



Re-visiting post-breast surgery pain syndrome: risk factors, peripheral nerve associations and clinical implications

George Kokosis, Karan Chopra, Halley Darrach, A. Lee Dellon, Eric H. Williams

Department of Plastic and Reconstructive Surgery, Johns Hopkins University, Baltimore, MD, USA

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Correspondence to: George Kokosis, MD. Department of Plastic and Reconstructive Surgery, 601 North Caroline Street, JHOC 8152A, Baltimore, MD 21287, USA. Email: gkokosis@jhmi.edu.

Abstract: Aesthetic and reconstructive breast surgery is among the most common operations performed by plastic surgeons. The prevalence of persistent pain after breast surgery remains underappreciated by plastic surgeons. Post breast surgery pain syndrome (PBSPS) is reported to range between 20–60%. It is the purpose of this paper to revisit chronic pain as a combination of the breast intervention and relate this to the peripheral nerve(s) transmitting the pain message, in order to understand the underlying etiology and to improve breast pain treatment outcomes.

Keywords: Breast surgery; breast pain; post mastectomy pain; nerve surgery

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Introduction

The introduction of the Breast Q, in 2007, as an outcome instrument for the evaluation of women having breast surgery (1) has enabled an understanding of quality of life issues in this large group of patients (2-5). Breast Q has a section addressing pain. To further evaluate pain, a numerical scoring system or the McGill pain questionnaire is typically added (6). The impact of pain in women having breast surgery is however not well defined and therefore underestimated.

In contrast, from 1986 through, and including the present (7,8), the term Post-Mastectomy Pain Syndrome has been used to discuss pain ramifications of breast interventions. The International Association for the Study of Pain (IASP) defines it as persistent pain soon after mastectomy or lumpectomy affecting the anterior thorax, axilla and/or upper arm (9). The literature related to this chronic pain after breast surgery suggests the magnitude of this problem may be as high as 50% of patients having

mastectomy (10,11). However, post breast surgery pain is not limited to mastectomy patients. Other types of surgical procedures of the breast, including reconstruction after mastectomy, cosmetic breast surgery and breast reduction (12-15). Therefore, a more appropriate term to discuss pain after breast surgery that is not limited to mastectomy is “post breast surgery pain syndrome” (PBSPS) which for the purpose of simplifying our review will be used for the remainder of the manuscript.

Peripheral nerve involvement in PBSPS has been suggested by the use of topical Capsaicin to relieve pain, by directing treatment at the end terminals of the unmyelinated nerve fibers (16). In contrast, a peripheral nerve itself, the intercostal-brachial nerve, has been suggested as the cause of the pain in at least seven patients (17).

It is the purpose of this paper to revisit chronic pain as a combination of the breast intervention and relate this to the peripheral nerve(s) transmitting the pain message, in order to understand the underlying etiology of PBSPS to improve breast pain treatment outcomes.

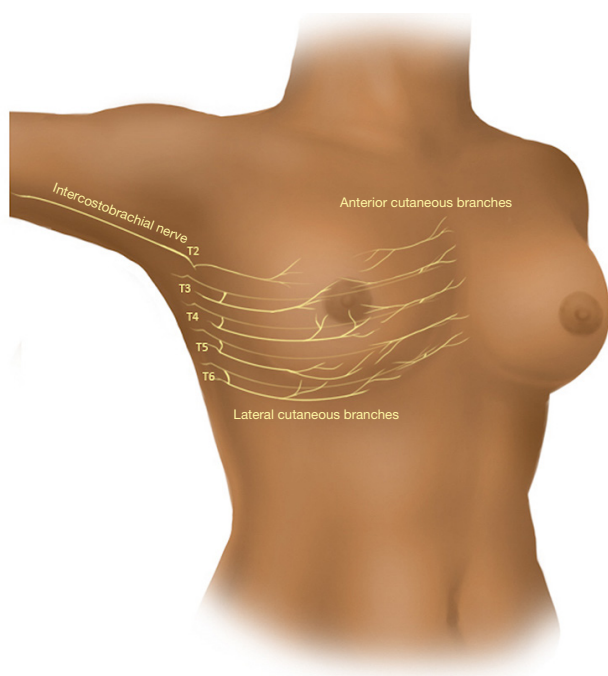


Figure 1 Anatomical considerations and associated nerves in breast surgery.

Definition

There is no universal definition of “post breast surgery pain syndrome” (PBSPS) as it is referred to by many authors. As summarized by Waltho *et al.* in their literature review of 23 studies, PBSPS is pain that occurs after any breast surgery, is of at least moderate severity, possesses neuropathic qualities, is located in the ipsilateral breast/chest wall, axilla, and/or arm, lasts at least 6 months, occurs at least 50% of the time and may be exacerbated by movements of the shoulder girdle (18). Characteristics of the pain that are mostly discussed between different authors are therefore the type of pain, its severity as well as its location, duration, frequency and exacerbating factors. Duration of the pain has been argued as more than 3–6 months (10,19,20).

Jung *et al.* proposed a classification of neuropathic pain following breast surgery:

- (I) Phantom breast pain (painful *vs.* non-painful). Non-painful is when the patient has the sensation that the removed breast tissue is still present. Painful is the same sensation but with associated pain.
- (II) ICBN (intercostobrachial nerve) injury.
- (III) Neuroma formation. This is the result of direct

injury to nerves innervating the surgical field. Axons can be trapped in the scar formed resulting in painful neuroma formation. Ducic *et al.* have described danger zones of potential injury during breast surgery (21), and it is in these zones that the intercostal nerves can be injured causing the painful neuroma (15).

Anatomical considerations (Figure 1)

The innervation of the breast parenchyma and overlying skin is through the medial and lateral cutaneous branches of the ventral ramus of the intercostal nerves T3–T6.

The lateral cutaneous branch of the second intercostal nerve (ICBN T2) crosses the axilla to innervate the upper medial arm and the anterolateral chest wall.

The anterior branch of the lateral branch of the T2 and T3 intercostal nerves have skin territories on the anterior chest, so that numbness/pain in the axilla and upper inner arm can be combined with pain over the upper lateral breast quadrant, and cause pain in the breast with arm movements, especially overhead movement. Hence the term, “intercostobrachial” nerve (ICBN).

The nipple is innervated through the lateral branch of T4. Injury to the above will cause allodynia, paresthesias and dysesthesia, and numbness related to the PBSPS.

The pectoralis major muscle is innervated through the medial and lateral pectoralis nerves. The long thoracic nerve to the serratus runs along the posterior part of the medial wall of the axilla. The thoracodorsal nerve to the latissimus dorsi runs vertically through the axilla in proximity to the subscapular artery and vein. All the above nerves are motor, and injury to any of the above will result in paralysis or weakness of the respective muscles. These nerves have no direct cutaneous innervation. Injury to these motor nerves may give referred pain to skin territories related to the motor nerve roots for these muscles (22).

Risk factors

Risk factors associated with the development of PBSPS vary significantly between different studies. It is important to clarify that nerve injury can either be a direct traumatic nerve transection with subsequent neuroma formation, or scar tissue resulting in stretch injury. Blunt *et al.* discuss the potential implication of postoperative hematoma to developing pain post-mastectomy (23). Gulluoglu *et al.* and Amichetti *et al.* report post-operative radiation as

potential risk factor (24,25). The mechanism underlying the radiation induced chronic pain is believed to be due to radiation neuritis, a process involving perineurial and intraneurial fibrosis, causing pain by compression of those nerve fibers, as well as the possibility loss of inhibitory input (26,27). Additionally, many authors have found young age

(<40–50) to be associated with higher chances of developing the syndrome (10-12,19). Possible explanations as to why younger age is associated with higher risk are discussed by Couceiro *et al.* as increased nerve sensitivity and lower threshold due to anxiety, more prevalent in this age group. Also the more aggressive nature of breast cancer in the younger population and more aggressive surgical treatment in this age group result in more anxiety (19). Other authors (Couceiro *et al.*, Wallace *et al.*, Smith *et al.*) have identified high BMI (>26) as a risk factor (12,19,27).

Another risk factor identified is prior history of headaches, with the most reasonable explanation being central sensitization (28,29). Preoperative pain has been found to be a risk factor for postoperative pain after mastectomy, perceived as breast pain (phantom pain) which is used as part of the classification of the syndrome by some authors (30).

Table 1 Development of PBSPS can be seen after different treatment modalities

Cosmetic surgery
Breast augmentation
Breast mastopexy
Fat grafting to breast
Mastectomy
Simple, with/without lymph node sampling
Including axillary node dissection
Including pectoralis major/minor resection
Breast reconstruction
Implant based
Implant with muscle flap
Autologous (pedicled, free, with or without muscle)
Breast reduction
Alternate approaches (circumareolar, inverted T incisions)

In this table, the syndrome is broken down as seen after cosmetic surgery, mastectomy alone or followed by reconstruction and breast reduction. PBSPS, post breast surgery pain syndrome.

Classification

Identification of the PBSPS early in its course is paramount for prompt management and relief of what could become disabling chronic pain. We discuss different surgical approaches that can potentially result in PBSPS (*Table 1, Figure 2*). The type and location of surgery is also associated with direct injury to specific nerves eliciting the chronic pain (*Table 2*).

- (I) Cosmetic breast surgery. Breast augmentation with implants can result in chronic pain in different ways. The approach/incision (peri-areolar,

Table 2 Development of PBSPS can be seen after injury to different nerves as listed on the table depending on the surgical approach, eliciting symptoms in different locations

Peripheral nerve	Pain location	Type of surgery/approach
Intercostobrachial nerve (ICBN)	Axilla, lateral upper chest/breast, upper medial arm	Mastectomy, axillary lymph node sampling/dissection, transaxillary augmentation
Intercostal T3	Anterior-central chest/breast	Mastectomy, periareolar augmentation, mastopexy, breast reduction, breast reconstruction
Intercostal T4	Anterior-central chest/breast, Nipple areolar complex	Mastectomy, periareolar augmentation, mastopexy, breast reduction, breast reconstruction
Intercostal T5	Inferior chest/breast	Mastectomy, inframammary augmentation, mastopexy, breast reduction, breast reconstruction
Intercostal T6	Inferior chest/breast	Mastectomy, inframammary augmentation, mastopexy, breast reduction, breast reconstruction
Infraclavicular brachial plexus	Superior chest/breast	Breast reconstruction (superior implant migration)

PBSPS, post breast surgery pain syndrome.

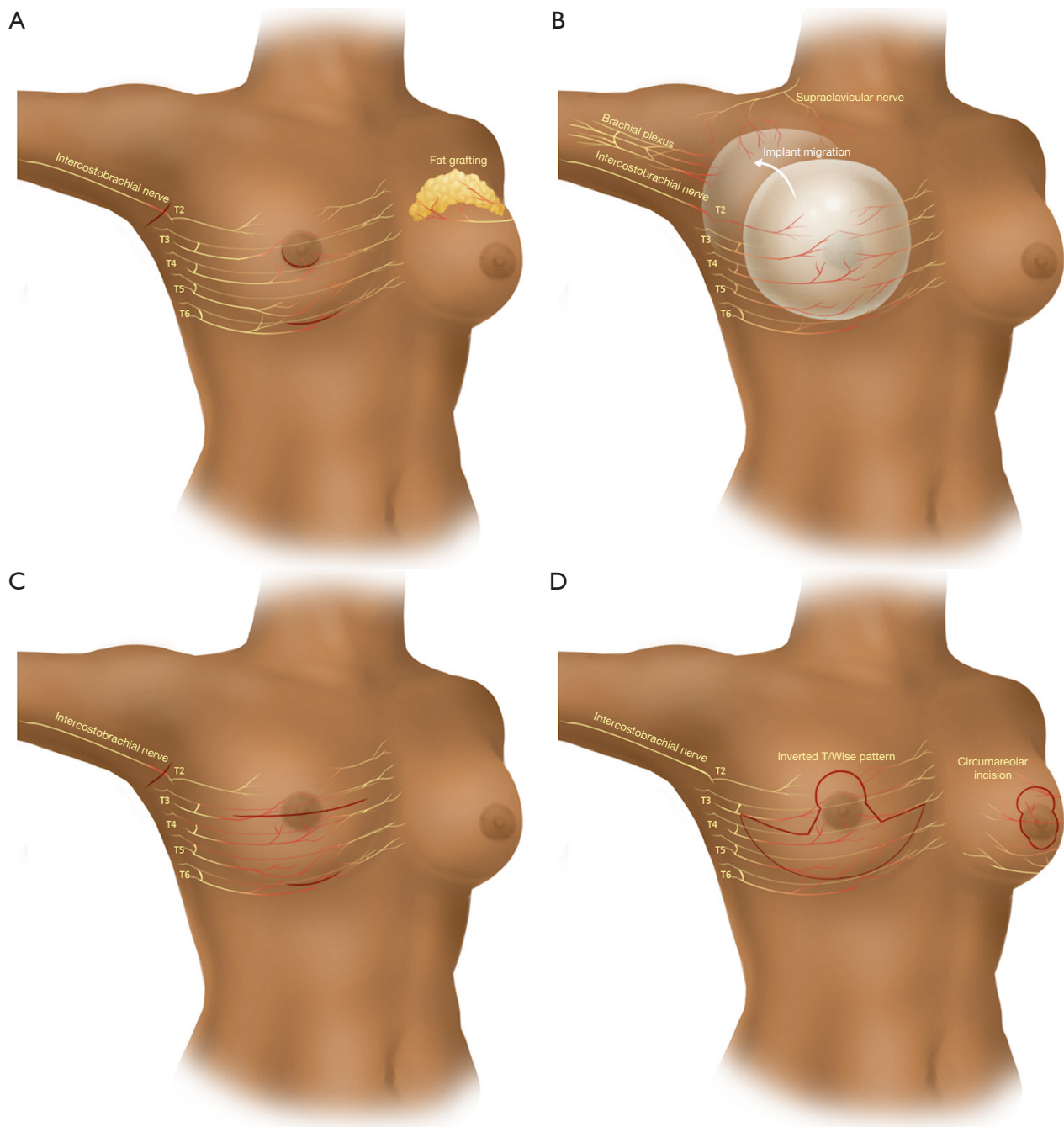


Figure 2 Illustration of nerves potentially injured in breast surgery (A), depending on different approaches to implant placement and fat grafting (B), implant location and capsular contracture (C), mastectomy or lumpectomy and/or axillary lymph node sampling or dissection (D).

inframammary fold, transaxillary) can directly injure nerves or the scar tissue from the incision healing can have the same effect. Additionally, submuscular or subglandular placement of the implants and subsequent capsular contracture can

cause pain from stretching adjacent structures, or entrapment of a nerve in the capsule itself. In the case of subglandular implants the skin nerve supply is involved and in case of subpectoral placement the pectoralis major may be a source of referred

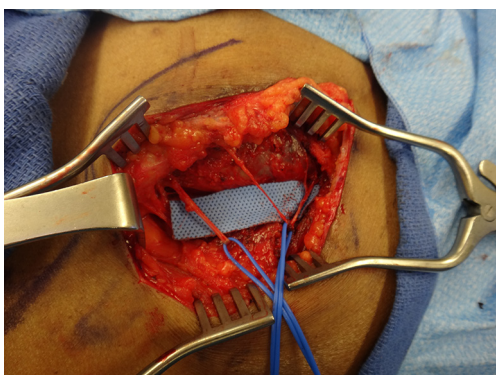


Figure 3 This is a patient that underwent breast augmentation through a wise incision about 1 year before she presented to our clinic with burning pain over the distribution of her second and third intercostals. Neuromas were found that were excised and buried in the muscle with appropriate outcome as evident by the resolution of her burning pain after the procedure.

pain or the intercostal nerve may be adherent to the capsule around the breast implant. Fat grafting for augmentation can also result in nerve pain from direct injury during the grafting process or compression from the volume of fat injected. A clinical example is provided (*Figure 3*).

- (II) Mastectomy or lumpectomy with or without axillary lymph node sampling or dissection. The ICBN is most commonly involved, especially during dissection in the axilla and the main reason for postoperative chronic pain following mastectomy or lumpectomy with lymph node dissection or sampling. Additionally, intercostal nerves can be injured during the process of removing the breast parenchyma. A clinical example is provided (*Figure 4*).
- (III) Breast reconstruction. If the mode of reconstruction is implant-based, as discussed above, the capsular contracture and stretching of the muscle when the pocket is made sub-muscularly can cause pain. Migration of the implants can cause direct pressure to the brachial plexus in its infraclavicular location (*Figure 5*). Reconstruction with a pedicled or free flap that results in pain should raise concerns about direct nerve injury and neuromas during dissection of the breast pocket. A clinical example is provided (*Figure 6*).
- (IV) Breast reduction. Different types of incisions are used to approach the breast reduction, including

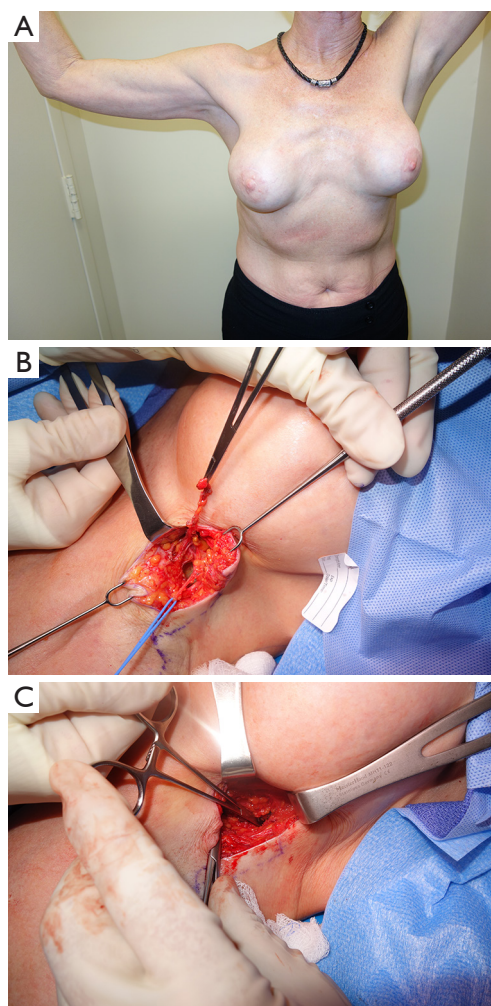


Figure 4 This is a patient that had right partial mastectomy and lymph node sampling, followed by simple mastectomy for positive margins about 2 years ago. She was seen in our office for persistent pain over her axilla and inability to raise her arm above the level of the shoulder due to pain (A). A neuroma of the intercostobrachial nerve was found and resected (B) and implanted into the muscle under tension (C) to avoid scarring and neuroma reformation if left at the operative field.

an inverted-T pattern, vertical pattern and circumareolar. Regardless of the incision, the pedicle design determines the breast parenchyma to be resected. Intercostal nerves T3-T6 are invariably prone to injury depending on the pedicle design. The sensation to the nipple-areolar complex is mostly affected (decreased) with the superior pedicle.

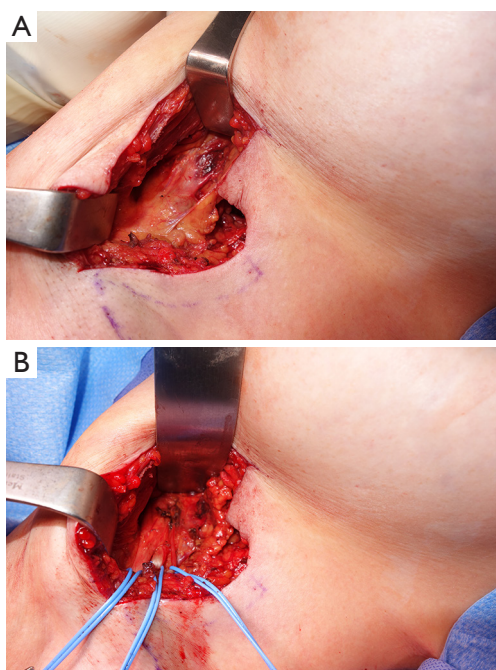


Figure 5 The patient discussed in *Figure 4* also had evidence of ulnar neuropathy and numbness along the medial antebrachial cutaneous nerve. The infraclavicular plexus was found to be scarred (A) and neurolysis (B) resulted in resolution of the paresthesias.

Discussion

Persistent pain following mastectomy has been described as early as 1978 (31). However, pain can develop after any type of breast surgery and not only mastectomy. Chronic pain of this nature can be disabling and a source of considerable distress. The incidence of PBSPS is described to be anywhere between 20% and 60% (10). The resulting debilitating pain persists for years with reported incidence as high as 40% in 3 years post-breast surgery (32). This is partially due to the poor understanding of the syndrome but also the lack of appropriate treatment. Kojima *et al.* performed a survey among medical providers in Japan regarding identification and treatment of this syndrome (33). The authors yielded a 34.7% response rate and found that 70.5% recognized PBSPS but only 47.7% treated it. The majority prescribed NSAIDs to treat PBSPS, therefore the treatment was ineffective. This study underlines the importance of physician education in managing PBSPS. It is important to remember that PBSPS is a chronic pain syndrome and as such, it is a multifactorial condition, linked to anatomical, behavioral and socioeconomic factors (34).

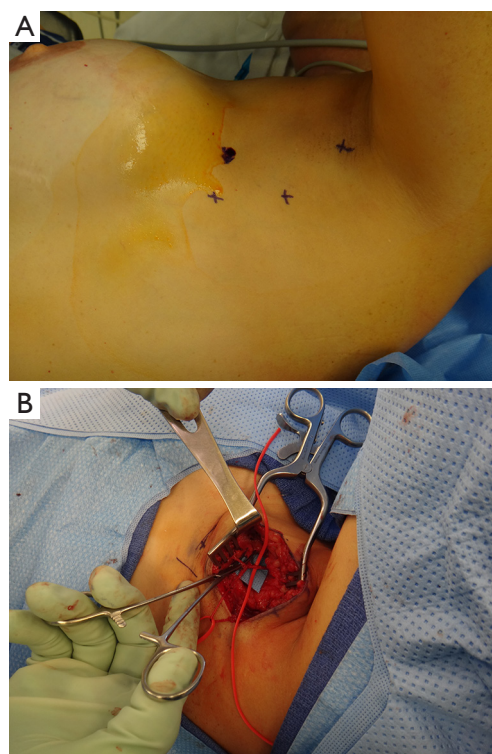


Figure 6 This patient presented with significant pain of her left lateral breast (A) following breast reconstruction with submuscular implant placement after breast resection for cancer. On exploration, neurolysis of the intercostal nerves stretched by the muscle pocket was performed (B). Her symptoms resolved after surgery.

While the contribution of the non-anatomical factors is ambiguous, anatomical reasons for PBSPS are easier to identify and deal with. There is no universal definition and classification of the syndrome in the literature. Different terms have been used before including Post-Mastectomy Pain Syndrome (PMPS), but that term by itself only covers the cases of pain following mastectomy but no other types of breast surgery. We are therefore re-visiting the PBSPS by breaking it down to subcategories based on the location of the pain and the type of surgery. Breast augmentation, mastectomy or lumpectomy and breast reconstruction, mainly implant-based as well as breast reduction surgery can all cause pain due to different pathways of nerve injury as described above. Ducic *et al.* performed a systematic review to identify the incidence of chronic pain following aesthetic breast surgery and found rates between 13.57% to 15.44% (35). The nerves involved were found to be the intercostal nerves, the intercostobrachial nerve as well as the

long thoracic nerve and brachial plexus (35). In the breast augmentation patients, submuscular placement of implants has been shown to result in increased pain compared to subglandular placement (50% vs. 21% respectively) (27). This is most likely related to capsular contracture and stretching of the muscle, a process that is more pronounced in the submuscular location as the nerves innervating the muscle travel underneath and potentially get incorporated within the newly formed capsule. Alternative explanation is direct brachial plexus compression, mainly from migration of the implants (13). However the systematic review by Ducic *et al.* showed no difference in symptoms when comparing the different implant pockets (35). The authors of this study found that implant volume is also not associated with increased risk for PBSPS (35). The intercostobrachial nerve injury is also a main risk factor for developing PBSPS after axillary lymph node dissection (ALND) or sampling for sentinel lymph node biopsy (SLNB) (10,11,17). This has led authors such as Vecht *et al.*, who described seven cases of patients with persistent pain in the distribution of the ICBN after ALND, to suggest the use of post-axillary dissection pain syndrome to better characterize this distinct clinical entity following ALND (17). With ALND, there can be difficulty preserving the ICBN. Abdullah *et al.* conducted a randomized trial where patients would have their ICBN preserved during ALND or resected (36). Interestingly enough, in the nerve preservation group only in 65% was the nerve actually preserved, highlighting the difficulty in protecting the ICBN during ALND. The incidence of sensory deficits among the patients whose nerve was preserved was significantly lower at discharge and during follow-up in 3 months, highlighting the importance of nerve preservation. Implant-based breast reconstruction has found to increase the incidence of postoperative chronic pain (50% rate with implant reconstruction vs. 30% rate without) (27). The same study revealed that delayed implant reconstruction has been found to be associated with higher incidence of pain as well (59% vs. 21%) (27). An explanation of this effect is that immediate reconstruction patients are usually lower risk profile patients that can tolerate a well vascularized breast flap (either pedicled or free flap) with or without a smaller size implant and the lack of progressive tissue expansion before a larger implant is placed. Breast reduction is associated with 22% incidence of PBSPS (14). It is believed to be due to injury to intercostal and supraclavicular nerves. Injury to intercostal nerves (T2-T7) and neuroma formation as the cause of pain after either implant base reconstruction, augmentation, mastopexy or

reduction has also been suggested by Broyles *et al.* (15). Regardless of the type of injury and the nerve involved, it is imperative that the provider involved in the care of patients complaining of pain after breast surgery is able to identify when symptoms point towards nerve injury rather than any other more common complications. Identification of the underlying etiologic factor can then tailor the appropriate treatment. This can be either surgical with nerve release and/or fat grafting or non-surgical, including pharmacologic treatments, local (capsaicin cream, botulinum toxin injections) or systemic (antidepressants) (8,35,37). The diagnostic algorithm and thorough assessment of the treatment of these nerve injuries is beyond the scope of this article.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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