Volume 11 • Number 3 • 2008
http://www.blackwell-synergy.com/loi/ner

ORIGINAL ARTICLE

Spinal Cord Stimulation Has Comparable Efficacy in Common Pain Etiologies

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ABSTRACT

Objectives. The probability of success with spinal cord stimulation (SCS) depends largely on appropriate patient selection. Here, we have assessed the predictive value of pain etiology as it relates to pain relief with SCS as part of a prospective multicenter clinical trial. **Methods.** Sixty-five subjects with chronic and intractable pain tested an epidural SCS system. Subjects reported pain ratings (visual analog scale) with stimulation off and stimulation on at scheduled follow-up visits for up to 18 months after activation of the system. Visual analog scale scores were averaged and stratified by dominant pain etiologies, comprising failed back surgery syndrome, complex regional pain syndrome, and a subgroup of subjects with miscellaneous other pain etiologies. **Results.** More than 70% of subjects in each subgroup had successful outcomes during the temporary trial period and similar percentages of subjects from each etiology subgroup subsequently went on to permanent implantation. After permanent implantation, all subgroups reported more than 50% pain relief, on average, at each follow-up time point. No predictive value of pain etiology was observed. **Conclusions.** Spinal cord stimulation is an effective therapy for neuropathic pain arising from a variety of causes. Failed back surgery syndrome, complex regional pain syndrome, and pain of other etiologies responded equally well to SCS.

KEY WORDS: *Back pain, complex regional pain syndrome, dorsal column stimulation, electrical stimulation, failed back surgery syndrome.*

Introduction

Since its first report in 1967, debate about spinal cord stimulation (SCS) therapy for chronic pain has centered on strategies to improve its efficacy (1). Although results were variable when the technology was first introduced, the clinical efficacy of this treatment modality has dramatically increased due to improvements in technology, surgical techniques, and patient selection (2–4). Indeed, recent registry data reported that 87% of SCS patients consider SCS to be a valid treatment for their condition and would make the same choice again (5). Today's typical SCS patient can reasonably expect a 60% or better chance of successful pain reduction, which is typically defined as greater than or equal to 50% relief of baseline pain (3,6,7). It is important to note, however, that in published reports regarding adequacy of pain relief with SCS, "success" may refer to the percentage of subjects electing a permanent implant after a temporary trial period, or

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Dr. Oakley died on April 18, 2006, and is greatly missed.

alternately, the degree and stability of pain relief over time after permanent implantation (6).

Some published reports have attempted to identify patient selection criteria that may be predictive of good outcome with SCS, such as pre-implant psychological profiles, results of diagnostic procedures such as sympathetic blockade and somatosensory evoked potentials, and pain relief during a temporary SCS trial (8–13). Pain etiology also has been examined as a possible predictor of SCS efficacy. SCS is generally recognized to be best suited for pain of neuropathic origin (14,15). In the United States, SCS is most commonly used for treating back and leg pain secondary to failed back surgery syndrome (FBSS) and pain associated with complex regional pain syndrome (CRPS) (16–19). Recent reviews of the literature concluded that SCS can successfully relieve pain in both syndromes, although few well-controlled studies exist and no studies have directly compared outcomes of subjects with each condition (20,21).

Spinal cord stimulation is most often initiated after one or more unsuccessful conservative procedures; a majority of patients realize modest or good pain relief (22). A 2005 report of a randomized clinical trial discussed the efficacy of spinal cord stimulation vs. re-operation for subjects with the chronic pain of FBSS. More SCS subjects (9 of 19 subjects) than re-operation subjects (3 of 26 subjects) reported satisfactory pain relief. Subjects also had the option to cross over and receive the other treatment option; fewer SCS subjects (5 of 24 subjects) elected to cross over than those subjects originally randomized to the re-operation group (14 of 26 subjects). Six of the 14 subjects who failed re-operation later went on to successful pain relief with SCS (23).

One randomized clinical trial of subjects with CRPS examined the relative efficacy of SCS plus physical therapy vs. physical therapy alone. Thirty-six subjects were randomized to the SCS group; 24 of these subjects went on to permanent implantation of the SCS system after a successful temporary trial period. Eighteen subjects were assigned to physical therapy alone. After six months, average pain scores of the SCS group significantly improved relative to the physical therapy-alone group (24). The improved outcome persisted for up to two years, suggesting that with careful patient selection and a successful temporary trial, SCS may provide a more attractive option than physical therapy for patients with CRPS (25).

The purpose of this report is to present new information on the predictive value of pain etiology for pain relief outcomes with SCS. A prospective study using SCS for the treatment of chronic, intractable pain of the trunk and/or legs was conducted with subjects suffering from FBSS, CRPS, and a variety of other neuropathic pain conditions. Data were stratified by diagnosis subgroups to assess the relationship between the etiology of pain and the short-term and long-term success of SCS. The data presented here are re-analyses of already-published data. More detailed information about study conduct and outcomes can be found in the previous report (26).

Methods

Subjects

Sixty-five subjects were recruited from investigators' practices under ethics committee approval at seven geographically diverse clinical pain management sites in the United States. In all respects, this study was conducted pursuant to the Declaration of Helsinki.

Study Design

The design of this study has been described in detail elsewhere (26). Briefly, subjects reported baseline levels of pain on a 10-cm visual analog scale for pain (VAS; 0 cm = no pain, 10 cm = worst imaginable pain) (27–29). Subjects were implanted with an epidural percutaneous SCS system (Precision™; Boston Scientific Neuromodulation, Valencia, CA, USA). All subjects underwent a temporary trial period using an external stimulator. Dependent on adequate pain relief during the trial, a permanent SCS system with one or two percutaneous lead(s) was implanted and activated. At follow-up visits (2-week, 3-, 6-, 12-, and 18-month post-activation), subjects repeated their pain ratings on the VAS. Pain scores over the past week, with stimulation and without stimulation, were gathered at each visit.

Statistical Analyses

Descriptive statistics were calculated including the number of observations, mean, standard error of the mean (SEM), treatment effect ($VAS_{stimulation\ off} - VAS_{stimulation\ on}$), and confidence interval. Hypothesis testing of pain rating data was performed using single factor analysis of variance (ANOVA) (Microsoft Excel, Redmond, WA, USA), and survival analysis log rank tests for numbers of days with pain relief above 50% (SAS, Cary, NC, USA). All significance levels were set at $p < 0.05$.

Results

Subjects

Demographics

A total of 65 subjects were enrolled. The sample included 39 men (60%) and 26 women (40%), with an average age of 52.0 years (range: 28–84 years). Forty subjects were diagnosed with FBSS, nine subjects with CRPS, and 16 subjects experienced pain arising from a number of different other etiologies.

Subject enrollment was graduated over a period of 15 months; when the study was closed by the sponsor,

TABLE 1. Demographics of All Enrolled Subjects, Including Sex, Age at Implant, and Etiology of Pain. Numbers of subjects in each group at each time point also are presented; fewer subjects participated at later time points due to study closure, not attrition

Enrolled subjects	Male	39	60%
	Female	26	40%
	Mean age at implant(years)	52	
Etiology of pain	Failed back surgery syndrome (FBSS)	40*	62%
	Complex regional pain syndrome (CRPS)	9	14%
	Other	16	25%
	Radiculopathy/neuropathy ($N = 4$)		
	Scoliosis/spinal stenosis ($N = 1$)		
	Amputation pain ($N = 1$)		
	Vascular disease ($N = 1$)		
	Unknown ($N = 9$)		
	Total	65	100%

Numbers of subjects

	Visit						
Group	Baseline	Activation	2-week	3-month	6-month	12-month	18-month
FBSS	28	28	27	22	21	8	2
CRPS	8	8	8	7	5	1	0
Other	13	12	12	9	7	3	2

*Three FBSS subjects each had one additional pain complaint: postoperative pain, cauda equina syndrome, and coccydynia.

subjects had completed varying numbers of follow-up visits. Thus, fewer subjects participated in follow-up visits at later time points, especially at 12- and 18-month postactivation. Withdrawal rates were low; instead of attrition, the apparent diminution in participation at later time points was an artifact of a hard cut-off for study activities (Table 1) (26).

Pain Relief Outcomes During Trial Period

All 65 enrolled subjects underwent surgical procedures to place trial leads in the epidural space. Table 2 shows average VAS scores during the trial period for all subjects, stratified by pain etiology. In general, SCS relieved a substantial portion of subjects' pain. Subjects rated their pain before SCS implant (baseline), and at later time points with stimulation turned off, as approximately 8 on the VAS (0–10). With stimulation, subjects reported pain scores of 3–4 on the same scale. No statistically significant differences between the VAS scores of the three diagnosis subgroups were found at any time point (all ps > 0.05). Figure 1 summarizes these data graphically.

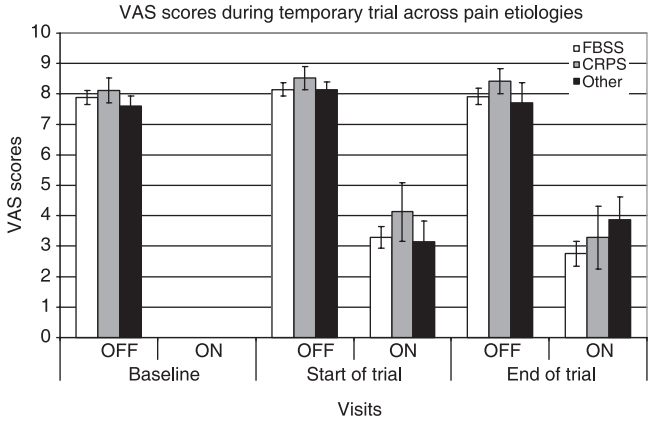

FIGURE 1. The trial-period visual analog scale (VAS) scores with stimulation on (ON) and stimulation off (OFF) at baseline, initial activation of the trial leads (start of trial), and the follow-up visit at the end of the trial for all subjects, based on etiology of pain. No statistically significant differences in pain relief scores between the three diagnosis-based subgroups were found (ps > 0.05). Column heights represent means ± SEM.

Ultimately, 16 subjects (12 with FBSS, one with CRPS, and three with other types of pain) withdrew from the study after the temporary trial period. Most subjects cited ineffective therapy as the primary reason for withdrawal; no pattern of reasons for withdrawal was found between the pain etiology groups. The 49 remaining subjects (75% of the total sample) proceeded to a permanent implant. Across the diagnosis subgroups, 70% of subjects with FBSS (28 of the 40 enrolled subjects), 89% of subjects with CRPS (eight of nine enrolled subjects), and 81% of subjects in the group with pain of other etiologies (13 of 16 enrolled subjects) received permanent implants.

Stimulation-on VAS scores of subjects who withdrew after the trial period were high, indicating poor pain relief, relative to the VAS scores of subjects who proceeded to permanent implants (Fig. 2). Due to small numbers in some subgroups, however, hypothesis testing to elucidate

TABLE 2. Effectiveness of Stimulation During the Trial Period, Based on Etiology of Pain. On average, SCS use was associated with pain relief for all pain etiologies. No relationship between diagnosis and outcome was found

	FBSS ($N = 40$)					CRPS ($N = 9$)					Other ($N = 16$)				
	Baseline	Start of trial		End of trial		Baseline	Start of trial		End of trial		Baseline	Start of trial		End of trial	
Visit	$N = 40$	$N = 37$	$N = 37$	$N = 33$	$N = 33$	$N = 9$	$N = 9$	$N = 9$	$N = 9$	$N = 9$	$N = 16$	$N = 16$	$N = 16$	$N = 16$	$N = 16$
Stimulation	OFF	OFF	ON	OFF	ON	OFF	OFF	ON	OFF	ON	OFF	OFF	ON	OFF	ON
Average VAS score	7.89	8.15	3.29	7.92	2.75	8.11	8.51	4.12	8.42	3.29	7.60	8.15	3.13	7.71	3.88
(± SEM)	(0.23)	(0.22)	(0.36)	(0.27)	(0.41)	(0.40)	(0.39)	(0.95)	(0.41)	(1.03)	(0.35)	(0.25)	(0.70)	(0.64)	(0.73)

Numbers of subjects experiencing improvement of VAS scores during stimulation

	FBSS		CRPS		Other	
	Start of trial	End of trial	Start of trial	End of trial	Start of trial	End of trial
Pain relief (%)						
90–100	4	6	2	1	4	3
80–89	6	6		3	3	1
70–79	4	7	1	1	1	2
60–69	6	1	1	1	1	1
50–59	5	3			1	2
40–49	4	3	1	1	2	
30–39	2	3	2			1
<30	6	4	2	2	4	6
Missing data	3	7				

CRPS, complex regional pain syndrome; FBSS, failed back surgery syndrome; SCS, spinal cord stimulation; VAS, visual analog scale.

differences between groups was not performed. Regardless, graphical trends clearly demonstrate that the averages of the three pain etiology groups were similar.

Pain Relief Outcomes After Permanent Implantation

Outcomes Based on Diagnosis

The majority of enrolled subjects received permanent implants and were followed for up to 18 months after activation of the permanent SCS system. Qualitatively, subjects of all etiologies had good pain relief outcomes across all time points, with stimulation-off scores of approximately 7–9 on the VAS scale and stimulation-on scores of approximately 2–4 (Table 3 and Fig. 3, top). The treatment effect, which we defined as the difference score of $VAS_{stimulation\ off} - VAS_{stimulation\ on}$, therefore, showed an improvement of approximately 5–6 VAS points after permanent activation (Fig. 3, bottom). We tested the null hypothesis that the means of the three groups were equal with ANOVA at each time point (stimulation off and stimulation on, separately). No statistically significant differences in pain scores were found between the pain etiology groups (all Fs < 2.8, all ps > 0.05).

Because this inconclusive statistical finding may have been the result of a type II error, we endeavored to determine whether the pain etiology groups were equivalent in terms of clinical outcomes. We reasoned that if the 95% confidence intervals around the mean treatment effect of each group fell within a range of VAS points that were not clinically distinguishable, then the groups were likely equivalent (see examples in Fig. 4). According to a recent report, patients with chronic back pain report that an improvement in two VAS points is the minimum change that is clinically important; therefore, an improvement of less than two VAS points in not clinically relevant (30). Given this, we plotted the treatment effect scores for each group, normalized to the overall means for each time point, over a two-VAS-point reference zone of "clinical indifference" (Fig. 4). Beginning with activation of the device and progressing through the six-month follow-up, all groups were clinically equivalent (eg, means and entire 95% confidence interval ranges were within two VAS points). The results at 12- and 18-month follow-ups also suggested clinical equivalence because the upper- and lower-bound limits of the 95% confidence intervals of each group fell within the two-VAS-point reference zone; however, these data are more ambiguous because some means were more extreme. Small numbers of subjects contributed to the trends at the later time points (Table 1); larger samples may have generated different results.

Survival Analysis

The durability of pain relief was assessed in all subjects with permanent implants. The duration of response for

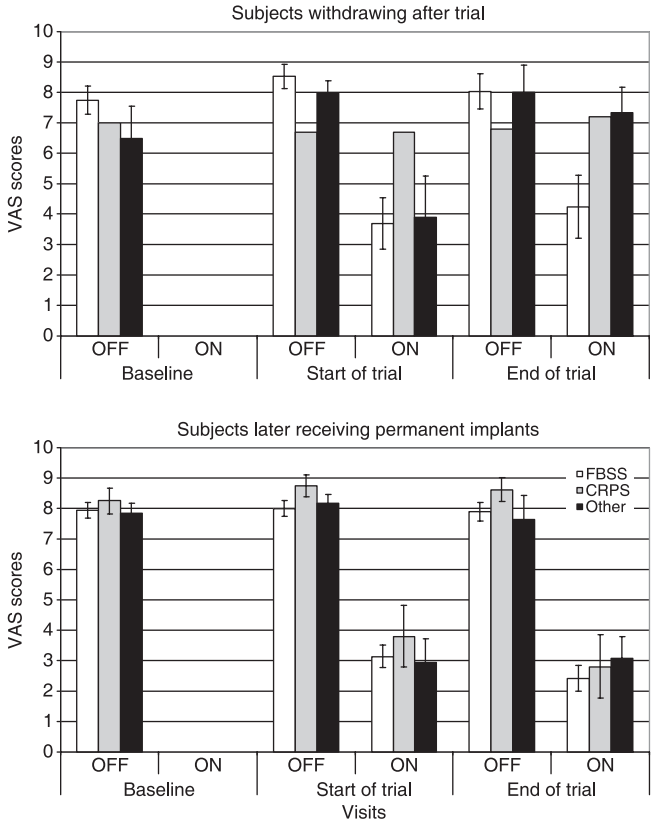

FIGURE 2. The trial-period visual analog scale (VAS) scores presented in Figure 1 are separated here into those subjects who withdrew after the trial (top) and those who later received a permanent spinal cord stimulation (SCS) system (bottom). Subjects who withdrew after the trial reported less, and more variable, pain relief than those who chose to be implanted with a permanent SCS system. Column heights represent means ± SEM. No error bar indicates that column represents data from one subject. Baseline scores were calculated independently for each cohort.

each subject was defined as the days elapsed from the date on which 50% or better pain relief was first reported until the first of two consecutive reports of 50% less pain relief, or the end of the study. The duration of response for subjects who never reported greater than 50% pain relief was defined as zero days. The Kaplan–Meier median duration of response for subjects with FBSS was 343 days (95% confidence intervals: 163 days—upper limit could not be estimated). The median duration of response for subjects with CRPS and pain of other etiologies could not be estimated because the Kaplan–Meier estimator for these data never reached a failure probability greater than 0.50. A log rank test showed no statistical difference in median duration of response in the three pain etiology groups ($p = 0.91$). A Kaplan–Meier survival analysis plot of the duration of response in each etiology group is presented in Fig. 5.

Discussion

Subjects

The average age of study subjects was 52 years, and 60% were male. FBSS and CRPS comprised 76% of subjects' pain etiologies, although the two diagnosis subgroups had unequal numbers of subjects. Subjects with FBSS ($N = 40$) comprised 61.5% of the 65 subjects, while subjects with CRPS ($N = 9$) represented 13.8%, and subjects with other etiologies of pain ($N = 13$) represented 20%. Taken together, the subject cohort was roughly representative of the chronic pain population and typical SCS patients in the United States (3).

Outcomes of Temporary Trial Period

A temporary trial of SCS allows the patient and physician to assess the individual benefits before implantation of a permanent device (31–33). While the majority of subjects proceeded to a permanent implant, sixteen subjects withdrew from the study during the trial period. The withdrawal rate was similar across all diagnosis subgroups and no patterns among the reasons for withdrawal were found between the diagnosis subgroups; ineffective therapy was the reason for withdrawal cited by the majority of subjects. Thus, success during the trial is likely independent of diagnosis of the pain etiology. One finding in the temporary trial data was that subjects who ultimately went on to receive permanent implants had better pain relief during the trial than those subjects who chose to withdraw from the study during the trial period. This observation is intuitive, given that a patient's outcome during a temporary SCS trial is commonly accepted as a predictor of later success and may primarily determine whether he or she should proceed to a permanent SCS implant (31).

Outcomes After Permanent Implantation

At all time points after permanent implantation, average stimulation-on VAS scores were significantly better than average stimulation-off VAS scores and also were significantly better than average baseline VAS scores. The majority of subjects experienced significant pain relief; at each follow-up interval, the percentage of subjects experiencing 50% or better reduction in pain was between 55% and 100%.

The etiology of pain held no predictive value for outcome with SCS; subjects in each group benefited equally well from SCS. We reached this conclusion after hypothesis testing to demonstrate statistical equivalence, as well as critical examination of the confidence intervals around each mean to demonstrate clinical equivalence. Having reached the same conclusions via different tests provides a compelling argument that the means of each pain etiology group do not vary enough to be meaningful to a patient with pain, or to a clinician weighing treatment options. Although a prior report indicated that FBSS as

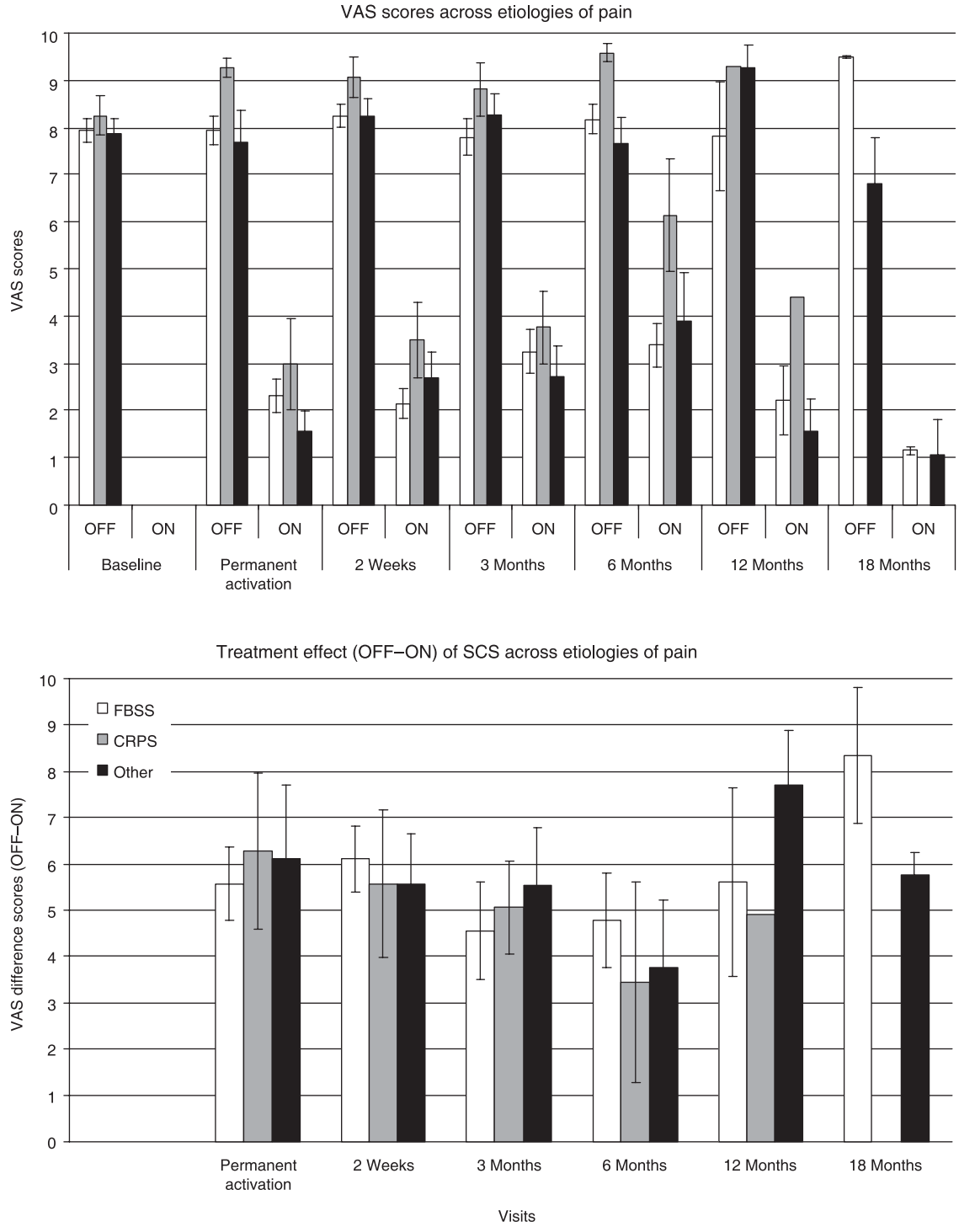

FIGURE 3. Top: Visual analog scale (VAS) scores at follow-up time points after activation of the permanent system for subjects diagnosed with failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS), and other etiologies of pain. Subjects reported more pain relief with stimulation on than when stimulation was off. No relationship between diagnosis and pain relief outcome was found ($ps > 0.05$). Column heights represent means ± SEM. No error bar indicates that column represents data from one subject. Bottom: Treatment effect of spinal cord stimulation (SCS) for pain in subjects diagnosed with FBSS, CRPS, and other etiologies of pain. Treatment effect scores were calculated by subtracting $VAS_{stimulation\ on}$ scores from $VAS_{stimulation\ off}$ scores at a given time point for each subject. No systematic differences in treatment effects were noted across etiologies of pain. Error bars indicate the 95% confidence intervals around the mean. No error bar indicates that column represents data from one subject.

TABLE 3. Effectiveness of Stimulation After Permanent Implantation, Based on Etiology of Pain. On average, SCS use was associated with pain relief for all etiologies of pain. No relationship between diagnosis and outcome was found

Subjects with FBSS: VAS scores with permanent implant ($N = 28$)

	Baseline	Activation		2-week		3-month		6-month		12-month		18-month	
Visit	$N = 28$	$N = 27$	$N = 28$	$N = 27$	$N = 27$	$N = 22$	$N = 22$	$N = 21$	$N = 21$	$N = 8$	$N = 8$	$N = 2$	$N = 2$
		OFF	ON	OFF	ON	OFF	ON	OFF	ON	OFF	ON	OFF	ON
Average VAS Score	7.94	7.94	2.31	8.25	2.15	7.80	3.25	8.18	3.39	7.81	2.20	9.50	1.15
(± SEM)	(0.26)	(0.31)	(0.34)	(0.23)	(0.33)	(0.39)	(0.46)	(0.31)	(0.46)	(1.15)	(0.73)	(0.03)	(0.09)

Subjects with FBSS: numbers of subjects experiencing improvement of VAS scores during stimulation

Pain relief (%)	Baseline	Activation	2-week	3-month	6-month	12-month	18-month
90–100		7	6	3	3	2	1
80–89		3	6	2		1	
70–79		5	3	3	4	1	1
60–69		3	7	4	3		
50–59		3	2	1	1	1	
40–49		4		3	6	2	
30–39			2	3	2		
<30		2	1	3	2	1	
Missing data		1	1	6	7	20	26

Subjects with CRPS: VAS scores with permanent implant ($N = 8$)

	Baseline	Activation		2-week		3-month		6-month		12-month		18-month	
Visit	$N = 8$	$N = 8$	$N = 8$	$N = 8$	$N = 8$	$N = 7$	$N = 7$	$N = 5$	$N = 5$	$N = 1$	$N = 1$	$N = 0$	$N = 0$
		OFF	ON	OFF	ON	OFF	ON	OFF	ON	OFF	ON	OFF	ON
Average VAS score	8.25	9.26	2.99	9.08	3.50	8.81	3.76	9.58	6.14	9.30	4.40		
(± SEM)	(0.42)	(0.20)	(0.97)	(0.42)	(0.80)	(0.56)	(0.75)	(0.18)	(1.20)	(n/a)	(n/a)		

Subjects with CRPS: numbers of subjects experiencing improvement of VAS scores during stimulation

Pain relief (%)	Baseline	Activation	2-week	3-month	6-month	12-month	18-month
90–100		1	1				
80–89		3	2				
70–79		1		2	1		
60–69			1	3			
50–59		1	2		1	1	
40–49		1	1	1			
30–39					1		
<30		1	1	1	2		
Missing data				1	3	7	8

Subjects with other pain: VAS scores with permanent implant ($N = 13$)

	Baseline	Activation		2-week		3-month		6-month		12-month		18-month	
Visit	$N = 13$	$N = 12$	$N = 12$	$N = 12$	$N = 12$	$N = 9$	$N = 9$	$N = 7$	$N = 7$	$N = 3$	$N = 3$	$N = 2$	$N = 2$
		OFF	ON	OFF	ON	OFF	ON	OFF	ON	OFF	ON	OFF	ON
Average VAS score	7.85	7.69	1.57	8.25	2.69	8.27	2.71	7.66	3.90	9.27	1.57	6.80	1.05
(± SEM)	(0.34)	(0.67)	(0.43)	(0.37)	(0.55)	(0.46)	(0.65)	(0.57)	(1.02)	(0.48)	(0.67)	(1.00)	(0.75)

TABLE 3. *Continued.*

Subjects with other pain: numbers of subjects experiencing improvement of VAS scores during stimulation ($N = 13$)

Pain relief (%)	Baseline	Activation	2-week	3-month	6-month	12-month	18-month
90–100		4	1	1		1	1
80–89		3	3	2		1	
70–79		1	3	3	2	1	1
60–69			2		2		
50–59		3	1		1		
40–49				2			
30–39			1	1			
<30		1	1		2		
Missing data		1	1	4	6	10	11

CRPS, complex regional pain syndrome; FBSS, failed back surgery syndrome; SCS, spinal cord stimulation; VAS, visual analog scale.

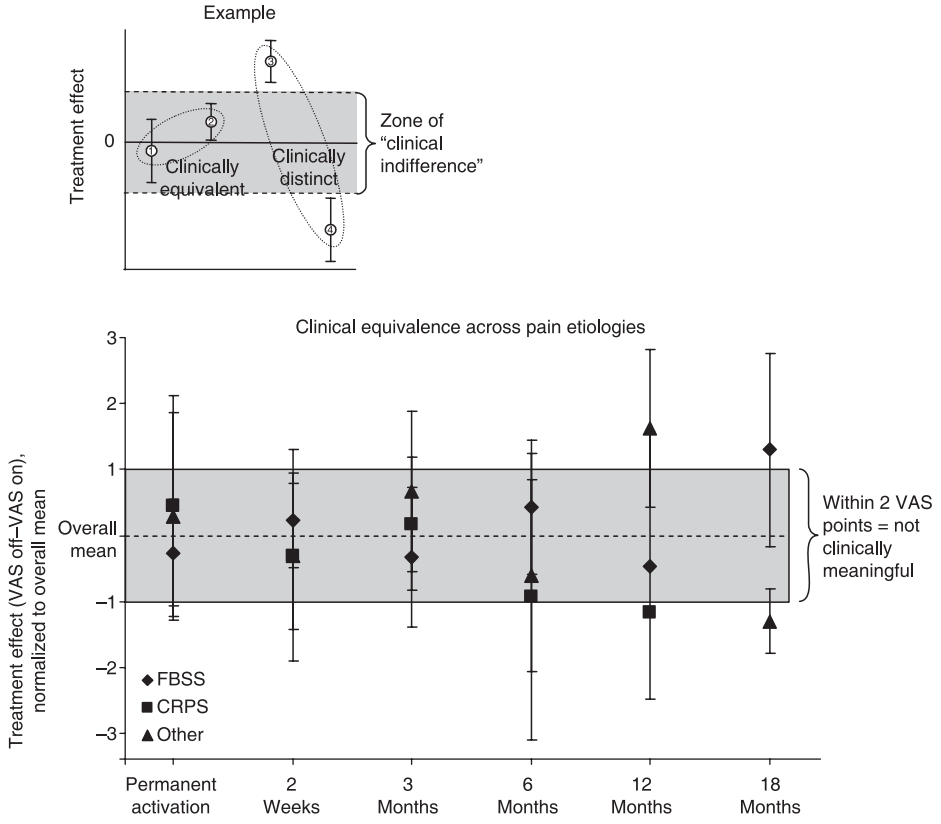

FIGURE 4. The example (top) shows a graph in which the shaded area is a zone of clinical insignificance, within which any group score difference is defined to be unimportant to clinical outcomes. The means and the entire range of the 95% confidence intervals of groups 1 and 2 fall within the shaded area, and these groups are thus very likely to be clinically equivalent. Groups 3 and 4, however, lie completely outside of the shaded area, showing strong evidence that the data in each group are clinically distinct. The data chart (bottom) shows the mean treatment effect (eg, visual analog scale [VAS] difference scores) of each pain etiology group over time, normalized to the overall mean at each time point. The shaded region represents 2 VAS points, a clinically insignificant range. The means of all groups fall within the shaded area from activation of the device through the six-month follow-up, suggesting that the means are clinically equivalent. Although the outcomes at the 12- and 18-month follow-ups are more ambiguous, the upper- and lower-bound ranges of the 95% confidence intervals do fall within the shaded range; this, and the small numbers (see Table 1) at these time points, suggest clinical equivalence at these time points as well.

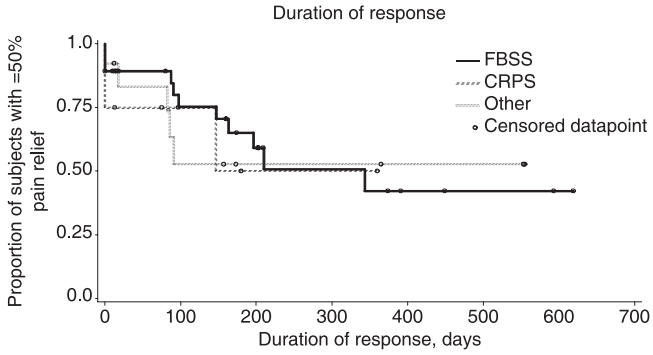

FIGURE 5. Survival analysis showing the duration of pain relief for subjects stratified by pain etiology. Duration of response was defined as the period of time that elapsed between the first report of greater than 50% pain relief to the date on which the pain relief dropped below 50%, as confirmed by similar outcome in a subsequent report. The median duration of response for subjects with failed back surgery syndrome (FBSS) was 343 days. Median duration of response for subjects with complex regional pain syndrome (CRPS) and other etiologies of pain could not be calculated because more than half of these subgroups never reached less than 50% pain relief.

the primary etiology of pain (vs. chronic leg and back pain of other etiologies) may have prognostic validity for selecting appropriate patients for SCS, we did not replicate this finding (21). In fact, published literature supports SCS as an effective treatment for a variety of pain conditions (34). A retrospective outcomes analysis of 138 SCS patients with various neuropathic pain etiologies reported that 74.7% of patients received a permanent implant after a successful (ie, greater than 50% improvement in pain) trial period; of these patients, 84.4% retained greater than 50% pain relief after one year. Opiate use, ability to perform activities of daily living, and employment status also were improved for some patients (32). Another retrospective study of 102 SCS patients with pain of various etiologies reported good pain relief in 68% of patients (as rated by the clinicians). Pain relief ratings by patients and clinicians agreed in 72% of cases, with patients tending to self-report more favorable outcomes than clinicians (35). Similar to the above examples, most published SCS studies include subjects with a wide variety of pain diagnoses in a single data analysis. This report represents an attempt to directly compare the outcomes of subjects with different diagnoses. We encourage future studies to consider similar analyses.

In a survival analysis, we found that for subjects with FBSS, at least half of the subjects reported 50% or better pain relief for 343 days after activation of the device. For subjects with CRPS and other etiologies of pain, survival analyses could not be performed because a majority of subjects in these subgroups reported better than 50% pain relief at all time points. These findings suggest that SCS with this system is a durable therapy, and may provide 50% pain relief for a majority of patients for a year or more.

Limitations and Future Directions

A major limitation of the analysis presented in this report is the possibility that our conclusion of equivalence across pain etiology groups may be due to a type II error. If so, it may be that SCS may have different efficacy for different pain etiologies, but the study was not powered to determine this with any degree of certainty. Statistical analysis of differences between diagnosis subgroups was complicated by the unequal group sizes; while 40 subjects with FBSS were enrolled, only nine subjects with CRPS and 13 subjects with pain of other etiologies were. Because a sample with uneven subgroup sizes has less statistical power than a sample with the same total size and equal subgroup sizes, our ability to detect potential statistically significant differences between the pain etiology groups may be limited by low power. Thus, it is possible that the small group differences in this study may have reached statistical significance with equal groups, or larger groups (36). The small numbers of subjects included in later time points, particularly the 12- and 18-month follow-ups, preclude rigorous hypothesis testing. Although few conclusions can be drawn from the data at these time points, we have presented them here in the interest of fully describing our dataset.

Certain aspects of individual subject information were not gathered as study data. For instance, the pain precipitators and type/numbers of surgeries were not gathered for FBSS subjects, and diagnostic nerve blocks were not required for subjects with CRPS, and, thus, it is unknown whether these subjects experienced pain that was sympathetically maintained or sympathetically independent. If this information was available, additional subset analyses may have been performed. Further conclusions about appropriate treatment for pain etiologies with SCS may have been able to be drawn. We encourage future studies to adopt thorough analysis of demographic and medical history data.

Another limitation in this study is that multiple etiologies of pain (neuropathy, amputation pain, etc.) were combined in the "other" group because of the small number of subjects with any one etiology of pain. Any systematic contribution of these etiologies may have been obscured by the small numbers of subjects. A future study may specifically focus on one or more of these indications. Also of note is that the etiology of pain for nine subjects was recorded as "unknown"; as such, we are unable to draw conclusions regarding the relationship between these subjects' pain conditions and their pain relief outcomes with SCS.

Conclusions

The utility of SCS for its two major indications in the United States, FBSS and CRPS, is supported in the literature by case studies, prospective studies, and retrospective/review articles (18,19,36–38). Outcomes of this study were in agreement with previous reports and highlight the efficacy of this SCS system both in the short term (ie, percentage of subjects proceeding to permanent implantation of the system after trial) and the long term (ie, stability of pain relief over time after permanent implantation). Furthermore, these results indicate that outcomes were comparable for three subgroups of subjects, based on diagnosis prior to implantation. We recommend that all patients with pain with a neuropathic component should be evaluated for suitability for SCS therapy, regardless of particular diagnosis groups.

Acknowledgments

This study was sponsored by Boston Scientific Neuromodulation. This clinical trial was performed in compliance with the US Food and Drug Administration Code of Federal Regulations (21 CFR 812) and Investigational Device Exemption (FDA IDE G030004, approved 01/30/2003). The authors thank Lilly Chen, MSc, for statistical assistance. Dr. Foster is an employee of Boston Scientific Neuromodulation.

Conflict of Interest

The authors reported no conflict of interest.

References

1. Shealy CN, Mortimer JT, Reswick JB. Electrical inhibition of pain by stimulation of the dorsal columns: preliminary clinical report. *Anesth Analg* 1967;46:489–491.

2. Bradley K. The technology: the anatomy of a spinal cord and nerve root stimulator: the lead and the power source. *Pain Med* 2006;7 (Suppl. 1):S27–S34.

3. Kumar K, Hunter G, Demeria D. Spinal cord stimulation in treatment of chronic benign pain: challenges in treatment planning and present status, a 22-year experience. *Neurosurgery* 2006;58:481–496.

4. Mironer YE, Brown C, Satterthwaite JR, Cohen M, Tonder LM, Grumman S. A new technique of "midline anchoring" in spinal cord stimulation dramatically reduces lead migration. *Neuromodulation* 2004;7:32–37.

5. Soldati E. National Italian register of implantable systems for spinal cord stimulation (SCS): analysis of preliminary data. *Neuromodulation* 2002;5:7–15.

6. Kumar K, Toth C, Nath R, Laing P. Epidural spinal cord stimulation for treatment of chronic pain—some predictors of success. A 15-year experience. *Surg Neurol* 1998;50:110–121.

7. De Mulder PA, te Rijdt B, Veeckmans G, Belmans L. Evaluation of a dual quadripolar surgically implanted spinal cord stimulation lead for failed back surgery patients with chronic low back and leg pain. *Neuromodualtion* 2005;8:219–224.

8. Burchiel KJ, Anderson VC, Wilson BJ, Denison DB, Olson KA, Shatin D. Prognostic factors of spinal cord stimulation for chronic back and leg pain. *Neurosurgery* 1995;36:1101–1110.

9. Hord ED, Cohen SP, Cosgrove GR et al. The predictive value of sympathetic block for the success of spinal cord stimulation. *Neurosurgery* 2003;53:626–632.

10. Sindou MP, Mertens P, Bendavid U, Garcia-Larrea L, Mauguiere F. Predictive value of somatosensory evoked potentials for long-lasting pain relief after spinal cord stimulation: practical use for patient selection. *Neurosurgery* 2003;52:1374–1383.

11. Villavicencio AT, Burneikiene S. Elements of the preoperative workup, case examples. *Pain Med* 2006;7 (Suppl. 1):S35–S46.

12. Ruchinskas R, O'Grady T. Psychological variables predict decisions regarding implantation of a spinal cord stimulator. *Neuromodulation* 2000;3:183–189.

13. Simpson BA. Stimulation for pain: are we selecting the patients and assessing the outcome appropriately? *Neuromodulation* 2003;6:199–200.

14. Carter ML. Spinal cord stimulation in chronic pain: a review of the evidence. *Anaesth Intensive Care* 2004;32:11–21.

15. Rasche D, Ruppolt MA, Kress B, Unterberg A, Tronnier VM. Quantitative sensory testing in patients with chronic unilateral radicular neuropathic pain and active spinal cord stimulation. *Neuromodulation* 2006;9:239–247.

16. Costantini A. Spinal cord stimulation. *Minerva Anestesiol* 2005;71:471–474.

17. Cameron T. Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: a 20-year literature review. *J Neurosurg* 2004;100:254–267.

18. Leveque J-C, Villavicencio AT, Bulsara KR, Rubin L, Gorecki JP. Spinal cord stimulation for failed back surgery syndrome. *Neuromodulation* 2001;4:1–9.

19. Bennett DS, Alo KM, Oakley J, Feler CA. Spinal cord stimulation for complex regional pain syndrome I (RSD): a retrospective multicenter experience from 1995 to 1998 of 101 patients. *Neuromodulation* 1999;2:202–210.

20. Taylor RS, Van Buyten J-P, Buchser E. Spinal cord stimulation for complex regional pain syndrome: a systematic review of the clinical and cost-effective literature and assessment of prognostic factors. *Eur J Pain* 2006;1:91–101.

21. Taylor RS, Van Buyten J-P, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. *Spine* 2004;30:152–160.

22. Wetzel FT, Hassenbusch S, Oakley JC, Willis KD, Simpson RK, Ross EL. Treatment of chronic pain in failed back surgery patients with spinal cord stimulation: a review of current literature and proposal for future investigation. *Neuromodulation* 2000;3:59–74.

23. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery* 2005;56:98–107.

24. Kemler MA, Barendse GAM, van Kleef M et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Engl J Med* 2000;343:618–624.

25. Kemler MA, De Vet HCW, Barendse GAM, Van Den Wildenburg FAJM, Van Kleef M. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two

years' follow-up of the randomized clinical trial. *Ann Neurol* 2004;55:13–18.

26. Oakley JC, Krames ES, Prager JP et al. A new spinal cord stimulation system effectively relieves chronic, intractable pain: a multicenter prospective clinical study. *Neuromodulation* 2007;10:262–278.

27. Duggleby W, Lander J. Cognitive status and postoperative pain: older adults. *J Pain Symptom Manage* 1994;9:19–27.

28. Williams J, Holleman D, Simel D. Measuring shoulder pain with the shoulder pain and disability index. *J Rheumatol* 1995;22:727–732.

29. Valvano M, Leffler S. Comparison of bupivacaine and lidocaine/bupivacaine for local anesthesia/digital nerve block. *Ann Emerg Med* 1996;27:490–492.

30. Ostelo RWJG, de Vet HCW. Clinically important outcomes in low back pain. *Best Pract Res Clin Rheumatol* 2005;19:593–607.

31. North RB, Wetzel FT. Spinal cord stimulation for chronic pain of spinal origin: a valuable long-term solution. *Spine* 2002;27:2584–2591.

32. Sundaraj SR, Johnstone C, Noore F, Wynn P, Castro M. Spinal cord stimulation: a seven-year audit. *J Clin Neurosci* 2005;12:264–270.

33. Frank ED, Menefee LA, Jalali S et al. The utility of a 7-day percutaneous spinal cord stimulator trial measured by a pain diary: a long-term retrospective analysis. *Neuromodulation* 2005;8:162–170.

34. Alo KM, Redko V, Charnov J. Four year follow-up of dual electrode spinal cord stimulation for chronic pain. *Neuromodulation* 2002;5:79–88.

35. Quigley DG, Arnold J, Eldridge PR et al. Long-term outcome of spinal cord stimulation and hardware complications. *Stereotact Funct Neurosurg* 2003;81:50–56.

36. Forouzanfar T, Kemler MA, Weber WEJ, Kessels AGH, van Kleef M. Spinal cord stimulation in complex regional pain syndrome: cervical and lumbar devices are comparably effective. *Br J Anaesth* 2004;92:348–353.

37. Harke H, Gretenkort P, Ladleif HU, Rahman S. Spinal cord stimulation in sympathetically maintained complex regional pain syndrome type I with severe disability: a prospective clinical study. *Eur J Pain* 2005;9:363–373.

38. Van Buyten J-P. Neurostimulation for chronic neuropathic back pain in failed back surgery syndrome. *J Pain Symptom Manage* 2006;31:S25–S29.