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ORIGINAL REPORT

# Breast Cancer Subtype Approximated by Estrogen Receptor, Progesterone Receptor, and HER-2 Is Associated With Local and Distant Recurrence After Breast-Conserving Therapy

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## ABSTRACT

### Purpose
To determine whether breast cancer subtype is associated with outcome after breast-conserving therapy (BCT) consisting of lumpectomy and radiation therapy.

### Patients and Methods
We studied 793 consecutive patients with invasive breast cancer who received BCT from July 1998 to December 2001. Among them, 97% had pathologically negative margins of resection, and 90% received adjuvant systemic therapy. No patient received adjuvant trastuzumab. Receptor status was used to approximate subtype: estrogen receptor (ER) or progesterone receptor (PR) positive and human epidermal growth factor receptor 2 negative = luminal A; ER+ or PR+ and HER-2+ = luminal B; ER– and PR – and HER-2+ = HER-2; and ER– and PR – and HER-2– = basal. Competing risks methodology was used to analyze time to local recurrence and distant metastases.

### Results
Median follow-up was 70 months. The overall 5-year cumulative incidence of local recurrence was 1.8% (95% CI, 1.0 to 3.1); 0.8% (0.3, 2.2) for luminal A, 1.5% (0.2, 10) for luminal B, 8.4% (2.2, 30) for HER-2, and 7.1% (3.0, 16) for basal. On multivariable analysis (MVA) with luminal A as baseline, HER-2 (adjusted hazard ratio [AHR] = 9.2; 95% CI, 1.6 to 51; $P = .012$) and basal (AHR = 7.1; 95% CI, 1.6 to 31; $P = .009$) subtypes were associated with increased local recurrence. On MVA, luminal B (AHR = 2.9; 95% CI, 1.3 to 6.5; $P = .007$) and basal (AHR = 2.3; 95% CI, 1.1 to 5.2; $P = .035$) were associated with increased distant metastases.

### Conclusion
Overall, the 5-year local recurrence rate after BCT was low, but varied by subtype as approximated using ER, PR, and HER-2 status. Local recurrence was particularly low for the luminal A subtype, but was less than 10% at 5 years for all subtypes. Although further follow-up is needed, these results may be useful in counseling patients about their anticipated outcome after BCT.

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## INTRODUCTION

Microarray analysis has identified breast cancer subtypes with distinct gene expression profiles.[1,2] Among the estrogen receptor (ER)-positive tumors, the two major subtypes are luminal A and luminal B, and they are biologically distinct in that luminal A tumors tend to have a higher expression of ER-related genes and a lower expression of proliferative genes than luminal B.[2-4] Among the ER-negative tumors, the major subtypes are the human epidermal growth factor 2 (HER-2) array subtype, most of which tend to be clinically HER-2 positive, and the basal-like subtype, which tend to have a low expression of ER, progesterone receptor (PR) and HER-2.[1,2,5]

These subtypes have been shown to be clinically meaningful, and can divide patients into groups with distinct tumor morphologies and distinct outcomes. For example, the HER-2 and basal subtypes are significantly more likely to be grade 3 than the luminal A tumors.[2] The luminal A subtype appears to be associated with the best prognosis, whereas significantly worse recurrence rates and overall survival have been observed for the HER-2 and basal subgroups.[2,4-6]

Currently, the impact of breast cancer subtype on local control is unknown, and among women



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with early-stage breast cancer, management decisions about local therapy are generally made without regard to the breast cancer subtype. Having information about whether certain subtypes are likely to have poorer local control would allow for better tailoring of local therapy.

One of the challenges to examining the association of breast cancer subtype with local control is that local recurrence for early-stage breast cancer is a relatively uncommon event, occurring in approximately 5% or less of women at 5 years, and therefore large numbers of patients would be required for enough power to detect a meaningful difference.[7] However, gene expression profiling in large databases is often impractical because of the time and expense required. Therefore, some have proposed that readily available clinical receptors be used to approximate breast cancer subtype. Specifically, using the ER, PR, and HER-2 status of a tumor, breast subtype can be approximated as follows: luminal A (ER+ or PR+ and HER-2–), luminal B (ER+ or PR+ and HER-2+), HER-2 (ER– and PR– and HER-2+), and basal (ER– and PR– and HER-2–).[3,6]

The purpose of this study is to determine whether breast cancer subtype, as approximated by ER, PR, and HER-2, is associated with local or distant recurrence among women with invasive breast cancer who receive breast-conserving therapy (BCT).

**Table 1.** Patient Baseline Characteristics (N = 793)

| Characteristic | No. | % |
|---|---|---|
| T stage | | |
| T1a | 97 | 12.2 |
| T1b | 192 | 24.2 |
| T1c | 343 | 43.3 |
| T2 | 155 | 19.5 |
| T3 | 6 | 0.8 |
| No. of positive nodes | | |
| cN0 (no nodes sampled) | 73 | 9.2 |
| 0 | 494 | 62.2 |
| 1 to 3 | 180 | 22.7 |
| 4 to 9 | 37 | 4.7 |
| > 9 | 9 | 1.1 |
| Grade | | |
| 1 | 212 | 26.7 |
| 2 | 317 | 40.0 |
| 3 | 252 | 31.8 |
| Unknown | 12 | 1.5 |
| ER or PR positive | 672 | 84.7 |
| HER-2 positive | 109 | 13.7 |
| LVI present | 204 | 25.7 |
| Menopausal status | | |
| Post- | 490 | 61.8 |
| Peri- | 53 | 6.7 |
| Pre- | 246 | 31.0 |
| Unknown | 4 | 0.5 |
| Systemic therapy | | |
| Yes | 712 | 90 |
| Node positive | 222 | 98 |
| Node negative | 490 | 86 |
| No | 81 | 10 |
| Node positive | 4 | 2 |
| Node negative | 77 | 14 |
| Margins | | |
| Negative | 664 | 83.7 |
| Close | 102 | 12.9 |
| Positive | 26 | 3.3 |
| Unknown | 1 | 0.1 |
| Age at diagnosis, years | | |
| 35 or less | 28 | 3.5 |
| 35-45 | 124 | 15.6 |
| 45-55 | 244 | 30.8 |
| 55-65 | 216 | 27.2 |
| 65-75 | 123 | 15.5 |
| > 75 | 58 | 7.3 |

Abbreviations: ER, estrogen receptor; PR, progesterone receptor; LVI, lymphovascular invasion.

## PATIENTS AND METHODS

### *Patient Selection*

The study cohort included 793 consecutive women with invasive breast cancer who received BCT at Dana-Farber Cancer Institute (DFCI)/Brigham and Women's Hospital (BWH; Boston, MA; n = 447) or Massachusetts General Hospital (MGH; Boston, MA; n = 346) from July 1998 through December 2001 and had information on the ER, PR, and HER-2/*neu* status of their primary tumor (Table 1). Patients with prior malignancy (except nonmelanoma skin cancers), synchronous bilateral breast cancer, or treatment with preoperative systemic therapy were excluded. This study was approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board.

### *Treatment*

A total of 720 patients (91%) had a surgical lymph node evaluation. Adjuvant chemotherapy was delivered to 88% of node-positive (199 of 226) and 29% of node-negative (165 of 567) patients. Among ER+ or PR+ patients, 88% (593 of 672) received hormonal therapy. No patient received adjuvant trastuzumab. All patients received external-beam radiation therapy to the whole breast. The most common doses were 45 Gy in 1.8-Gy fractions to the whole breast, plus a tumor-bed boost to 61 Gy, or 50 Gy in 2.0-Gy fractions to the whole breast, plus a tumor-bed boost to 60 Gy. A separate supraclavicular or axillary field was not typically added after axillary dissection unless there were four or more nodes positive.

### *Follow-Up*

Patients were generally seen in follow-up 4 to 6 weeks after completion of radiation therapy, and then every 6 months thereafter with annual breast imaging. For patients who discontinued follow-up at DFCI/BWH or MGH, attempts were made to obtain follow-up information from their primary care physician. In total, 55 patients (7%) were lost to follow-up. Follow-up time was counted from the date of diagnosis to the date of the first event, as outlined later herein, or to the last known confirmed date of breast cancer disease-free status. Median follow-up time was 70 months (range, 1.3 to 107 months).

### *Classification of Groups*

Patients were categorized based on the receptor status of their primary tumor as follows: luminal A (ER+ or PR+ and HER-2–), luminal B (ER+ or PR+ and HER-2+), HER-2 (ER– and PR– and HER-2+), and basal (ER– and PR– and HER-2–). ER and PR status was determined on the basis of immunohistochemistry (IHC) staining. Tumors were considered HER-2 positive only if they were either scored 3+ by IHC or if they were 2+ by IHC and also HER-2 amplified (ratio > 2.0) on the basis of fluorescence in situ hybridization (FISH). In the absence of positive FISH data, tumors scored 2+ by IHC were considered negative for HER-2.[8,9]

### *End Points*

The primary end point of this study was time to local recurrence as a first event. This end point included any ipsilateral in-breast recurrence (invasive or noninvasive) without evidence of distant metastases. Patients diagnosed with distant metastases within 4 months of a local recurrence were considered to have had simultaneous local and distant recurrence and were therefore not considered to have had the primary end point. The secondary end point was time to distant metastases.

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### Statistical Analysis

The $\chi^2$ test was used to compare the distribution of baseline characteristics among the four subtypes. Cumulative incidence curves of time to local recurrence were estimated for each subtype. We used Gray's competing risks multivariable analysis (MVA) to analyze the association between subtype and time to local recurrence as a first event.[10] Luminal A was the baseline group. The competing events were isolated regional nodal recurrence, distant metastasis, contralateral breast cancer, second malignancy (excluding nonmelanoma skin cancer), death without recurrence, and loss to follow-up. The covariables were age (continuous variable), radiation dose in Gy (continuous), tumor size in centimeters (continuous), number of nodes positive (continuous), margins (positive *v* < 2 mm *v* ≥ 2 mm), lymphovascular invasion (positive *v* negative), histologic grade (3 *v* 2 *v* 1), use of systemic therapy (hormonal and/or chemotherapy *v* none), and menopausal status (premenopausal *v* perimenopausal *v* postmenopausal). An identical methodology was used for the end point of time to distant recurrence, except that local and regional recurrences were not considered competing events. All analyses were performed in Stata 9.0 (StataCorp, College Station, TX). All statistical tests were two sided.

## RESULTS

### Association Between Subtype and Other Prognostic Indicators

Among the four breast cancer subtypes, there was a substantial difference in the overall distribution of histologic grade ($P < .001$), lymphovascular invasion ($P = .001$), node positivity ($P = .004$), pathologic T stage ($P < .001$), and median age ($P = .005$; Table 2). HER-2 and basal subtypes were more frequently high grade and of larger size, and occurred in younger patients than the luminal subtypes.

### Local Recurrence

After a median follow-up of 70 months, there were 18 (isolated) local recurrences. The 5-year cumulative incidence of local recurrence for all patients was 1.8% (95% CI, 1.0% to 3.1%). For patients in the luminal A subgroup, the 5-year cumulative incidence of local recurrence was 0.8% (95% CI, 0.3% to 2.2%), compared with 1.5% (95% CI, 0.2% to 10%) for luminal B, 8.4% (95% CI, 2.2% to 30%) for HER-2, and 7.1% (95% CI, 3.0% to 16%) for basal patients, respectively (Fig 1).

On MVA with the luminal A group as the baseline, both the HER-2 subtype (adjusted hazard ratio [AHR] = 9.2; 95% CI, 1.6 to 51), $P = .012$) and the basal subtype (AHR = 7.1; 95% CI, 1.6 to 31), $P = .009$) were associated with an increased risk of local recurrence. There were no other factors on MVA significantly associated with local recurrence.

### Distant Metastases

The 5-year cumulative incidence of distant metastases for the entire study cohort was 6.3% (95% CI, 4.7% to 8.3%). For patients in the luminal A subgroup, the 5-year cumulative incidence of distant metastases was 3.3% (95% CI, 2.1% to 5.2%), compared with 12% (95% CI, 6.6% to 22%) for luminal B, 19% (95% CI, 9.2% to 38%) for HER-2, and 16% (95% CI, 9.8% to 27%) for basal patients, respectively (Fig 2). On univariable analysis (UVA) with luminal A as the baseline, each of the other three subtypes was associated with an increased rate of distant metastases, with unadjusted hazard ratios of 3.9 for luminal B (95% CI, 1.9 to 8.1; $P < .0001$), 5.3 for HER-2 (95% CI, 2.2 to 13.1; $P < .001$), and 4.6 for basal (95% CI, 2.3 to 9.0; $P < .001$). However, on MVA, after adjusting for grade, tumor size, number of positive nodes, and the use of systemic therapy, only the luminal B group (AHR = 2.9; 95% CI, 1.3 to 6.5; $P = .007$) and the basal group (AHR = 2.3; 95% CI, 1.1 to 5.2; $P = .035$) showed a significantly greater risk of DM compared with luminal A (Table 3).

## DISCUSSION

In this series, we found a low overall 5-year rate of local recurrence of 1.8% among women who received BCT; however, the rates varied by subtype as approximated using readily available ER, PR, and HER-2 status information. We found that, on MVA with luminal A as baseline, the HER-2 and basal subtypes were the only factors associated with increased local recurrence, and neither margin status, tumor size, age, nor nodal status was significant. However, it should be noted that there were few patients with positive margins (3.3%) or age younger

**Table 2.** Patient Baseline Characteristics Stratified by Subtype

| Characteristic | All Patients (N = 793) | Luminal A (n = 595) | Luminal B (n = 77) | HER-2 (n = 32) | Basal (n = 89) | *P* |
|---|---|---|---|---|---|---|
| T1, % | 80 | 84 | 75 | 66 | 62 | < .001 |
| LVI, % | 26 | 23 | 38 | 47 | 31 | .001 |
| Node positive, % | 28 | 26 | 36 | 50 | 34 | .004 |
| ≥ 4 positive nodes | 6 | 5 | 9 | 13 | 9 | .056 |
| Grade 3, % | 32 | 23 | 47 | 80 | 88 | < .001 |
| Systemic treatment, % | 90 | 92 | 91 | 72 | 83 | .001 |
| Hormonal | 77 | 88 | 90 | 9 | 16* | < .001 |
| Chemotherapy | 46 | 37 | 68 | 66 | 76 | < .001 |
| Margins positive, % | 3 | 3 | 5 | 3 | 4 | NS |
| Median dose, Gy | 60 | 60 | 60 | 60 | 61 | NS |
| Median age, years | 55 | 56 | 54 | 49 | 51 | .005 |

NOTE. All comparisons by $\chi^2$ test except dose and age (Kruskal-Wallis test).
Abbreviations: HER-2, human epidermal growth factor receptor 2; LVI, left ventricular infarction.
*The reasons for hormonal therapy in triple-negative patients were chemoprevention (n = 10), extensive ductal carcinoma in situ found with tumor (n = 1), prior use of estrogen supplementation (n = 1), weak estrogen-receptor positivity on a prior biopsy not confirmed on excision (n = 1), equivocal finding of weak estrogen-receptor positivity "0 to 1+" (n = 1).


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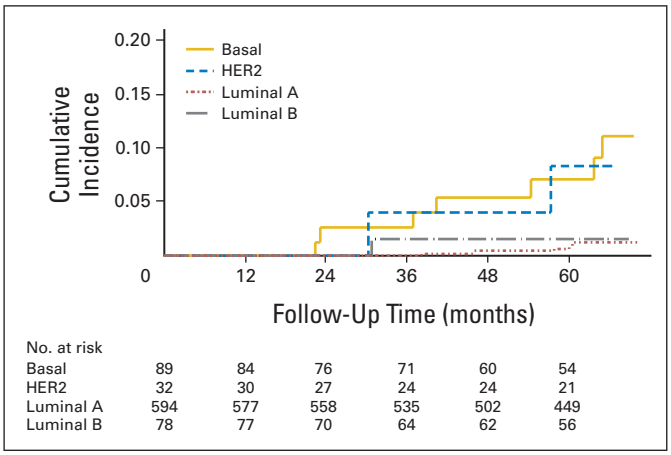


**Fig 1.** Cumulative incidence of local recurrence by breast cancer subtype. HER2, human epidermal growth factor receptor 2.

than 35 years (3.5%), which may have limited the ability to detect the impact of these factors on local recurrence.

There are currently limited data on the relationship between breast cancer subtype and the risk of local recurrence. Haffty et al[11] previously examined the Yale experience of 482 women treated with BCT who had available ER, PR, and HER-2 data. In that study, there was no difference seen in ipsilateral breast relapse-free survival between the 117 triple-negative (basal-like) patients and the rest of the study cohort (83% *v* 83%, respectively, at 5 years), although there was a significant difference in isolated regional nodal recurrence-free survival (94% for triple negative *v* 99% for all others; $P = .05$). In another study by Dent et al[12] of patients treated with mastectomy or BCT, triple-negative cancers had similar overall local recurrence rates to those of the non–triple-negative group (13% *v* 12%; $P = .77$), but there was a significantly shorter mean time to local recurrence seen among the triple negative patients (2.8 *v* 4.2 years; $P = .02$).

Differences in the study populations of the other two series compared with ours could potentially explain the differences in the results. In particular, our series included only patients treated between July 1998 and December 2001, whereas the Haffty et al and Dent et al series both included patients from an earlier era, some of whom were treated

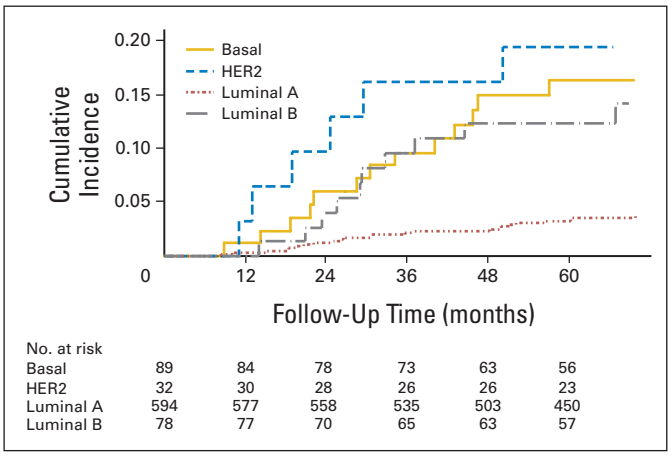


**Fig 2.** Cumulative incidence of distant metastases by breast cancer subtype. HER2, human epidermal growth factor receptor 2.

**Table 3.** Multivariable Analysis of Time to Distant Metastases

| Predictor | AHR | 95% CI | *P* |
|---|---|---|---|
| Luminal B* | 2.9 | 1.3 to 6.5 | .007 |
| HER-2* | 1.4 | 0.5 to 4.3 | NS |
| Basal* | 2.3 | 1.1 to 5.2 | .035 |
| Grade 3† | 5.2 | 1.4 to 19.2 | .013 |
| Tumor size, cm | 1.3 | 1.0 to 1.7 | .046 |
| No. of positive nodes | 1.2 | 1.1 to 1.2 | < .001 |
| Systemic treatment‡ | 0.3 | 0.1 to 0.8 | .015 |
| Grade 2† | | | NS |
| Age, years | | | NS |
| Dose, Gy | | | NS |
| LVI positive | | | NS |
| Margin positive | | | NS |
| Margin close | | | NS |
| Premenopausal | | | NS |
| Perimenopausal | | | NS |

Abbreviations: AHR, adjusted hazard ratio; HER-2, human epidermal growth factor receptor 2; NS, not significant; LVI, lymphovascular invasion.
*Compared with luminal A as baseline.
†Compared with grade 1 as baseline.
‡Compared with no systemic therapy.

in the 1980s. Similar to other centers, we have over time observed a progressive decline in local recurrence with better preoperative breast imaging, greater attention to achieving clearly negative margins, and more frequent use of increasingly effective adjuvant systemic therapy regimens. This decline in local recurrence has been particularly notable in patients with luminal or hormone-responsive cancers, who comprised nearly 85% of our series. As a result, our 5-year rate of local recurrence was less than 2% for the non–triple-negative group as a whole, compared with 17% in the Haffty et al study and 13% in the Dent et al study. Hence, the major difference between the studies is that our rates of local recurrence in the non–triple-negative group were much lower, reflecting results now seen in more recent series.

If confirmed by other studies, the results of this study would suggest that approximations of breast cancer subtype using ER, PR and HER-2 immunophenotype are useful in estimating the risk of local recurrence after BCT; however, the rates of local recurrence for all subtypes were less than 10% at 5 years. The highest rates of local recurrence were seen in the patients with the HER-2 and basal subtypes. Basal subtype patients do not benefit from the favorable interaction seen for hormonal therapy and radiation therapy among the luminal subtypes and potentially for trastuzumab and radiation therapy among the HER-2 subtype. Some of the patients with the basal subtype will prove to have BRCA mutations[4,13,14] for which mastectomy may be the preferred local treatment, but there is nothing from this study to suggest that BCT would not be appropriate for patients with the basal subtype who do not have a *BRCA* mutation, as the overall rate of local recurrence observed in this group (7.1% at 5 years) was still quite low. Currently, investigators are attempting to identify new targets in patients with the basal subtype, and such newer targeted therapies might be useful combined with radiation therapy in reducing local recurrence.

Regarding the HER-2 subgroup, the finding of an increased risk of local recurrence must be tempered by the fact that none of our patients received adjuvant trastuzumab, which has now become part of the standard of care for patients with HER-2+ early-stage breast

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cancer.[8,9] In the two largest randomized studies, the use of adjuvant trastuzumab among HER-2+ patients led to a relative improvement in disease-free survival of 46%[8] and 52%.[9] Although local recurrence was not tested statistically as an end point, trastuzumab reduced the number of local or regional recurrences as a first event from 35 to 15 in the National Surgical Adjuvant Breast and Bowel Project (NSABP) *N*-31 trial (of 872 and 864 people in each arm) and from 22 to 12 in the North Central Cancer Treatment Group (NCCTG) N9831 trial (of 807 and 808 people in each arm), and from 3.0% to 1.6% in the HERA (Herceptin Adjuvant) trial.[8,9] In the current study, it is unknown whether the differences seen in the rate of local recurrence between the HER-2 (AHR = 9.2; 95% CI, 1.6 to 51; $P = .012$) and luminal A groups would have been observed if the HER-2 patients had received adjuvant trastuzumab.

Unadjusted analysis showed that, compared with luminal A, all of the other subtypes were associated with an increased risk of distant metastases. However, part of this effect could be explained by the significant association between the subtypes and other important prognostic factors. On MVA, both the luminal B subtype (AHR = 2.9; 95% CI, 1.3 to 6.5; $P = .007$) and the basal subtype (AHR = 2.3; 95% CI to 1.1, 5.2; $P = .035$) remained significantly associated with time to distant metastases, whereas the association for the HER-2 subtype was no longer significant. Of note, the results for patients in the luminal B group, defined as ER positive or PR positive and HER-2 positive, must also be tempered by the fact that none received adjuvant trastuzumab, which reduces the risk of distant metastases for HER-2+ patients.[8,9]

The results for distant metastases are consistent with prior microarray-based studies in which breast cancer subtype, as defined by gene expression profiling, was significantly associated with distant outcome.[5,15] Haffty et al similarly found that the triple-negative/basal subtype was associated with a shorter time to distant metastases on both univariable and MVA, with an AHR of 2.15 (95% CI, 1.31 to 3.53; $P = .002$), which is similar to the AHR of 2.3 seen in our study for the basal subtype.

There are several potential limitations to this study. First, classifications based on ER, PR, and HER-2 status are only approximations of the underlying genotype-based breast cancer subtype, and conclusions based on the receptor-based approximations cannot necessarily be applied to the genotype-based subtypes. For example, Carey et al[6] reported that only 30% to 50% of luminal B tumors defined by genotyping are HER-2 positive, so our approximation of the luminal B group as ER or PR positive and HER-2 positive may miscategorize a proportion of the true luminal B group as luminal A. However, because receptor status information is much more readily available than genotyping, this method appears to have the most clinical applicability for the time being. In the future, as the technology of molecular markers improves, more sophisticated markers than ER, PR, and HER-2 immunophenotype may become available. For example, the 21-gene recurrence score assay has helped to risk-stratify patients for distant metastases, and there is preliminary evidence that it is also useful in estimating the risk of local recurrence.[16] Recently, Nuyten et al attempted to find a gene signature for local recurrence by screening profiles that had demonstrated value in predicting for distant metastases.[17] They found that a wound-response signature was significantly associated with the development of local recurrences, and that on MVA including age, tumor size, and the use of a boost, the wound-response signature was in fact the only variable significantly associated with local recurrence, which is similar to the result we found for breast cancer subtype.

Another possible limitation to the current study relates to the relatively small numbers seen in certain subgroups, particularly the HER-2 group, which contained only 32 patients, which widens the CI about all outcome estimates for that group. Finally, we have provided results at only 5 years, and longer follow-up may be needed to assess outcome. This is especially true for the luminal groups, where it is known that their hazard rates for recurrence are protracted well beyond 5 years.[18]

One additional caveat to consider is that it is currently unknown whether a local recurrence for any given patient represents inadequate patient selection/inadequate local treatment or is simply a manifestation of a biologically aggressive disease. The former can be prevented with better patient selection or more aggressive local treatment, but the latter likely cannot. The observation that patients with the basal and HER-2 subtypes have substantially higher rates of distant metastases suggest that these subtypes are biologically more aggressive than the luminal A subtype. Further study with a larger numbers of patients is needed to establish this. Until this issue is clarified, it is prudent to continue to try to prevent all local recurrences, given the data from the Oxford overview suggesting that for every four local recurrences prevented at year 5, one fewer breast cancer death will occur at year 15.[19]

In summary, this study suggests that the breast cancer subtype, as approximated by ER, PR, and HER-2 status, is significantly associated with both local and distant recurrence after BCT. In particular, subtype was the only factor on MVA associated with local recurrence. Further study is needed to determine whether these findings will hold for women who receive adjuvant trastuzumab. Although further follow-up is needed, these results may be useful in counseling individual patients about their anticipated outcome after BCT.

## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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# ERRATA

The April 20, 2008, article by Saltz et al entitled, "Bevacizumab in Combination With Oxaliplatin-Based Chemotherapy As First-Line Therapy in Metastatic Colorectal Cancer: A Randomized Phase III Study" (J Clin Oncol 26:2013-2019, 2008) contained errors in the last two columns of Table 1.

The columns were labeled as FOLFOX-4 + Placebo and FOLFOX-4 + Bevacizumab, whereas they should have been labeled as **XELOX + Placebo** and **XELOX + Bevacizumab**, respectively. The no. of patients was given as 351 and 349, whereas it should have been **350** in both columns. The median age was given as 60, whereas it should have been **61** in both columns. The age range was given as 26-83 and 19-82, whereas it should have been **18-83** and **18-86**, respectively.

The online version has been corrected in departure from the print.

DOI: 10.1200/JCO.2008.17.8616

The April 20, 2008, Diagnosis in Oncology article by Zota et al, entitled "Eosinophilia With *FIP1L1-PDGFRA* Fusion in a Patient With Chronic Myelomonocytic Leukemia" (J Clin Oncol 26:2040-2041, 2008) contained errors. The authors were listed out of order in the author list. The corrected author list is reprinted below in its entirety.

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The online version has been corrected in departure from the print.

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The May 10, 2008, article by Nguyen et al entitled, "Breast Cancer Subtype Approximated by Estrogen Receptor, Progesterone Receptor, and HER-2 Is Associated With Local and Distant Recurrence After Breast-Conserving Therapy" (J Clin Oncol 26:2373-2378, 2008) contained an error. In the legend for Table 2, LVI should have referred to lymphovascular invasion.

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