



Preservation of the nipple–areola complex in skin-sparing mastectomy for early breast cancer

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Abstract

Purpose Skin-sparing mastectomy (SSM) enables a radical cure of breast cancer while overcoming the cosmetic issues related to surgery. We review our experience of performing SSMs and assess whether preservation of the nipple–areola complex (NAC) could have been an option for some patients who underwent SSM.

Methods The subjects of this retrospective study were women who underwent SSM that utilized four incision types; namely, the so-called tennis racket incision, a periareolar and midaxillary incision, an areola-sparing and midaxillary incision, and a small transverse elliptical incision. We assessed whether preservation of the NAC would have been an option in SSM, based on histologic examination of three serial cut surfaces of the specimen around the nipple, ruling out the option when evidence of the malignant lesion/s was found in at least one of the following locations: in the nipple, within a 1-cm radius from the base of the nipple, or within 1 cm from the surface of the NAC.

Results We performed 193 SSMs. The cumulative 10-year local disease-free survival rate was 98%, with 89% of patients reporting levels of satisfaction with the reconstructed breast, of excellent, very good, or good. We evaluated that 70 of the 193 procedures could have been performed as nipple-sparing mastectomy (NSM).

Conclusions The outcomes of SSM in this series were excellent and NSM might have been an option for about one-third of the patients.

Keywords Breast cancer · Nipple-sparing mastectomy · Skin-sparing mastectomy

Introduction

In systemic therapy for breast cancer, local control is the major objective of surgery [1], and breast-conserving surgery is the mainstream treatment. However, based on the size or site of the lesion and the extent of intraductal involvement, about one-third of women with breast cancer still choose mastectomy [2]. Skin-sparing mastectomy (SSM) with immediate breast reconstruction (IBR), as first described by Toth and Lappert in 1991, is the method of choice for radical cure of breast cancer with optimal cosmetic results [3]. We have been achieving excellent outcomes with this procedure at Jikei University Kashiwa Hospital since July, 2003 [4], and after some trial and error, we have adopted

four types of skin incision chosen according to the needs of the patient [5, 6].

Cense's team first used “nipple-sparing mastectomy” (NSM) as a technical term in 2001 to describe SSM that preserves the skin tissue of the nipple–areola complex (NAC). They reviewed the literature and concluded that there was limited indication for the procedure because of an unacceptably high risk of local relapse [7]. We present an overview of our experience of performing SSM and assess retrospectively whether NSM might have been an option for these patients.

Patients and methods

The subjects of our retrospective study were Japanese women who underwent SSM with IBR at Jikei University Kashiwa Hospital between July 1, 2003 and March 31, 2017. Breast surgeons performed the mastectomy procedures, and plastic surgeons performed the breast reconstructions. All

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patients were advised of their choices for adjuvant therapy based on the findings of postoperative pathological examination and provided informed consent for implementation of the selected treatment.

SSM was planned so as to remove the nipple, with or without the areola complex, biopsy scars (excluding the core needle biopsy scar), and the entire breast parenchyma [3]. Four types of incisions were used for SSM: Type A, a periareolar incision with lateral extension (the so-called tennis-racket incision); Type B, a periareolar incision with a midaxillary line incision; Type C, a straight incision with a small elliptical incision at the baseline of the nipple, within the areola complex in a mediolateral (C1) or craniocaudal (C2) direction (the so-called areola-sparing incision, with caudal extension added if needed for Type C2) and a midaxillary line incision; and Type D, a small transverse elliptical incision encompassing the entire NAC with a transverse axillary incision (Fig. 1).

We assessed the cumulative local and distant disease-free survival rates and the cumulative overall survival rate using the Kaplan–Meier method; the level of satisfaction of the patients and their breast surgeons with the reconstructed breast according to their responses on a 5-point questionnaire (excellent/very good/good/not very good/poor); and the suitability of preservation of the NAC as an option in SSM based on histopathologic examination of three serial cut surfaces of the specimen, including the section through the nipple and the two cut surfaces adjacent to the nipple (Fig. 2a). We considered NSM as an option for all patients, except those in whom malignant lesion/s were identified in

at least one of the following locations: the nipple, within a 1-cm radius from the base of the nipple in the section through the nipple, or within 1 cm from the NAC surface or surgical margin of the skin side (Fig. 2b). We analyzed statistics using the Chi-square test and *t* test, with $P < 0.05$ considered significant.

Results

We performed SSM in 193 of 666 mastectomies. Table 1 delineates the characteristics of the patients, their tumors, the operative procedures, and the type of axillary management, according to the incision types. Tumors were staged based on the system of the American Joint Committee on Cancer. Types C and D incisions were used for device-based reconstructions (tissue expander [TE] or silicone breast implant [SBI]).

We applied Type A for all patients during the first 4 years, and less frequently thereafter until 2010. Type B and Type C were introduced in 2007 and 2008, respectively, to achieve better cosmetic outcomes. Type D was introduced in 2011 and then Type C2 was introduced in 2015 in response to the increase in device-based breast reconstruction. In accordance with that increase, we have adopted the Type C2 incision even for patients with a small areola, often extending the incision to the caudal side to better expose the operative field. The number of device-based breast reconstructions has increased remarkably since 2011.

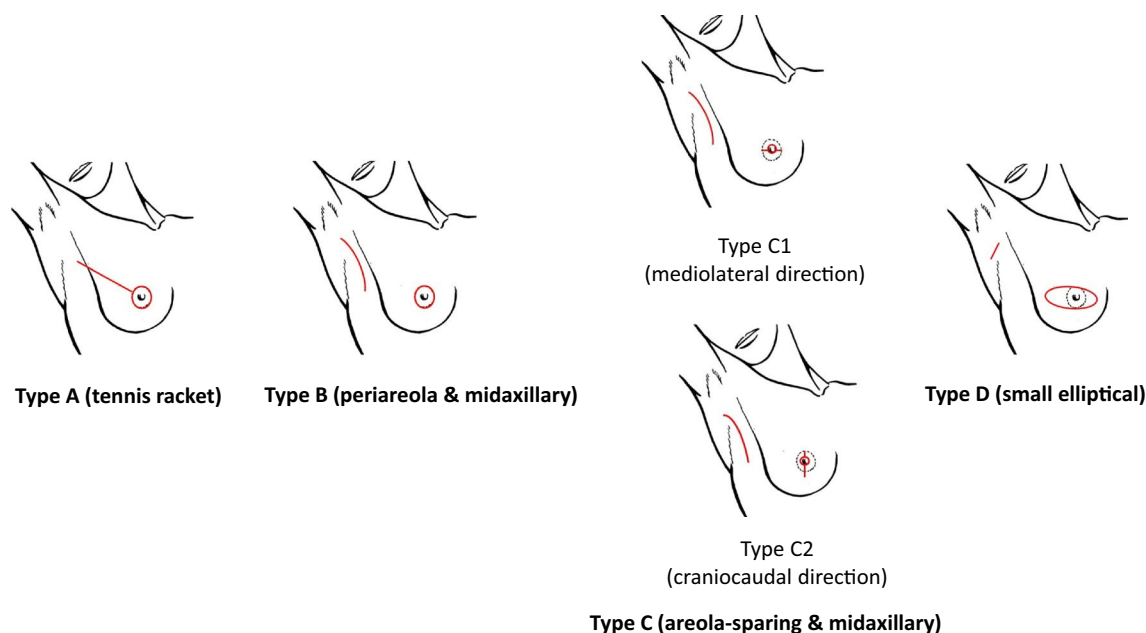


Fig. 1 Types of skin incisions used for skin-sparing mastectomy

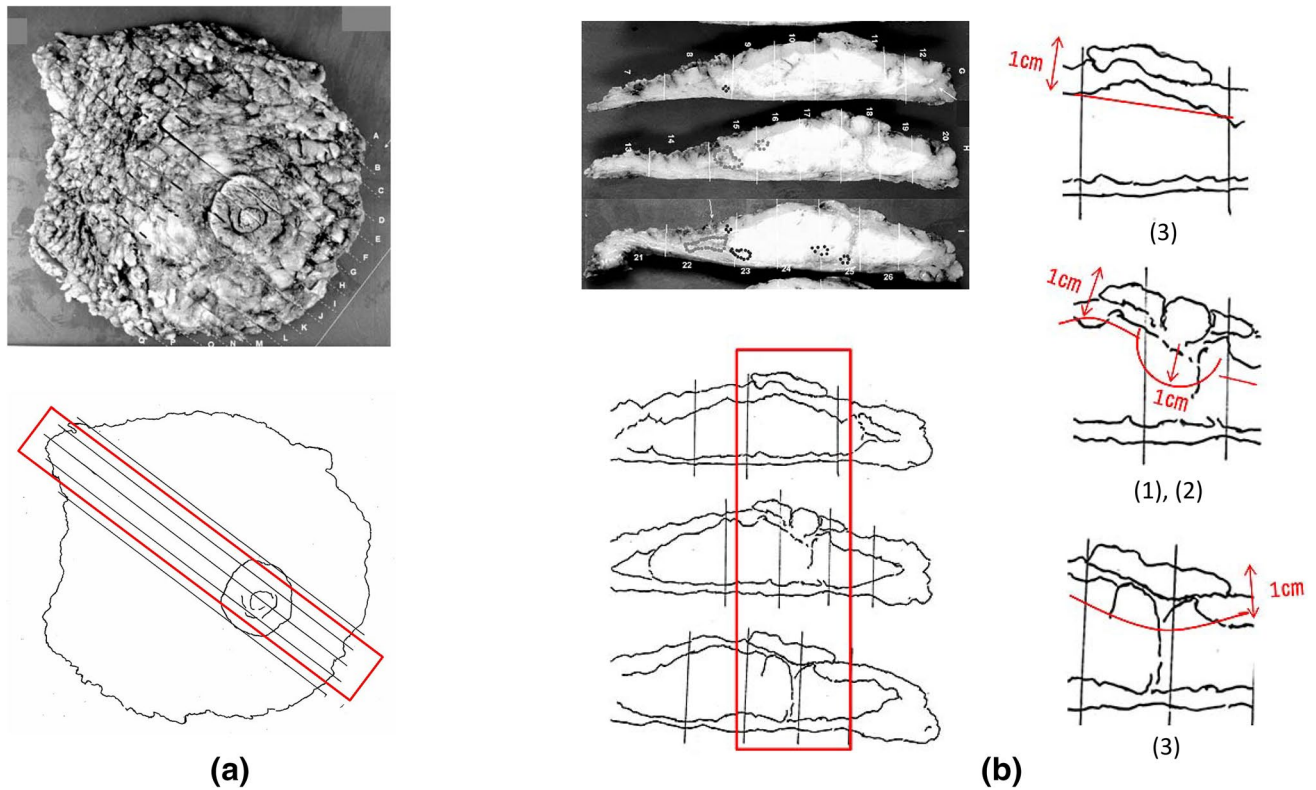


Fig. 2 **a** Three-slice cutting line of serial sections of a specimen from skin-sparing mastectomy, including a section through the nipple and two cut surfaces adjacent to the nipple. **b** Three cut surfaces were used to assess involvement of the nipple-areola complex

(NAC), to identify the presence of malignant lesion/s (1) in the nipple, (2) within a 1-cm radius from the base of the nipple in the section through the nipple, or (3) within 1 cm from the NAC surface

Table 1 Characteristics of patients, their tumors, operative procedures, and type of axillary management according to the incision used

	Type A	Type B	Type C		Type D
			C1	C2	
Number of patients	26	97	26	26	18
Age (years)	44.5 ± 8.6 (32–62)	46.8 ± 9.3 (29–71)	49.0 ± 10.5 (33–74)	50.2 ± 8.8 (34–67)	50.4 ± 10.2 (37–71)
0, Tis	4 (15.4)	18 (18.6)	6 (23.1)	8 (30.8)	7 (38.9)
I	9 (34.6)	26 (26.8)	9 (34.6)	6 (23.1)	4 (17.2)
IIa	10 (38.5)	36 (37.1)	9 (34.6)	11 (42.3)	4 (17.2)
IIIb	3 (11.5)	17 (17.5)	2 (7.7)	1 (3.8)	3 (16.7)
Diameter of areola (mm)	34.0 ± 6.8 (20–50)	37.6 ± 8.0 (25–74)	44.6 ± 9.4 (25–65)	33.0 ± 4.9 (25–45)	31.1 ± 5.9 (20–45)
Extended incision (mm)	–	–	–	–	–
Reconstruction procedure (%)					
LDMC	6 (23.1)	46 (47.4)	3 (11.6)	1 (3.8)	0
TRAM	15 (57.7)	32 (33.0)	7 (26.9)	0	0
DIEP	5 (19.2)	19 (19.6)	11 (42.3)	0	0
TE/SBI	0	0	5 (19.2)	25 (96.2)	18 (100.0)
Axillary management (%)					
SLNB	2 (7.7)	59 (60.8)	19 (73.1)	23 (88.5)	15 (83.3)
SLNB → ALND	1 (3.8)	18 (18.6)	5 (19.2)	2 (7.7)	3 (16.7)
ALND	23 (88.5)	20 (20.6)	2 (7.7)	1 (3.8)	0

ALND axillary lymph node dissection, DIEP deep inferior epigastric perforator, LDMC latissimus dorsi musculocutaneous, SBI silicone breast implant, SLNB sentinel lymph node biopsy, TE tissue expander, TRAM transverse rectus abdominis musculocutaneous

The mean follow-up period was 64.5 (5–171) months. The cumulative 5-year local disease-free survival rate was 99.3%, the cumulative 10-year local disease-free survival rate was 98.0%, and the cumulative overall survival rates were 97.0% at 5 years and 89.2% at 10 years (Fig. 3).

Postoperative complications included hemorrhage that required reoperation ($n = 1$); deep vein thrombosis ($n = 1$); insufficient circulation ($n = 8$), resulting in skin necrosis ($n = 6$) and flap loss ($n = 2$); and infection at the surgical site requiring removal of the tissue expander ($n = 3$).

Surveys about satisfaction with the reconstructed breast were returned by 168 patients (87.0%) and 190 breast surgeons (98.4%). Most patients (88.7%) and breast surgeons (95.3%) expressed that their level of satisfaction with the cosmetic results of the reconstructed breast was excellent, very good, or good (Fig. 4). Most patients who expressed levels of satisfaction that were not very good, or were awful, were unhappy with the size and/or shape of the

reconstructed breast. Only one patient expressed dissatisfaction about malposition of the NAC.

We assessed the option for NAC preservation in 164 of the 193 patients, after the exclusion of 24 patients with bloody nipple discharge that was positive for malignant cells and 5 with Paget’s disease. Table 2 summarizes the patient and tumor characteristics. We concluded that NSM would have been an option (convertible group) for 70 of the 164 patients treated with SSM and classified the other 94 for whom we felt NAC preservation was not an option (unconvertible group) according to the location of the malignant lesion/s as follows: in the nipple ($n = 15$), within a 1-cm radius from the base of the nipple in the section through the nipple ($n = 58$), and within 1 cm from the NAC skin surface ($n = 21$).

The mean age of the patients was 48.3 years in the convertible group and 47.8 years in the unconvertible group. The two groups did not differ significantly with regard to staging classification, histologic type, tumor size, lymphovascular

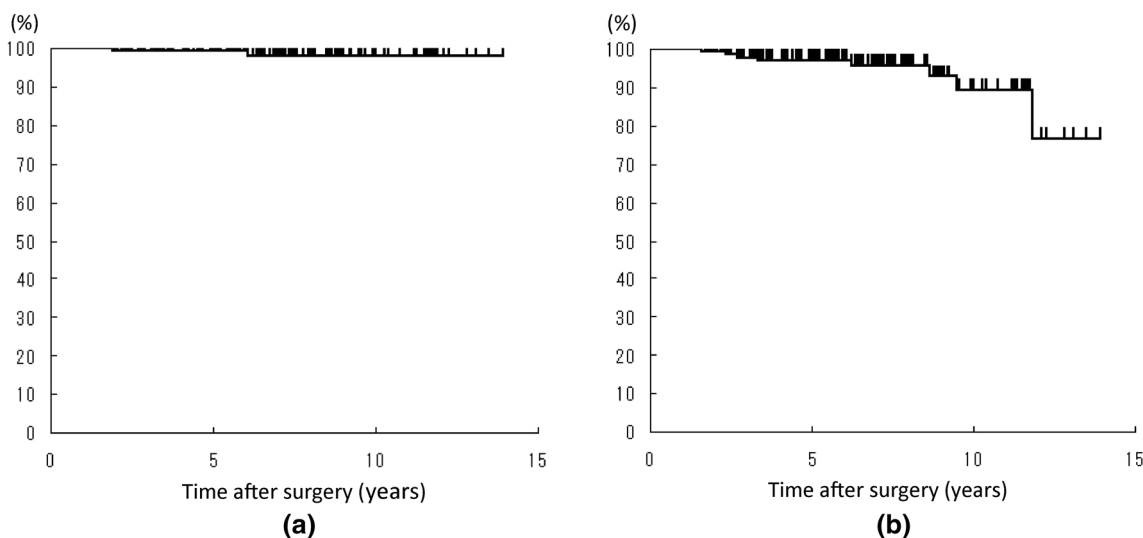


Fig. 3 Kaplan–Meier curves showing survival rates over time: **a** local disease-free survival (LDFS) after 5 years (99.3%) and 10 years (98.0%); **b** overall survival (OS) after 5 years (97.0%) and 10 years (89.2%)

Fig. 4 Results of surveys regarding the satisfaction of patients and their surgeons with their breast reconstruction surgery

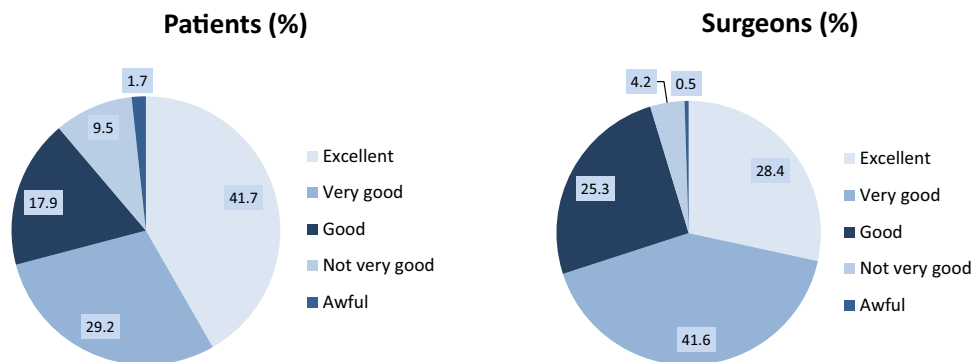


Table 2 Characteristics of patients and their tumors according to suitability for nipple-sparing mastectomy (convertible group) or not (unconvertible group) in skin-sparing mastectomy

	Unconvertible	Convertible	<i>P</i> value
Number of cases	94	70	
Age (years)	47.8±9.2	48.3±9.1	NS
Stage			
0, Tis	20	11	
I	25	20	NS
IIa	37	29	
IIIb	12	10	
Histologic type			
IDC	71	52	
ILC	10	3	
MC	2	3	NS
IMPC	1	0	
DCIS	10	12	
Tumor size (mm)	27.3±10.6	25.8±8.3	NS
NTD (mm)	12.1±14.1	21.0±13.1	0.0001
ATD (mm)	-6.1±13.7	2.5±12.3	0.0004
MR imaging	86	67	
Absence of IDS on image	14	25	0.003
Inconvertible on image	72	24	
Convertible on image	14	43	
Extent of invasion (mm)	18.3±14.3	17.1±12.6	NS
Extent of ductal spread (mm)	46.7±22.4	32.6±18.3	0.0001
Cases of negative LVI	50	44	NS
Cases of lymphnode metastasis	33	24	NS
Cases of negative EIC	64	51	NS

ATD distance between areola and tumor, *DCIS* ductal carcinoma in situ, *EIC* extended intraductal component, *IDC* invasive ductal carcinoma, *IDS* intraductal spread, *ILC* invasive lobular carcinoma, *IMPC* invasive micropapillary carcinoma, *LVI* lymphovascular invasion, *MR* magnetic resonance, *MC* mucinous carcinoma, *NTD* distance between nipple and tumor, *NS* not significant

invasion (LVI), number of patients with positive nodes, and number of patients with a positive extended intraductal component (EIC; referring to invasive breast cancer in which at least 25% of the tumor is composed of an intraductal component that extends beyond the invasive tumor [8]).

Magnetic resonance imaging (MRI) was done for 157 of the 164 patients. Based on the MR images, 72 (83.7%) of the 94 unconvertible group procedures were judged as unconvertible, and 43 (64.2%) of the 70 convertible group procedures were judged as convertible (sensitivity 64.2%, specificity 83.7%, accuracy 75.2%). We observed significant differences between the convertible vs. unconvertible groups in the distance between the nipple and the tumor, being 21.0 vs. 12.1 mm, respectively ($P=0.0001$); between the areola and tumor, being 2.5 vs. -6.1 mm, respectively ($P=0.0004$); in the histological extent of intraductal spread,

being 46.7 vs. 32.6 mm, respectively ($P=0.0001$); and in the absence of intraductal spread on MRI, seen in 25 vs. 14 patients, respectively ($P=0.003$).

Discussion

Modern radical surgery for breast cancer was established when William Stewart Halsted performed a standard radical mastectomy in 1882 [9]. At the end of the nineteenth century, most of these operations were performed for locally advanced disease, and widespread belief in Sappey's theory (1885) of centripetal lymphatic drainage of the breast toward the subareolar lymphatic plexus [7, 10] precluded consideration of NAC preservation. However, demonstration by Turner-Warwick (1959) and Handley (1964) of the downward lymphatic drainage of the breast, not toward the subareolar lymphatic plexus, but toward the deep pectoral lymphatic plexus, implied that preservation of the NAC might be safe [7, 10]. In 1962, Freeman reported sparing the NAC in subcutaneous mastectomy, but advocated the procedure's use only for benign lesions and not in therapeutic mastectomy or risk-reducing prophylactic mastectomy [11, 12]. It was not until the 1980s that breast-conserving surgery became common practice for breast cancer [13] and NAC preservation was accepted, although George Crile [14], a pioneer in breast cancer surgery, had performed a partial mastectomy as early as 1957.

A study reported by De La Cruz et al. in 2015, utilizing the Surveillance, Epidemiology, and End Results of the National Cancer Institute, demonstrated almost doubling of the number of NSM procedures performed between 2005 and 2009 in the United States [15]. However, many of these NSMs were performed for risk-reducing prophylactic mastectomy [16], and the numbers differed greatly by country, ranging from 0% in Norway to 49% in the United States [17]. As noted, risk-reducing prophylactic NSM is not covered by Japan's national health insurance. In their meta-analysis of 20 studies involving 5594 patients, the De La Cruz team detected no adverse oncologic outcomes of NSM in carefully selected women with early stage breast cancer [15].

Although preservation of the nipple-areola complex in the treatment of breast cancer may significantly impact a woman's body image, its value remains controversial because of concerns about possible residual cancer in the nipple [18]. Nipple involvement is defined as ductal carcinoma in situ (DCIS), invasive carcinoma, or Paget's cells within 1 cm of the NAC [7]. Anatomically, 15–20 mammary ducts branch from the terminal ductal lobular units to form the lactiferous sinus under the NAC, then branch again and rise toward the nipple surrounded by a network of vessels. When mastectomy is performed, a skin flap is raised in the plane of Cooper's ligament. However, there are neither

Cooper's ligaments nor subcutaneous fat between the skin and underlying glandular tissue of the breast at the NAC. The creation of a retro-nipple–areolar flap that is too thin can compromise the cosmetic results, and if the flap is too thick, oncologic safety is at risk because of the possibility of residual tumor cells. Torresan's group reported an association between a high prevalence of glandular breast tissue and residual disease in the skin flap with flap thickness greater than 5 mm [19]. It can be technically difficult for the breast surgeon to create a retro-nipple–areolar skin flap that is thinner than 5 mm. This is why we consider NAC preservation for within a 1 cm radius from the base of the nipple and the NAC skin surface.

The incidence of nipple involvement has been reported to range from 0 to 58% among patients with breast cancer [7, 10] and from 0 to 14% among patients selected to undergo therapeutic NSM according to strict criteria [20]. Moreover, most studies reported tumor recurrence in the NAC in fewer than 1% of cases [20]. Patient selection is most important for the safe outcome of NSM, and various methods have been proposed to assess nipple involvement before, during, and after surgery. Studies reporting the usefulness of MRI in predicting nipple involvement prior to surgery [21–25] have suggested a correlation between nipple involvement and distance between the nipple and tumor of no greater than 2 cm or distance between the nipple–areola complex and tumor of no greater than 0.5 cm. Fortunato et al. reported the usefulness of intraoperative histological examination and concluded that NSM can be performed safely if the margin of the retro-areolar resection is clear and the maximal surgical margin clearance is performed [26]. Petit's group delivered a single intraoperative dose of radiation (ELIOT) to the NAC and observed no recurrence in the NAC after 19 months of follow-up [27]. However, intraoperative radiation is not widely available, and therefore, not an option for most centers.

According to Murthy et al., the best available evidence suggests that NSM can be considered for patients whose tumor is smaller than 2.5 cm and located more than 4 cm from the nipple with negative axillary status, LVI, or EIC [10]. However, only one of our 164 patients treated with SSM satisfied all these criteria.

We judged that only 70 of our 193 patients (36.3%) would have been suitable candidates for NSM. Among the total 193 patients who underwent SSM, including the 24 with positive bloody nipple discharge and 5 with Paget's disease, none were considered candidates for sparing NAC. However, SSM was safely completed in all these patients, with 88.7% of them and 95.3% of their breast surgeons reporting levels of satisfaction with the reconstructed breast that were excellent, very good, or good. Furthermore, local control failed in only two patients (1.0%) during a median follow-up of 65 months. Based on the results of our small retrospective

study, excluding cases of risk-reducing prophylactic NSM for gene mutation, we identified few candidates for therapeutic NSM convertible from SSM for early breast cancer.

Conclusion

We achieved excellent oncological safety and cosmetic outcomes in 193 patients treated with SSM and judged that nipple preservation might have been an option for 70, representing about one-third of our study patients. We believe that NSM can be an option in SSM, but should be considered only for carefully selected women with early stage breast cancer to avoid the risk of residual cancer in and around the nipple–areola complex.

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Compliance with ethical standards

Conflict of interest We have no conflicts of interest to declare.

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