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Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: a 20-year literature review

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Object. The purpose of this report was to examine the available literature to determine the safety and efficacy of spinal cord stimulation (SCS) for the treatment of chronic pain of the trunk and limbs.

Methods. The author identified 68 studies that fulfilled the efficacy inclusion/exclusion criteria, grouped on the basis of pain indication, with an overall population of 3679 patients. Fifty-one studies fulfilled all safety inclusion/exclusion criteria. Based on the literature review, the author found that SCS had a positive, symptomatic, long-term effect in cases of refractory angina pain, severe ischemic limb pain secondary to peripheral vascular disease, peripheral neuropathic pain, and chronic low-back pain, and that, in general, SCS was a safe and effective treatment for a variety of chronic neuropathic conditions.

Conclusions. Despite the positive findings, there is an urgent need for randomized, controlled, long-term studies on the efficacy of SCS involving larger patient sample sizes.

KEY WORDS • spinal cord stimulation • chronic neuropathic pain • angina • failed–back surgery syndrome • complex regional pain syndrome • ischemic limb pain

THE use of implanted electrode–induced electrical stimulation was introduced in 1967 when Shealy, et al.,[87] used electrical stimulation to stimulate the dorsal columns to treat chronic, intractable pain. Since that time, dorsal column stimulation or SCS has been applied to a wide variety of pain disorders, including tumors, brachial plexus injuries, SCI, phantom limb pain, RSD, ischemic limb pain, multiple sclerosis, peripheral vascular disease, arachnoiditis, and pain after failed spinal surgery.[22,50,56,61,78,88,99] It has been estimated that 12,000 SCS systems are sold every year worldwide.[55]

Two different SCS systems are routinely used: those involving percutaneously placed electrode leads and those requiring laminectomies to allow placement of the electrodes. The first system involves the percutaneous insertion of electrodes into the epidural space and either transcutaneous connection to an external generator, allowing a trial period of stimulation, or subcutaneous connection to an implanted RF-controlled receiver or an IPG. The second system requires implantation of paddle-type leads into the epidural space after laminectomy. Similar to percutaneously placed electrodes, the electrode leads may be connected to an external generator, allowing a trial period of stimulation or may be connected subcutaneously to an RF receiver or an IPG. The RF receiver is activated by an external battery-powered transmitter, which operates through an antenna placed over the receiver. The IPG contains a battery that supplies power to the electrodes.

The exact anatomical placement of SCS leads depends on the location of the painful region. The SCS leads have been placed in locations from C-1 to L-5 to treat pain of the trunk and/or limb.[6] To achieve optimal pain relief effects, stimulation paresthesias should cover the area of pain.

Complications due to SCS may be technical or biological. The most frequently reported technical complications are electrode dislocation and breakage, as well as pulse generator or battery failures.[63,64] The most frequently reported biological complications are infection, CSF leakage, and pain located at the incision, electrode, or receiver site.[63]

The goal of this literature survey was to analyze the long-term benefits and risks of SCS for people with chronic neuropathic pain, including pain of the trunk and limbs, ischemic pain (peripheral vascular disease), or angina pain. The indications for SCS implantation, the proportions of patients that benefited from SCS, and the types and rates of complications were examined. Papers were identified by performing a MEDLINE search (January 1981 to the present) and were included after determining if they met detailed inclusion criteria. Articles were grouped according to the type of study and the indication for treatment. Finally, the indications most successfully treated by SCS therapy were also sought.

Abbreviations used in this paper: CABG = coronary artery bypass grafting; CRPS = complex regional pain syndrome; CSF = cerebrospinal fluid; IPG = implanted pulse generator; MRSA = methicillin-resistant *Staphylococcus aureus*; NHP = Norttingham Health Profile; NYHA = New York Heart Association; QOL = quality of life; RF = radiofrequency; RSD = reflex sympathetic dystrophy; SCI = spinal cord injury; SCS = spinal cord stimulation; VAS = visual analog scale.

Clinical Material and Methods

Literature Search

Two separate searches were performed of the available literature associated with the following key words or features: 1) electrical stimulation therapy, 2) IPG/RF stimulators, 3) articles published in English after January 1981, and 4) prospective randomized controlled studies; or 5) nonrandomized prospective studies; or 6) prospective no control studies; or 7) retrospective studies, 8) human experience, and 9) pain of trunk and limbs. Ovid was used first to search MEDLINE for pertinent studies published between January 1981 and the present. A second search was performed for articles published in the journal *Neuromodulation*, which was established in 1998 for the publication of articles specifically relating to the effects of electrical or chemical modulation on the nervous system. These articles were not identified by the MEDLINE searches, and thus a manual review was performed using the aforementioned search criteria.

Selection of Studies

Studies were examined for their inclusion in the efficacy analysis, safety analysis, or both.

Efficacy Analysis Selection Criteria. Criteria included the following. 1) Patients exhibited pain of the trunk and/or limbs. 2) Means, percentages, or statistics were reported by authors to be available. 3) The study was conducted to examine the effectiveness of SCS. 4) Pain measurements included the VAS, 50% or greater reduction in pain on a three- or four-point scale, number of angina attacks, and/or narcotic consumption or a comparison to relevant control group. 5) The number of patients studied was stated.

An article was excluded from the evaluation if it involved any one of the following criteria. 1) It was a review article, case study, or foreign-language article. 2) It included nonhuman animals. 3) Patients received implants before 1981.

Safety Analysis Selection Criteria. Criteria included the following 1) Patients exhibited chronic pain of the trunk and/or limbs and 2) complications were listed. An article was excluded from the evaluation if it met any one of the following criteria: 1) no complications were listed; 2) was a review article; 3) was a foreign-language article; or 4) included nonhuman animals.

Extraction of Data

Data were extracted from the articles according to the headings listed in Tables 1 through 5 (name of first author and date of publication, indication[s] for treatment and type of study, type of device, number of patients who received permanent implants and mean length of follow-up period, pain severity and narcotics consumption, and success rate). Papers in which angina pain was examined were also reviewed for the number of angina attacks and nitrate consumption.

Data regarding complications were also extracted from the articles.

Data Synthesis

Articles were grouped according to the following pain indications: 1) back and leg pain studies; 2) CRPS I or II pain studies; 3) ischemic limb pain studies; 4) angina pain studies; and 5) studies involving various pain diagnoses. Articles were then subgrouped by the type of study: 1) prospective randomized controlled or prospective nonrandomized controlled; 2) prospective noncontrolled; and 3) retrospective. Data obtained from studies in which investigators used similar success outcome measures were analyzed together. Similar outcomes were pooled and means and standard deviations calculated.

All studies in which complications were cited were included in the analysis. Complications were grouped according to type, including lead migration, infection, epidural hemorrhage, seroma, hematoma, paralysis, CSF leakage, over- or understimulation, intermittent stimulation, pain covering the area of the implant, allergic reaction, skin erosion, lead breakage, hardware malfunction, loose connection, other biological reaction specific to an IPG, and battery failure. The incidences of each complication were calculated.

Results

One hundred twenty-one articles were initially identified, from which 68, comprising 367 patients, fulfilled the efficacy inclusion/exclusion criteria. Grouped on the basis of the pain indication, these included 16 back and leg pain studies (Table 1), 12 CRPS I or II pain studies (Table 2), 13 ischemic limb pain studies (Table 3), 11 angina pain studies (Table 4), and 18 studies involving various pain diagnoses (Table 5). Fifty-one studies fulfilled all the safety inclusion/exclusion criteria. Four papers were included in the safety review that were not included in the efficacy review. Studies were grouped by complication type (Table 6), and included lead migration, infection, epidural hemorrhage, seroma, hematoma, paralysis, CSF leakage, over- or understimulation, intermittent stimulation, pain over the implant site, allergic reaction, skin erosion, lead breakage, hardware malfunction, loose connection, other biological reaction specific to an IPG, and battery failure.

Effectiveness of SCS Systems

Successful treatment in patients in whom SCS systems were implanted for chronic pain or ischemic limb pain was defined as either greater than 50% pain relief or significant reduction in VAS scores. In 49 studies reporting a long-term (> 6-month) success rate, investigators reported that 67% of the patients (2520) reported successful pain relief. When patients were grouped according to diagnosis, long-term success rates ranged from 57% (21 cases) in the SCI group to 83% (224 cases) in the CRPS I or II group (Table 7). Failed–back surgery syndrome, stump or phantom limb pain, and peripheral neuropathy were successfully treated in the majority of cases (62% [747 patients], 62% [eight patients], and 67% [36 patients], respectively), whereas SCS treatment of ischemic limb pain, CRPS I and II, and postherpetic neuralgia was associated with higher success rates (77% [629 cases], and 83% [224 cases], 82% [11 cases], respectively). In addition to pain reduction, the authors of 20 studies examined the effects of SCS on narcotic medication (or nitrate) intake. These authors reported that 345 (45%) of 766 patients had

TABLE 1

*Summary of studies involving SCS treatment for back and leg pain**

Authors & Year (study type)	Indication	No. of Cases Examined Long Term	Mean FU SCS Device	Length (mos)	Group (no. of cases)	No. w/ Reduced or Discontinued Narcotics at FU	SCS Pain Outcome
prospective controlled							
Marchand, et al., 1991	chronic back pain	8	IPG	NA	therapeutic SCS (8); placebo SCS (8)	not collected	pain scores significantly reduced ($p = 0.03$)
North, et al., 1995	FBSS	27	RF	6	SCS (12); back surgery (15)	not collected	significantly more crossed from surgery to SCS than vice versa ($p = 0.018$)
prospective w/out controls							
Leibrock, et al., 1984	lumbar arachnoiditis, root injury	11	RF	unknown		8 (72%) of 11	72%
Shatin, et al., 1986	low-back & leg pain	90	IPG	14.5		20 (54%) of 37	70%
LeDoux & Langford, 1993	FBSS	26		24		26% used daily compared w/ 61% at baseline	74%
Burchiel, et al., 1996	back & extremity pain	70	IPG/RF	12		not collected	56% successful; pain scores significantly improved over baseline ($p < 0.005$)
Ohnmeiss, et al., 1996	back & leg pain	40	IPG	24		21 (66%) of 32	26%; SIP significantly improved ($p < 0.05$)
Rainov, et al., 1996	FBSS	29	RF	29		not collected	86%
Kavar, et al., 2000	low-back & leg pain	25	IPG	18.5		6 (32%) of 19	56% successful; significant reduction in VAS score ($p < 0.05$)
Barolat, et al., 2001	FBSS	41	RF	12		not collected	88.2% successful
retrospective							
Waisbrod & Gerbershagen, 1985	FBSS	16	unknown	16		not collected	75
Probst, 1990	FBSS	92	unknown	54		40%	67%
Meglio, et al., 1994	low-back & leg pain	21	IPG/RF	45.5		not collected	62%
Fiume, et al., 1995	FBSS	34	IPG	55		19 (61%) of 31	56%
Devulder, et al., 1997	FBSS	69	IPG/RF	59		25 (58%) of 43	62%
Van Buyten, et al., 1999	FBSS	17	RF	9		76%	pain scores were significantly reduced over baseline ($p < 0.001$)

* FBSS = failed–back surgery syndrome; FU = follow up; NA = not available; SIP = Sickness Impact Profile.

TABLE 2

*Summary of studies involving SCS for CRPS I and II pain**

Authors & Year (study type)	Indication	No. of Patients Examined Long Term	SCS Device	Mean FU Length (mos)	Group (no. of cases)	No. W/ Reduced or Discontinued Narcotic Use at FU	SCS Pain Outcome
prospective controlled							
Kemler, et al., 2000	RSD	54	IPG	6	physical therapy (18); SCS & physical therapy (36)	not collected	pain scores significantly improved compared w/ control group ($p < 0.001$) & Pain Rating Index ($p = 0.02$)
prospective w/o controls							
Calvillo, et al., 1998	CRPS (upper extremity)	31	IPG	36		44.4% reduced by 50%	significant reduction in VAS score compared w/ baseline ($p < 0.0001$)
Oakley & Weiner, 1999	CRPS	16	IPG/RF	7.9		not collected	80% successful; significant reduction in VAS ($p < 0.05$)
Ebel, et al., 2000	CRPS (2 cases), phantom limb (1 cases)	3	IPG	36		not collected	100% successful
retrospective							
Broseta, et al., 1982	causalgia	11	RF	13		not collected	64% successful
Barolat, et al., 1989	RSD	15	IPG/RF	14		not collected	73% successful
Robaina, et al., 1989	RSD	6	unknown	10–36		5 (83%) of 6	100% successful
Robaina, et al., 1989	RSD, Raynaud syndrome	11	unknown	27		not collected	91% successful
Sanchez-Ledesma, et al., 1989	deafferentation pain, casualgia, RSD, postherpetic neuralgia	36	IPG/RF	66		80%	80% successful
Kumar, et al., 1997	RSD	12	IPG	41		not collected	100% successful
Bennett, et al., 1999	RSD	101 (30/71)	IPG/RF	18.7/23.5		not collected	70% quadripolar; 91% octopolar; significant improvement in VAS score in both groups compared w/ baseline ($p < 0.0001$)
Kemler, et al., 1999	RSD	18	IPG	32		not collected	57% much improved GPE score; significant pain reduction ($p < 0.001$)

* GPE = Global Perceived Effect.

TABLE 3

Summary of studies involving SCS for ischemic limb pain

Authors & Year (study type)	No. of Cases Examined Long Term	SCS Device	Mean FU Length (mos)	Group (no. of cases)	Reduced or Discontinued Use at FU	SCS Pain Outcome
prospective randomized control						
Jivegard, et al., 1995	51	IPG	18	SCS & oral analgesics (25); oral analgesics alone (26)	not collected	SCS pain scores significantly improved compared w/ controls ($p = 0.01$)
Klomp, et al., 1999	120	IPG	19	SCS & best medical treatment (60); best medical treatment (60)	medication significantly reduced in SCS group ($p < 0.05$) in short term	no intergroup difference; significantly reduced pain scored compared w/ baseline ($p < 0.001$)
prospective w/ controls						
Graber & Lifson, 1987	9	IPG/RF	7		not collected	80% successful
Horsch & Claeys, 1994	177	IPG	35.6		not collected	78% successful
Rickman, et al., 1994	25	IPG	6		not collected	72% successful
Petrakis & Sciacca, 2000	60	IPG	18		not collected	78% successful
retrospective						
Broseta, et al., 1986	37	RF	25		not collected	81% successful
Bracale, et al., 1989	27	unknown	unknown		not collected	80% successful
Fiume, et al., 1989	45	unknown	48		not collected	64% successful
Sampere, et al.,1989	17	IPG	2–27		not collected	71% successful
Francaviglia, et al., 1994	15	IPG	12–72		not collected	78% successful
Petrakis & Sciacca, 1999	150	IPG	71		not collected	75% successful
Huber, et al., 2000	17	IPG	32		not collected	100% successful

reduced their narcotics consumption at the time of follow-up examination.

Either a reduction in number of angina attacks, a decrease in the consumption of nitrate, or an improvement in QOL determined success for SCS-treated patients with angina pain. In a total of 11 studies investigators examined the effects of SCS on angina pain. A significant reduction in the number of angina attacks compared with baseline was reported in four studies. A long-lasting clinical response was documented in three studies, a significant improvement in NYHA class in two, a significant improvement on the NHP in one, and a significant reduction in hospital admission rates in one study. The authors of six studies found a reduction in nitrate consumption, which was significantly reduced compared with baseline in three studies.

Back and Leg Pain Studies. Sixteen studies, comprising 616 patients, were conducted to examine back and leg pain. Two were prospective controlled studies, eight were prospective without matched controls, and six were retrospective. Marchand, et al.,[59] examined patients with chronic back pain who acted as their own controls and were randomly assigned to receive either normal stimulation or placebo stimulation first. During four separate sessions, patients rated their pain in response to different stimulation parameters. In the first two sessions, the authors investigated clinical pain ratings, whereas in the last two sessions ratings of thermal pain were investigated. The authors found that pain scores were significantly reduced ($p = 0.03$) when using SCS compared with placebo.

In a prospective study North, et al.,[68] used a con-trol group but did not randomize their patients. They compared the results of two groups of patients with failed–back surgery syndrome, one undergoing SCS and the other undergoing additional back surgery. The primary outcome measure was the frequency of crossover, with patients permitted to cross over to the alternative group if the results of their procedure were unsatisfactory after 6 months. Significantly more patients crossed over from the surgery group to the SCS group (15 cases) compared with those that crossed over from the SCS group to the surgery group (two cases) ($p = 0.018$).

There were eight prospective studies without matched controls, and in these the overall success rate was 65% (332 cases).

Ohnmeiss, et al.,[71] found that only 26% of their patients experienced successful pain relief. They reported, however, that 65.6% reduced their medication intake, and that the QOL of the total group was significantly improved (according to results of the Sickness Impact Profile). They hypothesized that their pain scores may have been lower than those in other studies because they put more emphasis on increasing activity than on decreasing pain.

Six studies were retrospective without matched controls, and in these the overall success rate was 64% (232 cases). Van Buyten, et al.,[94] did not list their success rate, but they did report that pain scores were significantly reduced compared with baseline and that pain medication was reduced in 76% of their patients.

Complex Regional Pain Syndrome I or II Pain Studies. Of the 12 studies in which authors examined only CRPS I or II, one was a prospective controlled study, three were prospective without matched controls, and eight were retrospective in design. These studies comprised 260 patients.

In the prospective controlled study, Kemler, et al.,[44] examined the effects of SCS in patients with chronic pain in whom CPRS I (RSD) was diagnosed. Patients were randomly assigned to a group that underwent SCS and physical therapy or a group that received physical therapy alone. Outcome measures included pain measurements (VAS and McGill Pain Questionnaire) and QOL measurements (the NHP and short version of the Sickness Impact Profile). Patients were assessed at 1, 3, and 6 months, and data were analyzed using an intention-to-treat analysis. At 6 months, a significant improvement was demonstrated in the group assigned to receive SCS and physical therapy ($p < 0.0001$). The 24 patients who were actually treated with SCS exhibited a significant improvement in the pain component of the NHP ($p = 0.02$). No functional improvement was observed in either group.

Of the three prospective studies without matched controls, the overall success rate was 84% (19 cases). A study by Calvillo, et al.,[18] did not report a success rate, but they did find a significant improvement in pain scores compared with baseline.

In eight retrospective studies without matched controls, 192 patients (84%) reported success from SCS on one or both measures. In addition to pain reduction, the authors of two studies also reported a decrease in narcotic medication intake in a mean of 80% of patients.[80,83]

Ischemic Limb Pain Studies. Thirteen studies were classified as ischemic limb pain. Additionally, in four studies classified as those involving various pain diagnoses, investigators examined patients with ischemic limb pain. Of the studies in which authors examined ischemic limb pain only, two were prospective controlled studies, four were prospective without matched controls, and seven were retrospective in design. These studies comprised 750 patients.

Two studies were prospective randomized and controlled. Klomp, et al.,[45] examined 120 patients randomly assigned to either SCS with best medical treatment or best medical treatment alone. Critical limb ischemia was diagnosed in all cases. The purpose of the studies was to examine the effects of SCS on the treatment of ischemic pain and the avoidance of amputation. The mean follow-up period was 19 months. Analysis of results demonstrated no significant improvement in pain scores between the two groups. The quantity of pain medication in the short term, however, was significantly reduced in the SCS groups ($p < 0.05$). Jivegard, et al.,[41] also examined the effects of SCS in 51 patients with chronic limb ischemia. They randomized patients to a group receiving oral medication and SCS or one treated with oral medication alone. The authors found a significant improvement in pain scores in the SCS-treated group compared with the non-SCS-treated group ($p = 0.01$).

Four studies were found to be prospective without matched controls. Analysis of data demonstrated that a mean of 78% of the patients (271 cases) reported successful relief. Seven studies were found to be retrospective without matched controls. Analysis of these studies for success regarding one or both measures revealed that 76% of the patients (308 cases) reported success.

TABLE 4

Summary of studies involving SCS for angina pain

Authors & Year (study type)	No. of Cases Examined Long Term	SCS Device	Mean FU Length (mos)	Group (no. of cases)	Reduced or Discontinued Narcotics at FU	SCS Pain Outcome
prospective randomized controlled						
de Jongste, et al., 1994	17	IPG	2	SCS (8); delayed SCS (9)	significant reduction of nitrates compared w/ baseline ($p < 0.005$) and control ($p < 0.05$)	significant reduction in number of attacks compared to baseline ($p < 0.005$) & controls ($p < 0.05$)
Hautvast, et al., 1998	25	IPG	1.5	SCS (13); delayed SCS (12)	significant reduction of nitrates compared w/ baseline ($p < 0.01$)	significant reduction in number of attacks compared to baseline ($p < 0.01$) & controls ($p < 0.01$)
Mannheimer, et al., 1998	104	IPG	6	SCS (52); CABG (51)	both groups significantly reduced nitrate consumption ($p < 0.0001$); NS between groups	both groups w/significantly reduced angina attacks ($p < 0.0001$); no significance between groups; CABG group had higher mortality rate
prospective w/o controls						
Eliasson, et al., 1994	19	IPG	8		not collected	significant reduction in incidence of angina attacks ($p < 0.05$)
Sanderson, et al., 1994	23	IPG	45		9 tablets/day to 1.5 tablets/day	significant decrease in NYHA grade ($p < 0.01$)
Andersen, 1997	60	IPG	24		78%	78%
Bagger, et al., 1998	10	IPG	60		not collected	57% w/ long-lasting clinical response
Vulink, et al., 1999	26	IPG	12		not collected	significant improvement in NHP grade ($p < 0.05$)
retrospective						
Murphy & Giles, 1987	10	IPG/RF	unknown		100%	80%
Murray, et al., 1999	19	unknown	33		not collected	significant reduction in hospital admission rate ($p < 0.02$)
Ten Vaarwerk, et al., 1999	517	unknown	23		not collected	significant improvement in NYHA grade ($p < 0.01$)

Angina Pain Studies. Eleven studies were classified as involving angina pain, and comprised 830 patients. Three were prospective controlled studies, five were prospective with no matched controls, and three were retrospective in design.

Mannheimer, et al.,[58] examined 104 patients accepted for CABG. The patients were randomized to receive either CABG (51 cases) or SCS (53 cases). Results were compared on the basis of an intention-to-treat analysis. A significant reduction in the number of angina attacks and nitrate consumption was observed in both groups ($p < 0.0001$); however, there was no significant intergroup difference regarding these parameters. The CABG group was found to have a higher mortality rate. De Jongste, et al.,[24] examined the efficacy of SCS in treating angina pain. In this study, patients were randomized to active treatment with SCS or to a control group. In the control group an SCS device was not implanted until after the study period (2 months). At that time, these patients also received an SCS implant, and both groups were followed for 12 months. Both the incidence of angina attacks and the amount of nitrate consumed significantly decreased in the SCS-treated group ($p < 0.05$). In the remaining study to examine the effects of SCS on angina pain, Hautvast, et al.,[36] examined the efficacy of SCS in patients with stable angina pectoris. There was an SCS group and a control group in both of which the device was implanted; however, the treatment group was instructed to use the stimulator three times per day for 1 hour and additionally whenever angina-related symptoms occurred, whereas in the control group the device was inactivated. At the end of 6 weeks, the two groups were assessed. Compared with baseline and the control group parameters, a significant reduction in both the number of daily angina attacks and in the consumption of nitrates ($p < 0.01$) was demonstrated in the treatment group. The SCS-treated patients also exhibited an increased exercise duration and time to angina episode with exercise compared with the control group ($p < 0.03$ and $p < 0.01$, respectively).

Five studies were found to be prospective without matched controls. In all studies the authors reported a benefit. Eliasson, et al.,[28] reported a significant reduction in the number of angina attacks ($p < 0.05$). Sanderson, et al.,[84] reported a significant improvement on the NYHA grade and a reduction in nitrate intake. Andersen[2] and Bagger, et al.,[5] reported a long-lasting clinical response due to SCS in 78 and 57% of their patients, respectively. Vulink, et al.,[97] reported a significant improvement based on results of the NHP ($p < 0.05$).

There were three retrospective studies in this category. Murray, et al.,[66] found a significant reduction in hospital admission rates ($p < 0.02$), Ten Vaarwerk, et al.,[91] documented a significant improvement in NYHA class ($p < 0.01$), and Murphy and Giles,[65] reported that 60% of treated patients experienced a continued benefit, and nitrate consumption was reduced in all patients.

Studies Involving Various Pain Diagnoses. In 18 studies comprising a total of 1192 patients, the various investigators examined patients with a variety of pain diagnoses. Four studies were prospective without matched controls, and 14 were retrospective in nature. An analysis of the success rate found that 67% of the patients (51 cases) reported success. Alo, et al.,[1] did not report a success rate but found a significant improvement in pain scores compared with baseline. Daniel, et al.,[21] noted a success rate of only 24%. Their study relied on primitive SCS systems, had weak inclusion and exclusion criteria, and no predefined follow up.

Eighteen studies were found to be retrospective without matched controls. An analysis of these studies for success on one or both measures found that 59% of the patients (1062 cases) reported SCS-induced success. In one study the authors reported a success rate of less that 50%. The investigators, Cioni, et al.,[20] examined the efficacy of SCS in a population of paraplegic patients with chronic pain.

In addition to pain reduction, a decrease in narcotic intake was also documented in seven studies. A mean of 69% of the 344 patients reported a reduction in their narcotic consumption.

Safety of SCS Systems

The reported complications found in the literature search are summarized in Table 6, which includes data obtained from 51 papers comprising 2972 patients overall. Complications were categorized as follows: lead migration, infection, epidural hemorrhage, seroma, hematoma, paralysis, CSF leakage, over- or understimulation, intermittent stimulation, pain over the implant site, allergic reaction, skin erosion, lead breakage, hardware malfunction, loose connection, other biological reaction specific to an IPG, and battery failure.

Most complications were not life threatening and could usually be resolved by removing the device. The most common complication was lead migration. The most serious complication was paralysis, although only one case was identified. This occurred after a bacterial infection located at the lead tip.[61] Reports of subcutaneous hematoma were also found;[61] however, the three involved patients were undergoing anticoagulation therapy at the time of surgery.

Ohnmeiss, et al.,[71] described one patient with diabetic peripheral neuropathy who required the removal of the unit due to local skin erosion; however, the skin lesion resolved and an SCS unit was eventually replaced. Barolat, et al.,[9] reported on one patient in whom excessive positional changes were demonstrated in the stimulation threshold. Paresthesias were felt when in the supine position but were greatly reduced when standing or sitting.

There have been seven reported cases of aseptic meningitis associated with the implantation of an SCS system.[20,61,62] All cases resolved without permanent damage. Two of the cases resolved spontaneously, whereas the remaining five required the removal of the system. All reported cases of aseptic meningitis were treated at the same center.

In addition to complications, side effects such as headache, asthenia, and dizziness have been reported. In two patients with spinal cord lesion, SCS increased muscle spasms. Three patients described muscle twitches due to radicular stimulation, and in one patient muscular contraction resulting from activation of the pyramidal tract was observed.[61] Numerous case studies were identified in which complications occurred. These case studies were not included in the data analysis.

TABLE 5

*Summary of studies involving SCS treatment for various pain diagnoses**

Authors & Year (study type)	Indication	No. of Cases at Long-Term FU	SCS Device	Mean FU Length (mos)	Incidence of Reduced or Discontinued Narcotics at FU	SCS Success Rate
prospective						
Daniel, et al., 1985	mixed	17	unknown	12.9	not available	24%
Tesfaye, et al., 1996	peripheral neuropathy	7	RF	14	86%	86%, SCS pain scores significantly improved compared w/ baseline ($p < 0.05$)
Alo, et al., 1998	mixed	79	RF	30	not collected	pain scores significantly reduced compared w/ baseline ($p < 0.05$)
Villavicencio, et al., 2000	mixed	27	IPG	34	70%	89%
retrospective						
Garcia-March, et al., 1987	brachial plexus	6	unknown	28	not collected	50%
Koeze, et al., 1987	mixed	26	unknown	28	58%	50%
Meglio, et al., 1989	ischemic limb, low-back, paraplegic, deafferentation, postherpetic, & cancer pain	41	IPG/RF	12	not collected	80%
Simpson, 1991	mixed	60	IPG/RF	29	not collected	70%
Spiegelmann & Friedman, 1991	RSD, nerve root avulsion, postherpetic neuralgia, ischemic limb pain, FBSS, central deafferentation	28	IPG/RF	13	9 (69%) of 13	63%
North, et al., 1993	mixed	171	RF	84	58%	52%
Broggi, et al., 1994	mixed	232, 132, 68	IPG/RF	12, 24, 36	not collected	60%, 43%, 28%
Kupers, et al., 1994	mixed	70	unknown	42	not collected	52%
Van de Kelft & De La Porte, 1994	FBSS, ischemic limb pain, postherpetic neuralgia, peripheral nerve injury, phantom limb pain, spinal cord lesion	84	IPG/RF	47	91%	54%
Cioni, et al., 1995	paraplegic pain	9	unknown	37.2	not collected	44%
Hassenbusch, et al., 1995	arachnoiditis, epidural fibrosis, RSD, peripheral neuropathy, SCI	42	IPG (26), pump (16)	25	13 (81%) of 16	62%
Barolat & Ketcik, 1998	mixed	80	IPG/RF	45	not collected	51%
Kumar, et al., 1998	FBSS, ischemic limb pain, peripheral neuropathy, MS, RSD, spinal cord lesion, perirectal pain, cauda equina lesion, bone & joint syndromes, stump pain	189	IPG/RF	66	not collected	59%
Segal, et al., 1998	mixed	24	IPG	21	not collected	83%

* MS = multiple sclerosis.

A case of recurrent ulcerative colitis after SCS was reported by Kemler, et al.,[44] who described a patient with left-sided ulcerative colitis that was in remission and who experienced two successive relapses. These recurrences were thought to be related to the use of an SCS system.

Loubser[57] reported a case in which SCS adversely affected bladder function. This patient was undergoing SCS to reduce SCI-induced pain. The SCS was found to be causing urethral sphincter spasms resulting in urine retention and recurrent urinary tract infections. The author proposed that urodynamic function should be tested during trials of SCS in SCI patients.

Law[52] reported unexplained temporary paralysis in 1.8% of patients and multidermatonal, painful allodynia in 4.2%. The author hypothesized that this was due to cord ischemia caused by vasospasm, triggered by pain within or near the spinal canal. One possible way to prevent these complications is by selective injection of an epidural anesthetic.[52]

Finally, there have been some recent reports of interference that occurs when a patient with an SCS system enters an electromagnetic field created by a security system. In one such case the patient experienced permanent neurological injuries due to the uncontrolled activation of the cervical SCS device.[27]

Discussion

One of the main criticisms lodged against reports in the SCS literature has been the role of placebo. Because a patient cannot be blinded to the therapy, few well-controlled studies have been attempted to determine the effects of placebo in SCS therapy. In this literature survey eight prospective controlled studies were identified. Of these studies only one, that by Marchand, et al.,[59] attempted to control for the placebo effect. The authors examined the effects of SCS on patients with chronic back pain. They concluded that SCS did appear to affect pain; however, this effect was modest. The remaining studies involved either a best-medical-treatment control group or a delayed-treatment control group. In one study, Kemler et al.,[44] used a control group that received physical therapy; however, this treatment had been previously shown to be ineffective in this group. Therefore, the control group more closely resembled a nontreatment group. The study by Klomp, et al.,[45] compared SCS treatment with best medical treatment. The authors concluded that SCS, combined with best medical treatment, was no more effective than best medical treatment in preventing the need for amputation and in providing pain relief. Although there was a significant reduction in analgesic intake in the SCS group, its effect faded over time, and no intergroup difference in QOL was observed at any time point.

There are several studies conducted to investigate the short-term effects of SCS in angina pectoris.[24,36,84] In these studies it was suggested that the antianginal effect of stimulation may be secondary to an antiischemic effect. This effect may be secondary to a decrease in myocardial oxygen consumption or a redistribution of coronary blood flow. Furthermore, myocardial ischemia during treatment with SCS leads to anginal pain, and thus the treatment does not conceal symptoms of myocardial ischemia.[3]

Mannheimer, et al.,[58] compared patients with angina randomized to either SCS or CABG. A significant reduction in the incidence of angina attacks and nitrate consumption was documented in both groups; however, there was no significant intergroup difference regarding these parameters. The CABG group was found to have a higher mortality rate than the SCS group. In two other studies investigators examined the effectiveness of SCS on angina pain. Although they found a significant improvement with respect to the control group, because the control group did not receive any real treatment, it was really only equivalent to a baseline group.

Despite the lack of well-controlled studies and an understanding of the exact mechanism by which SCS produces its effect, SCS has become an indispensable therapeutic tool for treating many chronic pain conditions and has many benefits over alternate therapies. First, unlike ablative surgeries, the SCS device is completely removable. The SCS leads are placed in the epidural space remote from any neural tissue and can be removed at any time, causing little discomfort to the patient. Second, unlike the numerous systemic side effects of oral opioid agents, there are no long-term side effects of SCS use. Although intrathecal administration of opioid agents has greatly reduced the side effects seen with oral opioids, many complications remain, including pruritus, nausea, urinary retention, constipation, respiratory depression, and edema, as well as the additional complications due to the surgical procedure.

Treatment-Related Complications

Lead migration is the most common complication associated with SCS. Lead migration results in a loss of proper paresthesia coverage and a subsequent reduction in pain relief. Andersen,[2] reporting on the use of SCS for angina, found that the most frequent complication requiring repeated operation was lead migration (23%). The incidence was statistically lower in patients with quadripolar leads (11%) than in those with monopolar electrodes (45%) ($p < 0.003$). Because there was no difference in the frequency of electrode migration between the two types of electrodes, proper paresthesia coverage was most often recaptured by reprogramming with the multipolar leads. North, et al.,[67] reported SCS treatment in 62 patients with chronic pain. They found that surgical revision was necessary in 23% of the cases in which simple bipolar leads were placed to obtain optimal paresthesia coverage. Surgical revision, however, was required in only 16% of those cases with multichannel devices.

The introduction of multichannel leads has greatly reduced the need for repeated operation as the result of lead migration. North, et al.,[67] found that programmable multichannel systems have a significantly greater clinical reliability than single-channel systems. Alo, et al.,[1] reported that only 3.8% of their patients who lost paresthesia required revision of lead placement to improve capture. They claimed this was the result of using the eight-electrode lead and complex programming.

As with any surgical procedure, SCS involves the risk of infection. Although most infections that occur as a result of an SCS implantation can be resolved either with antibiotic therapy or with the removal of the SCS unit fol-

TABLE 6

*Summary of SCS-related complications culled from the literature**

Complication	No. of Events	Total No. of Cases	Incidence (%)
lead migration	361	2753	13.2
infection	100	2972	3.4
epidural hemorrhage	0	2972	0.0
seroma	0	2972	0.0
hematoma	8	2972	0.3
paralysis	1	2972	0.03
CSF leak	8	2972	0.3
unwanted stimulation	65	2753	2.4
intermittent stimulation	0	2753	0.0
pain over implant	24	2753	0.9
allergic reaction	3	2753	0.1
skin erosion	1	2753	0.2
lead breakage	250	2753	9.1
hardware malfunction	80	2753	2.9
loose connection	12	2753	0.4
battery failure	35	2107	1.6
other	38	2753	1.4

* Studies asterisked in the Reference list are used for this table only, and are not mentioned within the text of this paper.

TABLE 7

Summary of values after grouping studies according to diagnosis

Diagnosis	Overall Number			% Success
	Studies	Patients	Patient Months	
FBSS/low-back & leg pain	21	747	27,200	62
ischemic limb pain	14	629	24,394	77
CRPS I and II	13	224	7,237	84
peripheral neuropathy	4	36	1,620	67
SCI	5	21	615	57
postherpetic neuralgia	3	11	349	82
stump (phantom limb) pain	2	8	498	62
mixed	8	683	27,295	57

lowed by antibiotic therapy, life-threatening infections can occur. Torrens, et al.,[93] described one such case. This particular patient was found to have an MRSA infection. The authors suggested that the patient population typically identified for SCS systems may have a higher risk of MRSA infection because of frequent and prolonged hospitalization for severe neuropathic pain and antibiotic courses for various infections. In addition, they indicated that patients with diabetes mellitus are more susceptible to infection. The authors suggested that screening for MRSA colonization would help in identifying patients at risk for infection. Although one patient developed paralysis due to bacterial infection located at the lead tip,[61] this complication is extremely rare.

Cerebral spinal fluid leakage occurs after accidental dural puncture with the epidural needle, guidewire (lead blank), or leads during the surgical procedure. A CSF leak can lead to headache, which usually occurs in the early postoperative period. The characteristic features are those of headache that may be frontal or occipital, relieved by recumbency, and accompanied by tinnitus, diplopia, neck pain, and nausea. The headache is thought to result from decreased hydraulic support for intracranial structures.[15] Small dural punctures typically heal spontaneously and the headache can be treated conservatively.[48] An injection of autologous blood into the patient's epidural space is commonly used to treat dural puncture–related postural headache if conservative measures are unsuccessful.

Changes in stimulation may occur over time. These changes can be the result of cellular changes in tissue around the electrodes or temporary changes in the electrode position. There are reports in the literature of painful stimulation as well as cases of ineffective stimulation or loss of stimulation over time.

Barolat, et al.,[9] reported on one patient who experienced excessive positional changes in the stimulation threshold. Paresthesias were felt when in the supine position but were greatly reduced when standing or sitting. In a recent study, Cameron and Alo,[19] examined these postural effects in patients in whom a percutaneous SCS lead had been previously implanted. The mean threshold for paresthesia was lowest when recumbent, whereas in three patients it was lowest while sitting. The mean range and standard error of stimulation required to achieve paresthesias at all three posture levels was 0.51 ± 0.2 μC for leads in the cervical region (11 cases) and 1.52 ± 0.2 μC for leads in the thoracic region (19 cases). These changes in threshold with respect to posture were the result of spinal cord movement. When patients are lying on their back, their spinal cord moves ventral and therefore closer to the electrodes, reducing the level of stimulation needed to reach threshold. In addition to spinal cord movement, the thickness of the CSF layer can also affect stimulation thresholds. At the thoracic level, the CSF is reduced again, decreasing the distance between the electrode and the spinal cord.

Whenever there is a disruption of body tissue, temporary pain due to the healing process results. The typical location of the pain after an SCS is implanted is the incision site. Pain can also occur at the site of the implant. This type of pain usually subsides after 7 to 14 days. The actual tissue reaction resolves within 2 to 3 weeks. Tenderness can occasionally occur over the receiver site or at the connector at the spinous process. The latter does not resolve with time, but in many cases this tenderness does not require removal of the unit.

Although all the materials that come in contact with human tissue have been confirmed to be biocompatible, there have been documented cases of allergic reactions, which occur when there is an immune reaction to a foreign substance. When an allergic reaction does occur after the implantation of an SCS system, the implant must be removed. This complication is very rare. Diabetic peripheral neuropathy can result in pain of the extremities and has become an indication for the use of SCS. Peripheral neuropathy, however, can also result in skin incidents, which can be exacerbated by an implant. When skin erosion can be attributed to the IPG or receiver, the device is usually removed.

Device failure can be classified into several subsets, including electrode breakage, hardware malfunction, and loose connections. Overall, 227 of these failures were the result of lead breakage, 77 of hardware malfunctions, and 12 of a loose connection.

In addition to the complications summarized in Table 6, Heidecke, et al.,[37] specifically focused on hardware failures associated with SCS for failed–back surgery syndrome. They performed a retrospective analysis of 42 patients with failed–back surgery syndrome examining only hardware failures. These patients had undergone implantation of a Medtronic RF system. The most common hardware-related problem was lead breakage (eight cases). In addition, he found two cases of extension cable breakage and two cases of receiver insulation failure at the plug connection site.

Because the battery of an IPG is located within the device, when it is depleted, replacement requires repeated operation. When a battery requires replacement before the expected date (determined by the parameters being used by the patient), it is considered a battery failure. Battery failure occurred in 32 (1.7%) of the 1900 cases, although in 22 of 32 cases battery failure occurred after more than 3 years.

Efficacy of SCS

Spinal cord stimulation systems are relatively simple to implant, with many of the stimulation parameters being controlled by the patient. This has led to the use of SCS in a wide array of painful conditions, often without regard to the underlying origin or pathophysiology.[23] Thus, the authors of numerous early reports published success rates ($>$ 50% pain relief) in fewer than 25% of the implant-treated patients. The main reason cited for this low success rate was the diverse group of pain conditions treated with SCS and the use of poor patient selection criteria. Since that time, more stringent selection criteria have been followed. It is now recognized that the most appropriate patients for SCS are those with chronic, nonmalignant pain of neuropathic origin.[89] Another important selection criterion is psychological condition. Patients are now routinely screened to eliminate those with major personality disorders, secondary gain issues, or drug abuse indications.[17,32,77]

Although the SCS literature remains weak due to lack of placebo-controlled trials, it was found in the present literature survey that a number of studies supported the effectiveness of SCS for the treatment of certain chronic pain syndromes. Of the eight prospective controlled studies, a positive effect of SCS was noted in three. In the study by North, et al.,[68] although it was preliminary and lacked randomization, the authors found that a significant number of patients crossed over from the surgery to the SCS group. Jivegard, et al.,[41] reported a significant reduction in pain due to peripheral vascular disease in the SCS group compared with the control group. Finally, Mannheimer, et al.,[58] demonstrated that SCS and CABG were equally beneficial in reducing the number of angina attacks, while also being associated with a lower mortality rate.

The efficacy of SCS was further supported by the remaining 61 reviewed studies. Based on these studies the most common disorder treated with SCS was low-back and leg pain (with or without surgery). The success rate in this population of 747 patients was 62%. The next most frequently treated disorder was ischemic limb pain (peripheral vascular disease) with a success rate of 77%. Complex regional pain syndromes I and II were found to be the third most commonly treated disorders involving SCS. These patients respond best to SCS, with a success rate of 84%. Angina pain also favorably responded to SCS. In all studies involving examination of the effectiveness of SCS on angina pain, the investigators found significant improvement compared with baseline.

Although few randomized controlled studies examining the efficacy of SCS have been reported, there is a paucity of hard evidence to support overwhelmingly the use of SCS in the treatment of most chronic pain conditions.

Conclusions

Based on review of the studies examined in this survey, it is difficult to make any definite conclusions regarding the long-term efficacy of SCS in different chronic pain conditions. There is some evidence to indicate that SCS has positive, symptomatic, long-term effects on refractory angina pain, severe ischemic limb pain secondary to peripheral vascular disease, CRPS I and II, peripheral neuropathic pain, and failed–back surgery syndrome pain. There is an urgent need for proper, randomized, controlled, long-term studies of the efficacy of SCS involving a sufficient number of patients.

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Tracy Cameron is an employee of Advanced Neuromodulation Systems, Inc., and adjunct faculty at University of Texas Southwestern Medical School. The former designs and manufactures medical devices for chronic pain.

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