Current status and future perspectives of spinal cord stimulation in treatment of chronic pain

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1. Introduction and history of spinal cord stimulation for chronic pain

In 1959, the neurosurgeon Willem Noordenbos30 reported that a signal carried along large diameter fibers for “touch, pressure or vibration” may inhibit the signal carried by the thinner “pain” fibers. Consequently, the concept of interaction between thick non-nociceptive fibers and thin nociceptive fibers, and the control of this at the spinal dorsal horn, was born. From this, Melzack and Wall introduced the “Gate-control” theory of pain.24,25 This gate theory postulates that stimulation of large myelinated fibers suppresses the response of dorsal horn neurons to input from small, unmyelinated peripheral pain fibers and provided the theoretical foundation for the use of spinal cord stimulation (SCS) as a clinical treatment for chronic pain. The experimental clinical use of SCS was first reported 2 years after the introduction of the classical gate-control theory.26 The first fully implantable SCS system was developed in 1970;35 the first clinical trials in patients suffering from intractable chronic pain were performed in the early seventies.27,29

2. Spinal cord stimulation: indications and evidence

2.1. Conventional spinal cord stimulation (Con-SCS)

The present day conventional (tonic) SCS (Con-SCS) originates from 1980s with the creation of permanently implantable percutaneous leads for epidural placement. In Con-SCS, the leads are placed midline in epidural space, and for the stimulus, a frequency of 35 to 80 Hz is used with pulse width of 210 to 450 microseconds (μs), amplitude (3.6-8.5 mA), and a charge per pulse of 1.2 to 5 microCoulombs (μCb).26 The patient experiences a tingling feeling (paresthesias) in the covered area. During trial stimulation, the correct electrode placement is ascertained by carefully shifting the electrode along the dorsal column while in constant communication with the patient. Paresthesias should cover the painful area. This can be accomplished mostly with one lead but if necessary 2 leads. The effect of Con-SCS is due to modulation of excitatory amino acids connected to the local spinal inhibitory GABA system.9,40 Experimental studies in rats have shown that reduced intracellular GABA levels are only present during SCS treatment in responders.7 Furthermore, pain relief in Con-SCS seems to be predominantly due to a segmental spinal mechanism as SCS of the dorsal columns at the level where the injured fibers enter the spinal cord dorsal horn has resulted in much better pain-relieving effects than SCS at more rostral levels.39

Current indications for Con-SCS are diabetic neuropathy,5,38 radicular pain in failed back surgery syndrome,18,31 complex regional pain syndrome type-1 (CRPS-I),11 chronic intractable angina pectoris,42 and peripheral vascular disease.43 Two randomized controlled trials (RCT) have shown that Con-SCS is successful in diabetic neuropathy (>50% pain relief) in 40% to 65% of patients for at least 6 months.5,38 The evidence for CRPS-I11 and failed back surgery syndrome18 are each based on one large RCT. Several studies provide evidence for long-term clinically important treatment effects. However, these studies also showed that patients who initially respond well to SCS treatment success rates are not always able to maintain their initial gains over a period of years.8,12,23 A prospective study with follow-up over 12 years showed that after 3 years of treatment, 40% of initially successfully treated (>30% pain relief) cases turned into failures, and that 60% failed after 12 years (Fig. 1).8

In conclusion, the evidence for effective pain relief regarding Con-SCS for diabetic neuropathy is good and for CRPS-1 and failed back surgery syndrome is based on one RCT each. For intractable angina pectoris and peripheral vascular disease, the evidence is still limited. It is clear that large-scale, well-designed studies are still needed to evaluate effectiveness and long-term outcome of Con-SCS. Conventional spinal cord stimulation is not successful in all patients and pain relieving effects often decline over the years. For these reasons, the search for new stimulation modalities and new techniques to improve SCS are ongoing.

2.2. New spinal cord stimulation modalities

2.2.1. High-frequency burst spinal cord stimulation (HF-burst-SCS)

Various new stimulation modalities, such as HF-burst-SCS and HF-SCS, are in principal based on the gate-control theory where the stimulation of the non-nociceptive Aδ fibers in the dorsal columns might modulate the incoming small fiber nociceptive input.
The suggested mechanism of action for HF-burst-SCS is that a stimulation signal delivered in bursts is more similar to endogenous activation patterns in the nervous system, including the pain neurons in the dorsal horn as well as those at higher supraspinal levels. In burst stimulation, the stimulus is delivered at a low frequency of 40 Hz with 5 closely spaced pulses (1 ms) at 500 Hz per burst, or 4 pulses at 100 Hz, followed by a single repolarization pulse. Generally with this type of stimulation, the patient does not feel paresthesias.

Although HF-burst-SCS is characterized by a lower charge per pulse, at the same time a higher charge per second (120 μCb/s) is delivered to the dorsal column fibers as compared to Con-SCS. The higher charge per second and burst frequency are believed to produce modulation of the pain neurons in the dorsal horn and hypothesized to improve the patient’s attention to pain and changes in pain. This is based on encephalogram analyses that show that burst stimulation activates the dorsal anterior cingulate and right dorsolateral cortex more than Con-SCS.

At present, evidence for effectiveness of HF-burst-SCS is based on studies that compare HF-burst-SCS to Con-SCS in patients who where pretreated (with more or less success) with Con-SCS: 2 small RCTs, mainly in failed back surgery syndrome patients, and 2 larger prospective studies in failed back surgery syndrome and diabetic neuropathy patients collected evidence for HF-burst-SCS to additionally improve the pain relieving effect in patients with these conditions. There is some evidence that this stimulation approach has an effect on the patients’ focus on pain and reduces the attention that is paid to pain and pain changes.

In conclusion, HF-burst-SCS is a new stimulation modality for which treatment indications and (long-term) effectiveness need to be established in well-designed large-scale studies.

2.2.2. High-frequency SCS (HF-SCS)

With high-frequency stimulation (HF-SCS), the stimulus is delivered at the dorsal columns at a frequency of 10,000 Hz, pulse width of about 30 μs, low amplitude (1.6-3.8 A), high charge per second (480-1140 μCb/s).

The electrode implantation technique including lead placement, contact size, and spacing of the lead tips differs from Con-SCS stimulation. For back and leg pain, expert opinion up to now is that 2 leads should be used and that the lead tips should be placed midline in the posterior epidural space at disc level T9 to T10. In HF-SCS, the patient experiences no paresthesias because of the low charge per pulse (0.05-0.11 mCb/pulse) and subthreshold stimulation of the Aβ fibers in the dorsal column. Although one randomized trial and one prospective study provided evidence that HF-SCS (10,000 Hz) is superior to Con-SCS for back and leg pain, one study has reported no difference between HF-SCS and Con-SCS. Of note is that in the latter study, HF-SCS was performed at 5000 Hz.

In conclusion, HF-SCS may be a promising new treatment modality with the potential advantage for the patient that no paresthesias are noticed. On the other hand, there is evidence that some patients undergoing SCS seem to prefer the presence of paresthesias. In conclusion, HF-SCS is an interesting option but one that needs to be further explored in well-designed large-scale studies that examine both short-term and long-term effectiveness.

2.2.3. Dorsal root ganglion stimulation (DRG-STIM)

The dorsal root ganglion (DRG) is located at each segmental level of the spinal column in the lateral epidural space within the spinal foramen. It contains the cell bodies of the primary sensory neurons. The DRG is involved in the transduction of pain to the central nervous system. It was experimentally shown that DRG-STIM and the direct application of electrical fields to the DRG results in reduced excitability of the DRG neurons. It has been reported that incoming afferent pain signals spread over the different levels of the spinal cord and dorsal root ganglia and as a consequence communication between the segmental levels takes effect. Dorsal root ganglion stimulation might modulate the intersegmental integration and spreading of primary afferent inputs. Potential clinically meaningful are some prospective clinical studies that show that the DRG could be a stimulation target for peripheral neuropathic pain syndromes such as lumbosacral and genitofemoralis neuropathy, CRPS, CRPS, phantom limb pain, disk-related back pain, and radicular pain.

In conclusion, of the possible advantages of DRG-STIM are: (1) an improved ability to achieve pain relief in locations that are typically hard to target with Con-SCS and (2) enhanced stability of the stimulation regardless of body position. Evidence for treatment indications and (short term and long term) effectiveness should be established in well-designed large-scale studies.

3. Complications and side effects

Complications and side effects (adverse events) acquiring reinterventions often occur during treatment with SCS. Complications include deep and superficial infections or equipment-related side effects like hardware malfunction, lead migration, fractured electrode, pulse generator discomfort, and battery replacements. Localized pain over the implanted hardware occurs regularly, on average in 6% of cases. This pain, for instance, can present as pain around the implanted pulse generator or over the lead. Such pain typically leads to replacement of the lead and therefore an additional surgery. Removal of the SCS system may be necessary in cases of deep infection or treatment failure. A prospective study performed over 12 years showed adverse events in 61% of patients. However, the complication rate was significantly reduced during the last 4 years of the study from
an annual mean of 30% to 22%. The authors concluded that this was likely due to technological developments and improvements in the SCS hardware. Another explanation for this reduction is that the physicians treating patients gradually gain experience in a particular implant technique. New implantation techniques like DRG-STIM have been reported to cause more complications and it has been concluded that refinement and optimization of the technique are needed to minimize adverse events.

4. Cost-effectiveness of spinal cord stimulation

At present, the costs for a Con-SCS implant procedure (including the costs of the device, screening, implantation, and reprogramming sessions) is estimated at approximately $17,000. Based on a systematic review and economic evaluation, in which cost-effectiveness is examined for CRPS and failed back surgery syndrome, the British National Institute for Health and Care Excellence (NICE) Technology Appraisal Guidance recommends SCS as a treatment option for chronic pain of neuropathic origin. The British National Institute for Health and Care Excellence states that the choice of device or modality depends on the specific pain pattern and the preferences of the patient and clinician. To determine the costs and health care outcomes of SCS, the decision model for economic evaluation that NICE used considers device longevity to be 4 years and takes into account that the pain relieving effect can be up to 15 years. Spinal cord stimulation is not recommended by NICE as a treatment option for adults with chronic pain of ischemic origin except in the context of research as part of a clinical trial. A recent study showed that HF-SCS is more cost-effective than Con-SCS for failed back surgery syndrome.

In conclusion, the NICE guideline supports treatment with Con-SCS for all chronic pain of neuropathic origin. However, it should be noted that at present, there is only evidence available for the cost-effectiveness of Con-SCS for CRPS and failed back surgery syndrome and for HF-SCS in failed back surgery syndrome. For other all other indications and stimulation modalities, cost-effectiveness still needs to be established.

5. Future perspectives of spinal cord stimulation

Recent technical developments have made possible new stimulation modalities and direct stimulation of the DRG. These innovations are potentially quite interesting and may have important implications for the treatment of chronic pain patients. At the same time, it is clear that these new approaches require further development, scientific investigation, and refinement. Before they are used routinely in clinical settings, their effectiveness needs to be established for each clinical diagnosis by large-scale RCTs and cost-effectiveness studies.

With advances in clinical research, it is possible that in the future, one may be better able to “tailor-make” stimulation approaches for each individual patient and that patients’ preferences for stimulation type or system can be taken into account. However, this possibility also means that pain management with SCS will become more complex. Providing choices with regard to systems, treatment modalities, and potential targets may prove challenging. Spinal cord stimulation requires experienced physicians, a multidisciplinary approach to selection, and ongoing care of patients. This includes 24-hour availability for detection and management of potentially serious problems. Therefore, in the future, it is even more important that SCS treatment be performed in specialized pain centers by experienced specialists in a multidisciplinary setting.

A point of concern is that, at present, cost-effectiveness of SCS is impeded by the high cost of the device and the high incidence of complications and side effects requiring reinvention and surgery. Consequently, SCS treatment is not accessible for everyone in the world and up to now is only available for selected indications.

In conclusion, recent advancements in SCS therapy could be promising, new studies have been published that claim superior effectiveness for new modalities. However, the current evidence still points to the fact that Con-SCS is the best SCS pain treatment option in CRPS-1 and diabetic neuropathy. For failed back surgery syndrome, evidence is accumulating to show that HF-SCS might be superior to Con-SCS. Dorsal root ganglion stimulation could be promising for peripheral neuropathic pain. Intractable chronic neuropathic pain syndromes unsuccessfully treated with Con-SCS, or when SCS treatment fails over time, all stimulation modalities or DRG-STIM could be considered preferable under study conditions.

Goals for the future development of SCS include: (1) collecting evidence for its long-term effectiveness and (cost-)effectiveness for a wider variety of clinical conditions and stimulation modalities, (2) reduce the costs of SCS devices, and (3) improve the technology in ways that lead to reduced complication rates and longer time effectiveness.

In the management of pain using SCS, we believe that patient selection, implantation, and follow-up should take place in specialized pain centers by experienced pain interventional specialists in a multidisciplinary setting.

Conflict of interest statement
The authors have no conflict of interests to declare.

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References


