Sensory reinnervation after mastectomy with implant-based reconstruction

Anne Warren Peled¹, Ziv M. Peled²

¹Private Practice and Sutter Health California Pacific Medical Center, San Francisco, CA, USA; ²Peled Plastic Surgery, San Francisco, CA, USA *Contributions:* (I) Conception and design: Both authors; (II) Administrative support: Both authors; (III) Provision of study material or patients: Both authors; (IV) Collection and assembly of data: Both authors; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

Correspondence to: Anne Warren Peled, MD. 2100 Webster Street, Suite 318, San Francisco, CA 94115, USA. Email: drpeled@apeledmd.com.

Abstract: As breast cancer therapies continue to improve, increasing focus has been placed on quality-oflife issues after breast cancer and breast cancer risk-reducing treatments. The loss of sensation that typically occurs after mastectomy can have significant negative psychological, sexual, and functional impact on patients after surgery. In order to minimize this impact, more recent attention has been paid to ways to both avoid nerve injury at the time of mastectomy and reconstruct injured nerves either during mastectomy or at the time of delayed reconstruction. These advances have been facilitated by anatomic studies investigating different variants of intercostal anatomy and better understanding the course of the nerves innervating the mastectomy skin and nipple-areolar complex. With improved knowledge of the intercostal nerve anatomy, surgeons are able to carefully preserve nerves at the time of mastectomy, thus improving sensory outcomes. Additionally, nerve reconstruction techniques have advanced, particularly with newer nerve allograft technologies, which allows for nerve reconstruction to be done both at the time of mastectomy, as well as in a delayed fashion. Much of the current literature on intercostal nerve reconstruction to improve postmastectomy sensation has been performed in the setting of autologous reconstruction, but several more recent studies have assessed outcomes following implant-based reconstruction. The focus of this article is to describe the current state of sensory preservation and reinnervation for mastectomy with implant-based reconstruction and the advances that have allowed for these new approaches.

Keywords: Mastectomy; implant reconstruction; breast sensation; sensory reinnervation

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Post-mastectomy sensation following traditional approaches

Loss of breast sensation after mastectomy has gained more attention recently, particularly as it has been shown to be associated with a negative psychosocial impact for patients and certainly contributes to the decreased breastspecific sensuality and quality of life outcomes seen after mastectomy (1,2). Although there have been remarkable overall advancements in oncologic as well as reconstructive treatment since Halstead first described the radical mastectomy in the late 19th century (3,4), optimal sensation following mastectomy and breast reconstruction still remains one of the final hurdles in the field of breast cancer treatment.

Advances in mastectomy techniques such as preservation of the entire skin envelope through nipple-sparing mastectomy have certainly improved aesthetic outcomes (5), though hoped for improvements in sensation haven't been seen to the same degree. A number of studies have looked at sensation outcomes following nipple-sparing mastectomy and found overall relatively low rates of sensation preservation. Dosset *et al.* found measurable sensation in the nippleareolar complex (NAC) in only 28% of patients undergoing nipple-sparing mastectomy at least a year following their reconstruction with either expanders/implants or autologous tissue (6). Moreover, the degree of measured sensation that was present was quite poor. Rodriguez-Unda *et al.* similarly reported decreased post-operative breast sensation following reconstruction in both skin-sparing mastectomies and nipple-sparing mastectomy patients (7). Yet another study from Sweden reported similar significantly impaired breast sensibility when comparing patients undergoing prophylactic, mastectomy with free nipple grafting (8). The same study further demonstrated that ability to experience sexual sensation was lost, perhaps explaining a primary reluctance of many women to undergo risk-reduction surgery.

Having immediate reconstruction at the time of mastectomy can certainly optimize aesthetic results, but also could potentially have been thought to improve sensation as well. However, results with sensation following mastectomy with immediate reconstruction have also been sub-optimal. Yueh et al. looked at 17 breasts in 10 patients who underwent nipple-sparing mastectomy with immediate reconstruction. While there was some measurable sensation in the NAC in a number of patients post-operatively, the degree of sensation was quite low (9). In a larger cohort, Djohan et al. reported that a majority of patients described fair or poor NAC sensation after nipple-sparing mastectomy and immediate reconstruction, even with a mean follow-up of greater than four years (10). Patientreported outcomes from this study showed that this loss of sensation was the part of the patients' results that they would most like to change. Finally, data from Peled et al. in patients undergoing nipple-sparing mastectomy with immediate expander-implant reconstruction demonstrated that only 3% of patients were "very satisfied" and 21% of patients "somewhat satisfied" with their NAC sensation (11).

Relevant breast anatomy for facilitating sensory reinnervation

Ongoing study of the sensory innervation to the breast has helped to better define the anatomy and allow for targeted nerve preservation and reinnervation. Specifically, sensation to the breast skin envelope derives predominantly from the 1st-6th medial intercostal and 2nd-7th lateral intercostal nerves (12). Most papers also describe the sensory innervation to the NAC itself primarily from the medial and lateral superficial branches of the 3rd-5th intercostal nerves (13,14). Understanding of this anatomic landscape has allowed a number of authors to suggest modifications to established oncologic and reconstructive breast surgical procedures to help minimize sensory loss postoperatively.

Schulz et al. described limiting dissection within the inferolateral quadrant of the breast during reduction mammaplasty to optimize NAC sensation post-surgery (15). The lateral intercostal nerves typically have both superficial and deep branches, with the former often coursing in the subcutaneous tissues of the lateral skin flap and the former taking intra-parenchymal routes to reach the sub-areolar region and innervate the nipple-areolar complex. Knackstedt et al. defined the anatomy of the lateral intercostal nerve as emerging within 2 cm of the lateral border of the pectoralis minor muscle and predictably travelling under the adjacent vessels (16). They opined that recognition of this anatomy during mastectomy could aid the operative surgeon in identifying and ideally preserving the relevant nerve(s) to optimize post-operative sensation. Although consideration of mastectomy skin flap thickness has been described as it relates to reconstructive and oncologic outcomes (17,18), the correlation between skin flap thickness and sensory nerve preservation has not been well-studied.

In addition to the sensory anatomy of the breast, a better understanding of feasible donor nerve anatomy in those for whom an autologous reconstruction is contemplated has also developed. With DIEP reconstruction, several authors have described the donor nerve(s) for a possible sensate flap utilizing the 10^{th} – 12^{nd} intercostal nerves in the upper abdomen (19). Momeni *et al.* additionally described limiting donor nerve harvesting to the more distal, sensory portion of those caudal intercostal nerves (20).

Advances in post-mastectomy sensory preservation and nerve reconstruction

Given the low reported rates of sensation preservation following traditional mastectomy as described above, surgeons have begun to develop better techniques to help preserve and restore sensation. Until recently, the approaches have solely involved restoring sensation with autologous reconstruction, though a few newer studies have shown promising outcomes with implant-based reconstruction.

Some of the earliest studies of breast neurotization were done with neurotized TRAM flaps, which showed potential benefit with regards to improving sensation, but a definitive improvement from neurotization as compared to spontaneous sensory recovery was unclear (21). Sensory restoration with autologous reconstruction has evolved over time and has been reported in several studies using neurotized DIEP or other perforator flaps, primarily to improve sensation with delayed reconstruction using direct neurotization (22,23). Some larger studies have shown results with both immediate and delayed reconstruction using both nerve conduits and direct innervation of flap skin islands, with significant improvement in recovery of sensation when compared to controls (24,25). Emphasis on standardization of technique and outcomes measurements has been seen in recent years to help optimize outcomes (26) including the creation of a multi-site prospectively collected registry that has been shown to have promising early results (27).

To date, the literature on sensation reinnervation with implant reconstruction is very limited given the technique has only recently been adopted and in a small number of centers. The two published studies specifically addressing outcomes after neurotization with implantbased reconstruction were both done with immediate neurotization done at the time of mastectomy. Our previously reported work (28) presented proof of concept and efficacy data on intercostal nerve preservation as well as nipple-areolar complex neurotization done at the time of nipple-sparing mastectomy in the setting of immediate, pre-pectoral, direct-to-implant reconstruction. Results from 32 mastectomies in 17 patients showed preservation of sensation as measured with two-point discrimination in 88% of cases. 94% of patients had gross sensation to light touch throughout all 4 quadrants of their mastectomy skin. Although overall outcomes showed good return of sensation in the patient cohort, quantitative outcomes measures specifically looking at skin flap sensation were limited, as was follow-up time and patient-reported outcomes data. Another recent study from Djohan et al. (29) demonstrated similar results in patients undergoing nippleareolar complex neurotization at the time of implant-based reconstruction. Their study presented sensory outcomes from 15 mastectomies in 8 patients using a pressurespecified sensory device to assess sensation. They found overall improvements in mastectomy skin and nippleareolar complex sensation over time, though acknowledged that their follow-up was limited and that further recovery could be anticipated with additional follow-up. Additionally, their study did not include any patient-reported data and their cohort size was small and heterogeneous.

Outcome metrics to gauge breast sensation have also seen improvements with time. Older methods of assessing breast sensibility have included gross light touch, pin-prick, perception of pain to electric stimulation, sensitivity to vibration, thermal sensation and most commonly, Semmes-Weinstein monofilament testing (30,31). More recently, use of cutaneous pressure thresholds (pressure-specified sensory device measurements) have been utilized to measure post-surgical breast sensation with several advantages (29,32). First, the results obtained are linear as opposed to logarithmic (for Semmes-Weinstein monofilaments) thus making them more amenable to statistical analysis. Second, cutaneous pressure thresholds are able to be tested for both static and moving stimuli allowing evaluation of both Merkel cell-neurite/Raffini complexes as well as Meissner/ Pacinian corpuscles, respectively. Calibration is also easily performed making the results more reliable and accurate (33). Furthermore, with the advent of the BREAST-Q, validated and reliable PROMs are readily accessible to study the effects of mastectomy and reconstruction, including sensation (34).

Practice experience with sensation-preserving mastectomy and implant reconstruction

We began performing sensation-preserving mastectomies with immediate implant-based reconstruction in our practice in February 2018 and have now done over 200 of these procedures. The technique, which has been previously described (28), involves both intercostal nerve preservation and nerve grafting from intercostal nerves to subareolar nerves. Briefly, during mastectomy (almost exclusively nipplesparing mastectomy in our practice), care is taken during the lateral dissection to preserve the lateral, superficial branches of the 3rd, 4th or 5th intercostal nerves whenever possible at the thoracic cage. Preservation is done when considered oncologically safe as defined by favorable anatomy with the nerves running within the subcutaneous tissue and not through the breast parenchyma itself (Figure 1). If identified nerves are found to be running through the breast parenchyma, they are carefully dissected out to length within the parenchyma until no longer oncologically safe, at which point the nerves are sharply transected. In order to optimize oncologic safety, no glandular breast tissue is intentionally left behind during the mastectomy for the sake of nerve preservation.

For those nerves that are transected, nerve reconstruction is performed using an Avance nerve allograft (Axogen, Jacksonville, FL, USA) coapted from the transected lateral intercostal nerve to an identified subareolar nerve (*Figures 2,3*). The nerve reconstruction is done after pre-pectoral implant reconstruction with anterior, acellular dermal matrix (ADM) coverage with the reconstructed nerve lying in the plane Page 4 of 7



Figure 1 Carefully preserved lateral intercostal nerve running within the subcutaneous tissue.



Figure 2 Proximal connector-assisted coaptation of lateral intercostal nerve, showing the nerve allograft running anterior to the acellular dermal matrix covering the implant reconstruction.

between the ADM and subcutaneous tissue. In addition, connector-assisted repairs are performed to reduce tension at the nerve coaptation site, to reduce suture burden at the coaptation site and to minimize collateral sprouting (35).

Outcomes measures for sensation have included both neurosensory testing with a pressure-specified sensory device (PSSD) (Axogen, Jacksonville, FL, USA) and patient-reported outcomes regarding nipple and skin flap sensation. Review of outcomes in patients with a



Figure 3 Distal connector-assisted coaptation of subareolar nerve.

minimum of 6 months follow-up shows return of sensation to good or excellent levels in over 80% of patients, which continues to improve at the 1 year follow-up timepoint (unpublished data). Similar results are seen with patientreported outcomes assessing nipple and overall breast sensation. Importantly, no patients have reported long-term dysethesia, allodynia or symptoms of neuroma formation.

As we have developed our techniques over time, we have worked on optimizing the degree of sensation preservation and timing of return of sensation, as well as better defining patient selection and setting patient expectations. Technical adaptations have included attempting to preserve as much length as possible for nerves that have to be transected in order to allow for shorter nerve allograft reconstruction. While we are still collecting more and longer-term data that will make subgroup analysis possible, early review of our data shows a quicker time to sensory recovery with shorter nerve grafts, consistent with data from upper extremity reconstruction (36,37). As the length of nerve that can be preserved is unpredictable and unable to be determined prior to surgery, patients need to be counseled pre-operatively that implant size may be limited to allow for a tension-free nerve reconstruction with the longest commercially available nerve allograft (7 cm in length). We have found that nerve reconstruction can be reliably performed with implants under 400-450 cc in size, though larger implants may be used for cases of complete nerve preservation or those with nerve reconstruction if longer native nerve lengths can be achieved.

We have found that the technique of nerve preservation during mastectomy and nipple-areolar complex neurotization in the setting of implant-based reconstruction

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certainly has a learning curve when first implementing the approach into practice. Optimal candidates when first starting would be patients having prophylactic surgery who have not had prior radiation and are not anticipated to have radiation or chemotherapy adjuvantly; patients with a C cup breast or smaller who do not want to be any larger at the completion of their reconstruction; and patients having direct-to-implant reconstruction so the optimal nerve graft length can be determined at the time of surgery. Close partnership and discussion pre-operatively and intraoperatively between the breast and plastic surgeons are also essential to ensure the steps of the procedure are optimized, particularly during dissection of the breast off of the chest wall so that nerve length can be preserved as much as is oncologically possible.

Conclusions

Sensory preservation or restoration after mastectomy is the next frontier in breast reconstruction. Recent advances in the understanding of nerve anatomy, allograft technology, and nerve repair techniques allow surgeons to more widely offer sensation-preserving approaches, though much of the published literature to date has been in the setting of autologous reconstruction. While the data on sensory reinnervation following implant-based reconstruction is still limited, results show promising objective and patient-reported outcomes. Given that the significant majority of breast reconstructions performed are implantbased, expanding these techniques beyond autologous reconstruction is essential to provide more patients the quality-of-life benefits of retaining sensation after mastectomy.

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