

Advances in Nipple-Sparing Mastectomy: Oncological Safety and Incision Selection

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Abstract

Background: With the evolution of breast reconstruction and oncoplastic techniques, more aesthetic mastectomies are being offered to patients. Nipple-sparing mastectomy (NSM) has been controversial, but an expanding body of published experience has allowed this concept to gain momentum.

Objectives: The authors review their experience with NSM.

Methods: From 2007 to 2009, 112 consecutive patients (204 breasts) who were candidates for NSM presented to one of two private plastic surgery practices. All patients underwent preoperative magnetic resonance imaging to assess the size of the tumor, its distance from the nipple, and any additional disease within the ipsilateral/contralateral breast or axillae. Exclusion criteria included tumors larger than 3 cm, clinical invasion of the nipple-areolar complex, tumors within 2 cm of the nipple, evidence of multicentric disease, a positive intraoperative retroareolar frozen section, or nodal disease (excluding isolated immunohistochemistry positivity). Fourteen patients were excluded from the study for one of these reasons, leaving a total of 98 patients (186 breasts) who underwent NSM.

Results: Risk-reducing mastectomies were performed on 45 patients. Therapeutic mastectomies were performed for Stage 0 cancer (ductal carcinoma in situ) in 26 patients, for Stage 1A in 24 patients, and for Stage 1B in three patients. Disease-free survival was calculated from the date of surgery to any local, regional, or distant relapse (whichever occurred first). As of the writing of this article, follow-up ranged from nine months to three years, and there has been no local or regional recurrence in any patient.

Conclusions: NSM is evolving and should be considered a good treatment option in carefully-selected patients. These findings add to the growing body of evidence showing that, with proper patient selection and operative technique, NSM is a safe and effective intervention for patients requiring therapeutic or prophylactic mastectomy.

Keywords

nipple sparing mastectomy, breast reconstruction, oncological guidelines

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During the last century, breast reconstruction has evolved from a rarely-performed surgical venture to a daily occurrence that has become an important part of the rehabilitation process following mastectomy or lumpectomy. Improved aesthetic quality of the reconstructions has been fostered by the desire to offer patients better results, as well as by important technical advances. Reconstruction results have therefore emerged from amorphous blobs appearing as breast mounds to nearly-normal-appearing breasts. Symmetry, which was hardly possible and seldom achieved before, is now the standard. Along the same lines, the surgical management of breast cancer has undergone an evolution from radical mastectomies to less invasive breast conservation therapies and now to aesthetic mastectomies, of which nipple-sparing mastectomy (NSM) is the ideal, when appropriate. NSM is a procedure that combines skin-sparing mastectomy with preservation of the

nipple-areolar complex (NAC). Several recent studies attest to the efficacy and safety of this procedure.¹⁻¹⁴

In the majority of women who have undergone mastectomy, the devastating psychological and emotional impact of the loss can be mitigated by breast reconstruction. The cosmetic outcome following immediate breast reconstruction is

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enhanced by preservation of the native skin envelope, inframammary fold, anterior axillary fold, and (when appropriate) NAC. In this regard, Toth et al¹⁵ described the importance of involving a plastic surgeon in preoperative planning and decision-making regarding the placement of the incision. Several studies on skin-sparing mastectomy have now been published, showing that the incidence of local recurrence is similar to the rate following simple mastectomy.¹⁶⁻²⁷ No studies have prospectively investigated the comparative new primary cancer rate in simple versus skin-sparing mastectomy in the context of risk-reducing surgery. However, given that the rate of new primary cancers following either simple or subcutaneous mastectomy is low, it is unlikely that simple mastectomy could show a statistically or oncologically significant advantage that outweighs the major aesthetic disadvantages.^{28,29}

One may ask, why consider saving the nipple when advanced reconstructive techniques can achieve similar goals? Nipple-areolar reconstruction has always represented the final stage of breast reconstruction, whereby a reconstructed breast mound is transformed into a breast with maximal realism when compared with the patient's opposite breast. However, there are problems with reconstructed nipples, the greatest being loss of projection over time. There is the additional need for tattoos, which fade over time, to provide pigmentation of both nipple and areola.³⁰ There are also the issues of the patient's reconstructed breast appearing different or "alien" and the interval between surgery and nipple reconstruction, when the patient may feel incomplete. Essentially, all postmastectomy patients suffer distress brought on by the diagnosis of breast cancer and the severe alteration of body image with resultant adverse psychological consequences.³¹ As surgeons, we strive to reconstruct the most aesthetic breast form following mastectomy to reduce the psychological burden. Therefore, if a patient is a candidate for NAC preservation, this may further enhance our goal.

NSM was attempted in the 1980s but never gained popularity owing to the controversies surrounding oncological safety.³² Now, better technologies for preoperative staging and assessment of lesion distance from the NAC, along with an increased understanding of the anatomy of the breast ducts with relation to the nipple, are encouraging a return to the concept. One of the key publications that renewed and increased enthusiasm for this technique was the multicenter publication of 192 patients undergoing NSM with only four recurrences, all of which occurred distant from the NAC. Recurrences were seen in the upper outer quadrant, where nearly all recurrences are found with simple mastectomies, at the junction of the tail of the breast and axillary tissue.³³

In recent years, there has been a sudden increase in reports of NSM for prophylaxis and cancer treatment. Of the approximately 1868 NSM procedures performed for breast cancer treatment and published in recent literature,^{7-13,16,17,33-46} only three local recurrences within the NAC have been reported,^{8,16,17,36} representing 0.16% of local events attributed to patients with NAC preservation. Note, however, that most of these studies have short

follow-up periods, thus rendering definitive conclusions premature. The purpose of this study was to evaluate our series of NSM patients. In this report, we describe our technique for aesthetic mastectomy, recommend criteria for selection of patients, and describe proper incision selection based on patient characteristics.

METHODS

From 2007 to 2009, 112 consecutive patients presented to one of two private plastic surgery practices as candidates for NSM. All patients underwent preoperative magnetic resonance imaging (MRI) to assess for tumor size, tumor distance from the nipple, and multicentricity. Exclusion criteria included tumors larger than 3 cm, clinical invasion of the NAC, tumors within 2 cm from the nipple, evidence of multicentric disease, a positive intraoperative retroareolar frozen section, and nodal disease, excluding isolated immunohistochemistry positivity. On the basis of these criteria, fourteen patients were excluded from the study because of positive retroareolar frozen sections necessitating nipple removal. A total of 98 patients (186 breasts) were included in the study and underwent NSM.

All mastectomies were performed by a team of plastic surgeons and breast surgeons. All incisions were pre-marked by plastic surgeons, who were present during mastectomy. Nipple positions were marked on mastectomy specimens for accurate distance calculation during pathological analysis.

Reconstruction proceeded with one of three techniques. All patients who received both an expander and an implant underwent two-stage reconstructions, with placement of an expander and acellular dermal matrix at the first stage, followed by placement of the silicone prosthesis along with additional acellular dermal matrix and fat injection during the second-stage reconstruction. All patients in the autologous group (TRAM/DIEP) also underwent two-stage reconstructions, with initial insertion of an expander followed by autologous reconstruction. Patients in the latissimus/implant group underwent two-stage reconstructions that included placement of expander in addition to the latissimus at the first stage, followed by placement of a silicone implant and fat injection at the second stage.

During follow-up, disease-free survival was calculated from the date of surgery to the date of any local, regional, or distant relapse (whichever occurred first) or to the last visit date, in case of no events.

RESULTS

Of the 98 patients, 45 underwent NSM for risk reduction. The rest of the procedures were performed for Stage 0 cancer in 26 patients (ductal carcinoma in situ), Stage 1A in 24 patients, and Stage 1B in three patients.

All patients underwent immediate reconstruction with either expander/implant or autologous reconstruction (Table 1). Two patients who underwent risk-reducing

Table 1. Number of Mastectomies and Type of Reconstructions

	Breasts, n	Patients, n
Mastectomies	204	112
Nipple sparing	186	98
Areolar sparing	18	14
Reconstructions		
Immediate	204	112
Delayed	0	0
Type of reconstruction		
Expander/implant	182	96
TRAM/DIEP	4	2
Latissimus with implant	16	14

procedures were positive for malignancy with Stage 0 tumors (ductal carcinoma in situ), which were at least 2 cm away from the NAC. The distance of these tumors from the nipple was accurately quantified by MRI and correlated with pathology and did not necessitate excision of the nipple. (If biopsy was positive for “atypical cells,” the nipple would have been sacrificed.) At the time of submission, follow-up ranged from nine months to three years, and no patient had local or regional recurrence. Complete tumor characteristics are outlined in Table 2. Clinical results are shown in Figures 1-4.

DISCUSSION

Plastic surgeons strive to create an aesthetically-pleasing breast form following mastectomy. By selecting appropriate candidates and preserving the breast envelope while upholding oncologically-sound treatment, surgeons can achieve better cosmetic outcomes in these situations. Clearly, good breast reconstruction begins with an excellent mastectomy. The aesthetic mastectomy can be performed for two distinct purposes: risk reduction and cancer treatment.

The management of women at high risk for breast cancer presents a clinical dilemma to the healthcare provider as well as to the woman herself. Current options include surveillance, prophylactic surgery (mastectomy and/or oophorectomy), and/or chemoprevention.⁴⁷ These patients can be divided into three groups: patients with BRCA1/BRCA2 mutation, patients with a personal or family history of cancer following unilateral mastectomy for cancer, and patients with severe fibrocystic disease with a strong family history of cancer. Hartmann et al²⁹ showed that prophylactic mastectomy is associated with a substantial reduction in the incidence of subsequent breast cancer not only in women identified as being at high risk on the basis

Table 2. Patient and Tumor Characteristics

Characteristic	Patients, n
Total	98
Age	
< 35	40 ^a
35-55	46 ^b
>55	12
Positive lymph nodes, n	
0	50
1-3	3 ^c
> 3	0
Histiotype	
Ductal	47
Lobular	7
Mixed	1
Benign	43 ^d

^a26 risk reducing.

^b19 risk reducing.

^cImmunohistochemistry positive.

^dRisk reducing.

of a family history but also in women who are known BRCA1 or BRCA2 mutation carriers. McDonnell et al⁴⁸ concluded that the incidence of contralateral breast cancer seems to be significantly reduced after contralateral prophylactic mastectomy in women with a personal and family history of breast cancer. Although mastectomy with or without immediate reconstruction has been established as the standard treatment for risk reduction with acceptable rates of local recurrence, NSM has evolved as an alternative technique to improve women’s overall quality of life. In the setting of prophylactic mastectomy, NSM can be considered in virtually all patients after ruling out malignancy and discussing the risk-reducing strategies. Preoperative evaluation for NSM should include complete imaging studies (preferably, breast MRI), a detailed family history, and a physical exam.

There is no question that risk-reducing mastectomy provides the lowest rate of local recurrence.⁴⁹ In conjunction, NSM provides a natural-appearing nipple with a better cosmetic outcome. With the current outcomes reported for NSM, this technique should be considered not only for risk reduction but also as a treatment option for patients with existing breast cancer. NSM for the treatment of cancer is more controversial, however. It is imperative for the plastic surgeon and breast surgeon team to select good candidates for this operation. The goal, as with any case of breast cancer, is foremost to treat the breast cancer with the best

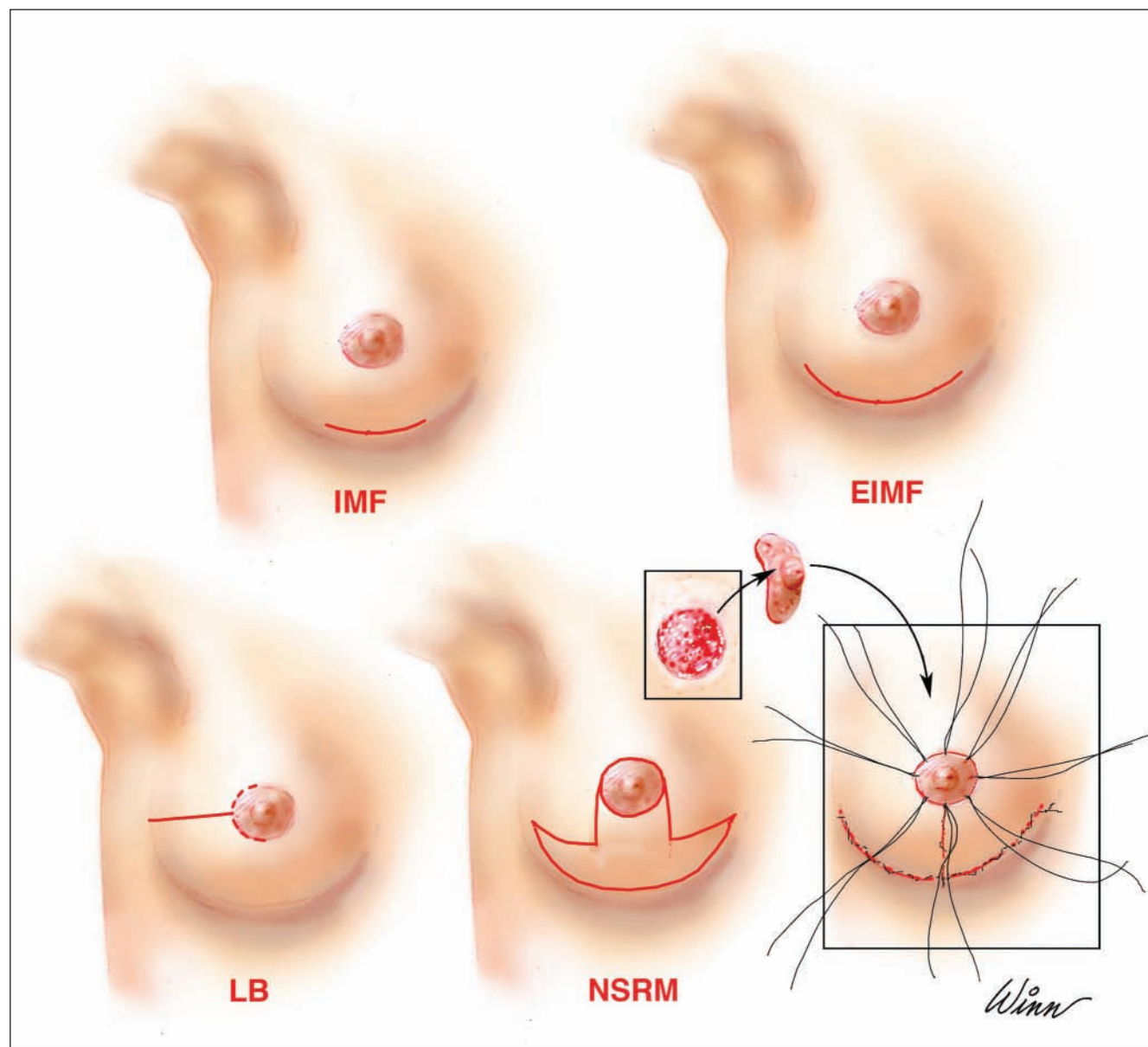


Figure 1. Incision options for nipple-sparing mastectomy. IMF, inframammary fold incision; EIMF, extended IMF; LB, lateral breast; NSRM, nipple-sparing reduction mastectomy.

possible oncological surgery, followed by reconstruction.

Given the data from the recent literature as well as our own experience, we have selected specific criteria to evaluate the candidacy of a patient for NSM.^{46,50} First, tumors should be 3 cm or less in size and have a distance of at least 2 cm from the center of the nipple. Second, the patient should have a clinically-negative axilla and a negative sentinel node. Furthermore, a patient with any skin involvement, inflammatory breast cancer, or multicentric disease should not undergo NSM. Clearly, tumor characteristics should be taken into account. Current evidence suggests that local failure is a manifestation of tumor biology rather than preservation of the NAC.⁴⁵ This procedure

should therefore be discouraged in patients with extensive nodal involvement and in those who have triple-negative tumors (ER/PR negative and Her-2 neu negative). However, patients with an immunohistochemistry-positive sentinel node may be candidates for NSM. These patients do not require additional treatment of the axillae, and each patient should be treated individually on the basis of personal/family history and available tumor data. Our goal is to achieve longevity with high quality of life; therefore, superior oncological management should always be the primary treatment. One can argue that the criteria listed above may be slightly more conservative than other published lists.⁹⁻¹²

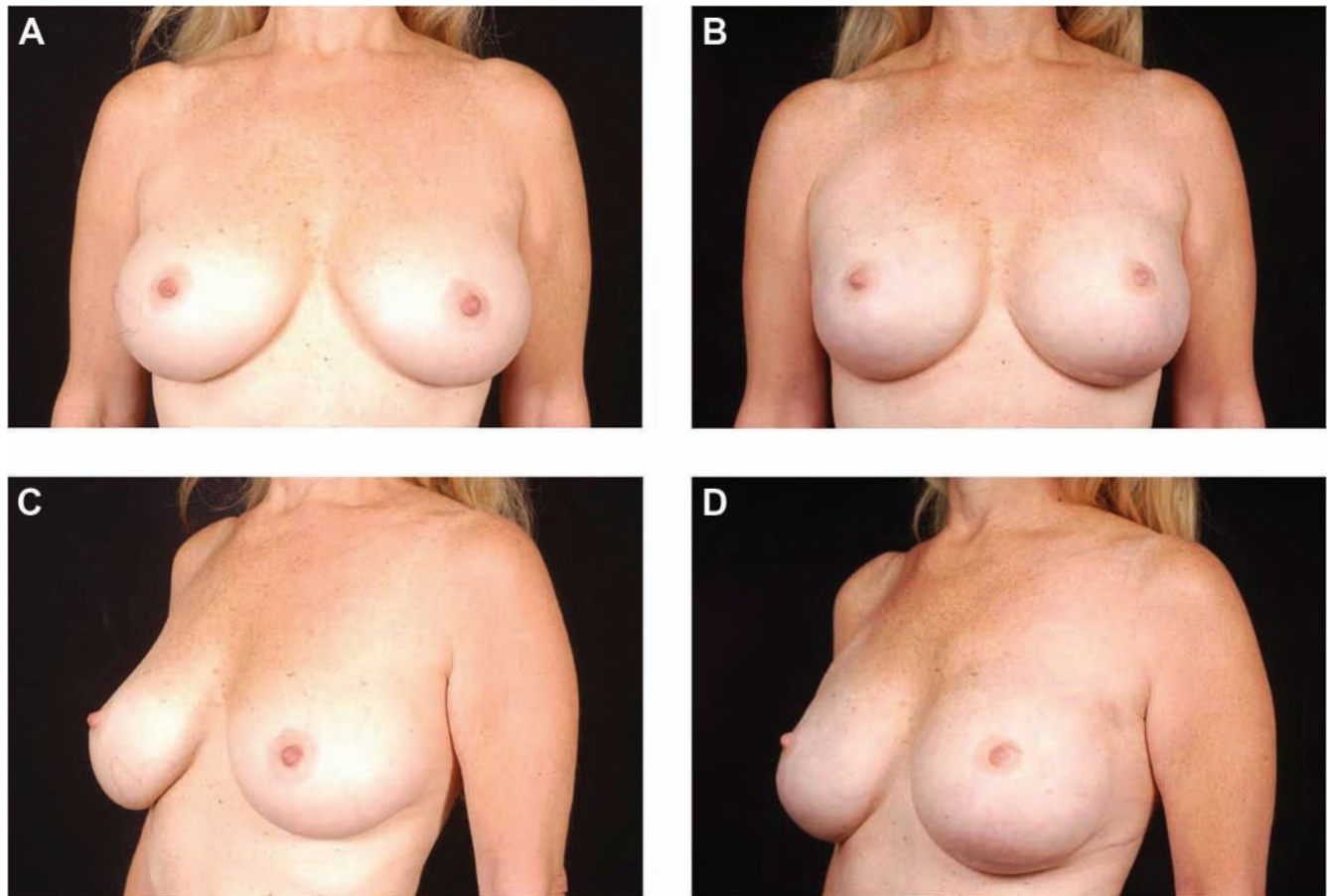


Figure 2. (A, C) This 43-year-old woman presented with Stage 1 ductal carcinoma in her left breast. (B, D) Eighteen months after nipple-sparing mastectomy with left sentinel node biopsy and two-stage breast reconstruction with form-stable, highly-cohesive gel anatomical implants (Style 410 FX, 495 gm; Allergan, Inc., Irvine, California), acellular dermal matrix, and fat injection (30 cc). Editor's Note: The anatomical implants placed in this patient are not currently FDA-approved in the United States.

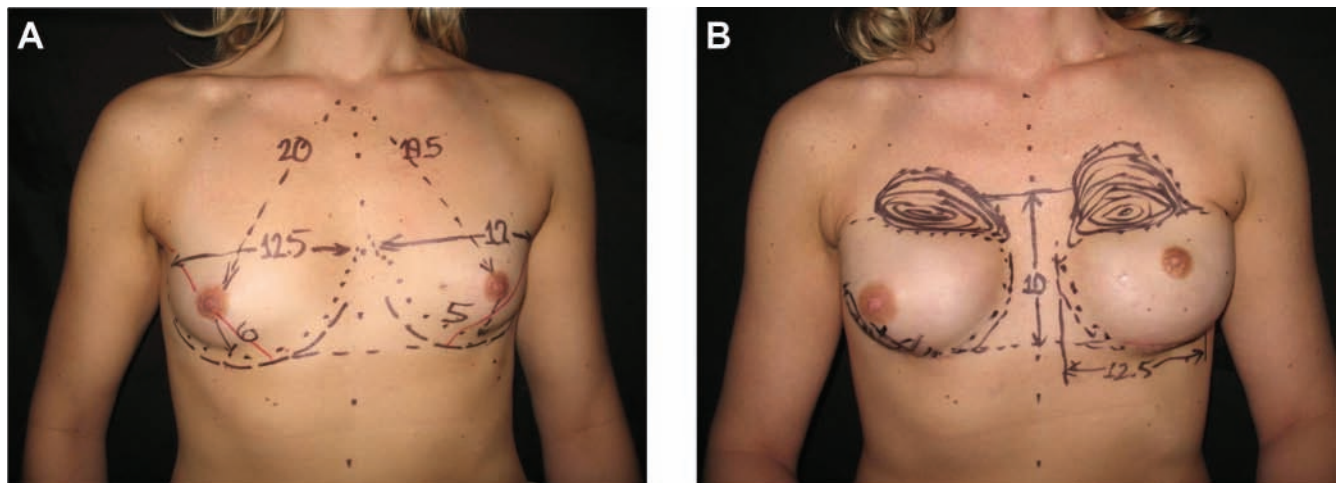


Figure 3. (A) Preoperative markings for an inframammary incision. (B) Preoperative markings for the patient's second-stage reconstruction, eight weeks after bilateral nipple-sparing mastectomy with left sentinel node biopsy and placement of 133 LV expanders.

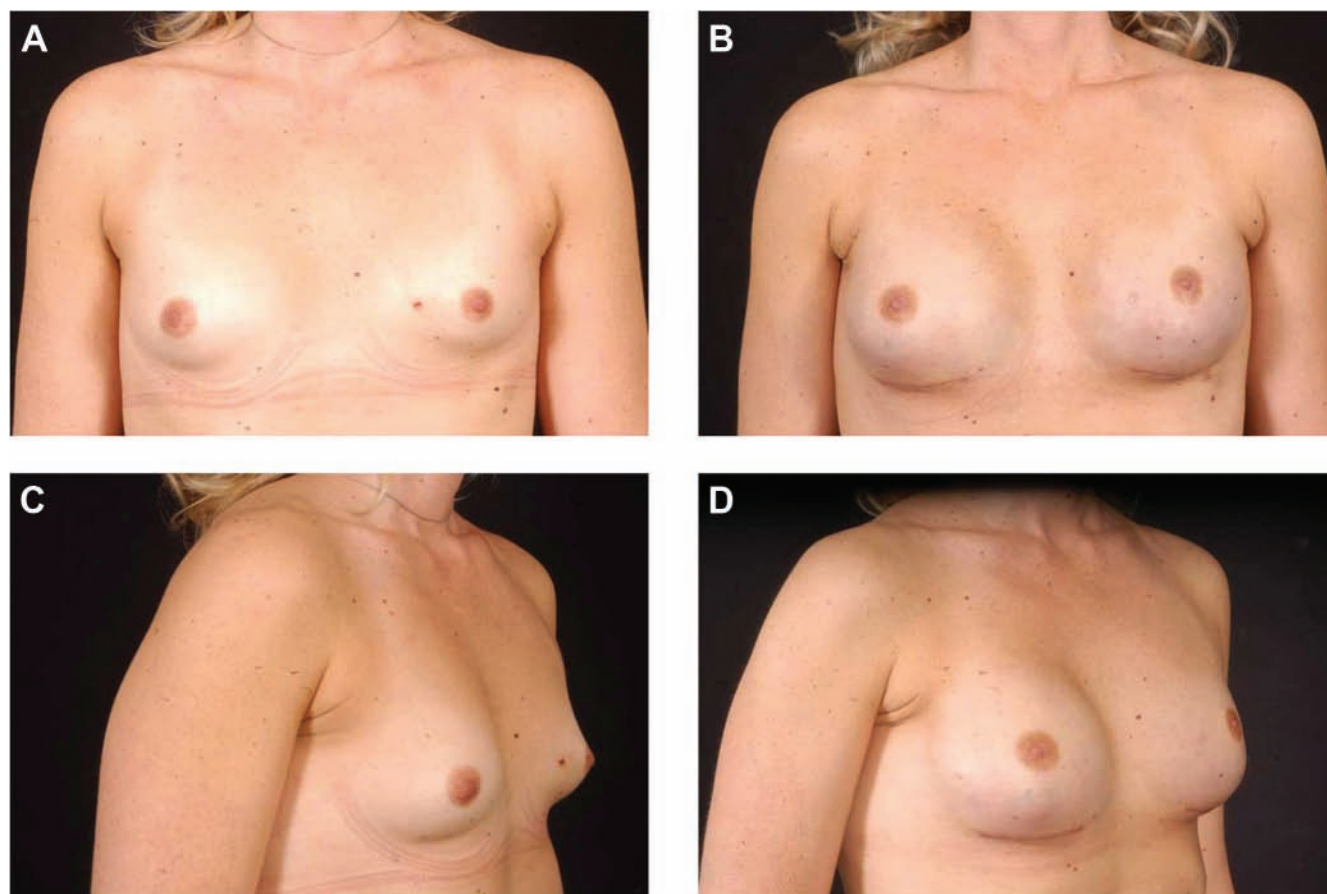


Figure 4. (A, C) The 31-year-old woman in Figure 3 presented with ductal carcinoma in situ in her left breast. (B, D) Fourteen months after nipple-sparing mastectomy with left sentinel node biopsy and placement of 133 LV expanders, followed by breast reconstruction with form-stable, highly-cohesive gel anatomical implants (Style 410 LX, 365 gm; Allergan, Inc., Irvine, California), acellular dermal matrix, and fat injection (40 cc). Editor's Note: The anatomical implants placed in this patient are not currently FDA-approved in the United States.

NSM is an excellent alternative in patients who are poor candidates for breast conservation therapy (BCT). NSM is not meant to replace BCT, but it does serve as an option for informed patients who choose mastectomy over BCT or for those who need mastectomy because of an anticipated poor result with BCT (ie, patients with small breasts or close lumpectomy margins).^{51,52} As new data continue to accumulate on the long-term risk of recurrence with BCT,⁵¹ we have begun to ask ourselves if mastectomy should be considered more strongly in younger women—especially those at high risk (ie, ER/PR negative). In addition, as we continue to improve our ability to preserve the aesthetic breast envelope (including the NAC), NSM may serve as a viable alternative in this patient population.

Preoperative radiographic evaluation plays an important role, whether with MRI or ultrasound-guided Mammotome biopsy of the duct and posterior nipple tissue. At our institutions, most patients undergo MRI evaluation to assess the breast and the axilla. The results for this study provide

information regarding the patient's candidacy for NSM. The tumor size and the distance of the tumor from the NAC are evaluated, along with the presence of other suspicious masses in the breast and axilla. Of course, the final decision on whether to keep the nipple is made intraoperatively, following results of the frozen section and, finally, the permanent pathology. At times, the frozen section has been interpreted as being benign while the result was positive. In these cases, we generally wait three to four weeks to completely excise the nipple in the office, following recovery of both the tissues and the patient.

In this series, the majority of our patients requested implant-based reconstructions. All patients had expanders placed during their first stage of reconstruction. Patients who had undergone prior radiotherapy received reconstruction with a latissimus dorsi flap in addition to the expander, to render a new vascularized pocket.

Despite all these criteria, the bottom line is the patient's preference among the available options in terms of which

procedure will place her most at ease while not compromising oncological management. In choosing the incision, the size of the breast and the degree of ptosis are the two most important factors. Regardless of the etiology, classifying patients according to their degree of ptosis is a useful tool. It is important to clarify with the patient preoperatively what her goals are in terms of the final appearance of her breast. Regnault's^{53,54} classification system should then be used to grade the extent of ptosis. The amount of preoperative ptosis can then be used as a guide to select the operation necessary to achieve the patient's preferred correction and symmetrization (Table 3, Figure 1). At one end of the spectrum, for patients with small- and medium-sized nonptotic breasts, an inframammary incision is safe and effective (Figures 2-4); at the other end, for patients with larger and more significantly ptotic breasts, a nipple-sparing reduction mastectomy can be performed to excise all breast tissue (Figures 5 and 6). There are two factors to consider here. First, with larger breasts, an inframammary incision may not allow for complete excision superiorly, and alternative incisions should be planned. Second, with more ptotic breasts (and when the patient expresses a desire for a smaller breast), a reduction of the skin envelope will be necessary, and this can be performed with only a vertical component or with a combined variant-size horizontal component. With nipple-sparing reduction mastectomy, the NAC is excised and banked over the mastectomy flap. If a concurrent autologous reconstruction is performed, this can be banked over the new tissue. The precise dissection and retention of the blood flow to the mastectomy flaps will be crucial for the graft to completely take over the mastectomy flap. If there is concern about the mastectomy flaps, the NAC can be banked at another site until the vascularity of the mastectomy flaps is confirmed.

Table 3. Surgical Incision Options Based on Breast Size and Degree of Ptosis

Breast Size	Nonptotic	Pseudoptosis	Ptosis		
			Grade 1	Grade 2	Grade 3
Small	IMF	IMF, EIMF	IMF, EIMF, LB	EIMF, LB, NSRM	NSRM
Medium	IMF	IMF, EIMF	IMF, EIMF, LB, NSRM	EIMF, LB, NSRM	NSRM
Large	IMF, EIMF, LB, VB	IMF, EIMF, LB VB	EIMF, LB, VB, NSRM	NSRM	NSRM

IMF, inframammary fold; EIMF, extended inframammary fold; LB, lateral breast; VB, vertical breast; NSRM, nipple sparing reduction mastectomy.

CONCLUSIONS

NSM is evolving and serves as an important option in carefully selected patients. These findings add to the growing body of evidence showing that, with proper patient selection and operative technique, NSM is a safe and effective intervention for patients requiring therapeutic or prophylactic mastectomy. The guidelines provided in this article are not intended to replace good clinical judgment but rather to serve as another avenue worth considering. The combination of preoperative patient selection, multidisciplinary collaboration, pathological analysis of the NAC, and attention to incision placement is paramount and unique for each patient and should be considered individually on the basis of available data.

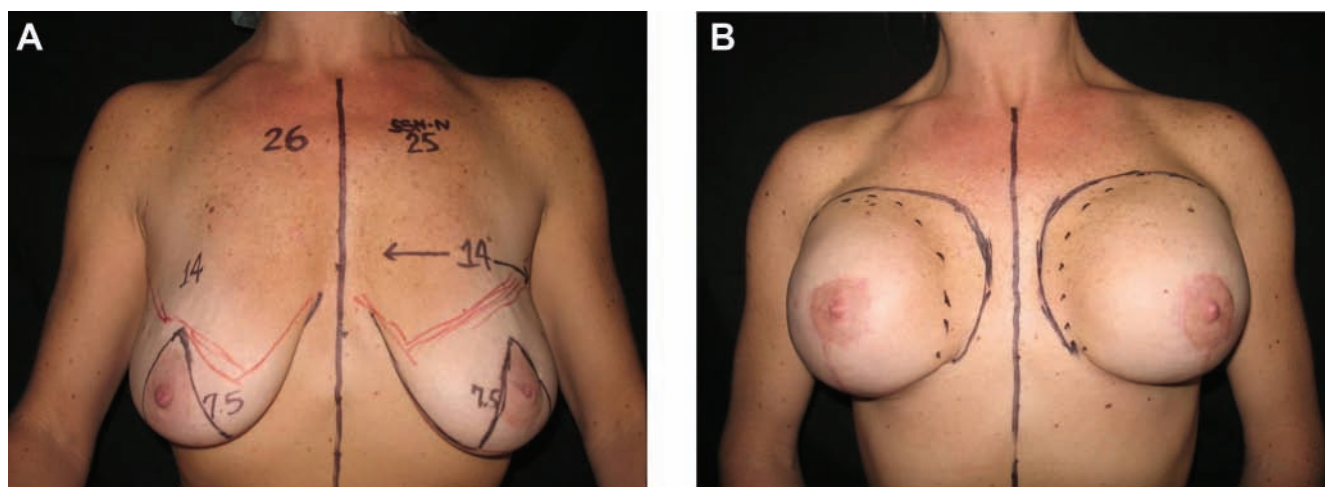


Figure 5. (A) Preoperative markings for a nipple-sparing reduction mastectomy. (B) Preoperative markings for the patient's second-stage reconstruction, three weeks after bilateral nipple-sparing mastectomy with left sentinel node biopsy and placement of 133 MV expanders.

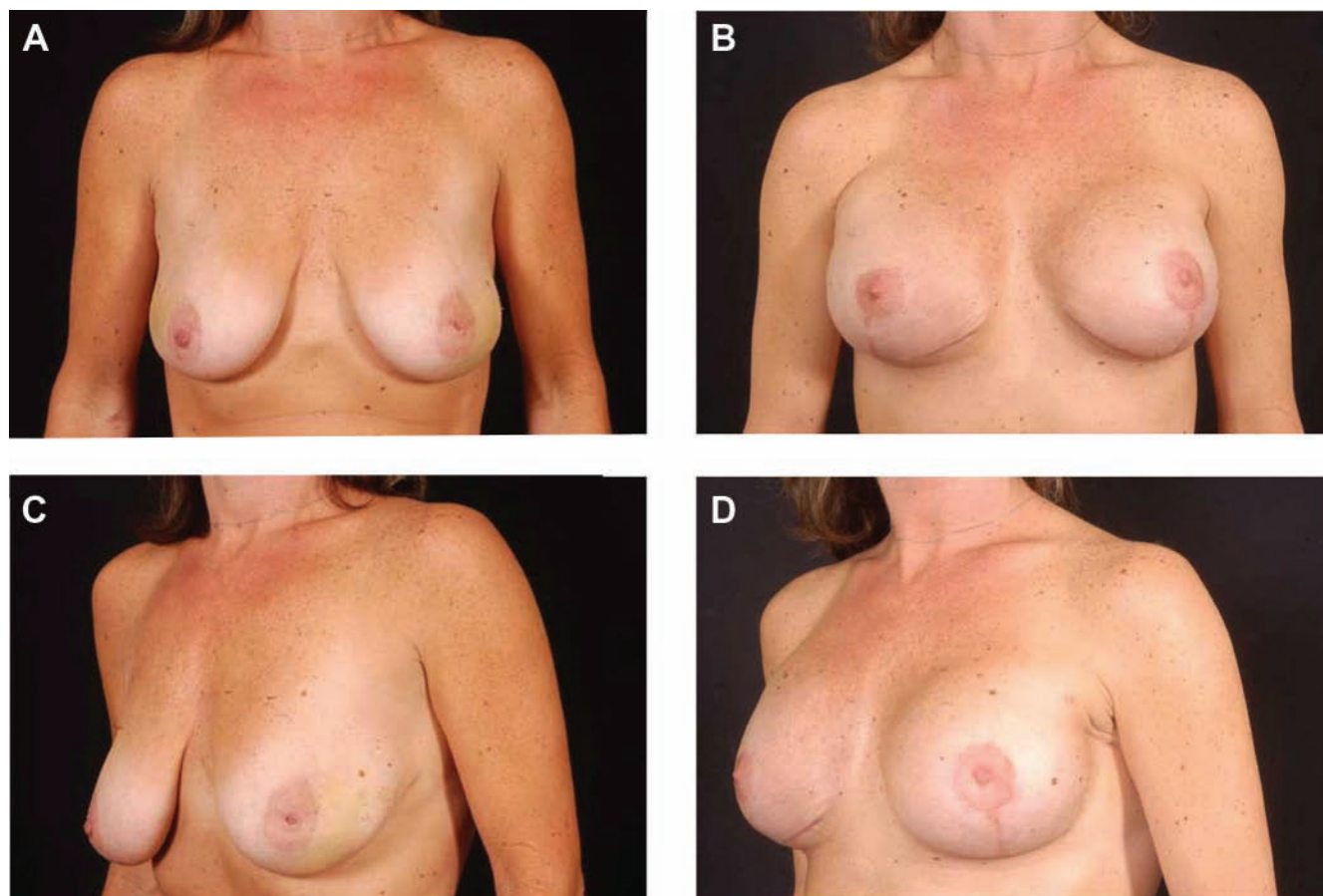


Figure 6. (A, C) The 39-year-old woman in Figure 5 presented with ductal carcinoma in situ in her left breast. (B, D) Eighteen months after nipple-sparing mastectomy with left sentinel node biopsy and placement of 133 MV expanders, followed by breast reconstruction with form-stable, highly-cohesive gel anatomical implants (Style 410 MX, 445 gm; Allergan, Inc., Irvine, California), acellular dermal matrix, and fat injection (30 cc). Editor's Note: The anatomical implants placed in this patient are not currently FDA-approved in the United States.

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