

Spinal Cord Stimulation for Chronic Pain

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Abstract

Spinal cord stimulation (SCS) is one of the most effective modalities for management of refractory neuropathic pain unresponsive to conservative therapies. The SCS has been successful in providing analgesia, improving function, and enhancing quality of life for patients suffering from chronic pain conditions such as failed back surgery syndrome, complex regional pain syndrome, ischaemic and phantom limb pain, and coronary artery disease. This technique has proven to be cost effective in the long term despite its high initial cost. In this review article, we discuss the history of SCS development, mechanism of action, and indications for SCS.

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Introduction

In 1967, Shealy¹ first introduced dorsal column stimulator for patients suffering from terminal cancer pain based on the gate control theory of pain proposed by Melzack and Wall.² In the first decade after its introduction, the success of follow-up rate was poor, and the spinal cord stimulation (SCS) soon fell into disrepute due to poor patient selection and technical difficulties. Only in the last decade, the outcome of SCS has improved significantly and became widely accepted therapy for chronic neuropathic pain. While not all patients are suitable for SCS therapy, careful patient selection and evaluation by a multidisciplinary pain management team can improve the selection of appropriate patients.^{3,4} The search for objective criteria to predict optimal outcome for implantable systems should include a comprehensive psychosocial evaluation to ensure all patients give his or her consent and are mentally sound or received appropriate medication for their mental state.

Advances in technology have also contributed to the acceptance of the device among the healthcare pain-management community. In the early years, the plated-type leads were surgically implanted directly over the spinal cord via laminectomy. Such method leads to undesirable complications including cerebrospinal fluid (CSF) leakage, localised fibrosis, and arachnoiditis. To avoid such complications, the leads have been implanted in the epidural space. Subsequently, the less invasive

percutaneous technique via a modified Tuohy epidural needle was introduced. The percutaneous system allows insertion of the lead without the laminectomy. Moreover, the technique easily allows a trial stimulation to assess suitability for a permanent implant. Currently, the protocols for SCS implantation stipulate a screening period using temporary percutaneous placement of the leads with an external pulse generator.

During the trial implantation, the patient is asked to indicate the location of paresthesia. The optimal position of the electrode placement depends on the location of the patient's pain. It is important to confirm that the resultant paresthesia overlaps with the painful area to achieve good analgesia. The trial lead is connected to an external impulse generator. During the trial period, which can last from a few days to a few weeks, the amount of pain relief and functional improvement are monitored with usual daily activities. The accepted benchmark for successful trial is a minimum of 50% reduction in baseline pain. If the patient is satisfied with the results of the trial, then implantation of the permanent SCS system is performed.⁵

Equipments

The SCS system consists of electrode lead, pulse generator, and a programmer. The electrodes developed initially were unipolar, and shortcomings were apparent with its limited field of paresthesia and application. Hence

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bipolar, quadripolar, and octapolar leads were subsequently developed. Currently, there are 2 types of leads available in the market: namely percutaneous and surgical. The cylindrically shaped percutaneous electrode can be inserted via Tuohy needles and is ideal for both trial and permanent implant; while paddle-type surgical electrode is suitable for patients with a medical history of lead migration or difficult trial lead placement. Placement of paddle lead requires more invasive laminectomy, but offers advantage of greater stability and less propensity to migrate.

The implanted leads are connected to the pulse generator, and the system is programmed by adjusting amplitude, pulse width, and frequency. The programmable multiple-electrode arrays have shown to be superior to the single-channel devices by allowing anode-cathode guarding and polarity changes to facilitate optimal current steering.⁶ Two types of systems that are currently available: an Internal Pulse Generator (IPG) or a radio-frequency (RF) coupled pulse generator with an implantable receiver. The IPG is powered by a lithium battery. Activation and programming of stimulator occur through an external transcutaneous telemetry device. Life span of the battery depends on usage and level of parameters utilised (voltage, frequency, pulse width, etc.). On average, most patients can expect a battery life of 2.5 to 4.5 years. The longer the battery life, fewer replacements were needed and thereby, resulting in lesser surgical risk and indirectly leads to potential cost savings.⁷ But recent introduction of rechargeable IPG, up to a total of 10-year life span is expected and can deliver frequencies up to 1400 Hz. The disadvantage of RF system is that the RF transmitter needs to be worn over the implanted antenna. Patients may find it troublesome to have transmitter taped to the skin, and the equipment is not waterproof. Besides that, external batteries must be replaced on a regular basis. Hence, rechargeable IPG is gaining popularity due to its small size and ease of maintenance.

Mechanism of SCS

Although a number of researchers have contributed to understanding the theory of SCS-induced analgesia, the exact mechanisms of action of SCS still remain elusive. The mechanism of action of SCS was based initially on the Gate Control Theory of pain described by Melzack and Wall.² They described stimulation of large myelinated fibres of peripheral nerves (A- β fibres), which carry non-painful touch sensations, inhibited the activity of small nociceptive projections (A- δ and C) in the dorsal horn of the spinal cord. However, this theory does not adequately explain the mechanism of action of SCS, since not all types of pain are modulated uniformly. SCS primarily affects neuropathic pain and non-nociceptive pain. Oakley and Prager⁸ suggested that several mechanisms are attributed to SCS induced analgesia. The computer simulation showed that stimulating

dorsal aspect of the epidural space causes formation of complex electrical fields that can influence a number of structures.⁹⁻¹³ A conduction block in spinothalamic track has been proposed by a number of authors,¹⁴ whereas others have implied activation of supraspinal systems involving spinobulbar, spinocortical, and spinothalamic track.¹⁵ The animal sciatic nerve injury model showed that SCS inhibit hyperexcitability of the wide dynamic range (WDR) cells in the dorsal horn.¹⁶ The predominant anti-nociceptive effect of SCS appears to occur via A- β fibres.^{17,18}

SCS attenuates hyperactivity of sympathetic nerve system as shown by anti-ischaemic and antianginal characteristics.⁸ The antianginal effect may be also attributed to the suppression of central nerve system, stabilisation of intracardiac neuronal activity, or release of adenosine.⁸ The anti-ischaemic effects appear to activate afferent fibres in the dorsal roots antidromically causing release of calcitonin gene-related peptide (CGRP) peripherally which in turn produce vasodilation.¹⁹

At the cellular level, animal studies suggest that SCS promotes the release of substance P, serotonin, noradrenaline, glycin, and gamma-aminobutyric acid (GABA) in the dorsal horns,²⁰ activation of the GABA-B receptor may be associated with reduction of glutamate and other excitatory amino acids release leading to pain modulation.²¹

Indications

SCS is particularly effective for pain of neuropathic origin. The most common indications include failed back surgery syndrome (FBSS) with radicular pain, complex regional pain syndrome, chronic arachnoiditis, peripheral neuropathy, phantom limb pain, angina, and ischaemic limb pain. Previous reports have also showed successful treatment of intractable pain due to spinal cord injury, postherpetic neuralgia, cervical neuritis, thoracic outlet syndrome, and visceral pain.

Holshimer et al²² and Oakely et al²³ have used computer modelling to develop tripole configuration to channel the current more accurately to the areas of interest. The transverse tripole array (+, -, +) enables selective recruitment of axons deeper in the dorsal column at the same time shielding nerve roots with 2 lateral anodes. This technique allows enhanced paresthesia coverage of axial back region, while minimising stimulation of nerve roots.

Failed Back Surgery Syndrome

One of the most common indications for SCS is FBSS. FBSS is a poorly defined pain conditions which persist after back surgery; the symptoms range from chronic back pain to radiculopathy. The systematic review of the literature cited by Tylor et al²⁴ concluded that the level of evidence for the efficacy of SCS in chronic back and leg pain secondary to

FBSS remains “moderate.” North et al²⁵ reported that in patients with postsurgical lumbar arachnoid or epidural fibrosis, SCS is superior to repeat surgical interventions or dorsal ganglionectomy. In this study, 50 patients with FBSS who averaged 3.1 operations prior to SCS implantation were included. Successful outcome (at least 50% pain relief and patient satisfaction with the result) was obtained in 53% of patients after 2.2 years and in 47% of patients after 5 years. North et al²⁶ also conducted a prospective study randomising patients with FBSS to either repeat back surgery or undergo SCS implantation. After 6 months, 17% (i.e. 2/12) of SCS patients requested cross-over to back surgery compared to 67% (i.e. 10/15) of the control group (back pain surgery) sought cross-over to SCS. Kumar et al^{27,28} compared SCS and conventional medical management (CMM) in 100 patients with neuropathic pain secondary to FBSS with predominant radicular pain. Compared to the CMM group, the SCS group experienced superior leg and back pain relief and greater treatment satisfaction at 6 month follow-up (Table 1). At 12 months, 48% of the SCS group and 9% of the CMM group achieved at least 50% pain relief.²⁷ At 24-month follow-up, 42 out of 52 patients on SCS reported significant relief of radicular pain, health-related quality of life (HRQoL), functional capacity, and satisfaction with treatment.²⁸

In general, SCS is much more effective in reducing radicular pain than the axial back pain. This is due to the difficulty in obtaining paresthesia coverage along the physiologic midline.²⁹ However; a recent study has shown that stimulation of the low back can be obtained more consistently with tripole²³ or quadripolar electrode at T8-T10 levels.³⁰

Neuropathic Pain

Complex regional pain syndrome (CRPS) is the second most common indication for SCS in the USA. Early evidence

suggested that SCS resulted in the relief of pain in over 73% of CRPS patients and helped to reduce the edema associated with the condition.^{31,32} Kemler et al⁵ carried out a prospective, randomised, controlled study in patients with chronic CRPS type I to determine whether SCS plus physiotherapy was more effective than physiotherapy alone. Results showed that, in patients treated with SCS plus physiotherapy, the pain intensity was reduced by 3.6 cm on the visual analog scale (VAS) compared with an increase of 0.2 cm in the physiotherapy alone group. In addition, a significantly greater number of SCS-treated patients (58%) described a “much improved” global perceived effect compared to the physiotherapy alone group (6%). Although there was no clinically significant improvement in functional status in either group, the overall HRQoL score improved by 11% for the SCS group; the SCS resulted in significant improvement in the pain-rating index ($P = 0.02$) as well as the HRQoL for patients with CRPS of both upper ($P = 0.02$) and lower extremities ($P = 0.008$). The results of 2 years of follow-up of this trial have demonstrated that SCS improved the pain intensity ($P < 0.001$) as well as the improvement in perceived effect, and HRQoL.³³ In 2008, Kemler et al³⁴ assessed the effectiveness of SCS in reducing pain due to CRPS-I at the 5-year follow-up. The results showed that SCS does not produce a durable and statistically significant improvement in the pain, but patient satisfaction at the 5-year follow-up remains high. They concluded that despite the diminishing effectiveness of SCS over time, 95% of patients with an implant would repeat the treatment for the same result. In a prospective study of 19 CRPS patients treated with SCS, Oakley et al³⁵ have shown that 80% of patients experienced at least 50% improvement in McGill Pain Rating Index, Sickness Impact Profile, Beck Depression Inventory, and VAS after an average follow-up period of 7.9 months.

Angina

SCS appears to be a promising technique for patients with refractory angina. The first stimulator was implanted for intractable angina in Australia in 1987.³⁶ SCS has shown to improve New York Heart Association (NYHA) functional class, reduce hospital admissions, and improves quality of life.^{37,38} These improvements appear to be persistent without causing additional risks to the patients. Mannheimer et al³⁹ studied a group of high surgical risk patients randomly assigned to coronary artery bypass graft (CABG) surgery or SCS. Both groups displayed a significant reduction in angina frequency and reduction in short-acting nitrate requirements, whilst only the surgical group showed significant improvement of exercise induced ischaemia at 6 months. However, the surgical group had a high procedural mortality rate compared to no deaths in the SCS group. Therefore, SCS may be a therapeutic option for high-risk

Table 1. Outcomes for Failed Back Surgery Syndrome (FBSS) with Spinal Cord Stimulation (SCS) Compared to Conventional Medical Management (CMM) at 6-month Follow-up²⁷

	CMM group (n = 44)	SCS group (n = 50)	P value
≥50% leg pain relief* – n (%)	4 (9%)	24 (48%)	<0.001
Leg pain VAS – mean (SD)	66.6 (24.0)	39.9 (26.3)	<0.0001
Back pain – VAS – mean (SD)	51.6 (26.7)	40.6 (24.9)	0.008
Treatment satisfaction – n (%)	8 (18%)	33 (66%)	0.001

VAS: visual analog scale; SD: standard deviation

*: Primary outcome

patients unsuitable for surgery. The benefit of SCS may be attributed to suppression of intrinsic cardiac neurons during myocardial ischaemia, reduction in pain perception, reduced sympathetic outflow, and antidromic vasodilation.⁴⁰⁻⁴² For angina, the electrode is generally placed at C6-T1 at the left of the midline. This provides paresthesia in the area corresponding to angina pain. Although this prevents adequate blinding of the therapy, several randomised controlled trials have convincingly established the clinical efficacy of SCS in chronic refractory angina pectoris.^{43,44}

Peripheral Ischaemic Limb Pain

Patients with non-reconstructible critical limb ischaemia (CLI) often require amputation. Cook et al⁴⁵ suggested that SCS may avert the need for amputation in patients with CLI. Several literature studies report significant long-term pain relief with SCS.⁴⁶⁻⁴⁹ In 51 patients with inoperable lower limb ischaemia, Jivegard et al⁴⁷ showed that the amputation-free survival was superior for the SCS group than the control group (62% vs. 45%, $P > 0.05$) at 18 months. The prospective randomised trial by Guarnera et al,⁵⁰ comparing efficacy of SCS vs distal arterial reconstruction, clearly demonstrated a favourable outcome with SCS (72%) than with distal arterial reconstruction (40%). A Cochrane review, evaluating the results of 6 studies (5 of which were randomised controlled trials) comprising nearly 450 patients, concluded that SCS was superior to medical management for treating patients with non-reconstructible CLI.⁵¹ Horsch et al⁵² reported on 177 patients with untreatable CLI, including Fontaine's stage III (chronic ischaemic rest pain, $n = 114$) and Fontaine's stage IV (ischaemic pain and ulcers or dry gangrene, $n = 63$). Greater than 75% of the patients on SCS reported significant pain relief, and limb salvage was achieved in 110 patients at 35.6 months follow-up. In 11 patients with limb salvage, pain reduction was between 50% and 70%. At 4-year follow-up, a 66% cumulative limb salvage rate was observed with SCS. Pain reduction with trial stimulation correlates well with successful limb salvage,^{52,53} and delayed wound healing is highly predictive of tissue hypoxia. Hence, transcutaneous oxygen pressure (TcPO₂) measurement is a non-invasive method useful for assessing efficacy of tissue perfusion. Patients without clinical improvement also fails to show increase in TcPO₂, subsequently requiring limb amputation.^{53,54} Pain reduction and TcPO₂ augment are the selection criteria generally used for the permanent implantation of SCS.⁵⁵ Spincemaille et al⁵⁶ recommend that patients with greater than 50% pain relief and better than 15% increase in TcPO₂ during the trial stimulation should be considered for permanent SCS implantation.

Complications

Turner et al⁵⁷ conducted a systemic review of efficacy and complication of SCS on patients with FBSS and CRPS.

On average, 34.3% of patients who received a stimulator experienced complications. They found the following incidence of complications: additional revision (23.1%), hardware malfunction (10.2%), infection (4.6%), biological complication other than infection or local pain (2.5%), pain at the pulse generator site (5.8%), and stimulator removal (11.0%). Complications are usually minor with a proper implantation technique. The most dreadful complication is neurological damage due to nerve root or cord injury and epidural haematoma.⁵⁸ The most common complication is electrode migration. The lead migration occurs most frequently within the first few days after the implantation. The incidence was statistically lower in patients with quadripolar leads (11%) than in those with monopolar electrodes (45%).⁵⁹ Percutaneous electrodes have higher incidence of migration than the surgical leads. The incidence of infection is 3% to 5%. The full course of antibiotics and explantation of hardware is often required to manage infection.^{60,61} To minimise likelihood of infection, a strict aseptic technique should be observed during the implantation. A single dose of antibiotic should be administered intravenously prior to the procedure.^{62,63} Inadvertent dura puncture is not uncommon complication during the implantation of SCS. The clinical presentation is usually positional headache. The majority of headache is amendable to epidural blood patch. However if the headache persists, myelogram may be required to localise the site of CSF leak. Rarely surgical exploration is necessary. Painful stimulation, necessitating either repositioning or removal of the electrode, has also been reported in a number of cases.⁵⁹ Persistent pain at the implant site must be carefully differentiated from an indolent infection of the implanted equipment.

Cost efficacy

Data available so far have shown that despite the high initial costs, SCS is cost-effective in the long term. A cost-effectiveness analysis study performed by Kemler et al⁶⁴ showed that treatment with SCS plus physiotherapy in CRPS resulted in a lifetime cost saving of €8,471 per patient compared to the standard treatment alone. Ubbink et al⁵¹ reviewed 6 studies comprising nearly 450 patients with CLI who were poor candidates for vascular graft surgery. They found that the average overall costs (1 study) at 2 years were €36,500 (SCS group) and €28,600 (conservative group), and the cost difference (€7900) was significant ($P < 0.009$). In a prospective, randomised, controlled study involving 100 patients with FBSS, Manca et al⁶⁵ compared HRQoL and cost implications of SCS plus CMM vs CMM alone. They showed that the 6-month mean total healthcare cost for the SCS group (CAN\$19,486; €12,653) was significantly higher than in the CMM group (CAN\$3994; €2594). However, HRQoL with SCS over the same period

of time was markedly superior in the SCS group.

Contraindication

Commonly-accepted contraindications are as follows:

(i) Absolute

- Sepsis, coagulopathy, or other conditions associated with an unacceptable surgical risk
- Previous surgery or trauma that obliterates the spinal canal
- Localised infection at the implantation site
- Spinal bifida

(ii) Relative

- Physical and/or cognitive/psychological disability
- Unresolved major psychiatric disorder,
- Unmanaged substance abuse or cognitive disorders,
- Pregnancy
- Presence of a cardiac pacemaker or defibrillator

Conclusion

SCS has demonstrated positive therapeutic effects in many painful syndromes. Though the initial costs may be high, the technique has proven to be cost effective in the long term. In combination with comprehensive medical management that may include physical and psychotherapy, SCS can provide long-term pain relief with concomitant improvement in the quality of life, daily function, and patient satisfaction. The key to successful SCS outcomes are: good understanding of indication of SCS, applying rigorous patient selection criteria, as well as acquiring sound surgical implantation techniques. In addition, careful follow-up of patients is necessary for long-term satisfaction.

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