Feasibility of Breast-Conserving Therapy for Younger Women With Breast Cancer

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**Objective:** To determine if breast-conserving therapy (BCT) consisting of segmentectomy, axillary lymph node dissection, and postoperative irradiation is a feasible approach to breast cancer in younger women, whose breast tissue is dense and whose tumors can be difficult to detect and successfully excise.

**Design and Patients:** We studied BCT in 59 women 35 years old or younger (mean age, 31.7 years) treated for breast cancer since 1982. Ninety percent of their cancers were palpable; 44% were not visible by mammography. Most (93%) had T1 or T2 lesions (≤5 cm). Invasive ductal carcinoma was the predominant histologic diagnosis (68%).

**Results:** Segmentectomy with axillary dissection was the initial operative procedure for 39 (66%) of the 59 patients; of these, 21 (54%) had microscopically positive segmentectomy margins. Nine patients (23%) with diffusely positive segmentectomy margins and four patients (13%) with local recurrences after BCT required conversion to mastectomy. Three patients (8%) underwent reexcision to achieve negative margins. The 39 patients required a total of 22 additional surgical procedures for local control. Thirty-three (56%) of the 59 patients underwent mastectomy during the mean 68-month follow-up period; 20 (34%) underwent mastectomy as the initial definitive treatment. Reasons for primary mastectomy included multifocality or multicentricity (35%), large tumor size (30%), patient preference (15%), and occult primary tumor (10%). During the same time period, 474 (64%) of 745 women older than 35 years underwent BCT as treatment of breast cancer. Two percent required conversion to mastectomy and 1% required repeated excision. Twenty-four patients (5%) required mastectomy for local recurrence after BCT. After excluding mastectomies performed because of patient preference, significantly fewer older women required mastectomy to achieve local control (21% vs 50%, P<.001).

**Conclusions:** Breast-conserving therapy is significantly more difficult in younger women despite surgeon and patient commitment. Patients and physicians should be encouraged to consider BCT but should be aware of the potential difficulty in obtaining adequate local control and the possible need for additional operative procedures.

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**B**reast-conserving therapy (BCT) (surgery with postoperative radiation therapy) is an effective and desirable local therapy for women with breast cancer. Not only does breast preservation have possible psychological advantages over mastectomy, but there is no significant survival difference between mastectomy and a breast-preserving regimen of partial mastectomy, axillary lymph node dissection, and postoperative irradiation.

Women 35 years old and younger represent a significant population of patients treated for breast cancer, ranging from 1% to 25% of all women with breast cancer. The impact of young age on local recurrence and overall survival is controversial. Several studies of partial mastectomy with axillary dissection and postoperative irradiation have identified youth (generally defined as ≤35 years old) as a risk factor for local recurrence, but other reports have not. In addition, there is no consensus regarding the impact of youth on survival for each stage of breast cancer.

We undertook this analysis to examine the feasibility of breast preservation in young women with breast cancer and to identify factors that may limit the success of BCT.

**RESULTS**

The mean age of the 59 study patients at diagnosis was 31.7 years, with a range of 23 to 35 years. Follow-up was maintained for 4 to 156 months, with a mean duration of 68 months.

See Patients and Methods on next page
PATIENTS AND METHODS

Women treated for invasive and noninvasive breast cancer between 1982 and 1995 were followed prospectively for local, regional, and distant recurrence. Those 35 years old and younger at the time of initial surgery were selected for evaluation; those older than age 35 served as a comparison group. Local recurrence was defined as the finding of carcinoma in the previously treated breast at any time during the period of follow-up, even after regional or distant metastasis. All patients underwent definitive surgery and were followed at the John Wayne Cancer Institute, Santa Monica, Calif, but some had undergone initial biopsy or radiotherapy elsewhere. There were 59 women in the evaluation group and 745 women in the comparison group.

STUDY VARIABLES

Preoperative study variables included age, method of tumor diagnosis, and clinical stage. Using the TNM system, preoperative tumor size was prospectively staged according to the diagnostic modality (palpation, ultrasonography, or mammography) yielding the largest tumor diameter. Initial and subsequent operative procedures and their rationale were recorded. Postoperative information included tumor size and histopathologic features, pathologic stage, estrogen and progesterone receptor status, and nodal involvement. Additional analysis included duration of follow-up; presence or absence of local, regional, or systemic recurrence; and the use of adjuvant chemotherapy.

Physical examination was the most common method of diagnosis; 53 (90%) of 59 cancers presented as a palpable mass. Four patients (7%) presented with bloody nipple discharge, while the remaining two patients (3%) had screening mammographic abnormalities. Only 33 of 59 (56%) biopsy-proven cancers were mammographically detectable.

Invasive ductal carcinoma was the predominant histologic diagnosis, occurring in 24 patients (41%). Sixteen patients (27%) had invasive ductal carcinoma with ductal carcinoma in situ (DCIS). Nine patients (15%) had extensive DCIS with foci of microinvasion, six patients (10%) had invasive lobular carcinoma, and four patients (7%) had medullary cancers.

In 41 of the 59 young patients, tumor size could be assessed before and after surgery. Preoperative clinical assessment yielded 16 T1 lesions (39%), 22 T2 lesions (54%), two T3 lesions (5%), and one T4 lesion (2%). Postoperative histopathologic assessment showed that seven (44%) of the 16 T1 lesions were histologically T2 (4/16, 25%) or T3 (3/16, 19%), while six (27%) of the 22 T2 lesions were actually T3 primaries. Thus, in 13 patients (32%) primary tumor size was increased after final pathologic assessment was available (Figure 1).

When the clinical assessment of tumor size was the same as the postoperative histopathologic size (T1 and T1, T2 and T2), BCT successfully preserved the breast in seven (78%) of nine patients having T1 lesions and eight (50%) of 16 patients having T2 lesions. If the clinical tumor size underestimated the histopathologic size (T1 to T2 or T3, T2 to T3), BCT was successful for only two (15%) of 13 patients (Figure 2).

Breast-conserving surgery was the primary operative procedure for 39 (66%) of the 59 study patients. Twenty-one (54%) of the 39 had microscopically positive segmentectomy margins. Thirteen (33%) of the 39 required conversion to mastectomy, nine for positive segmentectomy margins and four for local recurrence. Three patients (8%) underwent repeated excision to achieve tumor-free margins. Breast preservation was ultimately successful in 26 (44%) of the 59 patients. This group required 22 other surgical procedures to achieve satisfactory local control.

Thirty-three (56%) of the 59 patients underwent mastectomy during the period under study, with mastectomy the initial operative approach for 20 (34%). Reasons for mastectomy as a primary procedure included tumor multicentricity or multifocality (35%), large tumor size (30%), patient preference (15%), and occult primary with malignant adenopathy (10%) (Table 1).

Completion or salvage mastectomy was performed in 13 (22%) of the 59 patients (Table 2). Nine patients (23%) undergoing attempted BCT had diffusely positive segmentectomy margins and required conversion to mastectomy. Four (13%) of the remaining 30 patients completing BCT subsequently underwent mastectomy after developing local recurrence.

Twenty-nine patients (49%) had histologically con-
firmed malignant adenopathy. Twenty-one (40%) of 53 tumors were estrogen-receptor positive, and 17 (33%) of 51 tumors were progesterone-receptor positive. Forty-one patients (69%) received systemic chemotherapy.

In the study group of the 59 women, there were six local recurrences (12%; four after BCT and two after primary mastectomy), no axillary recurrences, three supraclavicular recurrences (5%), and 12 distant metastases (20%). At the last follow-up visit, 46 patients (78%) remained free of disease, five patients (8%) were alive with disease, and eight patients (14%) were deceased.

In the comparison group of 745 older women treated during the same period, BCT was undertaken in 474 patients (64%), with a success rate of 93% (441/474)—significantly higher than the 66% success rate in the study group of younger women ($P<.001$) (Table 3). The rationale for primary mastectomy included patient preference (43%), large tumor size (22%), and multifocal or multicentric disease (8%). Breast preservation failed in nine patients (2%) who required conversion to mastectomy for diffuse positive margins and in 24 patients (5%) requiring salvage mastectomy for local recurrence. Five patients (1%) underwent reexcision. The mean duration of follow-up for patients older than 35 years was 75 months. When compared with the study group of younger women, fewer older women underwent mastectomy (41% vs 56%, $P=0.09$). After excluding patients who selected mastectomy as their preference over BCT, significantly fewer older than younger women required mastectomy (21% vs 50%, $P<.001$).

Breast cancer in younger women ($\leq 35$ years) often escapes diagnosis for many months,\textsuperscript{22} usually because its diagnosis in this age group is complicated by a high rate of benign conditions such as fibrocystic disease and fibroadenomas. Once breast cancer has been diagnosed, BCT is desirable for both younger and older women. Breast-conserving therapy can be undertaken in some patients whose lesions are larger than 5 cm, but most studies comparing BCT with mastectomy restrict primary tumor size to $\leq 3$ cm, to preserve cosmesis while minimizing the risk of local recurrence.\textsuperscript{23}

Methods of preoperative tumor diagnosis and staging remain suboptimal in the younger woman. Noninvasive diagnostic techniques such as mammography are frequently compromised by the denser breast parenchyma of younger women. Only 3% of our study pa-

### Table 1. Reasons for Primary Mastectomy

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<th>&amp; % of Patients</th>
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<tr>
<td>$\leq 35$ y of Age</td>
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<tr>
<td>Multifocal/multicentric tumor</td>
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<td>Large tumor</td>
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<tr>
<td>Patient preference</td>
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<td>Occult tumor</td>
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<td>Inflammatory cancer after chemotherapy</td>
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<td>Unfavorable location of tumor</td>
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<td>Paget's disease</td>
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<td>Contraindications for radiation therapy</td>
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* $P<.001$, $\chi^2$ test.

### Table 2. Reasons for Conversion to Mastectomy (Secondary Mastectomy)

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<th>&amp; No. (%) of Patients</th>
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<tr>
<td>$\leq 35$ y of Age</td>
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<tr>
<td>BCT\textsuperscript{*} not successful</td>
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<tr>
<td>Diffusely positive segmentectomy margins</td>
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<td>Local recurrence after BCT</td>
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* BCT indicates breast-conserving therapy.
\dagger $P<.001$, $\chi^2$ test.

### Table 3. Effect of Patient Age on the Success of BCT\textsuperscript{*}

<table>
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<th>&amp; No. of Patients</th>
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<tr>
<td>$\leq 35$ y of Age</td>
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<tr>
<td>Total No. of patients</td>
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<tr>
<td>BCT attempted</td>
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<tr>
<td>BCT successful</td>
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<td>BCT success rate, % (successful BCT/attempted BCT)</td>
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* BCT indicates breast-conserving therapy.
\dagger $P<.001$, $\chi^2$ test.
tients had tumors that were diagnosed mammographically, and the overall sensitivity of this technique was only 56%.

Although physical examination detected nearly all (97%) of the breast tumors in our group of younger women, all diagnostic modalities together underestimated nearly a third of these patients. This discrepancy is similar to that reported by Holland et al.24 for patients whose tumors were measured clinically and mammographically. Preoperative understaging significantly affects the success of BCT. In our study, accurate clinical tumor size assessment led to successful completion of BCT in 60% of the younger patients. Conversely, underestimation of tumor size was a significant predictor of BCT failure. Since increased local recurrence rates have been associated with tumor-involved segmentectomy margins,15,26 success of BCT also depends on the ability to excise the tumor with a margin of noninvolved tissue. This is much easier when the patient has a focal, discrete, palpable mass whose edges can be easily identified and surgically circumscribed. Not surprisingly, breast cancers with an extensive intraductal component (EIC) have been associated with an increased rate of local recurrence.12,13,27 which Schnitt et al.28 attribute to the clinically inappropriate tumor burden in the vicinity of the primary site. Other authors maintain that margin status supersedes EIC as a risk factor for local recurrence. There is evidence that the inability to define the extent of disease within the breast, when combined with the finding of extensive DCIS, is associated with local recurrence rates as high as 71% after 8 years of follow-up.27 Recht et al.12 state that in their experience, EIC is the most important predictor of breast cancer recurrence. The incidence of invasive ductal carcinoma with EIC is higher in young breast cancer patients.12,13,28,29 and tends to have a wider extension in this group.29 In these patients, therefore, indiscernible tumor margins combined with a high incidence of wide tumor extension underscore the need to ensure tumor-free margins for local control.

The relationship between youth and multifocal or multicentric disease is not clear. Lagios et al.26 noted an increased incidence of multicentric invasive carcinoma (47%) in patients with larger foci of EIC. Similarly, Holland et al.24 after excluding 8% of their mastectomy series for “diffuse invasive cancer,” found that using 3- to 4-cm margins during excision of tumors smaller than 4 cm yielded a 7% to 9% risk of residual foci of invasive cancer and a 4% to 9% risk of DCIS in the remaining breast. In our series, significantly more mastectomies were performed for tumor multifocality or multicentricity in younger patients than in older patients (35% vs 8%, P < .001). The more frequent multifocality and multicentricity of younger patients’ tumors may contribute to the difficulty of BCT in this group.

Finally, the success of BCT depends on technical factors such as careful intraoperative palpation. In our experience, a firm cancer is more easily palpated in a fatty breast; a cancer in a young woman’s dense breast tends to have indistinct margins. The specimen should be carefully oriented and inked for accurate margin assessment. Again, every effort should be made to ensure negative margins. Primary sites with locally positive margins may be treated with liberal reexcision or a boost dose of radiation to the tumor bed. Mastectomy is reserved for patients with diffusely positive margins, those having multicentric disease, and, of course, those preferring this procedure over BCT.

In our experience, clinical understaging of the primary lesion, the increased breast density of younger patients, and the likelihood of multicentric or multifocal disease combine to make tumor-free margins difficult to achieve. This is not to say that BCT should be attempted less frequently in younger patients. Rather, both younger patients and treating physicians should be encouraged to attempt BCT but should be aware of the potential difficulty in obtaining adequate local excision and the possible need for additional operative procedures.

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Reprint requests to the John Wayne Cancer Institute, 2200 Santa Monica Blvd, Santa Monica, CA 90404 (Dr Giuliano).

REFERENCES

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Henry Ingersoll Bowditch (1808-1982) served as a staff member of the Massachusetts General hospital from 1838 to 1892. In a series of papers starting in 1852, he pioneered the operation for removal of pleural effusions (paracentesis thoracis) with trocar and suction pump. The technique had first been suggested by Morrill Wyman (1812-1903), a Boston physician and inventor of the pump, but it was most successfully employed by Bowditch, who garnered for it the support of the medical profession. By 1863, Bowditch had performed the procedure 150 times on 75 individuals. That year he wrote about the operation, "It cannot cure all... has relieved many, and will continue to do so... It is certainly innocuous and gives so little pain... that patients have begged for it to be repeated again and again. In my opinion it ought never... be allowed to fall into disuse by the profession."