

Letters to the Editor

Correspondence re: J. Russo, A. L. Romero, and I. H. Russo,
Architectural Pattern of the Normal and Cancerous Breast
under the Influence of Parity. *Cancer Epidemiol.,
Biomarkers & Prev.*, 3: 219-224, 1994.

Letter

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In their recent paper Russo *et al.* (1) counted the number of different types of breast lobules (Lob 1, 2, and 3) in nulliparous and parous women with and without breast cancer. Lob 1 represents the least differentiated type of lobule; all lobules are of this type during puberty. Lobules of type Lob 1 differentiate into Lob 2 and Lob 3 after puberty under the influence of parity and possibly age (2).

Russo *et al.* (1) found no difference in the proportion of lobules of type Lob 1 in breasts of nulliparous women with or without cancer (57.3 and 59.6%, respectively), but the proportion of Lob 1 was found to be higher in parous women with cancer than in parous women without cancer (52.6 versus 25.8%, respectively). The summarized results are given in Table 1. Russo *et al.* (1) concluded that Lob 1, or more specifically the Lob 3:Lob 1 ratio, may be a risk factor for breast cancer in parous women. They suggested "that pregnancy in these women [with breast cancer] did not succeed in inducing the same degree of differentiation achieved by the breast of parous women free of malignancies." This is a most interesting observation.

The results given in Table 1 show that the parous women with breast cancer were older than the parous women without cancer, so one would presume that this result would be even stronger if the women had been matched on age. The only possible problem with these results comes from an abstract published by the same authors (3), where the amount of Lob 3 was found to be more common in parous women ages 18-42 years and that it decreased thereafter, whereas Lob 1 increased again after age 42 years. It would be helpful if the authors would comment on this.

Russo *et al.* (1) also found that the total number of lobules (Lob 1 + Lob 2 + Lob 3), was much lower in women with cancer than in women without cancer. They concluded that "these observations indicate that for developing breast cancer it is not required a greater parenchymal mass." The data in fact appear to show that having more lobules is protective; this is a most peculiar result. A possible reason for these findings could be that the women without cancer were much younger than the women with cancer. The menopausal involution of the breast may begin as early as age 35 years, although the drastic reduction in glandular tissue occurs after age 45 years, after a decline

Table 1 Percentage of Lob 1 and total number of lobules in nulliparous and parous women with and without breast cancer^a

	Ages (yrs)	Mean age (yr)	% of Lob 1	Total no. of lobules
Nulliparous women				
Without cancer	20, 21, 30, 61	33.0	59.6	21,205
With cancer	39, 48	43.5	57.3	1,984
Parous women				
Without cancer	20, 25, 28, 30, 37, 46, 63	35.6	25.8	82,188
With cancer	39, 51, 58	49.3	52.6	22,626

^a From Russo *et al.* (1).

in ovarian function (4). In the study by Russo *et al.*, all women with cancer, but only 4 of 11 women without cancer, were above age 35 years, and 3 of 5 women with cancer, but only 3 of 11 women without cancer, were above 45 years of age (Table 1).

References

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3. Rivera, M. R., Russo, I. H., and Russo, J. Influence of age and parity on human breast development. *Proc. Am. Assoc. Cancer Res.*, 32: 204a, 1991.
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Reply

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I truly appreciate the interest and thoroughness of Drs. Ursin and Pike in reviewing our data. I am pleased with their comment that they find interesting our observation that Lob 1, or more specifically the Lob 3:Lob 1 ratio, may be a risk factor for breast cancer in parous women, and our suggestion that pregnancy in women with breast cancer did not succeed in inducing

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the same degree of differentiation achieved by the breast of parous women free of malignancies.

I found very useful the construction of Table 1, based on our results published in *Cancer Epidemiol., Biomarkers & Prevention*, 3: 219–224, 1994, which shows, as stated by Drs. Ursin and Pike, that the parous women with breast cancer were older than the parous women without cancer. The only possible problem that Drs. Ursin and Pike envisioned from these results, based on data presented in our abstract published in the *Proc. Am. Assoc. Cancer Res.*, 32: 204a, 1991, is the fact that Lob 3 are more abundant in parous women ages 18–42 years; their number decreased thereafter, whereas Lob 1 increased again after age 42 years. Their appreciation is correct. Our results were confirmed in a full paper published in *Breast Cancer Res. Treat.*, 23: 211, 1992 (data shown in Fig. 6 of that publication).

To answer those valid concerns, I have matched by age the two groups of women, eliminating all data from parous women without cancer ages 20, 25, 28, and 30 years. The comparison of these three parous women without cancer, ages 37, 46, and 63 years (mean age, 48.6 years), thus, provides a good age match with the three parous women with cancer, ages 39, 51, and 58 years (mean age, 49.3 years). The new values reveal that parous women without cancer have an average of 29.2% Lob 1, *versus* 52.6% in the parous women with cancer, values that are similar to those published previously, thus, indicating that even after matching for age, parous women with cancer still have a

higher percentage of lobules that are type 1 than do parous women without cancer.

Drs. Ursin and Pike mention that menopausal involution of the breast may begin as early as age 35 years, although the drastic reduction in glandular tissue occurs after age 45 years after a decline in ovarian function. Our observations support these views, although at morphological level, the actual decline in number of Lob 3 starts after age 39 years, and the increase in Lob 1 does not become significant until age 44 years, as published in *Influence of age and parity on the development of the human breast (Breast Cancer Res. Treat.*, 23:211, 1992). They indicated the possibility that the total number of lobules could be greater in parous women without cancer because of the fact that they were much younger than women with cancer. Their postulate is correct because when we eliminated the four younger parous women without cancer from this group, the total number of structures found in the area of breast tissue examined was reduced. However, the observation that the Lob 1:Lob 3 ratio was maintained, confirmed the original observation that the presence of Lob 1 in women with cancer was higher than in parous women without cancer. Much more work needs to be done in order to fully understand the relationship between the pattern of breast development and neoplasia. I hope this work will encourage additional studies along these lines.