Current Challenges in Spinal Cord Stimulation

Krishna Kumar, MBBS, MS*; David L. Caraway, MD†; Syed Rizvi, MD*; Sharon Bishop, BNurs, MHlthSci*

Objectives: This study aims to review the current state of spinal cord stimulation for the treatment of chronic pain associated with failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) and to describe intraspinal targets and stimulation parameters, patient selection, therapy cost-effectiveness, and strategies to improve outcomes.

Materials and Methods: We drew on professional literature spanning four decades, our work with national and international professional societies, and our own extensive clinical experience to summarize contemporary knowledge of the safety, efficacy, cost-efficiency, and challenges associated with spinal cord stimulation in treating chronic pain.

Results: The safety, efficacy, and cost-efficiency of spinal cord stimulation in treating chronic pain associated with FBSS and CRPS are well established through randomized controlled trials and long-term observational studies. Challenges include reducing wait-times before implant, which are associated with lower success rates; increasing awareness of this therapy among referring physicians, patients, and payers; decreasing device-related complications by incorporating advanced technology, improved operative and trialing techniques, and appropriate patient selection; and capturing functional and quality-of-life outcomes. Spinal cord stimulation must be part of an overall treatment plan to manage chronic pain, and must engage physicians, patients, their families, pharmacists, nursing staff, and mental health experts in supporting a return to employment, if possible, and to a full domestic and social life.

Conclusions: Innovation in spinal cord stimulation therapy has intensified with numerous new technical capabilities, safety advances, and novel stimulation targets. This progress holds hope for the many sufferers of chronic pain.

Keywords: Chronic pain, complex regional pain syndrome, failed back surgery syndrome, net monetary benefit, quality adjusted life years, spinal cord stimulation

INTRODUCTION

Neuromodulation utilizes implantable devices discharging electricity or pharmaceutical agents that modify signal transmission in order to achieve inhibition, excitation, or modulation of the activity of neuronal groups and networks. Spinal cord stimulation (SCS) is a reversible therapy that is approved by the Food and Drug Administration (FDA) in the United States to treat chronic pain of the trunk and limbs. Approved labeling varies from country to country, and in some countries, SCS is approved for indications other than chronic pain. SCS has developed over the past 40 years as a viable and highly effective option for the management of chronic pain. Clinical results are dependent on precise lead placement as well as the underlying pathology being treated. However, SCS continues to present its own unique set of challenges that must be acknowledged and addressed if this therapy's full potential is to be realized. The purpose of this article is to highlight the issues and discuss the controversies in using SCS for chronic pain.

CURRENT STATE OF SCS

The often-cited genesis of the use of electrical stimulation to modulate pain signals sprang from the work of Melzack and Wall when in 1965 they published a new theory, called the gate theory, about how pain is perceived and modulated (1). The concept that electrical inhibition plays a role in the normal physiology of pain transmission was quickly applied to clinical trials. Shealy described implanting a bipolar electrode through a laminectomy to stimulate the dorsal columns of the spinal cord for the treatment of cancer-related pain (2). The first leads consisted of plate-style electrodes placed in the subarachnoid space directly over the spinal cord. This technique was fraught with complications including cerebrospinal fluid (CSF) leak, poor quality paresthesia, and arachnoiditis.
Subsequently, neurosurgical techniques for percutaneous epidural electrode trial and implant were offered (3).

By 1968, Medtronic Inc., (Minneapolis, MN, USA) began to supply radiofrequency (RF) coupled dorsal column stimulators (DCSs) modified from a cardiac device used to stimulate the carotid sinus for hypertension (4). Within ten years of the initial presentation of the gate theory, permanently implantable percutaneous leads had gained popularity and were placed into the epidural space through a modified Tuohy needle to treat chronic pain (5–8). Although the basic procedural approaches for placing both surgical and percutaneous leads have changed little since that time, technological advancement has continued at a remarkable rate. The elucidation of the importance of dermatomal mapping and overlapping the distribution of pain with comfortable paresthesia led to the creation of multiple contact arrays and then to multiple array lead arrangements (9). Advances in battery and pacemaker design fostered the application of cardiac technology to what became known as SCS, with fully implantable programmable systems becoming available in the early 1980s (10).

The use of SCS has burgeoned over the past two decades. For example, in the U.S. Medicare population alone, an increase of 159% in spinal cord implants occurred over the ten-year period from 1997 to 2006 (11). It is estimated that current annual sales of SCS systems total 35,000 units globally, and the number is rising (12). Reasons for the increase include not only the development of low-morbidity percutaneous trial and implant techniques but also device advancements (13). Improved lead design with better ability to capture complex pain patterns coupled with fewer technical failures, higher powered generators, rechargeable systems that reduce the frequency of battery replacement surgery, and multiple array capabilities—as well as the emerging understanding of clinically important targets and stimulation parameters—have all contributed to improved outcomes and patient acceptance (14).

Lead Design and Selection

In addition to surgically placed lead arrays with embedded insulated plate electrodes, percutaneously placed cylindrical leads have evolved and include a variety of configurations and performance characteristics. Although the percutaneous leads have generally been accepted as the lead of choice for performing trials of SCS therapy, much scholarly debate has ensued regarding the relative merits of using one type or the other for permanent implantation. As is the case in most areas of medical device design, the decision requires balancing the advantages and disadvantages of each approach for a given clinical application (15).

Historically, surgical paddle-style leads were favored in settings of high power requirements because of the inherent improved efficiency of unidirectional stimulation fields compared with the omnidirectional stimulation pattern of cylindrical leads (16). The thicker and larger cross-sectional area of paddle-style leads reduced the dorsal CSF thickness, thereby positioning the electrodes closer to the spinal cord (17,18). However, with the advent of rechargeable generators and low-impedance leads, this electrical advantage has been mitigated, and the advantages must be weighed against the less invasive percutaneous approach. Although percutaneous implantation of the leads performed under mild sedation may facilitate intraoperative confirmation of adequate paresthesia coverage, surgical leads may allow a more stable spatial relationship among columns of leads (19). Examples of such leads include a tripolar array, which may offer a superior ratio of dorsal column to dorsal root activation (e.g., Specify 5-6-5°, Medtronic Inc.) or the five-column array (Penta, St. Jude Medical Inc., Plano, TX, USA), both designed to improve lateral coverage (20,21).

Physician practice structure, specialty training, and reimbursement strategies influence device selection. An increasingly common approach is for responsibilities to be distributed between one physician who selects the patient, performs the trial, and manages the patient and another physician, often a spine surgeon, who performs the implant. The trialing physician may insert a percutaneous trialing lead and then refer to the implanting physician, who may place a permanent surgical paddle lead.

Although this arrangement may capitalize on the training of the physicians and suit the practice environment, some caveats merit mention. The trialing lead is not the same as the implanted lead and, therefore, the patient may have a different experience during trial than after implant. This referral pattern is the usual case with surgical lead implantation, which makes effective communication between the trialing physician and implanting surgeon critical to ensure that the distribution pattern of necessary paresthesia is well understood and that the permanent, implanted lead can be reasonably expected to perform at least as well as the trial lead. Some centers use a permanent lead for trialing to overcome this potential hurdle. To accomplish this, the implanting surgeon must add a lead extension, which is then externalized so that trial stimulation may commence. The key advantage of this technique is that once satisfactory paresthesia coverage is achieved a second lead reimplantation procedure can be avoided. Choice of implantable pulse generator (IPG) characteristics and location should be discussed and agreed upon by the physicians and the patient before implant.

Guidelines developed by Dr. Richard North and the Neuromodulation Foundation (22) provide an overview of clinical considerations for surgical vs. percutaneous lead selection. The first set of considerations applies to the stimulation trial and lead insertion/removal. In obese patients, percutaneous catheter electrode placement, using specially designed Tuohy needles, is typically easier than placing plate/paddle electrodes. Placement of a surgical plate/paddle electrode requires a laminectomy or laminotomy, and removal requires laminotomy. Insertion/removal of the percutaneous catheter electrode requires neither. Thus, patients are likely to experience more pain after the insertion of the plate/paddle electrode than the percutaneous catheter electrode. In addition, a percutaneous electrode facilitates paresthesia mapping with relatively easy access to multiple spinal levels. A surgical plate/paddle electrode, however, might be required if a percutaneous catheter electrode cannot access the epidural space. Targeting specific sites may be simpler with a transverse tripole electrode configuration, according to robust computer modeling by Holsheimer and others (18,23,24). The three-column design, in which lateral anodes bracket a central cathode, may reduce segmental side-effects. Limited clinical experience with tripole electrodes requires further study to confirm the validity of the computer models. Finally, if patients are satisfied with the result of the percutaneous catheter electrode screening trial, they might choose it for the permanent implant.

The second set of considerations addresses potential complications associated with the two lead styles. When implanted using proper technique, fracture rates are similar (25). However, extraneous stimulation of nerve fibers in the ligamentum flavum, seen in a small fraction of patients, may be mitigated by insulated surgical leads. A percutaneous catheter electrode, on the other hand, retains a greater potential to migrate, even after encapsulation in fibrous tissue. New anchoring techniques may minimize this possibility. A
surgical plate/paddle electrode, due to its shape, resists migration once it is encapsulated, and multiple columns of contacts remain fixed in their relative positions. Yet if revision becomes necessary, the scarring around a plate/paddle electrode presents a greater surgical challenge than revising a percutaneous catheter electrode.

Published literature discusses the effects of the number of contacts, spacing, and size of the individual electrodes, the spatial arrangements of the electrode arrays, the number of arrays, and the shape and size of the lead itself. Manufacturers have provided a panoply of lead choices that allow the physician an opportunity to tailor device selection to specific patient characteristics. At the same time, convincing clinical evidence of superiority of any specific design, in terms of either efficacy or durability, is lacking (26). Distinguishing marketing initiatives from actual benefits of design for specific indications should be the aim of future clinical research.

Implanted Pulse Generator Design

The mid-1980s saw the development and approval of the primary cell, fully implantable generator with sufficient energy to power a single quadripolar array of electrodes (Itrel®; Medtronic Inc.) (27). For most patients, this was a significant improvement over the RF-coupled generators that were in widespread use. This improvement was not attributable to enhanced efficacy. In fact, the external RF power sources were capable of providing higher power for as long as the internal system remained intact, whereas the IPG required surgical replacement at the end of battery life. Battery life is a variable function of cumulative use and power requirements. Thus, much clinical time was spent “managing the battery” using various strategies, such as cycling the device on and off to minimize battery expenditure. From a patient perspective, the disadvantage of the RF system is that the RF transmitter needs to be worn over the implanted antenna. Patients often did not like having the transmitter taped to the abdomen because it was prone to detachment, was not waterproof, and the batteries in the unit required frequent changes. Thus, IPGs, despite their shortcomings, quickly gained dominance in the market. This is a striking example of how patient acceptance, perhaps more than cost-effectiveness, efficacy, or even reduced morbidity, may drive innovation.

The first rechargeable implantable pulse generator (RIPG) was introduced in 2004 (Precision SCS System, Boston Scientific Corp., Valencia, CA, USA). Relative to primary cell IPGs, RIPGs have the potential advantage of providing high power outputs with smaller size, less frequent need of surgical replacement, and therefore reduced longitudinal costs of therapy. Because the devices are rechargeable, the patient can use the generator at higher power whenever desired with less concern about battery longevity. For these reasons, all of the major device manufacturers now have rechargeable SCS generators, and RIPGs have become the dominant segment of the market in North America. In Europe, for various reasons, the primary cell IPG remains the dominant device. Yet not all patients are well suited to the present RIPG technology. In a UK study using the National Institute for Health and Clinical Excellence (NICE) model, rechargeable devices were cost-effective only if the primary cell IPG required replacement before four years (29). Statistical models (used in the United States) of the average difference in total lifetime costs between a rechargeable and nonrechargeable generator demonstrate that savings for a rechargeable system range from U.S. $104,000 to $168,833 (30). However, these analyses are not based on actual practice patterns and a number of the assumptions implicit in the model may not hold true in practice. Further cost-effectiveness research is warranted to define more clearly the actual benefit of being rechargeable.

Today, IPGs are available with various patient-controlled programming options to improve paresthesia coverage and patient satisfaction (31). In the more advanced devices, multiple parameters including anode/cathode contact configuration, amplitude, pulse width, and frequency are preconfigured and assigned by the clinician into sets of patient-selectable programs. Icons can be associated with these programs so that the patient can easily select a defined set of stimulation parameters specifically tailored to the patient’s activity and/or position.

These alterations in the programs are needed because the thickness of the dorsal CSF (dCSF, distance from the dura to the surface of the dorsal horn of the spinal cord) at the level of stimulation is the most important physiologic variable affecting paresthesia threshold. With postural changes, the cord moves relative to the electrode array, significantly altering this distance and thus the amount of intervening CSF (32). Regardless of the control system of the device (constant current or constant voltage), these positional changes are not sensed or accommodated as the total system impedance does not change appreciably (32). Therefore, the patient can experience painful paresthesia, for example, when going from standing to lying down and the reverse, or the patient may have understimulation when rising from bed to walk. For this reason, many clinicians assign icons that are easily identifiable and patient selectable to apply programs for sleeping, sitting, or walking. Still, this technology requires that changes in position must be anticipated, and the patient must intervene to maintain constant paresthesia.

Once again, advances in cardiac device technology are being applied to SCS to improve patient experience and satisfaction. For a decade, accelerometers have been incorporated into cardiac devices that can monitor patient activity and adjust therapy (33). Multiaxial accelerometers can reliably determine patient position and record activity data (34). A new IPG (RestoreSensor®, Medtronic Inc.) that incorporates accelerometer technology is now commercially available in most countries where the therapy is offered. The manufacturer asserts that the proprietary adaptive stimulation technology (AdaptiveStim®, Medtronic Inc.) monitors the individual’s movement and automatically adjusts settings as needed each time the patient changes position. Each program can have a different amplitude setting assigned to each of the six different positions. Because the system can provide four interleaved programs with any given position, selecting a variety of the four programs to provide therapy for each position allows changes in pulse width, rate, and electrode settings per position.

The device also records the amount of time a patient spends in each of six positions between interrogations of the device, and documents the number of times a patient changes position in the lying position to help assess the quality of rest. These data, which are provided in 24-hour averages, can be accessed to use in patient assessment and care if desired. A recently published multicenter, prospective, randomized, crossover design study has confirmed early patient surveys of the need for stimulators that adapt to positional changes, as well as high levels of satisfaction with the new device (35). In the study, appropriate candidates were selected and
screened in the usual fashion for conventional SCS. After a successful trial, all patients were implanted with the adaptive stimulation system, which incorporates the accelerometer-based technology. All study participants were initially programmed to conventional stimulation (no postural-sensing technology) for a four-week postoperative period to ensure wound healing and proficiency using the neurostimulation system. Subsequently, the study patients were randomized into two groups: one group continued with conventional stimulation for six additional weeks while the other group had the AdaptiveStim feature activated and programmed. At the end of this six-week period, the two groups crossed over to the other treatment for an additional six weeks. The primary end point was based on a two-dimensional assessment of both improved pain relief and/or improved convenience. In the intention-to-treat analysis, 86.5% of patients met the primary success goal of improvement in at least one of these domains, with most perceiving improvement in pain relief and convenience. The majority (90.1%) reported they intended to use the device in adaptive stimulation mode (35,36).

Boston Scientific has recently won FDA approval for a new IPG (Precision Spectra, Boston Scientific, Valencia, CA, USA) that has four lead ports and can support a total of 32 electrodes. The manufacturer claims the new device and leads with advanced programming algorithms can provide more coverage of the spinal cord, and thereby increase therapy flexibility and physician control (37). No study supports the launch of this new device. Whether this extended coverage of the spinal cord results in greater pain relief remains to be proven in clinical trials.

TECHNOLOGICAL ADVANCES
Stimulation Targets

Just as the gate theory of Melzack and Wall propelled SCS, the slow unraveling of the complex pathophysiology of chronic pain has led to technological developments that exploit our growing knowledge to treat the many people who suffer chronic pain. It is clear that multiple anatomic sites, extending from the brain to the peripheral nerve endings, may be amenable to the application of neuromodulatory techniques to treat chronic pain. In the past decade, many observational reports have been published about neurostimulation of peripheral nerves to treat various pain complaints (38,39). These reports have led to a significant increase in the use of these techniques even though rigorous supporting evidence has yet to be published. Regulatory approval has not been granted in the United States (40). One company has received CE mark approval for peripheral nerve stimulation in the European Union (Medtronic, May 2011). Two clinical trials by Medtronic are currently under way in Europe and the United States to establish the efficacy of this therapy (41).

Recent basic science research has illuminated the role of the dorsal root ganglion (DRG), an intraspinal structure, in the propagation and maintenance of chronic pain. In the classic understanding of ascending pain pathways and processing, input emanating from the peripheral nociceptors passes along Aδ fibers and C fibers in the peripheral nerves to the cell body in the DRG and then enters the spinal cord at the nerve root, synapsing with the central nervous system and ascending pathways. Current understanding, however, is that the DRG function is much more than a simple way station for neuronal traffic (Fig. 1). Rather, the DRG has been identified as a key player in the neuropathophysiologic cascade of neuropathic pain (42). Trauma or other pathology can lead to increased sensory neuronal discharges of multiple mediators that ultimately cause hyperexcitability of the DRG cell membranes, causing them to fire pain messages without an external stimulus (43–45). This abnormal electrophysiologic excitability of the DRG has been described as the “primary cause of neuropathic pain” (40).

The DRG may be a useful target for SCS. It has a consistent location between the medial and lateral aspects of the pedicle and, with the appropriate device, can be accessed easily via the epidural space. Because the DRG is not enveloped in CSF, power requirements for effective paresthesia are reported to be about 5% of that required for conventional SCS (46). For the same reason, postural changes may not result in the dramatic changes in paresthesia threshold seen with SCS. Somatotopic mapping of the DRG reveals that very specific anatomic regions can be stimulated, yet convergent pathways exist that allow stimulation-based paresthesia to cover similar anatomic regions at different spinal levels (Fig. 1).

An investigational, fully implantable neurostimulation device that targets the DRG is currently undergoing clinical trials in Europe and Australia. Preclinical results are promising (43). A recently published observational study of ten patients in the United States reported an average reduction of pain by 70% against baseline measurement. Eight subjects completed the study; 75% reported at least 50% reduction in pain (47).

High-Frequency Stimulation

Since the first application of SCS, the basic treatment paradigm has been that the painful area must be overlapped with paresthesia to be successful. Most of the technological advancements in the past 40 years have been aimed at making this goal achievable. Now, however, emerging clinical research may challenge this dictum.
Clinical techniques using high frequency (HF) and burst stimulation, while unproven, may be promising for treating pain without paresthesia (48). A recently published open-label, European, multicenter clinical trial indicates that a novel spinal neuromodulation device using HF stimulation (2–10 kHz) may significantly reduce back and leg pain without inducing paresthesia (49). The authors of this study concluded that more than 70% of this cohort of subjects with difficult-to-treat chronic back pain experienced significant and sustained low back and leg pain relief. Notably, this was achieved without paresthesia. The device (Nevro Corp., Menlo Park, CA, USA) has received CE mark approval in Europe and Australia. A large clinical study in the United States is under way. Should such a system prove effective, the advantage will be that no sensory mapping would be required and uncomfortable or painful paresthesia and/or decreased pain relief associated with positional changes may be avoided. The device does require high power, and the investigators reported that the current investigational RIGP requires daily recharging, which could be burdensome to patients.

A recently published study by Perruchoud et al. compared HF stimulation (5 kHz) with sham stimulation to assess global impression of change as the primary outcome and pain intensity and quality of life as secondary outcomes in 40 subjects (50). Complete data were available for 33 subjects. The proportion of patients responding to HF stimulation was 42.4% compared with 30.3% of sham stimulation patients. The mean benefit of the HF vs. sham stimulation was not statistically significant. However, the “period effect” was highly statistically significant regardless of treatment received, with 51% of patients improving at visit three and 21.2% improving at visit five. The mean pain visual analog scale (VAS) was 4.35 with HF and 4.26 with sham. The mean EuroQol five-dimensional (EQ-SD) index with HF was 0.480 compared with 0.463 with sham. Long-term efficacy is yet to be established.

**Magnetic Resonance Imaging (MRI) Compatibility**

A significant technological handicap for patient and clinician acceptance has been device incompatibility with MRI. The patient population indicated for neuromodulatory devices has a higher MRI requirement than the general population (51). Intrathecal infusion systems have FDA-approved labeling for conditional MRI compatibility (MR imaging under specified conditions) and have been available for many years manufactured by Medtronic Inc. and recently by Codman and Flowonix (Mt. Olive, NJ, USA). Note that specific conditions for safe MR imaging vary among manufacturers. However, MRI-compatible SCS systems have only recently achieved FDA approval and CE mark (SureScan® neurostimulation system with Vectris leads, Medtronic Inc.) to allow full-body MR imaging under specified conditions. Lead heating, device damage, and unintentional stimulation as well as patient sensory concerns, including vibration or movement of the generator, have been the primary areas of safety concern (52). Thermal tissue damage due to lead heating from interaction with the RF energy of the MRI scanner is the most serious concern, and this appears to have been resolved by adding a shielding layer to the lead body, which dissipates the energy over the length of the lead (53). Other system modifications are incorporated to address the other areas of concern. All major manufacturers recognize this important need and are working toward MRI-safe products.

**Improving Clinical Outcomes**

Technological advancements do not always result in better outcomes and even the most elegant theoretical analysis when subse-quent applied to treatment strategies may not lead to significant clinical improvement (54–58). We are in a competitive era that continues to generate rapid innovation, persuasive marketing, and early adoption—but perhaps too often without evidence of improved clinical utility. At present, it is our opinion that the impact of clinical variables, such as the etiology and distribution of pain, timeliness of treatment, and presence of psychologic or other comorbidities, are better understood and may have a greater impact on successful treatment than the nuances of device selection (58,59). This is not to diminish the importance of ongoing technological advancement. Tantamount to this, however, is solid research that guides appropriate application of these various technologies to specific clinical problems with the goal of improved outcomes.

**INDICATIONS**

SCS has been used for a variety of pain conditions with the most common indications in the United States being failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS). Labeled indications are considerably broader in Europe, Canada, and Australia, where the evidence requirements for approval are different (58,60–88). As clinical experience and basic science have progressed, it has become apparent that the use of SCS in certain pathologies yields a higher success rate than in others. It can be anticipated that in the coming years the scope of indications where electrical stimulation has proved useful will expand.

**FBSS**

FBSS is the most common indication for SCS and constitutes approximately 70% of the patients treated. While several case series and meta-analyses have reported beneficial outcomes, two randomized controlled trials (RCTs) have been published (60,61,63). The primary outcome in both studies was the proportion of people who achieved 50% or greater pain relief compared with other treatments.

The PROCESS Study recruited 100 patients (52 patients were assigned to the SCS group and 48 patients to conservative medical management [CMM]) with follow-up at six, 12, and 24 months (60,61). Compared with the CMM group, the SCS group experienced improved leg and back pain relief, quality of life, and functional capacity, as well as greater treatment satisfaction (p ≤ 0.05 for all comparisons). North et al. demonstrated that patients initially randomized to SCS were significantly less likely to cross over than were those randomized to re-operation (five of 24 patients vs. 14 of 26 patients, p = 0.02) (63). Patients randomized to SCS significantly reduced opiate intake compared with those randomized to re-operation (p < 0.025). SCS was more effective than re-operation as a treatment for persistent radicular pain after lumbarosacral spine surgery, and in the great majority of patients obviated the need for re-operation.

**CRPS**

Kemler et al. investigated the effect of SCS in combination with physical therapy (SCS + PT) compared with PT alone (64–66,89). SCS + PT was significantly more effective than PT alone in reducing pain at six months and at two years. In the main analysis, based on an intention-to-treat principle, SCS + PT produced results similar to PT alone for pain relief and all other measured variables at five years.
follow-up. However, in a subgroup analysis, the results with regard to global perceived effect ($p = 0.02$) and pain relief ($p = 0.06$) in 20 patients with an implant exceeded those in 13 patients who received PT ($p = 0.04$). The precise cause for reduced effectiveness of SCS over time in this study is unknown but may have been influenced by a number of other factors including disease progression with pain increase in the SCS group, exaggeration of pain relief in the trial period, or the possibility that the PT group had some spontaneous improvement. However, a long-term study of 25 patients indicated sustained improvement in functional capability, quality of life, depression, and pain levels. The greatest improvements in functional capability were demonstrated in patients who received the intervention within the first year of symptom onset (88). A recent systematic review of the literature on neuromodulation for CRPS by Levy supports the clinical effectiveness of SCS for this condition (90).

**PATIENT SELECTION**

Careful patient selection is vital to the success of SCS therapy. Considerations include chronic pain; failure of conventional treatment for at least six months; corrective remedial surgery inadvisable; no major psychiatric disorder, including somatization; the ability to operate the device controls; the ability to give informed consent for the procedure; willingness to stop inappropriate drug use before implantation; and no secondary gain or litigation involved. Once the patient is deemed a suitable candidate, psychological testing is desirable (58,91).

The issue of chronic pain and psychiatric overlay continues to perplex clinicians and researchers. Conventional wisdom suggests significant untreated psychologic or psychiatric illness as a contraindication to implant (58). However, this also is problematic as it excludes a large group of patients who would otherwise stand to benefit. To date, no consensus exists regarding which psychologic characteristics to assess or tests to undertake (92). Most studies examining the matter lack long-term follow-up. Sparkes et al. pointed out that depression has been identified as a factor that reduces efficacy but as a condition that improved after successful SCS in other studies (92). Prudence, good judgment, and individual patient analysis are regarded as superior tools in assessing candidacy for therapy (92). A better appreciation of psychosocial issues and concomitant management is needed before instituting SCS therapy.

Although healthcare professionals are correctly concerned about falsely raising patients’ hopes of a “total cure” as a benefit of SCS, they must remain mindful of the patient’s level of acceptance and adjustment to their injury. The neuromodulation team must actively assist patients in setting realistic goals and expectations before implantation. Chiefly, patients must come to accept that SCS therapy offers largely symptomatic improvement, that pain generator(s) (if they exist) are not removed, and that any underlying defect—whether anatomic or functional—remains uncorrected.

**THERAPY COSTS**

In the past, concerns over the high initial cost of SCS, coupled with the limited availability of high-quality evidence, have hindered adoption of this therapy (67). In recent years, however, the tide has turned dramatically. High-quality evidence, consisting of RCTs and long-term observational studies, attests to the cost-effectiveness of SCS where initial expenditures are easily defrayed by postimplant healthcare cost reductions. Unequivocally, SCS therapy has been shown to improve a patient’s state of health and quality of life. When contrasted with competing interventional and noninterventional therapies, the promise of SCS grows even stronger (60–66).

Costs related to SCS include initial implantation costs (from approximately Canadian $32,000 to $60,000 depending upon implant site), annual maintenance costs, and complication costs. It is suggested that approximately 18% per year be added to initial implantation costs to cover annual maintenance and complications (12,29,68).

**Cost-Effectiveness**

There is a common misconception in the medical community that SCS is a costly therapy relative to other treatment options and that its efficacy is questionable. To dispel this myth, we present cost-effectiveness and efficacy studies for FBSS and CRPS, identify strategies to improve outcomes, and provide a preview of new and exciting developments in neurostimulation.

**FBSS**

Since 1997, various analyses have examined the medical costs of SCS therapy for FBSS compared with alternative regimens of surgical or nonsurgical interventions (29,69,93,94). Earlier studies focused on recovery of absolute costs without explicitly addressing quality of life. These revealed that initial hardware costs are recouped within 2.1 to 2.5 years (93,94). As SCS is now being rigorously examined through the lens of health-economics research, the paradigm has shifted to include an analysis of improvement in patients’ quality of life against society’s willingness to pay (WTP) for each year of perfect health. Only a handful of papers have addressed this issue (29,95).

Kumar et al. performed both deterministic and probabilistic sensitivity analyses and constructed a Markov model to simulate costs and quality-adjusted life years (QALYs) derived from EQ-5D over a ten-year period. They judged cost-effectiveness conservatively, using a maximum WTP threshold of Canadian $20,000 to $50,000/QALY (95). In this model, patients were divided into three cohorts: 1) successful treatment with SCS (success-SCS); 2) failed SCS after initial success, hardware explanted, and patient subsequently maintained on CMM (failed-SCS); or 3) CMM alone. The analysis confirmed that success-SCS is the most cost-effective strategy with a cost-effectiveness ratio (CER) of $18,504, followed by failed-SCS (CER: $39,998) (Table 1). Clinically, even if the effectiveness of SCS dissipates over three years, requiring hardware removal and revision to CMM, failure is more cost-effective than CMM, which is the least cost-effective option (CER: $46,180). The CER for successful SCS therapy is well below the societal WTP thresholds of $20,000 to $50,000 per QALY. The lower end of this range is often applied in Canada, whereas the higher end is commonly cited in the United States. Patients in the CMM strategy lost 3.51 QALYs over ten years compared with the success-SCS strategy, whereas patients in the failed-SCS strategy lost only 1.34 QALYs during the same time period. The sensitivity analyses revealed that the cost-effectiveness of success-SCS was exceptionally resistant to parameter uncertainty, remaining cost-effective compared with the alternatives throughout the analyses. Initially higher costs borne by the SCS group were recouped within two to three years (Fig. 2).

The net monetary benefit (NMB) analysis showed substantial savings for the SCS groups. In the case of success-SCS, the NMB was positive at a WTP $18,501. For failed-SCS and CMM, the NMB thresholds were much higher at WTP of $40,000 and $48,000, respectively (Fig. 3). The success-SCS strategy had a 99% probability...
of being cost-effective for WTP ≥ $5500. The rechargeable IPG system proved slightly more cost-effective than the primary cell IPG, with CERs of $15,672/QALY and $16,439/QALY, respectively (95). Analyses indicate that when the longevity of a primary cell IPG is less than 4.25 years, a rechargeable (initially more expensive) IPG is more cost-effective (96).

CRPS

Using probabilistic simulations, Kumar et al. (unpublished data) created a cost-effectiveness acceptability curve for CRPS (Fig. 4). Nonparametric bootstrapping methods were used to estimate the distribution of incremental costs and effects associated with SCS compared with CMM. The cost-effectiveness acceptability curve represents the probability that SCS is a more cost-effective alternative to CMM at various WTP thresholds. At a WTP threshold of $50,000/QALY, the likelihood that SCS will be more cost-effective than CMM in the management of CRPS is 85%.

Kemler et al. analyzed patient outcomes and healthcare costs over a 15-year period from the perspective of the U.K. National Health Services (65). The incremental cost-effectiveness ratio of SCS compared with CMM was £3562 per QALY, a finding that was robust across sensitivity analyses, with an 87% probability that SCS is cost-effective at a WTP of £30,000. These findings supported policymakers in endorsing SCS as a good CRPS treatment value for the money.

**Table 1. Cost-Effectiveness of Spinal Cord Stimulation (SCS).**

<table>
<thead>
<tr>
<th></th>
<th>Base case</th>
<th>Analysis</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Success-SCS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td>$104,197</td>
<td>$83,357</td>
<td>$125,036</td>
</tr>
<tr>
<td>Effectiveness (QALY)</td>
<td>5.63</td>
<td>4.50</td>
<td>6.76</td>
</tr>
<tr>
<td>Cost-effectiveness ratio (CER)</td>
<td>$18,504</td>
<td>$14,803</td>
<td>$22,205</td>
</tr>
<tr>
<td><strong>CMM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incremental cost</td>
<td>−$7,197</td>
<td>−$5,757</td>
<td>−$8,636</td>
</tr>
<tr>
<td>Incremental effectiveness</td>
<td>−3.51</td>
<td>−2.81</td>
<td>−4.21</td>
</tr>
<tr>
<td>Cost/effectiveness</td>
<td>$46,180</td>
<td>$36,944</td>
<td>$55,416</td>
</tr>
<tr>
<td><strong>Failed-SCS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incremental cost</td>
<td>$67,628</td>
<td>$54,103</td>
<td>$81,154</td>
</tr>
<tr>
<td>Incremental effectiveness</td>
<td>−1.34</td>
<td>−1.07</td>
<td>−1.60</td>
</tr>
<tr>
<td>Cost/effectiveness</td>
<td>$39,998</td>
<td>$31,998</td>
<td>$47,997</td>
</tr>
</tbody>
</table>

Successful spinal cord stimulation (success-SCS) proved to be the most cost-effective strategy (CER of $18,504/QALY), while conservative medical management (CMM) was the least cost-effective strategy (CER of $46,180/QALY). Even failed-SCS was more cost-effective than CMM, signifying that reversion to CMM after SCS is no longer effective is still more cost-effective than CMM alone. Patients in the CMM strategy lost 3.51 QALYs of ten years compared with the success-SCS strategy, whereas patients in the failed-SCS strategy lost only 1.34 QALYs (95).

QALY, quality-adjusted life year.
STRATEGIES TO IMPROVE OUTCOMES

Early Intervention and Reduced Wait-Times

Not long ago, SCS was perceived as a treatment of last resort, held in reserve for refractory chronic pain when most medically and surgically invasive therapies had failed (69). Longitudinal observational data reported by Kumar and Wilson support the use of SCS earlier in the management of neuropathic pain than commonly occurs (97). Regrettably, however, many patients are unable to achieve the full benefits of SCS therapy due to excessive delays in treatment. At Regina General Hospital, the time from symptom development to implantation averaged six years and patients underwent an average of 2.9 operations before evaluation for SCS (60). In the PROCESS study, more than 50% of patients had undergone more than one surgery, and the time delay since the last surgery was a mean of 4.7 operations before evaluation for SCS (98). North et al. reported that patients in a five-year follow-up study had been in pain for a mean of 11.7 years before treatment with SCS and had undergone an average of 3.1 previous operations (99). Despite long delays, wait-times have declined during the past three decades (Fig. 5).

Kumar et al. studied the impact of implantation delay and were the first to establish a clear, linear, inverse relationship between intervention success and implantation delay (58,88,91,100). Success rates decreased from approximately 85% for a delay of less than two years to approximately 9% at 15 years or longer (p < 0.001) (Fig. 6). This response to treatment may be related to adaptation of the nervous system to pain, learned behavior, or worsening/natural history of the underlying disease over time. The situation has improved, with patients now waiting approximately 4.5 years for an implant, which secures a success rate of approximately 45%. These data from Kumar et al. suggest that shifting the curve to the left to achieve a higher success rate of 75–80% appears to be possible when implantation occurs within two years of symptom onset (Fig. 7) (58,91).

Kumar et al. also found that the referral stream was inefficient, with the greatest delays attributed to anesthesiologists and orthopedic surgeons, whose treatment interventions further delayed implantation (100). By contrast, neurologists and neurosurgeons were quicker to recognize the efficacy of SCS in this patient population and were more likely to seek a timely referral. Crucially, this study indicates that

![Cost-Effectiveness Acceptability Curve: SCS vs. CMM](Figure 4. Acceptability of spinal cord stimulation vs. conservative medical management for treatment of complex regional pain syndrome. The cost-effectiveness acceptability curve represents the probability that spinal cord stimulation (SCS) is a more cost-effective alternative to conservative medical management (CMM) at various willingness-to-pay thresholds (x-axis). The probability of cost-effectiveness (which ranges from 0 to 1) is plotted on the y-axis. For instance, at a willingness-to-pay threshold of $50,000 per quality adjusted life year, there is an 85% likelihood that SCS is more cost-effective than CMM in the management of complex regional pain syndrome (Kumar et al. unpublished data).

![Spinal cord stimulation wait-times (months) for chronic pain sufferers during three decades.](Figure 5. Spinal cord stimulation wait-times (months) for chronic pain sufferers during three decades. Wait-times have improved over the past three decades. On average, however, patients with chronic pain experience a five-year wait-time from development of chronic pain to SCS implantation (60). In order to improve long-term outcomes with SCS, wait-times must continue to decline (Kumar et al. unpublished data).)
SCS therapy in order to deny coverage. One striking example is Washington State’s refusal to fund SCS on the pretext that it does not restore patients to their original functional status (67). In the past decade, there has been a tremendous growth in documentation supporting the safety and efficacy of neuromodulation therapies. The strength of these data has been confirmed by impartial third-party reviews, including the NICE, which provides guidance for the National Health Services in the UK (103). The NICE recommended that SCS be used as a treatment for chronic neuropathic pain after the failure of CMM and after a successful trial of stimulation. Similar recommendations have been echoed by the Institute for Clinical Systems Improvement, the European Federation of Neurological Societies, and the Reflex Sympathetic Dystrophy Syndrome Association (103–106).

The dilemma confronting various pain societies lies in public education, rallying political support and hospital administrators to recognize that SCS is a clinically established means of controlling chronic pain, with the caveat that SCS is adjunctive therapy not intended to restore all anatomic and physiologic functional loss caused by the initial pathology responsible for the pain in the absence of other treatment.

The elucidation of novel applications for SCS implicitly draws resistance, discomfort, and disagreement, as other new technologies have in the past. The reasons for this marked discrepancy between perceived efficacy and utilization likely include limited studies describing basic mechanisms of neuromodulation for the pathology in question, lack of RCTs demonstrating superior efficacy to a reasonable comparator, unfamiliarity, comfort level of referring physicians, lack of regulatory approval for some devices in some countries, and insurance coverage and reimbursement issues (87).

Reducing Complications

The long-term complication rate for SCS hovers around 18% and may be as high as 32% in the first six months (29,60,61). Clearly, there is room for improvement. Device manufacturers face this challenge and must commit further resources to developing technical solutions. Scrupulous implant technique and use of recommended anchoring techniques can also contribute to the improvement of these statistics. Complications can be divided into three categories: 1) hardware-related (27–30%), 2) biologic (3–5%), and 3) other (3–4%) (58,91,94,107,108). The most common hardware-related complications are lead migration (13%), fracture (9%), and hardware malfunction (3%). Biologic complications are related to infection (3–5%), CSF leak (0.3%), symptomatic hematoma (0.3%), or pain located at the incision, electrode, or IPG site. Battery exhaustion is not a complication per se, but primary cells, regardless of manufacturer, must be replaced every three to four years, depending upon usage.

New technology has the ability to reduce complication rates. With the use of octapolar leads and complex programming, surgical revision rates have been reduced from 15% to 3.8% (109). Novel fixation devices have recently been marketed to reduce the incidence of lead migration. Improved titanium and silicone anchors and tissue adhesive provide a holding force significantly higher than that of earlier generation silicone anchors. These tools help reduce lead fatigue and fracture risk (25,107,110).

Similarly, good operative technique is essential. Professional organizations need to ensure that practitioners performing neuromodulation procedures are adequately trained and skilled to perform these procedures safely and with a minimum of complications. An expert panel recommends intraoperative imaging such as

**Figure 6.** Long-term spinal cord stimulation success rates. The rate of success of SCS is inversely related to the time interval between the beginning of the chronic pain syndrome and the time of implantation. The success rate decreases from 85% with a delay of less than two years to approximately 8% if the delay is 15 years or greater. Reproduced with kind permission from Springer Science and Business Media from Kumar K, Wilson JR. Factors affecting spinal cord stimulation outcome in chronic benign pain with suggestions to improve success rate. Acta Neurochir Suppl 2007;97(1):91–99 (97).

**Figure 7.** Spinal cord stimulation success vs. failure (% of patients) as a function of implantation delay (years). Success and failure lines intersect at five years, indicating that, to achieve best results, patients should be implanted within five years of their symptoms onset. Reproduced with kind permission from Springer Science and Business Media from Kumar K and Wilson JR (97).

profound defects persist in timely disease recognition, patient management, and access to effective treatment (Fig. 8).

Concerning CRPS, an emerging stream of thought favors more aggressive use of neurostimulation before permanent dystrophic changes occur (88,96). In a study of 25 patients with CRPS, multiple regression analysis indicated that longer delays in seeking treatment or treatment at a later stage of the disease hindered optimal pain relief and limited improvements in functional status and depression ($r > 0.6$). Pain relief and health-status improvement were best achieved in patients treated within the first year of symptom onset (88). These findings are supported by the International Association for the Study of Pain Expert Group, which recommends institution of SCS as early as 12–16 weeks if conventional treatment fails (101,102).

**Education and Awareness**

Payers and regulatory bodies, at times, hide behind a cloud of misinformation, questioning the efficacy and cost-effectiveness of
C-arm fluoroscopy to increase flexibility in imaging of the placement of both the needle and lead (107). A paramedian, shallow angle (<45° of introduction) of insertion facilitates lead steering and helps minimize the potential for compression of neural structures as a result of bending of the relatively stiff lead. The recent introduction of the Epiducer lead delivery system (St. Jude Medical Inc.) enables the placement of multiple electrodes through a single point of entry and may reduce the need for a more complicated procedure (111). While promising, the long-term effectiveness of this tool has yet to be demonstrated either in clinical trials or clinical practice.

Time spent in the operating room for trial stimulation is time well spent in assuring optimal results, given that approximately 15–18% of patients fail trial stimulation (58,91,94,95). Intraoperative screening appears to have good predictive value for successful long-term control of chronic low back and/or lower extremity pain (107). One should try to obtain at least 80% paresthesia coverage of the painful area. Ideally, surgical lead insertion should occur using either spinal or local anesthesia, thus obviating the need to rely on radiographic confirmation or somatosensory-evoked potentials to ascertain proper placement when using general anesthesia. IPG selection is dependent on patient age, stimulation parameters, energy requirements during trial, and the probability of utilizing multiple programs.

A Multidisciplinary Approach

SCS must be conceived as part of, and not independent from, an overall treatment plan to manage chronic pain. Interprofessional collaboration is a requisite both before and during the course of SCS therapy. The challenge in assessing candidacy for SCS lies in the physician’s ability to engage patients, their families, pharmacists, nursing staff, and mental health experts so that realistic expectations are fostered and any outstanding issues frankly discussed. If implantation is accomplished, ongoing follow-up is needed and stimulation adjustment may be required to address patients’ changing needs and ensure optimal outcomes. The patient must be integrated into a rehabilitation program that addresses deconditioning and emphasizes building functional capacity, return to active employment if appropriate, and active participation in both domestic and social life. Additionally, SCS has the capacity to reduce the need for pharmacologic interventions, notably narcotic and non-narcotic analgesics (60,61,88). A weaning protocol and specially trained facilitators should be available.

An open dialog with patients is vital for continued therapeutic maintenance and timely surveillance. At our centers, patients are longitudinally followed by treating physicians in a neuromodulation clinic staffed with specially trained midlevel professionals who optimize neuromodulation therapy, offer ongoing counseling, and help to manage acute complications. This approach has produced high patient-satisfaction rates, aided research and academic inquiry, and generated expertise at the institutional level (58,88,91).

Realizing Functional Outcomes

Historically, the benefits of SCS were proved through a reduction in a patient’s perception of pain. The expectation has been that a 50% reduction in validated pain score during the trial period before proceeding to implant will be sustained postimplant. However, this measure is now regarded as highly variable and subjective, arbitrary, and a poor correlate of a patient’s quality of life (112,113). Consequently, a paradigm shift has occurred as clinicians and academics have changed focus to how SCS impacts patients’ ability to live their lives and contribute in their activities of daily living, whether social, economic, or domestic. Ultimately, it is on this metric that SCS therapy should be judged by patients, society, and payers alike (66,67,95).

Contemporary literature attests to the transformative capacity of SCS therapy for chronic refractory pain. It is therefore imperative that neuromodulation programs actualize and expand on documented success (60,61,68,114). Returning to work if appropriate and resumption of activities of daily living should be a goal set by...
physicians and their patients. Employment status, however, depends upon many factors beyond pain control, including the patient’s training and education, field of employment, work history, length of unemployment, overall physical condition, and age. While not documented by RCTs, retrospective analysis demonstrates and the authors believe that if SCS is offered earlier in the treatment continuum, more disabled patients will to be able to return to work (88). Even in a refractory population of patients with CRPS, five out of 25 patients returned to gainful employment (88). Harke et al. prospectively recorded an impressive 70% back-to-work rate (114). In the PROCESS trial, the gain in health-related quality of life was markedly greater in the SCS group, with a mean EQ-5D score difference of 0.25 (p < 0.001) and 0.21 (p < 0.001) at three and six months, respectively, compared with the CMM group (68).

THE FUTURE OF NEUROSTIMULATION

SCS has earned a well-established role in contemporary chronic pain management. Now, foundationally secure and resolutely grounded in evidence-based medicine, the future heralds an era of renewal and revitalization. SCS will undoubtedly move further up the treatment ladder of chronic pain conditions as new applications are realized (115). In many instances, however, innovation—whether technical or therapeutic—has outpaced the quality of clinical research. The indications for SCS therapy are growing, and the technology involved is rapidly advancing. However, the challenge lies in developing confirmatory scientific evidence to support this form of therapy. Practical limitations often arise due to difficulties in masking and randomization to control groups.

Technology: Costs and Outcomes

New technology has led to increased expenditures and while efficacy has been demonstrated, cost-effectiveness of advanced devices remains to be adequately assessed (116). Historically, single-lead arrays have been used to produce pain relief in both unilateral and bilateral pain of the upper or lower extremities. Presently, implanters have a choice between cylindrical leads (with up to 16 contact points) and paddle leads (with up to 20 contact points). Technological advances have led to the introduction and extensive use of multichannel leads that enable bipolar or tripolar stimulation and are considered superior (99,117–119). Cost-effectiveness, however, has yet to be proved.

More complex and efficient microprocessor-based equipment, consuming less power with improved efficiency, is being developed. To maximize patient comfort, the IPG footprint (size and volume) continues to decrease, with special attention paid to shape and form. However, with miniaturization of the IPG, capacitor size decreases, thus necessitating frequent recharging. Manufacturers must counter this limitation by devising novel devices that increase charging interval.

Improving axial back pain control remains a modern challenge. A fundamental hurdle is the lack of consensus over the definition of the term “back.” While official nomenclature is likely to be clarified soon under the auspices of the spine section of the Congress of Neurosurgeons, experts have informally divided the back into two segments in the meantime: 1) the “upper back” encompassing the lower margin of the rib cage to the level of the iliac crest; 2) and “lower back” defined from the level of the iliac crest to the sacrococcygeal junction. Preliminary results from a three-center, multinational collaborative study (unpublished data) indicate that the specified 5-6-5 (Medtronic Inc.) using the tripole configuration is effective in significantly reducing lower back pain in 50% of cases and upper back pain in 12%. A recent study by Rigoard et al. confirms that multicolumn leads can reliably generate back pain coverage and favorable pain relief outcomes (120).

The scientific community has yet to establish 1) the optimal number of contact points required to maximize clinical outcome (i.e., eight, 16, 20, 32 electrodes, or more); 2) the relevance of electrode spacing in stimulation depth of the dorsal column; 3) the extent to which current steering is improved by multiple independent current control, or whether each electrode contact having its own, dedicated power source matters; and 4) whether Holsheimer’s computer modeling is fully valid in clinical practice (16,18,31,55,119).

Networked Programming

Currently, SCS programming is an urban phenomenon due to lack of telemetry in less populated locations. With the impending genesis of networked programming and remote telemetry, physical distances will become less of a deterrent to neurostimulation. Sophisticated data collection and management will reduce the need for time-consuming and costly programming trials, adjustments, and associated travel. Once this challenge is met, distributed computing infrastructure will emerge. A local programming device communicating with a network device, such as a server that maintains a data base, offers distinct advantages in reducing the burden associated with executing complex programming algorithms and secure data storage (121).

Storage of programs within a common data base allows for sharing stimulation treatment information, which will enable a clinician to provide better results. The programmer may then access useful information, such as suggested programs or programming protocols, that are effective for the specific pain type and location. Using the information stored in the data base, the server might provide information that leads to testing fewer programs. Additionally, information collected from a large number and variety of cases is a useful research resource (121). As is the case for all electronic records, privacy issues must be thoroughly considered, and appropriate safeguards must be implemented.

Wireless Communication and Signal Integration

Lead wires contribute to the risk of lead fracture, and wireless systems could eliminate these complications entirely (122). Another exciting development involves the implementation of an integrated system that can acquire neuronal signals from spinal cord dorsal horn neurons, wirelessly transmit the signals to a computer/ receiver, and recognize nociceptive signals. The program is integrated with a wireless neurostimulator to form a feedback loop to recognize and inhibit these nociceptive signals, thus potentially abolishing the perception of pain (123).

Precise Programming and the Patient

The goal of neuromodulation has become precise targeting of electrically excitable neuronal structures within the spinal cord. Newer leads, for instance, enable upwards of 20 contact points, and the industry trend is to continue increasing the number of contacts. IPGs can now adjust the electric field in 1% increments and achieve tight spacing of contacts to within 1 mm (124). The neuromodulation system is thus claimed to have an unprecedented
degree of control and organization in both programming and lead placement. While this level of control is impressive, no clinical data exist to demonstrate whether it affects therapy outcomes. The true challenge of improving therapy delivery lies in achieving optimal paresthesia coverage during surgical placement and translating almost infinite programming possibilities into reliable, highly steerable, durable pain relief. Formal training programs complemented by standardized industry-supported continuing education are necessary to ensure uniformity of treatment with SCS and to actualize optimal outcomes.

New Applications

As technology and therapy continue to evolve, SCS could find broader acceptance in the management of more and more complex painful conditions. Stimulators could also become capable of generating simultaneous stimulation from a single source delivered at multiple levels (125).

Pulse Waveforms

There is an ability to control the amount of current flow from each and every contact along the lead. Newer modes of pulse waveforms could be developed to treat specific conditions. For instance, animal studies for urinary tract dysfunction indicate that charge-balanced waveforms are as effective in evoking detrusor contraction as monophasic square pulse waveforms. Thus, it could be beneficial in clinical practice to replace the monophasic pulse waveform by charge-balanced waveforms as the stimulation power, thus improving efficacy and lowering energy requirements (126).

Synergistic Therapy

In the future, it might be possible to combine SCS with implanted drug delivery systems within a single unit to produce synergistic effects while minimizing side-effects and complications (125). Up to 18% of patients fail trial stimulation ("nonresponders") and in some patients, the effect of SCS may diminish with time (64,127). Nonresponders do not receive permanent device implantation. Truin et al. discovered that the combination of SCS with a subtherapeutic dose of intrathecal ketamine in nonresponder rats converted them into SCS responders (128).

Schectmann et al. conducted a randomized, double-blind, placebo-controlled clinical trial of 10 patients experiencing neuropathic pain with insufficient pain relief with SCS alone (129). Active drugs and saline (control) were intrathecally administered by bolus injections in combination with SCS. Seven of 10 patients reported significant pain reduction when SCS was combined with active drugs. The mean VAS ratings were reduced by more than 50% with each drug combined with SCS.

It is of clinical interest to consider using a low dose of intrathecal agents in patients who do not respond to trial SCS. Furthermore, in the group of patients who do respond to SCS but where the benefit is slowly diminishing over time, additional pharmacologic treatment might be considered in order to prolong the pain-relieving effect of SCS (64,88,128).

CONCLUSIONS

SCS has been a commercially available therapy for more than 40 years. Its pace of adoption has expanded quickly as device technology has improved, complications have been reduced, and its effectiveness and cost savings have been demonstrated in randomized controlled clinical trials and long-term observational studies. The industry is in a phase of intense innovation characterized by miniaturization of devices, safety advances, improvements in recharging, adaptive stimulation to improve the patient experience of stimulation, experiments with alternative frequencies, and novel targets of stimulation. Neurostimulation has a strong pipeline, with a number of companies engaged in the development of novel products and studying new indications (130,131). Focused healthcare allocation coupled with research and development and growing disease burden is expected to drive future adoption.

REFERENCES

45. Kovalsky Y, Amir R, Devor M. Simulation in sensory neurons reveals a key role for
44. Lirk P, Poroli M, Rigaud M et al. Modulators of calcium influx regulate membrane
38. Richter E, Abramova M, Sure D, Alò K. Nerve root, sacral, and pelvic stimulation. In:
33. Braunschweig F, Mortensen PT, Gras D et al. Monitoring of physical activity and
28. Lam CK, Rosenow JM. Patient perspectives on the efficacy and ergonomics of
22. North R, Shipley J. Practical parameters for the use of spinal cord stimulation in the
18. Holsheimer J, Wesselink WA. Effect of anode-cathode configuration on paresthesia
58. Kumar K, Hunter G, Demeria D, Mohr M, Al¢ E, Kressin NR. Spinal cord stimulation in the
50. Perruchoud C, Eldabe S, Battenham A et al. Analytic efficacy of high-frequency spinal cord stimulation: a randomized double-blind placebo-controlled study. Neurolo-
48. Keeling RS, Abdi S, Holsheimer J. Effect of spinal cord stimulation, overall, and the
differing effect of spinal cord stimulation technologies on pain, reduction in pain
47. Kemler MA, Furnee CA. Economic evaluation of spinal cord stimulation for chronic
65. Kemler MA, Furnee CA. Economic evaluation of spinal cord stimulation for chronic
57. Slavin KV, Burchiel KJ, Anderson VC, Cooke B. Efficacy of transcutaneous tripo-
62. North RB, Kidd DH, Long DM. Spinal cord stimulation for chronic
54. Haddadan K, Krames ES. The effect of spinal cord stimulation, overall, and the
53. Manca A, Kumar K, Taylor RS et al. Quality oflife, resource consumption and costs
50. Perruchoud C, Eldabe S, Battenham A et al. Analytic efficacy of high-frequency spinal cord stimulation: a randomized double-blind placebo-controlled study. Neurolo-
48. Keeling RS, Abdi S, Holsheimer J. Effect of spinal cord stimulation, overall, and the
differing effect of spinal cord stimulation technologies on pain, reduction in pain
2002;5:156–166.
2007;8:S200–S275. Updated at
2007;8:S200–S275. Updated at
2006;103:533–540.
2006;89:1765–1771.