

## Safely Expanding the Use of Nipple-Sparing Mastectomy in BRCA Mutation Carriers

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This past year, I presented data supporting the safety of nipple-sparing mastectomy (NSM) to a Latin American audience. After the talk, one of the participants thanked me for the talk but she was disheartened that the local medical oncologist described my presentation to his colleagues as nothing less than blasphemy. Although recently more accepting of NSM, our medical community also questions the oncologic safety of NSM. Should it be limited to prophylactic procedures? Is it safe for women with more advanced disease or with BRCA mutations?

Women with BRCA mutations have a significant lifetime risk of developing breast cancer, and it is well-established that prophylactic mastectomy significantly reduces that risk. For BRCA mutation carriers diagnosed with cancer, bilateral mastectomies are typically performed due to the high risk of second breast cancer events. Many of these women are young at the time of surgery but, regardless of age, improving cosmetic results with reconstruction make this aggressive surgery more palatable. NSM can successfully reduce cancer risk and it also offers an improved cosmetic outcome with reconstruction; a woman's native nipple is typically cosmetically superior to a reconstructed nipple. However, the high breast cancer risk associated with a BRCA mutation mandates that the surgery be as effective as possible at reducing future breast cancer events.

In the article that accompanies this editorial, Yao et al. report on a series of 397 NSMs performed at two different institutions on 201 women with documented BRCA1 and BRCA2 mutations.<sup>1</sup> This retrospective study adds to a

growing body of literature supporting the safety of NSM in general, but it is especially valuable due to its focus on women with BRCA mutations, on whom there is limited data. This study is also unique in that it includes these high-risk women undergoing NSM for cancer treatment ( $n = 51$ , 25%) in addition to women undergoing prophylactic surgery only ( $n = 150$ , 75%).

In order to answer the question of whether NSM is safe for women with BRCA mutations, it is important to first define the procedure, and to contrast it to subcutaneous mastectomy, which is not an oncologic procedure. During a subcutaneous mastectomy, a thick skin flap (and therefore breast tissue) is left behind with the nipple and areolar complex (NAC). Despite the intentional retention of some breast tissue, prophylactic subcutaneous mastectomies have actually been associated with low rates of subsequent cancer.<sup>2</sup> However, a modern NSM aims to remove as much breast parenchyma as possible, up to the base of the nipple and often including a core of tissue within the nipple. Done appropriately, the NSM only differs from the now well-accepted skin-sparing mastectomy in the preservation of the areolar skin and the skin of the nipple.

If the NAC is retained, how often is this tissue involved with cancer recurrence or with new cancer development? Yao et al. nicely summarize the available data regarding nipple recurrence in Table 4 of their article.<sup>1</sup> Large series of NSM have now been reported, with low rates of cancer recurrence overall and with NAC recurrences occurring only rarely. Indeed, of the over 3,000 patients included in Table 4, less than 1 % developed disease in the retained NAC. These studies did not focus on women with BRCA mutations. In the current study, four patients of the entire cohort experienced disease recurrence; the only isolated in-breast event occurred in a patient whose NSM was performed for risk reduction. One patient experienced a simultaneous distant and in-breast recurrence, and two patients experienced isolated axillary recurrences. No

recurrences at the NAC were seen in any patient, with a median follow-up of 32.6 months. Gerber et al. published the longest available follow-up, a mean of 101 months, and reported only one NAC recurrence in 60 women treated with therapeutic NSM,<sup>3</sup> and therefore it is expected that NAC recurrences will remain uncommon with longer follow-up.

These excellent oncologic results do depend on careful patient selection and on surgical technique. There is a consensus that NSM is not appropriate for women with inflammatory breast cancer, overt nipple and skin involvement, Paget's disease, or bloody nipple discharge. National guidelines define NSM eligibility conservatively, recommending that the procedure be limited to women with early-stage disease and low risk of local recurrence.<sup>4</sup> While many surgeons offer the procedure to women with more advanced disease, there is agreement that the nipple margin needs to be evaluated separately and the location indicated to the pathologist. In the series by Yao et al.<sup>1</sup> three of the 51 patients (1.5 %) undergoing therapeutic NSM were found to have disease at the nipple margin. No positive nipple margins were seen in the prophylactic group. Some surgeons send this tissue intraoperatively for touch prep or frozen section and, if disease is identified, immediately remove the nipple. Disease identified at the nipple margin on final pathology otherwise mandates return to the operating room to remove the nipple.

Prophylactic mastectomy specimens should also undergo careful pathologic evaluation due to the risk of occult cancer, which might be higher in the BRCA carrier population. In this series, incidental cancers were seen in 2.7 % of the prophylactic mastectomies and in 3.9 % of the therapeutic mastectomy patients (in the contralateral breast). Only one of these six total incidental cancers was invasive and therefore the authors concluded that, as with the non-BRCA population, sentinel lymph node biopsy was optional with prophylactic NSMs.

As surgeons become more comfortable with the procedure and eligibility is expanded to include more patients,<sup>1,5</sup> it is important to note that there is a learning curve to this procedure. A skin-sparing mastectomy is often technically challenging given the small incision size, need to access the axilla, and given competing demands of removing all breast tissue but maintaining perfusion of the skin flap. Given different incision choices and the careful dissection needed behind the NAC, NSM is even more difficult. Close collaboration with a reconstructive plastic surgeon is mandatory. While optimizing the cosmetic result and minimizing surgical complications are very important, this is a procedure designed to treat and prevent cancer, and adequately removing the breast tissue should be the primary goal. While NSM is a safe procedure for many patients with breast cancer and at high risk for developing cancer, including women with BRCA mutations, it is a technique that mandates careful patient selection and counseling.

**DISCLOSURES** None.

## REFERENCES

1. Yao K, Liederbach E, Tang R, et al. Nipple sparing mastectomy in *BRCA1/2* mutation carriers: an interim analysis and review of the literature. *Ann Surg Oncol*. 2014. doi:10.1245/s10434-014-3883-3.
2. Hartman LC, Schaid DJ, Woods JE, et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *N Engl J Med*. 1999;340:77-84.
3. Gerber B, Krause A, Dieterich M, Kundt G, Reimer T. The oncologic safety of skin sparing mastectomy with conservation of the nipple-areola complex and autologous reconstruction: an extended follow-up study. *Ann Surg Oncol*. 2009;249:461-8.
4. National Comprehensive Cancer Network Breast Guidelines, version 3.2014. [www.nccn.org](http://www.nccn.org). Accessed 24 Jul 2014.
5. Coopey WB, Tang R, Lei L, et al. Increasing eligibility for nipple-sparing mastectomy. *Ann Surg Oncol*. 2013;20:3218-22.