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Breast

Long-term course of the changes in the nipple position after breast-conserving surgery

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Abstract

Purpose: Even if favorable cosmetic outcomes are obtained shortly after breast-conserving surgery (BCS), cosmetic changes may occur up to several years after BCS. In the present study, we evaluated cosmetic changes while focusing on changes in the nipple position after BCS.

Methods: We examined the long-term course of changes in the nipple position over time after BCS using the proportion of the distance between the sternal notch and nipple (PDSN) in 196 patients. We also evaluated risk factors for long-term nipple position changes.

Results: The median follow-up period was 9.9 years. Nipple position changes occurred within eight years after BCS and seemed to plateau beyond that point. The body mass index (BMI), breast size, proportion of excision volume and axillary treatment were significantly associated with the nipple position changes within one to five years after BCS. The BMI, breast size, axillary treatment, chemotherapy and hormonal therapy were significantly associated with the nipple position changes within five to eight years after BCS.

Conclusions: After BCS, the nipple position changes occur within about eight years. Obesity, large breast size, large excision volume, axillary treatment, chemotherapy and hormone therapy were factors that affected the treated breast shrinkage and increase in the left-right difference after BCS.

Keywords: Breast-conserving surgery, Oncoplastic breast surgery, Nipple position

INTRODUCTION

Breast cancer is the most common cancer among Japanese women [1]. Breast-conserving surgery (BCS) is the standard treatment for early breast cancer. Several randomized clinical trials have shown that BCS and radiotherapy are equivalent to mastectomy in terms of both the disease-free and overall survival [2, 3]. The cosmetic outcomes after BCS are thought to be better than those after mastectomy. These outcomes are an important point of BCS, as a better cosmetic outcome is associated with a better quality of life in women who undergo BCS [4-7].

However, several studies have indicated that even if favorable cosmetic outcomes are obtained shortly after BCS, cosmetic changes may occur up to several years after BCS [8-10]. The majority of patients diagnosed with breast cancer who undergo BCS survive for relatively long periods [11]. Thus, it is very important to characterize the long-term cosmetic outcomes after BCS. However, there are limited data available regarding the long-term cosmetic changes over time after BCS.

It is difficult to examine the cosmetic changes over time because numerous factors are involved. However, one of the factors affecting these cosmetic changes is the decrease in breast size over time. We often encounter cases wherein the treated breast shrinks over time, causing the nipple to shift to the cranial side. Treated breast shrinkage and changes in the nipple position have a significant effect on the cosmetic results of BCS; however, there have been no detailed studies about when the shrinkage stops and what factors are involved.

In the present study, we examined the long-term cosmetic changes, focusing on changes in the nipple position over a long period of time after BCS using our new cosmetic evaluation method. We also evaluated the risk factors for long-term changes in the nipple position after BCS.

METHODS

We conducted a retrospective cohort study of the cosmetic outcomes. In particular, we focused on changes in the nipple position to monitor how the treated breast shrinks over time after BCS. This study was approved by the Mie University School of Medicine Ethics Committee (registration no: 3204). The patients gave their written informed consent for participation in clinical trials. Instead of obtaining written informed consent from each patient, using an opt-out method, we disclosed information and ensured that patients had the opportunity to refuse to participate in or discontinue participation in the study. Permission to take photographs for clinical use was obtained in writing from all patients. Patients were able to opt-out of the use of photographs for clinical trials. The policy regarding the usage of photographs was approved by the Ethics Committee.

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Method for evaluating the changes in the nipple position

We initially attempted to evaluate the change in breast shape by breast retraction assessment (BRA) measurements [12]. The percentage BRA (pBRA) value is a useful objective method for evaluating the cosmetic outcome at a single point; however, it is difficult to evaluate the changes in the breast size over time. Within the first year after surgery, the treated breast is often swollen and bigger than the contralateral breast due to irradiation and the operation itself [13]. However, the pBRA is the same value, regardless of whether the treated breast is bigger or smaller than the contralateral breast. Thus, we considered a new evaluation method that applied the pBRA.

We defined the proportion of the distance between the sternal notch and the nipple position of the treated breast to the distance of the contralateral breast as the “proportion of the distance between the sternal notch and nipple (PDSN)” (Figure 1). Using pictures, we measured the distance from the sternal notch to the nipple position of the treated and contralateral breast. The evaluation of the PDSN is a new simple method for assessing the changes in the nipple position. Unlike the pBRA, a PDSN of >1 means that the treated breast is bigger and the nipple lower than the contralateral breast, while a PDSN of <1 means that the treated breast is smaller and the nipple higher than the contralateral breast. We therefore decided to use the PDSN.

Patients

Although this study examining the nipple position changes over time was a retrospective study, we considered it desirable for the analysis to not be affected by the level of surgical technique or the photography conditions. However, it would be difficult to collect cases under the same conditions in a study examining multiple photographs over a long period of time. We therefore decided to consider cases in which the same surgeon performed the operation and in which all postoperative photographs were taken by the same person so that the conditions would be as uniform as possible. In addition, the position of the nipple is affected by the position of the breast tumor because it tends to shift toward the excision site after BCS. Particularly in tumors in the inferior portion, the nipple tends to deviate to the caudal side, resulting in poor cosmetic results [14, 15]. In cases with poor cosmetic results in which the nipple is deviated immediately after BCS, the deviation becomes noticeable over time, even in tumors in the upper portion. For that reason, tumors in

the inferior portion or cases with poor cosmetic results within one year after the operation were excluded from this study. By limiting the cases in this manner, we felt that changes in the nipple position over time would be similar to changes in the breast size over time.

Between April 2008 and December 2015, 280 patients with primary unilateral breast cancer or a benign breast tumor underwent BCS or lumpectomy (>4 cm) performed by a single surgeon (TO) in our hospital. Among these, 38 patients were excluded. Among 242 patients, the 199 for whom pictures with a frontal view were obtained at a minimum of 2 time points (within 1 year after BCS and ≥2 years after BCS) were eligible for inclusion in the present study. Among these 199 patients, 3 patients whose cosmetic results within 1 year after BCS were judged by a single surgeon (TO) to be poor were excluded from the study. Finally, we investigated the cosmetic changes focusing on the nipple position and factors that influenced the nipple position change after BCS in 196 patients. The patient flow chart is shown in Figure 2.

Study methods

A single surgeon (TO) photographed the patients from a frontal view in an upright position during postoperative routine follow-up visits (every three to six months). Using these pictures, we measured the distance from the sternal notch to the nipple position of the treated and contralateral breast. All measurements were performed by the same person (MK). We calculated the change in the PDSN. We decided to confirm the PDSN changes at one to five years after surgery as early postoperative changes and PDSN changes beyond five years after surgery as late postoperative

changes. We evaluated the association of the change in the PDSN with various clinical and pathological factors using a multiple regression analysis.

Using pictures, the breast size, ptosis [16] and excision volume in comparison to the total breast volume were subjectively judged by two or more of the coauthors of this paper.

Statistical analyses were preformed using the IBM® SPSS® Statistics software program, version 26.0 (IBM® Corp., Armonk, NY, USA). P-values of <0.05 were considered to indicate statistical significance.

RESULTS

The patient characteristics are shown in Table 1. The median time from BCS to the last follow-up examination was 9.9 (range, 5.7 to 13.3) years. The average PDSN seemed to gradually decline for eight years after BCS. The average PDSN at 1 year after BCS was 0.957 (n=196), that at 5 years was 0.940 (n=122), that at 8 years was 0.919 (n=82), and that at 11 years was 0.915 (n=5). The decline in the PDSN seemed to plateau at eight years after BCS (Figure 3). Photographs of a typical case are shown in Figure 4.

The relationships between the change in PDSN from one to five years after BCS and various clinicopathological factors are shown in Table 2. The BMI (p=0.027), breast size (p=0.046), proportion of excision volume (p=0.008) and axillary treatment (p=0.005) were significantly associated with nipple position changes at 1 to 5 years after BCS. Regarding the surgical procedure, the volume replacement technique (VR [17, 18]) group tended to have less marked changes over time than the volume replacement technique (VD [19, 20]) group, but there was no significant difference (p=0.06). The details of the surgical procedures are shown in Table 3.

Since there were few cases in which nine years or more had passed since surgery, the changes in PDSN from five to eight years after BCS should be correlated with clinicopathological factors as late postoperative changes. The relationships between the change in PDSN from five to eight years after BCS and various clinical and pathological factors are shown in Table 4. The BMI (p=0.001), breast size (p=0.03), axillary treatment (p=0.03), chemotherapy (p=0.004) and hormonal therapy (p=0.044) were significantly associated with the nipple position changes at five to eight years after BCS.

In all cases, whole-breast radiation was delivered at 50 Gy in 25 fractions, and in some cases, boosts were added at 10 Gy in 5 fractions. No significant association was found between changes in the PDSN and radiation therapy (RT) in either the early or late postoperative period.

DISCUSSION

There is no consensus concerning the optimal method for assessing cosmetic results after BCS. Both subjective and objective methods have been frequently used in previous studies. A representative subjective method was proposed by Harris et al. in 1979 [21]. They defined four stages of “excellent,” “good,” “fair” and “poor”. However, this method is criticized as being less appropriate and reproducible than objective methods. A representative objective method is the BCCT.core [22]. The BCCT.core is objective, reproducible, time-efficient and easy to use [23]. However, it is influenced by the photography conditions, and the performance declines with poor-quality photography [22]. Our previous study [24] revealed a clear difference between the subjective method (Harris’s method [21]) and the objective method (the BCCT.core [22]). In the daily outpatient setting, it is difficult to align the photography conditions to appropriately determine the BCCT.core.

Thus, in the present study, we used the PDSN as a new method for evaluating the changes in the nipple position after BCS. The PDSN quantitatively evaluates the nipple position change of the affected breast in comparison to the contralateral breast. It is a simple, easy to evaluate, and reproducible method that only requires a frontal view without any rigid photography conditions. Although the PDSN is inadequate for assessing cosmetic outcomes after BCS, if the breast is well-shaped and undistorted, we considered the change in PDSN to reflect the change in breast size. In order to make this simple method useful, patients whose tumors were located in the inferior portion of the breast and patients with a bad breast shape were excluded from this study. In addition, in order to reduce differences in the way photographs are taken, photographs recorded over time by the same surgeon were used. By limiting and homogenizing the cases in this way, it

was possible to clarify that the change in breast size subsides at approximately eight years after surgery.

Since we evaluated the change in the ratio between the treated breast and the contralateral breast over time, the large difference in PDSN between the two points means that the treated breast shrank or the contralateral breast drooped or enlarged during that period. The breast size significantly affected the expansion of the left-right difference in both the early and late postoperative periods. Contralateral large breasts tended to droop more over time than small breasts. Therefore, it is possible that the breast size affected the expansion of the left-right difference over time, as we performed measurements using a frontal photograph in this report. Obese patients have fatty breasts in many cases. Thus, the contralateral breast tends to droop over time as well, and as a result, the left-right difference may expand throughout the postoperative period. Treatment with chemotherapy or hormone therapy significantly promoted changes over time in the late postoperative period. This may be due to drug-induced mammary gland atrophy and, in the case of hormone therapy, an enlargement in the contralateral breast as it tends to gain weight. It was found that the laterality increased over time, even in cases in which axillary treatment was performed, which is considered to be due to decreased blood flow to the residual mammary gland and mammary gland atrophy due to axillary treatment.

Cases treated with the VD alone tended to show a greater change over time in the early postoperative period than cases treated with the VR. The larger the amount of excision, the greater the change over time in the early postoperative period. However, it is possible to maintain a good cosmetic outcome not only

immediately after surgery but also for a long period after BCS with the appropriate use of the VR, even in operations involving excision of a large amount of tissue.

That RT affects the cosmetic results after BCS is well known, and there have been several reports on the changes in cosmetic results over time that occur in association with RT [13, 25, 26]. However, according to the multiple regression analysis of our study, RT was not identified as a significant factor. Notably, our findings do not deny those of any previous reports. We believe that this was due to the fact that there were only 21 non-irradiated cases. RT is presently performed for almost all BCS cases. In our study as well, most of the non-irradiated cases were benign cases or those with a small tumor diameter treated before 2013. Therefore, it was likely difficult to accurately evaluate the effects of RT.

Several limitations associated with the present study warrant mention. First, this was a retrospective study with a relatively small population and performed in a single institution. Further prospective studies are therefore required. Second, patients whose tumors were located in the inferior portion of the breast and patients with poor cosmetic outcomes within one year after BCS were not included in this study, as we believe that the PDSN is not able to appropriately evaluate breast size changes in such patients. However, in the future, it will be necessary to use a tool that can also evaluate cases with tumors in the lower area and cases with a poor cosmetic outcome. In addition, the PDSN is useful for evaluating the change over time in breast size in cases with good cosmetic outcomes, but it is not adequate for evaluating changes over time in other factors, such as the breast shape, surgical wound, skin tone or condition. Finally, in our study, we only considered the doctor's perspective. We did not use any instruments (e.g. Breast Q^{TM} [27]) to investigate the patients' perspectives or satisfaction.

Despite these limitations, however, this study was still able to show that treated breast shrinkage occurs within about eight years after BCS. In addition, we were able to clarify the factors that influence the expansion of the left-right difference after BCS. We feel that this is very important when explaining the postoperative course to patients.

CONCLUSIONS

After BCS, the nipple position changes associated with breast size reduction occur gradually for eight years, after which the changes in the nipple position plateau. The patient factors that affect the expansion of laterality over time after BCS are obesity and large breast size. The therapeutic factors that affect the expansion of laterality over time include large resection, axillary treatment, chemotherapy and hormone therapy. However, if the amount of tissue that is excised is the same, the appropriate use of the VR may enable a good cosmetic outcome to be maintained for a long time after operation.

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Legends

Fig. 1 Proportion of the distance between the sternal notch and nipple (PDSN)

Fig. 2 Patient flow chart

Fig. 3 Change in the average PDSN

Fig. 4 Photographs of patients' breasts before and after the operation. The frontal view with the patient in an upright position. The treated breast is on the patient's right side. (a) PDSN: 0.879, 1 year, (b) PDSN: 0.848, 5 years, (c) PDSN: 0.831, 8 years after the operation

Table 1. Patient characteristics (n=196)

Characteristics		Findings (N=196)
Age (years)	median (range)	52.0 (23-80)
Body mass index	median (range)	21.8 (16.3-38.9)
Menstruation	pre	88
	post	108
Breast size	extra small	30
	small	93
	medium	51
	large	13
	extra large	9
Ptosis	non-ptosis	115
	grade 1	46
	grade 2	30
	grade 3	5
Proportion of excision volume (%)	Less than 20	102
	20-29	84
	30-39	7
	40 or more	3
Axillary treatment	none (breast surgery only)	16
	sentinel lymph node biopsy only	152
	axillary dissection	28
Surgical procedures	VD*	163
	VR**	33
Chemotherapy	Yes	153
	No	43

Hormonal therapy	Yes	89
	No	107
Radiation therapy	No	21
	whole breast (50 Gy/25 fr)	146
	whole breast and boost (60 Gy/30 fr)	29
Evaluation at 1 year after BCS	excellent	91
	good	78
	fair	27

***** volume displacement technique

**volume displacement technique + volume replacement technique

BCS, breast-conserving surgery

Table 2 Association of the proportion of the distance between the sternal notch and nipple (PDSN) change with various clinical or pathological factors within 1 to 5 years after breast conserving surgery (n=189)

Characteristics		PDSN change	p-value
Age (years)	continuous variable	-	0.69
Body mass index	continuous variable	-	0.026
Menstruation	pre	-0.025	0.37
	post	-0.019	
Breast size	extra small	-0.016	0.047
	small	-0.020	
	medium	-0.026	
	large	-0.030	
	extra large	-0.024	
Ptosis	non-ptosis	-0.022	0.25
	grade 1	-0.021	
	grade 2	-0.023	
	grade 3	-0.026	
Proportion of excision volume (%)	continuous variable	-	0.009
Axillary treatment	none (breast surgery only)	-0.005	0.005
	sentinel lymph node biopsy only	-0.023	
	axillary dissection	-0.028	
Surgical procedures	VD	-0.023	0.060
	VR	-0.018	
Chemotherapy	Yes	-0.024	0.077
	No	-0.021	

Hormonal therapy	Yes	-0.023	0.47
	No	-0.021	
Radiation therapy	No	-0.012	0.30
	whole breast (50Gy/ 25fr)	-0.022	
	whole breast and boost (60Gy/ 30fr)	-0.029	
Evaluation in 1 year	excellent	-0.020	0.80
after BCS	good	-0.024	
	fair	-0.021	

Table 3 Surgical procedures and Proportion of excision volume (n=196)

Surgical procedures		Proportion of excision volume (%)	
Volume displacement technique	163		
Glandular rotation flap (including Extended grandular flap[19])	122	Less than 20	69
		20-29	51
		30-39	2
		40 or more	0
Round block technique	20	Less than 20	9
		20-29	10
		30-39	1
		40 or more	0
Modified round block technique[20]	16	Less than 20	12
		20-29	4
		30-39	0
		40 or more	0
Medial mammoplasty	2	Less than 20	0
		20-29	2
		30-39	0
		40 or more	0
Lateral mammoplasty	2	Less than 20	0
		20-29	2
		30-39	0
		40 or more	0
B-plasty	1	Less than 20	0
		20-29	0

		30-39	1
		40 or more	0
Volume displacement technique + Volume replacement technique (Immediate reconstruction)	33		
Glandular rotation flap (including Extended grandular flap[19]) + Abdominal advancement flap[17]	16	Less than 20	9
		20-29	5
		30-39	2
		40 or more	0
Round block technique + Abdominal advancement flap[17]	2	Less than 20	1
		20-29	1
		30-39	0
		40 or more	0
Modified round block technique[20] + Abdominal advancement flap[17]	1	Less than 20	0
		20-29	1
		30-39	0
		40 or more	0
Medial mammoplasty + Abdominal advancement flap[17]	3	Less than 20	1
		20-29	2
		30-39	0
		40 or more	0
Lateral mammoplasty + Abdominal advancement flap[17]	5	Less than 20	0
		20-29	4
		30-39	0
		40 or more	1
Extended grandular flap[19] + Lateral tissue flap	3	Less than 20	1
		20-29	2

		30-39	0
		40 or more	0
Extended grandular flap[19] + Inframammary adipofascial flap[18]	3	Less than 20	0
		20-29	0
		30-39	1
		40 or more	2

Table 4. Association of the PDSN change with various clinical or pathological factors within 5 to 8 years after BCS (n=55)

Characteristics		PDSN change	p-value
Age (years)	continuous variable	-	0.12
Body mass index	continuous variable	-	0.001
Menstruation	pre	-0.007	0.72
	post	-0.009	
Breast size	extra small	-0.002	0.030
	small	-0.006	
	medium	-0.013	
	large	-0.018	
	extra large	-0.005	
Ptosis	non-ptosis	-0.006	0.62
	grade 1	-0.013	
	grade 2	-0.009	
	grade 3	-	
Proportion of excision volume (%)	continuous variable	-	0.33
Axillary treatment	none (breast surgery only)	-0.003	0.030
	sentinel lymph node biopsy only	-0.006	
	axillary dissection	-0.015	
Surgical procedures	VD	-0.008	0.92
	VR	-0.008	
Chemotherapy	Yes	-0.013	0.004
	No	-0.005	
Hormonal therapy	Yes	-0.0080	0.044
	No	-0.0077	

Radiation therapy	No	-0.002	0.82
	whole breast (50 Gy/25 fr)	-0.008	
	whole breast and boost (60 Gy/30 fr)	-0.014	
Evaluation at 1 year after BCS	Excellent	-0.005	0.20
	good	-0.011	
	fair	-0.008	

PDSN, proportion of the distance between the sternal notch and nipple; BCS, breast-conserving surgery

Fig 1

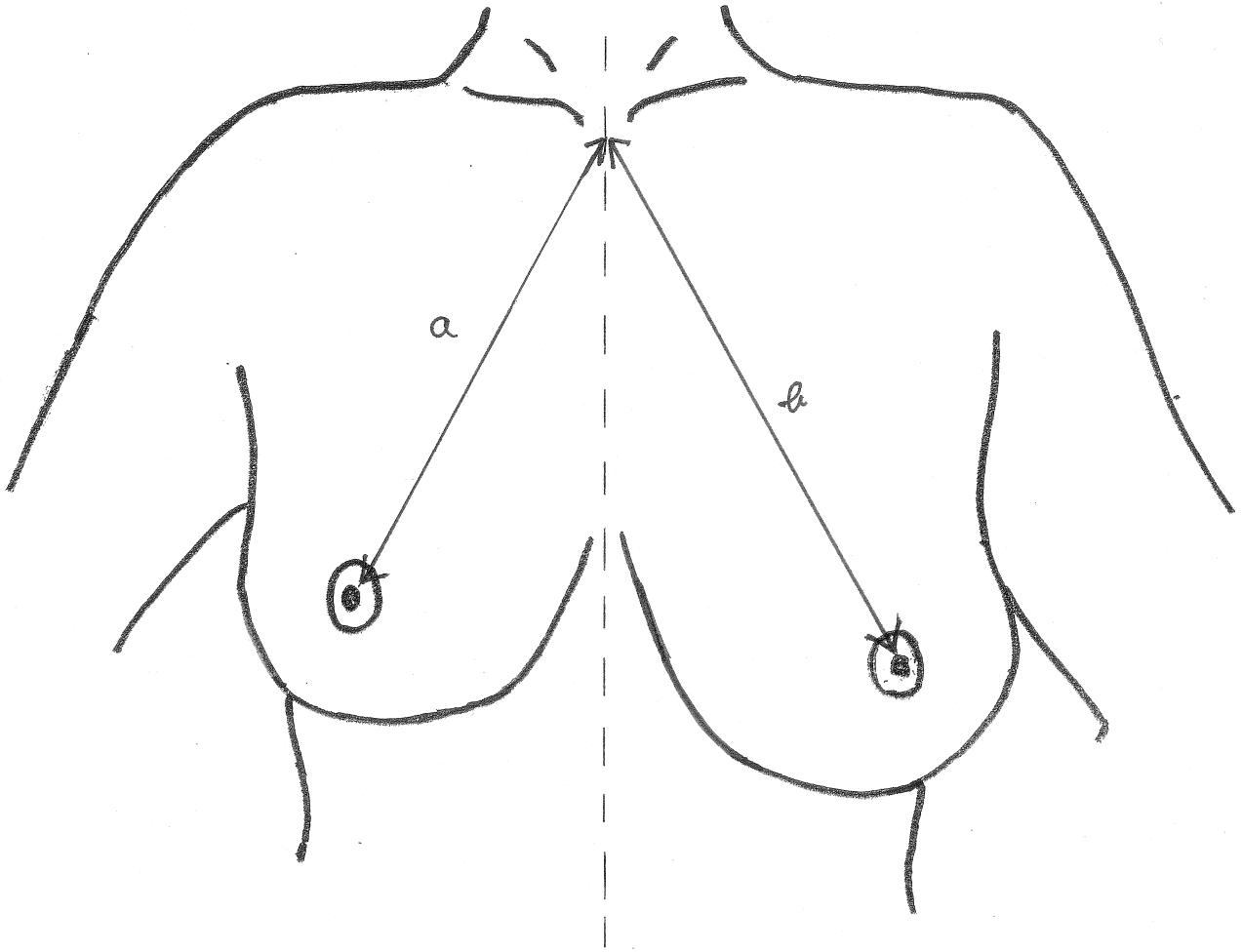


Fig 2

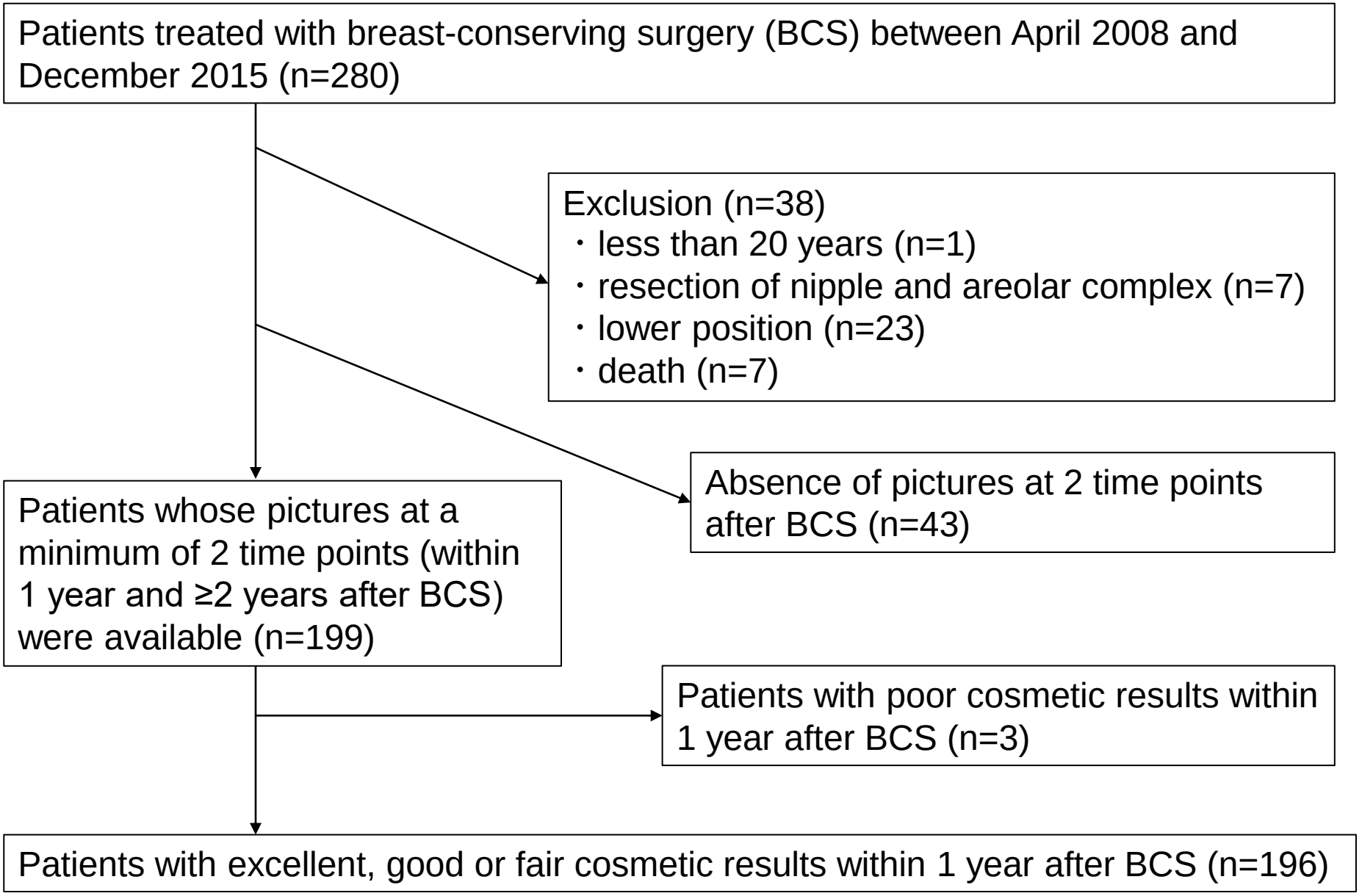

Patients treated with breast-conserving surgery (BCS) between April 2008 and December 2015 (n=280)
Exclusion (n=38)
・less than 20 years (n=1)
・resection of nipple and areolar complex (n=7)
・lower position (n=23)
・death (n=7)
Absence of pictures at 2 time points after BCS (n=43)
Patients whose pictures at a minimum of 2 time points (within 1 year and ≥2 years after BCS) were available (n=199)
Patients with poor cosmetic results within 1 year after BCS (n=3)
Patients with excellent, good or fair cosmetic results within 1 year after BCS (n=196)

Fig 3

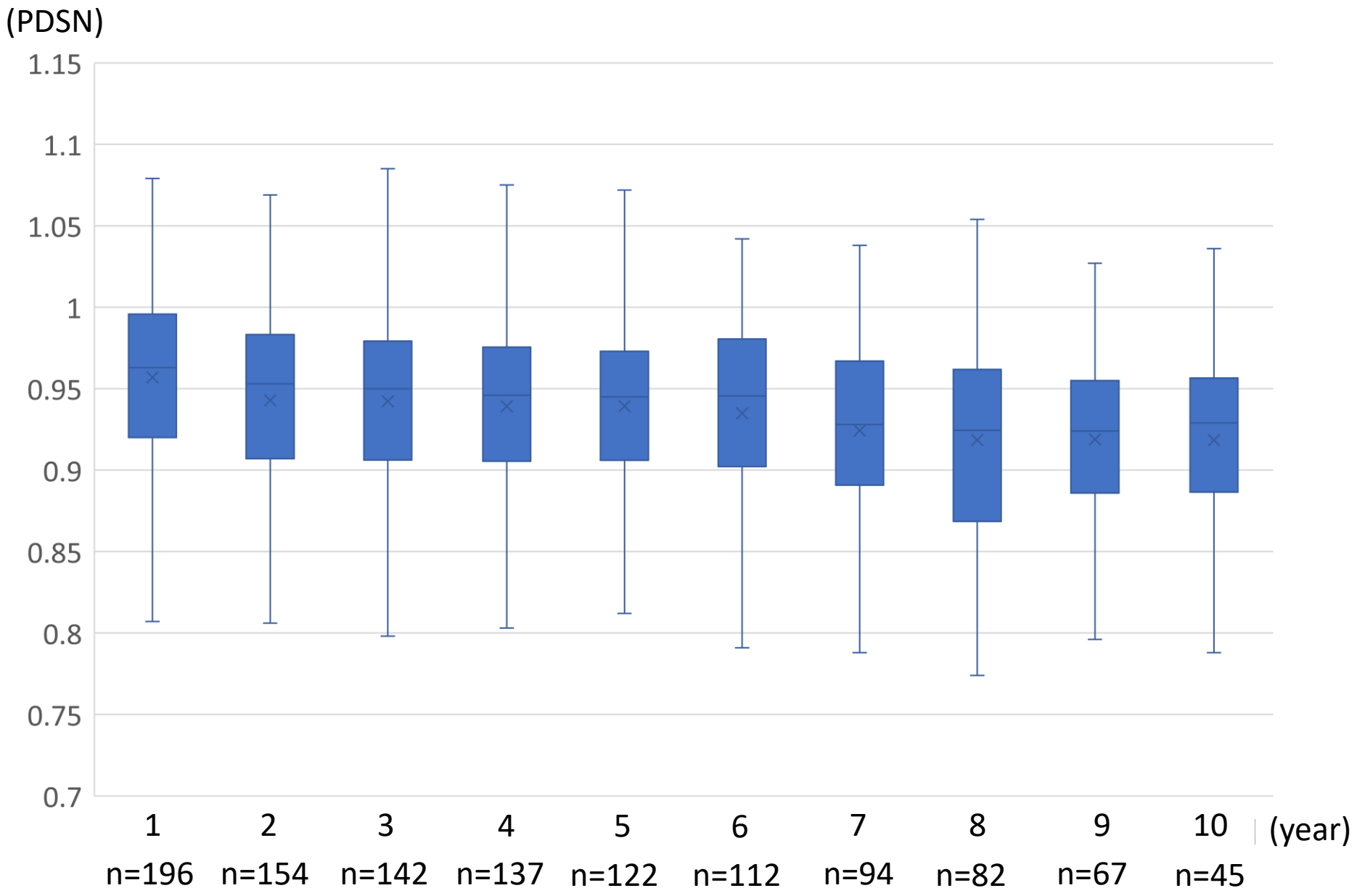
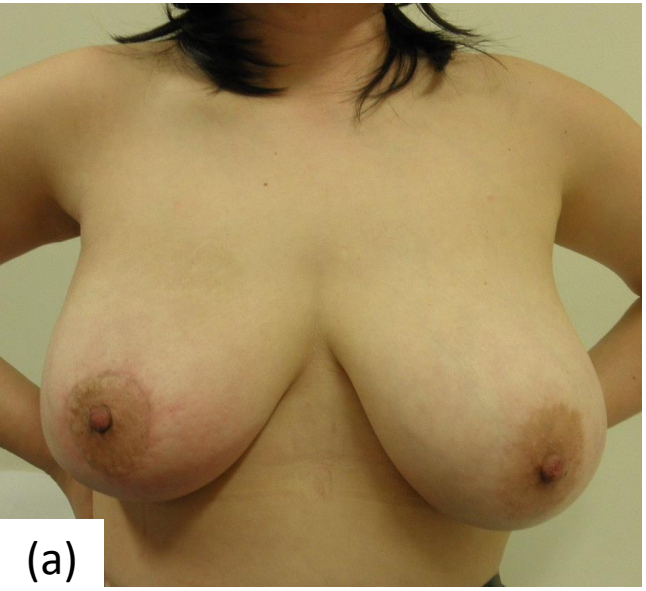
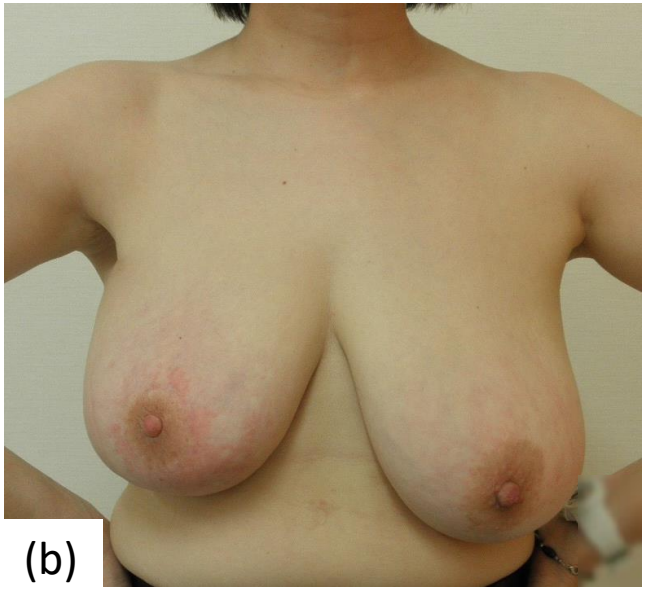

(PDSN)
1.15
1.1
1.05
1
0.95
0.9
0.85
0.8
0.75
0.7
1
2
3
4
5
6
7
8
9
10
(year)
n=196
n=154
n=142
n=137
n=122
n=112
n=94
n=82
n=67
n=45

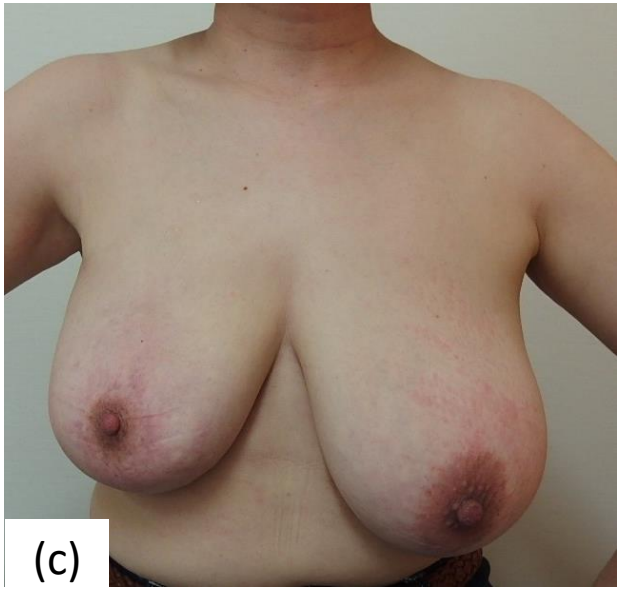
Fig 4



(a)



(b)



(c)