

Update on the Indications for Nipple-Sparing Mastectomy

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The surgical management of breast cancer has changed in the past 30 years from Halsted's radical mastectomy to breast-conserving surgery in the early 1990s. Breast cancer treatment is still evolving to include more conservative and cosmetic approaches. Advances in plastic surgery techniques have made immediate breast reconstruction available to the majority of patients undergoing mastectomy. These advances and increasing patient concerns about cosmesis have led surgical oncologists and plastic surgeons to explore approaches that combine oncologic safety and aesthetic results.

The need for removal of the nipple-areola complex (NAC) as part of mastectomy is an area of renewed interest. Nipple-sparing mastectomy (NSM), which combines skin-sparing mastectomy (SSM) with preservation of the NAC, is a controversial procedure lacking general consensus. Physicians involved in the management of breast disease should be familiar with the possible indications for the use of this procedure.

Historic Perspective

Before oncologic criteria for breast cancer were established, many factors contributed to the classic dogma that the NAC should be removed along with the specimen during mastectomy for any indication. Early descriptions of centripetal lymphatic drainage toward the subareolar plexus played a major role in this widespread concept, despite later studies showing that the lymphatic drainage is downward to the deep pectoral lymphatic plexus and the axilla.¹⁻³

In the prereconstructive era, there were no at-

Abstract There is renewed interest in the use of nipple-sparing mastectomy (NSM), which combines skin-sparing mastectomy with preservation of the nipple-areola complex. NSM may be an oncologically safe treatment in a subgroup of patients who are candidates for breast-conserving surgery but still prefer to undergo mastectomy. A combination of newer techniques and good coordination between plastic and oncologic surgeons can achieve excellent cosmetic results and a low incidence of postoperative complications. However, major concerns about NSM include the persistent risk for breast cancer development when it is used for prophylaxis as well as the potential failure of local control when it is used for treatment. The reported experience with these newer techniques lacks the power to generate a consensus for its indications because of limited reported series with small populations. Although the current role of NSM seems to be more defined as a prophylactic procedure in high-risk patients, prospective studies and reports are needed to better define its indications.

tempts to preserve the NAC and excess skin during mastectomy. Sparing the NAC was historically reported by Freeman^{4,5} in the 1960s with subcutaneous mastectomy. He advocated the procedure in the presence of benign breast lesions, but did not address its role for prophylaxis in high-risk patients or cancer treatment.

Biologic Considerations

Issues that arise when considering preservation of the NAC are safety, cosmesis, and function. The major concern about this procedure is the risk of breast cancer development of residual major ducts. The risk of cancer developing de novo in preserved tissue should be distinguished from the risk of cancer involving the nipple by direct extension. Involvement of the nipple by direct extension is more common than are de novo lesions.

PAGET'S DISEASE OF THE NIPPLE

Paget's disease represents a form of carcinoma in situ that arises from a lactiferous sinus near the nipple and grows up onto the surface of the nipple epidermis. Its incidence ranges from 0.5%

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Table 1**Occult Nipple Involvement in Reported Series**

PRIMARY AUTHOR	YEAR	NO. OF MASTECTOMY SPECIMENS	DEPTH OF NIPPLE BLOCKS (mm FROM SKIN)	NO. OF SECTIONS PER BLOCK	NIPPLE INVOLVEMENT (%)
Smith ¹²	1976	541	5	2	12
Parry ¹³	1977	200	NR	NR	8
Andersen ¹⁴	1979	40	10	14	50
Lagios ¹⁵	1979	149	4	NR	30
Wertheim ¹⁶	1980	1,000	NR	8	23
Quinn ¹⁷	1981	45	10	14	25
Morimoto ¹⁸	1985	141	20	NR	31
Luttges ¹⁹	1987	166	10	3	38
Santini ²⁰	1989	1,291	10	5–7	12
Menon ²¹	1989	33	small rim of subareolar tissue	9	58
Verma ²²	1997	26	10	4	0
Vyas ²³	1998	140	NR	6–8	16
Laronga ²⁴	1999	286	horizontal sectioning of NAC	NR	6

Abbreviations: NAC = nipple-areola complex; NR = not reported

to 2.8%, and it is associated with an underlying breast carcinoma in 97% of cases.^{6–8} Of the 158,621 pathologically confirmed female and male breast cancer registrants from the Surveillance, Epidemiology, and End Results (SEER) registry of the National Cancer Institute, 1,775 (1.1%) had histologic Paget's disease.⁹

DCIS INVOLVING THE NIPPLE

Nipple involvement is defined as ductal carcinoma in situ (DCIS), invasive carcinoma, or Paget's disease cells within 1 cm of the NAC. The incidence of nipple involvement in patients with DCIS has been evaluated in a few studies. Lagios et al¹⁰ found involvement of the nipple in 8 of 40 (20%) mastectomy specimens from patients with DCIS who presented with mammographic calcifications or who had DCIS as an incidental finding. Of these eight cases, five were Paget's disease and three had involvement of the lactiferous ducts.

RISK OF CANCER INVOLVING THE NIPPLE BY DIRECT EXTENSION

Occult nipple involvement in mastectomy specimens of patients with invasive ductal carcinoma (IDC) has been reported in several studies¹¹ (Table 1^{12–24}) and in 0% to 58% of cases.

Laronga et al²⁴ reported on a series of 286 patients undergoing SSM. An incidence of NAC involvement of 5.6% (16 of 286 patients) was shown when specimens were reviewed. Their analysis did not show significant differences between groups regarding tumor size, nuclear grade, histologic subtype, or estrogen and progesterone receptor status. Significant differences were observed regarding the location of the primary tumor (subareolar or multicentric) and positive axillary lymph node (ALN) status. Failure to associate tumor size and nuclear grade was attributed to a median tumor size of only 1.2 cm and to most cases having a moderate to high nuclear grade. The authors concluded that in patients with

negative ALN status and tumors located on the periphery of the breasts, the probability of missing an occult tumor with a NSM is less than 2%.

Simmons et al²⁵ performed a retrospective analysis of 217 patients treated with mastectomy and examined malignant involvement of the nipple, areola, or both. The overall frequency of malignant nipple involvement was 10.6% (23 of 217 cases). Comparisons of patients with tumors < 2 cm with tumors \geq 2 cm as well as comparisons of nuclear grade did not show a significant difference in nipple involvement. Likewise, there were no significant differences regarding the number of positive ALNs or the stage at diagnosis. The only variable that reliably predicted nipple involvement was tumor location. When a tumor was located in any of the four quadrants, the nipple was involved in only 6.4% of cases; when tumors were located in central, diffuse, or retroareolar areas, the nipple was involved in 27.3% of cases. It was also observed that only two patients (0.9%) had areolar involvement; both were at stage III with a retroareolar tumor > 5 cm. This last finding led investigators to propose preservation of the areola with removal of the nipple only.

RISK OF CANCER DEVELOPING IN THE NAC

IDC arising from the underlying tissue of the nipple as an index lesion is uncommon. When present, it is usually suspected on physical examination. The risk of development of a primary invasive carcinoma after NSM has been previously addressed. Hartmann et al²⁶ reported on seven cases (1.2%) with subsequent development of an invasive carcinoma from 575 high-risk patients treated with subcutaneous bilateral prophylactic mastectomy. Although studies such as this have been cited to conclude that preservation of the NAC may be suboptimal for prophylaxis,¹² the development of invasive disease in these cases did not necessarily occur within the NAC (only 1 of 7 cases occurred in the NAC, which accounts for 0.2%). This may also be attributed to the amount of redun-

Table 2**Previous Reports of NSM for Treatment or Prophylaxis**

PRIMARY AUTHOR	YEAR	NO. OF CASES	INDICATION FOR NSM	FOLLOW-UP	CASES WITH INCIDENCE OR RECURRENCE OF BREAST CANCER (%)	CASES WITH COMPLICATIONS (%)
Hartmann ^{a,26}	1999	575 (SCM)	Prophylaxis	14 years	7 (1%)	NR
Hartmann ^{a,27}	2001	26 (SCM)	Prophylaxis	13.4 years	0 (0%)	NR
Petit ²⁸	2003	25 (NSM)	Treatment	6 months	NR	1 (4%) TNN
Gerber ²⁹	2003	61 (NSM)	Treatment	4.9 years	6 (5%)	6 (10%) PNN
Crowe ³⁰	2004	44 (NSM)	Both	6 weeks minimum	NR	3 (6%) PNN

^aAnalysis of a subgroup of BRCA carriers in same series of patients

Abbreviations: NSM = nipple-sparing mastectomy; NR = not reported; PNN = partial nipple necrosis; SCM = subcutaneous mastectomy; TNN = total nipple necrosis

dant breast tissue left due to differences in surgical technique, which are discussed later in this article.

Results with NSM for Treatment or Prophylaxis

Limited studies have reported results and follow-up of NSM series either for treatment or prophylaxis of breast cancer (Table 2^{26–30}). Hartmann et al²⁶ reported results of bilateral prophylactic mastectomy. From 1960 to 1993, 1,065 women underwent bilateral subcutaneous mastectomy (performed with an inframammary incision and preservation of the NAC) or total mastectomy (included removal of the NAC with the specimen), 639 of whom had a family history of breast cancer. The group was divided into high- and moderate-risk subgroups, with 214 and 425 patients, respectively. After a median follow-up of 14 years, the risk reduction for breast cancer was 90%–94% in the high-risk group and 89.5% in the moderate-risk group. In this study, 575 cases (90%) had undergone subcutaneous mastectomy; 64 cases (10%) underwent total mastectomy. No significant differences were observed in the incidence of breast cancer between these two procedures (7 of 575 [1.2%]; 0 of 64 cases; $P = 0.38$).

The same series was further analyzed; of the 214 high-risk patients, 26 carriers of the BRCA1/2 mutation were identified. After a median follow-up of 13.4 years, the risk reduction in this subset was 89.5%–100%.²⁷

A novel technique introduced by Petit et al²⁸ for treating intraductal or invasive carcinoma preserves the NAC with a glandular layer of 0.5 cm to avoid jeopardizing its vascular supply. A frozen-section analysis (FSA) of the retroareolar tissue is performed. This step is followed by a single dose of electron-beam intraoperative radiotherapy (ELIOT) delivered to the remaining tissue behind the areola and immediate reconstruction. Their experience consisted of 27 NSMs in 25 patients, including 8 cases of DCIS and 19 of IDC. With a mean follow-up of only 6 months, the analysis was limited to immediate complications and early cosmetic results showing promising findings, with only 1 case (3.7%) of total necrosis of the NAC with subsequent removal.

Other authors have advocated the use of intraoperative FSA as part of the decision-making process. Gerber et al²⁹ performed NSM in 112 patients with IDC for whom modified radical mastectomy (MRM) was indicated; they compared the

results with those of 134 patients who underwent MRM. After intraoperative FSA of the NAC adjacent tissue, the NAC could be preserved in 61 cases (54.4%) and was resected in 51 of the 112 patients (45.5%). After a mean follow-up of 59 months, 6 recurrences (5.4%) were observed in the SSM group (3 in the group with preserved NAC and 3 in the group without conservation) and 11 (8.2%) in the MRM group ($P = 0.6$). There was noninvasive disease recurrence in the preserved NAC of one case that was treated with wide excision of the nipple with preservation of the areola. Partial necrosis of the nipple occurred in 6 patients (9.8%); 46 (75%) reported sensation in the preserved NAC, and depigmentation occurred in 26 patients (43%).

Crowe et al³⁰ reported their experience with 54 attempted procedures for NSM in 44 patients. Indications for the procedure were IDC (tumors measuring 0.1–3.5 cm) in 30 cases (56%), DCIS in 7 cases (13%), and prophylaxis in 17 cases (31%). Intraoperative FSA revealed six cases (12%) with occult nipple involvement; these cases were converted to total mastectomy. Neoplastic involvement of the nipple was found in 5 of 30 cases (17%) with IDC, 1 of 7 cases (14%) with DCIS, and none of the prophylactic cases. Of the 48 completed procedures, 45 maintained postoperative viability of the NAC, and 3 cases (6%) had partial loss of the NAC.

Surgical Techniques

Subcutaneous mastectomy, which is a nipple-sparing procedure, has been criticized because of the increased likelihood of retained breast tissue under the skin flaps and the NAC. This concern may not be a trivial issue for patients with a genetic predisposition to breast cancer, because deposits of ductal tissue can harbor a neoplastic predilection. In an autopsy series reported by Goldman and Goldwyn³¹ in 1973, 12 subcutaneous mastectomies were performed on 6 cadavers; subsequent biopsies of the subareolar tissue revealed retained breast tissue in all cases.

It is important to highlight that the current technique of NSM differs from that of the classic subcutaneous mastectomy. With the current NSM technique, the skin flaps are thinner, and a 2- to 3-mm thick nipple-areola flap remains, with scant or no ductal tissue. The technique is predominantly the



Figure 1 Transareolar, Perinipple Incision With Lateral Extension



Figure 2 Transareolar, Transnipple Incision With Medial and Lateral Extensions

same as that for a standard SSM; however, in NSM, there are several options for the skin incision that allow preservation of the NAC and its blood supply.³²

At Memorial Sloan-Kettering Cancer Center, we have performed four different approaches.

1) *Transareolar, perinipple incision with lateral extension.* This incision is made from the medial aspect of the NAC in a transverse plane, transecting the areola through the inferior border of the nipple and extending laterally (Figure 1).

2) *Transareolar, transnipple incision with medial and lateral extensions.* This approach bivalves the NAC symmetrically in a transverse plane, providing optimal exposure of intranipple and retroareolar ducts (Figure 2).

3) *Inferior-lateral mammary crease incision.* Incision is made in the inframammary crease with lateral extension. This approach is a modification of the classic subcutaneous mastectomy (incision along the inframammary crease) with better exposure and excellent cosmesis (Figure 3).

4) *Nipple-sparing omega (mastopexy) incision.* A semicircular skin island along the superior aspect of the NAC is excised with the mastectomy specimen, allowing an upward reposition of the NAC. This approach allows NSM in patients with slightly larger, minimally ptotic breasts (Figure 4).

Necrosis and partial loss of the NAC are common postoperative complications to be discussed with patients who consider NSM. Medial incisions may compromise blood flow to the nipple. In 48 completed NSMs reported by Crowe et al,³⁰ 45 cases performed through a lateral incision remained with a fully intact and well healed NAC. The three procedures performed through more medial incisions presented with partial loss of the NAC postoperatively. Currently, data are still limited, and larger studies are needed to determine the best approach.

Discussion

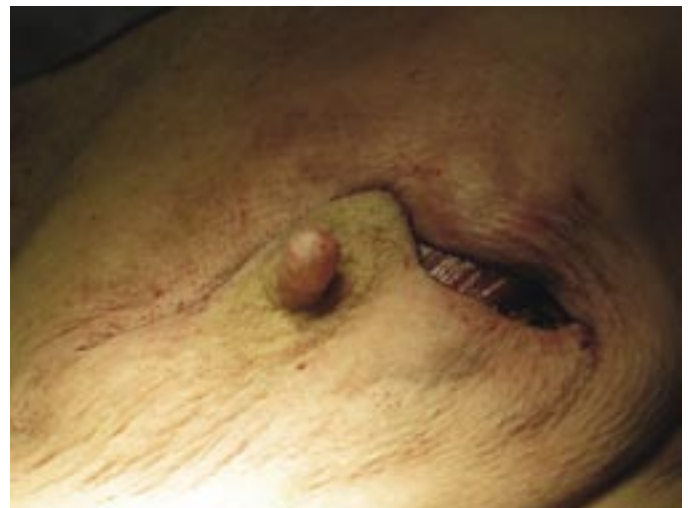
Preservation of the NAC in breast surgery is driven mostly by patient concerns. Removal of the NAC significantly chang-



Figure 3 Inferior-Lateral Mammary Crease Incision



Figure 4 Nipple-Sparing Omega (Mastopexy) Incision



es the appearance of a breast, often being perceived by patients as mutilation. Hence, efforts to consider its preservation have reemerged in the past 20 years.

NSM may be an oncologically sound treatment in breast cancer patients with tumors measuring < 2 cm, which are peripherally located (at least 2.5 cm from nipple) and have negative ALNs. In other words, NSM could be an option for a subset of patients who are candidates for breast-conserving surgery but still prefer to undergo mastectomy. Since the use of this procedure is still under study, prospective trials with a large number of cases are required to document patient selec-

tion and generate a consensus.

A better-defined role for NSM is in high-risk patients with no proven malignancy who decide to undergo bilateral prophylactic mastectomy. Current techniques allow excision of breast and ductal tissues to an extent that decreases the likelihood of malignant potential and provides a good cosmetic result with a low risk of postoperative complications (nipple ischemia, misplacement, loss of sensitivity, and erectile function). The risk of these complications should be discussed with patients who choose to undergo this procedure, and close coordination between plastic and oncologic surgeons should decrease this risk.

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