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# Post-Breast Surgery Pain Syndrome: Shifting a Surgical Paradigm

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**Summary:** Post-mastectomy pain syndrome and the less well-described post-breast surgery pain syndrome are long-term neuropathic pain conditions that may affect more than 50% of patients after mastectomy and breast surgery. While the etiology, risk factors, and management have been reviewed in our literature, we offer here a focused outline that will gear the plastic surgeon with tools to lead a multidisciplinary, algorithmic approach to the care of patients with post-mastectomy pain syndrome/post-breast surgery pain syndrome. After reading this article, we hope the reader will have improved awareness of post-mastectomy pain syndrome/post-breast surgery pain syndrome, and thus be able to incorporate appropriate treatments and preventative steps into their primary surgical routine. *(Plast Reconstr Surg Glob Open 2021;9:e3720; doi: 10.1097/GOX.0000000000003720; Published online 22 July 2021.)*

## INTRODUCTION

The reported prevalence of post-mastectomy pain syndrome (PMPS) ranges from less than 10% to more than 50% of patients after mastectomy.[1–4] This chronic pain is believed to be related to injury of the sensory nerves to the breast, chest, and upper arm/axilla. In the past, when concern was predominantly on patient survival, this pain was often considered acceptable. However, as breast cancer patients continue to survive for many years after their diagnosis, there has been increased focus on optimization of patient quality of life after treatment, which PMPS can significantly hinder.

## DEFINITION AND DIAGNOSTIC CRITERIA

Pain following mastectomy was first described in 1978.[5] Since then, there have been many publications on the subject, yet definitions of PMPS in the literature remain varied. Waltho and colleagues propose a definition of pain that occurs after any breast surgery, is of at least moderate severity, has been present for at least six months, is located in the ipsilateral breast/chest wall, axilla, or arm, possesses neuropathic qualities, is present at least 50% of the time, and may worsen with shoulder girdle movement. Furthermore, they recommend broadening the term to post-breast surgery pain syndrome (PBSPS), of which PMPS is a subset.[6] Similarly, Kokosis et al make the important distinction that neuropathic pain does not only arise following oncologic breast cancer treatments, but rather, all breast surgeries, including breast reconstruction, cosmetic breast surgery, and breast reductions.[7]

One key diagnostic criterion for PMPS/PBSPS is the presence of neuropathic pain. Jung et al provide a more nuanced description and classification system for neuropathic pain following breast surgery.[8] They divide neuropathic pain into phantom breast pain, injury to the intercostobrachial nerve, neuroma formation (from direct injury or from entrapment of nerve in scar), and other nerve injury pain that does not fall into any of the preceding categories.

## ANATOMY

The breast parenchyma and chest wall are innervated by the medial and lateral branches of the ventral rami of intercostal nerves T2-T6. One or more of these branches may be injured during mastectomy or other breast surgery. Another commonly injured nerve associated with PMPS is the intercostobrachial nerve, a lateral cutaneous branch arising from the second intercostal nerve, which supplies sensation to the skin of the upper medial arm and anterolateral chest wall. The course of this nerve through the axilla puts it at risk for either direct or traction injury during complete axillary node dissection, and less commonly, sentinel lymph node biopsy. Both Kokosis et al and Ducic et al outline the anatomic relationship between breast, axilla, and chest wall innervation and various surgical procedures and incisions.[7,9] Although awareness of

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the anatomy of breast innervation can help guide surgical decision-making and possibly prevent direct nerve injury, the inevitable presence of scarring, postoperative radiation, and other factors make nerve injury unavoidable in some patients.

## PREVALENCE

There have been many studies attempting to quantify the prevalence of neuropathic breast pain, the majority of which only include those patients who have undergone prior mastectomies (PMPS). Postoperative, nonmastectomy neuropathic breast pain (PBSPS) has been less frequently studied. Reported frequency of PMPS has a wide range from as low as 8%–9% to as high as 70%[1–4,10–14] (Table 1). PMPS is also dynamic and fluctuates with time, arising in some patients many years after initial breast surgery.[1–3] Kojima et al describe a survey of 242 Japanese breast surgeons on their awareness and treatment of PMPS. Amongst respondents, the presumed prevalence of PMPS was over 70%, but less than 50% prescribed treatment for their patients.[10] In another study of patients with PMPS, although 36.2% of participants had diagnosed PMPS, only 11.8% sought treatment for their symptoms.[11] In these studies, the discrepancy between true prevalence, the challenge in diagnosis and administration of treatment is seen.

## RISK FACTORS

It is useful to organize risk factors for PMPS/PBSPS into three groups: preoperative, intraoperative, and postoperative—as described by Tait et al in their comprehensive review.[15] Preoperative risk factors include younger patients, higher BMI, and presence of preexisting pain.[1–3,11–16] It has also been shown that there is a correlation between preoperative mood disorders and increased risk of PMPS.[2,17] Regarding PBSPS, Urits et al reviewed the risk factors associated with chronic pain specifically after cosmetic breast procedures, and found similar risk factors to PMPS, including younger age, larger BMI, postoperative hyperesthesias, and depression, anxiety, and catastrophizing pain scores.[18]

Intraoperatively, performing complete axillary lymph node dissection has been shown to increase risk of PMPS, compared with sentinel lymph node biopsy.[1,12,13] Surprisingly, Mustonen et al showed that patients undergoing breast-conserving therapy have a greater risk of chronic neuropathic pain, compared with patients undergoing mastectomy, even when controlling for postoperative radiotherapy.[2] However, Gärtner et al have shown no difference in PMPS between breast-conservation surgery and mastectomy.[19] Intraoperative damage or transection of the ICBN has also been implicated in development of PMPS. In their meta-analysis of studies examining preservation or transection of the ICBN, Warrier et al found that nerve preservation led to fewer sensory disturbances postoperatively.[20] Even among patients with intraoperative injury to their ICBN, not all patients develop neuropathic pain postoperatively.[2]

It is also important to consider the impact of breast reconstruction on the development of PMPS/PBSPS. Reghunathan et al showed that breast reconstruction after mastectomy (either immediate or delayed) had no impact on the development of PMPS.[21] In their prospective study, Roth et al showed that patients with abdominally-based autologous reconstruction had more severe pain at 2-years postoperatively than those patients who underwent expander/implant-based reconstruction.[4] However, other studies conclude that patents who undergo tissue expander/implant-based reconstruction have a higher incidence of PMPS.[22,23]

With regard to PBSPS in the cosmetic setting, Ducic et al examined the rate and risk factors of neuropathic pain after primary breast augmentation. In their meta-analysis, they found no correlation between dissection plane, incision type, or implant volume on the occurrence of nerve injury or pain postoperatively.[24] Other studies have shown variable effects of implant placement, incision type, and implant size on the development of postoperative neuropathic pain after noncancer breast surgeries.[25]

Certain postoperative findings have also been associated with increased risk of PMPS. Multiple studies have shown patients who have increased levels of immediate postoperative pain have a higher risk of developing chronic PMPS.[26,27] Additionally, there is also a well-documented link between radiation therapy and development of PMPS.[19]

## PMPS TREATMENT

Current literature addresses several different aspects of PMPS treatment, including pharmacological interventions, regional anesthesia, physical therapy, and surgery. It is also important to understand the preventative measures available to minimize the risk of PMPS/PBSPS from occurring following breast surgery.

**Table 1. Study Results Reporting the Prevalence of PMPS/PBSPS**

| Author, Year | PMPS or PBSPS | No. Subjects | Prevalence of PMPS/PBSPS |
|---|---|---|---|
| Wallace et al, 1996[23] | PMPS/PBSPS | 282 | 49% in mastectomy + reconstruction group, 31% in mastectomy alone, 22% in breast reduction |
| Caffo, 2003[14] | PMPS—including reconstruction | 529 | 39.7% |
| Macdonald et al, 2005[3] | PMPS | 113 | 52% |
| Gärtner, 2009[19] | PMPS | 3754 | 47% reporting pain, 13% with severe pain |
| Fabro et al, 2012[12] | PMPS | 174 | 52% |
| Mejdahl, 2013[1] | PMPS | 2411 | 22%–53% |
| Mustonen, 2019[2] | PMPS in patients with ICBN transection | 251 | 55% |
| Cui et al, 2018[11] | PMPS | 420 | 36.2% |
| Roth, 2018[4] | PMPS—including reconstruction | 1996 | 8%–9% moderate pain; 2%–3% severe pain |

### Pharmacological Pain Management

#### Treatment of Existing PMPS/PBSPS

There are many described pharmacologic treatments for PMPS, the majority of which are from the pain management literature. However, results have been mixed in terms of effectiveness for many of these modalities. In their systematic review of six studies, Larsson et al describe the statistically significant reduction of pain symptoms associated with PMPS with use of various drugs, including antidepressants (amitriptyline and venlafaxine).[28] Other reported drugs shown to improve PMPS include nefopam (nonopioid analgesic) and memantine (NMDA receptor antagonist).[29] Other studies have examined the role of topical capsaicin cream on the treatment of PMPS. In their double-blinded randomized control trial, Watson and Evans show that PMPS symptoms decrease after 4–6 weeks of treatment with capsaicin cream, compared with a placebo.[30]

#### Prevention of PMPS/PBSPS

In addition to these pharmacologic treatment options for patients with existing PMPS/PBSPS, it is important for plastic surgeons to be aware of the described benefits of perioperative therapies shown to reduce the risk of acute postoperative pain, the latter of which has been shown to be associated with subsequent development of PMPS. Recently, there has been much research into the use of enhanced recovery after surgery (ERAS) protocols in reducing postoperative pain and minimizing opioid dependence. One study by Morin et al showed that use of a perioperative multimodal analgesic ERAS protocol reduced postoperative pain at 1 day and 1 week postoperatively. The authors also found that patients with higher BMIs had increased rates of persistent pain, despite use of ERAS.[31] Other publications have also shown a reduction in opioid use and overall pain postoperatively with ERAS protocols. However, many of these studies focus on the abdominal donor site (for autologous breast reconstruction), rather than the breast and chest wall, and many only report on ERAS efficacy for acute pain management, rather than long-term neuropathic pain.[32–34]

Gabapentin has also been shown to reduce immediate postoperative pain following mastectomies and other breast surgeries, and is often a component of ERAS protocols.[35,36] In their randomized control trial, Fassoulaki et al found that combining perioperative gabapentin and local anesthesia led to a significant decrease in chronic pain 3 months after surgery, supporting the importance of a multimodal approach to preventing PMPS.[35] Another trial examining the use of perioperative intravenous methylprednisone at the time of breast augmentation surgery showed a reduction in hyperesthesias, but not pain, 1 year following surgery.[25]

### Regional Anesthesia

#### Treatment of Existing PMPS/PBSPS

Administration of regional anesthesia has also shown promising results in patients who have chronic PMPS/PBSPS.[29] Given the described role that ICBN injury plays in the development of PMPS, Wijayasinghe et al describe their technique of ultrasound-guided ICBN blockade in a group of six patients with PMPS. Despite the fact that the sample size is small, the results—with all patients experiencing a postprocedure decrease in pain intensity scores—are promising.[37] Other nonsurgical strategies have been described to help alleviate PMPS/PBSPS symptoms, including injection of dilute botulinum toxin percutaneously into the breast,[38] and stellate ganglion blocks, either with local anesthesia or with thermal radiofrequency.[39,40]

#### Prevention of PMPS/PBSPS

In addition to blockade of the ICBN, other studies have examined use of regional anesthesia targeting other nerves that may be implicated in PMPS. In their randomized control trial, Fujii et al examined the effects of two different intraoperative interfascial thoracic blocks on both acute and chronic pain following mastectomy. Their results showed that a pectoralis nerve block decreased the rate of moderate to severe chronic pain at 6 months postoperatively, compared with a serratus anterior block.[41]

Multiple studies also show that regional paravertebral blocks improve postoperative pain, decrease intravenous opioid usage, and reduce hospital length of stay following both tissue expander/implant and autologous-based reconstruction.[42,43] While high levels of postoperative pain have been associated with an increased risk of PMPS/PBSPS, there is minimal information in the plastic surgery literature on the effects of regional anesthetic blocks specifically on long-term neuropathic postoperative pain, nor do many of these studies delineate between neuropathic and nonneuropathic pain.[44]

### Physical Therapy

Chronic pain in the upper arm, axilla, and chest may lead patients to reduce use of the upper extremity and shoulder, which leads to long-term stiffness, reduced range of motion, and often compounds pain. Most current literature on the effects of postoperative physical therapy is variable, with some studies showing a greater reduction in pain than others.[45–47] Furthermore, many studies only examine physical therapy and its role in acute pain management postoperatively, without reporting long-term results.

### Surgical Interventions

#### Treatment of Existing PMPS/PBSPS

Surgical treatment for PMPS/PBSPS is another option for patients who have little or no response to the above measures. Broyles et al described their surgical approach to PMPS by first identifying affected intercostal nerves with a diagnostic local anesthetic block, and then dissecting these nerves and implanting them into local muscle. The majority of patients in their study achieved lasting pain relief after this procedure.[48] In the thoracic surgery literature, Williams et al describe a similar technique of intercostal nerve resection and implantation into surrounding muscle in their treatment of intercostal neuralgia.[49] Other studies have described the benefits of postoperative fat grafting in areas of painful scar retraction and nerve entrapment in patients who developed PMPS following mastectomy, axillary dissection, and radiotherapy.[50,51]

**Prevention of PMPS/PBSPS**

There has been much research into the prevention of phantom limb and neuroma pain after extremity amputations. In the context of breast surgery, O'Brien et al recently described their approach to PMPS prevention using targeted muscle reinnervation. During the primary surgery, they identify transected lateral or anterior intercostal nerves and perform neurorrhaphy between these damaged nerves and redundant motor nerves to adjacent muscles.[52] Similarly, Gatherwright and Knackstedt described the use of cadaveric nerve grafts for targeted reinnervation of damaged intercostal nerves to mastectomy skin flaps.[53] The use of porcine nerve caps to prevent neuroma formation in animal limbs has also been described. Whether these nerve caps have a role in prevention of PMPS remains to be seen.[54]

## OUR APPROACH TO PMPS/PBSPS TREATMENT

Just as the etiology of PMPS is multifactorial in nature, so too is the appropriate treatment algorithm (Fig. 1). We utilize a multidisciplinary approach in the care and treatment of patients with PMPS/PBSPS. Patients with PMPS/PBSPS may present to any member of the multidisciplinary team, the core of which is composed of a plastic surgeon, a pain specialist, and physical therapist. Additional practitioners may be enlisted as needed (surgical and medical oncologists, radiologists, and clinical psychologists). A diagnosis of PMPS/PBSPS is made once other nonneuropathic causes for pain (such as infection, musculoskeletal, or oncologic recurrence) are excluded. Once a diagnosis is made, treatment is provided based on the outlined algorithm.

Physical therapy is instituted for all patients to address mobility and strength deficiencies, and is continued throughout the patient's recovery. The pain specialist

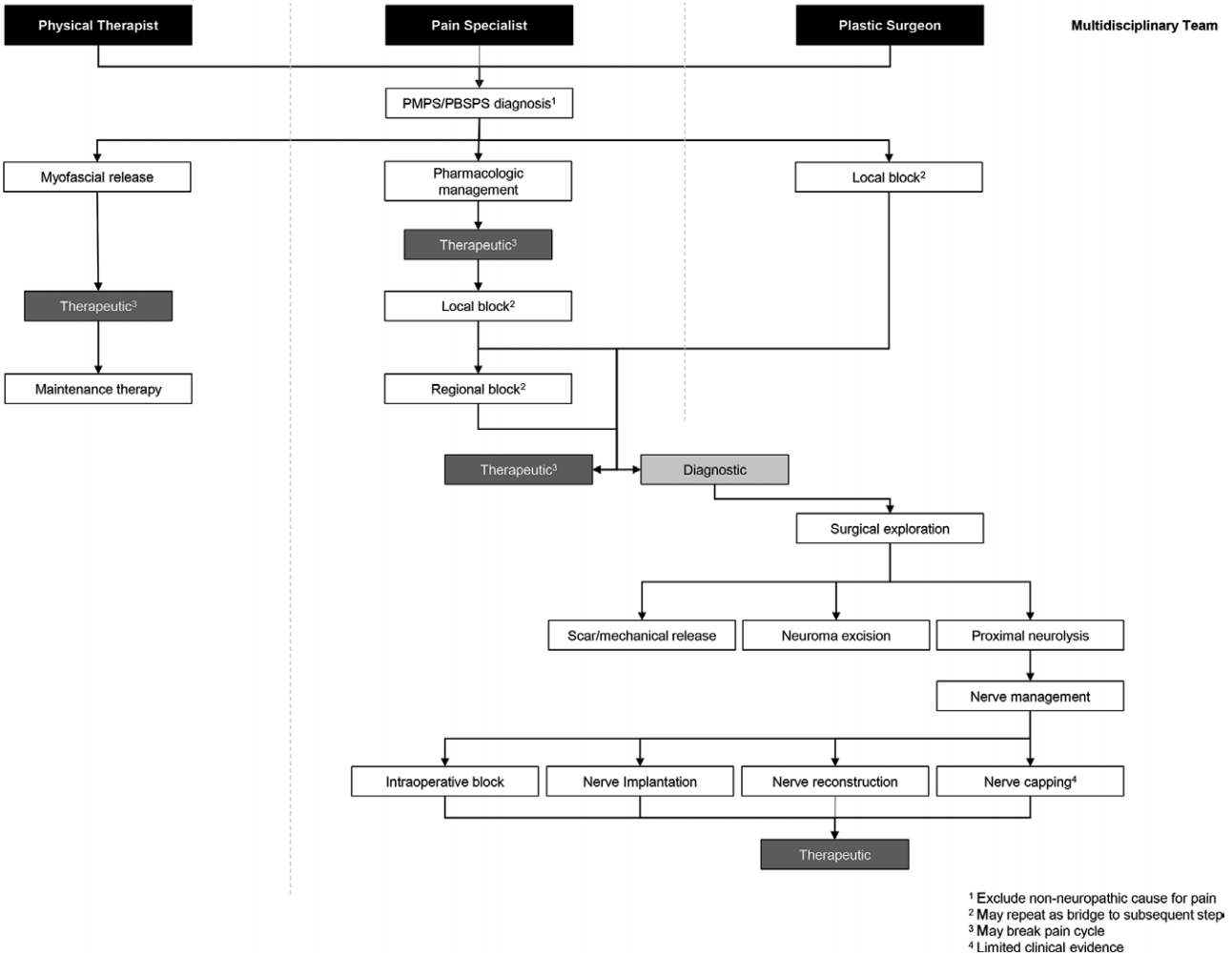


**Fig. 1.** Our outlined algorithmic, multidisciplinary approach to the care of patients with PMPS/PBSPS. Our treatment team is composed of plastic surgeons, physical therapists, and pain specialists, who work together to diagnose and treat patients with PMPS/PBSPS. As seen in the algorithm, local blocks can be used both for diagnosis and for symptom management, and can be performed either by the plastic surgeon or by the pain specialist. Surgical intervention is rarely the first-line treatment option, but rather, is offered after other, less-invasive options have been attempted.

manages a multimodal medication regimen and introduces local and regional blocks as necessary.

Surgical intervention is rarely the first option to be offered, as it is prudent to exhaust other modalities before embarking on invasive procedures, which include the potential risk of worsening symptoms. Failure of surgical intervention to improve symptomatology should be discussed as part of the informed consent, and a backup plan should be prepared should this occur.

Preoperatively, areas of maximal point tenderness are marked. Exploration is performed, and a neuroma, scar tissue, or a mechanical obstruction (ie, surgical clips or suture material) may be encountered. If a nerve is clearly seen entering the scar bed, it is dissected proximally until healthy nerve bundles are found. If no other reconstruction is being performed and there are no suitable distal nerve targets, the proximal nerves are buried into non-scarred tissue.[55] Our preferred reconstructive method is to perform coaptation of the proximal nerve stump to a sensory nerve in the context of free flap reconstruction. Alternatively, we consider using allogeneic nerve grafting to regional nerves, nerve conduit or allograft nerve.

Although our approach above outlines how to treat patients with existing PMPS/PBSPS, it is important to note that our increasing awareness of this problem has enabled us to take steps to prevent it from happening at the index surgery. Similar to searching the surgical field to obtain hemostasis, we also attempted to identify damaged, transected, or clipped nerves, especially in high-risk areas, such as the lateral breast and chest wall. This is often performed in conjunction with our surgical oncology colleagues.

## CASE EXAMPLES

**Case 1**

A 48-year-old woman, previously treated for breast cancer with bilateral mastectomies and implant-based reconstruction, was unhappy with her reconstruction, and presented with bilateral implant malposition and bilateral capsular contracture. Additionally, she reported chronic

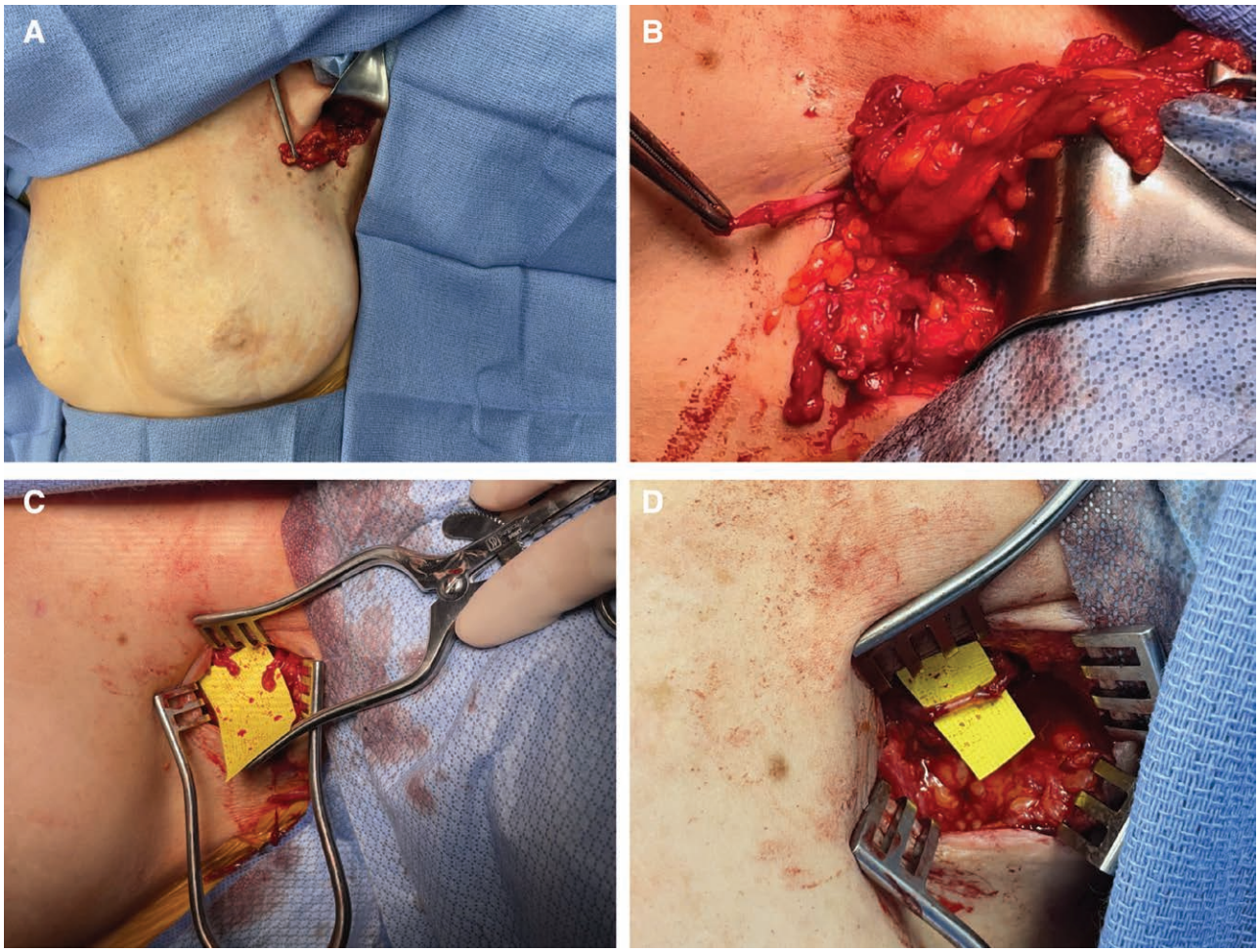


**Fig. 2.** A 51-year-old woman presented with left subaxillary tenderness at the site of a previous sentinel lymph node biopsy. After a thorough workup and exclusion of other, nonneuropathic causes of her pain, surgical exploration was performed. The previous incision was opened (A), and two ligated ends to the intercostobrachial nerve were identified (B). These ends appeared damaged under loupe magnification, and were trimmed back to healthy-appearing nerve ends (C). A 10-mm nerve connector was used to coapt the ends together to ensure a tension-free connection (D). The patient experienced almost instantaneous postoperative improvement in her pain.

pain of neuropathic character in the left lateral chest wall. Examination revealed significant tenderness to palpation in the anterior axillary line at the level of the fourth rib.

Intraoperatively, both implants were removed, and bilateral capsulectomies and pectoralis muscle repositioning were performed. Additionally, a clipped neurovascular bundle in the left lateral T4 region was identified. The nerve was dissected free of the vessels, and was connected to a sensory nerve that was transferred along with an ipsilateral transverse upper gracilis flap. A nerve graft was used to create a tension-free coaptation. The right breast was also reconstructive with an ipsilateral transverse upper gracilis flap with nerve coaptation to provide protective sensation. The patient reported immediate and complete resolution of her pain during the postoperative period and throughout her 1-year follow-up period.

**Case 2**

A 62-year-old woman who had previously undergone a Wise-pattern breast reduction presented with chronic pain in the right lateral chest and breast. This pain led to chronic narcotic use and multiple injections by pain management physicians over the 18 months following her original surgery. Point tenderness at the lateral T4 and T5 locations was elicited on examination. This pain was immediately, but temporarily, alleviated with direct injection of local anesthesia. Based on her pain symptoms, attempted prior treatments, and responsiveness to local block, surgical exploration was recommended.

Through the lateral aspect of the right transverse Wise-pattern incision, a cut edge of a lateral T5 intercostal nerve was identified. In addition, a clipped T4 intercostal nerve was also discovered. The two nerves were dissected free of the surrounding tissue and connected using a 15-mm nerve connector. The patient reported resolution of her pain after surgery and stopped her pain medications. However, at six months postoperative, she continued to have mild paresthesia of the right lateral nipple–areola complex, unchanged from before nerve exploration.

**Case 3**

A 51-year-old woman presented with left subaxillary tenderness and hypoesthesias at the site of a previous sentinel lymph node biopsy (Fig. 2). Surgical exploration revealed two ligated edges of the ICBN. The proximal edge was notably edematous and hypervascular on gross inspection. The nerve ends were trimmed and coapted using a 10-mm nerve connector. Immediate postoperative pain relief was noted, and continued throughout a three-month follow-up period.

## CONCLUSIONS

Although many studies are contradictory, it is clear that PMPS/PBSPS can be a significant problem for patients, which occurs following both breast cancer surgery/reconstruction, as well as noncancer-related breast surgery. Given the negative impact that this chronic pain can have, all patients should be treated as if they are at risk for this problem and it is crucial that providers have awareness of both the preventative and treatment options available. We believe that treatment of breast cancer, associated reconstructive efforts, and other noncancer breast surgeries should be considered truly successful only if patients are pain-free. Given the magnitude of breast surgeries performed annually, even a small percentage reduction in patients with PMPS/PBSPS will have a significant impact. By educating ourselves, our patients, and our breast surgery and oncology colleagues, we may be able to positively affect women who are currently affected by PMPS/PBSPS and have not been properly treated thus far.

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