

Post Breast Therapy Pain Syndrome (PBTPS)

Sabrina Selim, MD, Richard Shapiro MD, E. Shelley Hwang, MD and Ernest Rosenbaum, MD

Introduction

[Back to the Table Of Contents](#)

Definition: Post Breast Therapy Pain Syndrome (PBTPS) depends on the *characteristics, duration and location* of pain. It is defined as typical neuropathic pain and associated symptoms (numbness, dysesthesia, edema, allodynia) located in the chest wall, axilla, arm, or shoulder of the surgical side, and persists beyond the typical 3 month healing period. It includes many of the symptoms associated with post mastectomy pain syndrome (PMPS) and post axillary pain syndrome (PADS) reported in previous articles.

Post Breast Therapy Pain Syndrome (PBTPS) is an underreported condition believed to affect 10- 30% of women who have undergone surgical procedures for breast cancer. ¹ While prior studies have looked at post mastectomy (PMPS) or post axillary dissection pain syndromes (PADS), recent articles have reported a more encompassing condition which we term PBSPS. PBSPS not only results from injury to nerves during surgery; it is now believed that radiation and chemotherapy play a role in aggravating the condition. ² Because of its multivariate causes, PBSPS encompasses many different symptoms which can range from mild to debilitating in severity: chest and upper arm pain, numbness, edema, continuous aching and burning associated with chronic dysesthesia, allodynia (hypersensitivity to pain) and phantom breast tactile sensation/pain. The onset of symptoms can range from directly following breast surgery: mastectomy, axillary dissection, or other invasive procedure, to 6 months after. ³ Symptoms generally persist beyond the normal 3 month healing period.

Quality of life issues surrounding women diagnosed with PBTPS have prompted us to look at this recently acknowledged condition. Forty percent of women diagnosed with PBSPS reported increased pain with movement, leading to arm restriction and *frozen shoulder* syndrome. ¹ Over 50% of women experience pain during their daily chores, and over half reported sleep disturbances. ² Because these chronic symptoms are more widespread, and therefore affect the quality of life of many more women than the 4-6% reported by physicians, ⁴ it is important for healthcare professionals to consider the consequences when discussing treatment options and post-operative care with patients. Minimizing invasive procedures (sentinel lymph node biopsies and lumpectomies rather than traditional axillary node dissections and mastectomies, respectively) improving surgical technique and using adequate analgesics during and following surgery have been shown to reduce the incidence of PBSPS^{3, 5, 6}. Nevertheless for those women who still develop symptoms that interfere with a comfortable/productive life, advancements in pharmacological and more holistic treatments (acupuncture, massage, biofeedback, etc.) provide women with a range of treatment options.

Etiology

[Back to the Table Of Contents](#)

PBTPS is primarily a neuropathic disorder believed to be caused by a number of factors including injury to nerves/tissue due to surgery, radiation therapy, chemotherapy or secondary neuroma development. The most common theory for its onset is the injury to intercostobrachial nerves, which are sensory nerves that exit chest wall muscles and provide sensation to the shoulder and upper arm. It is believed that this nerve is injured in 80-100% of mastectomy patients who undergo an axillary dissection. ² Because of the extensive/invasiveness of a complete axillary dissection (CAD) as compared to sentinel node biopsies (SLND), in which only the lymph nodes draining a cancer are removed, there is a higher chance that nerves and vasculature be severed.

Furthermore, retraction compression during CAD can lead to PBTPS. It was shown that, even if the brachial plexus and peripheral nerves are spared, compression damage leads to neuropathic pain. Days or weeks following injury, ectopic neural activity may originate at the nerve injury site and dorsal root ganglion. The resulting increased sensitivity to chemical or mechanical stimuli results in spontaneous sensations, including pain. ² Studies supporting the theory that minimizing invasiveness decreases morbidity have shown that PBSPS correlates with the extent of axillary surgery (although this is being debated): ^{3, 5, 7, 9} 20-25% of women who received CAD showed signs of neuropathic pain, ⁵ SLND¹⁸, (which is believed to be as accurate in staging of the axilla) has resulted in fewer referrals to a pain clinic for treatment of PMPS. ³ It should be noted that if SLND results are positive for cancer, a CAD is generally performed to determine the extent of spread. Other studies have shown that the CAD group reported an increase in arm circumference, increased lymphedema, pain, numbness and decreased arm motility. Quality of life, however, was not significantly impacted by these symptoms. ⁸

Post Breast Therapy Pain Syndrome (PBTPS)

Sabrina Selim, MD, Richard Shapiro MD, E. Shelley Hwang, MD and Ernest Rosenbaum, MD

In a small study, intercostal neuromas (where the intercostal nerve was transected during mastectomies and breast reduction surgery and became embedded in scar tissue) were also briefly noted as contributing to incidence of PBTPS. The study, which involved the surgical resection of intercostal neuromas, found complete pain relief in all 5 patients. ²

In addition to intra-operative damage to the intercostobrachial and other¹⁰ nerves (long thoracic, thoracodorsal, lateral and medial pectorals, and branches of the brachial plexus) that innervate the breast, radiation therapy can either cause or aggravate the injury initiated by surgery. In this case, pain is deafferentation-type (the interruption of sensory nerve impulses by destroying or injuring the sensory nerve fibers) and generally occurs in regions (anterior thorax, axilla and medial upper arm) innervated by the damaged nerves. Because radiation-induced fibrosis or tumor involvement in the brachial plexus may also cause similar symptoms to PBTPS, it is frequently misdiagnosed as brachial plexopathy or disease recurrence. ³ **The healthcare provider is encouraged to emphasize that PBSPS does not signify a recurrence in cancer.**

Furthermore, chemotherapy (such as Taxol, Vincristine, and Platinum) can contribute to polyneuropathies similar to those induced by radiation therapy; this can intensify the pain and impairment caused by surgery.

Some patients were found to suffer from severe and chronic pain which in turn results in the remodeling of parts of the brain that processes painful stimuli. ⁵ It was shown that the limbic system becomes hypersensitized to painful stimuli and results in a feedback between injured sensory nerves and the *emotional pain* centers of the brain. Furthermore, neural pain receptor networks within the spinal cord were found to play a role in the perpetuation of painful sensations from the operative site. In these cases, psychological counseling and neurotropic drugs (anti-depressant and neurontin) were shown to decrease the severity of chronic pain. ⁵ It should be noted however, that while many women with PBTPS are understandably afflicted with symptoms of depression, PBSPS is not a manifestation of chronic depression or behavior/mental illness.

	Mastectomy	Lumpectomy	Complete Axillary Dissection (CAD)	Sentinel Node Dissection (SLND)
Definition	<ul style="list-style-type: none"> -Radical Mastectomy Complete removal of breast tissue; radical mastectomy includes the removal of lymph nodes and chest wall muscles -Modified Radical Mastectomy Complete removal of breast tissue and lymph nodes. 	<p>Removal of a breast cancer (lump) and the surrounding tissue without removing the entire breast.</p>	<p>Removal of all axillary lymph nodes which are then reviewed by a pathologist to determine stage of breast cancer</p>	<p>Isosulfan blue or a radioisotope is injected into a tumor to determine the draining lymph node; this node is selectively removed thereby sparing other nodes</p>
Pro	<ul style="list-style-type: none"> -Removal of multifocal disease -Disease control and cure of large tumors -Prophylactic if there's a genetic 	<p>Lumpectomy + radiation -> decreased incidence of PBTPS vs. mastectomy; no difference in recurrence or overall survival ⁵</p>	<p>The <i>gold standard</i> against which other axillary node procedures are compared.</p>	<ul style="list-style-type: none"> -Nearly 0 morbidity due to minor dissection to avoid nerves and vasculature ⁸ -The ability to examine SLN through multiple sections therefore more

Post Breast Therapy Pain Syndrome (PBTPS)

Sabrina Selim, MD, Richard Shapiro MD, E. Shelley Hwang, MD and Ernest Rosenbaum, MD

	predisposition to breast cancer			accurate/increased detection of metastases ⁸
Cons	<p>-Up to 43% of women will develop PMPS over their lifetime ¹⁴</p> <p>-May need reconstructive surgery</p>	<p>-Breast defects</p> <p>-Not standard practice for multifocal or large tumors</p>	<p>- Increased pain with increased #ref LN removed or chemotherapy received ²</p> <p>- Surgery-related symptoms persist for majority of womenà dec. QOL, mental health</p>	<p>-Accuracy to detect micrometastases still being evaluated ⁸</p> <p>-Adverse reactions to Isosulfan blue ¹²</p>
PBTPS Symptoms Reported	<p>-12-55% of women (underreported?) experience phantom breast pain ²</p> <p>-3 months after mastectomy:⁶ 35% chest pain 39% axilla pain 39% arm pain 100% decreased sensation 61% chronic pain</p>	Presumed (preliminary reports) decreased pain vs. mastectomy	<p>- 20-25% of women experience symptoms overall ⁶</p> <p>-2-5 years after ALND:¹¹ 35% numbness 15% arm swelling 30% pain 8% limited arm motion</p> <p>-72% of women reported pain, weakness, numbness over their lifetime ¹¹</p> <p>-73% reported decreased range of motion ¹⁶</p>	-Nearly 0 morbidity is noted; however long-term data is currently lacking.

Prevalence + Risk Factors for PBTPS

[Back to the Table Of Contents](#)

There was no significant difference between women from varying demographic regions. ² More research is needed to verify the following correlates since several articles report contradictory results, ^{1, 3, 9} but an increased risk for developing PBTPS are believed to depend on:

Younger age: ^{3, 14} Why younger women have a statistically significant increased risk for developing PBTPS is not known. A study showed that 65% of women ages 30-49 developed PBSPS, while only 26% of those 70 or older were affected.

Several theories include: ¹⁴

- an increased sensitivity of nerve damage in younger women
- more extensive efforts at axillary dissection in younger women

Post Breast Therapy Pain Syndrome (PBTPS)

Sabrina Selim, MD, Richard Shapiro MD, E. Shelley Hwang, MD and Ernest Rosenbaum, MD

- the nature of breast cancer in pre-menopausal women
- increased anxiety, and therefore a lower threshold for unusual sensations, in younger women
- Increased body mass index (BMI) ¹⁴
- Larger tumor size ³
- Improper surgical technique ^{3, 13}
- Increased axillary node invasion ³
- Use of chemotherapy or radiation therapy ^{3, 14}
- Post-operative complications such as infection or bleeding ³

Pharmacologic Treatments

[Back to the Table Of Contents](#)

To minimize the deleterious effects of PBTPS, it is noted that prevention, through the preservation of nerves, is the best measure. Minimizing invasive procedures: using SLNB vs. CAD results in decreased injury to intercostobrachial and sensory nerves to the chest wall and axilla, and lumpectomy plus radiation were shown to be equally effective in preventing local recurrence while maximizing survival, as a mastectomy. ⁴ The American College of Surgeons Oncology Group is currently sponsoring 2 clinical trials which compare SLNB and CAD, and more should be known in the next several years.

Despite the availability of prescribed therapies, many women either don't know about their options or choose not to use them. A study showed that many breast cancer survivors with PMPS are not interested in pharmacological treatments due to the possibility of side effects or the perceived risk of chronic (versus short term) pain treatment. Furthermore, since PBTPS occurs after surgery, many women learn to cope with and accept pain. ⁴ Approximately 80% of the women interviewed for the study reported self-treatment with nonprescription therapies such as over-the-counter medications, massage, heat, rest, etc. ⁴

Additionally, another study noted that *complications that are considered minor by physicians' standards may still be troubling to patients but tend not to be noted in medical records. Numbness, for example, was virtually never described in medical records but was the most frequent patient-reported symptom, occurring in 35% of (ALND) patients.* ¹¹ This emphasizes the notion that PBTPS remains an underreported, yet debilitating, consequence of surgery. It is still not well recognized by physicians, so women are not educated about the risks of developing PBSPS. They consequently learn to accept/live with the pain and symptoms that detract from quality of life. While few treatments completely eliminate PBSPS, there are many methods to ameliorate the symptoms.

These medically directed therapies have been compiled from various sources: ^{5, 6, 12}

- Anti-inflammatory agents (Ibuprofen, Naproxyn and other NSAIDs)
- Low-dose antidepressants (Elavil, Pamelor and other SSRIs) although maximum benefit necessitates consistent usage for several weeks
- Topical counterirritants (capsaicin and mentholated creams) although the overall efficacy is poor. Capsaicin cream acts by interrupting transmission of pain impulses through small diameter nerves by decreasing substance P (a neurotransmitter). It is effective in patients with neuromas
- Local anesthetic and corticosteroid injections for scar neuromas -- serial injections over several weeks/months are often needed to see dramatic improvement. If there is only temporary but complete relief following injections, improvement may be seen with excision of the painful area of the scar along the neuroma. If there is no improvement following injection, removal of the scar is unlikely to be effective.
- EMLA (eutectic mixture of local anesthetics: 25mg lidocaine, 25mg prilocaine per ml water) application prior to surgery

Post Breast Therapy Pain Syndrome (PBTSP)

Sabrina Selim, MD, Richard Shapiro MD, E. Shelley Hwang, MD and Ernest Rosenbaum, MD

has been shown to decrease the need for post-operative analgesics, and the incidence/intensity of chronic pain. Since post-operative pain is associated with continuous firing of nervous system from the wound area and axillary lymph nodes, analgesic drugs are needed until the wound heals. Further confirmatory studies on EMLA are needed.

- For otherwise intractable pain, the following may be used as a last resort. There are a variety of options depending on the circumstance and personal need to control suffering:

- a) thoracic sympathectomy
- b) intermittent corticosteroid or anesthetic injections into the epidural space
- c) implantable spinal cord stimulators
- d) regional nerve blocks or neurolytic agents (alcohol)
- e) sacrifice nerves (surgical)

It should be noted that narcotics have been shown as ineffective against chronic neuropathic pain, and generally results in dependency.

Adjunctive Therapy

[Back to the Table Of Contents](#)

In addition to pharmacologic treatments, several studies have shown the importance of adjunctive therapies to improve the physical and psychological health of women diagnosed with PBCPS. Acupuncture, for example, was shown to significantly increase the range of arm motion, and reduce pain following axillary dissection.¹³ Other suggested modalities include:

- Guided imagery training
- Biofeedback
- Physical therapy to prevent "frozen shoulder" syndrome as a result of inadequate movement
- Psychological counseling has also been shown as effective: improvements in both comfort and function were seen when patients underwent behavior therapy in addition to their medication. By consulting with psychologists/psychiatrists trained in chronic pain syndromes, these patients were able to address the psycho-emotional component in the limbic pain reinforcement pathways.⁵

Aggravating and Alleviating Factors

[Back to the Table Of Contents](#)

Several studies used retrospective questionnaires and telephone interviews to evaluate symptoms from women who had undergone mastectomies and axillary node dissections.^{4, 11} All women interviewed were diagnosed with PMPS. Women noted the symptoms influencing their quality of life, noting adverse or alleviating effects. One study concluded *the need for clinical trials evaluating the effectiveness of nonpharmacologic or cognitive behavioral therapies in alleviating mild to moderate PMPS.*

Aggravating ^{4, 11}		Alleviating ^{4, 11}	
1) 62%	overuse of arm	1) 51%	medication
2) 59%	lifting arm	2) 49%	rest
3) 42%	straining	3) 46%	heat
4) 38%	sudden movements	4) 22%	exercise
5) 16%	cold	5) 19%	massage; stocking; lying down

Post Breast Therapy Pain Syndrome (PBTSP)

Sabrina Selim, MD, Richard Shapiro MD, E. Shelley Hwang, MD and Ernest Rosenbaum, MD

6) 14%	misc.: clothing, weather, stress, swelling	6) 11%	misc.: prayer, alcohol, no bra
7) 13%	coughing	7) 3%	ice
8) 11%	lack of movement; pressure on arm; prolonged standing		

Summary

[Back to the Table Of Contents](#)

The importance of educating both caregivers and breast cancer patients regarding surgery and therapy-induced PBTSP cannot be overemphasized. Through proper surgical technique, minimizing invasive procedures, using adequate analgesics during and after therapy and encouraging women to take part in their recovery, we hope to reduce the incidence of PBTSP. Further research to unravel the conflicting results regarding surgical techniques, patient ages and post-treatment recovery remains to be done. Furthermore, discovering appropriate pharmacologic and integrative therapies for those women who do suffer from chronic pain and resulting consequence to quality of life can only benefit the 200,000-400,000 women currently enduring symptoms of PBTSP.

References/Important Conclusions

[Back to the Table Of Contents](#)

1. Canadian consensus document from the Canadian Medical Association. Clinical practice guidelines for the care and treatment of breast cancer: the management of chronic pain in patients with breast cancer (summary of the 2001 update) 10. The management of chronic pain in patients with breast cancer Chris Emery, Romyne Gallagher, Maria Hugi, Mark Levine, for the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer *CMAJ* 2001;165(9):1218-9 special supplement to www.cancerlynx.com/breastpain.html
2. Lash TL, Silliman RA. Patient Characteristics and Treatments Associated with a Decline in Upper-Body Function Following Breast Cancer Therapy. *J Clin Epidemiol* 2000; 53:615-622.
3. Miguel RM Kuhn AM, Shons AR, Dyches P, Ebert MD, Peltz ES, Nguyen K, Cox CE. The Effect of Sentinel Node Selective Axillary Lymphadenectomy on the Incidence of Postmastectomy Pain Syndrome. *Cancer Control* 2001; 8:427-430.

Of 1009 women with breast cancer between 1991 and 1998, 55 were diagnosed with postmastectomy pain syndrome in a pain clinic. While 15 women were seen in the clinic in 1991, this number dropped to 3 in 1998; all but 1 of 55 had ALND and none had SLNB. **Conclusion:** PMPS is a complication of ALND. The increase in SLND performed has decreased the number of referrals to the clinic for treatment of PMPS thus SLND is associated with decreased morbidity.
4. Carpenter JS, Andrykowski MA, Sloan P, Cunningham L, Cordova MJ, Studts JL, McGrath PC, Sloan D, Kenady DE. Postmastectomy/Postlumpectomy Pain in Breast Cancer Survivors. *J Clin Epidemiol* 1998; 51:1285-1292.
5. Wascher, Robert, M.D.,FACS; PostMastectomy Pain Syndromes: A Surgeon's Perspective; <http://www.cancersupportivecare.com/surgerypain.html>
6. Fassoulaki A, Sarantopoulos C, Melemini A, Hogan Q. EMLA Reduces Acute and Chronic Pain After Breast Surgery for Cancer. *Reg Anesth Pain Med* 2000;25:350-355.

Post Breast Therapy Pain Syndrome (PBTSP)

Sabrina Selim, MD, Richard Shapiro MD, E. Shelley Hwang, MD and Ernest Rosenbaum, MD

Forty six women received either pre-operative and post-operative (4 days) EMLA or placebo. They were monitored for post surgical pain Three months later, they were asked if they had pain in the chest wall, axilla and/or medial upper arm, decreased sensation, if they required analgesics at home, and the intensity of their pain. **Conclusion:** application of EMLA reduced post-operative analgesic requirements and the incidence/intensity of chronic pain.

7. Fassoulaki A, Sarantopoulos C, Melemini A, Hogan Q. Regional Block and Mexiletine: The Effect on Pain After Cancer Breast Surgery. *Reg Anesth Pain Med* 2001; 26:223-228.

100 patients received either regional block and oral metxiletine (R + M), (placebo + M), (R + placebo), or (placebo + placebo) for the first 6 postoperative days after breast surgery. Postoperative pain was assessed. Three months later, patients were interviewed for the presence and intensity of pain, abnormal sensation and analgesic requirement. **Conclusion:** Regional block reduced analgesic requirement in early post-operative period, R + M reduced requirements during next 5 post-operative days and although chronic pain was not affected, late-abnormal sensation may be diminished by R + M.

8. Shrenk P, Reiger R, Shamiyeh A, Wayand W. Morbidity following Sentinel Lymph Node Biopsy versus Axillary Lymph Node Dissection for Patients with Breast Carcinoma. *Cancer* 2000; 88: 608-614.

Thirty-five women post-ALND were compared with 35 women post SLNB according to circumference of arm, subjective lymphedema, pain, numbness, arm strength, mobility and stiffness. Conclusion: SLNB is associated with negligible morbidity versus ALND.

9. Wong L. Intercostal Neuromas: A Treatable Cause of Postoperative Breast Surgery Pain. *Ann Plast Surg* 2001; 46:481-484.

Five patients with intercostal neuromas had surgery to retract nerve deep to intercostal muscle. Conclusion: 12-48 months post-operatively, all patients had complete symptomatic relief.

10. Netter, Frank. Atlas of Human Anatomy. New Jersey: Hoechstetter Printing Company. 1989.

11. Warmuth MA, Bowen G, Prosnitz LR, Chu L, Broadwater G, Peterson B, Leight G, Winer EP. Complications of Axillary Lymph Node Dissection for Carcinoma of the Breast: A Report Based on a Patient Survey. *Cancer* 1998; 83:1362-1368.

Mailed survey of 330 Stage I and II breast cancer patients free from recurrence 2-5 years after axillary lymph node dissection. Conclusion: mild symptoms, especially pain and numbness, are common 2-5 years after ALND, frequency of inflammation and infection were greater than previously appreciated for women who had received radiation therapy following ALND, but that overall quality of life was not overly impacted due to complications of symptoms of ALND

12. Barnett, Jim, MD; Persistent Pain after Breast Surgery; www.cancerlynx.com/breastpain.html

13. He JP, Friedrich M, Ertan AK, Muller K, Schmidt W. Pain-Relief and Movement Improvement by Acupuncture after Ablation and Axillary Lymphadenectomy in Patients with Mammary Cancer. *Clin Exp Obstet Gynecol* 1999; 26:81-84.

14. Smith WCS, Bourne D, Squair J, Phillips DO, Chambers WA. A Retrospective Cohort Study of Post Mastectomy Pain Syndrome. *Pain* 1999; 83:91-95.

Retrospective cohort of mastectomy patients over 6 years. 408 women completed questionnaires which revealed that 43% had suffered from PMPS and 29% reported current symptoms. Body weight, height and age (younger) were associated with the frequency of PMPS.

15. Tasmuth T, Blomqvist C, Kalso E. Chronic Post-Treatment Symptoms in Patients with Breast Cancer Operated in Different Surgical Units. *Eur J Surg Oncol* 1999; 25:38-43.

Post Breast Therapy Pain Syndrome (PBTPS)

Sabrina Selim, MD, Richard Shapiro MD, E. Shelley Hwang, MD and Ernest Rosenbaum, MD

16. Hack TF, Cohen L, Katz J, Robson LS, Goss P. Physical and Psychological Morbidity after Axillary Lymph Node Dissection for Breast Cancer. *J Clin Oncol* 1999; 17:143-149.
17. Leong, SPF, Donegan E, Hefferon W, Dean S, Katz JA. Adverse Reactions to Isosulfan Blue During Selective Sentinel Lymph Node Dissection in Melanoma. *Ann of Surg Oncol*. 2000; 7:361-366.
18. Robert A. Wascher, MD, FACS. Overview Of The Sentinel Lymph Node Concept *CancerLynx.com* 2002; www.cancerlynx.com/sln.html

Additional References

[Back to the Table Of Contents](#)

- Kwekkeboom KL. Pain Management Strategies used by Patients with Breast and Gynecologic Cancer with Postoperative Pain. *Cancer Nurs* 2001; 24:378-86.
- Gottrup H, Andersen J, Arendt-Nielsen L, Jensen TS. Psychophysical Examination in Patients with Post-Mastectomy Pain. *Pain* 2000; 87:275-284.
- Carpenter JS, Sloan P, Andrykowski MA, McGrath P, Sloan D, Rexford T, Kenady D. Risk Factors for Pain after Mastectomy/Lumpectomy. *Cancer Pract* 1999; 7:66-70.

This section written by: Sabrina Selim, B.A., Medical Student, Dartmouth Medical School, Richard Shapiro M.D., Chief of Anesthesiology, Union Memorial Hospital, and Ernest Rosenbaum, M.D., Clinical Professor of Medicine, UCSF Comprehensive Cancer Center and Stanford Hospital and Clinics, Shelley Hwang, MD Assistant Professor, Surgery, UCSF