

## Breast Cancer After Augmentation Mammoplasty

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**Background:** It is thought that implants interfere with breast cancer diagnosis and that cancers in women who have had breast augmentation carry a worse prognosis.

**Methods:** A prospective breast cancer database was reviewed, comparing augmented and nonaugmented patients for details of histology, palpability, tumor size, nodal status, mammographic status, receptor status, nuclear grade, stage, and outcome.

**Results:** Ninety-nine cancers in augmented women and 2857 cancers in nonaugmented women were identified. Among these women, mammography was normal in 43% of those who had had augmentation and in 5% of those who had not. Augmented women were more likely to have palpable cancers (83% vs. 59%) and nodal involvement (48% vs. 36%), and less likely to have ductal carcinoma in situ (DCIS) (18% vs. 28%). When comparing only women younger than 50, the differences in invasiveness and nodal status lost significance. Cancers diagnosed in the 1990s were more likely to be nonpalpable and noninvasive than those diagnosed in the 1980s. This trend was more pronounced in the augmented population.

**Conclusions:** Augmented patients were more likely to have palpable cancers, although the overall stage and outcome were similar to those of nonaugmented women. Although there have been significant improvements in our ability to diagnose early breast cancer over the past two decades, mammography continues to be suboptimal in augmented women.

**Key Words:** Breast cancer—Augmentation Mammoplasty.

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Augmentation mammoplasty was first described in the 1950s. The first silicone breast implants were marketed in 1962, and they rapidly came into widespread use. It is estimated that before 1992, when the FDA issued the restricted usage guidelines, more than 2 million women had undergone cosmetic breast augmentation with silicone gel implants. Although several studies have clearly documented no increase in the risk of breast cancer in the augmented population,<sup>1–5</sup> we can expect over 250,000 of these women to develop breast cancer in their lifetimes based on current population incidence statistics.<sup>6</sup> Cur-

rently, breast cancers following augmentation are relatively rare. Less than 150 cases have been reported in the literature, in a number of small series.<sup>7–12</sup> The largest population-based epidemiologic study found only 41 cases in 11,670 women with cosmetic breast augmentation over 20 years in Alberta, Canada.<sup>13</sup> This rarity likely reflects the young age at which most women undergo augmentation and the relative newness of the procedure. As the augmented population ages, we can expect to see an increasing incidence in cancers in these women.

The published data regarding breast cancer following augmentation mammoplasty are limited and contradictory. Several small series report that cancers in augmented women usually are more advanced at the time of detection,<sup>7,8</sup> whereas others have reported no difference in tumor size or stage at the time of diagnosis in augmented women compared to nonaugmented women.<sup>10–12</sup> Several authors have reported that breast implants interfere with mammographic detection of breast cancers.<sup>10,14,15</sup> It is clear that standard compression views are inefficient at visualizing the bulk of the breast tissue in augmented women. In 1988, Eklund<sup>16</sup> described implant

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displacement views, which allow significantly improved visualization of the native breast tissue. However, Silverstein et al.<sup>17</sup> performed pre- and postaugmentation mammography on a group of women and showed a significant decrease in the measurable tissue area visualized even with Eklund's displacement views. Therefore, there continues to be significant concern that augmentation mammoplasty causes a delay in breast cancer diagnosis because of an inability to screen efficiently with mammography. Grace et al.<sup>18</sup> have reported that breast cancers in women with breast augmentation were visualized mammographically; however, five of the six cancers reported in this study were palpable cancers and so do not qualify as mammographically detected lesions. Leibman and Kruse<sup>19</sup> reported a series that documents 40% of breast cancers in augmented women detected on screening mammography alone, which is similar to the rate in the general population.

We have reviewed our experience with cancer following augmentation mammoplasty to determine whether augmentation interferes with breast cancer diagnosis, resulting in cancers diagnosed at a later stage, and whether breast cancers in women with augmentation carry a worse prognosis, after controlling for differences in stage at presentation.

## MATERIALS AND METHODS

A prospective breast cancer database was reviewed for cases diagnosed in the period from January 1, 1980 to December 31, 1999. Patients in this cohort who were diagnosed with either invasive breast cancer or ductal carcinoma in situ (DCIS) after having undergone cosmetic augmentation mammoplasty were compared to nonaugmented patients with the same diagnoses. Patients with the diagnosis of only lobular carcinoma in situ were excluded. Information obtained from the database included age at diagnosis, augmentation status, time from augmentation to diagnosis, presence and degree of capsular contractions (augmented patients only), invasiveness, palpability, tumor size, nodal status, mammographic status (if positive, calcifications or mass), estrogen receptor (ER) status, nuclear grade, T stage, overall stage, Van Nuys Prognostic Index (for DCIS patients), surgical treatment (mastectomy or breast conservation), reconstruction, date at diagnosis, and outcome.

Breast cancers were considered palpable if they could be appreciated on physical examination by at least one physician prior to treatment. Nonpalpable tumors were identified through abnormal imaging studies. Pretreatment mammograms were obtained in the majority of

patients. From 1980–1988 these studies consisted of two standard compression views of each breast. Abnormalities were further studied radiologically as deemed appropriate by the radiologist at the time of evaluation. From 1989 on, all augmented women also were studied with implant displacement views.<sup>16</sup> Based on the extent of tumor, physician recommendation, and patient preference, patients underwent either mastectomy or breast conservation therapy (lumpectomy with or without radiation therapy). Women with invasive cancers routinely underwent lymph node dissection and postoperative radiotherapy if electing breast conservation. All women undergoing mastectomy were offered immediate or delayed reconstruction. Tumor size, nodal status, invasiveness, receptor status, and nuclear grade were obtained from the pathology report at the time of definitive treatment. Patients were followed with physical examination at 6-month intervals and mammography at least annually following treatment to identify recurrence.

The objectives of the analysis were (1) to compare tumor and patient characteristics at diagnosis between women with augmented and nonaugmented breasts and (2) to compare outcome between these groups. Special attention was given to controlling for age at diagnosis, because breast augmentation is more prevalent in younger women, who also would tend not to be undergoing routine mammographic screening for breast cancer, and to period of diagnosis (1980s or 1990s), to investigate the effect of advances in imaging technologies and improved screening/breast cancer awareness. Comparison of frequencies of tumor and patient characteristics between different groups were based on the simple  $\chi^2$  test,<sup>20</sup> or the Cochran-Mantel-Haensel test and Mantel-Haensel odds ratio (OR) estimate when these were adjusted for age or other variables.<sup>21</sup> Comparisons of means were based on the two-sample *t*-test.<sup>20</sup> Differences in breast cancer-specific survival (BCSS) and overall survival (OS) were analyzed using product limit estimates with Greenwood standard errors and the stratified log-rank test.<sup>22</sup> All quoted *P* values are two-sided.

## RESULTS

### Patients

Between 1980 and 1999, 95 women who had previously undergone cosmetic augmentation mammoplasty were treated for 99 breast cancers. Their mean age was 46.1 years (range, 29–71). In the vast majority (84%) the implants were placed in the submammary position. During the same period, 2680 women with nonaugmented breasts were treated for 2857 breast cancers. Their mean age was 53.6 (range, 22–94 years; *n* = 2639; difference

**TABLE 1.** All cancers in augmented and nonaugmented patients

	Augmented	Nonaugmented	Odds Ratio	P value
No. Cancers	99	2857	n.a.	
% Palpable	82.8	58.7	4.64 <sup>a</sup>	<.001 <sup>a</sup>
% Invasive	81.8	72.1	1.84 <sup>b</sup>	.028 <sup>b</sup>
% Invasive (palpable tumors only)	95.1	93.4	1.48 <sup>b</sup>	.60 <sup>b</sup>
Average size (mm)	25.8	25.7	n.a.	.97
Average size (mm) (palpable tumors only)	25.5	29.7	n.a.	.17
Average nuclear grade	2.3	2.2	n.a.	.45

<sup>a</sup> Adjusted for age and invasiveness.

<sup>b</sup> Adjusted for age only.

$P < .0001$ ). The average time from augmentation to diagnosis of breast cancer was 10.6 years (range, 0.5–37 years,  $n = 92$ ). Capsular contraction was noted in 94 of 99 augmented breasts (96%), with an average severity of 2.1 on a scale of 1 to 4.

A similar proportion of women with an without breast augmentation underwent breast-conserving surgery (59% vs. 55%, age- and pathology [invasive vs. in situ]-adjusted OR 1.20,  $P = .40$ ). However, women with breast augmentation who underwent mastectomy ( $n = 43$ ) were more likely to elect to undergo breast reconstruction (72%) than nonaugmented women ( $n = 1177$ ) (59%; age-adjusted OR = 2.48;  $P = .015$ ).

### Comparison of Cancers in Women With and Without Breast Augmentation

Women in the cohort who had had breast augmentation presented more often with tumors that were invasive (82.8% vs. 58.7%,  $P < .001$ ) and palpable (81.8% vs. 72.1%,  $P < .028$ ) (Table 1). However, there was no significant difference in the size or nuclear grade. When comparison was restricted to palpable tumors only, augmented and nonaugmented patients had similar frequencies of invasive cancer (95.1% vs. 93.4%,  $P = .60$ ). The palpable lesions in the augmented women tended to be slightly smaller than those in the nonaugmented women (25.5 mm. vs. 29.7 mm,  $P = .17$ ), although the difference was not statistically significant.

Of the in situ tumors (DCIS), there was no difference between the augmentation and nonaugmentation cancers comparing nuclear grade, size, or Van Nuys Prognostic

Index (Table 2), although the small number of augmented patients with DCIS limited the ability to detect differences in these comparisons.

Of the invasive tumors, the cancers in augmented women were more likely to be node-positive (48.1% vs. 36.0%,  $P = .029$ ). However, there was no difference in the T stage, overall stage, ER status, or nuclear grade (Table 3).

### Comparison of Women Aged 50 Years or Younger

The women with breast augmentation represent a younger age group than the nonaugmented women, because 70% were diagnosed under the age of 50. Comparing only the patients diagnosed at the age of 50 or below, augmented women continued to be more likely to present with palpable lesions (82.9% vs. 63.8%,  $P = .001$ ); they were no more likely, however, to have invasive disease than their nonaugmented counterparts. The palpable lesions in the augmented women again tended to be smaller than those in the nonaugmented women (25.0 mm vs. 30.4 mm,  $P = .137$ ), although the difference was not statistically significant. Young augmented women with invasive breast cancer were not significantly more likely to have nodal involvement (Table 4).

### Mammography in Augmentation Cancers

Ninety percent of the augmented patients and 85% of the nonaugmented patients underwent pretreatment mammography. Mammography was interpreted as ab-

**TABLE 2.** Noninvasive cancers in augmented and nonaugmented patients

	Augmented	Nonaugmented	P value
No. Cancers	18	797	
Average size (mm)	30.7	26.1	.47
Average nuclear grade	2.39	2.25	.44
Average VNPI	6.83	6.11	.078

VNPI, Van Nuys Prognostic Index.

**TABLE 3.** Invasive cancers in augmented and nonaugmented patients

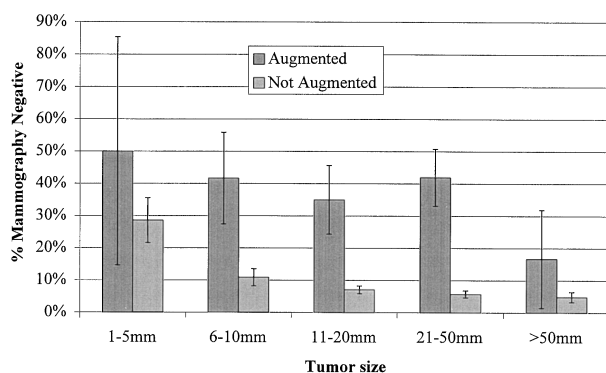
	Augmented	Nonaugmented	P value
No. Cancers	81	2060	
% Node-positive	48.1	36.0	.029
Average T stage	1.60	1.56	.59
Average stage	1.79	1.65	.79
% ER-positive	67.7	73.1	.32
Average nuclear grade	2.28	2.24	.64

ER, estrogen receptor.

**TABLE 4.** *Cancers in augmented and nonaugmented patients diagnosed at  $\leq 50$  years*

	Augmented	Nonaugmented	P value
No. Cancers	70	1243	
% Palpable	82.9	63.8	.001
% Invasive	80.0	72.0	.144
Average size (mm) (palpable tumors only)	25.0	30.4	.137
% Node-positive (invasive cancers only)	50.0	39.0	.145

normal in 66.3% of the augmented patients and 94.6% of the nonaugmented patients ( $P = .001$ ). Position of the implant made no difference in the efficacy of mammography: 65.7% of mammograms were abnormal in women with submammary implants, compared to 66.7% in women with subpectoral implants. Augmentation cancers were less likely to be detected by mammography regardless of tumor size ( $P < .001$ ). Abnormalities identified in the augmented women included calcifications (27%), mass (59%), or both (14%). Even in the presence of a palpable mass, mammography was abnormal in only 62.5% of augmented women with breast cancers, compared to 92.7% of women without implants ( $P = .001$ ). Although detectability on mammography increased with tumor size in both augmented and nonaugmented patients ( $P < .001$ ), the size of the palpable mass did not obviously affect the efficacy of mammography in the augmented patient unless the lesion was larger than 5 cm (Fig. 1). The rate of increase in detectability with size was not statistically different between the two groups.

**FIG. 1.** The percentage of patients with palpable cancers whose pretreatment mammogram was interpreted as negative, stratified by tumor size (mm.). Augmented patients are represented by dark bars and nonaugmented patients by light bars. Error bars represent  $\pm 1$  standard error.

### The Effect of Date of Diagnosis

Some significant improvements were made in our ability to diagnose early breast cancer in both augmented and nonaugmented women during the time of this study (Table 5). Cancers diagnosed in the 1990s were more likely to be nonpalpable (OR = 2.58,  $P < .001$ ) and noninvasive (OR = 1.71,  $P < .001$ ) than were the cancers diagnosed in the 1980s. These improvements were more pronounced in the augmented women than in the nonaugmented women, although the differences in the odds ratios between augmented women and nonaugmented women approached statistical significance only for palpability ( $P = .088$ ). There was no significant improvement in the incidence of nodal involvement.

### Follow-up and Survival

There was no difference in completeness of follow-up between patient groups. Median follow-up time in augmented and nonaugmented patients was 6.2 and 6.4 years, respectively. Median follow-up in DCIS and invasive cancer patients was 6.2 and 6.5 years, respectively. Overall, 79% of patients were followed for more than 2 years, and 26% were followed more than 10 years. There were no differences in breast cancer-specific survival between the augmented and nonaugmented patients with either invasive or noninvasive breast cancer ( $P = .78$ , stratified log-rank test, Fig. 2).

## DISCUSSION

Several authors have reported that breast cancers in augmented women present at a later stage or are more aggressive tumors than those arising in nonaugmented women.<sup>7-9</sup> There are several possible explanations for these findings: (1) women with augmented breasts tend to be younger and may not be undergoing routine breast cancer screening; (2) augmented breasts are more difficult to screen mammographically; (3) augmented breasts may be more scarred or deformed as a result of the surgery, making palpable lesions more difficult to detect; (4) breast cancer in the augmented patient may be a more aggressive disease; or (5) there may be a bias inherent in the series, due to size, referral patterns or some other unidentified factor. We have reviewed our experience with breast cancer in women following cosmetic augmentation mammoplasty to determine whether these cancers are different from those arising in nonaugmented women and the impact of each of the possible causes.

Cancers in augmented women are significantly more likely to present as a palpable mass (83% vs. 59%). The converse is that augmentation cancers are significantly less likely to present as a mammographic abnormality in



**TABLE 5.** Cancers Diagnosed in the 1980s Compared to Those Diagnosed in the 1990s

	Augmented		Nonaugmented		Year difference OR ( <i>P</i> value) <sup>a</sup>	Non-homogeneity <i>P</i> value <sup>b</sup>
	1980s	1990s	1980s	1990s		
No. Cancers	37	62	1504	1353		
% Palpable	97.3	74.2	68.8	47.5	2.58 (<.001)	.088
% Invasive	91.9	75.8	77.1	66.6	1.71 (<.001)	.25
% Node-positive (invasive only)	52.9	44.4	56.2	36.0	0.99 (.93)	.46

<sup>a</sup> OR of year vs. palpability, invasiveness, or node status, averaged over augmentation status.

<sup>b</sup> Test of difference in OR between augmented and non-augmented patients.

OR, odds ratio.

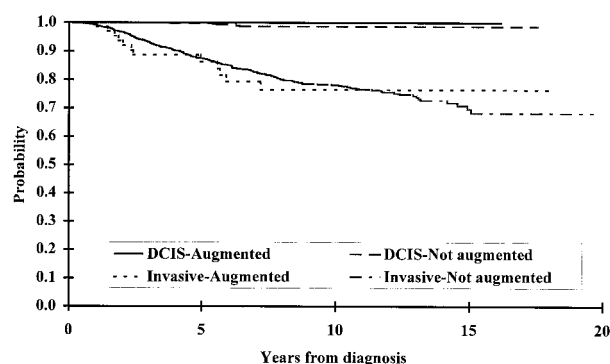
the absence of physical findings. This suggests that mammography may not be a good screening tool in augmented women. In 1992, the American Cancer Society (ACS) recommended routine annual screening mammography after the age of 50.<sup>23</sup> This was then updated in 1997 to recommend routine annual screening mammography beginning at the age of 40.<sup>24</sup> Because the mean age of the augmented cohort in this study was 46.1 years, whereas that of the nonaugmented cohort was 53.6 years, there is a difference between the two cohorts in terms of the recommended screening regimen that applied, which would bias the augmented group toward more palpable lesions. To correct for this possible bias, we limited our analysis to women diagnosed at the age of 50 or younger, for whom the same screening regimen would apply. When looking only at this younger age group, the augmentation cancers still were significantly more likely to be palpable (83% vs. 64%). Unfortunately, it was impossible to determine what proportion of these women were

taking part in a mammographic surveillance program and whether there was a difference between the two groups contributing to the observed difference in presentation. This is one potential source of bias.

To assess the efficacy of mammography in detecting cancers in the two groups, we looked at its ability to detect known palpable lesions. Only 63% of palpable cancers in augmented women were detectable on pre-treatment mammography, compared to 93% in nonaugmented women, confirming the unreliability of mammography in the augmented patient. Palpable augmentation cancers were less likely to be detected on mammography regardless of tumor size, and only if the tumors were larger than 5 cm. was mammography able to detect over 70% of the masses. Thus, mammography continues to be suboptimal in the augmented breast, and we should continue to look for more effective screening modalities.

There is no evidence to suggest that breast augmentation interferes with our ability to detect breast cancers on physical examination. Although more of the augmentation cancers presented as a palpable mass, tumors in the two cohorts were of equivalent size, T stage, and overall stage. If anything, the palpable masses in the augmented women tended to be slightly smaller than those detected in nonaugmented women (25.5 mm vs. 29.7 mm), although this difference was not statistically significant ( $P = .17$ ). Clark et al. also have reported that palpable tumors in the augmented patients were smaller than those in nonaugmented women,<sup>11</sup> and Birdsell et al. reported that cancers in women who had had breast augmentation were smaller than those in women with nonaugmented breasts.<sup>13</sup> Cancers in augmented women may be more easy to detect on physical examination as a result of smaller native breast volume or because the implant splays the breast tissue out in a way that makes it easier to examine.

Cancers diagnosed in women with augmented breasts were more likely to be both invasive and node-positive.



**FIG. 2.** Breast cancer-specific survival by augmentation status for both invasive breast cancers and ductal carcinoma in situ (DCIS). Median follow-up time was 6.2 years for women with breast augmentation and 6.4 years for women with nonaugmented breasts. Breast cancer-specific survival was defined as the minimum time from diagnosis to death attributable to breast cancer. Patients who were alive at last follow-up or whose death was from a cause other than breast cancer were censored in these analyses. Survival curves were generated using the product limit estimate.

Invasiveness was related to palpability: when considering only the palpable cancers, there was no difference in the incidence of invasive cancers between the two groups of women (95.1% in augmented women and 93.4% in nonaugmented women). There is some age bias associated with the findings: when only the women aged 50 or younger were considered, the differences in invasiveness and nodal status were no longer statistically significant. Finally, the relatively high incidence of DCIS in the nonaugmented group (27.9%) reflects our referral patterns, which are weighted toward DCIS. Two large population-based epidemiological studies from Alberta, Canada and Los Angeles, California have shown that the incidence of DCIS is equivalent in unselected augmented and nonaugmented populations and is on the order of 6% to 12% of all cancers diagnosed.<sup>5,13</sup>

Although the increased incidences of invasive disease and nodal positivity suggest that cancers in women with breast augmentation may, in fact, be more aggressive than those diagnosed in nonaugmented women, our data do not support this conclusion. There was no difference between the two groups in several prognostic indicators, including tumor size, T stage, overall stage, receptor status, and nuclear grade. Further, there was no difference between the two cohorts in breast cancer-specific survival. Both the Alberta and the Los Angeles studies show a similar stage distribution in cancers in augmented and nonaugmented women, and the Alberta study found no difference in overall survival in the cohorts.<sup>5,13</sup> Given that there is no difference between the groups in distribution of prognostic markers or survival, there is no evidence that augmentation cancers are inherently more aggressive than cancers arising in nonaugmented women.

Breast augmentation was introduced in the 1960s and is most commonly performed in women in their 20s and 30s. Women who underwent breast augmentation in the 1960s, then, are now entering the time of life when they are at most risk of developing breast cancer, and we, as clinicians, can expect to see cancers in women with breast augmentation with increasing frequency over the next decade. It is important to build on what we have learned about these cancers over the past two decades. There have been significant improvements in our ability to diagnose early breast cancers in both augmented and nonaugmented women over the past 20 years, with fewer women having palpable or node-positive disease at the time of diagnosis. These improvements are likely due, at least in part, to significant improvements in mammography and other imaging modalities as well as to a general increase in breast cancer awareness and breast cancer screening over this time period. The time trends were

more marked in the augmented group. This can be attributed to a number of factors. In 1988, implant displacement views were described that markedly improved the efficacy of imaging the augmented breast.<sup>16</sup> With the well-publicized controversy in the early 1990s regarding health risks associated with silicone implants, women with augmentation are likely to have become more focused on their breasts and any potential problems, and to seek medical advice at the first sign of any changes in their breasts. Further, many women underwent aggressive radiologic evaluation to assess for evidence of implant leakage in the wake of the controversy, and so may have had their cancer diagnosed early as a result. Finally, the augmented population is aging and so is becoming a population that is aggressively screened for breast cancer. The challenge for the next decade is to improve our screening efficacy in the augmented population in order to detect more of their cancers at a preclinical stage. Despite our current limitations, however, we can be reassured that augmented women with breast cancer fare just as well as nonaugmented women.

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