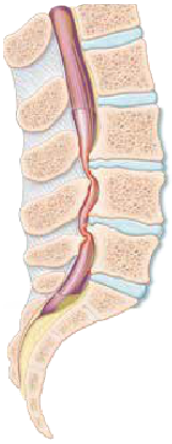




# Spinal Cord Stimulation for the Management of Neuropathic Pain in Failed Back Surgery Syndrome


## ABSTRACT

Chronic pain is a complex disease state associated with substantial individual disability and suffering alongside societal economic impact. The entity of neuropathic pain is a diagnosis of specific clinical characteristics and underlying pathophysiology. Failed back surgery syndrome represents persistent neuropathic leg pain following structurally corrective spinal surgery, often being refractory to escalated pharmacological management. In appropriately selected patients, spinal cord stimulation is a surgical technique that may offer reduced disability and pain, and improved economic outcomes for patients where medical management has been unsuccessful. Contemporary technological advances continue to improve this approach with greater success, lessened morbidity, and expanding indications.


KEYWORDS: failed back surgery syndrome, neuropathic pain, spinal cord stimulation, neuromodulation

## Introduction

The International Association for the Study of Pain (IASP) has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1] The categorization of pain as chronic is then furthered by temporal extension over a certain of period of time (generally 3-6 months) or by pathological definition once residual pathology can no longer explain the presence or extent of the patient's suffering. Chronic pain can have a profound impact, with worldwide prevalence estimates of 13-53% and associated interference with activities of daily living, rates of health-related unemployment, impaired psychological function, and greater utilization of health care resources.[2-8]

***Mohammed F. Shamji MD, PhD, FRCSC***
*Division of Neurosurgery, Toronto Western Hospital, Department of Surgery, University of Toronto, Toronto, Ontario, Canada.*

***Alina Shcharinsky RN (EC), MN, CNN(C)***
*Division of Neurosurgery, Toronto Western Hospital, Toronto, Ontario, Canada*

Neuropathic pain is a specific subtype of this disease where maladaptive plasticity induced by a lesion has affected the somatosensory system to a degree that pain is felt in the absence of a stimulus or that responses to both innocuous and noxious stimuli are enhanced. Spontaneous features include burning pain and tightness with unpredictable lancinating features. Stimulus-evoked features include hyperalgesia (a heightened response to a normal painful stimulus) and allodynia (a pain response to a normally non-painful stimulus). The clinical diagnosis is established in 2-3% of the developed world population,[9] with underlying diagnoses including painful diabetic neuropathy, lumbosacral radiculopathy, post-herpetic neuralgia, post-infectious or post-chemotherapy neuropathy, complex regional pain syndrome, and failed back surgery syndrome (FBSS).

The general approach to managing neuropathic leg pain following structurally corrective spinal surgery involves an escalating pharmacological regimen established by the Canadian Pain Society in 2007,[10] which if unsuccessful, can be followed by techniques of greater invasiveness. The use of electrical stimulation for analgesia hails back to Scribonius in 15AD with the fortuitous observation that inadvertent contact with a torpedo fish provided relief of gout pain.[11] Spinal cord stimulation (SCS) has been demonstrated in prospective randomized controlled trials to have benefit in the management of leg-dominant FBSS.[12-14]

## Overview of Neuropathic Pain

Despite the high prevalence of neuropathic pain, estimated to affect one million Canadians,10 there remains substantial ambiguity about this clinical entity. In the context of FBSS, the residual neuropathic pain has been assumed to arise from ischemic or fibrotic changes to the nerve.[15-19] Such permanent changes cannot be predicted preoperatively and may be invisible to even intraoperative assessment, with the subsequent diagnosis considered only upon the postoperative failure of clinical resolution despite adequate decompression, realignment or stabilization. Complicating this ambiguity is the fact that the diagnosis is made on a set of symptoms and subjective descriptions that are challenging to measure objectively. Indeed, most objective structural and functional testing is employed to investigate the presence of an alternate diagnosis.

The definition of neuropathic pain put forth by the IASP describes two main types of pain mechanisms, being either of peripheral or central origin, as well as a number of associated pain

terms. However, an operational definition that can be used by practicing clinicians for distinguishing neuropathic pain from other types of pain has remained elusive, yielding instead to a constellation of different features as detected by various screening tools.[20, 21] Table 1 delineates some of the characteristic findings and descriptions used to operationalize making this diagnosis in the clinical setting. The specific qualities of evoked pain during the examination include allodynia, hyperalgesia, hyperesthesia, and hyperpathia. Allodynia is an altered quality of sensation, whereby a painful response is elicited to a non-painful stimulus. Hyperalgesia is an augmented painful response only to those stimuli that are normally painful, whereas hyperesthesia more broadly represents augmented sensitivity to all stimuli. Hyperpathia is a pain condition whereby an abnormally painful response occurs in response to a stimulus, particularly repetitively applied. The clinician is faced with interpreting subjective responses to the clinical examination into patterns of pain behavior. A number of screening tools have been developed to help delineate the clinical presentations as neuropathic pain or not, and Table 2 summarizes the most common screening tools including their sensitivity and specificity. The most consistent elements include burning and lancinating quality, the presence of paresthesia, and clinical findings of allodynia.[20-24] More recent diagnostic methods include Quantitative Sensory Testing (QST) and electrodiagnostic studies.[10,25] QST is performed by administering various standard noxious stimuli (thermal, mechanical, electrical) under controlled settings to identify a dysfunctional sensory response. Electromyography (EMG) and nerve conduction

**Table 1: Clinical Features of Neuropathic Pain**

| | Spontaneous Pain | Evoked Pain |
|---|---|---|
| **Stimulus** | Independent | Dependent |
| **Onset** | Unpredictable | Dynamic (vibration or brush) or static (pressure or pinprick) stimulus |
| **Duration** | Continuous or Intermittent | During and for a predictable period after stimulus |
| **Quality** | **Continuous:** burning, throbbing, shooting, intense tightness, lancinating<br>**Intermittent:** shooting, stabbing, electrical | Allodynia<br>Hyperalgesia<br>Hyperesthesia<br>Hyperpathia |

studies (NCS) used in the workup of these patients may additionally offer objective confirmation of chronic and invariable neural injury, supporting the pathophysiological basis of neuropathic pain.

## What is Spinal Cord Stimulation?

The use of electrical stimulation in clinical practice was formalized following the introduction of Melzack and Wall's Gate Control Theory in 1965, suggesting that pain resulting from noxious inflow is modulated by transmission of nerve impulses from afferent fibers to spinal cord transmission cells through a spinal gating mechanism in the dorsal column.[26] They postulated that opening of the "gate" for pain perception occurred when more small diameter C-fibers were activated rather than large affer-

**Table 2: Common Validated Screening Tools for Neuropathic Pain**[20,21,23]

| Screening Tool | Description | Sensitivity | Specificity |
|---|---|---|---|
| Leeds Assessment of Neuropathic Symptoms and signs (LANSS) | 5 self-reported items<br>2 examination items | 82-91% | 80-94% |
| Neuropathic Pain Questionnaire (NPQ) | 10 self-reported items<br>2 mood and affect items<br><br>Short form available with only 3 discriminative properties (numbness, tingling, pain increase in response to touch | 66% | 74% |
| Douleur Neuropathique en 4 questions (DN4) | 7 self-reported items<br>3 examination items | 83% | 90% |
| painDETECT | Self-reported questionnaire with 9 items relating to symptoms (7 descriptors, 2 special)<br><br>No clinical examination items | 85% | 80% |
| ID-Pain | 5 descriptor items<br>1 item identifying joint pain (nociceptive)<br>No examination items | Not available | Not available |
| McGill Pain Questionnaire (MPQ) | 3 major descriptors (sensory, affective, evaluative)<br>3 major measures:<br>Pain rating index<br>Number of specific descriptors<br>Present pain intensity (1-5) | Not available | Not Available |

ent fibers which would otherwise inhibit small fiber transmission. Conversely, closure of the "gate" was facilitated by substantial activation of large afferent fibers to block small fiber transmission. It was suggested that electrical stimulation of large afferent fibers would precipitate selective "gate closure" that would in turn block painful input to the central nervous system.[27]

More recent investigations suggest that the mechanisms by which SCS achieves analgesia are more complex than this tidy hypothesis suggests. Table 3 summarizes the variety of active research in this field. Certainly effects are seen both antidromically, where interaction between small C and large Aβ may recapitulate the gate theory, and orthodromically, where direct supraspinal nuclear activation may generate secondary downward modulation currents. Clinical evidence that there is more than the "gate"

**Table 3: Proposed Mechanisms of SCS Analgesia**[27,29,31]

| | |
|---|---|
| **Dorsal Column activation** | Dorsal column axonal activation is the anatomical substrate of paraesthesias experienced during stimulation<br>Stimulated depolarization of large myelinated afferent DC fibers leads to:<br>• Orthodromic activation of Aβ-fibers projecting to the DC nuclei and then further activating the periaqueductal gray and the thalamus.<br>• Antidromic activation via Aβ-collaterals into the dorsal laminae to suppress C-fibers and wide dynamic range (WDR) neurons in the dorsal horn.<br>• Antidromic activation to the peripheral dendrites of the Aβ dorsal root (DR) fibers. |
| **Supraspinal pathways** | • SCS may activate brainstem noradrenergic projections that then activate a spinal-supraspinal-spinal feedback loop generating an SCS-induced descending analgesic effect.<br>• Serotonin, substance P, adenosine, and muscarine receptor are also thought to be involved in the analgesic effect of SCS through both supraspinal and spinal segmental mechanisms. |
| **Neurochemical transmission in the dorsal column** | Neurochemical changes in pain transmission in the dorsal horn result in central sensitization<br>Spinal cord stimulation alters the neurotransmitter profile including decreasing release of excitatory aspartate and glutamate and increasing the release of tonic GABA inhibitory activity as well as serotonin and adenosine |
| **Sympatholytic mechanisms** | SCS suppresses efferent sympathetic activity resulting in lesser peripheral vasoconstriction<br>SCS produces peripheral vasodilation by activating interneurons that:<br>• Reduce the activity of spinothalamic tract and sympathetic preganglionic neurons<br>• Reduced release of norepinephrine from sympathetic preganglionic neurons<br>• Antidromic activatation of the dorsal root afferent fibers<br>• Release of calcitonin gene related peptide and nitric oxide |

DC-dorsal column; GABA- gamma-amino-butyric acid; WDR-wide-dynamic-range; NS- nociceptive-specific; SCS-spinal cord stimulation

to be considered include the lack of influence of SCS on nociceptive pain and induced acute pain, the ability to generate pain by activation of large afferent fibers, obliteration of cutaneous hyperalgesia by selective blockage of large fibers, and the fact that analgesic effects of SCS may outlast the duration of the stimulation. Indeed, multiple sites within the neuromatrix are likely involved,[27-31] and more recent molecular analyses also reveal that SCS can influence levels of cerebrospinal fluid compartment neurotransmitters including increases in GABA, serotonin, Substance-P, norepinephrine, acetylcholine, and adenosine, and decreases in glutamate and aspartate. At an operational level stimulation is considered successful when the painful region of interest is replaced by active paresthesias following stimulator activation. The goal is to establish the perception threshold where paresthesia are felt and avoid the discomfort threshold where the stimulation is intolerable.[27]

## Patient Selection for SCS

Patient selection for SCS to manage leg-dominant FBSS remains challenging, even for experienced pain physicians and neurosurgeons; a fact reflected in variable rates of conversion from trial stimulation to permanent implantation. Fundamental contraindications to device implantation include untreated psychiatric comorbidity, presence of correctable structural pathology, cognitive impairment leading to inability to provide surgical consent or apply the technology, clotting disorders, and active infection.[28] Ongoing legal action can be a contraindication, as can the need for future serial MRI scans for any reason.

Because of these challenges a multidisciplinary team is generally involved in assessing patient suitability for SCS. The disciplines include:

a) Spinal surgery – assessment of whether a structurally-correctable basis for ongoing leg pain exists

b) Psychology – assessment and management of comorbid mood and anxiety disorders

c) Comprehensive pain medicine – escalating pharmacological management of neuropathic pain as well as postoperative weaning from the medication regimen

## Structural Spine Pain

Leg pain that persists following spinal surgery may be due to a variety of different etiologies. The surgeon should question the nature of the initial diagnosis, the structural effectiveness of the surgical intervention, and the consequent sequelae of that intervention. The diagnostic armamentarium must include both structural and functional evaluations of the mus-

culoskeletal and nervous system. Magnetic resonance imaging, enhanced with gadolinium, will provide insight into the presence of ongoing nerve compression or development of epidural fibrosis. Computed tomography scans and dynamic (flexion-extension) radiographs will demonstrate the presence of lateral recess and foraminal stenosis as well as the development of any post-surgical instability. EMG and NCS have utility in establishing the diagnosis as being radiculopathy and differentiating it from a peripheral nerve entrapment neuropathy or other neurological diagnosis. The role of further spinal interventions including complex revision spinal surgery must be explored as the index surgery may not have achieved the goals of neural element decompression and or adequately addressed the spinal alignment and stability. Non-surgical interventions are summarized in Table 4 and may be used for managing ongoing radiculopathy, facet arthropathy, epidural fibrosis, and discogenic pain syndromes. Revision surgical interventions may be targeted at completing the initial decompression, correcting any pre-existing or new deformity, and stabilizing any previously occult or newly created iatrogenic instability.

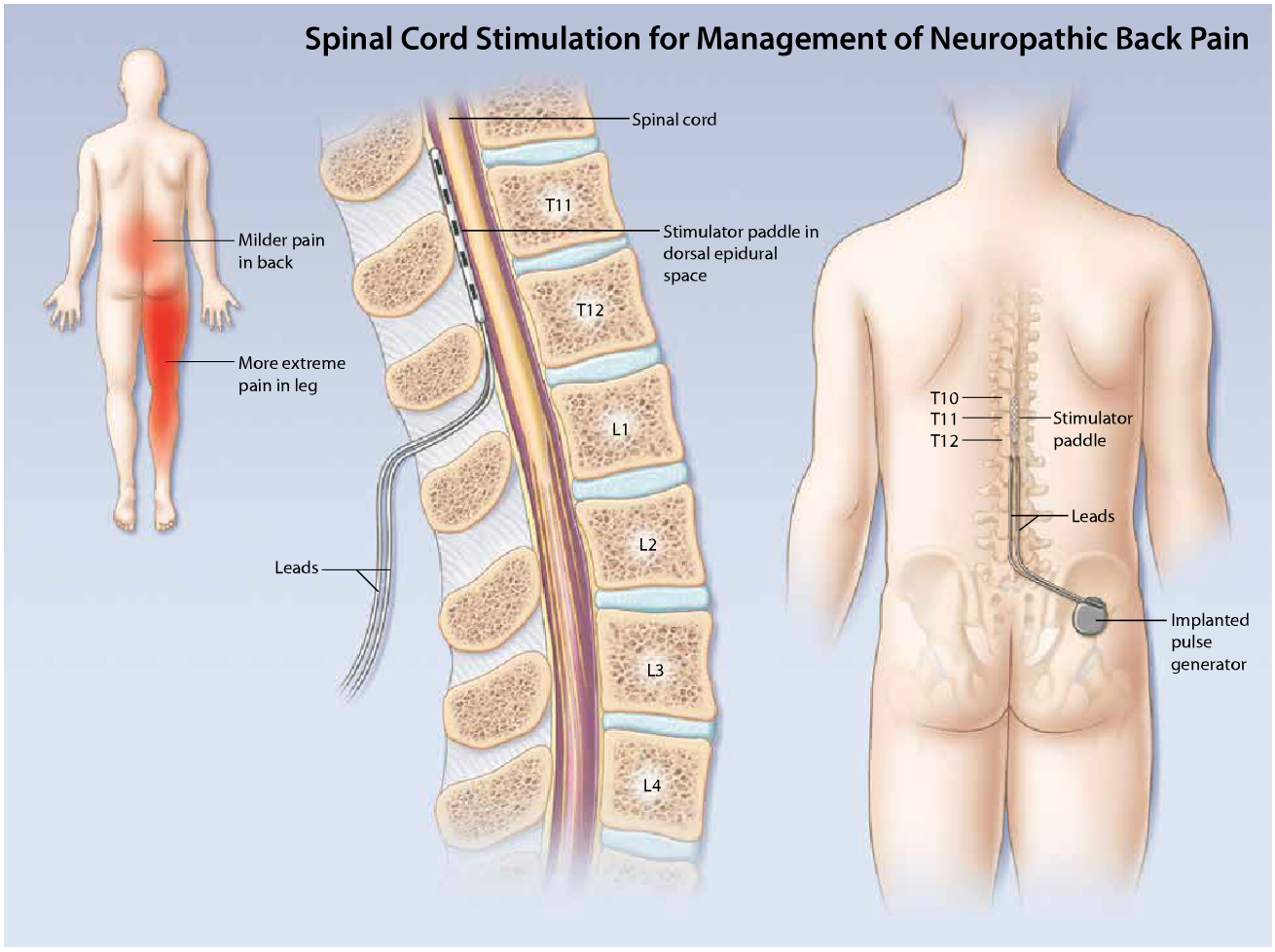
## Psychological Assessments

Individual pain experiences and responses to various manage-

**Table 4: Summary of Common Interventional Pain Procedures in FBSS**

| Indication | Procedure Type |
|---|---|
| Radiculopathy | Epidural injections, transforaminal injections, selective nerve root blocks (local anesthetic or steroid) |
| Facet Arthropathy | Facet joint procedures<br>• Intra-articular joint steroid injection<br>• Medial branch block (anesthetic solution)<br>• Radiofrequency ablation (RFA) |
| Epidural or intra-dural fibrosis | Adhesiolysis (percutaneous and endoscopic) |
| Discogenic lower back and leg pain | Disc Interventions<br>Thermal annular procedures<br>• Intra-discal electrothermal therapy (IDET)<br>• discTRODE<br>• Biacuplasty<br><br>Nucleoplasty<br><br>Mechanical decompression |

ment modalities including SCS are influenced by comorbid psychopathology.[25] Mood and anxiety disorders are the most common abnormalities, found in 50%-80% of patients afflicted with chronic pain. Further, self-reported levels of depression, anxiety, poor coping, somatization, and hypochondriasis all correlate with poorer treatment related benefits.[32] Other predictors of unsuccessful treatment include pain chronicity, negative emotional impact, pain-related catastrophizing, substance abuse, cognitive dysfunction, poor social support, and history of abuse or trauma.[33] Formal psychological assessment and optimization of mood and anxiety disorders is recommended prior to permanent device implantation. Clinicians should reinforce that the goal of SCS is to provide symptomatic improvement with respect to pain control, and not to correct underlying pathology; complete pain relief is unrealistic. Identification and treatment of significant vulnerabilities earlier in the process may improve patient satis-



faction and their response to SCS therapy and decrease the rates of unsuccessful trials.[25]

## Comprehensive Pain Management

Treating neuropathic pain secondary to FBSS requires a comprehensive pain medicine approach, involving both non-pharmacological and pharmacological initiatives. After active physiotherapy and psychotherapy, the multi-tier stepwise pharmacological approach recommended by the Canadian Pain Society[10] is often the next treatment. This must be supplemented with secondary goals including improving sleep, functional status, and overall quality of life. The goals of therapy must be clearly established. These are rarely obliterating pain completely but rather making the pain bearable and improving both the patient's function and quality of life.

## SCS Process

Once patients are deemed appropriate candidates (summarized in Table 5), then the general process includes an externalized trialing process, which if positive is followed by internalization of the implantable pulse generator (IPG). The details of each of these steps varies by center and by surgeon – procedures may be under general anesthesia or conscious sedation, trialing may be by percutaneous or surgically implanted leads and the IPG may be implanted at vari-

**Table 5: Screening Criteria for Use of SCS in the Management of Leg-Dominant FBSS**

| |
|---|
| Presence of persistent leg +/- lower back pain lasting at least 6 months following the most recent successful spinal surgery (e.g. lumbar discectomies, laminectomies, forminectomies, spinal fusions; performed separately or in any combination) |
| Suboptimal response of leg +/- lower back pain to comprehensive conservative management |
| Possible underlying structural/lesional spinal and other pathology that may potentially account for back and leg pain has been ruled out |
| Sensory examination demonstrates intact dorsal column function (proprioception, vibration); somatosensory evoked potentials should be formally tested if clinical exam is doubtful |
| The patient demonstrates realistic expectations with respect to SCS: understands the nature of the procedure, trial process, and risks vs. benefits |
| The patient has a good support system |
| The patient does not have psychological "red flags" |
| The patient is willing to be actively engaged in their treatment course |
| The patient does not have an active medical condition that will require MRI following permanent device implantation |

ous body sites. For leg-dominant FBSS, implantation regions in the dorsal epidural space range between T9-10 and T12-L1, with varying lengths of laminectomy. Careful attention must be paid to lead positioning so that it is symmetrical on the longitudinal axis of the spinal canal and that its rostrocaudal location permits generation of limb paresthesia with minimal abdominal effect. The surgeon may choose to anchor the lead generally employing an epifascial strain relief loop. Figure 1 shows an example of an implanted system through the T12-L1 interspace centered behind the T11 vertebral body for the man-

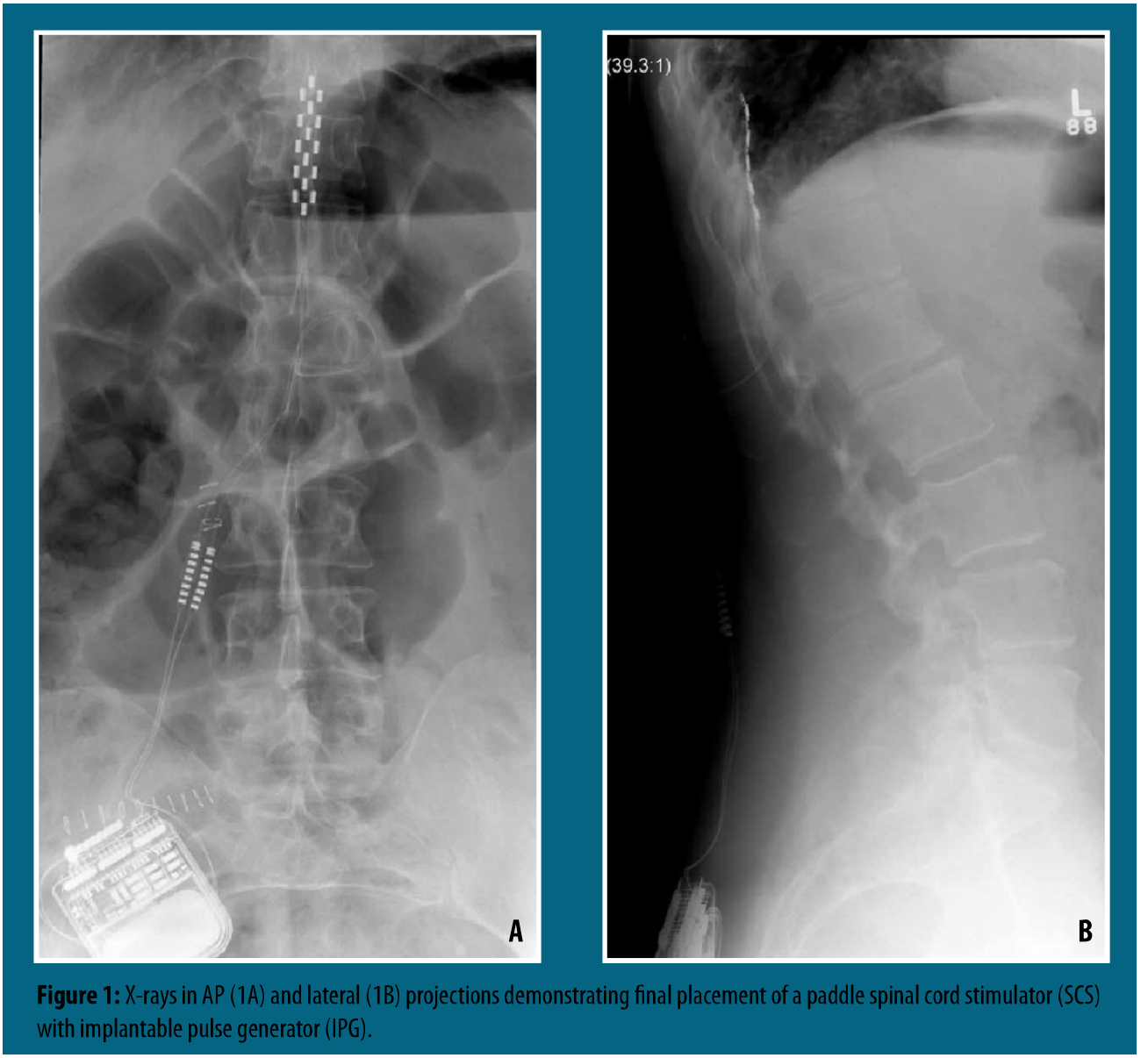



**Figure 1:** X-rays in AP (1A) and lateral (1B) projections demonstrating final placement of a paddle spinal cord stimulator (SCS) with implantable pulse generator (IPG).

## SUMMARY OF KEY POINTS

A variety of validated and reliable questionnaires based on sensory descriptions and sensory examination have been developed to guide clinicians in the diagnosis of Neuropathic Pain and to discriminate it from other types of pain.

The workup of the leg-dominant failed back surgery syndrome patient for spinal cord stimulation must include a multi-tier pharmacological approach, psychological optimization, and structural assessment from a complex spinal surgery service.

Predictors of success include short duration of symptoms following the index spinal surgery, well-managed mood and anxiety disorders, and the absence of allodynia as a presenting sign.

agement of left-sided S1 distribution pain. Current technological advances include minimally-invasive placement of the surgical leads to minimize surgical tissue trauma[34] and multi-columnar electrode leads that address various regions of neuropathic pain.[14] During the external trialing process, the patient has an opportunity to test various stimulation programs and define (1) whether the device is successful at creating paresthesia in the painful region and (2) whether the created sensation is acceptable compared with the neuropathic pain. Typically that represents greater than a 50% reduction. When both of those criteria are met and the patient wishes to proceed, internalization of the system with placement of an IPG is carried out. In addition to all the usual risks of spinal surgery, unique risks associated with the SCS device include battery depletion, lead migration, wire breakage or cutaneous erosion and infection around the device that can lead to epidural abscess. At present the use of postoperative MRI utilization is limited, although ongoing innovation in the field may remove this complication.

## SCS Outcomes

The utility of SCS in the management of leg-dominant FBSS has been well established. In a systematic review, Frey and coworkers[35] summarized the work of nine observational and two randomized studies. Among the observational studies, for 1035 patients who were implanted, 48-77% sustained more than 50% reduction in pain scores at one year postoperatively. The first randomized study, by Kumar and coworkers,[12,36] demonstrated significant reduction in pain for SCS patients (58%) compared with conventional medical management (17%) along with improved self-reported quality of life, albeit with short term higher health care resource costs. The second rand-

omized study, by North and coworkers,[13] revealed 47% improvement in pain among SCS patients compared with only 11% of patients undergoing repeated structural spinal surgery. The systematic review concluded that the technology can be both clinically and cost effective. Further, even when both FBSS back and leg pain scores are elevated, Rigaord and coworkers[14] demonstrate improvement in back pain (7.6 to 0.5) and leg pain (7.8 to 1.5) as well as in self-reported disability scores. Other important technique-related results suggest that there is no difference in outcome between patients who have the trial lead implanted under general anesthesia or under conscious sedation[37] and that higher success rates are observed among patients who are trialed with surgical rather than percutaneous leads.[38] Traditionally SCS has been considered the "last resort treatment" for patient with chronic pain syndromes who are refractory to conventional medical management but recent studies suggest that long-term efficacy of SCS is inversely related to the duration of pain prior to implantation. Some recommend that a trial of SCS be offered if suboptimal response to conventional multidisciplinary management is observed for 12 to16 weeks.[28,39-41] Indeed, Kumar and coworkers[28] reported success rates of over 85% if implantation occurs within 2 years following pain onset, and decreases to as low as 9% with delays of 15 years or longer.

## Conclusion

The management of persistent leg pain following spinal surgery can be challenging with treatments ranging from psychotherapeutic to pharmacological to neuromodulation. It is incumbent upon physicians manag-

## CLINICAL PEARLS

Postoperative leg pain following structurally-corrective spinal surgery can result from inadequate surgical decompression, implant malposition, iatrogenic instability, recurrent disease or epidural fibrosis, in addition to the neuropathic pain. The role of complex revision spinal surgery should be explored first.

Spinal cord stimulation should be considered for patients with neuropathic pain who are deemed refractory to multidisciplinary and multimodal management.

An early understanding of how mechanical, stimulated pain differs from neuropathic pain will aid in differentiating those patients in whom SCS technology can be helpful. Certain distinctive clinical symptoms including burning pain and paresthesia and signs including allodynia and hyperalgesia are very important elements of the diagnosis.

ing chronic pain to be familiar with the array of potential interventions. As technology advances, the utility of SCS will continue to grow. The technique has been rigorously evaluated and compared to both medical management and conventional spinal surgery. It has been found to reduce chronic pain and disability reliably and cost effectively.

## References


1. Pain terms: a list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. Pain. 1979;6:249.
2. Bouhassira D, Lanteri-Minet M, Attal N, et al. Prevalence of chronic pain with neuropathic characteristics in the general population. Pain. 2008;136:380-7.
3. van Hecke O, Torrance N, Smith BH. Chronic pain epidemiology and its clinical relevance. Br J Anaesth. 2013;111:13-8.
4. Smith BH, Macfarlane GJ, Torrance N. Epidemiology of chronic pain, from the laboratory to the bus stop: time to add understanding of biological mechanisms to the study of risk factors in population-based research? Pain. 2007;127:5-10.
5. Torrance N, Smith BH, Bennett MI, et al. The epidemiology of chronic pain of predominantly neuropathic origin. Results from a general population survey. J Pain. 2006;7:281-9.
6. Toth C, Lander J, Wiebe S. The prevalence and impact of chronic pain with neuropathic pain symptoms in the general population. Pain Med. 2009;10:918-29.
7. Nicholson B, Verma S. Comorbidities in chronic neuropathic pain. Pain Med. 2004;5 Suppl 1:S9-S27.
8. Dieleman JP, Kerklaan J, Huygen FJ, et al. Incidence rates and treatment of neuropathic pain conditions in the general population. Pain. 2008;137:681-8.
9. Gilron I, Watson CP, Cahill CM, et al. Neuropathic pain: a practical guide for the clinician. Cmaj. 2006;175:265-75.
10. Moulin DE, Clark AJ, Gilron I, et al. Pharmacological management of chronic neuropathic pain - consensus statement and guidelines from the Canadian Pain Society. Pain Res Manag. 2007;12:13-21.
11. Gildenberg PL. History of Electrical Neuromodulation for Chronic Pain. Pain Med. 2006;7:S7-S13.
12. Kumar K, Taylor RS, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. Pain. 2007;132:179-88.
13. North RB, Kidd DH, Farrokhi F, et al. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. Neurosurgery. 2005;56:98-106; discussion -7.
14. Rigoard P, Delmotte A, D'Houtaud S, et al. Back pain: a real target for spinal cord stimulation? Neurosurgery. 2012;70:574-84; discussion 84-5.
15. Kobayashi S, Yoshizawa H, Yamada S. Pathology of lumbar nerve root compression. Part 2: morphological and immunohistochemical changes of dorsal root ganglion. J Orthop Res. 2004;22:180-8.
16. Kobayashi S, Yoshizawa H, Yamada S. Pathology of lumbar nerve root compression. Part 1: Intraradicular inflammatory changes induced by mechanical compression. J Orthop Res. 2004;22:170-9.
17. Matsui H, Tsuji H, Kanamori M, et al. Laminectomy-induced arachnoradiculitis: a postoperative serial MRI study. Neuroradiology. 1995;37:660-6.
18. Bosscher HA, Heavner JE. Incidence and severity of epidural fibrosis after back surgery: an endoscopic study. Pain Pract. 2010;10:18-24.
19. Onder A, Serarslan Y, Aydin MD, et al. Spinal Arachnoiditis and The Axonal Degeneration of The Spinal Nerve Roots Due to Ischemia Induced By Vasospasm: An Experimental Study. Journal of Neurological Sciences (Turkish). 2009;26:416-23.
20. Bennett MI, Attal N, Backonja MM, et al. Using screening tools to identify neuropathic pain. Pain. 2007;127:199-203.
21. Bennett MI, Bouhassira D. Epidemiology of neuropathic pain: can we use the screening tools? Pain. 2007;132:12-3.
22. Dworkin RH. An overview of neuropathic pain: syndromes, symptoms, signs, and several mechanisms. Clin J Pain. 2002;18:343-9.
23. Dworkin RH, Turk DC, Revicki DA, et al. Development and initial validation of an expanded and revised version of the Short-form McGill Pain Questionnaire (SF-MPQ-2). Pain. 2009;144:35-42.
24. Timmerman H, Heemstra I, Schalkwijk A, et al. Assessment of neuropathic pain in patients with cancer: the interobserver reliability. An observational study in daily practice. Pain Physician. 2013;16:569-80.
25. Campbell CM, Jamison RN, Edwards RR. Psychological screening/phenotyping as predictors for spinal cord stimulation. Curr Pain Headache Rep. 2013;17:307.
26. Melzack R, Wall PD. Pain mechanisms: a new theory. Science. 1965;150:971-9.
27. Oakley JC, Prager JP. Spinal cord stimulation: mechanisms of action. Spine (Phila Pa 1976). 2002;27:2574-83.
28. Kumar K, Rizvi S. Historical and present state of neuromodulation in chronic pain. Curr Pain Headache Rep. 2014;18:387.
29. Meyerson BA, Linderoth B. Mechanisms of spinal cord stimulation in neuropathic pain. Neurol Res. 2000;22:285-92.
30. Meyerson BA, Linderoth B. Mode of action of spinal cord stimulation in neuropathic pain. J Pain Symptom Manage. 2006;31:S6-12.
31. Smits H, van Kleef M, Holsheimer J, et al. Experimental spinal cord stimulation and neuropathic pain: mechanism of action, technical aspects, and effectiveness. Pain Pract. 2013;13:154-68.
32. Celestin J, Edwards RR, Jamison RN. Pretreatment psychosocial variables as predictors of outcomes fol-

lowing lumbar surgery and spinal cord stimulation: a systematic review and literature synthesis. Pain Med. 2009;10:639-53.
33. Tunks ER, Crook J, Weir R. Epidemiology of chronic pain with psychological comorbidity: prevalence, risk, course, and prognosis. Can J Psychiatry. 2008;53:224-34.
34. Rigoard P, Luong AT, Delmotte A, et al. Multicolumn spinal cord stimulation lead implantation using an optic transligamentar minimally invasive technique. Neurosurgery. 2013;73:550-3.
35. Frey ME, Manchikanti L, Benyamin RM, et al. Spinal cord stimulation for patients with failed back surgery syndrome: a systematic review. Pain Physician. 2009;12:379-97.
36. Manca A, Kumar K, Taylor RS, et al. Quality of life, resource consumption and costs of spinal cord stimulation versus conventional medical management in neuropathic pain patients with failed back surgery syndrome (PROCESS trial). Eur J Pain. 2008;12:1047-58.
37. Falowski SM, Celii A, Sestokas AK, et al. Awake vs. asleep placement of spinal cord stimulators: a cohort analysis of complications associated with placement. Neuromodulation. 2011;14:130-4; discussion 4-5.
38. Villavicencio AT, Leveque JC, Rubin L, et al. Laminectomy versus percutaneous electrode placement for spinal cord stimulation. Neurosurgery. 2000;46:399-405; discussion -6.
39. Kumar K, Rizvi S. Cost-effectiveness of spinal cord stimulation therapy in management of chronic pain. Pain Med. 2013;14:1631-49.
40. Kumar K, Rizvi S, Nguyen R, et al. Impact of Wait times on Spinal Cord Stimulation Therapy Outcomes. Pain Pract. 2013.
41. Stanton-Hicks M, Kapural L. An effective treatment of severe complex regional pain syndrome type 1 in a child using high doses of intrathecal ziconotide. J Pain Symptom Manage. 2006;32:509-11.