Managing Chronic Pain With Spinal Cord Stimulation

Lawrence J. Epstein, MD and Marco Palmieri, DO

Department of Anesthesiology, Mount Sinai School of Medicine, New York, NY

OUTLINE

ABSTRACT

Since its introduction as a procedure of last resort in a terminally ill patient with intractable cancer-related pain, spinal cord stimulation has been used to effectively treat chronic pain of varied origins. Spinal cord stimulation is commonly used for control of pain secondary to failed back surgery syndrome and complex regional pain syndrome, as well as pain from angina pectoris, peripheral vascular disease, and other causes. By stimulating one or more electrodes implanted in the posterior epidural space, the patient feels paresthesias in their areas of pain, which reduces the level of pain. Pain is reduced without the side effects associated with analgesic medications. Patients have improved quality of life and improved function, with many returning to work. Spinal cord stimulation has been shown to be cost effective as compared with conservative management alone. There is strong evidence for efficacy and cost effectiveness of spinal cord stimulation in the treatment of pain associated with intractable angina, failed back surgery syndrome, and complex regional pain syndrome. In this article, we review the history and pathophysiology of spinal cord stimulation, and the evidence (or lack thereof) for efficacy in common clinical practice. ***Mt Sinai J Med 79:123–132, 2012.*** *© 2012 Mount Sinai School of Medicine*

Address Correspondence to:

Lawrence J. Epstein
Department of Anesthesiology
Mount Sinai School of Medicine
New York, NY
Email: lawrence.epstein@mountsinai.org

Key Words: chronic pain, complex regional pain, failed back surgery syndrome, intractable angina, spinal cord stimulation.

Shealy *et al.*[1] first reported the use of spinal cord stimulation (SCS) in 1967 in an elderly man suffering with terminal bronchogenic carcinoma and right-sided chest pain. The authors extrapolated from earlier cases in which peripheral nerve stimulation was used to treat intractable pain. The stimulation seemed to distract the patient from the primary pain. In this patient, a monopolar lead was placed via laminectomy and sutured to the dura at a level of T2-T3. The lead was connected to an external generator and then stimulated. The patient's pain was reportedly "completely abolished" for periods of 10–15 minutes, after which the pain would recur. The stimulation frequency was varied slightly and the pain would resolve for another 10–15 minutes. The cycle of pain relief and return continued for the next day and a half, until the

patient expired due to complications related to his malignancy.

MECHANISM OF ACTION

Gate Theory

Melzack and Wall[2] postulated that a "gate" existed in the dorsal horn of the spinal cord that determined the central transmission of neural activity signaling pain. This "gate" was opened when there was an abundance of small fiber (A-delta and C-fiber) nocioceptive input over large fiber (A-beta) activity in the peripheral nervous system. The gate was closed when there was excess large-diameter afferent activity. Therefore, on the basis of this gate theory, by selectively activating the large-diameter afferent fibers by electrical stimulation, one may electively close the gate and reduce or abolish painful inputs to the spinal cord, and thus the higher processing centers of the brain (Figure 1). Intraoperative monitoring performed in a patient undergoing placement of paddle lead at T9 via laminotomy shows "collision" and attenuation of cephalad transmission with the lead in place and stimulation on (Figure 2).

The gate theory, however, fails to address certain clinical observations, including: (1) both acute and chronic pain should be affected by this stimulation, but this is not the case; only chronic pain appears to be affe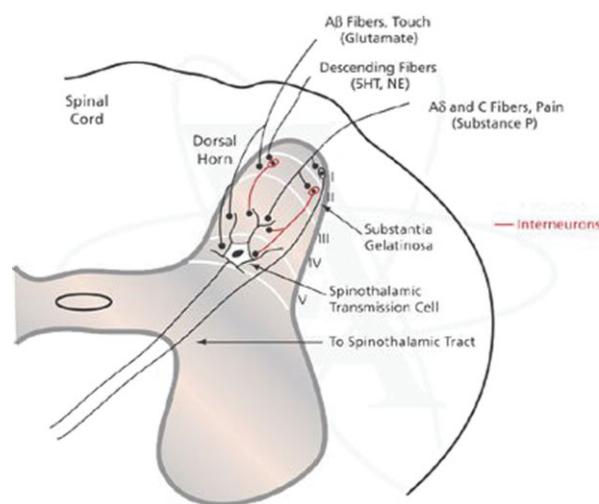cted; (2) the period of relief often outlasts the period of stimulation by minutes to hours; and (3) stimulation seems to be most effective for neuropathic or sympathetically mediated pain states.

Spinal Neurochemistry

There are few human studies available, but there appears to be no relationship between SCS and endogenous opioid pain-relieving mechanisms, as the effects are not blocked by the administration of naloxone.

Animal models of neuropathic pain have focused on the neurochemistry of the dorsal horn of the spinal cord. "In "normal" animals, a primary effect of SCS involves gamma-aminobutyric acid (GABA), which has been shown to increase after stimulation in responding rats but is unchanged in nonresponders (as defined by alteration in their pain behavior)."[3] In addition, it has been shown that these effects can be counteracted by the administration of bicuculline, a GABA antagonist.[4] Other substances known to be involved with pain modulation in the spinal cord, specifically substance P and serotonin, also are released by SCS.[5]

Spinal cord stimulation in rats has been shown to increase levels of GABA and acetylcholine in periaqueductal grey matter[6] in subjects that had a concomitant reduction in allodynic behavior (a pain response to a stimulus that would normally not be perceived as painful).[7] The reduction in allodynic behavior was blocked by muscarinic antagonists.

Vasodilation

Spinal cord stimulation has also been shown to inhibit sympathetic activity, reducing vasoconstriction and release of vasoactive agents from sensory fibers to cause vasodilation.[8,9]

GENERAL CONCEPTS

Modern SCS systems are made up of 3 components: leads/electrodes, a generator/power source, and a programmer/controller. Leads/electrodes can be divided into percutaneous or "wire" leads and paddle or "laminotomy" leads. The percutaneous leads are round wires with 4–8 circumferential contacts evenly spaced near the distal end. These leads are passed through a 14-gauge needle, inserted into the epidural space (usually) 4–6 levels caudal to the desired level and then threaded up under fluoroscopic guidance

Fig 1. Gate theory of SCS. Selective activation of the large diameter afferent fibers by electrical stimulation may electively close the "gate" and reduce or abolish painful inputs to the spinal cord and thus the higher processing centers of the brain. **Abbreviations:** 5HT, 5-hydroxytryptamine; NE, norepinephrine; SCS, spinal cord stimulation.
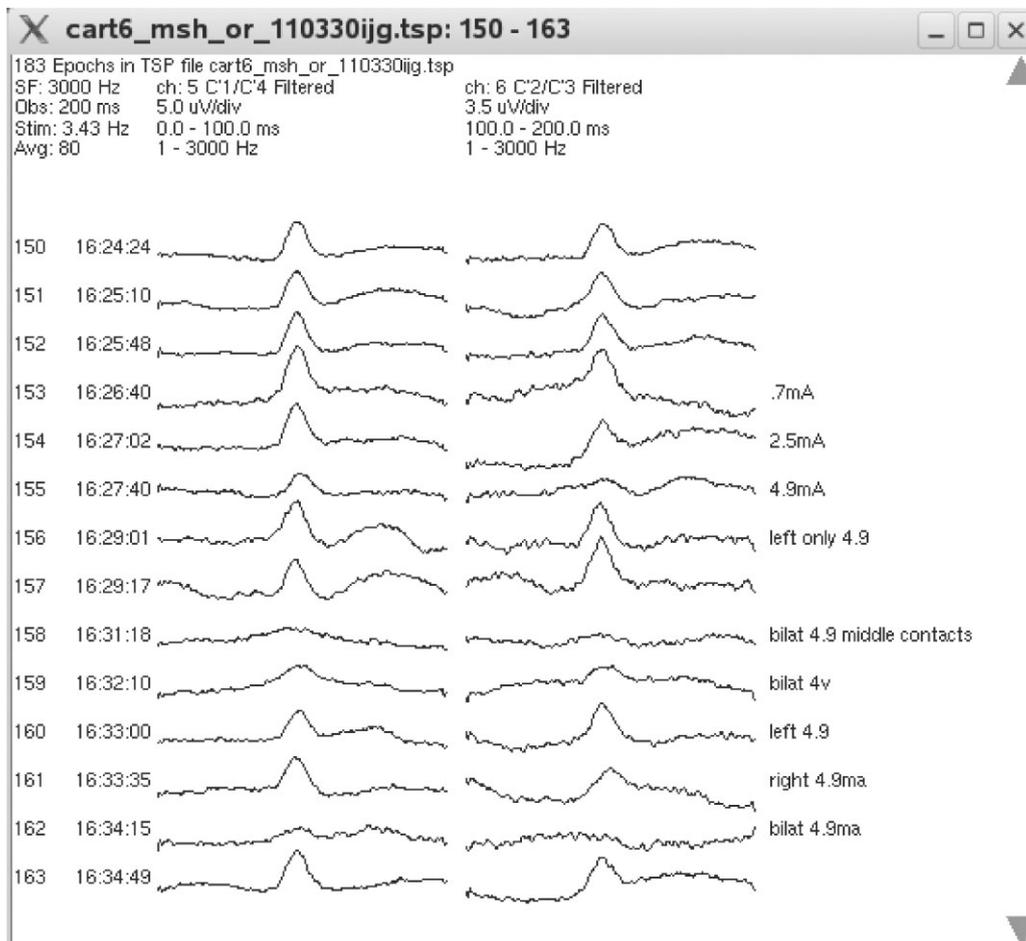
Fig 2.   Intraoperative monitoring of patient undergoing placement of SCS paddle lead at T9 via laminotomy. Monitoring shows "collision" and attenuation of cephalad transmission with the lead in place and stimulation on. **Abbreviation:** SCS, spinal cord stimulation.

and positioned in the posterior epidural space at or on either side of midline. The paddle leads are flat polymer leads with 1–3 rows of electrodes on 1 side only (Figure 3). Paddle leads are placed via a small laminotomy immediately below the level desired. Advantages of percutaneous leads are easier/less-invasive method of placement and lower initial cost. Paddle leads require a more invasive procedure for placement (1- or 2-level laminotomy) and higher initial cost, but are much less likely to require revision or repositioning due to spontaneous lead migration.[10] The procedure is performed in either an operating room or fluoroscopy suite, using sterile technique.

There are 2 types of generators: external battery with implanted radiofrequency receiver, or implanted battery. Implanted batteries are now available in either rechargeable or nonrechargeable versions (Figure 4). The early units were more commonly the radiofrequency variety, but as battery technology has improved, battery size has been decreased.
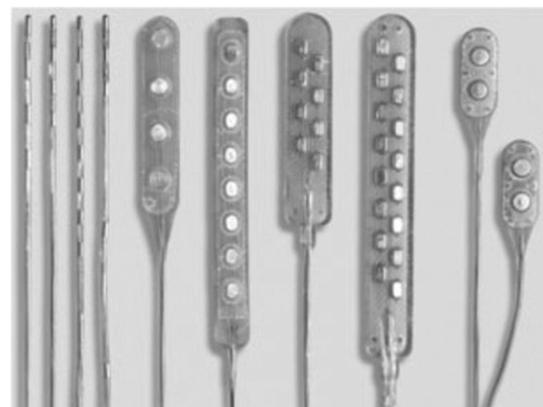

Fig 3.   Flat SCS polymer leads with 1–3 rows of electrodes on 1 side only. **Abbreviation:** SCS, spinal cord stimulation.

With the introduction of the rechargeable models, the radiofrequency units are now rarely used (Table 1).

Fig 4. Implantable batteries in rechargeable and non-rechargeable varieties.

Fig 5. Extending SCS pain coverage by adding lateral stimulation to dorsal column stimulation. **Abbreviation:** SCS, spinal cord stimulation.

The patient is issued a wireless/programmable controller (excepting radiofrequency units). This is a handheld device that gives the patient some control over the stimulation. The degree and range of control are programmed by the physician and can be changed at any time. Patients can turn the device on and off, can vary the intensity, and can be allowed to vary parameters such as pulse width and rate of stimulation wave. With modern generators, patients can be given multiple programs from which to choose, depending on position, pain intensity and location, or other factors.

leads immediately on either side of midline (on only the affected side if the patient has unilateral limb pain; 1 midline lead or 1 lead on either side of midline for axial pain). Most commonly, the goal is to stimulate the dorsal columns of the spinal cord (posterior, on either side of midline) without stimulating the lateral structures within the cord (dorsal horn or exiting nerve roots). This is accomplished through tight contact spacing in order to optimize the shape of the electrical field.[11] Lateral stimulation usually gives unwanted and uncomfortable paresthesias. In certain situations, lateral stimulation is intentionally performed in order to obtain coverage of areas not reachable with dorsal column stimulation (Figure 5).

Positioning of Electrodes

Electrodes are positioned such that the patient feels the stimulation (commonly described as a buzzing or vibration) in the same distribution as their pain. This is usually accomplished by positioning the

Trial/Screening

Most commonly, percutaneous lead(s) are inserted under local anesthesia. The leads are initially positioned empirically, according to the location and type of pain (eg, low back pain, T9; buttock and leg

Table 1. *Variable Features of Spinal Cord Stimulation Systems.*

	Advantages	Disadvantages
Radiofrequency	Small implanted components; low complexity of implant/lower failure rate; external batteries easily changed and available (9 V); lowest initial expense	External power source must be worn at all times when using device; irritation over receiver implant.
Nonrechargeable, implanted battery/generator	Low complexity for patient; large variety of programming/operating modes	Larger battery/generator implant; limited battery life (1–4 years depending on device/power settings) requiring surgical removal and replacement.
Rechargeable, implanted battery/generator	Large variety of programming/operating modes; longer battery life (~5–10 years); smaller battery/generator implant	Increased complexity for patient/need for regular recharging (every 3 days to 3 weeks depending on device/power settings); most expensive.

pain, T10-11; pelvic pain, T12-L1 [conus]). The leads are then stimulated and the patient is asked whether he feels the stimulation "everywhere you have pain." The leads are then repositioned, depending on the coverage. It is important to explain (prior to the procedure) that during placement of the trial leads, the physician is concerned with "coverage," meaning that the patient feels the sensation of the stimulation in all areas of pain. The patient must understand that he or she should not expect pain relief from the stimulation during the placement of the leads. Optimum positioning is such that the patient has best stimulation when using the middle electrodes of the lead(s) so that there is room for some migration of the leads. The leads are secured to the skin and a sterile dressing applied. After transfer to the post anesthesia care unit, the stimulator is programmed so that the patient has good coverage in multiple positions (supine, seated, and standing). Each position may require its own program, or 1 program may cover some or all positions. The patient is then educated on the use of the device as well as warning signs indicating possible complications (fever, new-onset weakness or numbness) and discharged home to use the device for 3–7 days (most commonly). During this period, it is critical that contact be maintained with the patient and coverage monitored. If the patient's coverage is not adequate, the device should be reprogrammed immediately. At the end of the trial period, the leads are removed and the patient reports whether the pain relief, quality-of-life improvement, and/or increased activity tolerance justifies permanent implantation. Permanent implantation is usually performed approximately 1 month later. In some cases (particularly if there is difficulty positioning the leads), a "permanent trial" may be performed, in which an incision is made at the time of trial and the leads implanted subcutaneously with an extension exiting some distance away. If the patient decides on permanent implantation, the extension is removed and the generator is implanted and connected. This eliminates the need for positioning new leads, but may be associated with a higher postimplantation infection rate In these authors' experience, approximately 65% of patients undergoing an SCS trial will proceed to permanent implantation. Some practitioners implant a much higher percentage of patients, and others question the need and validity of the trial. The authors have explanted multiple systems from patients who have either had no trial, or had permanent systems implanted after a trial that gave marginal relief with the explanation that they would "get better coverage with the permanent system." In light of this experience, we do not proceed to permanent implantation unless the patient describes a significant (from the patient's perspective) reduction in pain, as evidenced by decreased need for analgesic medications and/or improved function.

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Permanent Implantation

Permanent implantation is commonly performed approximately 1 month after removal of the trial leads. Permanent stimulation may be obtained using the same type of "percutaneous" or "wire" leads that were used in the trial. An incision is made at the needle-insertion level and the leads are again placed through the needle and positioned using fluoroscopy. Once positioned, the needles are removed and the leads secured to the interspinous ligament. Alternatively, a small laminotomy may be performed 1–2 levels below the desired level of the leads (as determined during the trial) and a "paddle" lead placed under direct vision (with fluoroscopic confirmation). The leads are then tunneled under the skin to the pocket that has been made to hold the battery/generator and connected. The skin is then closed over the insertion site and generator pocket. Common sites for placement of the generator include upper buttock, left or right lower quadrant, axilla/lateral chest wall, and infraclavicular.

INDICATIONS FOR SPINAL CORD STIMULATION

Postlaminectomy Syndrome/ Failed Back Surgery Syndrome

The most common indication for SCS in the United States is postlaminectomy syndrome or failed back surgery syndrome (FBSS). These are patients who

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have had previous spine surgery and have persistent pain postoperatively. The pain may be axial (low back pain or neck pain) or radiating to arms or legs. Some of these patients are also patients who are not candidates for corrective surgical repair.

Spinal cord stimulation has been shown to be cost effective compared with controls, with a 5-year cost of $29,000 in the stimulator group and $38,000 in the control group.[12] Another review of 3 studies[13] also concluded that SCS was more cost effective than conservative management. Mancia et al,[14] in a prospective, randomized, controlled, multicenter study, concluded that the patients with combined SCS and medical management were more costly to the healthcare system, but also had significant functional improvement. Kumar et al[15] showed a 5-year cost of $25,000 for the SCS group compared with $34,000 for the conventional-therapy group. Quality of life increased 27% in the SCS group versus 12% for the conventional-therapy group. Of the SCS group, 60% reported being very satisfied,

> *When spinal cord stimulation and control groups were compared with regard to 5-year cost, spinal cord stimulation was shown to be more cost effective (spinal cord stimulation cost: $29,000; control group cost: $38,000). The most cost-effective spinal cord stimulation option, despite higher initial cost, was a rechargeable generator, when the predicted generator longevity was >4 years.*

28% were satisfied, and 15% returned to work. No patients in the conventional-therapy group returned to work. A recent study by Kemler et al.[16] concluded that "in selected [complex regional pain syndrome] patients, SCS is a cost-effective option as an adjunct to conventional medical management." They also concluded that a rechargeable generator is the most cost-effective option, when the predicted generator longevity is >4 years, despite higher initial cost.

In a systematic review by Frey et al,[17] 85 studies were reviewed and ultimately 6 randomized trials and 28 observational studies were included. In one of these randomized trials[18] in which the primary outcome was 50% relief of leg pain at 1 year, 48% of SCS patients versus 9% achieved the primary outcome. In addition, the SCS group experienced improved leg and back pain, improved quality of life, increased functional capacity, and greater treatment satisfaction than the medical management group. In summary, the systematic review concluded that "there is level II-1 (evidence obtained from well-designed controlled trials without randomization) or II-2 (evidence obtained from well-designed cohort or case-control analytic studies, preferably from ≥1 center or research group) evidence for the effectiveness of SCS in relieving chronic, intractable pain of failed back surgery syndrome."

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North et al.[19] performed a randomized controlled trial of 50 patients comparing SCS versus reoperation for failed back surgery syndrome. Patients were followed for an average of 3 years postoperatively by a disinterested third party and were allowed to cross over to the alternative if they were dissatisfied. They found that patients in the SCS group were more likely satisfied and less likely to cross over than the reoperation group. Also, patients randomized to the surgical group required increased opioid analgesics more often than those randomized to the SCS group. They concluded that SCS was more effective than reoperation as a treatment for persistent radicular pain after lumbosacral spine surgery and, in the great majority of patients, it averts the need for surgery.

In a third-party review of the first 42 patients in a separate, randomized, controlled, crossover

trial comparing SCS with reoperation in patients with failed back surgery syndrome, North *et al.*[20] concluded that SCS was "less expensive and more effective than reoperation in selected patients and should be the initial therapy of choice."

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Complex Regional Pain Syndrome

Complex regional pain syndrome (CRPS) is a chronic pain condition that is believed to be the result of dysfunction in the central or peripheral nervous systems. Typical features include dramatic changes in the color and temperature of the skin over the affected limb or body part, which may be accompanied by intense burning pain, skin sensitivity, sweating, and swelling. Complex regional pain syndrome I (previously reflex sympathetic dystrophy) is frequently triggered by tissue injury; the term describes all patients with the above symptoms but with no underlying nerve injury. Patients with CRPS II (previously causalgia) experience the same symptoms, but their cases are associated with an obvious nerve injury.

A randomized controlled trial of SCS in the treatment of CRPS by Kemler[21] was carried out in which patients who carried the diagnosis of CRPS for ≥6 months' duration were randomized 2:1 into an experimental group (n = 36) with SCS and physical therapy (PT) versus a control group (n = 18) in which patients had PT alone. In this study, SCS therapy led to a reduction in pain intensity at 12 months' follow-up, whereas pain increased in the control group (PT alone). No significant improvement in functional capacity was observed between the 2 treatment groups.

The SCS group was followed up at 2 and 5 years by Kemler *et al.*[22,23] The 5-year follow-up showed that SCS does not produce a durable and statistically significant reduction of pain, but patient satisfaction at 5 years remains high. They found that despite the diminished pain relief, 95% of patients with a stimulator would repeat the procedure for the same results.

In a systematic review by Taylor *et al.*[24] totaling 500 patients in 25 case series followed for a mean of 33 months, 67% had >50% pain relief, with functional capacity and quality of life significantly improved. They also considered cost and concluded that "... SCS combined with physical therapy is both clinically effective and cost effective for the treatment of patients with CRPS type I."

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Intractable Angina

The first reported use of SCS to treat refractory angina was in the mid 1980s. Since then, there have been several studies that have shown benefit in reduction of symptoms and in improved quality of life.[25–28] The most appropriate location for electrode placement for the treatment of angina pectoris is most likely the lower cervical and upper thoracic region.

A study by DeJongste *et al.*[29] showed a significant reduction in the incidence of angina attacks and a reduction in the usage of nitrates in a group of patients followed for a period of 12 months.

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In a prospective study, Mannheimer et al.[30] randomized 104 patients accepted for coronary artery bypass grafting to receive either surgery (n = 53) or SCS (n = 51). Both groups experienced a significant reduction of both anginal attacks and usage of nitrates. The maximum workload capacity was lower in the SCS group, and the ST-segment depression on maximum workload was higher in the SCS group as well. There was, however, a significantly higher rate of cerebrovascular events in the surgical group, as well as a higher rate of mortality. They concluded that "it seems reasonable to conclude that SCS may be a therapeutic alternative for patients with an increased risk of surgical complications." The question of whether or not SCS can conceal the pain of an acute myocardial infarction was addressed by Anderson et al.[31] in a prospective study. During the observational period of up to 37 months, 10 out of 50 patients experienced a myocardial infarction. Nine of these 10 patients with acute infarction correctly recognized that their pain was clearly different and significantly more severe than their typical anginal pattern.

Peripheral Vascular Disease/ Critical Limb Ischemia

Cook et al.[32] were the first to suggest that SCS may avert the need for amputation in patients with critical limb ischemia. They placed spinal column stimulators in patients with chronic pain due to multiple sclerosis, and subsequently it was noted that there was an apparent improvement in lower-limb blood flow. Following this observation, they began to use this modality of treatment in patients whose primary problem was peripheral vascular disease. It was observed that patients had relief from rest pain, increased skin temperature, and healing of small cutaneous ulcers.

Jivegard et al,[33] in a randomized study of 51 patients with critical limb ischemia, placed participants into 2 groups, either treatment with oral medications alone or treatment with SCS with oral medications. It was reported that there was significant improvement in pain scores in the group treated with SCS and oral medications as compared with the group treated with oral medications alone. In addition, it was shown that the amputation-free survival was better for the group treated with SCS.

A Cochrane review[34] that analyzed 6 studies of SCS versus conservative treatment determined that limb salvage after 12 months was significantly higher in the stimulator group. There was no significant difference in ulcer healing between the 2 treatments.

In addition, pain relief was observed to be improved in both treatment groups, but was more prominent in the stimulator group.

Significant controversy remains as to whether SCS is indicated for the treatment of critical limb ischemia. In the United States, most insurance carriers will not recognize ischemia as an approved indication for SCS, although approval will frequently be granted with the indication of pain of ischemic origin.

Other Indications

Clinical observations support the potential use of SCS for various other painful conditions, such as postherpetic neuralgia, postamputation pain, multiple sclerosis, spinal cord injury or lesion, and diabetic neuropathy. A small prospective study of patients with intractable pain due to postherpetic neuralgia found that 82% (23 patients) obtained long-term pain relief from SCS.[35] These positive preliminary clinical results indicate that randomized controlled trials should be conducted to evaluate the benefit of SCS in patients with these and other painful neuropathic syndromes who have inadequate response to pharmacotherapy.

COMPLICATIONS

Complications from SCS implantation are usually minor with proper technique. Some of the more serious potential complications include epidural hematoma, accidental dural puncture, neurological damage due to nerve root or cord injury, and painful stimulation.

Taylor et al.[36] reported that 43% of patients had ≥1 complication, with more than half of those being problems with the lead(s), including lead migration or breakage. They reported a 6% infection rate and a 7% cerebrospinal fluid leak rate. No neurological complications were reported in this study.

In another systematic review by Turner et al,[37] 34.3% of patients who received a stimulator experienced complications. The following complications were also noted: additional revision (23.1%), hardware malfunction (10.2%), infection (4.6%), and pain at pulse generator site (5.8%).

CONTRAINDICATIONS

Contraindications to SCS placement include local or systemic infections, immune suppression, coagulopathy, insufficient patient cognitive function to manage

Table 2. *Contraindications to Spinal Cord Stimulation.*

Absolute	Relative
Local infection	Need for future MRI
Coagulopathy	Malignancy
Patient inability to understand/ use device	Immunosuppression

Abbreviations: MRI, magnetic resonance imaging.

the device, and need for future magnetic resonance imaging (Table 2).

CONCLUSION

Spinal cord stimulation can provide significant relief to patients with a variety of painful disorders including failed back surgery syndrome, CRPS, intractable angina, and peripheral vascular disease. Spinal cord stimulation has been shown to be safe and effective, and the technique is cost effective as compared with medical management alone.

DISCLOSURES

Potential conflict of interest: Nothing to report.

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