



# Sensate immediate breast reconstruction

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**Contributions:** (I) Conception and design: Both authors; (II) Administrative support: AW Peled; (III) Provision of study materials 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.

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**Abstract:** As breast cancer therapies and associated oncologic outcomes continue to improve, greater attention has been placed on quality-of-life 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. Further, injury of nerves not only leads to numbness, but can also cause chronic neuropathic pain, which can be very debilitating to affected patients. In order to minimize these impacts, there is expanding uptake of surgical approaches that preserve nerves at the time of mastectomy and reconstruct injured nerves either during mastectomy or during 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 (NAC). 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. The focus of this article is to describe the current state of sensory preservation and immediate reinnervation at the time of mastectomy and the advances that have allowed for these new approaches.

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

Submitted Oct 10, 2023. Accepted for publication Mar 18, 2024. Published online Apr 12, 2024.

doi: 10.21037/gS-23-416

View this article at: <https://dx.doi.org/10.21037/gS-23-416>

## Defining the problem: post-mastectomy sensation loss and chronic pain

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 breast-specific sensuality and quality of life outcomes seen after mastectomy (1,2). While advances in mastectomy techniques that allow for preservation of the entire breast skin envelope including the nipple-areolar complex (NAC) have improved the cosmetic outcomes and provided psychological benefit to patients (3), sensory outcomes following nipple-sparing mastectomy (NSM) have been universally poor.

A number of studies have assessed patient-reported outcomes on sensation following mastectomy and have found overall relatively low rates of return of NAC or skin flap sensation. Dossett *et al.* found measurable sensation in the NAC in only 28% of patients undergoing NSM and immediate reconstruction with either expanders/implants or autologous tissue (4), plus a very limited amount of sensation present in those that had any sensation. These results were echoed in another similar study of patients having immediate reconstruction at the time of NSM (5). Rodriguez-Unda *et al.* reported decreased post-operative overall breast sensation following reconstruction in both skin-sparing mastectomies and NSM patients (6). Not surprisingly, patients also specifically report significant

impairment in their ability to experience sexual sensation following mastectomy (7), which for some people can lead to significant impairment in their quality of life. In one of the larger cohorts assessed with a mean follow-up of greater than 4 years, Djohan *et al.* reported that the majority of patients had only fair or poor NAC sensation after NSM and immediate reconstruction (8); additionally patient-reported 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 NSM with immediate expander-implant reconstruction demonstrated that less than 25% of patients were either "very satisfied" or "somewhat satisfied" with their NAC sensation (9).

In addition to numbness, sensory nerves injured at the time of mastectomy often lead to chronic neuropathic pain, also known as post-mastectomy pain syndrome (PMPS). In fact, the incidence of PMPS has been shown to occur at rates ranging from 20% to 68% (10-12). While the likely etiology is multifactorial (e.g., nerve injury, scar contracture, muscle disinsertion/dysfunction), it is reasonable to assume that a significant portion of these patients have a neuropathic component to their pain (13). Therefore, strategies aimed at optimizing post-mastectomy sensation may also have beneficial effects on post-mastectomy pain. In fact, the concept of targeted re-innervation hinges upon giving injured nerves 'something to do' by coapting them to motor and sensory targets that become re-innervated in time instead of forming the disorganized, regenerating nerve ends seen in painful neuromas (14,15).

Given these clear limitations of traditional mastectomy, more recent advances have been made to better understand the nerve-related anatomy of the breast, use evolving technology to repair nerves that need to be transected during mastectomy, and develop improved outcomes measures for assessing the outcomes from these approaches.

### Relevant breast anatomy for facilitating nerve preservation and reconstruction

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 1<sup>st</sup>-6<sup>th</sup> medial intercostal and 2<sup>nd</sup>-7<sup>th</sup> intercostal nerves (16). Most papers also describe the sensory innervation to the NAC itself primarily from the medial and lateral superficial

branches of the 3<sup>rd</sup>-5<sup>th</sup> intercostal nerves (17,18). These medial and lateral T3, T4, or T5 branches are often the ones typically injured during mastectomy, contributing to both numbness and PMPS.

Anatomic studies have been done to better understand the locations of sensory nerves in the breast to help avoid injury to nerves during breast surgery and/or optimize nerve length for nerve reconstruction. Knackstedt *et al.* defined the anatomy of the lateral intercostal nerve as predictably emerging within 2 cm of the lateral border of the pectoralis major muscle and traveling under the adjacent vessels (19). Defining this location and demonstrating its consistency is invaluable for surgeons in attempting to identify and ideally preserve the relevant nerve(s) to optimize post-mastectomy sensation. Cadaveric studies done by Ducic *et al.* in the setting of consideration for targets for neurotized flap reconstruction reported on the anticipated course of the medial T2 and T3 intercostal nerves as potential recipient nerves given their proximity to recipient internal mammary vessels and also defined the T4 lateral intercostal nerve in its location lateral to the pectoralis major border (20). 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 latter taking intra-parenchymal routes to reach the sub-areolar region and innervate the NAC, which is why the deep branch is typically used for neurotization (21). Dissection in the inferolateral quadrant along the chest wall during other breast procedures including reduction mammoplasty and augmentation should be limited to avoid injury to these deep branches and potential associated NAC sensory loss (22,23).

With the increased attention paid to sensory nerves in the breast during mastectomy, there has also been a greater focus and interest in better understanding the sensory nerve anatomy to flaps used for autologous reconstruction, both to try to avoid sensory loss at the donor site and to allow for nerve harvest with flaps for intercostal nerve reconstruction or neurotization, which is particularly important in clinical settings where cadaveric nerve allograft is not available or cost-prohibitive. Authors have described the donor nerve(s) for sensate deep inferior epigastric perforator (DIEP) flap reconstruction utilizing the 10<sup>th</sup>-12<sup>th</sup> intercostal nerves in the upper abdomen (20,24). Zhou *et al.* additionally described limiting donor nerve harvesting to the more distal, sensory portion of those caudal intercostal nerves to optimize nerve reconstruction and outcomes (25).

### Immediate sensory nerve reconstruction: technique and outcomes

Although more recent attention has been paid to post-mastectomy sensation loss and restoration, including in the lay press (26), the foundation for sensory preservation and breast nerve reconstruction was actually laid several decades ago. Early studies focused on delayed autologous reconstruction, with initial reports describing the use of neurotized transverse rectus abdominis musculocutaneous (TRAM) flaps to help restore chest sensation (27). As autologous flap reconstruction has evolved to muscle-sparing options, neurotization with these flaps has been reported as well, initially primarily in the setting of delayed reconstruction using direct neurotization (28,29).

Performing immediate neurotized autologous reconstruction at the time of mastectomy has been adopted by many microsurgeons in recent years, particularly as timing of reconstruction has shifted towards immediate rather than delayed (30). Neurotization with immediate flap reconstruction is typically described in a similar fashion to that performed during delayed reconstruction, with a nerve from the flap coapted either directly to medial or lateral intercostal nerves or by using a nerve allograft (31). Other studies have reported neurotization of the NAC from a lateral intercostal nerve identified during the mastectomy without any neural connection to the flap, with excellent rates of sensory return (32). Emphasis on standardization of technique and outcomes measurements has been seen in recent years to help optimize outcomes, including the creation of a multi-site prospectively collected registry that has been shown to have promising early results (33). Most recently, Djohan *et al.* reported outcomes from a large case-control study looking at neurotization with nerve allografts in combination with nerve conduits during abdominally based free flap reconstruction, with significantly improved sensation seen at 1-year follow-up in the neurotized cohort (34). Another large study assessing delayed-immediate reconstruction with neurotized DIEP flaps showed return to baseline sensation in nearly all quadrants of the breast at 2-year follow-up (35). Although there is certainly a learning curve in performing flap neurotization as with any procedure, in the hands of experienced microsurgeons the additional operative time for performing neurotization is minimal (36).

Particularly with more widespread usage of cadaveric nerve allografts and success using allografts for larger gap reconstructions in the extremities (37), there has been increasing exploration of the option of neurotization with implant-based reconstruction where the donor nerves

used in flap reconstruction are not available. Our previously reported work presented proof of concept and efficacy data on intercostal nerve preservation as well as NAC neurotization done at the time of NSM in the setting of immediate, prepectoral, direct-to-implant reconstruction (38). Results from 32 mastectomies in 17 patients showed preservation of sensation as measured with two-point discrimination in 88% of cases. In total, 94% of patients had gross sensation to light touch throughout all four quadrants of their mastectomy skin. Another similar study from Djohan *et al.* reporting on their early results of patients undergoing NAC neurotization with cadaveric allografts at the time of implant-based reconstruction also demonstrated efficacy of this approach (39). Their study presented sensory outcomes from 15 mastectomies in 8 patients using a pressure-specified sensory device to assess sensation. They found overall improvements in mastectomy skin and NAC sensation with NAC neurotization and have highlighted in this work and others (40) the importance of careful nerve identification and preservation by the oncologic surgeon whenever possible, a sentiment echoed by other teams implementing this approach in their practice as well (41).

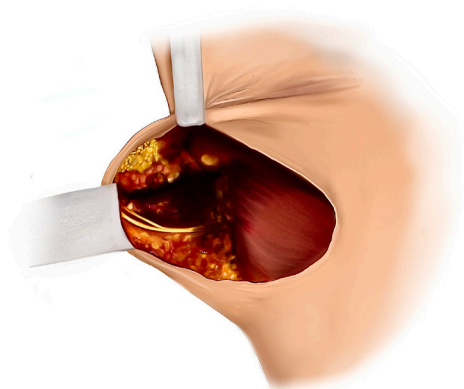
An additional important clinical area where sensation preservation and NAC neurotization are relevant is gender-affirming mastectomy. In recent years, several groups have described their outcomes performing NAC neurotization at the time of gender-affirming mastectomy (42,43). In these studies, primary repair is performed either with coaptation of lateral intercostal nerves to subareolar nerve ends or direct coaptation to skin, with significant improvement in nipple, areolar, and peripheral breast skin sensation demonstrated with these approaches by 1-year follow-up.

Although restoration of sensation following mastectomy is not a new concept to some degree, the recent increased focus on preserving sensation at the time of mastectomy and sensory assessment to track outcomes has highlighted the importance of defining terms and addressing the limitations of current research. *Table 1* describes different technical aspects of the procedures and when they might be utilized. Published recent studies on sensory outcomes vary widely with regards to approach used and heterogeneity of techniques even within the study, which makes comparison across studies challenging. Additionally, there are few prospectively assessed studies including baseline/pre-operative sensory assessment and patient-reported outcomes and no randomized controlled data, which is certainly a limitation of the current literature and ones that will hopefully be addressed with future studies as

**Table 1** Definition of terms and techniques for sensory restoration and preservation

Term/technique	Definition	Technical pearls/details
Neurotized flap reconstruction	Coaptation of flap donor nerve to recipient intercostal nerve using direct repair, nerve conduit, or nerve allograft	Most frequently done with DIEP flap reconstruction; anterior branch of third intercostal nerve typically preferred to lateral given proximity to donor vessels
NAC neurotization	Targeted reinnervation of the NAC from the lateral intercostal nerve using either direct repair or repair with nerve allograft or autograft	Connector-assisted repair can be done if a subareolar nerve target can be identified; if not, coaptation to the dermis can be performed
Sensation-preserving mastectomy	Combined approach of nerve reconstruction/NAC neurotization and nerve preservation of lateral and medial intercostal nerves that can be safely preserved from an oncologic standpoint	Requires team approach of breast oncologic and reconstructive surgeons; can be performed with any type of reconstruction and aesthetic flat closure

DIEP, deep inferior epigastric perforator; NAC, nipple-areolar complex.

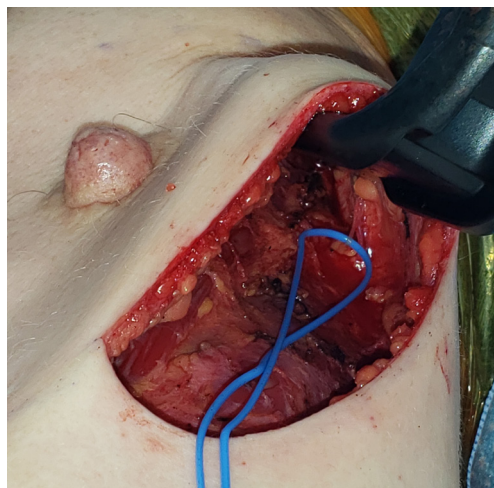


**Figure 1** Schematic depiction of a preserved T4 intercostal nerve that has been preserved and is seen coursing directly from its emergence at the intercostal space into the lateral subcutaneous tissues.

implementation of these approaches becomes more widely adopted into clinical practice.

### Pearls and pitfalls for implementation

We began performing what we have termed “sensation-preserving mastectomies” primarily with immediate implant-based reconstruction but also with aesthetic flat closure and DIEP flap reconstruction in our practice in February 2018 and have now done over 800 of these procedures. The technique, which has been previously described (38), involves both intercostal nerve preservation and nerve grafting from intercostal nerves to subareolar nerves. Briefly, during mastectomy (almost exclusively NSM in our practice), care is taken during the lateral dissection to preserve the lateral, superficial branches of the 3<sup>rd</sup>, 4<sup>th</sup>, or 5<sup>th</sup> intercostal nerves



**Figure 2** An intraoperative photograph demonstrating the anatomy seen in *Figure 1* on the contralateral side. The T3 intercostal nerve is seen within the vessel loop entering the subcutaneous tissues lateral to the lateral border of the pectoralis major muscle.

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 (*Figures 1,2*). 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 (*Figure 3*).

Through our experience with this technique, in addition to teaching other breast oncologic and reconstructive teams how to perform the procedure and help them incorporate it into practice, we have developed a set of recommendations



**Figure 3** An intraoperative photograph showing the trajectory of T4 intercostal nerve as it was passing through the parenchyma which has now been removed. In this case, the deep and superficial branches course into one nerve trunk distally. Approximately 6 cm of the nerve was able to be preserved prior to the need for transection.

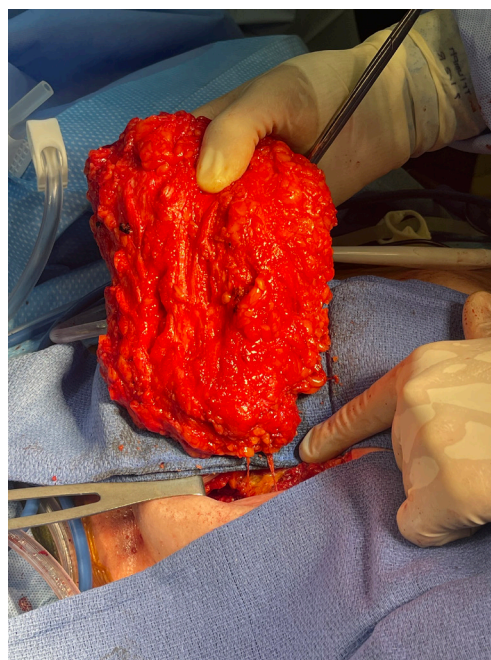
and “tips and tricks” for implementation.

### *Team approach*

Although well-coordinated care between the breast and plastic surgeons is best even for traditional mastectomy and reconstruction, it is essential for sensation preserving approaches. Identifying intercostal nerves that can be preserved and carefully dissecting out the ones to length that will be used for reconstruction is ideally done under loupe magnification jointly by the breast and plastic surgeons. Having microsurgical experience can help facilitate efficient nerve repair and reconstruction. Together the breast oncologic and reconstructive surgeons can determine the best “choreography” for their team with regards to identifying and repairing nerves and where these steps will fit into their overall mastectomy and reconstruction surgical plan.

### *Initial patient selection*

There is certainly a learning curve to identifying intercostal nerves, dissecting them out to length, and identifying a distal



**Figure 4** A near-complete extirpation of the breast tissue demonstrating a co-dominant nerve supply including both the T4 and T5 intercostals heading intra-parenchymal. Both nerves were ultimately transected distally and the more caudal and smaller nerve was harvested as an autograft to complete the nerve reconstruction in a manner similar to that depicted in the prior figure.

subareolar nerve target for reconstruction. To optimize this process and outcomes in early cases, ideal candidates would be patients having prophylactic mastectomy so that tumor location does not need to factor in to the nerve dissection, minimal ptosis, no history of radiation or plan for adjuvant radiation, and smaller reconstruction planned (ideally large B cup or smaller). By selecting patients with shorter distances to traverse for the nerve reconstruction, tension-free repair with either an autograft or allograft is more likely to be successful, plus return of sensation should occur more quickly and more completely.

### *Nerve identification and reconstruction*

As was described earlier in anatomic studies, we have found that the lateral intercostal nerves can almost always be identified within 1 to 2 cm of the lateral border of the pectoralis major muscle. We find that the ideal time to identify these is to look for them when the breast is being taken off of the chest wall from superior-medial to inferior-lateral (*Figure 4*). With this approach, significant native nerve length can often be achieved, as well as identification

of other non-dominant nerves that could be used for an autograft. For identification of the subareolar nerves, the nerve fibers are usually located adjacent to subareolar vessels which are typically located in a radial spoke-like configuration in this region (*Figure 5*). These tissues can be distinguished from the subareolar dermal tissues, which are



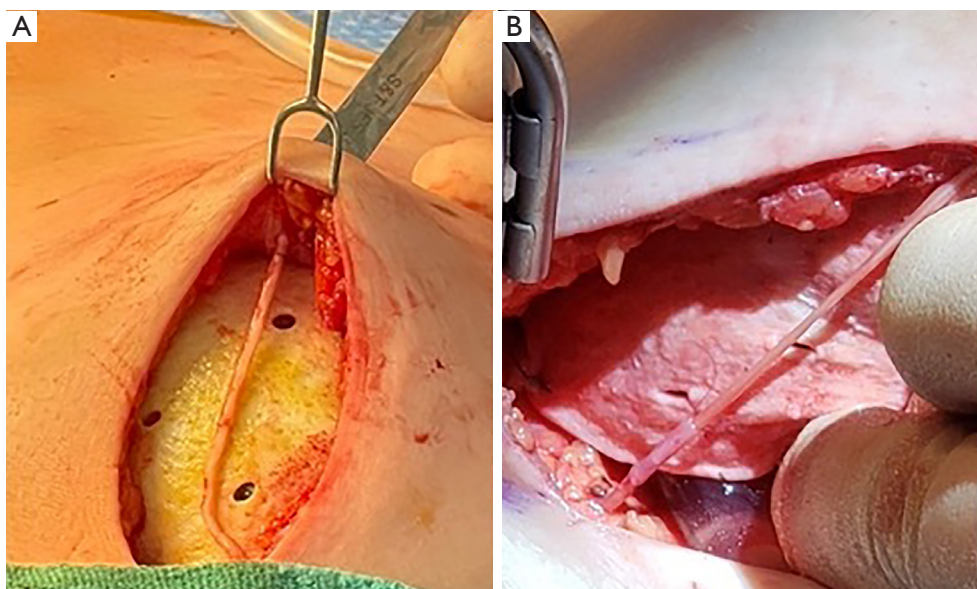
**Figure 5** A subareolar nerve that has been identified and dissected so that an end-to-end nerve reconstruction can be performed.

typically localized in a concentric pattern.

For the nerve reconstruction, using an implant sizer initially to measure the gap can be helpful to determine the ideal nerve graft length for a tension-free repair. We recommend selecting a nerve allograft that is at least 1cm longer than the measured gap with the sizer in place to ensure there is no tension on the final repair. While we were initially using 7 cm nerve allografts for all reconstructions, over time with increasing lengths of native nerve we often use 5 cm grafts and are frequently shortening those to some degree. Although we have not yet formally assessed our outcomes with different nerve allograft lengths, anecdotally while we have seen longer time for return to sensation with longer allografts, we have not seen overall decreased sensory return, consistent with data on other peripheral nerve repair sites (37). Minimizing suture burden is important to prevent intraneural scarring and to optimize neuronal growth through the coaptation. When a notable size mismatch is seen at one or both of the nerve coaptation sites, a nerve connector can be helpful to reduce tension at the site and to minimize collateral sprouting (44) (*Figure 6*).

## Conclusions

Immediate sensation restoration through nerve preservation



**Figure 6** The final nerve reconstruction is completed and demonstrated here located superficial to the acellular dermal matrix. (A) A nerve connector can be seen over the central portion of the allograft which will subsequently be slid over the coaptation site to complete a connector-assisted repair. (B) Completed connector-assisted repair.

or repair during 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. Assessment of outcomes using these approaches demonstrate not only superior return of sensation, but also significant reduction or even elimination of chronic neuropathic pain. Expansion of these techniques more widely into clinical practice will allow for more advanced understanding of outcomes, optimization of patient selection, and technical developments that will dramatically improve the experience and quality-of-life for patients undergoing mastectomy.

### Acknowledgments

*Funding:* None.

### Footnote

*Provenance and Peer Review:* This article was commissioned by the Guest Editors (Tine Engberg Damsgaard, C. Andrew Salzberg and Jørn Bo Thomsen) for the series “Hot Topics in Breast Reconstruction World Wide” published in *Gland Surgery*. The article has undergone external peer review.

*Peer Review File:* Available at <https://gs.amegroups.com/article/view/10.21037/gS-23-416/prf>

*Conflicts of Interest:* Both authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gS-23-416/coif>). The series “Hot Topics in Breast Reconstruction World Wide” was commissioned by the editorial office without any funding or sponsorship. A.W.P. is a consultant and speaker for Allergan (Abbvie), Sientra, and Axogen. Z.M.P. is a consultant and speaker for Axogen. The authors have no other conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All clinical procedures described in this study were performed in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for the publication of this

article and accompanying images.

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**Cite this article as:** Peled AW, Peled ZM. Sensate immediate breast reconstruction. *Gland Surg* 2024;13(4):552-560. doi: 10.21037/gs-23-416