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Nipple-Areolar Complex Neurotization in Implant-Based Breast Reconstruction: A Narrative Review of Anatomy, Surgical Techniques, and Clinical Outcomes

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Nipple-Areolar Complex Neurotization in Implant-Based Breast Reconstruction: A Narrative Review of Anatomy, Surgical Techniques, and Clinical Outcomes

Daniel Maliszewski [1,*], Wiktoria Stańkowska [2], Artur Bocian [3], Joanna Kufel-Grabowska [4], Julian Krul [5], Rafał Tarkowski [6], Sylwia Jałtuszewska [7] and Wojciech Jan Makarewicz [8]

[1] Department of General and Oncological Surgery, Provincial Hospital in Słupsk, Słupsk, Poland
[2] Senocore Sp. z o.o., Nowy Sącz, Poland
[3] Oncological Surgery Clinic, Holy Cross Cancer Centre, Kielce, Poland
[4] Clinic of Oncology and Radiotherapy, Medical University of Gdańsk, Gdańsk, Poland
[5] Department of General and Oncologic Surgery, M. Pirogow Provincial Specialist Hospital, Łódź, Poland
[6] Department of Surgical Oncology, Breast Unit, Regional Specialist Hospital Legnica, Poland
[7] Institute of Health Sciences, Pomeranian University in Słupsk, Słupsk, Poland
[8] 2nd Division of Radiology, Medical University of Gdańsk, Gdańsk, Poland
* Correspondence: danielmal2@gmail.com; Tel.: +48-501-784-896

Simple Summary

Nipple-sparing mastectomy with implant-based reconstruction can preserve the appearance of the breast, but it often leaves the nipple-areolar complex numb. This loss of sensation reduces protection from injury and may contribute to chronic chest-wall symptoms after surgery. To address this problem, surgeons have developed neurotization techniques that reconnect intercostal sensory nerves to the nipple during reconstruction using nerve grafts or adjacent nerve transfers. This review explains the key surgical anatomy that determines where donor nerves can be identified and safely managed, summarizes current approaches for nerve routing and coaptation around implants, and outlines what recent clinical studies suggest about safety, recovery timelines, operative complexity, and cost. The aim is to provide a practical, anatomy-based framework to help surgeons select appropriate donor nerves, choose reconstruction-compatible techniques, and counsel patients about realistic outcomes.

Abstract

Nipple-sparing mastectomy (NSM) with immediate implant-based breast reconstruction (IBBR) optimizes aesthetic outcomes, yet transection of intercostal sensory nerves commonly results in persistent nipple-areolar complex (NAC) anesthesia and, in some patients, denervation-related symptoms. NAC neurotization has emerged as an intraoperative strategy intended to improve protective sensation and potentially erogenous sensation by reconnecting donor intercostal nerves to the retroareolar plexus or to targets within the nipple. Here, we provide an anatomy-first narrative synthesis of the medial and lateral sensory corridors, with emphasis on the lateral cutaneous branches of T3–T5 and the reported anatomical landmarks that facilitate donor identification during NSM. We then review the biological constraints governing regeneration across the long trajectories typical of IBBR, including evidence suggesting reduced performance of acellular nerve allografts with increasing gap length and the rationale for autologous nerve transfers. Technical approaches are organized by (i) donor selection and harvest depth, (ii) graft choice, and (iii) distal coaptation strategies ranging from subareolar stump coaptation to targeted NAC reinnervation and direct nipple neurotization techniques. We also summarize the current clinical evidence regarding sensory recovery kinetics, safety and complications, operative time and cost, and propose practical

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checkpoints for intraoperative decision-making and standardized postoperative assessment. Collectively, available data support NAC neurotization as a feasible adjunct to NSM-IBBR, while highlighting the need for harmonized outcome reporting and longer follow-up to define comparative effectiveness among techniques.

Keywords: nipple-sparing mastectomy; implant-based breast reconstruction; nipple-areolar complex; neurotization; intercostal nerves; sensory restoration; nerve graft; nerve allograft; autograft; targeted reinnervation

1. Introduction

The surgical management of breast cancer has undergone a major shift from radical resections toward increasingly refined, tissue-preserving techniques. Today, nipple-sparing mastectomy (NSM) combined with immediate implant-based breast reconstruction (IBBR) is widely used in both therapeutic and risk-reducing settings. Long-term data suggest that NSM is not associated with significant differences in overall survival or breast cancer-specific survival compared with total mastectomy, supporting its oncologic safety in appropriately selected patients [1]. From an aesthetic perspective, preservation of the native breast skin envelope and the nipple-areolar complex (NAC) can produce outcomes that more closely resemble the natural breast and reduce the visible impact of extirpative surgery.

Despite these morphological advantages, standard NSM and IBBR commonly result in substantial sensory loss affecting the breast and NAC. Because extirpative dissection severs the intercostal sensory nerves supplying the breast skin and nipple, many patients are left with a numb reconstructed breast, with diminished or absent nipple sensation reported in up to 75% of cases [2,3]. Historically, this sensory loss was often accepted as an unavoidable consequence of oncologic treatment. However, as survivorship has improved, its impact on quality of life has gained increasing clinical attention and has been recognized in both the scientific literature and lay press as the problem of “numb new breasts” [4].

The consequences of an insensate breast extend beyond dissatisfaction with appearance or altered body image. Loss of protective sensation may increase the risk of thermal injury from common external heat sources, including heating pads, hot water bottles, or sun exposure [5]. In addition, reduced erogenous sensation and the development of post-mastectomy pain syndrome (PMPS), phantom breast pain, or neuroma-related symptoms may adversely affect psychosocial and sexual well-being [6,7]. As a result, patients and reconstructive surgeons are increasingly prioritizing not only restoration of breast form, but also recovery of sensory function [8,9].

To address this deficit, NAC neurotization has emerged as an intraoperative strategy intended to improve sensory recovery by reconnecting donor intercostal nerves to the retroareolar plexus or to targets within the nipple [10]. Although sensory restoration has been explored in autologous flap reconstruction for more than two decades [11], achieving reliable reinnervation in the more commonly performed IBBR setting remains challenging. Surgeons must navigate variable anatomy and bridge transected nerve stumps across the implant pocket to the NAC. This effort is constrained by the biology of nerve regeneration over long distances, the cost of acellular nerve allografts [12], and experimental evidence suggesting reduced regenerative performance in long grafts associated with Schwann cell senescence [13].

This narrative review provides a practical, anatomy-based framework to guide donor nerve selection, technique choice, and patient counseling in NAC neurotization during NSM-IBBR. We present an anatomy-first synthesis of the medial and lateral sensory pathways, with particular emphasis on the lateral cutaneous branches of T3–T5 and the reported landmarks that facilitate their identification during NSM. We then review the biological and technical considerations relevant to nerve grafting and transfer in IBBR, including the constraints of long regenerative trajectories and the rationale for autologous alternatives. Finally, we examine nerve routing within the implant

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pocket and summarize the principal contemporary strategies for distal target management at the NAC.

Unlike prior reviews that primarily summarize sensory outcomes or pool heterogeneous reconstructive settings, this review focuses specifically on nipple-sparing mastectomy with implant-based breast reconstruction as a distinct technical problem. Rather than emphasizing outcome pooling alone, we adopt a technique- and decision-pathway-focused approach centered on donor-nerve availability, graft-length biology, nerve-routing constraints, and distal target selection. By organizing the field around these reconstructive constraints, we aim to provide a practical anatomy-based framework for choosing among preservation, autograft, allograft, and targeted reinnervation strategies in oncologic implant reconstruction.

1.1 Scope and Literature Search

This article is a narrative review based on targeted searches of PubMed and Google Scholar conducted through February 2026. Search strings combined terms related to nipple-sparing mastectomy, implant-based breast reconstruction, breast neurotization, intercostal nerves, targeted reinnervation, and nipple or breast sensation. Reference lists of key anatomical studies, technical reports, and recent reviews were also hand-screened to identify additional relevant publications. We prioritized peer-reviewed studies that informed four domains: (i) surgical anatomy and donor-nerve landmarks, (ii) operative technique and target selection, (iii) biological constraints relevant to graft length and regeneration, and (iv) clinical outcomes, including sensation, denervation symptoms, complications, operative burden, and cost. Because the literature remains limited and heterogeneous, emphasis was placed on high-yield anatomical studies, technical reports, comparative cohorts, randomized evidence where available, and recent systematic reviews used to contextualize consistency and gaps in the field.

2. Surgical Anatomy of Breast Sensation

Successful neurotization requires a precise, granular understanding of the sensory nerve distributions and neurovascular territories that supply the breast skin. The primary sensory innervation of the breast is derived from two principal pathways: a medial corridor and a lateral corridor.

2.1 The Medial and Lateral Corridors

The medial corridor is supplied by the anterior cutaneous branches of the intercostal nerves (AICNs), typically arising from the second to sixth intercostal spaces [14]. After emerging parasternally and piercing the deep fascia and pectoralis major, these nerves divide into medial and lateral branches. The medial branches supply the skin directly over the sternum and course away from the breast, remaining outside the standard mastectomy field. By contrast, the lateral branches of the AICNs course toward the gland and supply the medial breast, providing the principal medial sensory contribution to the NAC [14,15].

The utility of the AICNs depends strongly on reconstructive context. In autologous reconstruction, the second and third AICNs are useful recipient nerves because they are naturally exposed during preparation of the internal mammary vessels and require no additional dissection. In deep inferior epigastric perforator (DIEP) reconstruction, this branch may represent the preferred option for reinnervation because, even with a short pedicle, it allows a stable coaptation with less technically demanding dissection. In implant-based reconstruction, however, they are generally less favorable for NAC reinnervation because they provide limited usable length and are vulnerable to transection or traction injury during medial mastectomy dissection.

Because of these limitations, contemporary NAC neurotization strategies primarily rely on the lateral cutaneous branches of the intercostal nerves (LICNs) [16]. These nerves emerge near the mid- to anterior axillary line and divide into anterior and posterior branches. The posterior branches

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course laterally and posteriorly to supply the lateral torso and back, whereas the anterior branches travel medially across the serratus anterior and pectoralis major toward the breast parenchyma and NAC. Their trajectory, caliber, and accessibility make the anterior branches of the LICNs the principal donor nerves used in breast and NAC reinnervation.

2.2 The Dominant Donor Nerve: The T4 Lateral Branch

Most anatomical studies identify the lateral cutaneous branch of the fourth intercostal nerve (T4) as the dominant sensory supply to the NAC. A recent meta-analysis of anatomical dissection studies reported T4 contribution to the NAC in approximately 89% of cases [15]. Upon emerging from the intercostal space, the lateral cutaneous branch divides into anterior and posterior divisions. In clinical practice, surgeons typically identify, preserve, and coapt the anterior division. The anterior division of T4 follows a relatively predictable trajectory toward the nipple, approximately at the 8 o'clock position in the right breast and the 4 o'clock position in the left breast. While the anterior division remains the standard clinical target, the posterior division, which courses away from the breast to supply the skin of the lateral torso and back, may also be harvested as an expendable free autograft when additional graft material is required.

However, reliance on T4 alone is an oversimplification. Anatomical studies indicate that the anterior divisions of the T3 and T5 lateral branches may also contribute to the NAC and inferior pole sensation, with reported frequencies of approximately 64% and 33%, respectively [15]. For this reason, contemporary surgical algorithms often emphasize identification and preservation of the anterior divisions of T3, T4, and T5 in order to maximize available axonal input for reinnervation [17–19].

The course of the anterior divisions may vary in depth before reaching the NAC. Some branches remain relatively superficial within the subcutaneous fat, whereas others follow a deeper trajectory through the breast parenchyma or along the pectoral fascia before looping anteriorly toward the NAC [17,18]. This variation is surgically important. Branches that remain superficial may sometimes be preserved, but deeper branches that traverse the glandular tissue being removed cannot be safely spared without compromising oncologic dissection. Recognizing this deep looping pattern early therefore helps guide operative strategy: rather than attempting to preserve a nerve intimately associated with the gland, the surgeon may dissect it several centimeters into the breast parenchyma and sharply divide it to obtain a longer proximal stump at the chest wall for subsequent grafting.

2.3 Surgical Landmarks and the "Danger Zone"

Locating these nerves intraoperatively requires precise triangulation. In a cadaveric study, the T4 lateral branch emerged at a mean distance of 13.1 ± 1.3 cm from the sternal border and 11.8 ± 2.2 cm from the midclavicular line [20]. Of greatest intraoperative importance, the nerve was found to emerge at the lateral border of the pectoralis minor muscle or within 2 cm of this border. This defines the surgical "Danger Zone": a 2-cm-wide vertical strip along the lateral pectoral border where electrocautery should be exchanged for blunt dissection in order to identify the emerging nerve stalks and avoid iatrogenic thermal injury [17,20]. The T4 branch typically measures approximately 2.0 mm in diameter, which is generally adequate for microsurgical coaptation (Table 1) [20].

Table 1. Anatomy-based landmarks and donor nerve options commonly used for NAC neurotization in NSM-IBBR.

Donor nerve	Landmark(s) for identification	Practical notes
T4 lateral cutaneous branch (LICN)	Emerges near the anterior mid-axillary line at/near the lateral border of pectoralis	Dominant contributor to NAC sensation; typically ~2 mm caliber; often paired with a

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	minor; cadaveric measurements ~13.1 ± 1.3 cm from the sternal border and ~11.8 ± 2.2 cm from the midclavicular line.	'sentinel' perforator within a neurovascular bundle.
T3 and T5 LICNs	Adjacent interspaces above/below T4; similar exit zone near the lateral pectoral border.	Supplement axon count and coverage of superior/inferior breast pole; may reduce effective graft length depending on target quadrant.

2.4 Mastectomy Incision Planning and Nerve Exposure

Locating these neurovascular landmarks intraoperatively begins with optimal mastectomy incision planning. Contemporary literature emphasizes that successful nerve preservation is highly dependent on surgical access. Coopey et al. and Gfrerer et al. both note that neurotization during IBBR is most easily performed through a radial or inframammary fold (IMF) [17,19]. Importantly, when utilizing an IMF approach, the incision must be planned more laterally than a standard cosmetic IMF incision—typically beginning at the breast meridian and extending along the lateral fold.

This specific inferolateral approach provides superior direct visualization and exposure of the lateral intercostal nerves as they emerge from the "Danger Zone" at the pectoralis border. Through this optimal exposure, the surgeon can initially localize the dominant T4 lateral branch to thoroughly evaluate its quality, caliber, and available length. If the primary T4 branch is damaged by the extirpative dissection or is deemed inadequate to facilitate a tension-free repair, this wide lateral access allows the surgeon to systematically extend the dissection to identify and harvest the adjacent T3 or T5 branches from within the same surgical field before proceeding with the reconstruction.

2.5 The Deep Neurovascular Anatomy

While the cutaneous branches serve as the primary sensory conduits to the skin and NAC, successful harvesting depends on recognizing their relationship with adjacent nutrient vessels. Anatomical studies show that the T4 nerve does not travel in isolation; rather, it is often accompanied by small perforating arteries and veins derived from the lateral thoracic or intercostal systems, together forming a local neurovascular bundle [20]. Preserving this bundle may offer a reconstructive advantage because, rather than stripping the vessels and devascularizing the neural tissue, it may help maintain vascular support to the graft. In addition, this approach encourages hemostasis with micro-clips rather than electrocautery, thereby reducing the risk of thermal injury to adjacent axons [17].

Tracing this neurovascular relationship proximally reveals the deep anatomy of the main intercostal nerve trunk, which is central to modern autologous neurotization techniques [21]. The main intercostal nerves travel anteriorly within the intercostal spaces along the subcostal groove at the inferior border of the corresponding ribs. In this location, the nerve remains part of the primary neurovascular bundle, coursing alongside the intercostal artery and vein and lying in close proximity to the parietal pleura before piercing the thoracic musculature to form its cutaneous divisions. During proximal dissection, the thoracodorsal vessels serve as a useful anatomical landmark, as the lateral intercostal nerve usually travels deep to these vessels before piercing the external intercostal and serratus anterior muscles. Within this neurovascular bundle, the structures are routinely arranged from superior to inferior as vein, artery, and nerve. Knowing this consistent anatomical relationship is crucial to avoid incidental vessel damage during nerve preparation.

From a practical standpoint, these anatomical data support a stepwise reconstructive hierarchy. When the anterior division of T4 can be identified and preserved without compromising oncologic dissection, it remains the preferred donor. When T4 is short, thin (in comparison to T3 and T5), deeply

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embedded, or oncologically inseparable from the gland, the surgeon should instead think in terms of a donor set rather than a single donor, incorporating T3 and T5 branches to increase axonal input and to reduce effective graft distance depending on the chosen NAC target [17–19].

3. Surgical Approaches to NAC Neurotization

3.1 Bridging the Nerve Gap: Biological and Surgical Considerations

While identifying the T3–T5 donor nerves is the critical first step for successful neurotization, the surgeon must then overcome the anatomical distance to the NAC. Recent anatomical and clinical assessments suggest that the average total nerve length required to reach the NAC in implant-based reconstruction is approximately 12.3 cm [22]. Standard mobilization of the anterior intercostal nerve stumps typically yields only 5.3 to 5.6 cm of usable length, resulting in a distinct nerve gap that routinely necessitates an interposition graft averaging 6.9 cm [22].

3.1.1 Acellular Nerve Allografts

To bridge this extensive gap, early implant-based neurotization strategies frequently relied on processed acellular nerve allografts (ANAs). However, the use of ANAs presents both financial and biological limitations. Financially, utilizing commercial nerve allografts adds a substantial mean cost of approximately $7,839 per breast [12]. Furthermore, the widespread adoption of ANAs has been supported in part by industry-funded literature, despite a lack of independent, high-quality comparative evidence demonstrating clear superiority over autografts [23]. Biologically, ANAs act as empty scaffolds that rely entirely on the host's living Schwann cells to migrate into the graft, proliferate, and pull regenerating axons across the gap. Basic science models demonstrate that while ANAs perform well in short gaps, they exhibit severely limited axonal regeneration at lengths of 40 mm and frequently fail to support regeneration at lengths of 60 mm or greater. Populating these long grafts places a substantial proliferative demand on host Schwann cells, causing them to undergo "cellular senescence"—a state of permanent growth arrest in which they cease to support axonal regeneration and may halt the advancing regenerative front before it reaches the target [13].

3.1.2 The Shift to Autologous Nerve Utilization

To overcome this deficit without relying on costly or biologically limited ANAs, contemporary surgical algorithms exploit the inherent anatomical redundancy of the chest wall. Meticulous proximal dissection of the lateral intercostal nerves can yield extended autologous segments of 9.0 ± 1.5 cm (up to 10.5 cm), occasionally permitting direct, tension-free coaptation to the NAC [21]. Alternatively, if the anterior division of the T4 lateral cutaneous branch is of insufficient length, the anterior divisions of T3 or T5, posterior divisions, or the medial branches of the anterior cutaneous nerves may be harvested from the mastectomy field and used as free nerve autografts to bridge the gap [18]. From a technical standpoint, utilizing an IMF incision facilitates the optimal initial exposure and evaluation of the dominant T4 branch; if intraoperative assessment reveals this nerve to be of inadequate length or caliber, this approach allows the surgeon to systematically extend the dissection from lateral to medial to identify and harvest the adjacent T3 or T5 branches [17].

3.2 Donor Nerve Harvesting Techniques

The foundation of successful NAC neurotization lies in securing an adequate donor nerve and, when necessary, sufficient autologous grafting material from the local mastectomy field. Based on patient anatomy and the required nerve length, two primary harvesting strategies are described in the literature: the deep main trunk harvest and superficial lateral branch transfer.

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3.2.1 Deep Main Trunk Harvest

When superficial nerve stumps are too short to allow for a tension-free direct coaptation to the nipple, a "deep harvest" can be performed to obtain a lengthy, vascularized intercostal nerve autograft directly from the mastectomy field. As pioneered by Chang et al. [21], this technique begins by tracing the transected lateral cutaneous branch proximally toward the chest wall. To access the deep intercostal space, the pectoralis major muscle is split parallel to its fibers. A self-retaining retractor is then applied to expose the subcostal groove at the inferior border of the respective rib.

At this level, the surgical anatomy becomes highly delicate and typically requires the use of an operating microscope. The main intercostal nerve travels as part of a neurovascular bundle, coursing intimately alongside the intercostal artery and vein, and lying in close proximity to the thin parietal pleura [21]. Fine bipolar cautery under microscopic magnification may be used to carefully separate the nerve from the accompanying vessels and achieve precise hemostasis, while strictly avoiding thermal or mechanical injury to the underlying pleura. By dividing the main branch more medially (near the sternum), the surgeon can harvest a robust, living autologous nerve graft of up to 20 to 25 cm. This may provide sufficient length to traverse the dome of a breast implant without tension [21]. The graft should be positioned in an antegrade orientation, allowing its fine branches to sprout outward properly and reinnervate the regional tissue and surface sensory receptors underneath the mastectomy skin flap.

Because this technique involves dissecting directly over the pleura, concerns regarding respiratory morbidity are understandable. However, a recent safety analysis evaluating donor-site morbidity following deep intercostal harvest found no statistically significant increase in major pulmonary complications, such as pneumothorax, when compared to standard non-neurotized reconstructions [24]. While the rate of postoperative pleural effusion was slightly higher in the neurotized cohort (12% vs. 4%), the vast majority of these cases were entirely asymptomatic, did not require invasive intervention, and were successfully managed with conservative treatment [24].

3.2.2 Superficial Lateral Branch Transfer and Posterior Branch Utilization

A less invasive alternative to the deep trunk harvest involves exploiting the inherent anatomical redundancy of the superficial lateral cutaneous branches. As previously established, current algorithms emphasize preservation of the T4 lateral branch as the primary sensory conduit. However, the adjacent T3 and T5 lateral branches are also routinely exposed during the extirpative dissection [17]. Rather than discarding these segments, surgeons can meticulously dissect and harvest the anterior divisions of these expendable adjacent nerves to serve as free autografts [18,21].

Technically, these superficial branches are best identified early in the mastectomy procedure. By applying gentle upward traction to the lateral breast tissue with a lighted retractor, the surgeon causes the nerves to physically “tent” approximately 1 to 2 cm lateral to the pectoralis major border, facilitating their early identification [17]. It is advisable to avoid the use of heavy electrocautery near these structures to prevent irreversible thermal axonal injury, relying instead on blunt dissection and micro-clips to manage small adjacent perforating vessels.

Furthermore, surgical strategy must account for complex or unfavorable anatomy. If the primary anterior branches are inadequate, the surgeon can trace and harvest these posterior divisions from within the existing surgical field, repurposing them as additional free grafting material. This maneuver ensures sufficient autologous tissue to construct the "neural bridge" – the vital interpositional conduit connecting the proximal viable nerve stump to the denervated NAC – without needing to use ANAs or access a distant, morbid donor site, such as the sural nerve [19].

Generally, in the implant-based setting, the attractiveness of acellular allograft declines as the required regenerative distance lengthens and as cost becomes harder to justify in the absence of high-quality comparative data. Accordingly, autologous local nerve strategies may be particularly compelling when the anticipated gap is long, adjacent expendable branches are available, and the surgical team is comfortable with additional dissection.

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3.3 Proximal Coaptation and Routing

Once donor nerves and graft material have been selected, proximal coaptation is performed, and the graft is strategically routed over the breast implant to reach the intended distal target. This phase of the operation is technically demanding and requires careful consideration of the tension placed on the nerve graft, as well as the prophylactic management of any newly created nerve stumps.

3.3.1 Management of the Proximal Stump and Neuroma Prevention

When utilizing adjacent expendable nerves (such as the T3 or T5 branches) as free autografts, the surgeon inherently creates new, raw proximal nerve stumps at the lateral chest wall. If left unaddressed, these actively regenerating stumps may form painful, symptomatic neuromas or contribute to PMPS. To ensure that restoration of nipple sensation does not come at the cost of donor-site pain, these proximal stumps should be managed prophylactically. Contemporary algorithms recommend targeted muscle reinnervation (TMR), in which the proximal nerve end is coapted to a small, expendable motor branch of the serratus anterior or pectoralis muscle, providing the regenerating axons with a physiological target [18]. Alternatively, the nerve end can be buried deep within the serratus muscle belly to provide a non-stimulatory environment. In patients considered at elevated risk for pain, a randomized controlled trial demonstrated that performing a "centrocentral" coaptation—directly connecting two adjacent transected intercostal nerve stumps into a closed loop—significantly reduced neuropathic pain scores in the early postoperative period without the need for additional grafting [6].

3.3.2 Routing and Tension Management

Regardless of whether an allograft or autograft is utilized, the physical routing of the neural construct over the breast implant is an important determinant of success. The required arc length of the nerve increases significantly once the final implant is positioned. A nerve coaptation that appears tension-free in an empty or deflated mastectomy pocket may become dangerously taut, or even avulse, upon closure or implant inflation [19].

To mitigate this, standard 5 cm allografts are frequently insufficient, emphasizing that "one size does not fit all" and highlighting the importance of taking final nerve length measurements only after the final implant sizers are placed [22]. The graft must be routed carefully over the acellular dermal matrix (ADM) or implant capsule, avoiding sharp edges that could act as a fulcrum and cause compression injury. In two-stage tissue expander reconstructions, surgeons must create significant redundancy ("slack") in the nerve graft to accommodate future expansion volumes. Furthermore, the graft should be routed laterally or inferiorly to the planned incision site for the second-stage exchange procedure to prevent inadvertent iatrogenic transection of the revascularizing nerve construct [19]. A summary of common distal targeting strategies is provided in Table 2.

3.4 Distal Coaptation and Target Management

Once the nerve graft has been successfully routed over the implant, the final and often most technically decisive step is distal coaptation to the nipple-areolar complex. Because the extirpative dissection severs the terminal branches of the intercostal nerves unpredictably, surgeons face significant anatomical variability at the recipient site. Consequently, the contemporary literature supports three distinct surgical strategies for distal target management.

3.4.1 Direct Nerve Coaptation

The most anatomically intuitive approach involves identifying a specific, severed subareolar nerve stump on the undersurface of the preserved NAC. This technique can begin during the mastectomy with a "tug test"; applying gentle traction to the proximal lateral intercostal nerve can create a visible dimple in the skin along the lateral border of the NAC, acting as a visual guide to identify the distal nerve stump [10]. Dissection under the NAC must be performed sharply, with

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avoidance of electrocautery, to minimize irreversible thermal damage to these microscopic neurovascular structures. Once identified, the distal end of the nerve graft is coapted directly to this stump, often utilizing a connector-assisted repair to shield the anastomosis. While this method creates a direct neural bridge, its primary limitation is anatomical variability. It is frequently difficult to visually differentiate tiny subareolar nerve endings from transected lactiferous ducts or fibrous bands in the mastectomy flap. To overcome this, surgeons may utilize intraoperative frozen section confirmation or immunohistochemical identification of neural elements (such as S-100 staining) before committing to the coaptation [19].

3.4.2 Targeted NAC Reinnervation

To overcome the challenge of finding a distinct subareolar stump, contemporary algorithms employ targeted nipple-areolar complex reinnervation (TNR). Rather than relying on a single macroscopic nerve target, this technique targets the broader dermatosensory peripheral nerve elements of the NAC. The distal end of the nerve allograft or autograft is carefully split into smaller, individual fascicles [18,19]. These fascicles are then fanned out and sutured directly to the retroareolar dermis across multiple clock-face points. The distal fascicles should be secured with fine 9-0 nylon sutures in a manner that avoids strangulation of the delicate fascicles.

In specific reconstructive scenarios, such as free nipple grafting, surgeons can de-epithelialize the recipient site and create a small, full-thickness subcutaneous tunnel through the mid-NAC. The distal ends of the nerves are passed through this tunnel and spread out over the surface area before the nipple graft is sutured into place. This fascicular fanning approach maximizes the total surface area of the reinnervation zone and may reduce the risk of focal hypersensitivity or point tenderness at the nipple [18,19].

3.4.3 Direct Nipple Neurotization

A third, simplified alternative bypasses the broader subdermal plexus in favor of the dense neurotrophic targets within the nipple core. Recent technical reports describe anchoring the distal nerve graft directly into the base or inferior pole of the nipple stroma [21,25]. Utilizing a 9-0 nylon suture to secure the distal tip to the deep dermis, surgeons aim to deliver regenerating axons straight into the highly innervated central papilla. This technique is particularly useful when nipple projection is well preserved following oncologic resection. By embedding the nerve into the nipple base, this approach provides robust sensory input without the need for extensive microscopic fascicular dissection or the search for a distinct distal stump.

3.4.4 Practical Selection of Distal Strategy

In practical terms, direct nerve coaptation is most appropriate when a reliable distal stump can be identified and preserved without ambiguity. Targeted NAC reinnervation is preferable when no discrete stump is visible but the retroareolar dermis is intact and can serve as a broad biologic target. Direct nipple neurotization may be useful when nipple projection is preserved and a simpler bulk-target strategy is preferred. In staged or expander-based reconstruction, surgeons should be especially cautious with routing, redundancy, and future access incisions in order to protect the revascularizing nerve construct.

Table 2. Common distal targeting strategies for NAC reinnervation in implant-based reconstruction.

Distal strategy	Concept	Typical distal target	Key advantage(s)	Key limitation(s)
Direct stump coaptation	Coapt donor/graft to an identifiable	Discrete subareolar stump at lateral NAC border.	Single coaptation; anatomically intuitive.	Target may be absent/indistinct; risk of mistaking

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	subareolar nerve stump.			ducts/fibrous bands.
Targeted NAC reinnervation (fascicular fanning / 'sleeve')	Split distal graft into fascicles and distribute across the retroareolar plexus.	Retroareolar subdermal plexus (e.g., multiple clock-face points) ± central tunnel.	Addresses caliber mismatch; broad target surface; may reduce focal hypersensitivity.	More microsurgical steps; requires careful positioning to avoid implant contact/traction.
Direct nipple neurotization	Anchor distal graft within the nipple base/stroma as a bulk target.	Inferior pole/base of nipple stroma.	Simplified targeting when nipple projection preserved; avoids needing a visible stump.	Mechanistic assumptions about target density; technique-specific outcome data remain limited.

4. Clinical Outcomes and Safety

The clinical evidence base remains early and methodologically uneven. Most studies are single-center series or nonrandomized comparative cohorts with small sample sizes, heterogeneous sensory endpoints, inconsistent baseline testing, and variable follow-up duration. As a result, current data are sufficient to support technical feasibility and signal potential clinical benefit, but they do not yet permit confident ranking of distal targets, graft materials, or harvesting strategies within oncologic NSM-IBBR.

4.1 Sensory Restoration and Quality of Life

Available evidence suggests that sensory outcomes are substantially poorer after standard NSM without neurotization than after reconstructive strategies that attempt to restore neural continuity. In a large analysis of 460 non-neurotized NSM cases, up to 70.9% of patients had completely absent NAC sensation postoperatively [2]. By contrast, neurotized reconstructions have shown more favorable sensory recovery. Using quantitative pressure-specified sensory device (PSSD), one study reported that by 12 months, 75% of breasts achieved "excellent" moving pressure thresholds, with an additional 21% classified in the "good" range [26].

Sensory recovery also appears to correlate with improved quality of life. In a prospective cohort study comparing neurotized and non-neurotized IBBR, the neurotized cohort demonstrated significantly higher psychosocial and sexual well-being scores [7]. Patients with restored sensation also reported greater satisfaction with their reconstructive surgeon and care team, suggesting that functional restoration may carry meaningful psychological benefit in addition to sensory improvement [7].

The kinetics of sensory recovery are influenced by patient population and reconstructive context. A recent systematic review and meta-analysis found that TNR improved sensation across studied populations, with faster and more consistent recovery reported in female-to-male (FTM) gender-affirming mastectomies [27]. In those cohorts, up to 88% of patients regained erogenous sensation by 12 months [27]. This more rapid recovery has been attributed to younger patient age and the relative absence of prior oncologic surgery, radiation, or neurotoxic systemic therapy.

In contrast, sensory return in oncologic breast reconstruction appears slower and more variable. In breast cancer patients, meaningful sensory improvement may not become apparent until approximately 12 months postoperatively, with continued gains reported up to 24–60 months [2,21]. These observations reinforce the need to counsel patients that neurotization is not an immediate intervention, but rather a long-term regenerative process. Importantly, outcomes from gender-affirming mastectomy should not be assumed to translate directly to oncologic NSM-IBBR, because differences in patient age, flap biology, prior treatment exposure, mastectomy-plane characteristics, and reconstructive goals may materially affect regeneration and sensory testing.

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4.2 Mitigation of Post-Mastectomy Pain Syndrome (PMPS) and Denervation Symptoms

In addition to sensory recovery, neurotization may help reduce PMPS and other denervation-related symptoms. Historically, one concern surrounding nerve dissection during mastectomy was the possibility of generating painful neuromas. However, contemporary evidence suggests that proactive nerve management may reduce this risk by providing regenerating axons with a structured pathway and physiological target rather than leaving them untreated within the mastectomy bed.

This concept has been supported by a double-blind randomized controlled pilot trial in which patients who underwent intercostal nerve coaptation reported significantly lower Short-Form McGill Pain Questionnaire (SF-MPQ) scores at 6 months than non-neurotized controls ($p = 0.038$), consistent with a reduction in neuropathic pain [6]. Similarly, prospective clinical data suggest that neurotized patients may experience fewer denervation-related symptoms, including severe itching and dysesthetic discomfort [7].

Taken together, these findings suggest that the benefits of NAC neurotization may extend beyond restoration of protective and erogenous sensation to include mitigation of pain and other postoperative denervation phenomena.

4.3 Operative Safety and Oncologic Considerations

Current evidence indicates that incorporating neurotization into IBBR does not compromise overall perioperative safety. In a matched-pair comparison, Boyd et al. found no statistically significant increase in major complications, such as implant loss or return to the operating room, or minor complications, such as delayed wound healing or skin flap necrosis, when NAC neurotization was compared with standard non-neurotized reconstruction [12].

Despite this favorable perioperative profile, a persistent concern regarding broader adoption is the possibility that nerve preservation could compromise oncologic clearance. In particular, critics have argued that sparing the nerve and its surrounding tissue cuff, or attempting to preserve elements of the subareolar plexus, might require retention of tissue that could harbor occult ductal carcinoma. However, contemporary anatomical and operative protocols aim to mitigate this risk. Coopey et al. emphasize that meticulous dissection of the intercostal nerves can be performed without intentionally leaving excess breast tissue behind, thereby preserving oncologic safety margins at the NAC [17]. To further balance functional restoration with oncologic caution, some contemporary algorithms incorporate real-time pathological confirmation. For example, Millesi et al. describe a “Frozen Section First” protocol in which a biopsy from the retroareolar base is submitted for intraoperative frozen section analysis before nerve coaptation is performed [25]. At the same time, an important evidence gap remains. A 2025 systematic review noted the absence of long-term oncologic outcome data specifically evaluating local recurrence rates in neurotized cohorts [28]. Thus, while early perioperative and margin-related safety appear reassuring, rigorous long-term oncologic follow-up remains necessary before the full safety profile of this approach can be considered established.

5. Limitations of the Current Evidence

Several limitations constrain interpretation of the present literature. First, most reports are small, retrospective, and single-institutional, limiting external validity. Second, sensory outcomes are measured with nonuniform tools and at inconsistent time points, often without true preoperative baseline data. Third, patient populations are heterogeneous, with studies variably mixing oncologic reconstruction, prophylactic mastectomy, and gender-affirming procedures. Fourth, technique reporting is often incomplete, particularly regarding graft length, donor caliber, coaptation details, implant plane, and staged versus direct-to-implant reconstruction. Finally, long-term oncologic endpoints and formal cost-effectiveness analyses remain sparse. These limitations mean that current evidence is best interpreted as supportive of feasibility and biologic plausibility rather than as proof of a single optimal neurotization strategy.

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6. Standardizing Protocols and Future Directions

While early reports of breast neurotization are encouraging, broader adoption remains limited by methodological heterogeneity and unresolved economic concerns.

6.1 Standardizing Sensory Assessment and Study Design

A 2025 systematic review identified several major methodological weaknesses in the current breast neurotization literature, including reliance on small uncontrolled case series, lack of standardized testing protocols, and absence of preoperative baseline sensory data [28]. To generate high-quality and reproducible evidence, future studies should adopt a standardized core outcome set and more robust comparative designs.

First, preoperative baseline sensory testing is essential, because claims of postoperative "recovery" cannot be interpreted meaningfully without knowledge of the patient's starting point. Second, objective postoperative testing should include Semmes-Weinstein monofilament assessment mapped across defined breast and NAC quadrants. Ideally, such testing should be performed in a blinded fashion to reduce reporting and observer bias [28]. Third, subjective outcomes should be measured using validated patient-reported instruments, particularly the BREAST-Q Sensation Module, in order to capture the lived impact of sensory return on psychosocial and sexual well-being [28].

Future protocols must also address timing and study design. Because peripheral nerve regeneration is inherently slow, definitive sensory assessment should not be limited to early postoperative intervals such as 3–6 months, which may reflect ongoing axonal growth rather than stable functional recovery. Follow-up extending to at least 12–24 months is likely to be more informative. In addition, stronger comparative designs, including matched controls or randomized trials, will be needed to define the true clinical efficacy and cost-utility of NAC neurotization [28].

6.2 Cost, Bias, and Future Translational Priorities

The economic implications of breast neurotization remain an important area of debate. The use of commercial acellular nerve allografts adds a substantial mean cost of approximately $7,839 per breast [12]. Given the scarcity of healthcare resources, this additional cost raises legitimate questions regarding value, particularly in the absence of high-quality evidence demonstrating clear superiority in long-term patient-centered outcomes.

Financial concerns are compounded by the influence of industry funding within the nerve allograft literature. A coauthorship network analysis of 185 studies found that 79% of the most academically influential authors in nerve allograft research had received financial payments from the nerve allograft industry [23]. Although such relationships do not invalidate the published data, they underscore the need for independent comparative studies and cautious interpretation of the evidence base [23].

To address both cost concerns and the biological limitations associated with long allograft constructs, future work should continue to evaluate autologous and in situ nerve transfer strategies. The use of expendable local intercostal branches offers a living Schwann cell scaffold without added implantable material cost and may represent a more biologically favorable option in selected cases. As the field matures, future priorities should include not only refinement of operative technique, but also stronger comparative effectiveness data, longer oncologic follow-up, and more rigorous cost-effectiveness analysis.

The next phase of the field should focus on three priorities: (i) standardized prospective sensory phenotyping with baseline and long-term follow-up; (ii) head-to-head comparison of allograft, local autograft, and in situ transfer strategies within clearly defined oncologic IBBR cohorts; and (iii) implementation studies that assess operative burden, learning curve, payer context, and cost-effectiveness. Without this transition from feasibility studies to comparative effectiveness research,

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neurotization will remain promising but difficult to standardize. The current landscape of clinical evidence domains, typical study designs, and their inherent limitations is summarized in Table 3.

Table 3. Clinical evidence domains and resource signals commonly reported in NAC neurotization studies.

Evidence domain	Representative study designs	Outcomes commonly reported	Resource signals	Typical limitations
Pain/denervation symptoms	Randomized trials; prospective cohorts; matched analyses.	Neuropathic pain scores; denervation symptoms (e.g., itching/paresthesia); analgesic use.	Added operative time for coaptation; follow-up burden.	Heterogeneous instruments and follow-up; limited blinding.
Objective sensation testing	Prospective cohorts; comparative series.	Two-point discrimination; Semmes-Weinstein monofilaments; thermal or vibration thresholds.	Training/standardization of testing; clinic time.	Nonuniform testing protocols; learning effects; ceiling/floor effects.
Complications and safety	Registry series; comparative cohorts.	Flap/skin necrosis; implant loss; infection; neuroma/hypersensitivity.	Potential for additional dissection-related morbidity.	Low event rates; underpowered comparisons.
Cost and value	Cost-minimization/value analyses; matched-pair cohorts.	Allograft cost; incremental OR time; downstream visits.	Material cost (allograft) vs time cost (autograft).	Assumptions about pricing and health-system context; limited long-term economic endpoints.

7. Conclusions

Nipple-areolar complex neurotization is an emerging functional adjunct to NSM-IBBR that seeks to restore protective and erogenous sensation while potentially reducing denervation-related symptoms. Although allograft interposition remains the most commonly reported approach because of its technical simplicity and avoidance of donor-site morbidity, its cost and biological limitations across long regenerative distances continue to drive interest in autologous alternatives. Autologous strategies, including deep main-trunk harvest and superficial lateral branch transfer, offer living Schwann cell support and potential cost advantages, albeit at the expense of additional dissection. Across all techniques, the key determinants of success are appropriate donor selection (T3–T5), adequate graft length and routing within the implant pocket, and effective distal targeting at the NAC. Current evidence supports the technical feasibility and clinical promise of NAC neurotization, but stronger comparative studies, standardized sensory assessment, transparent reporting of pain and denervation-related symptoms, and longer oncologic follow-up are required before its role in routine reconstructive practice can be defined with confidence.

In our view, an important next question is which reconstructive strategy is most justifiable for a given implant-based scenario. The most defensible contemporary approach appears to be selective

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rather than universal: donor choice, graft material, and distal target should be tailored to anatomy, oncologic constraints, anticipated gap length, and resource context. However, until comparative data mature, NAC neurotization should be regarded as a promising reconstructive adjunct supported by feasibility data rather than by evidence for a single standard approach.

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Abbreviations

The following abbreviations are used in this manuscript:

NAC	Nipple-areolar complex
NSM	Nipple-sparing mastectomy
IBBR	Implant-based breast reconstruction
AICN	Anterior cutaneous branch of the intercostal nerve
LICN	Lateral cutaneous branch of the intercostal nerve
DIEP	Deep inferior epigastric perforator
ANA	Acellular nerve allograft
TMR	Targeted muscle reinnervation
PMPS	Post-mastectomy pain syndrome
ADM	Acellular dermal matrix
TNR	Targeted nipple-areolar complex reinnervation
PSSD	Pressure-specified sensory device
FTM	Female-to-male
SF-MPQ	Short-Form McGill Pain Questionnaire
IMF	Inframammary fold

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