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Long-term sensory recovery of nipple-areola complex following superior-lateral pedicled reduction mammaplasty

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Abstract:	Background The aim of our study was to investigate nipple-areola complex (NAC) sensation at 48-month follow-up following superior-lateral-pedicled reduction mammaplasty (SLPRM) using the Pressure-Specified-Sensory-Device (PSSD). Patients and Methods NAC sensation for static and moving 1&2-point was collected from 30 active-group (AG) hypertrophic-breasted patients undergone SLPRM preoperatively (T0), at 6-months (T6) and 48-months (T48), and from a control-group (CG) of 30 unoperated women with normal-sized breasts. Breast volume assessments were performed using the BREAST-V. Statistical analysis using mixed effects model was performed with significant p-values <0.05. Results Nipple: static-1-point test showed mean pressure thresholds from the AG at T6 was 1.63 higher than T0 ((p=0.467), while at T48 was 4.10 and 4.19 times higher than T0 and CG (p<0.001) respectively; moving-1-point test showed mean pressure thresholds from the AG at T6 was 1.42 higher than T0 ((p=1.000), while at T48 4.08 and 3.23 times higher than T0 and CG (p<0.001) respectively. Areola: static-1-point test showed mean pressure thresholds in the AG at T6 was 1.21 higher than T0 ((p=0.912), while at T48 was 4.12 and 4.83 times higher than T0 and CG (p<0.001) respectively; moving-1-point test showed mean pressure thresholds from the AG at T6 was 1.38 higher than T0 ((p=0.001), while at T48 was 4.56 and 4.46 times higher than T0 and CG (p<0.001) respectively. Conclusions Despite an early, though not-significant worsening at 6-months after surgery, patients who have undergone SLPRM showed significant NAC sensibility reduction at 48-month follow-up. The NAC of hypertrophic-breasted patients was seen to be not significantly less sensitive than normal-sized breasts, while significant postoperative decrease of NAC sensibility compared to CG was observed following SLPRM.

Response to Reviewers:	Editorial review: 1. + Exceeds Word Count Limit Unfortunately, we have to impose word limits on all PRS publications. Original Articles have a cap of 3000 words (not including the abstract, tables, and reference list). Please reduce the number of words to number NO MORE than 3000 words. REPLY: We reduced text lenght to 2994 words without compromising essential contents of the manuscript. Reviewer #2: 1. The authors have made all necessary revisions, except the original study design. REPLY: We thank Reviewer #2 for her/his positive comments. Concerning the study design, our intentions were to investigate normal nipple-areola complex (NAC) sensibility and after reduction mammaplasty in a population of macromastia patients (with mean breast size of 1153cc). Therefore, we already used as a reference preoperative levels of NAC sensibility from this particular group of patients, then comparing their preoperative and postoperative NAC sensibility values with those coming from a normal breast sized group of unoperated women to assess eventual differences of sensibility levels. We did so in order to allow both surgeon and patient to fully understand which expectations and results in terms of volume and sensibility can have postoperatively. Investigations on normal NAC sensibility from different groups of hypertrophic-breasted patients are object of a study that will be submitted within the next weeks to PRS journal. Reviewer #3: 1. The authors have made the necessary revisions in my estimation. REPLY: We thank Reviewer #3 for her/his positive comments.

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Short Running Head: NAC sensibility after reduction mammaplasty

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Conflict of interest disclosure statement: We, hereby certify, that to the best of our knowledge none of the authors has a financial interest in any of the products, devices or drugs mentioned in this manuscript or any member of our immediate family or any individual or entity with whom or with which we have a significant relationship from any commercial source which is related directly or indirectly to the scientific work which is reported on in the article.

Abstract

Background

The aim of our study was to investigate nipple-areola complex (NAC) sensation at 48-month follow-up following superior-lateral-pedicled reduction mammaplasty (SLPRM) using the Pressure-Specified-Sensory-Device (PSSD).

Patients and Methods

NAC sensation for static and moving 1&2-point was collected from 30 active-group (AG) hypertrophic-breasted patients undergone SLPRM preoperatively (T_0), at 6-months (T_6) and 48-months (T_{48}), and from a control-group (CG) of 30 unoperated women with normal-sized breasts. Breast volume assessments were performed using the BREAST-V. Statistical analysis using mixed effects model was performed with significant *p*-values <0.05.

Results

Nipple: static-1-point test showed mean pressure thresholds from the AG at T_6 was 1.63 higher than T_0 ((p=0.467), while at T_{48} was 4.10 and 4.19 times higher than T_0 and CG (p<0.001) respectively; moving-1-point test showed mean pressure thresholds from the AG at T_6 was 1.42 higher than T_0 ((p=1.000), while at T_{48} 4.08 and 3.23 times higher than T_0 and CG (p<0.001) respectively.

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Conclusions

Despite an early, though not-significant worsening at 6-months after surgery, patients who have undergone SLPRM showed significant NAC sensibility reduction at 48-month follow-up. The NAC of hypertrophic-breasted patients was seen to be not significantly less sensitive than normal-sized breasts, while significant postoperative decrease of NAC sensibility compared to CG was observed following SLPRM.

Key words: Breast sensibility; Nipple sensitivity; Areola sensitivity; Breast reduction; Superior-lateral pedicled reduction mammaplasty.

Clinical Question/Level of Evidence: Therapeutic, II.

Background

Numerous breast reduction procedures have been proposed during the 20th century, all showing satisfactory aesthetic outcomes without compromising breast-feeding[1-14], though many controversies still exist on their effects on breast sensibility. However, most of these studies have used imprecise devices basing their results on debatable statistical methodology[15-24].

The recent introduction of the Pressure-Specified Sensory Device (PSSD) made it possible to conduct studies based on an objective assessment method providing realistic and reliable data on sensory restoration after a wide variety of surgical procedures, such as hand, oral cavity, and both breast reduction and reconstruction surgery[25-31].

The aim of this study was to investigate nipple-areola complex (NAC) sensation at 48-month follow-up following superior-lateral pedicled reduction mammaplasty (SLPRM) using the PSSD, comparing the resulting data to those obtained from a control group of unoperated women with normal-sized breasts.

Patients and Methods

A cohort of 30 women considered as active group (AG) was prospectively enrolled to investigate NAC sensation following SLPRM. Mean age was 46 years (range, 29-63), mean body mass index (BMI) was 25 kg/m^2 (range, 21-28). Preoperative mean volume of their 60 breasts was 1153cc (range, 805cc-2190cc), with a mean resection of 888cc (range, 379cc-1850cc), and a final mean breast volume of 515cc (range, 392cc-587cc). Thirty women with mean age of 41 years (range, 33-63), mean BMI of 23 kg/m^2 (range, 19-27) and mean volume of their 60 breasts of 553cc (range, 401cc-601cc) were recruited as control group (CG) (Table 1). Breast volume assessments were performed using the BREAST-V[32] by collecting preoperative anthropomorphic values from charts review in the AG and by direct measurements in the CG. All 60 patients had at least one pregnancy and had breastfed; exclusion criteria were: breast asymmetries, previous breast surgery, diabetes, neurological disorders and tobacco use.

All AG patients were operated on by the senior surgeon (F.S.) with the superior-lateral pedicled technique according to Blomqvist and Alberius[33]. NAC sensitivity from both AG and CG was investigated by a single evaluator (B.L.) using the PSSD; static and moving one and two-point discrimination of the nipple and the four areolar quadrants were collected from the CG, and from all AG patients preoperatively (T_0), at 6 months (T_6) and at 48 months (T_{48}) from surgery. Testing was repeated five consecutive times on each area. The highest and lowest results were discarded and the remaining values were averaged. Higher pressure thresholds indicate decreased sensibility.

Surgical Technique

The breasts are marked with patients in standing position preoperatively. Inframammary fold, breast midline, and new nipple position located along the latter at 21-22 cm from the sternal notch are drawn; finally, a keyhole Wise-pattern and the superior-lateral pedicle are marked according to Blomqvist and Alberius[33].

The operation is performed under general anesthesia with the patient in supine position and arms abducted to her sides, and one preoperative antibiotic prophylaxis dose of first-generation cephalosporin (Cefazolin, 1 g intravenously). In all breasts, incision lines are injected with a 500 ml saline solution with 10 ml of ropivacaine HCl (Naropin® 7.5 mg/ml - AstraZeneca, London, England), 20 ml of 2% lidocaine, and 1 ml of adrenaline 1 mg/ml. Then, the NAC is marked with a 42-mm areolotome, and both keyhole pattern and pedicle are dehepitelialized using a scalpel. After undermining the breast inferior pole, the breast parenchyma is excised inferiorly as for the Strömbeck procedure. Thereafter, the breast gland is incised midway between the borders of the areola and medial skin flap, straight through the dermal and subcutaneous tissue layers down to the pectoralis fascia, so as the superior-lateral pedicle is created. Furthermore, after creating a shallow pocket for the future positioning of the NAC in the superior-medial part of the pedicle, the NAC is easily transposed to its new position. After hemostasis, the areola is fixed into the keyhole by 4-0 interrupted nylon sutures, while the medial and lateral skin flaps and skin closure are sutured by two-layer interrupting 3-0 Vicryl™ (polyglactin 910) and 3-0 Prolene™ (polypropylene) sutures. No suction drains are placed in the breasts. Micropore adhesive tape (3M, St. Paul, Minn.) is used to cover incisions. All patients were discharged from the hospital 1 day after surgery, and followed up in the outpatient clinic every 3 days until postoperative day 14 when sutures are completely removed. They are instructed to wear a sports bra night and day for 1 month. Afterward, each patient was seen 1 month, 3 months, and 6 months after operation.

Statistical methodology

Analyses were stratified by location (areola or nipple), number of pressure points (one or two), and whether the test was static or moving. For each stratum, mixed effect models on the logarithm of pressure thresholds were estimated, with and without adjustment for BMI and age. A subject-specific random intercept was used to take into account dependence arising from repeated measurements on the same subject. The resulting p-values were adjusted for multiplicity using Bonferroni correction. We report the adjusted p-values, so that a $p<0.05$ can be deemed as statistically significant after multiplicity correction. All analyses were performed using the software R version 2.14.2.

Results

There were no total or partial nipple-areola losses, and the viability of the NAC was excellent in all treated breasts. Neither haematomas, seroma, wound infections nor lipolysis was experienced.

Static 1-point test at the nipple showed that mean pressure thresholds from the AG at T_6 was 1.63 times higher than T_0, although not significantly (p=0.47), while at T_{48} it was 4.10 times higher than T_0 (p<0.001). Furthermore, pressure thresholds at T_0 and T_{48} were respectively 0.91 (p=1.00) and 4.19 (p<0.001) times higher than CG.

Moving 1-point test at the nipple showed mean pressure thresholds from the AG at T_6 1.43 times higher than T_0, although not significantly (p=1.00), while at T_{48} it was 4.08 times higher than T_0 (p<0.001). Furthermore, pressure thresholds at T_0 and T_{48} were respectively 0.66 (p=1.00) and 3.23 (p<0.001) times higher than CG. Stating and moving 2-point discrimination at the nipple was barely measurable, giving unreliable and non-reproducible results thus not considered in the study.

No significant differences were found between the four areolar quadrants for static and moving 1-point and static 2-point values. Static 1-point test at the areola showed that mean pressure thresholds in the AG at T_6 was 1.21 times lower than T_0, although not significant (p=0.91), while at T_{48} it was 4.12 times higher than T_0 (p<0.001). Moreover, pressure thresholds at T_0 and T_{48} were respectively 1.20 (p=1.00) and 4.83 (p<0.001) times higher than CG. Moving 1-point test at the areola showed that mean pressure thresholds from the AG at T_6 was 1.38 times lower than T_0 (p=0.001), while at T_{48} was 4.56 times higher than T_0 (p<0.001). Moreover, pressure thresholds at T_0 and T_{48} were respectively 0.90 (p=1.00) and 4.46 (p<0.001) times higher than CG. Static 2-point test at the areola showed that mean pressure thresholds from the AG at T_6 was 1.56 times higher than T_0 (p<0.001), while at T_{48} was 2.71 times higher than T_0 (p<0.001). Moreover, pressure thresholds at T_0 and T_{48} were respectively 1.88 (p=1.00) and 5.34 (p<0.001) times higher than CG. Moving 2-point discrimination was barely assessable for each areola quadrants, giving unreliable and non-reproducible results thus not considered in the study (Table 2, 3).

Discussion

Dissimilar approaches have been used in different studies to investigate breast sensibility changes following reduction mammaplasty[15-19,23,29,34,35]. Early studies have been performed with Vitapulp device[15,16] and Semmes-Weinstein nylon monofilaments[17-21,24] (SWMs) yielding non-reproducible and reliable data that could not be statistically managed[36].

Objective investigations on NAC and breast sensibility following reduction mammaplasty have been performed using the Dermatomal Somatosensory Evoked Potentials (DSEP) and the Pressure-Specified Sensory Device (PSSD).

DelVecchyo et al[35] used the DSEP, a neurophysiologic method based on the anatomic knowledge of breast innervations and the congruent areas of dermatomal maps, showing an improvement of NAC and breast sensibility at 12-month follow-up following breast reduction with Mckissock technique. Moreover, they found that small breasts were statistically more sensitive than larger ones, and after reduction mammaplasty the latter presented no statistical difference in amplitude of breast sensibility compared to the small-breasted group. The complexity of the DSEP device and criticism of the selection method for breast volume samples using patient-stated bra cup size as a proxy of breast size, represent the main limitations of this study. It is well known that bra cup size is a weak determinant of breast volume and its accuracy is further compromised when considering that band size adds extra variability in the prediction of breast volume[37,38].

The development of the Pressure-Specified Sensory Device (PSSD) made it possible to collect data on continuous measurements of cutaneous pressure (g/mm^2). This allows for quantification of one-point static (slowly-adapting fibers including Merkel cell-neurite and Ruffini complexes), one-point moving (rapidly-adapting fibers stimulated by Pacinian and Meissner corpuscles), and two-point static and moving (density of innervation) discrimination.

Mofid et al[29] were the first to use the PSSD to establish the normal NAC sensation and to compare sensory outcomes between the inferior and the medial pedicled reduction mammaplasty technique. At 24-month follow up they found that despite the better pressure threshold observed in the medial pedicle technique sample, there were no significant differences in postoperative sensory outcomes in both inferior and medial pedicled techniques. However, the authors declared that the mass of the excised breast parenchyma was 60% greater in the medial pedicle group, probably having larger breasts than inferior pedicle group. This further confirms that bra cup size represents an inaccurate method to identify breast volume samples, potentially leading to biased results, and an objective tool is required to better define breast populations. Moreover, authors give no information about the sensibility changes between pre and postoperative sensory outcomes, thus not quantifying the effects of the investigated breast reduction procedures.

Ferreira at al[30] used the PSSD to compare pre and postoperative sensory data from patients addressed to upper-medial pedicled reduction mammaplasty, noting worsening of sensibility at 6-month follow up. However, Dellon commented that their results were not stable because of the short period of observation stating that data could be improved to sensibility levels of smaller breasts at a longer period of follow up[36]. Moreover, further criticism of Ferreira's study was the inaccurate method by which the authors defined their population in terms of breast size basing it on the mass of tissue resected. Therefore, from the latter two studies in which PSSD was applied, an issues remained unsolved: what are the real changes of NAC sensibility following reduction mammaplasty compared to preoperative pressure thresholds at long term follow up?

In 2007 Santanelli et al[31] pre- and postoperatively investigated NAC sensibility levels and innervation density in hypertrophic-breasted patients addressed to superior-lateral pedicled reduction mammaplasty. They evaluated the existence of sensibility changes between cup D and E/EE breasted patients and the impact of glandular resection and nipple elevation on NAC sensibility. All variables analyzed led to the same result: patients undergoing reduction mammaplasty according to Blomqvist should be carefully informed that their nipple-areola complex sensibility might change after surgery; it can be not significantly reduced, which is less detectable in large (cup E/EE) breasts because of lower preoperative levels of sensibility.

Since these conclusions emerged from data evaluation at 6-month follow-up, and for this reason can be considered transitory and unstable, we wanted to observe further modifications of NAC sensibility at a longer period of follow-up.

In our study we fixed the last follow up at 48 months after surgery, assuming that spontaneous sensory recovery of the NAC can be considered definitely stable at the end of this period. Dellon had already established 24 months as a sufficient time for a possible sensibility recovery[29,36], but we have further stretched the final evaluation time to collect and analyze data in a very long term follow up.

Moreover, quantitative preoperative breast dimension is very important as it gives the possibility to define and stratify breast population. In this context, both 3-dimensional analysis and anthropometric measurements were seen to be objective and reproducible tools, and respectively Canfield Vectra 3 pod system[39] and BREAST-V showed very accurate determination of breast volumes. Among them, the BREAST-V has the advantage to be a faster and easier method by using only 3 measures of the breast, being also cheaper as it can be downloaded for free from Apple store and Google Play Store respectively for iOS and Android devices. Therefore, we applied the BREAST-V to objectively define breast population of AG in terms of volume, and to enroll a CG of patients having a breast volume similar to the AG postoperatively. Furthermore, since pressure thresholds come from 120 breasts belonging to 60 women, it is clear that the observations are not all independent thus possibly providing biased estimates. Therefore, from a statistical point of view, we had actually fit a linear mixed effects model with subject-specific random intercept particularly useful in setting where repeated measurements are made on the same statistical unit (*e.g.* two breasts per each patient), thus better controlling for fixed or random individual differences.

From our statistical analysis emerged that large breasts (805-2190cc) are less sensitive than smaller ones (401-601cc) even if not significantly. Although our results compare with findings of other authors, the difference in breast sensibility between the two groups was found to be lower as expected. Our divergent result could be due to the linear mixed effects model and to the objective determination of breast volume with BREAST-V performed in our study that, to the best of our knowledge, is the first to use an objective tool to stratify breast volume samples. Nevertheless, as other authors[29,30], we do believe that large and heavy breasts potentially produce a chronic nerve traction injury causing an inverse relationship between breast volume and sensibility. However, objective investigations about the real impact of breast size on NAC sensibility thresholds should be object of future studies in order to better clarify the magnitude of their association.

In AG patients, we observed dissonant results between nipple and areola sensibility at T_6 compared to T_0, even if not significant; nipple was found to be less sensitive for both rapidly and slowly adapting fibers, while areola showed a sensibility improvement for static and moving 1-point discrimination. However, as previously discussed by Dellon[36], 6-month follow up gives transitory results that in our study could explain the observed alternate increased and decreased thresholds for nipple and areola respectively. Instead, a longer period of observation guarantees stable and realistic data, and at T_{48} both nipple and areola were found to be significantly less sensitive, 4.19 and 4.12 times respectively, if compared to preoperative thresholds (T_0) for slowly adapting fibers (static 1-point), while 4.08 and 4.56 respectively for rapidly adapting fibers (moving 1-point). Moreover, nipples of AG patients at T_{48} were found to be significantly less sensitive of 4.19 and 3.23 times than nipples of CG for 1-point static and moving discrimination respectively, while areola was found to be significantly less sensitive of 4.83, 4.46 and 5.34 times than areola of CG for static and moving 1-point, and static 2-point discrimination respectively. Such significant worsening in sensibility could be imputed to the superior-lateral pedicled reduction technique that certainly interrupts the medial innervation to the NAC coming from the anterior cutaneous branches of the 3rd, 4th and 5th intercostal nerves, while likely cuts also the lateral cutaneous branch of the 4th intercostal nerve along its course at its emerging point from the pectoralis fascia to run through the glandular tissue toward the posterior surface of the nipple[40]. However, because anatomical variations of NAC innervation are possible, superior-lateral pedicle reduction technique still entails variable and different risk for each patient of impairing NAC sensitivity. Furthermore, the fibrotic scar at the areolar edges could be responsible for the progressive sensibility worsening over time from 6 to 48 months, as autocrine and paracrine axonal growth mechanisms are contrasted and slowed down by fibrosis. It has been shown that scar fibroblasts express various axonal growthinibitory molecules such as tenascin-C, semaphoring 3A, NG2 proteoglycan and phosphacan[41, 42], thus entailing an inherent either physical and molecular attitude to obstacle physiological functions and regeneration of nerve axons which come into contact with them within the scar microenvironment. An interesting unexplored phenomenon is neural organization in the somatosensory system after reduction mammaplasty. Phantom sensations are reported as a consequence of partial and total breast amputation for cancer, possibly accounted for by both rearranging of peripheral nerves and remapping on deafferented subcortical and cortical somatosensory areas[43]. It has been reported that mislocation phenomena mainly involve the nipple, which is probably the portion of the breast most extensively represented in the brain. Reduction mammaplasty can also be considered as a partial breast amputation for aesthetic and functional purposes, but actually we do not know whether surgical-induced topographical remapping produces a cortical up- or downgrading of NAC sensibility of reduced breasts. Future studies comparing different reduction mammaplasty techniques in homogeneous breast volume samples at long-term follow-up are needed to confirm our presumed dynamics about sensibility worsening as a pathophysiological surgical result of a structurally and functionally impaired innervation to the NAC. Authors approaching investigations on this topic should apply objective measurements techniques to their populations in order to better understand and improve their surgical performances. In this context, the application of the PSSD and BREAST-V makes objective and reproducible investigations on breast sensibility representing an ideal solution for future researches in this field of plastic surgery.

Conclusion

Despite an early though not significant worsening at 6 months after surgery, patients who have undergone SLPRM showed significant NAC sensibility reduction at 48-month follow-up. The NAC of hypertrophic-breasted patients was seen to be not significantly less sensitive than control normal-sized breasts, while significant postoperative decrease of NAC sensibility compared to control group was observed following surgical reduction of breast volume. Therefore, patients undergoing SLPRM should be fully informed about the significant reduction of NAC sensibility they may experience after surgery at long term follow up.

Finally, the combined use of PSSD and BREAST-V was found to be an innovative and reproducible methodology to objectively investigate NAC sensation following reduction mammaplasty.

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Table 1. Descriptive statistics for patients' data.

Variable	CG (Mean value ± Standard Deviation)	AG (Mean value ± Standard Deviation)
Age (years)	41.82 ± 7.19	46.03 ± 7.50
Body Mass Index (kg/m^2)	23.31 ± 2.94	25.63 ± 4.06
Breast Volume* (cc)	553.10 ± 134.4	1153.70 ± 605.5 (preop) 515.55 ± 144.6 (postop)
Breast Volume (cc) (Median value)	525	1050 (preop) 495 (postop)

CG= control group; AG= active group

preop= preoperative volume; postop= postoperative volume

* Mean breast volume is considered for each breast, not for each patient.

Table 2. Mean cutaneous pressure thresholds**.

Variable	CG	AG (T_0)	AG (T_6)	AG (T_{48})
Nipple 1-sp (g/mm^2)	2.19 ± 0.35	2.45 ± 0.79	2.87 ± 2.91	6.97 ± 5.02
Nipple 1-mp (g/mm^2)	1.07 ± 1.95	1.17 ± 1.02	1.59 ± 2.29	4.53 ± 3.84
Areola 1-sp (g/mm^2)	3.27 ± 0.96	4.01 ± 2.46	3.46 ± 3.69	11.92 ± 3.55
Areola 1-mp (g/mm^2)	1.97 ± 3.94	2.25 ± 3.62	2.03 ± 1.16	7.67 ± 3.32
Areola 2-sp* (g/mm^2)	3.76 ± 3.89	6.27 ± 4.01	6.75 ± 2.03	17.45 ± 3.45

CG= control group; AG= active group

T_0= before surgery; T_6= 6 months after surgery; T_{48}= 48 months after surgery

1-sp= static 1-point; 1-mp= moving 1-point; 2-st= static 2-point

* distance between probes fixed at 10 mm

** Note that higher pressure thresholds mean worse sensibility

Table 3. Estimates and *p*-values from mixed effects statistical model.

Variable	T_6 vs T_0	T_{48} vs T_0	T_0 vs CG	T_{48} vs CG
Nipple 1-sp (*p*-value)	1.631 (0.467)	4.104 (<0.001)	0.907 (1.000)	4.186 (<0.001)
Nipple 1-mp (*p*-value)	1.428 (1.000)	4.076 (<0.001)	0.659 (1.000)	3.227 (<0.001)
Areola 1-sp (*p*-value)	1.214 (0.912)	4.122 (<0.001)	1.195 (1.000)	4.833 (<0.001)
Areola 1-mp (*p*-value)	1.383 (0.001)	4.557 (<0.001)	0.895 (1.000)	4.457 (<0.001)
Areola 2-sp (*p*-value)	1.575 (<0.001)	2.708 (<0.001)	1.883 (1.000)	5.339 (<0.001)

CG= control group

T_0= active group before surgery; T_6= active group at 6 months after surgery; T_{48}= active group at 48 months after surgery

1-sp= static 1-point; 1-mp= moving 1-point; 2-st= static 2-point

COVER LETTER

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Rod J. Rohrich, M.D.

Editor in chief

Plastic and reconstructive surgery®

University of Texas Southwestern Medical Center

5323 Harry Hines Blvd., HD1. 544

Dallas, TX 75390-8820

Dear Dr. Rod J. Rohrich, Editor in Chief,

On behalf of my co-authors, I am submitting the enclosed manuscript, *"*Long-term sensory recovery of nipple-areola complex following superolateral pedicled reduction mammaplasty*"*, for possible publication in Plastic and Reconstructive Surgery®. In this paper we investigated nipple-areola complex (NAC) sensation at 48-month follow-up following superolateral-pedicled reduction mammaplasty (SLPRM) using the Pressure-Specified-Sensory-Device (PSSD). NAC sensation for static and moving 1&2-point was collected from 30 active-group (AG) hypertrophic-breasted patients undergone SLPRM preoperatively (T_0), at 6-months (T_6) and 48-months (T_{48}), and from a control-group (CG) of 30 unoperated women with normal-sized breasts. Breast volume assessments were performed using the BREAST-V. Statistical analysis using mixed effects model was performed with significant *p*-values <0.05. Despite an early, though not significant worsening at 6-months after surgery, patients who have undergone SLPRM showed significant NAC sensibility reduction at 48-month follow-up. The NAC of hypertrophic-breasted patients was seen to be not significantly less sensitive than normal-sized breasts, while significant postoperative decrease of NAC sensibility compared to CG was observed following SLPRM.

We strongly believe the contribution of this study warrants its publication in the Plastic and Reconstructive Surgery®.

It has not been submitted for publication or has it been published in whole or in part elsewhere. I attest to the fact that all authors listed on the title page have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to Plastic and Reconstructive Surgery®.

Possible conflicts of interest, sources of financial support, corporate involvement, patent holdings, etc. for each author are disclosed in an accompanying letter.

Sincerely,

Benedetto Longo, MD PhD

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