

Targeted Nipple Areola Complex Reinnervation: Technical Considerations and Surgical Efficiency in Implant-based Breast Reconstruction

Lisa Gfrerer, MD, PhD*
 Jessica Erdmann Sager, MD†
 Olivia Abbate Ford, MD*†
 Matthew J. Carty, MD†
 Francys C. Verdial, MD*
 Michele A. Gadd, MD*
 Michelle C. Specht, MD*
 Jonathan M. Winograd, MD*
 Ian L. Valerio, MD*

Background: Despite promising pilot study results, adoption of neurotization of immediate implant-based reconstructions has not occurred.

Methods: For surgeons interested in adopting breast reinnervation techniques, we present ways to overcome initial barriers by decreasing operative time and maximizing chances of sensory recovery.

Results: We discuss the combined experience at two academic teaching hospitals, where neurotization of both immediate tissue expander cases and direct-to-implant reconstructions are performed through varying mastectomy incisions.

Conclusion: Initial barriers can be overcome by shortening operative time and providing an individualized reinnervation approach that aims to increase the chance of meaningful sensation. (*Plast Reconstr Surg Glob Open* 2022;10:e4420; doi: 10.1097/GOX.0000000000004420; Published online 25 July 2022.)

INTRODUCTION

The breast reconstruction surgeon provides women with the appearance of a restored feminine form after mastectomy. However, restoring breast function remains a challenge. The second to sixth intercostal nerves contribute to breast sensation, with the fourth lateral cutaneous branch cited as the main contributor to nipple areola complex (NAC) sensation.¹ These nerves are transected during mastectomy, resulting in diminished tactile sensation, which affects the ability to experience protective sensation and sensual touch.^{2,3} In patient-reported outcomes surveys, sensation and arousal stand alone in their poor outcome scores.^{4,5} In addition, phantom breast syndrome has been reported with a prevalence of 20%–80% after mastectomy with sensation of residual breast tissue, foreign feeling of reconstructed tissue or implants and phantom breast pain.^{6,7} Current innovations in breast reconstruction include neurotization, with the goal to create an aesthetic breast that also feels like a breast and provides function in the form of sensation. In addition,

neurotization may prevent chronic pain and phantom pain.

Breast neurotization during autologous reconstruction is not a novel concept.⁸ However, the high rates of implant-based breast reconstruction coupled with the increasing trend toward nipple-sparing mastectomy have spurred the need for comparable nerve reconstruction strategies in this population. Intercostal-to-NAC interposition allografts employed during implant reconstruction to stimulate nerve regrowth and sensory recovery have recently been reported.^{9,10} Peled and Peled¹⁰ first described a novel technique in which following mastectomy, transected lateral intercostal nerves are dissected and coapted to 7 cm nerve allografts that are then secured to target subareolar nerves after implant reconstruction is complete. In their pilot study of 23 breasts, 67% reported similar preoperative and postoperative breast and NAC sensation.

Despite promising pilot study results, widespread adoption of neurotization of immediate implant-based reconstructions has not occurred. This likely stems from the numerous barriers to neurotization which include patients' lack of understanding of sensation loss and the option to neurotize, insurance companies' reluctance to provide coverage, and surgeons' hesitation to add additional cost and/or time to the mastectomy and immediate

From the *Division of Plastic and Reconstructive Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, Mass.; and †Division of Plastic and Reconstructive Surgery, Brigham and Womens Hospital, Harvard Medical School, Boston, Mass.

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reconstructive procedure. For surgeons interested in adopting breast reinnervation techniques, we present ways to overcome initial barriers by decreasing operative time and maximizing chances of sensory recovery. Here, we discuss the combined experience at two academic teaching hospitals, where neurotization of both immediate tissue expander cases and direct-to-implant reconstructions are performed through various mastectomy incisions.

INTRAOPERATIVE SEQUENCING FOR IMMEDIATE IMPLANT-BASED RECONSTRUCTIONS

Breast reinnervation is a team-oriented procedure that may involve up to three surgeons and, therefore, requires careful coordination in the operating room. At our two different institutions, we have developed and trialed two team-based approaches that are feasible and efficient. We have found that these approaches add approximately 15–20 minutes on each side. Most of the time, neurotization at our institutions is performed by the plastic surgeon performing the breast reconstruction. Some reconstructive surgeons with no microsurgical background prefer involvement of a peripheral nerve surgeon.

Intraoperative sequencing is determined largely by whether the breast surgeon begins the mastectomy by elevating the breast from the chest wall first or by defining the mastectomy skin flaps first. If the breast surgeon prefers to start with elevation of the breast off the chest wall, then the reconstructive surgeon is present at the beginning of the procedure. In a bilateral case, the breast surgeon identifies the lateral border of the pectoralis muscle on the one side before moving to the other side to start the mastectomy. The reconstructive surgeon identifies the nerves on the one side. Once the nerves have been dissected to the maximal length that is oncologically safe and transected, they are safely tucked away at the lateral border of the breast. The breast surgeon switches to the side on which the nerves are tucked away to complete the mastectomy, whereas the reconstructive surgeon identifies the nerves on the other side. The reconstructive surgeon then prepares the allografts on the back table. After completion of the mastectomy, the reconstructive surgeon performs the implant-based reconstruction. After the implant-based breast reconstruction is complete, the reconstructive surgeon performs the nerve coaptations and closes the operative site. The reinnervation portion adds around 20 minutes per side to the procedure for the coaptation at the end. Importantly, the implant pocket/base width and donor nerve length must allow for coaptation of the nerve graft to the donor nerves on the chest wall. If the implant base width/pocket size is broad and the donor nerves are short, then the edge of the lateral implant may cover the donor nerves preventing coaptation to the nerve graft. In a scenario like this, we recommend coaptation of the nerve graft to the donor nerves on the chest wall before insertion of the implant. Some surgeons prefer completing the intercostal nerve coaptation before placement of a tissue expander or implant. For unilateral cases, the reconstructive surgeon is present

Takeaways

Question: Despite promising pilot study results, widespread adoption of neurotization of immediate implant-based reconstructions has not occurred.

Findings: We discuss the combined experience at two academic teaching hospitals, where neurotization of both immediate tissue expander cases and direct-to-implant reconstructions are performed through varying mastectomy incisions.

Meaning: Initial barriers can be overcome by shortening operative time and providing an individualized reinnervation approach that aims to increase the chance of meaningful sensation.

at the beginning of the case to identify the donor nerves. After dissection and transection of the donor nerves, they are tucked away on the lateral chest wall as the breast surgeon performs the mastectomy and the reconstructive surgeon performs implant-based breast reconstruction. Then, nerve coaptations are performed as described for bilateral cases.

If the breast surgeon elevates mastectomy skin flaps first, the reconstructive surgeon is called into the room when the breast surgeon starts elevating the breast off of the chest wall from medial to lateral over the pectoralis major muscle. The reconstructive surgeon identifies the intercostal nerve branches, dissects them to length, and transects them. The breast surgeon completes the mastectomy, and the reconstructive surgeon later returns to do nerve coaptations and placement of a breast prosthesis.

TYPE OF MASTECTOMY INCISIONS

Incision planning is important to allow for successful NAC neurotization. In our experience, neurotization during immediate implant-based reconstruction cases can be performed most easily through a radialateral incision or inframammary fold (IMF) incisions. Importantly, an IMF incision must be planned more lateral than a standard IMF incision, such that the incision begins at the meridian of the breast and extends along the IMF along the lateral aspect of the breast.

SURGICAL TECHNIQUE

See **Video (online)**, which demonstrates the targeted nipple areola complex reinnervation technique.

METHOD OF NEUROTIZATION

Even if an intercostal nerve branch is dissected to length and divided at the skin level, an interposition nerve graft must be used because nerves in situ travel directly through the breast parenchyma to reach their target, whereas a reconstructed nerve must travel around the lateral aspect of the tissue expander or implant. Our preference is to perform neurotization during immediate implant-based reconstructions with a cadaveric nerve allograft. Nerve autografts such as sural nerve grafts would be ideal from a

cost containment standpoint, but the donor site morbidity and added operative time make this option unappealing.¹¹ Nerve conduits are suboptimal due to inferior results following nerve repair with gaps of this size (5–7 cm).¹²

INTERCOSTAL NERVE BRANCH DISSECTION

After identification of the lateral border of the pectoralis major muscle, careful dissection along this border is performed to identify the lateral cutaneous branches of the third to fifth intercostal nerves (Fig. 1A).¹³ We strive to preserve all three nerves to increase the donor axon count available for reinnervation (Fig 1B). The maximum donor nerve length that is safe from an oncologic standpoint should be preserved. The nerves are transected as distal as possible, sometimes at the skin level. Small blood vessels that run with the donor nerves are not separated from the neural tissue to provide vascularized pedicled grafts. Oftentimes, a superficial nerve branch can be found in the lateral subcutaneous tissue of the mastectomy flap. This branch does not travel through the breast parenchyma and should be preserved.

TARGETED NAC REINNERVATION: COAPTATION AT THE CHEST WALL

Nerve coaptation at the chest wall is determined by the number of and length of intercostal nerves encountered and preserved. If all donor nerves are sufficiently long, they can be combined and sutured to the allograft in an end-to-end fashion (See figure 1A, Supplemental Digital Content 1, which shows an end-to-end donor nerve to allograft coaptation for nerves similar in length, <http://links.lww.com/PRSGO/C86>.) If there is a small length discrepancy between the intercostal nerve branches, but the branches

are close together, then the allograft is split into its fascicles proximally. The individual nerves are coapted to the individual fascicles. (See figure 1B, Supplemental Digital Content 1, which shows a nerve graft split proximally to allow for end-to-end donor nerve to allograft coaptation in nerves with length discrepancy, <http://links.lww.com/PRSGO/C86>.) If the nerve graft is split proximally, the best allograft diameter is 2–3 mm, as this graft will yield a sufficient number of fascicles and will provide a good size match at the lateral cutaneous nerve coaptation. If only two branches are present and/or the nerve branches are small, a 1–2 mm graft may be required. If there is a large length discrepancy between the donor nerve branches and/or the branches are far from each other, then an end-to-side coaptation between the short and long nerves is performed, and the long nerve is coapted to the allograft in an end-to-end fashion. (See figure 1C, D, Supplemental Digital Content 1, which shows an end-to-side anastomosis, <http://links.lww.com/PRSGO/C86>.) For the proximal coaptation of the intercostal nerves to the allograft, we recommend a standard epineurial repair using 9-0 or 8-0 Nylon suture. Our preference is to use a nerve wrap at the chest wall coaptation site.

If nerves are encountered that cannot be used for reinnervation because they are too proximal or distal, or if they have been transected in error at the level of the chest wall, our preference is to perform either targeted muscle reinnervation (TMR) or regenerative peripheral nerve interface reconstruction (RPNI) with the nerve endings to decrease the risk of chronic pain and possibly phantom sensations.^{14,15} TMR is a technique in which the proximal nerve end is coapted to a small muscle motor branch in close proximity to the nerve stump.¹⁶ RPNI is a technique in which the nerve stump is wrapped in a small muscle cuff.¹⁵

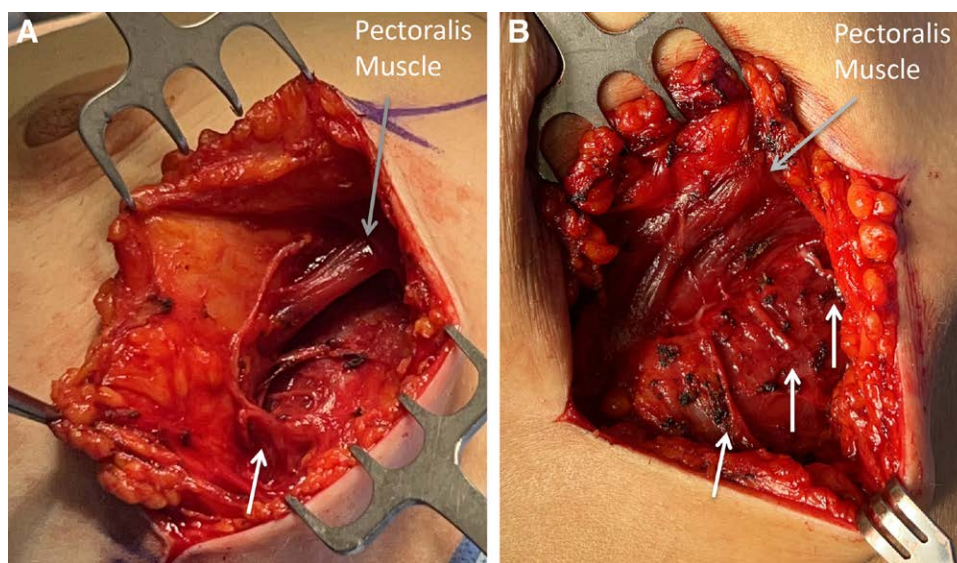


Fig. 1. Lateral cutaneous nerve dissection. A, The fourth intercostal nerve (white arrow) has been identified at the lateral border of the pectoralis muscle. B, The third to fifth intercostal nerves (white arrows) are dissected out and transected.

TNR: DISTAL NERVE TARGETS AND NERVE COAPTATION TO THE NAC

Peled and Peled described identification of a distal nerve target underneath the NAC.¹⁰ In our experience, it is not possible to differentiate ducts from small NAC nerve endings after nipple-sparing mastectomy without sending a confirmatory frozen section, which we believe is unnecessary (Fig. 2B). Possibly, this difference is related to variations in mastectomy techniques. To neurotize, we secure the distal nerve allograft to the NAC with suture fixation.¹⁷ Of note, the distal end of the allograft may be split into its fascicles to increase the reinnervation zone (Fig. 2A). The distal fascicles are then sutured to the NAC with 9.0 Nylon suture that importantly does not strangulate the fascicle (Fig. 2A). Before closing the mastectomy pocket, we ensure that the drains are placed in a position that will allow for drain pull without disturbing the nerve reconstruction.

SPECIAL CONSIDERATIONS IN DIRECT-TO-IMPLANT AND TISSUE TISSUE EXPANDER-BASED RECONSTRUCTION

In direct-to-implant reconstruction, it is important to recognize that implant size, implant projection, and implant base width influence the ability to perform breast neurotization. Large implants with broad base width and/or high projection increase the donor intercostal nerve to distal NAC target distance significantly. Currently, the longest commercially available allograft is 7 cm in length. Peled and Peled have shown that reinnervation of the NAC can occur over this 7 cm distance.¹⁰ Although it is possible that reinnervation is successful over longer distances, we do not recommend using a second graft. It is well known that the chances of reinnervation decrease with longer graft length and the cost of a

second graft is therefore not warranted in our opinion.¹⁸ When two-stage breast reconstruction with tissue expanders is performed, one must be cognizant of where the allograft is placed to avoid injury during the second-stage exchange procedure. When a radialateral mastectomy incision is used, our preference is to route the allograft inferior to the incision during the first stage of the procedure. During the second stage, when the radialateral incision is reopened, the allograft is not in the area of the incision as it travels inferior to the incision. When an inframammary fold mastectomy incision is used, we recommend placing the graft as far lateral as possible and exchanging the TE through the medial aspect of the incision. It is helpful to measure the position of the allograft from the most medial and lateral aspect of the incision and document this in the operative report. During the second-stage tissue expander exchange, the position of the allograft can be marked and avoided.

DISCUSSION

This article offers technical considerations and tips for efficiency in the operating room to help overcome early barriers encountered by surgeons who are interested in offering breast reinnervation after implant reconstruction to patients.

Breast reinnervation for implant-based reconstruction has been described by several authors.^{9,10} Our technique differs from current approaches in several ways. First, we aim to increase the donor axon-to-target density to maximize dermatome recovery by preserving all the nerves encountered during the mastectomy dissection. It has been shown that increased donor axon count results in improved functional outcomes after other reinnervation procedures such as facial reanimation and brachial plexus reconstruction.^{19,20} The likelihood that this principle applies to other reinnervation procedures is high. Furthermore, we do not separate small blood vessels from

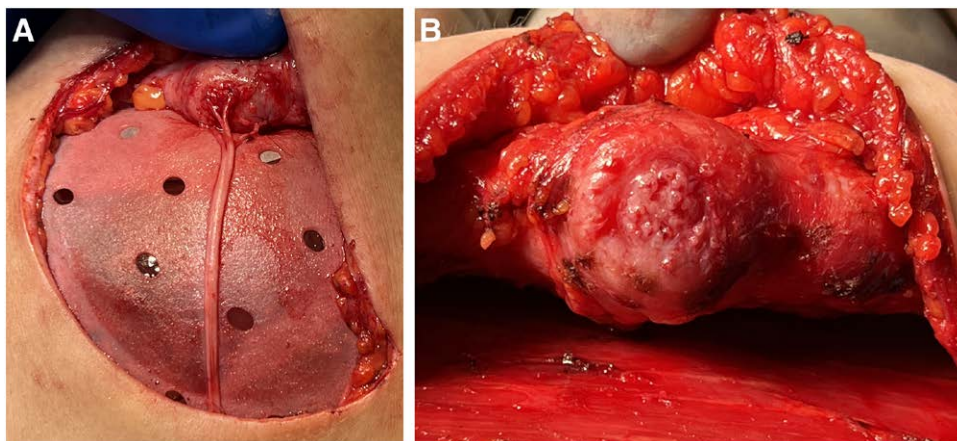


Fig. 2. TNR: separation of the nerve allograft to increase the reinnervation zone. A, The distal allograft is carefully split into its fascicles and (B) attached the dermosensory peripheral nerve fibers of the NAC. B, After nipple-sparing mastectomy, all the breast tissue is removed from underneath to the NAC. At this level, it is very difficult to differentiate small nerve endings from nipple ducts without sending a frozen section.

the epineurium of the donor nerves, as this may disrupt the epineurium. Although a direct comparison between vascularized and nonvascularized nerve grafts is not available, there is evidence to suggest that vascularized pedicled and free nerve transfers are superior to nonvascularized grafts.^{21,22} In addition, our technique is based on patient anatomy. In our experience it is easier to achieve a tensionless repair, maximum donor axon count, and donor nerve to allograft size match when the nerve reconstruction technique is individualized. Furthermore, the distal end of the allograft is split into fascicles and distributed throughout the NAC, rather than directing one large allograft to the dermis. Splitting fascicles has the potential to avoid focal hypersensitivity and to increase the zone of reinnervation. Last, we suture the distal allograft to the dermatosensory peripheral nerve fibers.¹⁷ We have found that it can be challenging to identify nerve endings at the NAC without frozen section which is time consuming. A recent animal study has shown that direct neurotization to dermis allows for axonal ingrowth into denervated skin.²³ Furthermore, the NAC has been shown to be rich in dermatosensory nerve fibers that are great recipients for axonal ingrowth.^{17,24} Therefore, axons growing across the allograft should be able to reinnervate the NAC.

Apart from sensory recovery, breast reinnervation has great potential to avoid chronic postmastectomy pain known as “postmastectomy pain syndrome”, which has been shown to occur in 25%–60% of women after mastectomy.^{25,26} We know from extremity peripheral nerve research that techniques to address nerve stumps after transection can prevent chronic pain and treat persistent pain when present.^{16,27} One of these methods employs reconstruction of the proximal nerve end with a long nerve allograft.^{28,29} This scenario is similar to the principles applied in breast reinnervation and should prevent chronic pain after mastectomy.

CONCLUSIONS

Breast reinnervation following mastectomy and implant-based breast reconstruction is a new development with potential to improve sensation of the breast. Initial barriers can be overcome by shortening operative time and providing an individualized reinnervation approach that aims to increase the chance of meaningful sensation.

Lisa Gfrerer, MD, PhD

Division of Plastic and Reconstructive Surgery
Massachusetts General Hospital
15 Parkman Street, WACC 435
Boston, MA 02114
E-mail: lgfrerer@partners.org

Ian Valerio, MD

Division of Plastic and Reconstructive Surgery
Massachusetts General Hospital
15 Parkman Street, WACC 435
Boston, MA 02114
E-mail: ivalerio@mg.harvard.edu

Jessica Erdmann-Sager, MD

Brigham and Womens Hospital
75 Francis Street
Boston, MA 02115

E-mail: jerdmansager@bwh.harvard.edu

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