PAIN MEDICINE CASE REPORTS

ISSN 2768-5152

Volume 5, Number 2, pp. 73-78

Received: 2020-09-17
Accepted: 2020-09-24
Published: 2021-03-31

Treatment of Postmastectomy Pain Syndrome with Spinal Cord Stimulation: A Case Series

Matthew Chung, MD
Harold Ray, MD
Tsun Hsuan Chen, PhD
Yinan Chen, MD, PhD
George Ansoanuur, MD
Christina Le-Short, MD

Background: Postmastectomy pain syndrome (PMPS) is a chronic pain syndrome that can be refractory to treatment by pain specialists. Spinal cord stimulation is a technique that has been approved for neuropathic pain and shown promise as a modality for targeted treatment. In this study, we report the outcomes of spinal cord stimulation in patients with refractory PMPS.

Case Report: A retrospective chart review was performed at The University of Texas MD Anderson Cancer Center to identify patients who underwent spinal cord stimulation during a 3-year period. Relevant outcomes for efficacy and safety were evaluated. The protocol was reviewed and approved by The University of Texas MD Anderson Cancer Center Institutional Review Board.

Seven patients with refractory PMPS were treated with spinal cord stimulation at our institution. All patients initially underwent trial spinal cord stimulation, with a mean preoperative Numeric Rating Scale (0-10) (NRS-11) score of 8.29 ± 1.70. Six of 7 (85.7%) patients reported a successful trial stimulation (> 50% pain reduction); however, only 5 received permanent implantation. Following implantation, the reported one-month postoperative NRS-11 score was 4.20 ± 1.79. The mean change in the pain score between pre- and postoperative intervention was 4.40 ± 1.34 (Cohen's d = 3.28, P = .002). The mean decrease in the morphine equivalent daily dose (MEDD) following implantation was 55.80 (SD 82.21, Cohen's d = 0.68, P = .125).

Conclusion: Spinal cord stimulation may be an effective therapy for patients experiencing chronic PMPS and should be considered in medically refractory cases. Future prospective studies are warranted to confirm the positive outcomes we demonstrated pertaining to pain scores and opioid medication changes.

Key words: Cancer pain, postmastectomy pain syndrome, neuromodulation, opioids

BACKGROUND

Postmastectomy pain syndrome (PMPS) affects 25% to 60% of women who undergo mastectomy (1). The pain can be debilitating, both emotionally and physically. It is thought to be multifactorial in origin and presents primarily as neuropathic pain (1,2) that results from damage to the surrounding nerves during surgery

From: Department of Pain Medicine, Division of Anesthesiology, Critical Care and Pain Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas

Corresponding Author: Matthew Chung, MD E-mail: mchung1@mdanderson.org
Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

(intercostobrachial nerve, lateral and medial pectoral nerves). This type of pain is notoriously difficult to treat. In addition, given its intimate location, PMPS is complicated by psychosocial distress, greatly impacting quality of life in most patients. This psychologic component is further evidenced by the increased risk of PMPS in patients with anxiety, depression, and somatization (3).

Treatment of PMPS primarily centers on slow-acting neuropathic agents (1) that are associated with unwanted side effects. Other medications, such as opioids, are also used; however, in our current political climate and as a result of social awareness about the potential for addiction and overdose, alternative therapies are being sought. Spinal cord stimulation (SCS) is a technique that has been approved for neuropathic pain (4). This technology has undergone many innovations in the last few years, as devices now provide new waveforms that target pain differently. In the following cases, we review the efficacy and outcome of SCS in patients with chronic PMPS.

METHODS

A retrospective chart review was performed to identify all patients from the Pain Medicine Department at The University of Texas MD Anderson Cancer Center (Houston, TX) who underwent SCS for PMPS from March 4, 2016 to October 21, 2019. The protocol was reviewed and approved by The University of Texas MD Anderson Cancer Center Institutional Review Board. Demographic variables were collected, including indication, comorbidities, age, and prior treatments. Pre- and postoperative Numeric Rating Scale (NRS-11) pain scores, postoperative complications, and narcotic medication doses were also collected. Narcotic medications were converted to morphine equivalent daily dose (MEDD) to provide consistency.

Statistical Analysis

Categorical variables were summarized as percentages, while continuous variables were reported as means, standard deviations (SDs), and ranges. Paired t tests (or the Wilcoxon signed rank test if the normality assumption was not met) and Cohen's d effect sizes were used to compare the mean NRS-11 pain scores and MEDD values before and after the spinal cord stimulator trial and one month post spinal cord stimulator implantation using SAS version 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

Case #1

A 56-year-old woman with right-sided breast cancer status post chemotherapy and mastectomy with tumor invasion of the brachial plexus presented with chronic right-hand pain with the greatest intensity in the lateral 3 fingers, extending to her right chest. The pain was described as shooting and stabbing. She had trialed venlafaxine, duloxetine, tramadol, and pregabalin, and was managed primarily on hydrocodone and gabapentin. She had also tried transcutaneous electrical nerve stimulation (TENS) therapy, physical therapy, acupuncture, and a stellate ganglion block with minimal relief. As the patient was limited from work due to her pain, she sought alternative means of pain relief, prompting pursuit of her trial.

A Burst DR stimulator (Abbott Laboratories, Plano, TX) was used for the trial and implantation. During the trial period, the patient reported > 75% pain relief, which led to subsequent implantation. One octrode lead was placed midline and advanced to the superior aspect of C2; an additional octrode lead was advanced to the superior aspect of C3. The patient continued to experience relief one year after implantation and continues to reduce her opioid regimen.

Case #2

A 54-year-old woman with right-sided breast cancer with a history of lumpectomy, chemotherapy, radiation, and hormone therapy presented with right-sided chest and armpit pain. She complained of pain in the right chest wall and axilla that radiated toward the inferior margin of the scapula and under her breast. She previously trialed acupuncture, trigger point injections, and intercostal nerve blocks with minimal pain relief. At the time of evaluation she was being managed with hydrocodone and gabapentin. Since her medications made it difficult to work, she sought alternative modalities of pain relief, prompting pursuit of a trial.

A Burst DR stimulator was used for the trial and implantation. Both octrode leads were placed slightly to the right of the midline, with one lead advanced to the T3 level and the second lead up to the T1 vertebral level. The patient reported 80% relief during the trial, which led to subsequent implantation. The patient's postprocedure course was complicated by lead migration following a traumatic mechanical fall that required revision. After revision, the patient

had shown enough improvement in pain control that she discontinued all opioid use. At her 15-month follow-up, she reported continued relief and was without opioids.

Case #3

A 64-year-old woman with breast cancer status post mastectomy, chemotherapy, and radiation therapy presented with multiple-site pain, including chronic back pain and right upper extremity pain. She complained of sharp pain in her right upper extremity that worsened with swelling from lymphedema. She had previously trialed acupuncture, intercostal nerve blocks, physical therapy, compressive wraps, methadone, tramadol, pregabalin, duloxetine, fentanyl patches, and gabapentin. She was managed on morphine and hydrocodone at the time of evaluation. Since the patient was limited at home and at work due to her pain and lymphedema, the decision was made to proceed with the trial.

A Burst DR stimulator was used for the trial, with one lead placed to the right of the midline and advanced to the C4 vertebral level. During the 7-day trial period, the patient experienced only 30% relief and minimal improvement in her lymphedema, so she did not proceed with implantation.

Case #4

A 65-year-old woman with left-sided breast cancer status post mastectomy, chemotherapy, and radiation presented with intractable left chest and arm pain. She described a constant shooting and stabbing pain in her chest that extended to her arm; pain was aggravated by pronation and adduction of her arm and alleviated by having her arm in a sling. She previously trialed physical therapy, arm elevation techniques, compression wrapping, and methadone. At the time of evaluation, she was managed on hydrocodone, oxycodone, and pregabalin. Due to her pain, lymphedema, and sedative effects of her medications, she decided to pursue a trial.

A tonic stimulator was used for the trial and implantation. During the trial period, she reported > 50% relief with improved lymphedema and functional use of her left arm and hand, prompting implantation. An octrode lead was placed to the left of the midline and advanced to the C2 vertebral body. The patient experienced substantial relief and had discontinued all opioid medications. Within a year of implantation, she passed away from progression of her ongoing disease that had been present prior to our evaluation.

Case #5

A 61-year-old woman with a history of right-sided breast cancer status post mastectomy, chemotherapy, radiation, and metastatic involvement to the brain presented with intractable right chest wall pain. She previously trialed gabapentin, methadone, hydrocodone, and hydromorphone with minimal relief and significant adverse effects. She had also trialed multiple intercostal nerve blocks, epidurals, physical therapy, and massage therapy with minimal relief. At the time of evaluation, she was being managed with tramadol and diclofenac. With her ongoing complaints, we proceeded with a spinal cord stimulator trial.

Tonic stimulation was used for the trial and implantation. Two octrode leads were used, with both placed slightly to the right of the midline. One lead was advanced to the T3/T4 interspace, and the second lead was advanced to the T5/T6 interspace. During the trial period, she reported > 75% relief, prompting the decision to pursue implantation; however, she passed away before surgery due to progression of her disease that was noted prior to the trial.

Case #6

A 53-year-old woman with a history of right-sided breast cancer status post mastectomy, chemotherapy, radiation, and neuropathy of her feet presented with intractable right chest spasms and right arm pain. She described muscle spasms in her right chest and shoulder, with stabbing, shooting pain extending from her right axilla to her hand. She had previously trialed baclofen, tizanidine, trigger point injections, stellate ganglion block, and paravertebral nerve blocks with minimal relief. Her insurance denied the use of botox for her spasms. At the time of her evaluation, she was being managed with hydrocodone, methadone, gabapentin, and methocarbamol. As the patient felt limited from her work due to her pain, spasms, and her medications, the decision to pursue a trial was made.

Tonic stimulation was used for the trial and implantation. During the trial period, the patient reported > 60% pain relief, with improved range of motion of her right hand and arm, prompting implantation. Two octrode leads were placed to the right of the midline, including one that was advanced to T1 and another that was advanced to T2. Due to neuropathy of her feet, she was unable to decrease her opioids but endorsed continued relief at her 3-year follow-up.

Case #7

A 64-year-old woman with a history of left-sided breast cancer status post mastectomy, lymph node dissection, chemotherapy, radiation, and chemotherapy-induced neuropathy of her bilateral distal extremities presented with intractable left chest and arm pain. She described her pain as a shooting pain that radiated down her left arm and hypersensitivity over her left thoracic region. She stated that her thoracic pain and arm pain were more severe than was her chemotherapy-related pain. She previously trialed multiple stellate ganglion blocks, intercostal nerve blocks, physical therapy, and hydrocodone. At the time of evaluation, she was managed with tramadol, gabapentin, and duloxetine. The patient felt limited from her daily activities due to her pain, prompting pursuit of a trial.

Tonic stimulation was used for the trial and implantation. During the trial period, the patient reported 70% pain relief, prompting implantation. Two octrode leads were placed slightly to the left of the midline, including one that was advanced to C5 and a second that was advanced to T8. She reported enough relief to decrease her opioid regimen and intentionally lose 11.8 kg after implantation, requiring subsequent battery placement revision. She reported continued relief at her most recent 3-year follow-up.

Prior to trial and implantation, discussion between the patient and their oncologist regularly included open discussion of expectations (including associated risks, availability of alternative treatments, and life expectancy). As this cancer population is regularly subject to changes in management related to their primary disease, we conducted regular correspondence including follow-up encounters.

Optimal lead placement and adjustment within the epidural space was determined intraoperatively with verbal feedback to confirm induction of paresthesia in areas of perceived pain. Among those with paresthesia-free based devices, placement was based on preoperative interview and examination.

All patients (see Table 1) underwent a trial with a mean preoperative NRS-11 score of 8.29 ± 1.70 (range, 5-10). One patient did not receive an implant because of insufficient pain relief, and a second patient passed away with palliative measures before follow-up. Of the 5 patients who underwent implantation after a successful trial, significant pain reduction was seen in the mean postoperative one-month follow-up NRS-11 score of 4.20 ± 1.79. The paired t test demonstrated the pre-post intervention difference (4.40 ± 1.34) was statistically significant ($P = .002$, Cohen's d = 3.28).

At one month's follow-up, all 5 patients who had undergone implantation demonstrated continued relief, with a notable reduction in their opioid medications and a mean decrease in the MEDD of 55.80 (SD 82.21, Cohen's d = 0.68, $P = .125$) (Table 2).

DISCUSSION

The purpose of this case series was to demonstrate that SCS may be a useful tool in the management of postmastectomy pain syndrome for improvement of pain, function, and quality of life. Although it is not well understood, stimulation of the dorsal columns of the spinal cord has been explained via the gate control theory, where large-diameter neurons are stimulated, inhibiting the communication of pain via smaller diameter pain neurons (4-6). Optimal placement of SCS electrodes over segments along the dorsal column alter pain perception as it relates to stimulation above C5 for shoulder pain, T1 for axilla, and T3-5 for chest wall pain. In recent years, the paradigm of SCS has expanded with the development of new waveforms and new stimulation targets (i.e., the dorsal root ganglion) and the belief that descending pain inhibition pathways are also activated, which plays a role in pain relief (7,8). Burst SCS systems may offer a more specific advantage over other waveforms because they target the emotional and affective component of pain by stimulating the medial pathway via the insula and anterior cingulate cortex (6). Anxiety, depression, and pain catastrophizing have been shown to be instrumental in the development of postmastectomy pain syndrome, and the mechanism by which burst stimulation provides increased firing to these low-frequency firing areas implicated in the unpleasantness and attention paid to pain may prove beneficial. It should be noted, however, that it is unclear how much pain reduction can be attributed to this effect and that SCS in general is relatively contraindicated in patients with depression and associated comorbidities, as these are negative predictors of a successful outcome. Technological advancements of SCS devices requiring further attention also include magnetic resonance imaging (MRI) conditionality. Until recently, patients with implanted SCS devices were recommended to be excluded from MRI study due to associated hazards incurred from the magnetic field on an implanted device (9). In this population, where MRI is part of regular oncologic practice towards assessment and decision-making (10), several factors must be considered in final patient and device selection.

Table 1. Summary of 7 cases considered for spinal cord stimulation for post mastectomy pain syndrome (PMPS).

Case	Age (Years)	Gender	Description of Pain	Description of Pain on Initial Examination	Duration of PMPS Symptoms (Months)	Previously Trialed Therapies	Pain Relief Reported Following Trial	Stimulator Status	Pre / Post Implant (1 month) NRS	Pre / Post Operative Morphine Equivalent Use (1 month)	Post-Operative Events and Complications
1	56	F	Shooting and stabbing in right hand extending to right chest	7	12	TENS, Acupuncture, Stellate ganglion block, PT, SCS	>75%	Permanent	8 / 3	60 / 10	No complications met
2	54	F	Aching, numbness and tingling from right chest wall and axilla extending below scapula and breast	Right: T2-T7	36	Intercostal nerve block, Acupuncture, TPI, SCS	80%	Permanent	9 / 7	10 / 0	Lead migration following fall requiring revision, without any complications since
3	64	F	Constant right sharp pain in axilla extending throughout her arm	Right: C4-T3	204	Intercostal nerve blocks, acupuncture, physical therapy, compressive wraps SCS	30%	Failed Trial	5 / NA	70 / NA	Relief was not sufficient on paramaters of pain and lymphedema so did not proceed with implantation
4	65	F	Constant shooting and stabbing pain in left chest and arm extending to hand	Left: C3-T2	12	PT, Arm elevation, compressive wraps, SCS	>50%	Permanent	8 / 3	199 / 0	Patient passed away within a year from implant due to progression of metastatic disease that was evident prior to stimulator consideration
5	62	F	Constant throbbing pain over right anterior wall	Right: T3-T8	12	Intercostal nerve blocks, Epidural injection, Massage therapy, SCS	>75%	Deferred Implant	10 / NA	20 / NA	Patient passed away 1 week prior to implantation from metastatic advancement (with comfort meausres) that had been evident prior to stimulator consideration
6	53	F	Spasms of right chest and shoulder, stabbing and shooting pain from axilla to the right hand	Right: C7--T2	12	Paravertebral nerve block, Trigger point injections, Stellate ganglion block, PT, SCS	60%	Permanent	10 / 5	22.5 / 22.5	Frequent battery charging and complaint of paresthesias in chest wall with alteration of settings
7	64	F	Allodynia and hyperesthesia over left anterior thoracic region and left upper extremity	Left: T1-T5	10	Stellate ganglion blocks, intercostal nerve blocks, PT, SCS	70%	Permanent	8 / 3	60 / 40	Lost 11.8 kgs, requiring subsequent revision in placement of battery

F – Female, NRS – numerical rating scale, TPI - trigger point injection, NA – Not available, SCS – spinal cord stimulation, PT – physical therapy

Table 2. Difference of mean pain and morphine equivalent daily dose (MEDD) following spinal cord stimulator implantation for post mastectomy pain syndrome.

	Pre		Post		Difference		*P* value	Effect Size
	Mean	Std	Mean	Std	Mean	Std		
Mean Pain	8.29	1.70	4.20	1.79	4.40	1.34	0.002	3.28
MEDD	63.07	64.37	11.21	15.01	55.80	82.21	0.125	0.68

Postmastectomy pain syndrome is broadly defined, with varying musculoskeletal and lymphedema pain sequela in addition to neuropathic pain (2). Patients may undergo a variety of treatment modalities based on their pain manifestations. In our case series, patients' symptoms varied from shooting pain in the hand to muscle spasm in the chest wall, which is not surprising as different nerves may be involved in different types of mastectomy surgeries (i.e., radical vs modified approaches). Prior to stimulator trial, our patients received various interventions in addition to pharmacological treatment with inadequate pain relief. SCS of the hand was able to provide satisfactory pain relief in 6 out of 7 patients, regardless of the pain distribution and nature. Less invasive pain interventions should still be considered for postmastectomy pain; however, when multiple interventions provide either insufficient or short-lived pain relief, SCS should be considered given its capacity to cover a wide range of symptoms. This emphasizes the importance of patient selection and further investigation into the effects of SCS on the many aspects of postmastectomy pain. Additionally, there have been other cases in which dorsal root ganglion stimulation has been used to target postmastectomy pain (7), which may be helpful in targeting specific pain foci. The continued innovation of the technology that is used in stimulation and neuromodulation as a whole will benefit our patients with the development of unique waveforms for each individual, as the pain experience varies for each patient.

There are limitations to the effect of SCS that we have presented in this report, including a small sample size and the retrospective nature of these complex postmastectomy pain cases. Given the heterogeneity in the level of pain relief that SCS has given across various types of pain (11), patient selection and understanding of the risk factors contributing to lower trial success is paramount. One prognostic factor that may need to be closely considered for postmastectomy pain patients is the duration of pain. In this case series, our only case who did not find sufficient relief also had the longest duration of pain (204 months). Although the association of higher duration of pain with lower pain reduction has been seen in other arenas of chronic pain (12), this would require further investigation on a larger scale.

SCS, in addition to physical therapy and conservative management strategies, provides an alternative to opioids and sedating neuropathic medications. However, SCS is not without its potential adverse effects, such as hardware-related issues (migration, lead fracture, malfunction, and pain at the implantable pulse generator site), hematoma or seroma at the implantable pulse generator site, infection, or rarely, epidural hematoma, cerebral spinal fluid leak, or neurological deficit (4). With an understanding of the potential adverse effects, the current trends of innovation, and the broadened indications for its use, SCS should be considered for appropriately selected patients who are interested in decreasing their dependence on medications.

REFERENCES

1. Larsson I, Sørenson J, Bille C. The post-mastectomy pain syndrome – A systematic review of the treatment modalities. *Breast J* 2017; 23:338-343.
2. Tait RC, Zoberi K, Ferguson M, et al. Persistent post-mastectomy pain: Risk factors and current approaches to treatment. *J Pain* 2018; 19:1367-1383.
3. Schreiber K, Martel M, Shnol H, et al. Persistent pain in postmastectomy patients: Comparison of psychophysical, medical, surgical, and psychosocial characteristics between patients with and without pain. *Pain* 2013; 154:660-668.
4. Dones I, Levi V. Spinal cord stimulation for neuropathic pain: Current trends and future applications. *Brain Sci* 2018; 8:138.
5. DeRidder D, Vanneste S. Burst and tonic spinal cord stimulation: Different and common brain mechanisms. *Neuromodulation* 2016; 19:47-59.
6. Kirketeig T, Schultheis C, Zuidema X, Hunter CW, Deer T. Burst spinal cord stimulation: A clinical review. *Pain Med* 2019; 20:S31-S40.
7. Morgalla MH. Dorsal root ganglion stimulation for the treatment of post-mastectomy pain: Case report. *Neuromodulation* 2019; 22:117-118.
8. Sivanesan E, Maher DP, Raja SN, Linderoth B, Guan Y. Supraspinal mechanisms of spinal cord stimulation for modulation of pain: Five decades of research and prospects for the future. *Anesthesiology* 2019; 130:651-665.
9. Rubino S, Adepoju A, Kumar V, et al. MRI conditionality in patients with spinal cord stimulation devices. *Stereotact Funct Neurosurg* 2016; 94:254-258.
10. Dregely I, Prezzi D, Kelly-Morland C, et al. Imaging biomarkers in oncology: Basics and application to MRI. *J Magn Reson Imaging* 2018; 48:13-26.
11. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: A systematic review and analysis of prognostic factors. *Spine* 2005; 30:152-160.
12. Taylor RS, Desai MJ, Rigoard P, Taylor RJ. Predictors of pain relief following spinal cord stimulation in chronic back and leg pain and failed back surgery syndrome: A systematic review and meta-regression analysis. *Pain Pract* 2014;14:489-505.