occurred, were documented along with any subsequent treatment. Local recurrence was defined as recurrence of cancer in the ipsilateral breast, and regional or distant metastases were recorded to determine metastasis-free survival. Actuarial survival curves were plotted for local recurrence-free, metastasis-free, and overall survival. Patients' clinical and pathologic findings and treatment variables were tested for relationship to local recurrence and distant metastases. The early treatment period (1980–1985) was compared with the subsequent treatment period (1985–1990) to evaluate for changes in treatment results. Fisher's exact test was used for comparisons.

RESULTS

Clinicopathologic Findings

Retrospective chart review yielded sufficient information in 93% (125/135) of cases initially identified as BCT patients. Eighty-five patients had documented completion of BCT and were the basis for this review (Table 1). Median age was 51 years, with a range of 29 to 79 years. Most patients were white or black, 58% and 39%, respectively. Younger patients (<40 years) made up 25% of the group. Clinical staging revealed 42 stage I cancers, 40 stage II cancers, 1 stage III cancer, and 2 unknown cases. In 62% of the cases, the lesion was discovered by the patient. Diagnosis was by fine-needle aspiration in 41% and open surgical biopsy in 55% of cases. Eighty-three percent of cases having open surgical biopsy underwent a re-excision of the biopsy site, and 58% of the re-excisions were positive for residual tumor. Only 6% of patients diagnosed by fine-needle aspiration required a re-excision of the lumpectomy site. Seroma (14%) and infection (6%) were the most common complications in the postoperative period.

Classification by pathologic stage showed 36 stage I cases, 32 stage IIA cases, and 17 stage IIB cases (Table 2). Invasive ductal carcinoma made up 89% of the cases. Detailed histologic evaluation identified the presence of the following tumor characteristics: any intraductal component, 45%; EIC, 21%; and lymphatic or vascular

Table 2. PATHOLOGIC FINDINGS IN BREAST CONSERVATION THERAPY CASES

Finding	Percent of 85 Cases
Stage	
I	42
IIA	38
IIB	20
Histologic subtype	
Invasive ductal	89
Medullary	7
Colloid	2
Lobular	1
Histologic features*	
Any intraductal component	45
EIC	21
Lymphatic/vascular invasion	26
High nuclear grade	39
Receptor status†	
ER postiive	53
PR positive	43
Margins	
Negative	93
Positive	2
Unknown	5
Specimen size‡	
≤5 cm	5
5.1–10 cm	56
>10 cm	33
Unknown	6

EIC = extensive intraductal component; ER = estrogen receptor; PR = progesterone receptor.

* Of those reevaluated (one fourth of cases had insufficient pathologic material available).

† Of those having hormone receptor status determined (two thirds for ER and one half for PR).

‡ Largest axis chosen to represent specimen size (either length, width, or thickness).

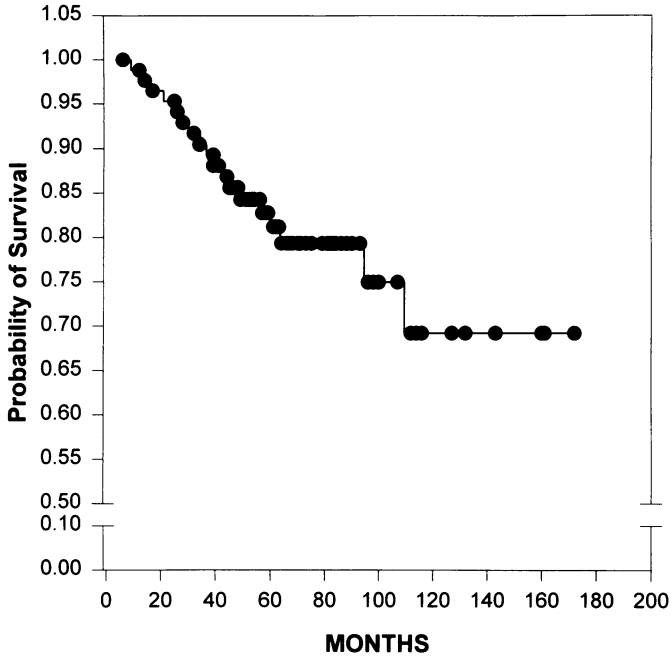

Figure 1. Actuarial overall survival of patients treated with breast conservation therapy.

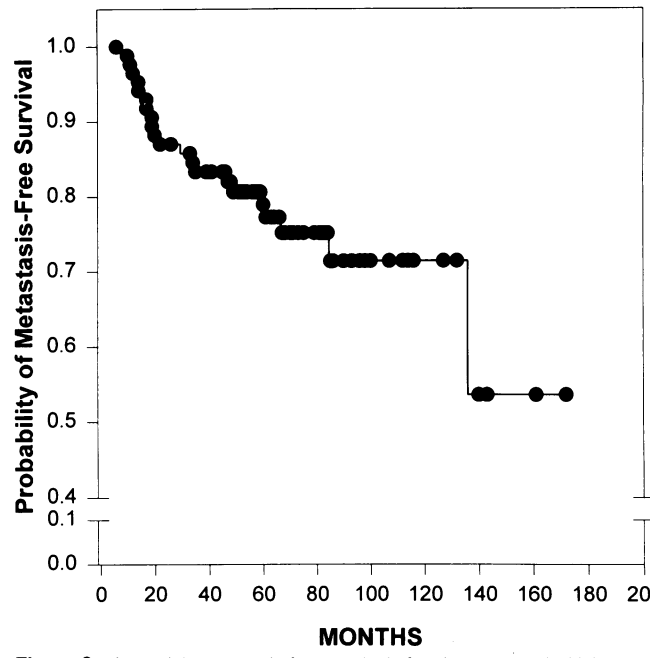

Figure 2. Actuarial metastasis-free survival of patients treated with breast conservation therapy.

invasion, 26%. Negative margins were achieved by surgery in 93% of cases, with the remainder of margins unknown (5%) or positive (2%). Of two patients with positive margins, one refused mastectomy and the other had only a focal positive margin and colloid carcinoma. Estrogen receptor analysis was available in two thirds of the cases, with 53% of those tested positive.

Total radiation dose (initial dose plus boost dose to tumor bed) was 45 to 49 Gy in2 cases, 50 to 59 Gy in 24 cases, 60 to 69 Gy in 41 cases, and ≥70 Gy in 11 cases; in the remaining 7 cases, the dose was unknown. Sixty-six percent of cases had a boost dose, usually with electrons (¾). Iridium 192 interstitial implant was used in seven cases, two for positive margins and five for margins ≤ 3 mm. Chemotherapy (most commonly either adriamycin/cyclophosphamide or cyclophosphamide/methotrexate/fluorouracil) was given to 34% (29/85) of patients, usually on an NSABP protocol (¾ of chemotherapy given). Of node-positive patients, 71% (20/28) received chemotherapy. Twenty percent of all patients received tamoxifen.

Outcome

Median follow-up was 5 years and ranged from 42 months to 172 months. Five-year overall and metastasis-free survival were 83% and 79%, respectively, with 10-year overall survival at 69% (Figs. 1 and 2). Crude local recurrence rate was 10.6% (9/85). Actuarial local recurrence rate at 5 years was 6.6% (Fig. 3). Age was the only factor significantly related to local recurrence (24% for patients age <40, *vs.* 6% for patients ≥ age 40 years, $p < 0.05$; Table 3). Older patients did not have a statistically significantly higher percentage of stage I disease (45%) compared with younger patients (33%), and rates of node positivity were

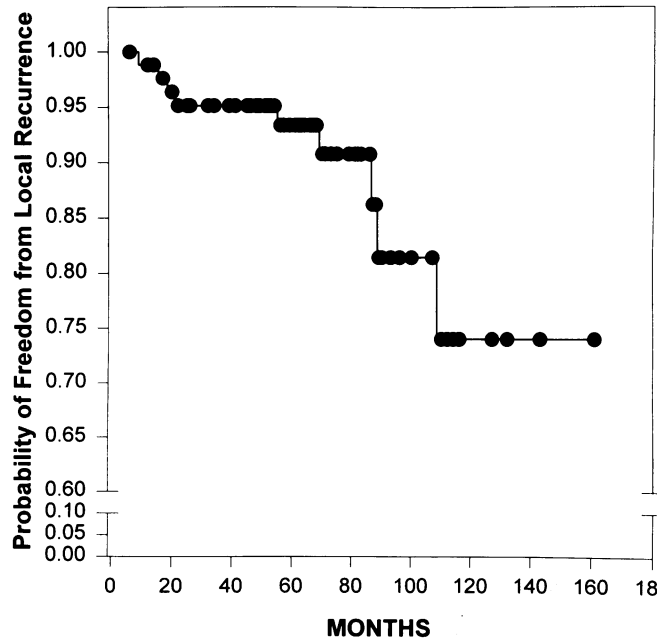

Figure 3. Actuarial local recurrence-free survival of patients treated with breast conservation therapy.

Table 3. UNIVARIATE ANALYSIS OF RISK FACTORS FOR LOCAL RECURRENCE (LR)

Variable		Percent LR	Significance*
Age	<40 *vs.* age ≥40	24% *vs.* 6%	$p < 0.05$
Stage (pathologic)	I *vs.* IIA and IIB	8% *vs.* 11%	NS
Stage (pathologic)	I and IIA *vs.* IIB	9% *vs.* 17%	NS
Nodes	+ *vs.* −	9% *vs.* 14%	NS
Intraductal component	+ *vs.* −	8% *vs.* 17%	NS
EIC	+ *vs.* −	15% *vs.* 8%	NS
Lymphatic/vascular invasion	+ *vs.* −	12% *vs.* 8%	NS
Margins	≤3 mm *vs.* > 3 mm	7% *vs.* 15%	NS
Radiation boost	Yes *vs.* no	11% *vs.* 14%	NS
Chemotherapy	Yes *vs.* no	10% *vs.* 15%	NS

LR = local recurrence; NS = not significant ($p > 0.05$) EIC = extensive intraductal component.
* Fisher's test.

approximately equal, 38% for younger *vs.* 33% for older patients. Factors not significantly related to local recurrence included tumor size, EIC, lymphatic invasion, and positive regional nodes. Treatment variables (margins, re-excision of biopsy site, lumpectomy specimen size, radiation boost, and use of chemotherapy) also did not affect local recurrence. For the nine patients with local recurrence, disease-free interval was > 5 years in four, and salvage mastectomy was performed in seven, with five still with no evidence of disease at last follow-up (Table 4). Distant metastasis developed in 25% of the total series (21/85). Only pathologic stage (19% for stage I and IIA *vs.* 47% for stage IIB, $p < 0.05$) predicted distant metastases. No statistically significant relationship was found between treatment variables and development of distant metastases.

Treatment Evolution

Analysis of earlier (1980–1985, 20 patients) and later (1986–1990, 65 patients) treatment groups revealed no significant changes in clinical characteristics or pathologic findings, except for surgical margins. Close tumor margins (≤ 3 mm) and focally positive margins were more frequent in the later time period (21% for earlier *vs.* 54% for later, $p < 0.05$), and a radiation boost to the lumpectomy site became more frequently used (40% earlier *vs.* 74% later, $p < 0.05$). The treatment guidelines adopted for the optimization of irradiation were instituted in 1988.[7] No change in need for re-excision (approximately 50%) could be documented. Use of chemotherapy was the same for both time periods.

DISCUSSION

As expected, the overall and metastasis-free survival at 5 years (83% and 79%, respectively) closely reflected the most recent determinations of the NSABP B06 5-year life-table estimates (84% overall survival and 74% distant

Table 4. CHARACTERISTICS OF LOCAL RECURRENCE CASES

Age (yrs)	Pathologic Stage	Histology* and Features†	Margins/Closest Distance	Radiation (Total Dose in Gy)/ Chemotherapy	Months to LR	Mastectomy (type)/Outcome
27	I, T1N0	2	Negative 5 mm	50 No	110	Salvage AWD
32	IIA, T2N0	1	Negative 12 mm	46 No	70	Salvage NED
32	IIB, T2N1	1 a, b, c	Negative 10 mm	50 Yes	12	Salvage NED
38	I, T1N0	1	Negative ? mm	60 No	56	Lost FU
39	IIB, T2N1	1	Negative 15 mm	60 Yes	22	Salvage DOD
43	IIA, T2N1	1 c	Negative ? mm	60 Yes	17	"Toilet" DOD
50	IIA, T2N0	1 a, b	Negative 4 mm	70 No	20	Salvage NED
58	IIA, T1N1	1	Negative 3 mm	60 No	87	Salvage NED
63	I, T1N0	1	Negative 3 mm	60 No	89	Salvage NED

* 1. infiltrating ductal, 2. medullary.
† a, intraductal component; b, EIC: c, lymphatic/vascular invasion.
LR = local recurrence; AWD = alive with disease; DOD = dead of disease; NED = no evidence of disease; Lost FU = lost to follow-up.

disease-free survival).[2] Our 10-year actuarial data showed 69% overall survival. In a retrospective study reviewing the long-term outcome of BCT, the University of Pennsylvania reported on 697 women with early-stage breast cancer and found the 10-year overall survival was 83%.[8] In their review, Fowble et al.[8] examined other retrospective studies with 10-year overall survival rates ranging from 61% to 86%. They concluded that their survival rates were at the high end of contemporary results, possibly reflecting the frequent use of adjuvant chemotherapy because 77% of node-positive patients were treated. The determination of prognostic factors affecting long-term outcome was a major objective of this review. Only pathologic stage was related significantly to development of metastatic disease, and 47% of stage IIB patients developed regional or distant relapse compared with 19% of stage I and IIA patients. At our institution, BCT has evolved such that it frequently is recommended and chosen for the treatment of early breast cancer, but long-term outcome results reinforce our longstanding commitment to participating in adjuvant systemic therapy trials.

Another important aspect of BCT is the identification of risk factors for local recurrence. Although local recurrence per se has not been shown to adversely affect long-term overall survival,[2,3,9] it is desirable to understand and prevent this distressing event. The NSABP B06 results clearly demonstrated an increased local recurrence rate when adjuvant radiation was not used (10% local recurrence for irradiation, *vs.* 39% local recurrence for none at 8 years).[2] Of the seven patients randomized to the NSABP B06 lumpectomy-only arm at our institution, 43% (3/7) recurred locally (patients not irradiated were not included in the BCT results reported here).

Several recent reports have suggested that young age (variously demarcated at 30–50 years of age) is a risk factor for local recurrence,[10–14] whereas others have not.[15,16] Analyses of this subject have described a variety of histologic features that may more commonly be present in the young patient with breast cancer: lymphatic stromal reaction, high histologic grade, EIC, lymph node involvement.[12,17] It has been hypothesized further that these histopathologic differences may contribute to the increased local recurrence rates found in this group.[12,17] We did not encounter higher rates of lymph node involvement, EIC, or high-grade tumors as described in some studies, but young age (< 40 years) still was associated with a higher rate of local recurrence in our study. Moreover, we did not find that any of these pathologic features were significant independent risk factors for local recurrence.

One study of 88 BCT cases in women younger than 35 years of age demonstrated no increase in local recurrence rate.[16] This result was attributed to aggressive pathologic axillary node staging and use of adjuvant chemotherapy for node-positive patients, as well as assessment of resection margins and liberal use of re-excision. Evidence that adjuvant chemotherapy decreases local recurrence rate in BCT has been reported,[2,18,19] and some of our patients were in randomized studies to investigate this. Most of our young patients had adjuvant chemotherapy for positive nodes. Even in series confirming higher local recurrence in younger patients, survival was not compromised compared with similar patients treated by mastectomy.[20] As stated by Harris and Gelman in their editorial on risk factor assessment for BCT, ". . . young patient age may be a prognostic factor for local recurrence, but is not necessarily of assistance in selecting the best form of local treatment."[6] (p648) Young patient age is not a contraindication to BCT, but additional prognostic markers are sought that predict which patients benefit from adjuvant chemotherapy, additional radiotherapy, or even mastectomy to prevent the problematic 24% local recurrence rate we found in this subset of patients.

From the perspective of the surgical oncologist, a negative margin in early breast cancer is one that requires no further excisional surgery. Pathologically, this mandates lack of tumor at the inked microscopic margin, although it may be close. Multiple studies demonstrate that margin status impacts on local recurrence rate, uniformly concluding that every effort should be made to attain negative microscopic margins.[21–23] Furthermore, studies on radiation dose and margin status have suggested that a radiation boost contributes to the successful local control of close (or sometimes even positive, depending on definition) margins.[7,24] Radiation oncologists have suggested that it is useful to analyze margin measurements in millimeter increments to optimize radiation treatment. As defined by Schmidt-Ullrich, a margin < 2 mm is essentially positive, a margin of 2 to 5 mm is considered close, and a margin > 5 mm is considered clear. The evolution in radiation treatment at our institution was examined, particularly as reflected by use of boost dose in relation to surgical margin. Our initial experience with BCT stemmed from participation in the NSABP B06 study, in which the lumpectomy plus radiation therapy arm of the protocol required negative margins and irradiation to 50 Gy (no boost allowed). However, our more recent experience (1988–present) sought to optimize radiation technique and doses according to the published guidelines noted.[7] The observed consequence of this radiation policy was that close and focally positive margins were both routinely tolerated and more frequently found (21% *vs.* 54% during the earlier and later time period, respectively). This reflects our confidence that carefully prescribed radiation boost ensures low local recurrence rates, despite close margin status. This also should im-

prove the cosmetic outcome, although that was not specifically evaluated in this series.

A controversial issue is the impact of EIC-positive cancer on local recurrence rate. Recent data have suggested that if margins were positive or not assessed, presence of an EIC predicted a high risk for local recurrence.[25] However, in cases in which microscopically negative inked margins were attained, local recurrence rates for EIC-positive cancers have been low.[6,14,26,27] Our number of EIC-positive cancers (21%) appears comparable to those of larger contemporary studies.[12,21] Attaining negative surgical margins has been a standard requirement for BCT at our institution, and thus, our results have not demonstrated higher rates of local recurrence in EIC-positive cancer. This emphasizes the critical role of surgery in BCT, and validates our longstanding policy of requiring a microscopically negative margin. The effect of EIC, therefore, is negated by use of re-excision as needed to attain negative margins. In addition, relegating patients in whom negative margins cannot be attained to mastectomy "censors" the effect of EIC somewhat.

Between 1980 and 1990, the option of BCT at the Medical College of Virginia evolved from experimental protocol to established practice. We have incorporated the surgical experience from participating in the NSABP trials, the proven treatment practices from our radiation oncology department, and the information reported in the literature to do so successfully. The long-term results of this experience demonstrate comparable overall and metastasis-free survival rates to other contemporary series for BCT. Patients younger than 40 years of age were found to be at increased risk for local recurrence. Negative microscopic margins, even when close, can provide low local recurrence rates when postoperative radiation therapy is administered. However, prolonged careful follow-up of these patients is essential because nearly half of the local recurrences seen occurred after 5 years.

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Discussion

DR. ROGER S. FOSTER, JR. (Atlanta, Georgia): Vice President Haller, Secretary Copeland, Members of the Southern, and Guests. I would like to take this opportunity to thank the Fellows for the privilege of election to this Association.

A member of this Association, the late George Crile, Jr., was an advocate of breast conservation surgery and began performing such procedures in 1955. However, despite the randomized trial data, there is evidence that even in recent years, many surgeons have remained skeptical about the safety of breast conservation, as indicated by both opinion surveys and by the wide variations in the use of breast conserving surgery versus total mastectomy.

If I could have the slide, please.

Illustrated on this slide are wide institutional and geographic differences in the selection of patients for breast conservation surgery. Data from the American College of Surgeons National Cancer database indicate that 31% of patients with stage 0 and I breast cancer had breast conserving surgery in 1986 through 1987, which had risen to 49% in 1992. The geographic variation in the use of breast conserving surgery in 1992 is illustrated by the rate of 62% in the Northeast, 44% in the South Atlantic and 38% in the South. Studies have indicated that these differences in rates are related more to the reluctance of surgeons to be totally convinced that breast conserving surgery is safe than to patient choice.

When I reviewed our breast cancer surgeries at the University of Vermont for 1989 and 1990, which corresponds to the last 2 years of today's study, we had performed 180 lumpectomies for invasive breast cancers and an additional 20 surgeries for ductal carcinoma *in situ*. In these 2 years, I was personally treating most of these patients. Seventy-three percent of all our invasive breast cancer patients had breast-conserving surgery; 86% for clinical stage I, 60% for stage II, and 33% for clinical stage III.

The authors of today's study have examined factors associated with in-breast recurrence and have emphasized two factors with which I would agree. In their experience and that of many others, younger age is a major predictor of ipsilateral recurrence but not a factor contraindicating breast conservation therapy. Although the authors felt that negative surgical margins were important, *i.e.*, that the tumor does not touch the inked margin of the specimen, beyond that, wider margins were of little importance in patients treated with radiotherapy.

This relatively small series did not demonstrate a significant association between chemotherapy and reduction of in-breast recurrence. Many other large studies, however, have demonstrated that when the patients are treated with systemic therapy, either cytotoxic therapy or tamoxifen there are quite low rates of in-breast recurrence and lower rates than were seen prior to the use of systemic adjuvant therapy.

For example, at 12 years in the National Surgical Adjuvant Breast Project (NSABP) BO6 trial for node-positive patients treated with chemotherapy, there was only a 5% in-breast recurrence rate after lumpectomy plus radiotherapy plus chemotherapy. Many multiple, more modern studies are showing rates of less than 2% at 5 years.

I have three questions for the authors.

What proportion of your patients were treated with breast conservation therapy?

You had only one patient with invasive lobular carcinoma. Why was that?

Was tamoxifen therapy associated with a lower in-breast recurrence rate in your patients?

Thank you.

DR. DANIEL E. KENADY, SR. (Lexington, Kentucky): Dr. Haller, Dr. Copeland, Members, and Guests. I appreciate the opportunity to discuss this paper. And, as Dr. Foster, I appreciate the honor bestowed on me by election into this Association.

This is a very elegant study by Dr. Bear and Dr. Neff, and there is a lot, obviously, in the manuscript that could not be brought out.

We went back and looked at our series at the University of Kentucky. We are in one of those areas, particularly Kentucky, to later really get on the bandwagon for breast conservation. It has really been in the last few years that our numbers have really increased. We have 69 patients that we have follow-up on dating back to 1986. In that group, we have three who developed distant metastases. We have not seen a local recurrence. But the point is not that we are better surgeons or we have better therapists. The factor is we do not have the follow-up, and this is what we need—more studies like this that have long follow-up. We are seeing a significant number of these patients recur at 10 years and even farther out. Our average follow-up is only 2 years.

Of the nine patients who Dr. Bear identified as demonstrating local recurrence, four were over 5 years, and one additional patient was just 4 months short of that 5-year mark. So long follow-up is definitely needed.

I feel there are three important tenets to take away from this study. Re-excision for positive margins is absolutely mandatory, and our feeling is when you do re-excise, that you need to excise the entire surgical cavity. There is actually no way to know for sure where that positive margin was, and you have to always worry about seeding.

Fifty-eight percent of the patients in this series did have additional tumor identified with the re-excision. And it is interesting that the 3-mm figure is becoming more and more accepted. We agree with that also. And even though it did not reach statistical significance in this study, those who had a margin of 3 mm or more had only a 7% local recurrence as opposed to a 15% local recurrence. So that is certainly concerning when you do get less than 3 mm.

The radiation boost, we feel, also should be proportional to