

Spinal Cord and Dorsal Root Ganglion Stimulation



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DESCRIPTION

Spinal cord stimulation (SCS), also known as dorsal column stimulator (DCS) involves the use of low-level epidural electrical stimulation of the dorsal columns of the spinal cord to block the sensation of pain. The neurophysiology of pain relief after SCS is uncertain but may be related to either activation of an inhibitory system or blockage of facilitative circuits. SCS is the most used implantable neurostimulation technology for the management of pain syndromes.

SCS is used for the treatment of pain that is neuropathic in nature, i.e., resulting from damage to the peripheral nerves. SCS has been used in a wide variety of chronic refractory pain conditions, including but are not limited to failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis (usually documented by the presence of high levels of proteins in the cerebrospinal fluid and/or by myelography or MRI), radiculopathies, phantom limb/stump pain and peripheral neuropathy/painful diabetic neuropathy. There has been an interest in SCS as a

treatment of critical limb ischemia, primarily in patients who are poor candidates for revascularization, pain associated with cancer and in patients with refractory chest pain (chronic stable angina pectoris).

Spinal cord stimulation (SCS) devices consist of several components: (1) the lead that delivers the electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source that generates the electrical stimulation. The lead may incorporate 4 to 8 electrodes, with 8 electrodes more commonly used for complex pain patterns. The patient's pain distribution pattern dictates at what level in the spinal cord the stimulation lead is placed. The pain pattern may influence the type of device used; for example, a lead with 8 electrodes may be selected for those with complex pain patterns or bilateral pain. Totally implantable systems are the most used.

Traditional spinal cord stimulation devices use electrical stimulation with a frequency on the order of 100 to 1000 HZ. Some devices allow adjustment of the frequency settings. In 2015 a spinal cord stimulation device using a higher frequency (10,000 Hz.) was approved by the FDA through the premarket approval process. The high-frequency stimulation is proposed to be associated with fewer paresthesia's, which are a recognized effect of traditional spinal cord stimulation devices. In 2016, the FDA approved a clinician programmer application that allows a SCS device to provide stimulation in bursts rather than at a constant rate. Burst stimulation is proposed to relieve pain with fewer paresthesia's. The burst stimulation device works in conjunction with standard SCS devices.

The incidence of adverse events related to spinal cord stimulation have been reported to occur in 30% to 40% of cases. Adverse events can either be hardware related or biological. Hardware related complications included lead migration or lead failure or fracture. Biological complications include infection and pain. More severe biological complications are rare, including dural puncture headache (estimated incidence, up to 0.3%) and neurological damage (estimated incidence 0.25%).

Types of Spinal Cord Stimulation Devices:

- **Conventional Systems:** (total implantable system): The leads are inserted in the epidural space above the spinal cord using a small needle or through a small incision. The exact location of the lead(s) depends on the specificity of the patient's pain. The generator is usually implanted in the abdomen or buttock region. This system requires little effort on the patient's part for maintenance. However, a minor surgical procedure is required to replace the power source when it runs out.
- **Radiofrequency Systems:** Are designed to sustain therapy over long periods at the highest output level. Because of its high- power capabilities, the RF system is suitable for the most challenging cases in which there is complex, multi-extremity pain. With this type of system, the patient must wear an external power source to activate stimulation.

- **Rechargeable Systems:** Are the newest type of SCS device. The patient is responsible for recharging the power source when it runs low. A rechargeable system typically lasts longer than a conventional System. Eventually a minor surgical procedure may be required to replace the power source if the time between recharges becomes impractical.

Patients being considered for spinal cord stimulation should ideally meet the following criteria:

- Pain is not associated with malignancy
- Poor response to conservative treatment for a minimum of 6 months
- Revision surgery not an option or would have a low chance of success
- No pacemaker or other medical contraindications
- No major psychiatric disorders, including somatization
- Willingness to stop inappropriate drug usage prior to implantation
- Ability to give informed consent for the procedure

Spinal cord stimulation is used only as a last resort; and other treatment modalities (pharmacological, surgical, psychological or physical therapies, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated.

Two - Step Process for Implantation of the spinal cord stimulator device:

Spinal Cord Stimulator Trial

The first step is to implant a device on a trial basis which is done in an outpatient visit. The patient's skin is numbed with a local anesthetic; leads are placed under the skin and attached to a small generator that the patient carries (much like a pager or cell phone); and using pre-set programs, electrical currents are emitted in a pattern to target the areas of pain. The trial phase can be beneficial for the following reasons:

- It can help the patient/physician analyze whether SCS effectively relieves pain
- It provides the patient/physician with an assessment period to determine which types of SCS technology works best
- It enables the patient/physician to evaluate different stimulation settings and programs.

The individual will keep a written log of the stimulation settings during different activities, along with the level of pain relief. If the trial is successful (reduction in pain of at least 50% or more) then a permanent spinal cord stimulator may be implanted.

There is no consensus on appropriate trial length, although on average, it lasts three to seven days. For patients who take anticoagulation or antiplatelet medications, the length of the trial may be shortened to minimize the risk of thrombotic complications off medications.

Permanent Spinal Cord Stimulator

If the SCS trial provides adequate pain relief (demonstrates a reduction in pain of at least 50% or more during the trial period), then a permanent system may be implanted. Documentation of the reduction of pain should be based on objective evidence of pain relief (e.g., decreased opioid usage, improved range of motion of the affected area, increased activity, increased pain relief according to the Visual Analog Scale (VAS) of the Numeric Pain Intensity Scale).

The trial electrodes are often removed, and implantation of new electrodes and the pulse generator are performed as a separate procedure. The permanent electrodes should be placed in the same spinal region(s) where the temporary trial produced the pain relief (example, trial in lumbar region results in permanent electrode placement in the lumbar region). The electrode placement for implantation may be performed by laminotomy or percutaneous approach. A small incision is made to allow insertion of epidural needles, anchoring of the leads after insertion, and tunneling of the lead extension cable. The leads are placed by fluoroscopy and tested for paresthesia. After stimulation is programmed, the level of sedation can be deepened as appropriate for generator placement. A second incision is made to create the pocket for the implantable pulse generator (IPG). The generator is usually implanted in the abdomen or buttock region. The extension cable must be tunneled under the skin between the lead connector and the IPG.

On rare occasions, surgical revisions may be needed if the neurostimulator electrodes migrate or move from the area needing stimulation. Also, if the individual is unable to tolerate the electrodes, the individual has an onset of neurological deficits, the modality itself becomes ineffective over time, or, if the leads and/or pulse generator become infected, the device may be removed.

Dorsal Root Ganglion stimulation

Another variation of spinal cord stimulation (SCS) is dorsal root ganglion stimulation (DRGS). A DRGS stimulator consists of electrical leads, which are threaded through the epidural space into the intervertebral foramen and directly overlie the dorsal root ganglion. Electrical fields are generated that can selectively stimulate different parts of the dorsal root ganglia. This is intended to allow focusing of stimulation onto specific nerve roots or parts of nerve roots. The leads are then connected to an implanted battery through extension wiring. The main difference between DRGS and traditional SCS lies in the type of fiber activation associated with the two types of stimulation. SCS involves stimulation of the dorsal columns resulting in broad electrical stimulation of multiple dermatomes. DRGS is more precise, directly activating the cell bodies of the very neurons that innervate the painful regions.

The purpose of dorsal root ganglion stimulation (DRGS) is to treat individuals who have treatment refractory neuropathic chronic pain similar to spinal cord stimulation (SCS) to provide a treatment option that is an alternative to or an improvement on existing therapies. Similar to spinal cord stimulation (SCS), DRGS is also performed in a two-step

process to include a trial basis and if the trial is successful (reduction in pain of at least 50% or more) then a permanent DRGS may be implanted.

Spinal Cord and Dorsal Root Ganglion Stimulation

Clinical Context and Therapy Purpose

The purpose of spinal cord stimulation (SCS) and dorsal root ganglion (DRG) stimulation in patients who have treatment refractory chronic pain, critical limb ischemia, chronic stable angina pectoris, heart failure, or cancer-related pain, is to provide a treatment option that is an alternative to or an improvement on existing therapies.

Populations

There are several populations of interest in this review:

- Patients with treatment-refractory chronic pain of the trunk or limbs
- Patients with critical limb ischemia
- Patients with treatment-refractory chronic stable angina pectoris
- Patients with heart failure
- Patients with cancer-related pain

Interventions

The therapies being considered include:

- Spinal cord stimulation (SCS): SCS uses low-level epidural electrical stimulation of the spinal cord dorsal columns. The mechanism of action is uncertain but may be related to either activation of an inhibitory system or blockage of facilitative circuits. SCS devices consist of several components: (1) the lead delivering electrical stimulation to the spinal cord; (2) an extension wire that conducts the electrical stimulation from the power source to the lead; and (3) a power source. The lead may incorporate four to eight electrodes, depending on the complexity of the pain pattern. A trial period in which the electrode is temporarily implanted in the epidural space is recommended, prior to the permanent implantation. Most SCS devices operate under a frequency of 100 to 1000 Hz.
- High-frequency spinal cord stimulation (HFSCS): HFSCS devices use a higher frequency (10000 Hz) compared with the standard SCS devices. HFSCS potentially lowers the incidence of paresthesia's compared with standard SCS.
- Dorsal root ganglion stimulation (DRGS): DRGS uses the same epidural approach technique as SCS but targets a different anatomical target, the DRGS.

Comparators

The standard of care, by population of interest consists of:

- Patients with treatment-refractory chronic pain of the trunk or limbs: medical therapy or surgical therapy
- Patients with critical limb ischemia: medical therapy or surgical therapy (revascularization surgery or amputation)

- Patients with treatment-refractory angina pectoris: medical therapy or coronary revascularization
- Patients with heart failure: medical therapy or coronary revascularization
- Patients with cancer-related pain: medical therapy

Outcomes

The general outcomes of interest include reduction in pain symptoms and improvements in quality of life (QOL).

Spinal Cord Stimulation for Refractory Chronic Pain of the Trunk or Limb

Standard Spinal Cord Stimulation

Systematic Reviews

In 2017, Visnjevac et. al. reported on a systematic review of the literature to evaluate the effects of spinal cord stimulation (SCS) on patients with complex regional pain syndrome (CRPS) for the following outcomes and provide summary levels of evidence regarding each outcome: perceived pain relief, pain score, resolution of CRPS signs, functional status, quality of life, psychological impact, sleep hygiene, analgesic medication utilization, and patient satisfaction with SCS therapy. Of 30 studies selected, seven systematic reviews were excluded, as were four studies reporting combination therapy that included SCS and other therapies (i.e., concurrent peripheral nerve stimulation, intrathecal therapy) without clear delineation to the effect of SCS alone on outcomes. A total of 19 manuscripts were evaluated. Perceived pain relief, pain score improvement, quality of life, and satisfaction with SCS were all rated 1B+, reflecting positive high-level (randomized controlled trial) evidence favoring SCS use for the treatment of CRPS. Evidence for functional status improvements and psychological effects of SCS was inconclusive, albeit emanating from a randomized controlled trial (evidence level 2B±), and outcomes evidence for both sleep hygiene and resolution of CRPS signs was either nonexistent or of too low quality from which to draw conclusions (evidence level 0). An analgesic sparing effect was observed in nonrandomized reports, reflecting an evidence level of 2C+. The authors concluded, spinal cord stimulation (SCS) remains a favorable and effective modality for treating CRPS with high-level evidence (1B+) supporting its role in improving CRPS patients' perceived pain relief, pain score, and quality of life. A paucity of evidence for functional improvements, resolution of CRPS signs, sleep hygiene, psychological impact, and analgesic sparing effects mandate further investigation before conclusions can be drawn for these specific outcomes.

In 2017, Kapural et. al. reported on a systematic review of the clinical data from prospective studies to assess the efficacy of spinal cord stimulation (SCS) in the treatment of failed back surgery syndrome (FBSS) in adults. A systematic literature review was performed using several bibliographic databases, prospective studies in adults using SCS for FBSS were included. Clinical evidence suggests that for patients with FBSS, repeated surgery will not likely offer relief. Additionally, evidence suggests long-term use of opioid pain medications is not effective in this population, likely presents

additional complications and requires strict management. The authors concluded that spinal cord stimulation (SCS) has been shown to be a safe and efficacious treatment for this patient population. Recent technological developments in SCS offer even greater pain relief to patient's refractory to other treatment options, allowing patients to regain functionality and improve their quality of life with significant reductions in pain.

In 2016, Grider et. al. reported on a systematic review to assess the role and effectiveness of spinal cord stimulation (SCS) in chronic spinal pain. RCTs of efficacy with a minimum of 12 months follow-up were considered for inclusion. For trials of adaptive stimulation, high frequency stimulation, and burst stimulation, shorter follow-up periods were considered. Results showed 6 RCTs with 3 efficacy trials and 3 stimulation trials. There were also 2 cost effectiveness studies available. Based on a best evidence synthesis with 3 high quality RCTs, the evidence of efficacy for SCS in lumbar failed back surgery syndrome (FBSS) is Level I to II. The evidence for high frequency stimulation based on one high quality RCT is Level II to III. Based on a lack of high-quality studies demonstrating the efficacy of adaptive stimulation or burst stimulation, evidence is limited for these 2 modalities. The limitations of this systematic review continue to require future studies illustrating effectiveness and superiority of high frequency stimulation and potentially burst stimulation. The authors concluded there is significant (Level I to II) evidence of the efficacy of spinal cord stimulation (SCS) in lumbar FBSS; whereas there is moderate (Level II to III) evidence for high frequency stimulation; there is limited evidence for adaptive stimulation and burst stimulation.

Randomized Controlled Trials

Six randomized controlled trials (RCTs) (total N=528 patients, range 36-218 patients) have evaluated spinal cord stimulation (SCS). Patient populations had failed back surgery syndrome (FBSS), diabetic neuropathy, and complex regional pain syndrome (CRPS). The comparators were primarily conventional medical management, although 1 RCT compared SCS with reoperation for FBSS, and another compared SCS with physical therapy. All RCTs reported results at 6 months. The most common primary outcome reported was a responder outcome of 50% reduction in pain; however, one study reported absolute change in visual analog scale (VAS) pain score. Consistent with clinical practice, RCTs included a trial period of SCS, usually a few days to a week. Patients not reporting improvement in pain during the trial period did not continue receiving SCS during the remainder of follow-up. In most RCTs, these patients were included in the intention-to-treat analyses either as failures to respond or using imputation techniques. All RCTs with the responder primary outcomes reported clinically and statistically significant differences in the primary outcomes at 6 months, favoring SCS (SCS range, 39%-63% vs comparator range, 5%-12%). Outcomes measuring the reduction in analgesic use were consistently numerically larger for SCS but not statistically significant in all studies. Four of the 5 studies did not report differences in functional, quality of life, or utility outcomes. Device-related complications ranged from 17% to 32%, with the most common being infection and discomfort or pain due to positioning or migration of electrodes or leads. However, 2 studies reported dural puncture headaches and one 26 ending in death. Two studies reported longer term results for both treatment groups. In

each, results continued to favor SCS at 2 years, but for one with 5 years of follow-up, results were not statistically significant at 5 years.

Section Summary

The evidence of the efficacy of standard spinal cord stimulation (SCS) for the treatment of chronic limb or trunk pain consists of a number with refractory pain due to failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS) or diabetic neuropathy. These trials were heterogenous regarding patient populations and participants were unblinded (no trials used sham surgeries or devices), but they consistently reported reductions in pain with clinically and statistically significant effect sizes and reductions in medication use for at least 6 months. Even with a sham-controlled surgery or device, blinded outcomes assessment may not be feasible for SCS, because active SCS is associated with paresthesias. Given the extensive treatment effects with consistent findings across studies, this evidence suggests that spinal cord stimulation (SCS) is a reasonable treatment option.

High Frequency Spinal Cord Stimulation

In 2015, an SCS device, using a higher frequency of electrical stimulation (10 kHz) than predicate devices (which use frequencies on the order of 100-1000 Hz), was approved by the U.S. Food and Drug Administration. Studies that offer direct comparisons between standard SCS and high-frequency SCS (HFSCS) were sought to evaluate the incremental benefit of HFSCS.

Systematic Reviews

In 2016, Bicket et. al. published a systematic review of controlled trials on high-frequency spinal cord stimulation (HFSCS). HFSCS has the potential to provide paresthesia-free pain relief for patients with chronic pain, in contrast to conventional spinal cord stimulation, which produces distracting and potentially unpleasant paresthesias. Reviewers searched for RCTs and controlled nonrandomized studies of adults with pain for at least 3 months who were treated with HFSCS (i.e., ≥ 1000 Hz) and prospectively assessed pain outcomes. Eight trials (236 participants randomized or 160 followed prospectively) met inclusion criteria. All trials of HFSCS focused on patients with chronic low back pain with one exception, which included patients with chronic migraine. All but one trial documented funding by industry. Performance bias due to unmasked participants, physicians, and outcome assessors limited the quality of all but one study. The authors concluded significant growth in the preclinical and clinical evidence base for HFSCS suggests that HFSCS may differ from conventional SCS in mechanism of action and efficacy of treatment, respectively. Addressing current knowledge gaps in clinical evidence will require standardization in trial reporting and leveraging the paresthesia-free characteristic of HFSCS to enable masking in high-quality randomized controlled trials.

Randomized Controlled Trials

In 2021, Petersen et. al., randomized 216 participants with painful diabetic neuropathy (baseline lower limb VAS ≥ 5 cm on a 10 cm scale) refractory to prior pharmacological

treatment to high-frequency spinal cord stimulation plus conventional medical management (n=113) versus conventional medical management alone (n=103). All participants were randomized to high-frequency spinal cord stimulation and underwent a trial stimulation period. Participants were eligible for permanent implantation of the stimulation device if at least 50% pain relief was achieved during the trial period. Participants remained in their randomized groups for 6 months, after which time they were eligible to crossover to the other group in the event of inadequate pain relief. The addition of high-frequency spinal cord stimulation to conventional medical management was associated with significantly improved pain scores at 6-month follow-up. Results from 12-month follow-up were consistent in finding a significant pain benefit for high-frequency spinal cord stimulation plus medical management versus medical management alone. Limitations of the study include a lack of blinding for participants and investigators.

De Andres et. al. (2017) compared one year follow-up in a prospective, randomized blind trial the efficacy of high-frequency spinal cord stimulation (HFSCS) versus conventional frequency spinal cord stimulation (CFSCS) on the patients with failed back surgery syndrome (FBSS). Seventy-eight patients with FBSS diagnosis based on internationally recognized criteria, and refractory to conservative therapy for at least 6 months, were recruited, and sixty subjects met the eligibility criteria and were randomized and scheduled for the trial phase. The patients were randomly assigned in either, one of the two groups: CFSCS or HFSCS. Within the study methods, special attention was paid to standardizing patient programming, so that these parameters would not impact the results. The trial period was considered successful if there was $\geq 50\%$ reduction in the NRS (numerical rating scale) from baseline. A total of 55 subjects successfully completed all assessments for one year follow-up. Change patterns in scores did not differ based on high versus conventional frequency, with significant global average reduction at 1 year similarly for both groups. Among all the items included in the Short Form-12 questionnaire (SF-12), only the variations in the social function score between the instants t1 and t2 are somewhat higher in the high frequency group. The authors concluded the evolutionary pattern of the different parameters studied in our patients with FBSS does not differ according to their treatment by spinal stimulation, with conventional or high frequency, in one year follow-up.

In 2016, Kapural et. al. compared long term results of spinal cord stimulation (SCS) delivered at 10 kHz (as in HF10 therapy) and traditional low-frequency SCS. A randomized, controlled, pivotal trial with 24-month follow-up was conducted across 11 comprehensive pain treatment centers. Subjects had Visual Analog Scale (VAS) scores of $\geq 5.0/10.0$ cm for both back and leg pain and were assigned randomly (1:1) to receive HF10 therapy or low-frequency SCS. The primary end point was a responder rate, defined as $\geq 50\%$ back pain reduction from baseline at 3 months with a secondary end point at 12 months (previously reported). In this article, 24-month secondary results are presented. Non-inferiority was first assessed, and if demonstrated the results were tested for superiority. In the study, 198 subjects were randomized (101 HF10 therapy, 97 traditional SCS). One hundred seventy-one subjects (90 HF10 therapy, 81 traditional

SCS) successfully completed a short-term trial and were implanted. Subjects averaged 54.9 ± 12.9 years old, 13.6 ± 11.3 years since diagnosis, 86.6% had back surgery, 88.3% were taking opioid analgesics. At 3 months, 84.5% of implanted HF10 therapy subjects were responders for back pain and 83.1% for leg pain, and 43.8% of traditional SCS subjects were responders for back pain and 55.5% for leg pain ($P < .001$ for both back and leg pain comparisons, non-inferiority and superiority). At 24 months, more subjects were responders to HF10 therapy than traditional SCS (back pain: 76.5% vs 49.3%; 27.2% difference, 95% CI, 10.1%-41.8%; $P < .001$ for non-inferiority and superiority; leg pain: 72.9% vs 49.3%; 23.6% difference, 95% CI, 5.9%-38.6%; $P < .001$ for non-inferiority and $P = .003$ for superiority). Also at 24 months, back pain decreased to a greater degree with HF10 therapy ($66.9\% \pm 31.8\%$) than traditional SCS ($41.1\% \pm 36.8\%$, $P < .001$ for non-inferiority and superiority). Leg pain also decreased to a greater degree with HF10 therapy ($65.1\% \pm 36.0\%$) than traditional SCS ($46.0\% \pm 40.4\%$, $P < .001$ for non-inferiority and $P = .002$ for superiority). The authors concluded this study demonstrates long-term superiority of HF10 therapy compared with traditional SCS in treating both back and leg pain. The advantages of HF10 therapy are anticipated to impact the management of chronic pain patients substantially.

In 2015, Kapural et. al., the objective of this randomized, parallel arm, noninferiority study was to compare long-term safety and efficacy of spinal cord stimulation (SCS) therapies in patients with back and leg pain. Current treatments for chronic pain have limited effectiveness and commonly known side effects. Given the prevalence and burden of intractable pain, additional therapeutic approaches are desired. Spinal cord stimulation (SCS) delivered at 10 kHz (as in HF10 therapy) may provide pain relief without the paresthesia's typical of traditional low-frequency SCS. A total of 198 subjects with both back and leg pain were randomized in a 1:1 ratio to a treatment group across 10 comprehensive pain treatment centers. Of these, 171 passed a temporary trial and were implanted with an SCS system. Responders (the primary outcome) were defined as having 50% or greater back pain reduction with no stimulation-related neurological deficit. At 3 months, 84.5% of implanted HF10 therapy subjects were responders for back pain and 83.1% for leg pain, and 43.8% of traditional SCS subjects were responders for back pain and 55.5% for leg pain ($P < 0.001$ for both back and leg pain comparisons). The relative ratio for responders was 1.9 (95% CI, 1.4 to 2.5) for back pain and 1.5 (95% CI, 1.2 to 1.9) for leg pain. The superiority of HF10 therapy over traditional SCS for leg and back pain was sustained through 12 months ($P < 0.001$). HF10 therapy subjects did not experience paresthesia's.

Perruchoud et. al. (2013) compared the efficacy of high-frequency spinal cord stimulation (HFSCS) and sham stimulation on the patient's global impression of change (PGIC), pain intensity, and quality of life. Forty patients who have achieved stable pain relief with conventional spinal cord stimulation (SCS) were recruited. After randomization, HFSCS and sham were initiated in a double-blind randomized two-period-crossover design. Complete data was available from 33 patients. The primary outcome was a minimal improvement in the PGIC. The proportion of patients responding under HFSCS was 42.4% (14/33 patients) vs. 30.3% (10/33 patients) in the sham condition. The mean

benefit of high frequency (HF) vs. sham was not statistically significant with a proportion of 11.2% in favor of HFSCS ($p = 0.30$). There was a highly statistically significant "period effect," irrespective of treatment received, with 51.5% of patients ($N = 17$) improving at visit 3 vs. 21.2% ($N = 7$) at visit 5 ($p = 0.006$). The mean pain visual analog scale (VAS) on sham was 4.26 vs. 4.35 on HFSCS ($p = 0.82$) and the mean EuroQol five-dimensional (EQ-5D) index with HFSCS was 0.480 vs. 0.463 with sham ($p = 0.78$). The authors concluded; this is the first randomized double-blind study on SCS. HFSCS was equivalent to sham for the primary outcome (improvement of PGIC) as well as for both the secondary outcomes (VAS and EQ-5D index). There was a highly statistically significant "period effect" ($p = 0.006$) with improved PGIC scores in the first study period regardless of the treatment. The same trend was seen for VAS and EQ-5D. It appears that the effect of HFSCS and sham is equal and only the order in the sequence, not the nature of the treatment, seems to dictate the effect.

Case Series

Al-Kaisy et. al. (2018) reported on a prospective, open label study designed to evaluate the long-term effectiveness of 10-kHz high-frequency spinal cord stimulation (HFSCS) in the treatment of chronic axial low back pain with no history of spinal surgery. Patients with chronic low back pain without previous spinal surgery underwent assessment by a multidisciplinary pain and surgical team to confirm eligibility. After a successful temporary trial of 10-kHz HFSCS therapy, defined by $\geq 50\%$ back pain reduction, enrolled subjects underwent permanent system implantation and were followed up for 36 months. Outcome measures consisted of a 100-mm visual analog scale (VAS) for pain intensity, the Oswestry Disability Index (ODI), and a standard measure of health-related quality of life. Twenty-one patients satisfied the inclusion/exclusion criteria. Following a temporary trial, 20 of 21 (95%) subjects were implanted with a pulse generator, and 17 of 20 reached the 36-month time point. From baseline to 36 months, the average VAS pain intensity decreased from 79 ± 12 mm to 10 ± 12 mm, the average ODI score decreased from 53 ± 13 to 19.8 ± 13 , and use of opioids decreased from 18 subjects to two subjects. One subject was deceased, unrelated to the study, one subject was explanted due to loss of effectiveness, and one subject was lost to follow-up. The authors concluded these results suggest that 10-kHz high-frequency SCS may provide significant, long-term back pain relief, improvement in disability and quality of life, and reduction in opioids for nonsurgical refractory back pain.

Section Summary

The evidence for high-frequency spinal cord stimulation (HFSCS) compared with standard spinal cord stimulation (SCS) consists of randomized controlled trials, systematic reviews and case series. In the randomized controlled trial that randomized 198 patients not previously treated with SCS and reported a clinically and statistically significant benefit associated with HFSCS. The crossover RCT enrolling patients with pain despite previous treatment with SCS reported no difference between HFSCS and sham stimulation. However, interpretation of this trial is limited due to the significant period effect. Based on systematic reviews, they suggest that HFSCS may differ from conventional SCS in mechanism of action and efficacy of treatment, respectively. The

evidence suggests that high-frequency spinal cord stimulation (HFSCS) may be a reasonable treatment option.

Spinal Cord Stimulation with Burst Stimulation

In 2016, a supplement to an SCS device (in the form of a clinician programmer application), which allows for the provision of burst stimulation, was approved by the Food and Drug Administration. Studies that offer direct comparisons between standard SCS and burst SCS were sought to permit evaluation of the incremental benefit of burst SCS.

Systematic Reviews

Hou et al (2016) published a systematic review of burst SCS for the treatment of chronic back and limb pain. Reviewers identified five studies of burst SCS in patients with intractable chronic pain of more than three months in duration who had failed conservative treatment. Three studies, with sample sizes of 12, 15, and 20, respectively, used randomized crossover designs to compare burst stimulation with tonic stimulation; 2 studies also included a placebo stimulation intervention. Also, there were 2 case series with sample sizes of 22 and 48 patients, respectively. Data were collected after one to two weeks of treatment. Study findings were not pooled. Using American Academy of Neurology criteria, reviewers originally rated four studies as class III and 1 study as class IV. However, given the small sample sizes and short durations of follow-up of the four studies, all were downgraded to class IV. Overall, the level of confidence in the evidence on burst SCS for treating chronic pain without paresthesia was rated as "very low."

Randomized Controlled Trials

Six crossover randomized controlled trials (RCTs) with a total of 199 patients (range, 12-100 patients) were identified, 5 of which were conducted in Europe and the other in the United States. The trials by De Ridder et. al. (2010, 2013) enrolled patients with neuropathic pain, the trial by Schu et al (2014) enrolled patients with failed back surgery syndrome, Kriek et. al. (2017) enrolled patients with CRPS, Deer et al (2018) enrolled patients with chronic intractable pain of the trunk and/or limbs, and Eldabe et. al. (2020) enrolled patients with chronic back and leg pain. All trials compared burst stimulation with spinal cord stimulation. Schu et. al. (2014), De Ridder et. al. (2013), Kriek et. al. (2017), and Eldabe et. al. (2020) also compared burst with a sham stimulation group. Schu et. al. (2014) and Eldabe et. al. (2020) included patients receiving standard spinal cord stimulation while De Ridder et. al. (2010, 2013) and Deer et al (2018) included patients not previously treated with spinal cord stimulation. It was not clear in Kriek et. al. (2017) whether patients had previously received spinal cord stimulation. Results were reported for 1 week of stimulation in Schu et al (2014) and De Ridder et. al. (2013), after 2, 1-hour sessions of spinal cord stimulation or burst in De Ridder et. al. (2010), after 2 weeks of stimulation in Kriek et. al. (2017) and Eldabe et. al. (2020), and after 12 weeks of stimulation in Deer et. al. (2018). All trials reported reductions in absolute pain scores (numeric rating scale or visual analog scale). Schu et. al. (2014) and De Ridder et. al. (2013) did not account for their crossover designs in data analyses, so analyses and p

values are incorrect and not reported. De Ridder et. al. (2010) did not provide between-group comparisons. Kriek et. al. (2017) reported only per-protocol analyses. Four trials reported numerically larger reductions in pain scores with burst than with spinal cord stimulation; Kriek et. al. (2017) did not report less pain for spinal cord stimulation at any frequency compared with burst. In Kriek et. al. (2017), 48% of patients preferred the 40-Hz spinal cord stimulation compared with 21%, 14%, 14%, and 3% that preferred 500-Hz spinal cord stimulation, 1200-Hz spinal cord stimulation, and burst and sham, respectively. In Eldabe et al (2020), the mean reduction in pain with 500-Hz spinal cord stimulation was significantly greater than that seen with sham (25%; 95% confidence interval [CI], 8%-38%; $p=.008$) or burst (28%; 95% CI, 13%-41%; $p=.002$), with no significant differences in pain visual analog score for burst versus sham ($p=.59$). The interpretation of 5 of the trials was limited by small sample sizes, short follow-up, and incorrect, inadequate, or missing statistical analyses.

The largest trial of burst stimulation is the Success Using Neuromodulation with BURST (SUNBURST) trial reported by Deer et al (2018). Success Using Neuromodulation with BURST (SUNBURST) was a 12-week, multicenter, randomized, unblinded, crossover, noninferiority trial evaluating traditional SCS or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs enrolled between January 2014 and May 2015. Patients were SCS-naive and completed a trial stimulation period. Forty-five patients were randomized to SCS then burst, and the remaining 55 were randomized to burst then SCS. At the end of the second crossover period, patients were allowed to choose the stimulation mode they preferred and were followed for one year. Patients' mean age was 59 years; 60% of patients were women; and 42% of patients had FBSS while 37% had radiculopathies. The primary outcome was the difference in mean VAS score, with a noninferiority margin of 7.5 mm. Analyses were intention-to-treat with missing values imputed using the hot deck method. Also, outcomes were imputed for patients who underwent invasive procedures for pain or had medication increases. The estimated difference in the overall VAS score between burst and SCS was -5.1 mm (95% upper confidence interval [CI], -1.14 mm), demonstrating noninferiority ($p<0.001$) and superiority ($p<0.017$). The proportion of patients with a decrease in VAS score of 30% or more was 60% (60/100) during burst stimulation and 51% (51/100) during SCS. The proportion of patients whose global impression was minimally improved, moderately improved, or very much improved was approximately 74% in both groups. There were no significant differences in Beck Depression Inventory scores ($p=0.230$). Patients were asked to rate their satisfaction levels for both periods: 78% were satisfied with both SCS and burst, 4% were dissatisfied with both SCS and burst, 7% were satisfied with SCS but not burst, and 10% were satisfied with burst but not SCS. However, more patients (70.8%) reported preferring burst stimulation over SCS stimulation after the 24-week crossover period. After 1 year of follow-up, 60 (68%) of the 88 patients completing follow-up reported preferring burst stimulation. The authors reported that the programming parameters were not standardized at the beginning of the study but a more standardized approach with lower amplitudes was implemented as the trial was ongoing. Trial limitations included the crossover design, which limits comparison of pain over longer periods of time, lack of blinding, and variable burst programming parameters.

Section Summary

SCS with burst stimulation has been evaluated in five crossover randomized controlled trials (RCTs). Four of the RCTs had fewer than 35 patients. Inferences drawn from these trials are limited by small sample sizes, short follow-up, and flawed statistical analyses. The largest RCT (Success Using Neuromodulation with BURST) (SUNBURST) was a 12-week, multicenter, randomized, unblinded, crossover, non-inferiority trial assessing traditional SCS or burst stimulation in 100 patients with chronic pain of the trunk and/or limbs. The burst was non-inferior to SCS for overall VAS score (at 12 weeks). The proportion of patients whose global impression was improved (minimally, moderately, or very much improved) was approximately 74% in both groups. Seventy-eight percent of patients reported being satisfied with both SCS and burst at the end of the 24-week crossover portion of the trial, while 7% were satisfied with SCS but not burst and 10% were satisfied with burst but not SCS. However, more patients (70.8%) reported preferring burst stimulation over SCS stimulation after the 24-week crossover.

Dorsal Root Ganglion Stimulation for Refractory Chronic Trunk or Limb Pain

Systematic Reviews

In 2021, Moman et. al. completed a systematic review and pooled analysis of incidence to determine the overall incidence of dorsal root ganglion stimulation (DRGS) infections, incidence at each stage (trial versus implant versus revision), infection characteristics and outcomes. Dorsal root ganglion stimulation (DRGS) is a newer form of neuromodulation that targets the dorsal root ganglion. DRGS has superior efficacy in complex regional pain syndrome compared to spinal cord stimulation (SCS) and may have efficacy in other forms of chronic pain. While decades of safety data are available for SCS, there is less available safety information for DRGS. Ten studies met inclusion criteria. Eight studies reported patients with trial data (n = 291), ten studies reported patients with implant data (n = 250), and seven studies reported data with revisions (n = 26). The pooled incidence of trial infections was 1.03% (95% CI 0.35-2.99%), implant infections was 4.80% (95% CI 2.77-8.20%), revision infections was 3.85% (95% CI 0.20-21.59%), and overall infections was 2.82% (95% CI 1.62-4.54%). There was a statistically significant difference in infection rates between the trial, implant, and revision stages, $X^2(2, N = 567) = 8.9839, p = 0.01$. The authors concluded DRGS trial appears to be low risk for infection, but that risk is significantly increased with DRGS implant. Our findings highlight the need for further study of infectious complications, their risks, and optimal prophylaxis.

Vuka et. al. (2019), conducted a systematic review about patient selection, efficacy, and safety of neuromodulation with electrical field stimulation (EFS) of dorsal root ganglion (DRG) in various painful conditions. Among the 29 included studies, only one was RCT, majority being case series and case reports. The evidence is based on studies with small number of participants (median: 6, range 1-152) with various painful conditions. Neuromodulation with EFS of DRG was mostly performed in participants who have failed other treatment modalities. Most of the authors of the included studies reported positive, but inconclusive, evidence regarding efficacy of neuromodulation with EFS of

DRG. Meta-analysis was not possible since only one RCT was included. The authors concluded, available evidence suggest that neuromodulation with EFS of DRG may help highly selected participants with various pain syndromes, who have failed to achieve adequate pain relief with other pharmacological and nonpharmacological interventions. However, these findings should be confirmed in high-quality RCTs with sufficient numbers of participants.

In 2017, Chang Chien et. al. published a systematic review on intraspinal stimulation of nondorsal column targets, including neurostimulation of the DRG for chronic pain. Reviewers included reports published through March 2015. They identified six studies of DRG stimulation: one conference presentation of the preliminary RCT data from A Safety and Effectiveness Trial of Spinal Cord Stimulation of the Dorsal Root Ganglion for Chronic Lower Limb Pain (ACCURATE, discussed below), four publications describing three prospective observational studies, and one retrospective chart review. In the 3 prospective observational studies (n=32, 10, and 8), follow-up ranged from 7 days to 12 months. The retrospective study reported on 25 patients with a follow-up to 32 weeks. Meta-analyses could not be conducted with one RCT.

Randomized Controlled Trials

Mekhail et. al. 2019, conducted a sub-analysis on the patients receiving dorsal root ganglion (DRG) stimulation in the ACCURATE study, this study explored treatment outcomes for DRG subjects who were paresthesia-free versus those who experienced the sensation of paresthesia, as well as the factors that predicted paresthesia-free analgesia. A retrospective analysis of therapy outcomes was conducted for 61 subjects in the ACCURATE study who received a permanent DRG stimulator. Outcomes of subjects who were paresthesia-free were compared to those who experienced paresthesia-present therapy at 1, 3, 6, 9, and 12-month follow-ups. Predictor variables for the presence or absence of paresthesia's with DRG stimulation were also explored. The percentage of subjects with paresthesia-free pain relief increased from 16.4% at 1-month to 38.3% at 12-months. Paresthesia-free subjects generally had similar or better outcomes for pain severity, pain interference, quality of life, and mood state as subjects with paresthesia-present stimulation. Factors that increased the odds of a subject feeling paresthesia were higher stimulation amplitudes and frequencies, number of implanted leads, and younger age. The authors concluded, some DRG subjects achieved effective paresthesia-free analgesia in the ACCURATE trial. This supports the observation that paresthesia is not synonymous with pain relief or required for optimal analgesia with DRG stimulation.

The ACCURATE study (NCT01923285) compared dorsal root ganglion (DRG) stimulation with standard spinal cord stimulation (SCS). As reported by Deer et al (2017), a pivotal, prospective, multicenter, randomized comparative effectiveness trial, was conducted in 152 subjects diagnosed with complex regional pain syndrome or causalgia in the lower extremities. Subjects received neurostimulation of the DRG or dorsal column (spinal cord stimulation, SCS). The primary end point was a composite of safety and efficacy at 3 months, and subjects were assessed through 12 months for long-

term outcomes and adverse events. The predefined primary composite end point of treatment success was met for subjects with a permanent implant who reported 50% or greater decrease in visual analog scale score from preimplant baseline and who did not report any stimulation-related neurological deficits. No subjects reported stimulation-related neurological deficits. The percentage of subjects receiving $\geq 50\%$ pain relief and treatment success was greater in the DRG arm (81.2%) than in the SCS arm (55.7%, $P < 0.001$) at 3 months. Device-related and serious adverse events were not different between the 2 groups. Dorsal root ganglion stimulation also demonstrated greater improvements in quality of life and psychological disposition. Finally, subjects using DRG stimulation reported less postural variation in paresthesia ($P < 0.001$) and reduced extraneous stimulation in nonpainful areas ($P = 0.014$), indicating DRG stimulation provided more targeted therapy to painful parts of the lower extremities. As the largest prospective, randomized comparative effectiveness trial to date, the results show that DRG stimulation provided a higher rate of treatment success with less postural variation in paresthesia intensity compared to SCS.

Case Series

The remaining evidence for the use of dorsal root ganglion (DRG) stimulation for chronic pain consists of case series.

The case series evaluated the Axium dorsal root ganglion (DRG) stimulator or an unnamed DRG stimulator in patients with FBSS, diabetic and non-diabetic peripheral nerve injury, postsurgical neuropathic pain, groin pain, and CRPS. Liem et. al. (2015) and Schu et. al. (2015), Liem et. al. (2015) had a larger sample size ($N=51$ vs $N=29$) and longer follow-up. Fifty-one patients with chronic pain of the trunk, lower back, or lower limbs who had failed conventional treatment underwent trial stimulation, and 32 underwent permanent implantation. Sample sizes ranged from 10 to 65 patients. One study had a six-month follow-up, most studies had one-year follow-up, and the largest study followed half of the patients for three years. For the studies reporting at least 1-year follow-up, the proportion of patients achieving a 50% or greater reduction in overall pain ranged from 49% to 83%. The largest case series, by Morgalla et. al. (2018), reported that after 3 years of follow-up, the patients continued to experience decreased Beck Depression Inventory scores, decreased Pain Disability Index scores, and 72% achieved a 50% or greater reduction in overall pain.

Deer et al (2019) compared the safety and complaint records from the manufacturers of dorsal root ganglion (DRG) stimulation ($n=500+$) and SCS ($n=2000+$) devices, from April 2016 through March 2018. The overall safety event rate for the study timeframe was 3.2% for DRG systems and 3.1% for SCS systems. Persistent pain was reported at a rate of 0.2% by patients with DRG implants and 0.6% by patients with SCS implants. Infection rates were 1.1% in both groups of patients. Cerebrospinal leaks were reported in 0.5% of patients with DRG implants and in 0.3% of patients with SCS implants.

Dorsal Root Ganglion Wireless Injectable Device

No controlled studies were identified. A case series, which included 11 patients, was published by Weiner et al (2016). This study included patients with FBSS who had chronic intractable neuropathic pain of the trunk and/or lower limbs. Five patients participated in phase 1 of the study (device not anchored), and six additional patients participated in phase 2 (device anchored). During phase 1, the device migrated more than was recommended and thus it was anchored in the remaining patients. Baseline VAS scores were five or higher in all patients. Seven (63%) of the 11 patients reported good to excellent overall pain relief (VAS score reduction, $\geq 50\%$), 2 patients reported fair overall intensity pain relief (25%-50% reduction), and 2 patients reported poor or no overall pain relief (0%-25%). No adverse events were reported.

Section Summary

One unblinded randomized controlled trial (RCT) and many case series have evaluated dorsal root ganglion (DRG) stimulators in patients with chronic trunk and/or limb pain. The RCT (n=152) found that patients receiving DRG stimulation had significantly higher rates of treatment success (physical functioning score and quality of life (QOL) measures) at 3 and 12 months compared with those receiving standard SCS devices. In addition, DRG stimulation was found to be non-inferior to SCS in percentage achieving $\geq 50\%$ pain reduction, emotional functioning score, and SF-36 scores. Both groups experienced paresthesia's but patients in the DRG group reported less postural variation in paresthesia and reduced extraneous stimulation in non-painful areas. Patients in the DRG group also reported more improvement in interference with physical functioning and mood states. Rates of serious adverse events were similar. Many case series have also been published; all reporting results consistent with the RCT. The percentages of patients achieving 50% or greater reduction in overall pain ranged from 49% to 83% among the case series. The largest series, which had the longest follow-up of 3 years, reported that 83% of patients at 12 months and 72% of patients at 3 years experienced 50% or greater reduction in overall pain

Spinal Cord Stimulation for Critical Limb Ischemia

Critical limb ischemia is described as pain at rest or the presence of ischemic limb lesions. If the patients are not suitable candidates for limb revascularization (typically due to insufficient distal runoff), amputation may be required in a substantial number of patients. SCS has been investigated in this subset of patients as a technique to relieve pain and decrease incidence of amputation.

An updated Cochrane by Ubbink and Vermeulen (2013) assessed the use of spinal cord stimulation (SCS) in peripheral vascular diseases. Reviewers included randomized controlled trials (RCTs) and non-RCTs evaluating the efficacy of SCS in adults with non-reconstructable chronic critical leg ischemia. Six trials were identified; all were conducted in Europe and five were single-country studies. SCS was compared with other nonsurgical interventions. One study was not randomized, and none was blinded. In a pooled analysis of data from all 6 studies, there was a significantly higher rate of limb survival in the SCS group than in the control group at 12 months (pooled risk difference,

-0.11; 95% CI, -0.20 to -0.02). The 11% difference in the rate of limb salvage means that 9 patients would need to be treated to prevent 1 additional amputation (95% CI, 5 to 50 patients). However, when the nonrandomized study was excluded, the difference in the rate of amputation no longer differed significantly between groups (risk difference, -0.09; 95% CI, -0.19 to 0.01). The SCS patients required significantly fewer analgesics, and more patients reached Fontaine stage II (intermittent claudication) than in the control group. There was no difference in ulcer healing (but only 2 studies were included in this analysis). In the 6 trials, 31 (15%) of 210 patients had a change in stimulation requiring intervention, 8 (4%) experienced the end of battery life, and 6 (3%) infections required device removal.

A systematic review of non-revascularization-based treatments by Abu Dabrh et. al. (2015), including SCS, for patients with critical limb ischemia also included 5 RCTs. In the pooled analysis, reviewers found that SCS was associated with reduced risk of amputation (odds ratio, 0.53; 95% CI, 0.36 to 0.79). However, they concluded that the evidence was of “relatively low quality mainly due to imprecision (i.e., small sample size and wide CIs) and the risk of bias.”

Section Summary

Based on review of the peer reviewed medical literature there were five relatively small RCTs comparing spinal cord stimulation (SCS) versus usual care for patients with critical limb ischemia. In some pooled analyses, SCS did not result in a significantly lower rate of amputation, although 1 systematic review and meta-analysis reported a significant difference. This evidence is insufficient to determine whether spinal cord stimulation (SCS) would improve net health outcomes for patients with critical limb ischemia.

Spinal Cord Stimulation for Other Medical Conditions

Refractory Angina Pectoris

Despite advances in medical and surgical therapies for angina patients, there remains a small number of patients with refractory angina. Spinal cord stimulation (SCS) at the T1 and T2 level has been studied in the management of refractory angina.

The mechanism of action is poorly understood. Spinal cord stimulation (SCS) may have beneficial effects on angina by suppressing the capacity of intrinsic cardiac neurons to generate activity during myocardial ischemia; alternatively, it may provide benefit by reducing sympathetic activity or by redistributing myocardial blood flow from nonischemic to ischemic areas.

Systematic Reviews

An UpToDate review evaluated newer medical and mechanical therapies for treating patients with refractory angina to include spinal cord stimulation. Overall, spinal cord stimulation is an unproven procedure given the current state of knowledge.

In 2017, Pan et. al. published a systematic review and meta-analysis to evaluate the efficacy and safety of conventional spinal cord stimulation (SCS) in the treatment of refractory angina pectoris (RAP). A total of 12 randomized controlled trials involving 476 RAP patients were identified. A trend of reduction in the angina frequency (MD=-9.03, 95% CI, -15.70 to -2.36) and nitroglycerin consumption (MD=-0.64, 95% CI, -0.84 to -0.45) could be observed in the SCS group. Compared with the control group, SCS showed benefit on increasing exercise time (MD=0.49, 95% CI, 0.13-0.85) and treatment satisfaction (MD=6.87, 95% CI, 2.07-11.66) with decreased VAS scores of pain (MD=-0.50, 95% CI, -0.81 to -0.20) and disease perception (MD=-8.34, 95% CI, -14.45 to -2.23). However, the result did not reach the significance level in terms of physical limitation (95% CI, -8.75 to 3.38; P=0.39) or angina stability (95% CI, -7.55 to 3.67; P=0.50). The authors concluded the meta-analysis suggested that SCS was a potential alternative in the treatment of RAP patients. Further investigation for finding the appropriate intensity of stimulation is required before this treatment should be widely recommended and applied.

In 2015, Tsigaridas et. al. published a systematic aimed to review randomized controlled trials (RCTs) that investigated the efficacy and safety of spinal cord stimulation (SCS) in patients with refractory angina. Nine RCTs were included in the systematic review. The included RCTs were categorized into two groups: RCTs comparing SCS either with optimal medical treatment or inactive mode or low stimulation SCS; and those comparing SCS with alternative therapeutic interventions. Follow-up was short-term (1-6 months) in most studies, showing no major complications. Two studies reported a neutral effect regarding mortality. Regarding efficacy, most RCTs were in favor of SCS mainly in the short term. The most recent, multicenter RCT reported no significant difference compared to the control group. The authors concluded RCTs investigating the efficacy of SCS were small and they demonstrated a small effect in angina improvement. Due to great differences in their design the interpretation of the results is complex. Before this method is recommended as a routine therapy for refractory angina, a larger, well-designed, multicenter RCT is needed.

Randomized Controlled Trials

A small, controlled trial from Italy by Lanza et al (2011) randomized 25 patients to 1 of 3 treatment groups: SCS with standard stimulation (n=10), SCS with low-level stimulation (75%-80% of the sensory threshold) (n=7), or very low intensity SCS (n=8). Thus, patients in groups 2 and 3 were unable to feel sensation during stimulation. After a protocol adjustment at 1 month, patients in the very low intensity group were re-randomized to one of the other groups of which there were 13 patients in the standard stimulation group and 12 patients in the low-level stimulation group. At the 3-month follow-up (2 months after re-randomization), there were statistically significant between-group differences in 1 of 12 outcome variables. There was a median of 22 angina episodes in the standard stimulation group and 10 in the low-level stimulation group (p=0.002). Nonsignificant variables included the use of nitroglycerin, quality of life, VAS, Canadian Cardiovascular Society angina class, exercise-induced angina, and scores on 5 subscales of the Seattle Angina Questionnaire.

In 2012, Zipes et. al. published an industry-sponsored, single-blind, multicenter trial with sites in the United States and Canada. The aim of this study was to evaluate the safety and efficacy of spinal cord stimulation (SCS) for refractory angina. This trial evaluated SCS in two patient groups: high stimulation (HS) (treatment) and low stimulation (LS) (control). The HS group controlled SCS with a programmer for a minimum of two hours four times daily. The LS group received SCS therapy above the paresthesia threshold for one min once daily. The primary efficacy endpoint was number of angina attacks recorded by patients at six months. The primary safety endpoint was the major adverse cardiac event (MACE) rate at six months. Due to slow enrollment, a futility analysis was performed, resulting in early termination of the study. Sixty-eight patients were randomized after implantation. Mean change in angina attacks per day from baseline to six months was -1.19 ± 2.13 (HS) and -1.29 ± 1.66 (LS). The difference from baseline was significant within each group (both $p < 0.001$) but not between groups ($p = 0.45$). Total exercise time and time to angina onset increased significantly from baseline to six months within each group (both $p = 0.02$ and 0.002) but not between groups ($p = 0.52$ and 0.51). MACE was similar between groups. The authors concluded although this study was terminated early, the results obtained at six months suggest that SCS (HS) is not more effective than the control (LS) in patients with refractory angina.

Section Summary

Spinal cord stimulation (SCS) has been used in the treatment of patients with refractory angina pectoris who fail to respond to standard pharmacotherapies and are not candidates for surgical interventions. Numerous small randomized controlled trials (RCTs) have evaluated SCS as a treatment for refractory angina. While some studies have reported benefit, most have not. In 2 more recent RCTs, there were no significant benefits for the primary outcomes. Overall, this evidence is mixed and insufficient to allow conclusions on whether net health outcomes are improved.

Heart Failure

In 2016, Zipes et. al. reported the results of the DEFEAT-HF trial, a prospective, multicenter, single-blind randomized controlled trial (RCT) trial comparing spinal cord stimulation (SCS) with active stimulation to sham-control in patients with New York Heart Association functional class III heart failure with a left ventricular ejection fraction of 35% or less. Sixty-six patients were implanted with a SCS and randomized in a 3:2 manner to SCS on ($n=42$) or SCS off (sham; $n=24$). For the study's primary end point (change in left ventricular end systolic volume index from baseline to 6 months), there was no significant difference between groups ($p=0.30$). Other end points related to heart failure hospitalization and heart failure related quality of life scores and symptoms did not differ significantly between groups. After completion of the 6-month randomization period, all subjects received active SCS. From baseline to 12-month follow-up, there were no significant treatment effects in the overall patient population from echocardiographic parameters ($p=0.36$). The nonsignificant difference between groups might have been the result of under-powering. However, the absence of any treatment

effects or between group differences is further suggestive of lack of efficacy of SCS for heart failure.

Findings of a small pilot crossover randomized controlled trial (RCT) evaluating spinal cord stimulation (SCS) for heart failure were published in 2014 by Torre-Amione et al. Eligibility included symptomatic heart failure despite optimal medical therapy, left ventricular ejection fraction less than 30%, hospitalization or need for intravenous inotropic support in the past year, and ability to walk less than 450 meters on a 6-minute walk test. All patients had an implanted heart device. Nine patients underwent SCS implantation and received 3 months of active treatment and 3 months of inactive treatment (off position), in random order. There was a 1-month washout period between treatments. The primary outcome was a composite of death, hospitalization for worsening heart failure, and symptomatic brady-arrhythmia or tachyarrhythmia requiring high-voltage therapy. Four patients experienced at least 1 of the events in the composite end point. The event occurred in 2 patients while the device was turned on and 2 while it was turned off. One patient died about 2 months after implantation while the device was turned off. The SCS devices did not interfere with the functioning of implantable cardioverter defibrillators.

Section Summary

Two randomized controlled trials (RCTs) have evaluated spinal cord stimulation (SCS) as a treatment for heart failure. One was a small pilot crossover trial (N=9) that reported at least 1 adverse event in 2 patients with the device turned on and in 2 patients with the device turned off. The other RCT (N=66) was sham-controlled; it did not find significant differences between groups but might have been underpowered.

Cancer Related Pain

A substantial number of patients with cancer pain do not obtain satisfactory relief with conventional first line approaches, including treatment of underlying causes, if possible, opioid based pharmacotherapy and noninvasive second line therapies. For some patient's interventional pain management strategies may offer safe and effective pain relief. Interventional pain management may include injection-based treatments, catheter-based infusion therapies, implanted devices such as spinal cord stimulation and some surgical approaches.

An UpToDate review (last updated May 2022) regarding interventional therapies in cancer pain management, that included spinal cord stimulation (SCS). Spinal cord stimulation (SCS) is rarely used for patients with advanced cancer. There are no randomized trials addressing the benefit of SCS for cancer-related pain. The cost of SCS and the need for active patient involvement in its use make it unsuitable for debilitated cancer patients near the end of life.

In a 2013, a Cochrane review was published on spinal cord stimulation (SCS) for treatment of cancer related pain in adults. The author did not identify any randomized controlled trials (RCTs) evaluating the efficacy of SCS in patients with cancer related

pain. Four case series using a before-after design with a total of 92 patients were identified. This review was updated in 2015 (Peng et. al.), no new studies meeting inclusion criteria were identified. The authors concluded “Current evidence is insufficient to establish the role of SCS in treatment refractory cancer related pain.

Section Summary

A Cochrane review did not identify any randomized controlled trials (RCTs) evaluating spinal cord stimulation for the treatment of cancer-related pain.

Postherpetic Neuralgia

Postherpetic neuralgia is a complication of shingles, which is caused by the chickenpox (herpes zoster) virus. Postherpetic neuralgia affects nerve fibers and skin, causing burning pain that lasts long after the rash and blisters of shingles disappear. Current treatment for postherpetic neuralgia includes antidepressants such as amitriptyline or nortriptyline, which are effective in treating nerve pain; antiseizure medications such as carbamazepine, which is effective for trigeminal neuralgia; short term narcotic pain medications; and topical creams with capsaicin. Spinal cord stimulation (SCS) has been proposed as a treatment option in the treatment of postherpetic neuralgia for pharmacological non-responders.

An UpToDate review last updated October 2021 on postherpetic neuralgia which included a review regarding neuromodulation that included spinal cord stimulation (SCS) which is considered investigational.

In 2018, Kurklinsky, et. a. reported on case reports and review of the literature on the use of spinal cord stimulation (SCS) and peripheral nerve stimulation (PNS) for the treatment of postherpetic neuralgia (PHN). Pubmed, Ovid, and EBMR databases were searched for all reports that had the following key words: postherpetic neuralgia, spinal cord stimulation, and peripheral nerve stimulation. A retrospective chart review was performed for all the patients that underwent peripheral nerve stimulation (PNS) for postherpetic neuralgia (PHN) at Mayo Clinic Florida (MCF). There were 20 original reports that described 309 patients with PHN who were treated with SCS. Sixteen reports had a permanent implantation of SCS, with a total of 255 patients, out of which 120 had long-term pain relief. There were six reports of subcutaneous PNS for PHN (in a thoracic area). Four reports provided data on success rates where all five patients received complete pain relief. In our practice, two patients underwent subcutaneous PNS for PHN (in the thoracic area) with good pain relief for 10 months and 2.5 years, respectively.

In 2017, Dao-Song et. al. evaluated the efficacy of short-term spinal cord stimulation (stSCS) in patients with refractory acute/subacute zoster related pain in a retrospective study. A total of 46 patients who presented with acute/subacute zoster-related pain, and had previously failed conventional therapies, underwent stSCS treatment. Visual analog scale (VAS), Short Form Health Survey 12 items (SF-12), and analgesic consumptions were recorded before stSCS, post-stSCS, 2 weeks, and 1, 3, 6, 9, and 12 months after stimulation. The VAS scores at post-stSCS, 2 weeks, and 1, 3, 6, 9, and 12 months after

stSCS treatment were significantly decreased compared with the baseline score ($P < 0.001$). Thirty-two patients (69.6%, 32/46) achieved the minimal clinically important difference (MCID), including 18 patients (39.1%, 18/46) who achieved complete pain relief ($VAS \leq 2$). During the follow-up period, the efficacy of stSCS did not decrease and VAS scores were declining. Similarly, SF-12 scores and analgesic consumptions improved after stSCS treatment. The efficacy of stSCS did not differ significantly among patients with different durations of acute/subacute zoster-related pain starting from the onset of rash. No serious adverse effects were observed in the entire follow-up period. This study was not a randomized prospective controlled study. They did not compare the outcomes with patients presenting with mild or moderate pain and did not compare the efficacy of stSCS treatment with conventional therapies.

Section Summary

Based on review of the peer reviewed medical literature for spinal cord stimulation (SCS) in the treatment of postherpetic neuralgia the evidence is limited. While some studies may show promise, further prospective randomized controlled trials (RCTs) comparing SCS to conventional therapies with larger sample sizes and long-term follow-up is needed to establish the safety and effectiveness of SCS in the treatment of postherpetic neuralgia. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Multiple Sclerosis (MS)

Based on review of the peer reviewed medical literature, case reports were found on the treatment of neuropathic pain and functional limitations associated with multiple sclerosis (MS) and the use of spinal cord stimulation (SCS). While case reports may show promise, high quality evidence is currently unavailable to support the use of SCS for this indication. Further prospective randomized controlled trials (RCTs) comparing SCS to conventional therapies with larger samples sizes and long-term follow-up is needed to establish the safety and effectiveness of SCS in the treatment of multiple sclerosis (MS). The evidence is insufficient to determine the effects of the technology on net health outcomes.

Fibromyalgia

Fibromyalgia is a disorder characterized by widespread musculoskeletal pain accompanied by fatigue, sleep, memory, and mood issues. Researchers believe that fibromyalgia amplifies painful sensations by affecting the way your brain processes pain signals. Symptoms sometimes begin after a physical trauma, surgery, infection, or significant psychological stress. In other cases, symptoms gradually accumulate over time with no single triggering event. Women are more likely to develop fibromyalgia than are men. While there is no cure for fibromyalgia, a variety of medications can help control symptoms. Exercise, relaxation, and stress-reduction measures also may help. Spinal cord stimulation (SCS) has been proposed as a treatment option related to neuropathic pain associated with fibromyalgia.

No randomized controlled trials (RCTs) were found for spinal cord stimulation (SCS) in the treatment of fibromyalgia. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Nociceptive Pain and Central Deafferentation Pain

Based on the peer reviewed literature spinal cord stimulation is generally not effective in treating nociceptive (pain which results from irritation, not damage to the nerves), or for central deafferentation pain (related to central nervous system damage from a stroke or spinal cord injury). The evidence is insufficient to determine the effects of spinal cord stimulation for these indications on net health outcomes.

Potential Adverse Events

Deer et. al. (2019) compared the safety and complaint records from the manufacturers of dorsal root ganglion neurostimulation (n=500+) and spinal cord stimulation (n=2000+) devices, from April 2016 through March 2018. The overall safety event rate for the study timeframe was 3.2% for dorsal root ganglion systems and 3.1% for spinal cord stimulation systems. Persistent pain was reported at a rate of 0.2% by patients with dorsal root ganglion implants and 0.6% by patients with spinal cord stimulation implants. Infection rates were 1.1% in both groups of patients. Cerebrospinal leaks were reported in 0.5% of patients with dorsal root ganglion implants and in 0.3% of patients with spinal cord stimulation implants.

Summary of Evidence

Treatment of Refractory Chronic Pain

For individuals who have treatment-refractory chronic pain of the trunk or limbs due to conditions such as failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS; formerly known as reflex sympathetic dystrophy), lumbosacral arachnoiditis, radiculopathy, phantom limb syndrome and peripheral neuropathy who receive standard spinal cord stimulation (SCS) the evidence includes systematic reviews, randomized controlled trials (RCTs) and case series. Available RCTs are mixed regarding underlying diagnosis in select patient populations. However, those trials including patients with underlying neuropathic pain processes have shown a significant benefit with SCS. Systematic reviews have supported the use of SCS to treat refractory trunk and limb pain, and patients who have failed other treatment modalities with few options. The evidence is sufficient to determine the technology results in a meaningful improvement in net health outcomes.

For individuals with who have treatment-refractory chronic pain of the trunk or limbs who receive high-frequency SCS (HFSCS), the evidence includes a systematic review and 4 randomized controlled trials (RCTs). One RCT comparing high-frequency with standard SCS in patients who had not previously been treated with SCS found a clinically and statistically significant benefit associated with high-frequency SCS (HFSCS). Another RCT in patients who had chronic pain despite previous treatment with standard SCS found no benefit for those receiving high-frequency stimulation compared with

sham-control; however, it is difficult to compare these findings with other trials of SCS due to the different patient populations, short treatment periods, and the crossover period effect. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have treatment-refractory chronic pain of the trunk or limbs who receive dorsal root ganglion (DRG) stimulation, the evidence includes systematic reviews, randomized controlled trial (RCT) and case series. The unblinded RCT found that patients receiving DRG stimulation had significantly higher rates of treatment success (physical functioning score and QOL measures), at 3 and 12 months compared with those receiving standard spinal cord stimulation (SCS) devices. DRG stimulation was found to be non-inferior to SCS in percentage achieving $\geq 50\%$ pain reduction, emotional functioning score, and SF-36 scores. Both groups experienced paresthesia's but patients in the DRG group reported less postural variation in paresthesia and reduced extraneous stimulation in non-painful areas. Rates of serious adverse events were similar between the two study arms. While most of the case series were small (sample sizes ranged from 10 to 65), all reported results that were consistent with the RCT results. The largest case series had the longest follow-up, reporting continued improvements in pain and psychological scores through three years. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Critical Limb Ischemia

For individuals who have critical limb ischemia who receive spinal cord stimulation (SCS), the evidence includes randomized controlled trials (RCTs). In some pooled analyses of these RCTs, SCS did not result in a significantly lower rate of amputation, although a systematic review and meta-analysis did report a significant difference. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Treatment Refractory Angina Pectoris

For individuals who have treatment-refractory angina pectoris who receive spinal cord stimulation (SCS), the evidence includes systematic reviews and randomized controlled trials (RCTs). Numerous small RCTs have evaluated SCS as a treatment for refractory angina. While some have reported benefit, most have not. In 2 more recent RCTs, there was no significant benefit on the primary outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

Heart Failure

For individuals who have heart failure who receive spinal cord stimulation (SCS), the evidence includes randomized controlled trials (RCTs). One small pilot crossover study (N=9) reported at least 1 adverse event in 2 patients with the device turned on and in 2 patients with the device turned off. A sham-controlled randomized trial (N=66) did not find significant differences between groups but might have been underpowered to do so. The evidence is insufficient to determine the effects of the technology on health outcomes.

Cancer Related Pain

For individuals who have cancer-related pain who receive spinal cord stimulation (SCS), the evidence includes no randomized controlled trials (RCTs). No RCTs evaluating SCS in this population were identified. A Cochrane review (2013) which was updated by Peng et. al. (2015) concluded “current evidence is insufficient to establish the role of SCS in treating refractory cancer-related pain.” The evidence is insufficient to determine the effects of the technology on health outcomes.

Postherpetic Neuralgia

Based on review of the peer reviewed medical literature for spinal cord stimulation (SCS) in the treatment of refractory postherpetic neuralgia the evidence is limited. While some studies may show promise, further prospective randomized controlled trials (RCTs) comparing SCS to conventional therapies with larger sample sizes and long-term follow-up is needed to establish the safety and effectiveness of SCS in the treatment of postherpetic neuralgia. The evidence is insufficient to determine the effects of the technology on net health outcomes

Multiple Sclerosis

Based on review of the peer reviewed medical literature, case reports were found on the treatment of neuropathic pain and functional limitations associated with multiple sclerosis (MS) and the use of spinal cord stimulation (SCS). While case reports may show promise, high quality evidence is currently unavailable to support the use of SCS for this indication. Further prospective randomized controlled trials (RCTs) comparing SCS to conventional therapies with larger sample sizes and long-term follow-up is needed to establish the safety and effectiveness of SCS in the treatment of multiple sclerosis (MS). The evidence is insufficient to determine the effects of the technology on net health outcomes.

Fibromyalgia

No randomized controlled trials (RCTs) were found for spinal cord stimulation in the treatment of fibromyalgia. Further studies are needed. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Nociceptive Pain and Central Deafferentation Pain

Based on the peer reviewed literature spinal cord stimulation is generally not effective in treating nociceptive (pain which results from irritation, not damage to the nerves), or for central deafferentation pain (related to central nervous system damage from a stroke or spinal cord injury). The evidence is insufficient to determine the effects of spinal cord stimulation for these indications on net health outcomes.

Practice Guideline and Position Statements

American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine

In 2010, the American Society of Anesthesiologists and the American Society of Regional Anesthesia and Pain Medicine updated and published guidelines for chronic pain management. The guideline concluded; spinal cord stimulation (SCS) may be used in the multimodal treatment of persistent radicular pain in patients who have not responded to other therapies. It may also be considered for other selected patients (e.g. those with complex regional pain syndrome (CRPS), peripheral neuropathic pain, peripheral vascular disease, or postherpetic neuralgia). Shared decision making regarding spinal cord stimulation should include a specific discussion of potential complications associated with spinal cord stimulator placement. A spinal cord stimulation trial should be performed before considering permanent implantation of a stimulation device.

American Society of Interventional Pain Physicians (ASIPP)

In 2013, The American Society of Interventional Pain Physicians updated their evidence-based guidelines for interventional techniques in the management of chronic spinal pain. The guidelines included the statement that there is fair evidence in support of spinal cord stimulation (SCS) in managing patients with failed back syndrome.

American Society of Pain and Neuroscience

In 2021, the American Society of Pain and Neuroscience issued a comprehensive guideline on the management of cancer-related pain. The guideline found the following regarding spinal cord stimulation (SCS):

- 1) treatment of refractory cancer pain (Level II-3-C evidence: multiple series compared over time, with or without intervention, and surprising results in noncontrolled experience; treatment is neither recommendable nor inadvisable), and
- 2) on a case-by-case basis for “pain that is related to cancer treatment such as chemotherapy-induced peripheral neuropathy”

(level III-C evidence: clinical experiences-based opinions, descriptive studies, clinical observations, or reports of expert committee; treatment is neither recommendable nor inadvisable).

International Modulation Society

The International Neuromodulation Society convened a Neuromodulation Appropriateness Consensus Committee (NACC) to develop best practices for the use of dorsal root ganglion (DRG) stimulation for the treatment of chronic pain syndromes. The NACC was comprised of experts in anesthesiology, neurosurgery, and pain medicine. The NACC performed a systematic literature search through June 2017 and identified 29 publications providing evidence for the consensus recommendations. The evidence was graded using the modified Pain Physician criteria and the U.S. Preventive Services Task Force criteria. The table below summarizes the consensus recommendations on the use of DRG stimulation.

NACC Consensus Recommendations for the Use of DRG Stimulation

Recommendation	Level	Grade	Consensus
DRG stimulation should be considered primarily for patients with focal neuropathic pain syndromes with identified pathology	I	A	Strong
DRG stimulation is recommended for CRPS type I or type II of the lower extremity	I	A	Strong
DRG stimulation for CRPS type I or type II of the upper extremity requires more study	II-2	A	Strong
DRG stimulation for DPN may be effective based on limited data. Since there is good evidence for SCS, the use of DRG must be justified.	III	C	Strong
Evidence for DRG stimulation for non-diabetic peripheral neuropathy is limited; use should be determined on a case-by case basis.	III	B	Moderate
Evidence for DRG stimulation for chronic postoperative surgical pain is limited; use should be determined on a case-by-case basis.	III	C	Moderate
DRG stimulation for pelvic pain should be used under strict	III	I	Moderate

criteria depending on mechanism of injury and visceral/somatic designation. Psychologic comorbidity is a contraindication.			
DRG stimulation for groin pain is recommended.	II-2	B	Strong
DRG stimulation is superior to standard SCS for unilateral focal pain from CRPS type I or type II of the lower extremity	I	A	Strong
No evidence for DRG stimulation over SCS for other indications			

National Institute of Health and Clinical Excellence (NICE)

In 2019, the National Institute for Health and Clinical Excellence (NICE) issued a guideline on Senza spinal cord stimulation system for delivering HF10 therapy to treat chronic neuropathic pain. The case for adopting Senza spinal cord stimulation (SCS) for delivering HF10 therapy as a treatment option for chronic neuropathic back or leg pain after failed back surgery is supported by the evidence. HF10 therapy using Senza SCS is at least as effective as low-frequency SCS in reducing pain and functional disability and avoids the experience of tingling sensations (paresthesia).

Neuropathic Pain Special Interest Group of the International Association for the Study of Pain:

In 2013, the Neuropathic Pain Special Interest Group of the International Association for the Study of Pain published recommendations on management of neuropathic pain. The interest group issued 2 recommendations on spinal cord stimulation (SCS); both were considered weak due to the amount and consistency of the evidence. The recommendations supported the use of SCS for failed back surgery syndrome and for complex regional pain syndrome (CRPS).

Regulatory Status

A large number of neurostimulator devices have been approved by the FDA through premarket approval process:

Device	Manufacturer	Original Approval Date	Indication
Algovita SCS System	Nuvector Corporation	November 2015	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, intractable low back pain, and leg pain.
Axiom (1 st generation) and Proclaim DRG (2 nd generation) Neurostimulator System	Abbott Medical	February 2016	Moderate to severe chronic intractable pain of the lower limbs in adult patients with Types I and II CRPS
Cordis Programmable Neural Stimulator Models 900a	Cordis Corporation	April 1981; Withdrawn in 2016	Stimulator, Spinal-Cord, Totally Implanted For Pain Relief
Freedom SCS	Stimwave Technologies	Aug 2016	Chronic, intractable pain of the trunk and/or lower limbs, including unilateral or bilateral pain
Genesis And Eon Family Neurostimulation (Ipg) System	St. Jude Medical/ Abbott Medical	Nov 2001	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome, intractable low back pain and leg pain
Itrel Totally Implantable SCS	Medtronic Neuromodulation	Nov 1984	Chronic, intractable pain of the trunk and/or limbs- including unilateral or bilateral pain associated with the

			<p>following conditions:</p> <ul style="list-style-type: none"> • Failed Back Syndrome (FBS) or low back syndrome or failed back • Radicular pain syndrome or radiculopathies resulting in pain secondary to FBS or herniated disk • Post-laminectomy pain • Multiple back operations • Unsuccessful disk surgery • Refractory Degenerative Disk Disease (DDD)/herniated disk pain • Peripheral causalgia • Epidural fibrosis • Arachnoiditis or lumbar adhesive arachnoiditis • Complex Regional Pain Syndrome (CRPS), Reflex Sympathetic Dystrophy (RSD), or causalgia • Diabetic peripheral neuropathy of the lower extremities
Precision SCS Systems	Boston Scientific Corporation	Apr 2004	Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with

			failed back surgery syndrome, Types 1 and 2 CRPS, intractable low back pain and leg pain
Senza SCS System	Nevro Corporation	May 2015	<p>Chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with the following: failed back surgery syndrome, intractable low back pain, and leg pain</p> <p>When programmed to include a frequency of 10 kHz: Chronic intractable pain of the lower limbs, including unilateral or bilateral pain, associated with diabetic neuropathy; non-surgical refractory back pain (intractable back pain without prior surgery and not a candidate for back surgery)</p>

In October 2016, the FDA approved BurstDR stimulation (St. Jude Medical, Plano, TX), a clinical programmer application that provides intermittent “burst”: stimulation for patients with certain St. Jude SCS devices.

PRIOR APPROVAL

Not applicable.

POLICY

Spinal Cord Stimulation

Implantation of a Temporary (Trial) Spinal Cord Stimulation (SCS) Device

A trial period using a temporary standard low frequency or high frequency spinal cord stimulator (SCS) device may be considered **medically necessary** when **All** the following criteria are met:

- 1) An individual has undergone careful screening, including evaluation by a multi-disciplinary team that confirms the existence of one of the following conditions:
 - Failed back syndrome or also known as post-laminectomy syndrome; **or**
 - Complex regional pain syndrome (CRPS), type I or type II (formerly known as reflex sympathetic dystrophy (RSD))
 - Type I CRPS is associated with symptomatic tissue injury
 - Type II CRPS is associated with nerve injury; **or**
 - Chronic neuropathic pain of certain origins:
 - lumbosacral arachnoiditis (arachnoiditis is usually documented by the presence of high levels of proteins in the cerebrospinal fluid and/or by myelography or MRI); **or**
 - Radiculopathies; **or**
 - Phantom limb syndrome (stump pain); **or**
 - Peripheral neuropathy/diabetic neuropathy.
- 1) There is documentation in the medical records of the failure of 6 months of conservative treatment modalities (pharmacological, surgical, psychological, or physical therapies), unless judged to be unsuitable or contraindicated; **and**
- 2) Further surgical intervention is not indicated (the treatment is used only as a last resort); **and**
- 3) There is documentation in the medical records the individual has been evaluated by a licensed psychologist, psychiatrist, or other licensed mental health professional; **and**
- 4) There is documentation in the medical records there is no evidence of existing untreated drug addiction; **and**
- 5) The individual does not have any contraindications to implantation (i.e., sepsis or coagulopathy issues).

Implantation of Permanent Spinal Cord Stimulation (SCS) Device

Placement of a permanent standard low frequency or high frequency spinal cord stimulator (SCS) device, or burst stimulation may be considered **medically necessary**

when the above medical necessity criteria for a trial (temporary) placement of spinal cord stimulation (SCS) are met, and **ALL** the following is also met:

- 1) There is \geq 50% reduction in pain with the trial of the temporary spinal cord stimulation (SCS) device as documented in the medical record; **and**
- 2) There is objective evidence per documentation in the medical records of pain relief (e.g., decreased opioid usage, improved range of motion of the affected area, increased activity, increased pain relief according to the Visual Analog Scale [VAS] or the Numeric Pain Intensity Scale).

Dorsal Root Ganglion (DRG) Stimulation

The implantation of a temporary (trial period) or permanent placement of dorsal root ganglion (DRG) stimulation is considered **medically necessary** when the individual meets the above medically necessary criteria for temporary (trial period) or permanent placement for spinal cord stimulation (SCS) above.

Combined use of spinal cord stimulation and dorsal root ganglion stimulation for any indication is considered **investigational** because the effectiveness of this approach has not been established.

Replacement of Spinal Cord or Dorsal Root Ganglion Stimulator Device

Replacement of standard low frequency, high-frequency or burst spinal cord stimulator and/or battery/generator may be considered **medically necessary** for an individual that meets the above medical necessity criteria and the existing stimulator and/or battery/generator are/is no longer under warranty and cannot be repaired.

Replacement of a properly functioning standard low frequency spinal cord stimulator (SCS) device with a high-frequency spinal cord stimulator (SCS) or a burst spinal cord stimulation device is considered **not medically necessary**.

Replacement of dorsal root ganglion stimulator and/or battery or generator may be considered **medically necessary** for an individual that meets the above medical necessity criteria for dorsal root ganglion stimulation (DRGS) and the existing stimulator and/or battery/generator are/is no longer under warranty and cannot be repaired.

Replacement for technological advancements or newly released upgrades to a standard dorsal root ganglion stimulator (DRGS) device when the original dorsal root ganglion (DRGS) device is still functioning properly and/or there are no changes in the individual's condition are considered **not medically necessary**.

Removal or Revision of Spinal Cord Stimulator or Dorsal Root Ganglion Device

The removal or revision of a standard low frequency, high-frequency or burst spinal cord stimulator (SCS) device or dorsal root ganglion stimulation (DRGS) device may be considered **medically necessary** for any of the following indications:

- Migration of lead(s)
- Loss of effectiveness
- Intolerance by individual
- Infection
- Painful generator site
- Development of neurological deficits
- Need for MRI study

Spinal cord stimulation (SCS) (standard low frequency, high frequency or burst) or dorsal root ganglion stimulation (DRGS) is considered **investigational** for all other indications including but not limited to the following because the safety and effectiveness cannot be established based on review of the available published peer reviewed medical literature. Additional randomized controlled trials (RCTs) with larger sample sizes and follow-up are needed to draw conclusions on the safety and effectiveness. The evidence is insufficient to determine the effects on net health outcomes:

- Treatment of cancer related pain
- Treatment of peripheral vascular disease
- Treatment of chronic pain of ischemic origin:
- Treatment of critical limb ischemia as a technique to forestall amputation
- Treatment of refractory angina pectoris
- Treatment of Multiple Sclerosis & spasticity disorders
- Treatment of axial and other musculoskeletal pain syndromes
- Treatment of nociceptive pain (resulting from irritation, not damage to nerves)
- Treatment of central deafferentation pain (related to central nervous system damage from a stroke or spinal cord injury)
- Treatment of post-herpetic neuralgia
- Treatment of heart failure
- Treatment of fibromyalgia

Definitions

Arachnoiditis

Painful condition caused by inflammation of the arachnoid, one of the three linings that surround and protect the brain and the spinal cord. The arachnoid can become inflamed due to a variety of reasons. These include irritation from chemicals present myelograms and epidural steroid injections; bacterial or viral infections; spinal cord injury; or complications from spinal surgery or other invasive spinal procedures. When arachnoiditis begins to impact the nerves, it can cause a number of symptoms, including numbness, tingling, and a distinctive stinging and burning pain the lower back and legs. Other symptoms may include debilitating muscle cramps, twitches, spasms, and bladder/bowel/sexual dysfunction. There is no cure for this condition, so the goal of treatment is to control pain and symptoms.

Arachnoiditis is usually documented by the presence of high levels of proteins in the cerebrospinal fluid and/or by myelography or magnetic resonance imaging (MRI).

Complex Regional Pain Syndrome (CRPS)

An uncommon nerve disorder which causes intense burning pain, usually in the arms, hands, legs, or feet. It can occur after an injury, either to a nerve or to tissue in the affected area. Along with pain, the patient may experience extreme skin sensitivity and changes in color, temperature, or moistness of the skin. The cause of CRPS is unknown, and there is no cure.

Failed Back Syndrome (FBSS) or post laminectomy syndrome (lumbar or cervical)

Persistent or recurrent pain, mainly involving the lower back and/or legs, even after prior anatomically successful spinal surgery. FBSS is considered a diagnosis of exclusion, so CT scans or MRIs must demonstrate that there are no surgically correctable lesions present. Patients with FBSS often have epidural/intraneural/perineural fibrosis or scar tissue, which generally will not respond to surgery but may respond to spinal cord stimulator (SCS).

Neuropathic Pain

Otherwise known as “nerve pain” is a complex, chronic pain state that usually is accompanied by tissue injury. With neuropathic pain, the nerve fibers themselves might be damaged, dysfunctional or injured. These damaged nerve fibers send incorrect signals to other pain centers. The impact of nerve fiber injury includes a change in nerve function both at the site of injury and areas around the injury.

Nociceptive Pain

Nociceptors are the nerves which sense and respond to parts of the body which suffer from damage. They signal tissue irritation, impending injury or actual injury. When activated they transmit pain signals (via the peripheral nerves as well as the spinal cord) to the brain. The pain is typically well localized, constant, and often with an aching throbbing quality. Visceral pain is the subtype of nociceptive pain that involves the internal organs. It tends to be episodic and poorly localized.

Nociceptive pain is usually time limited, meaning when the tissue damage heals, the pain typically resolves.

Central Deafferentation Pain

Central pain is defined as pain that is initiated by a primary lesion within the CNS. Central pain can occur in association with all types of CNS lesions related to wide variety of pathological processes. Deafferentation pain denotes a type of pain that results from complete or partial interruption of afferent nerve impulses. This type of pain results from lesions that interrupt the spinothalamic pathways at any level of the nervous system.

Patients with deafferentation pain usually display varying degrees of sensory loss characterized by disturbances with pain and temperature sensation.

Critical Limb Ischemia (CLI)

A severe blockage in the arteries of the lower extremities, which markedly reduces blood-flow. It is a serious form of peripheral arterial disease, or PAD. CLI is a chronic condition that results in severe pain in the feet or toes, even while resting. Complications of poor circulation can include sores and wounds that won't heal in the legs and feet. Left untreated, the complications of CLI will result in amputation of the affected limb.

Refractory Angina Pectoris (Chronic Stable Angina)

A chronic condition characterized by the presence of angina caused by coronary insufficiency in the presence of coronary artery disease which cannot be controlled by a combination of medical therapy, angioplasty, and coronary bypass surgery. The presence of reversible myocardial ischemia should be clinically established to be the cause of the symptoms. Chronic is defined as a duration of more than 3 months

Ischemic Pain

Caused by a reduction in oxygen delivery to the tissue, usually caused by reductive in blood flow because of constriction of blood vessel (vasospasm) or its obstruction by atheroma or embolus. Ischemic pain conditions include critical limb ischemia & refractory angina).

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 63650 Percutaneous implantation of neurostimulator electrode array, epidural
- 63655 Laminectomy for implantation of neurostimulator electrodes, plate/paddle, epidural
- 63661 Removal of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed
- 63662 Removal of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed
- 63663 Revision including replacement, when performed, of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed
- 63664 Revision including replacement, when performed, of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed
- 63685 Insertion or replacement of spinal neurostimulator pulse generator or receiver, direct or inductive coupling
- 63688 Revision or removal of implanted spinal neurostimulator pulse generator or receiver
- C1767 Generator neurostimulator (implantable) non-rechargeable
- C1778 Lead, neurostimulator
- C1787 Patient programmer, neurostimulator

- C1816 Receiver and/or transmitter neurostimulator (implantable)
- C1820 Generator neurostimulator (implantable), non- high frequency with rechargeable battery and charging system
- C1822 Generator neurostimulator (implantable), high frequency with rechargeable battery and charging system
- C1826 Generator, neurostimulator (implantable), includes closed feedback loop leads and all implantable components, with rechargeable battery and charging system
- C1827 Generator, neurostimulator (implantable), non-rechargeable, with implantable stimulation lead and external paired stimulation controller
- C1897 Lead neurostimulator test kit (implantable)
- L8679 Implantable neurostimulator, pulse generator any type
- L8680 Implantable neurostimulator electrode, each
- L8681 Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
- L8682 Implantable neurostimulator radiofrequency receiver
- L8683 Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
- L8685 Implantable neurostimulator pulse generator, single array, rechargeable includes extension
- L8686 Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
- L8687 Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
- L8688 Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension
- L8689 External recharging system for battery (internal)for use with implantable neurostimulator, replacement only
- 95970 Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain, cranial nerve, spinal cord, peripheral nerve, or sacral nerve, neurostimulator pulse generator/transmitter, without programming
- 95971 Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with simple spinal cord or peripheral nerve (e.g., sacral nerve) neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional

- 95972 Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with complex spinal cord or peripheral nerve (e.g., sacral nerve) neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional

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POLICY HISTORY		
Date	Reason	Action
August 2022	Annual Review	Policy Revised
August 2021	Annual Review	Policy Renewed
August 2020	Annual Review	Policy Renewed
August 2019	Annual Review	Policy Revised
August 2018	Annual Review	Policy Revised
August 2017	Annual Review	Policy Revised
August 2016	Annual Review	Policy Renewed
September 2015	Annual Review	Policy Revised
February 2015		Policy Revised
October 2014	Annual Review	Policy Revised
May 2014	Interim Review	Policy Revised
January 2014	Annual Review	Policy Revision, New Policy Created
January 2013	Annual Review	Policy Renewed
January 2012	Annual Review	Policy Renewed
February 2011	Annual Review	Policy Revised
October 2010	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
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