

# Diagnosis and Management of Neuropathic Breast Pain

Maria Bejar-Chapa, MD\*  
 Seamus P. Caragher, MD, MPhil\*  
 Lisa Gfrerer, MD, PhD†  
 Ian L. Valerio, MD, MS, MBA\*  
 Amy S. Colwell, MD\*  
 Jonathan M. Winograd, MD\*

**Summary:** Chronic postoperative pain after breast surgery is a significant concern, with studies indicating varying rates depending on the type of surgical procedure. The risk of developing neuropathic pain is notably increased with axillary lymph node dissection due to potential nerve injuries. Additionally, the method of breast reconstruction may influence postsurgical pain rates, with conflicting findings on the impact of reconstruction type. Recent advancements in techniques such as targeted muscle reinnervation, among others, show promise in addressing postoperative pain in these patients. As the prevalence of these procedures rises, future research is likely to focus on assessing and managing pain in this patient population. The development of patient-reported outcome measures specific to breast surgery pain can aid in clinical assessment and treatment planning. This review emphasizes the importance of gaining a deeper understanding of risk factors, nerve anatomy, and treatment options to enhance outcomes and quality of life for individuals undergoing breast surgery. (*Plast Reconstr Surg Glob Open* 2024; 12:e6266; doi: [10.1097/GOX.0000000000006266](https://doi.org/10.1097/GOX.0000000000006266); Published online 23 December 2024.)

## INTRODUCTION

### Incidence of Pain After Breast Surgery and Identified Risk Factors

Breast surgery accounts for more than 500,000 surgical procedures each year within the United States alone.<sup>1</sup> Unfortunately, a subset of these patients experience chronic postoperative pain. Several definitions of postbreast surgical pain have emerged in the literature. One frequently encountered definition is postmastectomy pain syndrome, marked by persistent discomfort in the chest, upper arm, and shoulder after mastectomy/lumpectomy, lasting beyond 3 months. It is neuropathic, with hypersensitivity, hyperesthesia, allodynia, skin pulling, and reduced sensitivity to pinpricks, cold, and touch.<sup>2</sup> Different definitions describe similar pain experiences after breast surgeries with differences concerning the duration of pain postsurgery. Persistent postoperative

pain is present after 3–6 months,<sup>3</sup> persistent postsurgical pain lasts beyond 3 months,<sup>4</sup> or chronic pain persists beyond 3–6 months.<sup>5</sup>

Several studies have identified these terms to be of limited utility in the clinical setting.<sup>6–9</sup> The mechanisms underlying postbreast surgery pain remain incompletely understood but include neuromas, which are disorganized outgrowths of nerve axons after injury.<sup>10</sup> Thoracic nerve neuromas have been reported, most frequently of the intercostal and intercostobrachial nerves.<sup>3,10–13</sup> In addition, scar tissue formation with subsequent nerve entrapment,<sup>14,15</sup> fibrosis of skin and muscles induced by radiation,<sup>16</sup> and myofascial tightening<sup>17</sup> have also been identified as drivers of postsurgical breast pain derived from the peripheral nervous system. In addition, the central nervous system may contribute to persistent pain. The contribution of the central nervous system to chronic neuropathic pain is a well-described and robust area of research.<sup>18</sup> Changes in brain areas responsible for pain sensation after surgery can generate maladaptive circuit dynamics, perpetuating chronic pain long after the initial surgical insult.<sup>19,20</sup>

Although specific estimates of pain after breast surgery vary, clearly, many patients experience consistent pain. Plastic surgeons are uniquely qualified to engage and treat these patients, given both their extensive experience

From the \*Division of Plastic and Reconstructive Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, Mass.; and †Division of Plastic and Reconstructive Surgery, Weill Cornell Medicine, New York City, N.Y.

Received for publication April 15, 2024; accepted August 27, 2024.

Drs. Bejar-Chapa and Caragher contributed equally to this work.

Copyright © 2024 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the [Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 \(CCBY-NC-ND\)](https://creativecommons.org/licenses/by-nc-nd/4.0/), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: [10.1097/GOX.0000000000006266](https://doi.org/10.1097/GOX.0000000000006266)

Disclosure statements are at the end of this article, following the correspondence information.

Related Digital Media are available in the full-text version of the article on [www.PRSGlobalOpen.com](http://www.PRSGlobalOpen.com).

operating on the breast tissue and expertise in the management of nerve reconstruction. This review highlights the large unmet need of patients with pain after breast surgery, beginning with exploring the likely prevalence of this issue by type of breast surgery, as well as the current tools available to treat these patients.

### Oncologic Breast Surgery

Surgery for breast cancer entails a range of procedures, including lumpectomy, mastectomy, sentinel lymph node biopsy, and axillary lymph node dissection (ALND). The specific intervention depends on the tumor type and stage. The exact incidence of pain after breast cancer surgery is unknown, but several studies provide a basis for estimation. A cohort including 1983 patients who underwent mastectomy without reconstruction found a post-mastectomy pain syndrome rate of 28.2%.<sup>21</sup> In a cohort of more than 23,500 breast cancer patients undergoing mastectomy or breast-conserving therapy (BCT), 48% of patients reported pain at 1 year.<sup>22</sup> A more recent meta-analysis of 297,612 patients undergoing mastectomy or BCT found a pooled pain prevalence of 46%.<sup>4</sup> These studies suggest rates between 30% and 45% within 1 year. Other studies explored pain over longer timeframes. A large prospective study with 3253 women who underwent BCT or mastectomy found a pain prevalence of 47% 2–3 years after surgery<sup>23</sup>; prevalence dropped to 20.4% by 7–9 years.<sup>24</sup> Although further long-term studies are needed, these data suggest that pain after breast surgery is common, gradually improves for roughly half of women, and often persists for years.

Many potential factors associated with pain after breast cancer surgery have been proposed, including operative technique. Studies have compared mastectomy and lumpectomy directly, including a recent case-control study of 407 women that found a slight but significant increase in pain among women treated with BCT compared with mastectomy with or without reconstruction.<sup>25</sup> Another study of 1606 patients identified higher chronic pain rates in patients treated with lumpectomy (46%) than with mastectomy (35.4%).<sup>26</sup> Of note, all of the lumpectomy patients had also undergone radiation, which carries its own risk for pain related to the effects of radiation. Radiation can induce cellular proliferation failure and chronic ischemia, resulting in fibrosis, nerve entrapment, demyelination, and blockage of neural conduction. Neurolysis, often accompanied by an adipose tissue wrap, is indicated when there is progressive motor weakness or when conservative therapy fails.<sup>27–29</sup>

Studies have consistently pointed to ALND as a risk factor for pain after breast surgery. A prospective study of 216 patients and the previously mentioned mastectomy cohort both identified ALND as an independent risk factor for chronic pain after breast surgery.<sup>5,21,30</sup> The large Wang meta-analysis of 297,612 patients confirmed ALND increases pain rates to 43%, compared with 26% with sentinel lymph node biopsy only.<sup>4</sup> The increased rates of pain in ALND are most likely due to the increased risk of injury to sensory nerves within that region, including the lateral cutaneous branch of the second intercostal nerve, the

### Takeaways

**Question:** How prevalent is pain after breast surgery and how is it best managed?

**Findings:** Pain after breast surgery is estimated to affect 20%–40% of patients. Management begins with delineation of nerve pain via questionnaires, physical examination, and nerve blocks. Imaging may be useful. Once identified as neuropathic, interventions may include fat grafting, lysis of scars, or novel nerve management techniques (eg, targeted muscle reinnervation, regenerative peripheral nerve interface, and nerve grafts).

**Meaning:** Plastic surgeons will encounter many of these patients and have unique skills for intervention via peripheral nerve techniques. Innovations are under development for management and prevention of pain after breast surgery.

intercostobrachial nerve. A systematic review combining cadaveric and operative studies of intercostobrachial anatomy found that, among more than 1500 axillae, this nerve arises from the T2 spinal nerve in 90% of patients; roughly half of patients have a single cord, whereas another 42% demonstrate a branching pattern.<sup>13</sup> This variability of nerve course may contribute to the increased risk of nerve injury during axillary dissection.

In patients who underwent mastectomy, the method of breast reconstruction influences rates of postsurgical pain. One early study in 1996 of 282 patients treated with mastectomy with and without reconstruction found reconstruction increased pain rates to 49% compared with 31% in mastectomy alone 1 year after surgery. However, the more recent Wang meta-analysis found no significant difference in pain prevalence based on the presence of reconstruction. Within the population of patients undergoing reconstruction, studies have assessed differences in implant-based and autologous tissue techniques. One study found that women with implant reconstruction had a higher rate of pain (53%) than those with tissue-based reconstruction (30%).<sup>31</sup> In contrast, a later study of 205 women undergoing transverse rectus abdominis myocutaneous flaps or implant-based reconstruction found no difference in rates of pain 2 years postsurgery.<sup>32</sup> This finding was further supported by a retrospective cohort of 310 women.<sup>33</sup> Finally, the Wang meta-analysis identified no difference in rates of pain after breast reconstruction with implant or tissue-based approaches.<sup>4</sup> It seems that type of reconstruction is less likely to influence risk of developing chronic pain. However, further study is needed, as we were unable to identify a study looking specifically at pain rates after reconstruction with deep inferior epigastric perforator (DIEP) flaps.

Intrinsic patient variables are also risk factors. Younger patients were consistently identified as more likely to develop postoperative breast pain regardless of intervention type<sup>5,30</sup>, although some studies suggest that there might be a relationship between younger age and increased postsurgical pain due to increased nerve sprouting,<sup>34</sup> clinical observations have yet to determine whether this stems

from a distinct pain perception, physiological alterations, a shift in subjective pain expression, or variances in physical activity levels compared with older patients.<sup>35</sup>

Likewise, elevated weight and metabolic dysfunction have been linked to increased postoperative pain.<sup>36,37</sup> Genetic predispositions to pain have also been identified. For example, women with certain genotypes for potassium channels expressed on nociceptive nerves were at increased risk of pain after breast surgery.<sup>38</sup> Psychological factors, such as catastrophizing, somatization, anxiety, and sleep disturbance, have been linked to higher rates of postsurgical chronic pain.<sup>5,39</sup> Preexisting mental health issues highlight the psychological basis of pain perception. Overall, these studies provide insight into which breast cancer patients are at heightened risk of chronic pain.

### Reduction Mammoplasty

Breast reduction surgery (BRS) for macromastia is associated with improvement in quality of life.<sup>40</sup> Despite 115,000 procedures per year in the United States,<sup>41</sup> studies of pain after BRS are rare, possibly because women tend to report high rates of satisfaction.<sup>42,43</sup> A study of 90 patients found that, although 43% reported back pain improvement, 28% described new pain in the breasts at 27 months.<sup>44</sup> Studies examining these patients using the BREAST-Q<sup>45</sup> have shown improved physical well-being subscores<sup>40,46–48</sup>; however, the lack of specific questions related to pain location may mask issues of postoperative pain. Further studies are needed to reveal the prevalence after reduction surgery. Risk factors for pain after BRS seem to parallel results from breast cancer surgery. In the previously mentioned cohort study of 90 women who underwent reduction, younger age was again associated with increased risk of pain.<sup>44</sup> It also showed that sensory abnormalities of the breast before surgery were correlated with increased rates of postoperative pain.

### Aesthetic Breast Surgery

Cosmetic surgery is a major share of breast surgery, with more than 225,000 breast augmentations or implant revisions and 87,000 mastopexies in 2020.<sup>41</sup> A systematic review of pain after breast augmentation identified lower rates of postoperative pain at approximately 15%.<sup>49</sup> One retrospective study of 95 breast augmentation patients found that 33.7% of patients experienced postsurgical chronic pain.<sup>50</sup> A larger study assessed 611 patients at 6 weeks and 6 months and found significant increases in quality of life over that time period, but a significant decrease in mean physical well-being, including pain.<sup>51</sup> Specific questions on pain were not provided, limiting interpretation. These studies suggest a significant percentage of augmentation patients experience chronic pain after surgery.

Factors associated with pain after cosmetic breast surgery parallel those in oncology. In 1 study of 265 augmentation patients, younger age was associated with increased risk of chronic pain. The study found lower satisfaction with cosmetic results were associated with higher rates of postoperative pain.<sup>52</sup> A smaller study of 95 augmentation patients identified early postoperative sensory changes as associated with chronic pain.<sup>50</sup> This connection between

alterations in sensation and risk of persistent pain was further supported by a study of 116 augmentation patients, assessed 1 and 4 years postoperatively.<sup>53</sup> Breast sensory changes may serve as early indicators of nerve dysfunction and injury, eventually resulting in chronic pain. With the exception of 2 studies,<sup>50,53</sup> all the references cited in this section investigated the potential correlation between implant size and postoperative neuropathic pain, yet none found a statistically significant association.

### Gender-affirming “Top” Surgery

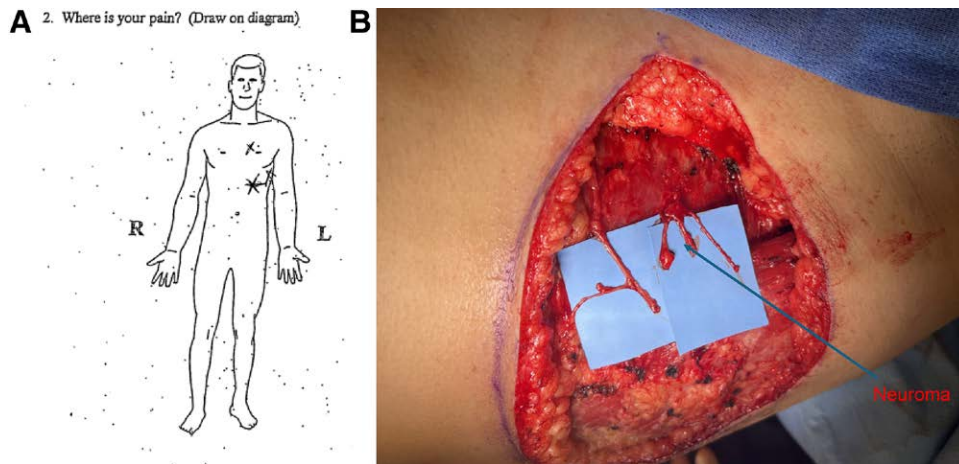
Gender affirmation surgery of the chest includes mastectomy and breast augmentation. More than 12,000 such breast surgeries occurred in 2020.<sup>41</sup> Postoperative pain has not yet been studied in large cohorts. A recent study of 84 transmen undergoing mastectomy found a rate of 27.4% of persistent postmastectomy pain with a follow-up of 24 months, though the majority (60.9%) was mild.<sup>54</sup> One study of 308 transwomen identified 5% with chronic pain, though the location was not specified.<sup>55</sup> As rates of these procedures increase,<sup>23</sup> future studies will likely include assessment of patient pain after chest surgery for gender affirmation.

One question raised by this population of breast surgery patients is the effect of concomitant hormonal therapy, a backbone of gender-affirming care in many cases.<sup>56</sup> One cohort study, including 26 transmale and 47 transfemale patients, identified that initiation of estrogens was associated with increased reports of pain, whereas testosterone was associated with decreased pain. Most patients with pain reported musculoskeletal and breast pain, or headaches.<sup>57</sup> The role hormones play on pain development, and perception is a rich and somewhat controversial area of inquiry (reviews<sup>58–60</sup>). Several preclinical models have reached the conclusion that testosterone has antinociceptive effects,<sup>50</sup> via induced endocannabinoid expression<sup>61</sup> and suppression of inflammatory pain modulators.<sup>62</sup> Likewise, estrogen and its metabolites have been shown to influence pain in preclinical models, although the specific influence of these molecules seems heterogenous.<sup>60</sup> These models, however, cannot account for the complex psychosocial dynamics of pain, especially chronic pain. Further clinical study is needed to explore the role of hormone therapy on postoperative pain.

## DIAGNOSIS AND MANAGEMENT OF NEUROPATHIC BREAST PAIN

### Diagnosis

Diagnosis requires a thorough delineation of the type of pain. Neuropathic pain can be assessed with different questionnaires that rely on the unique symptoms of neuropathic pain, including elevated sensitivity to non-noxious stimuli and pain to normally tolerable temperatures.<sup>63</sup> Many questionnaires have been developed to aid in the identification of neuropathic pain. They include the DN4,<sup>64,65</sup> the Neuropathic Pain Symptom Inventory,<sup>66</sup> the Leeds Assessment of Neuropathic Signs and Symptoms,<sup>67</sup> and the McGill Pain Questionnaire,<sup>68,69</sup> which the senior author has incorporated into our clinical practice (Fig. 1).



**Fig. 1.** Clinical presentation of post-breast surgery neuroma. A, A patient's pain diagram showing intercostal neuromas (marked X) after breast surgery, typical for this condition. Additionally, it includes an intraoperative photograph (B) of a large intercostal neuroma (arrow) found during a gender affirmation mastectomy after bilateral breast reduction. Image courtesy of Lisa Gfrerer, MD, PhD.

(See figure, Supplemental Digital Content 1, which displays the McGill modified pain questionnaire. Used with permission, <http://links.lww.com/PRSGO/D586>.) In addition, several breast-specific quality of life and patient-reported outcome measures (PROMs) have been developed. The BREAST-Q is the leading PROM for breast surgery,<sup>45,70</sup> including several pain-specific questions. In addition, the European Organization for Research and Treatment of Cancer has developed a range of PROM questionnaires for cancer patients, including both questions on pain and breast cancer-specific symptoms.<sup>71</sup> These questionnaires can be used in the clinic.

Next, a full sensory examination of the chest wall, axilla, and breasts should take place. Sensitivity to palpation or percussion should be noted. For example, a positive Tinel test, in which tapping on the area of concern elicits a tingling or shock-like sensation,<sup>72</sup> indicates axonal injury and in many cases, a sensory neuroma. Also, the presence of pain in the axillary region elicited on raising the arm over the head, should raise suspicion for neuroma of the intercostobrachial nerve.<sup>73</sup> In patients who underwent mastectomy, it is common to find a positive Tinel sign at the point of emergence of one or several of the lateral cutaneous branches of the intercostal nerves, which are routinely injured and may result in a painful neuroma.

If the history and physical examination suggest a sensory nerve injury, nerve blocks can then help to confirm the diagnosis and indicate that surgical intervention may confer substantial benefit. The use of blocks in this patient population is well-described,<sup>6,74</sup> and they are not only diagnostic but also temporarily therapeutic with the potential for longer lasting relief in some patients. The senior author refers patients to pain medicine specialists for blocks with local anesthetics and corticosteroids, which have been shown to increase the efficacy of blocks in clinical scenarios,<sup>75,76</sup> though the efficacy of this technique remains debated.<sup>77,78</sup> If the patient reports relief from symptoms for the duration of the block, then a surgical intervention

is considered. Typically, a reduction on the visual analog pain scale of 4 or greater out of 10 is considered a positive response to the nerve block.

#### Interventional Options

Nonsurgical options for neuropathic pain are vast and outside the scope of this article. They include a range of interventions from medical management, psychotherapy, and cognitive behavioral therapy<sup>79</sup> to injection of Botox.<sup>80</sup> We note with interest that many trials are ongoing related to psychological interventions on postoperative pain, given the possible contribution of the central nervous system to postsurgical breast pain.<sup>81,82</sup> Referral to pain specialists should be considered for all patients with pain after breast surgery. Interdisciplinary management has shown promise across a range of patients experiencing chronic, post-surgical pain.<sup>83</sup> Surgical interventions for refractory cases of chronic pain after breast surgery address the nerve injury directly (Table 1). For intact nerves compressed by scar tissue, neurolysis can be performed. Fat grafting has also been applied to these patients. A trial of 92 patients with chronic pain after lumpectomy and radiation found a significant reduction in pain scores in 57 patients after fat grafting.<sup>87</sup> A randomized control trial of 18 patients with unilateral mastectomy without reconstruction found a 55% reduction in pain with fat grafting.<sup>88</sup> A study of 98 patients found that fat grafting in patients with a previous mastectomy, ALND, and radiation reduced pain and pain medication usage compared with patients without fat grafting.<sup>89</sup> A dual-center study confirmed this result, with reduced pain scores at 1 and 6 months.<sup>90</sup> These studies pointed toward fat grafting as an intervention for pain. However, a double-blind study published in 2022 in which patients underwent scar release with fat grafting or saline injection found no additional beneficial effect for fat grafting.<sup>91</sup> Further research will clarify the efficacy of this technique as well as the possible mechanism, which are currently unknown.

**Table 1. Summary of Surgical Interventions for Pain after Breast Surgery**

Technique	Indications	Surgical Training	Pros	Cons
Neurolysis	Compression Scar tissue formation	Breast surgery, plastic surgery, or peripheral nerve surgery	Simple surgical technique	Possibility for scar tissue recurrence
TIM <sup>8,82</sup>	Neuroma Nerve transection with only proximal end identified	Breast surgery, plastic surgery, or peripheral nerve surgery	Simplest neuroma management technique Minimal time requirement	High rate of neuroma formation/recurrence in other locations Increased reoperation rate
TMR <sup>84</sup>	Neuroma Nerve transection with only proximal end identified	Plastic surgery, or peripheral nerve surgery	Lower neuroma recurrence rates than TIM in other locations Therapeutic and possibly preventative	Technically demanding Increased surgical time Sacrifice of motor nerve branches in nearby muscles
RPNI <sup>85</sup>	Neuroma Nerve transection with only proximal end identified	Breast surgery, plastic surgery, or peripheral nerve surgery	Lower neuroma recurrence rates than TIM in other locations Technically less challenging than TMR Therapeutic and possibly preventative	Must harvest free muscle grafts, adding morbidity Increased surgical time
Acellular nerve allografts <sup>86</sup>	Nerve transection with long gap injuries	Plastic surgery, or peripheral nerve surgery	Possibility for restoration of sensation to the innervated dermatome Compatible with free flap breast reconstruction	Technically demanding Use of cadaveric nerve grafts increases cost

TIM, transposition into muscle.

If a painful neuroma is present, excision is typically undertaken, followed by additional interventions. Historically, transposition into muscle of the free nerve end was used. Studies have shown positive effects in neuromas after breast surgery using this technique.<sup>3,6,7,74,92</sup> These studies have involved relatively few patients and follow-ups for less than 1 year. In neuromas of the extremity, management with neurectomy and implantation into muscle has been called into question given recurrence rates. Historic studies suggest a recurrence rate of more than 50% after excision and implantation.<sup>93</sup> More recent studies of neuroma management in the hand and extremities have reported recurrence rates of 7.8%,<sup>84</sup> 6.4%,<sup>94</sup> and 23%.<sup>95</sup> New techniques in development for nonintercostal neuroma management have been raised as possible interventions for intercostal neuromas.

One of these techniques, targeted muscle reinnervation (TMR), has gained attention as a method to limit symptomatic neuroma recurrence. In this technique, the neuroma is excised and the distal sensory intercostal nerve end is coapted into a nearby motor nerve branch, often from the serratus muscle, or the mixed sensory and motor intercostal nerve distally (a modified TMR) (Fig. 2). TMR has shown great promise in other areas of neuroma treatment, including amputations and headache surgery.<sup>85,96-98</sup> It has also been applied intraoperatively after mastectomy in a few cases to prevent pain.<sup>86</sup> Our group is currently undertaking a randomized control trial of the modified TMR described above compared with transposition into muscle for post-mastectomy patients with intercostal neuroma (Fig. 3).

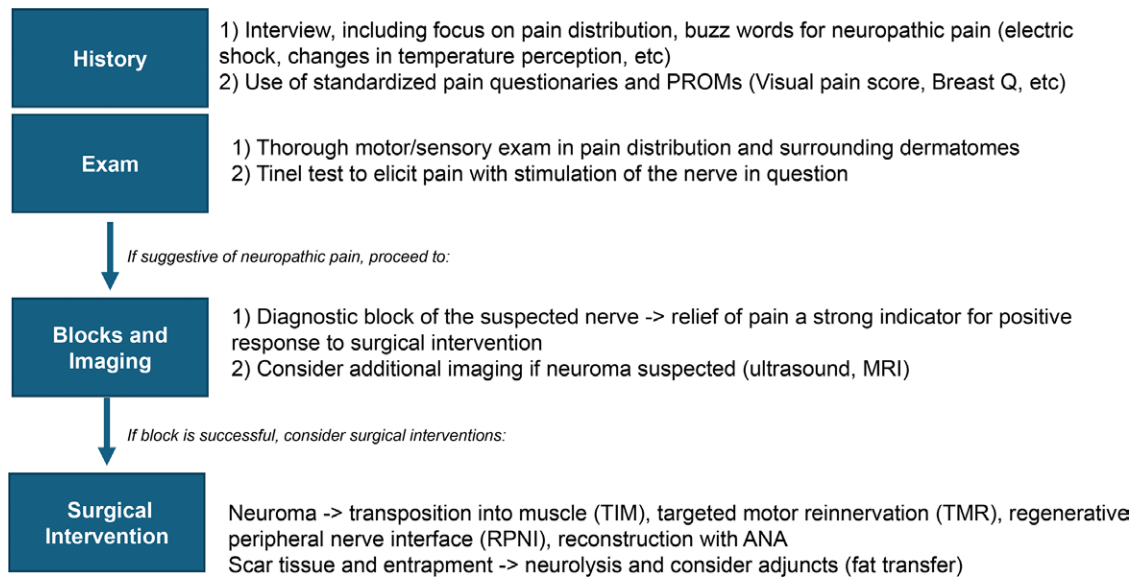
Regenerative peripheral nerve interfaces (RPNIs) have also demonstrated robust efficacy in reducing symptomatic neuroma recurrence. This technique relies on placing the proximal nerve end into denervated muscle grafts that serve as recipient sites to limit neuroma formation and neuropathic pain. Studies have shown its utility in a

range of surgical patients,<sup>99,100</sup> including breast surgery patients affected by postoperative pain.<sup>101,102</sup> An ongoing study exploring this question will further define the utility of RPNI in this population.<sup>103</sup>

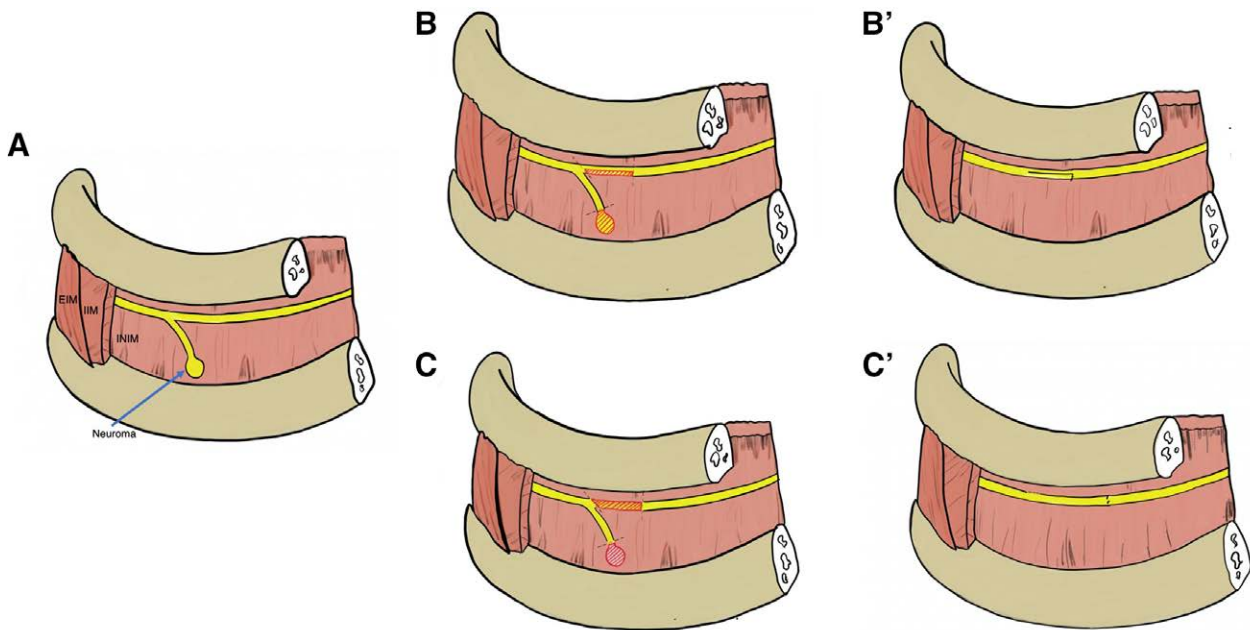
In addition, nerve grafting utilizing acellular nerve allografts (ANAs) has also been proposed to treat neuropathic pain, in patients with and without known neuroma.<sup>104</sup> A case report was recently published in which 3 patients with postmastectomy pain were successfully treated with cadaveric ANAs. Nerves causing pain were identified by diagnostic block and methylene blue injection; cadaveric ANAs were grafted from the nerve of interest to sensory nerves in the mastectomy flaps.<sup>105</sup> Interestingly, one of these patients subsequently underwent DIEP successfully with continued relief of pain.

## FUTURE DIRECTIONS

Various surgical interventions are available and under development for patients with chronic neuropathic pain after breast surgery. However, prevention may be the most effective approach. Prophylactic nerve treatments during initial surgery to limit neuroma formation have been successful in other areas, particularly the extremities, and are being adapted for breast surgery. A small cohort of 11 patients had TMR of the intercostal sensory nerve branches performed immediately after mastectomy as part of their reconstruction. An average of 1.8 nerves were found damaged in each patient. TMR was utilized without complication, and low pain scores at 8 months postoperatively were found.<sup>86</sup> It may be advantageous to deploy TMR, or other preventative treatments for neuroma such as RPNI, more broadly during initial breast surgery if sensory nerves are injured to decrease the likelihood of neuroma formation and the incidence of neuropathic pain.



**Fig. 2.** Diagnostic workflow for patient with postsurgical breast pain. Our evaluation begins with a history and physical examination, complemented by validated questionnaires designed for pain assessment. The physical exam includes detailed sensory testing and Tinel sign assessment. Targeted nerve blocks by pain specialists, are both diagnostic and therapeutic, with pain relief indicating potential benefit from surgical intervention. \*Defined as persistent neuropathic pain after breast surgery beyond 3–6 months. MPQ, McGill pain questionnaire; MRI, magnetic resonance imaging; SNRI, serotonin norepinephrine reuptake inhibitors; TCAs: tricyclic antidepressants; TIM, transposition into muscle; VAS, visual analog score.



**Fig. 3.** Schematic representations of TMR for intercostal neuroma. A, An intercostal neuroma formed on the cutaneous branch of the ICN branch running deep to the EIM and IIM, and superficial to the INIM. B and C, After neuroma excision, the main distal nerve branch is stimulated to identify motor fascicles that (B) can be isolated from the rest of the nerve. B', Isolated motor fascicles are transected and become the neurotization target for the sensory branch. Epineurium at the branch point where the motor fascicles are divided is closed. C, The distal ICN is monofascicular (distinct motor fascicles cannot be found). C', The cutaneous branch is coputed to the main distal intercostal branch and the epineurium at the branch point where the ICN is divided is closed. EIM, external intercostal muscle; ICN, intercostal nerve; IIM, inner intercostal muscle; INIM, innermost intercostal muscle.

In autologous breast reconstruction, neurotization of free flaps,<sup>106</sup> which similarly allows the intercostal sensory nerve(s) to regrow rather than just form a neuroma,

has shown potential to limit postsurgical pain and promote return of sensation.<sup>107</sup> One study comparing neurotized and nonneurotized transverse rectus abdominis

myocutaneous flaps found that nerve reconstruction improved patient-reported quality of life, including a reduction in “bodily pain.”<sup>108</sup> In some patients undergoing neurotized flap reconstruction, the removal of fibrosis after radiation therapy coupled with flap coverage could provide additional relief of pain directly related to scarring, which may be complementary to any additional benefit from preventing or alleviating neuropathic pain. A more recent study of necrotized DIEP flaps reported an improvement in quality of life based on the BREAST-Q.<sup>109</sup> Although subscores for pain were not reported, the study highlights the potential for neurotization as a bulwark against neuroma formation and the development of neuropathic pain after breast surgery. Nerve allografts may also be useful in this process, as described above, with the successful use of cadaveric grafts for neurotization of free flaps. By more easily providing the necessary length for an injured nerve to reach an end organ of interest, ANAs greatly expand the pool of patients who may benefit from nerve reconstruction. As such, we expect that continued development, refinement and implementation of nerve reconstruction as a routine part of autologous breast reconstruction will identify best practices for sensation restoration and neuropathic pain prevention.

Advancements in autologous reconstruction are notable, but questions linger about their efficacy in implant-based reconstructions, a common treatment in the United States. Our group and others have shared experiences with neurotization in implant-based reconstruction and gender-affirming top surgery.<sup>110–112</sup> Further research is needed to explore this promising opportunity.

In conclusion, neuropathic pain after breast surgery poses a significant challenge for many patients, compounded by its inherently subjective nature. Pain, deeply rooted in each individual’s perception and experiences, defies objective measurement or comparison. However, this challenge has sparked a heightened focus on pain prevention and treatment, which have become crucial objectives for breast and plastic surgeons alike. Moreover, there is a notable expansion in the adoption of techniques such as TMR, RPNI, and nerve reconstruction among this patient demographic. Shedding a light on these treatment options may serve as a catalyst for addressing this problem more effectively and fostering further research endeavors. Such studies could lead to enhanced strategies for mitigating neuropathic pain and preserving or restoring breast sensation.

**Jonathan M. Winograd, MD**

Division of Plastic and Reconstructive Surgery  
Massachusetts General Hospital  
15 Parkman Street, WACC Suite 453  
Boston, MA 02114  
E-mail: jwinograd@mgh.harvard.edu

## DISCLOSURES

Dr. Valerio is a consultant for Axogen, Inc., Integra Lifesciences, Inc., and Checkpoint, Inc. The other authors have no financial interest to declare in relation to the content of this article.

## REFERENCES

1. American Society of Plastic Surgeons. 2022 ASPS procedural statistics release. *Plast Reconstr Surg*. 2024;153:1–24.
2. International Committee for the Study of Pain, Subcommittee on Taxonomy. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. Prepared by the international association for the study of pain, subcommittee on taxonomy. *Pain Suppl*. 1986;3:S1–226.
3. Nguyen JT, Buchanan IA, Patel PP, et al. Intercostal neuroma as a source of pain after aesthetic and reconstructive breast implant surgery. *J Plast Reconstr Aesthet Surg*. 2012;65:1199–1203.
4. Wang L, Cohen JC, Devasenapathy N, et al. Prevalence and intensity of persistent post-surgical pain following breast cancer surgery: a systematic review and meta-analysis of observational studies. *Br J Anaesth*. 2020;125:346–357.
5. Spivey TL, Gutowski ED, Zinboonyahgoon N, et al. Chronic pain after breast surgery: a prospective, observational study. *Ann Surg Oncol*. 2018;25:2917–2924.
6. Broyles JM, Tuffaha SH, Williams EH, et al. Pain after breast surgery: etiology, diagnosis, and definitive management. *Microsurgery*. 2016;36:535–538.
7. Ducic I, Larson EE. Outcomes of surgical treatment for chronic postoperative breast and abdominal pain attributed to the intercostal nerve. *J Am Coll Surg*. 2006;203:304–310.
8. Chopra K, Kokosis G, Slavin B, et al. Painful complications after cosmetic surgery: management of peripheral nerve injury. *Aesthet Surg J*. 2019;39:1427–1435.
9. Kokosis G, Chopra K, Darrach H, et al. Re-visiting post-breast surgery pain syndrome: risk factors, peripheral nerve associations and clinical implications. *Gland Surg*. 2019;8:407–415.
10. Zabaglo M, Dreyer MA. Neuroma. In: *StatPearls [Internet]*. StatPearls Publishing; 2021.
11. Hill EJ, Patterson JMM, Yee A, et al. What is operative? Conceptualizing neuralgia: neuroma, compression neuropathy, painful hyperalgesia, and phantom nerve pain. *J Hand Surg Glob Online*. 2022;5:126–132.
12. Oliveira KM, Pindur L, Han Z, et al. Time course of traumatic neuroma development. *PLoS One*. 2018;13:e0200548.
13. Henry BM, Graves MJ, Pękala JR, et al. Origin, branching, and communications of the intercostobrachial nerve: a meta-analysis with implications for mastectomy and axillary lymph node dissection in breast cancer. *Cureus*. 2017;9:e1101.
14. Ducic I, Seiboth LA, Iorio ML. Chronic postoperative breast pain: danger zones for nerve injuries. *Plast Reconstr Surg*. 2011;127:41–46.
15. Lisa A, Maione L, Vinci V, et al. The use of autologous fat grafting for treatment of scar tissue and scar-related conditions: a systematic review. *Plast Reconstr Surg*. 2016;138:1076e–1077e.
16. Straub JM, New J, Hamilton CD, et al. Radiation-induced fibrosis: mechanisms and implications for therapy. *J Cancer Res Clin Oncol*. 2015;141:1985–1994.
17. De Groef A, Van Kampen M, Vervoesem N, et al. Effect of myofascial techniques for treatment of upper limb dysfunctions in breast cancer survivors: randomized controlled trial. *Support Care Cancer*. 2017;25:2119–2127.
18. Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. *Lancet Neurol*. 2010;9:807–819.
19. Chapman CR, Vierck CJ. The transition of acute postoperative pain to chronic pain: an integrative overview of research on mechanisms. *J Pain*. 2017;18:359.e1–359.e38.
20. Simons LE, Elman I, Borsook D. Psychological processing in chronic pain: a neural systems approach. *Neurosci Biobehav Rev*. 2014;39:61–78.
21. Gong Y, Tan Q, Qin Q, et al. Prevalence of postmastectomy pain syndrome and associated risk factors: a large single-institution cohort study. *Medicine (Baltim)*. 2020;99:e19834.

22. Davis LE, Bubis LD, Mahar AL, et al. Patient-reported symptoms after breast cancer diagnosis and treatment: a retrospective cohort study. *Eur J Cancer*. 2018;101:1–11.
23. Gärtner R, Jensen M-B, Nielsen J, et al. Prevalence of and factors associated with persistent pain following breast cancer surgery. *JAMA*. 2009;302:1985–1992.
24. Johannsen M, Christensen S, Zachariae R, et al. Socio-demographic, treatment-related, and health behavioral predictors of persistent pain 15 months and 7–9 years after surgery: a nationwide prospective study of women treated for primary breast cancer. *Breast Cancer Res Treat*. 2015;152:645–658.
25. Howes BHL, Watson DI, Xu C, et al. Quality of life following total mastectomy with and without reconstruction versus breast-conserving surgery for breast cancer: a case-controlled cohort study. *J Plast Reconstr Aesthet Surg*. 2016;69:1184–1191.
26. Admoun C, Mayrovitz H. Choosing mastectomy vs. lumpectomy-with-radiation: experiences of breast cancer survivors. *Cureus*. 2021;13:e18433.
27. Warade AC, Jha AK, Pattankar S, et al. Radiation-induced brachial plexus neuropathy: a review. *Neurol India*. 2019;67:S47–S52.
28. Johansson S, Svensson H, Larsson LG, et al. Brachial plexopathy after postoperative radiotherapy of breast cancer patients—a long-term follow-up. *Acta Oncol*. 2000;39:373–382.
29. Alessandri-Bonetti M, Egro FM, Persichetti P, et al. The role of fat grafting in alleviating neuropathic pain: a critical review of the literature. *Plast Reconstr Surg Glob Open*. 2019;7:e2216.
30. Miaskowski C, Cooper B, Paul SM, et al. Identification of patient subgroups and risk factors for persistent breast pain following breast cancer surgery. *J Pain*. 2012;13:1172–1187.
31. Wallace MS, Wallace AM, Lee J, et al. Pain after breast surgery: a survey of 282 women. *Pain*. 1996;66:195–205.
32. Roth RS, Lowery JC, Davis J, et al. Persistent pain following post-mastectomy breast reconstruction: long-term effects of type and timing of surgery. *Ann Plast Surg*. 2007;58:371–376.
33. De Oliveira GS Jr, Bialek JM, Nicosia L, et al. Lack of association between breast reconstructive surgery and the development of chronic pain after mastectomy: a propensity matched retrospective cohort analysis. *Breast*. 2014;23:329–333.
34. Fitzgerald M, McKelvey R. Nerve injury and neuropathic pain—a question of age. *Exp Neurol*. 2016;275 Pt 2:296–302.
35. Andersen KG, Kehlet H. Persistent pain after breast cancer treatment: a critical review of risk factors and strategies for prevention. *J Pain*. 2011;12:725–746.
36. van Helmond N, Timmerman H, van Dassel NT, et al. High body mass index is a potential risk factor for persistent post-operative pain after breast cancer treatment. *Pain Physician*. 2017;20:E661–E671.
37. Schreiber AK, Nones CF, Reis RC, et al. Diabetic neuropathic pain: pathophysiology and treatment. *World J Diabetes*. 2015;6:432–444.
38. Langford DJ, Paul SM, West CM, et al. Variations in potassium channel genes are associated with distinct trajectories of persistent breast pain after breast cancer surgery. *Pain*. 2015;156:371–380.
39. Belfer I, Schreiber KL, Shaffer JR, et al. Persistent postmastectomy pain in breast cancer survivors: analysis of clinical, demographic, and psychosocial factors. *J Pain*. 2013;14:1185–1195.
40. Coriddi M, Nadeau M, Taghizadeh M, et al. Analysis of satisfaction and well-being following breast reduction using a validated survey instrument: the BREAST-Q. *Plast Reconstr Surg*. 2013;132:285–290.
41. Surgeons, A.S.o.P. Plastic surgery statistics report: ASPS national clearinghouse of plastic surgery procedural statistics. 2021. Available at <https://www.plasticsurgery.org/news/plastic-surgery-statistics?sub=2020+Plastic+Surgery+Statistics>. Accessed March 1, 2024.
42. Rogliani M, Gentile P, Labardi L, et al. Improvement of physical and psychological symptoms after breast reduction. *J Plast Reconstr Aesthet Surg*. 2009;62:1647–1649.
43. Hermans BJ, Boeckx WD, De Lorenzi F, et al. Quality of life after breast reduction. *Ann Plast Surg*. 2005;55:227–231.
44. von Sperling ML, Høimyr H, Finnerup K, et al. Chronic postoperative pain and sensory changes following reduction mammoplasty. *Scand J Pain*. 2011;2:57–61.
45. Pusic AL, Klassen AF, Scott AM, et al. Development of a new patient-reported outcome measure for breast surgery: the BREAST-Q. *Plast Reconstr Surg*. 2009;124:345–353.
46. Gonzalez MA, Glickman LT, Aladegbami B, et al. Quality of life after breast reduction surgery: a 10-year retrospective analysis using the BREAST Q questionnaire: does breast size matter? *Ann Plast Surg*. 2012;69:361–363.
47. Crittenden TA, Watson DI, Ratcliffe J, et al. Outcomes of breast reduction surgery using the BREAST-Q: a prospective study and comparison with normative data. *Plast Reconstr Surg*. 2019;144:1034–1044.
48. Cogliandro A, Barone M, Cassotta G, et al. Patient satisfaction and clinical outcomes following 414 breast reductions: application of BREAST-Q. *Aesthetic Plast Surg*. 2017;41:245–249.
49. Ducic I, Zakaria HM, Felder JM, et al. Nerve injuries in aesthetic breast surgery: systematic review and treatment options. *Aesthet Surg J*. 2014;34:841–856.
50. Sperling ML, Høimyr H, Finnerup K, et al. Persistent pain and sensory changes following cosmetic breast augmentation. *Eur J Pain*. 2011;15:328–332.
51. Alderman AK, Bauer J, Fardo D, et al. Understanding the effect of breast augmentation on quality of life: prospective analysis using the BREAST-Q. *Plast Reconstr Surg*. 2014;133:787–795.
52. van Elk N, Steegers MA, van der Weij LP, et al. Chronic pain in women after breast augmentation: prevalence, predictive factors and quality of life. *Eur J Pain*. 2009;13:660–661.
53. Kaasa T, Romundstad L, Roald H, et al. Hyperesthesia one year after breast augmentation surgery increases the odds for persisting pain at four years: a prospective four-year follow-up study. *Scand J Pain*. 2010;1:75–81.
54. Lang CL, Day D-L, Klit A, et al. Low risk of persistent pain, sensory disturbances, and complications following mastectomy after gender-affirming surgery. *Transgend Health*. 2021;6:188–193.
55. de Blok CJ, Staphorsius AS, Wiepjes CM, et al. Frequency, determinants, and satisfaction of breast augmentation in trans women receiving hormone treatment. *J Sex Med*. 2020;17:342–348.
56. Baker KE, Wilson LM, Sharma R, et al. Hormone therapy, mental health, and quality of life among transgender people: a systematic review. *J Endocr Soc*. 2021;5:bvab011.
57. Aloisi AM, Bachiocco V, Costantino A, et al. Cross-sex hormone administration changes pain in transsexual women and men. *Pain*. 2007;132:S60–S67.
58. Mogil JS. Sex differences in pain and pain inhibition: multiple explanations of a controversial phenomenon. *Nat Rev Neurosci*. 2012;13:859–866.
59. Nasser SA, Afify EA. Sex differences in pain and opioid mediated antinociception: modulatory role of gonadal hormones. *Life Sci*. 2019;237:116926.
60. Gregus AM, Levine IS, Eddinger KA, et al. Sex differences in neuroimmune and glial mechanisms of pain. *Pain*. 2021;162:2186–2200.
61. Niu KY, Zhang Y, Ro JY. Effects of gonadal hormones on the peripheral cannabinoid receptor 1 (CB1R) system under a myositis condition in rats. *Pain*. 2012;153:2283–2291.
62. Vodo S, Bechi N, Petroni A, et al. Testosterone-induced effects on lipids and inflammation. *Mediators Inflamm*. 2013;2013:183041.
63. Campbell JN, Meyer RA. Mechanisms of neuropathic pain. *Neuron*. 2006;52:77–92.



64. Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain*. 2005;114:29–36.
65. Guastella V, Mick G, Soriano C, et al. A prospective study of neuropathic pain induced by thoracotomy: incidence, clinical description, and diagnosis. *Pain*. 2011;152:74–81.
66. Bouhassira D, Attal N, Fermanian J, et al. Development and validation of the neuropathic pain symptom inventory. *Pain*. 2004;108:248–257.
67. Searle RD, Simpson MP, Simpson KH, et al. Can chronic neuropathic pain following thoracic surgery be predicted during the postoperative period? *Interact Cardiovasc Thorac Surg*. 2009;9:999–1002.
68. Dworkin RH, Turk DC, Revicki DA, et al. Development and initial validation of an expanded and revised version of the short-form McGill pain questionnaire (SF-MPQ-2). *Pain*. 2009;144:35–42.
69. Ferreira VTK, de Oliveira Guirro EC, Dibai-Filho AV, et al. Characterization of chronic pain in breast cancer survivors using the McGill pain questionnaire. *J Bodyw Mov Ther*. 2015;19:651–655.
70. Cohen WA, Mundy LR, Ballard TN, et al. The BREAST-Q in surgical research: a review of the literature 2009–2015. *J Plast Reconstr Aesthet Surg*. 2016;69:149–162.
71. Bjelic-Radisic V, Cardoso F, Cameron D, et al; EORTC Quality of Life Group and Breast Cancer Group. An international update of the EORTC questionnaire for assessing quality of life in breast cancer patients: EORTC QLQ-BR45. *Ann Oncol*. 2020;31:283–288.
72. Lifchez SD, Means KR Jr, Dunn R.E, et al. Intra- and inter-examiner variability in performing Tinel's test. *J Hand Surg*. 2010;35:212–216.
73. Kim JS, Spiess AM. Surgical treatment of intercostal brachial nerve pain after mastectomy and axillary dissection. *Plast Reconstr Surg Glob Open*. 2021;9:e3935.
74. Wong L. Intercostal neuromas: a treatable cause of postoperative breast surgery pain. *Ann Plast Surg*. 2001;46:481–484.
75. Movafegh A, Razazian M, Hajimaohamadi F, et al. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. *Anesth Analg*. 2006;102:263–267.
76. Cummings KC, III, Napierkowski D, Parra-Sanchez I, et al. Effect of dexamethasone on the duration of interscalene nerve blocks with ropivacaine or bupivacaine. *Br J Anaesth*. 2011;107:446–453.
77. Shanthanna H, Busse J, Wang L, et al. Addition of corticosteroids to local anaesthetics for chronic non-cancer pain injections: a systematic review and meta-analysis of randomised controlled trials. *Br J Anaesth*. 2020;125:779–801.
78. Pehora C, Pearson AME, Kaushal A, et al. Dexamethasone as an adjuvant to peripheral nerve block. *Cochrane Database Syst Rev*. 2017;11:CD011770.
79. Tatrow K, Montgomery GH. Cognitive behavioral therapy techniques for distress and pain in breast cancer patients: a meta-analysis. *J Behav Med*. 2006;29:17–27.
80. Dessy LA, Maruccia M, Mazzocchi M, et al. Treatment of post mastectomy pain syndrome after mastopexy with botulinum toxin. *J Plast Reconstr Aesthet Surg*. 2014;67:873–874.
81. Lukas A, Theunissen M, Boer DK-d, et al. AMAZONE: prevention of persistent pain after breast cancer treatment by online cognitive behavioral therapy—study protocol of a randomized controlled multicenter trial. *Trials*. 2022;23:1–14.
82. Moorthy A, Lowry D, Edgley C, et al. Effect of perioperative cognitive behavioural therapy on chronic post-surgical pain among breast cancer patients with high pain catastrophising characteristics: protocol for a double-blinded randomised controlled trial. *Trials*. 2022;23:66.
83. Caragher SP, Khouri KS, Raasveld FV, et al. The peripheral nerve surgeon's role in the management of neuropathic pain. *Plast Reconstr Surg Glob Open*. 2023;11:e5005.
84. Wolvetang NH, Lans J, Verhiel SH, et al. Surgery for symptomatic neuroma: anatomic distribution and predictors of secondary surgery. *Plast Reconstr Surg*. 2019;143:1762–1771.
85. O'Brien AL, West JM, Gokun Y, et al. Longitudinal durability of patient-reported pain outcomes after targeted muscle reinnervation at the time of major limb amputation. *J Am Coll Surg*. 2022;234:883–889.
86. O'Brien AL, Kraft CT, Valerio IL, et al. Targeted muscle reinnervation following breast surgery: a novel technique. *Plast Reconstr Surg Glob Open*. 2020;8:e2782.
87. Maione L, Vinci V, Caviggioli F, et al. Autologous fat graft in postmastectomy pain syndrome following breast conservative surgery and radiotherapy. *Aesthetic Plast Surg*. 2014;38:528–532.
88. Juhl AA, Karlsson P, Damsgaard TE. Fat grafting for alleviating persistent pain after breast cancer treatment: a randomized controlled trial. *J Plast Reconstr Aesthet Surg*. 2016;69:1192–1202.
89. Caviggioli F, Maione L, Forcellini D, et al. Autologous fat graft in postmastectomy pain syndrome. *Plast Reconstr Surg*. 2011;128:349–352.
90. Lisa AVE, Murolo M, Maione L, et al. Autologous fat grafting efficacy in treating postmastectomy pain syndrome: a prospective multicenter trial of two Senonetwork Italia breast centers. *Breast J*. 2020;26:1652–1658.
91. Sollie M, Toyserkani NM, Bille C, et al. Autologous fat grafting as treatment of postmastectomy pain syndrome: a randomized controlled trial. *Plast Reconstr Surg*. 2022;149:295–305.
92. Williams EH, Williams CG, Rosson GD, et al. Neurectomy for treatment of intercostal neuralgia. *Ann Thorac Surg*. 2008;85:1766–1770.
93. Laborde KJ, Kalisman M, Tsai TM. Results of surgical treatment of painful neuromas of the hand. *J Hand Surg Am*. 1982;7:190–193.
94. Dellon AL, Mackinnon SE. Treatment of the painful neuroma by neuroma resection and muscle implantation. *Plast Reconstr Surg*. 1986;77:427–438.
95. Vlot MA, Wilkens SC, Chen NC, et al. Symptomatic neuroma following initial amputation for traumatic digital amputation. *J Hand Surg*. 2018;43:86.e1–86.e8.
96. Alexander JH, Jordan SW, West JM, et al. Targeted muscle reinnervation in oncologic amputees: early experience of a novel institutional protocol. *J Surg Oncol*. 2019;120:348–358.
97. Souza JM, Cheesborough JE, Ko JH, et al. Targeted muscle reinnervation: a novel approach to postamputation neuroma pain. *Clin Orthop Relat Res*. 2014;472:2984–2990.
98. Gfrerer L, Wong FK, Hickel K, et al. RPNI, TMR, and reset neurectomy/relocation nerve grafting after nerve transection in headache surgery. *Plast Reconstr Surg Glob Open*. 2022;10:e4547.
99. Kubiak CA, Adidharma W, Kung TA, et al. Decreasing postamputation pain with the regenerative peripheral nerve interface (RPNI). *Ann Vasc Surg*. 2022;79:421–426.
100. Woo SL, Kung TA, Brown DL, et al. Regenerative peripheral nerve interfaces for the treatment of postamputation neuroma pain: a pilot study. *Plast Reconstr Surg Glob Open*. 2016;4:e1038–e1038.
101. de Lange JWD, Hundepool CA, Power DM, et al. Prevention is better than cure: surgical methods for neuropathic pain prevention following amputation - a systematic review. *J Plast Reconstr Aesthet Surg*. 2022;75:948–959.
102. Hart S, Agarwal S, Hamill J, et al. Intercostal neurectomy and regenerative or dermatosensory peripheral nerve interface for chronic mastectomy pain [abstract]. *Plast Reconstr Surg Glob Open*. 2020;8:80–81.

103. Center, U.o.M.R.C. Surgical treatment of post-surgical mastectomy pain utilizing the regenerative peripheral nerve interface (RPNI). Available at <https://clinicaltrials.gov/ct2/show/NCT04530526>. Accessed March 1, 2024.
104. Chappell AG, Bai J, Yuksel S, et al. Post-mastectomy pain syndrome: defining perioperative etiologies to guide new methods of prevention for plastic surgeons. *World J Plast Surg*. 2020;9:247–253.
105. Gatherwright J, Knackstedt R. Targeted breast re-innervation (TBR) for post-mastectomy pain. *J Plast Reconstr Aesthet Surg*. 2019;72:1700–1738.
106. Spiegel AJ, Menn ZK, Eldor L, et al. Breast reinnervation: DIEP neurotization using the third anterior intercostal nerve. *Plast Reconstr Surg Glob Open*. 2013;1:e72.
107. Weissler JM, Koltz PF, Carney MJ, et al. Sifting through the evidence: a comprehensive review and analysis of neurotization in breast reconstruction. *Plast Reconstr Surg*. 2018;141:550–565.
108. Temple CL, Ross DC, Kim S, et al. Sensibility following innervated free TRAM flap for breast reconstruction: part II. Innervation improves patient-rated quality of life. *Plast Reconstr Surg*. 2009;124:1419–1425.
109. Cornelissen AJM, Beugels J, van Kuijk SMJ, et al. Sensation of the autologous reconstructed breast improves quality of life: a pilot study. *Breast Cancer Res Treat*. 2018;167:687–695. .
110. Gfrerer L, Sager JE, Ford OA, et al. Targeted nipple areola complex reinnervation: technical considerations and surgical efficiency in implant-based breast reconstruction. *Plast Reconstr Surg Glob Open*. 2022;10:e4420.
111. Peled AW, Peled ZM. Nerve preservation and allografting for sensory innervation following immediate implant breast reconstruction. *Plast Reconstr Surg Glob Open*. 2019;7:e2332.
112. Gfrerer L, Winograd JM, Austen WG Jr, et al. Targeted nipple areola complex reinnervation in gender-affirming double incision mastectomy with free nipple grafting. *Plast Reconstr Surg Glob Open*. 2022;10:e4251.