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Subcutaneous Stimulation as an Additional Therapy to Spinal Cord Stimulation for the Treatment of Lower Limb Pain and/or Back Pain: A Feasibility Study

Tanja E. Hamm-Faber, MA*, Hans A. Aukes, MD*, Frank de Loos, MD†, Ismail Gültuna, MD*

Objective: The objective of this study was to demonstrate the efficacy of subcutaneous stimulation (SubQ) as an additional therapy in patients with failed back surgery syndrome (FBSS) with chronic refractory pain, for whom spinal cord stimulation (SCS) was unsuccessful in treating low back pain.

Study Design: Case series.

Materials and Methods: FBSS patients with chronic limb and/or low back pain whose conventional therapies had failed received a combination of SCS (8-contact Octad lead) and/or SubQ (4-contact Quad Plus lead(s)). Initially leads were placed in the epidural space for SCS for a trial stimulation to assess response to suppression of limb and low back pain. Where SCS alone was insufficient in treating lower back pain, leads were placed superficially in the subcutaneous tissue of the lower back, directly in the middle of the pain area. A pulse generator was implanted if patients reported more than 50% pain relief during the trial period. Pain intensity for limb and lower back pain was scored separately, using visual analog scale (VAS). Pain and Quebec Back Pain Disability Scale (QBPDS) after 12-month treatment were compared with pain and QBPDS at baseline.

Results: Eleven FBSS patients, five male and six female (age: 51 $\pm$ 8 years; mean $\pm$ SD), in whom SCS alone was insufficient in treating lower back pain, were included. In nine cases, SubQ was used in combination with SCS to treat chronic lower back and lower extremity pain. In two cases only SubQ was used to treat lower back pain. SCS significantly reduced limb pain after 12 months (VAS_{bl}: 62 $\pm$ 14 vs. VAS_{12m}: 20 $\pm$ 11; $p = 0.001$, $N = 8$). SubQ stimulation significantly reduced low back pain after 12 months (VAS_{bl}: 62 $\pm$ 13.0 vs. VAS_{12m}: 32 $\pm$ 16; $p = 0.0002$, $N = 10$). Overall pain medication was reduced by more than 70%. QBPDS improved from 61 $\pm$ 15 to 49 $\pm$ 12 ($p = 0.046$, $N = 10$). Furthermore, we observed that two patients returned to work.

Conclusion: SubQ may be an effective additional treatment for chronic low back pain in patients with FBSS for whom SCS alone is insufficient in alleviating their pain symptoms.

Keywords: Chronic pain, failed back surgery syndrome, low back pain, neuromodulation, neuropathic pain, peripheral nerve field stimulation, subcutaneous stimulation

Conflict of Interest: Dr. I. Gültuna has received financial compensation as Advisory Committee member for Medtronic. The other authors reported no conflicts of interest.

INTRODUCTION

Spinal cord stimulation (SCS) involves placing leads in the epidural space, and applying electrical stimulation to the large myelinated fibers of the dorsal column. This has been shown as an effective long-term therapy for chronic limb pain in failed back surgery syndrome (FBSS) (1–4). Clinicians have reported greater success with radicular, lower extremity pain than with axial low back pain (5,6). Few studies have shown that axial low back pain in combination with limb pain responds well to SCS (7–10). Therefore, while SCS certainly benefits some FBSS patients with chronic low back pain, it is often inadequate. Many patients continue to experience significant pain, requiring frequent local injections, oral opiates, or other additional interventions (11).

Efforts to relieve low back pain with SCS have benefited from the development of programmable multicontact electrodes and improved techniques and strategies (11–13). Subcutaneous stimulation (SubQ) or peripheral nerve field stimulation (PNFS) appears to

Address correspondence to: Tanja E. Hamm-Faber, MA, Pain Treatment Center, Albert Schweitzer Hospital, Wilhelminastraat 75, 3361 XV Sliedrecht, PO Box 444, Dordrecht, The Netherlands. Email: t.hamm@asz.nl

* Albert Schweitzer Hospital, Pain Treatment Center, Dordrecht, The Netherlands; and

† Optimal Care Pain Clinic, Rotterdam, The Netherlands.

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have potential as a therapeutic modality in the treatment of chronic pain syndromes (14–18). In contrast to SCS, during SubQ leads are placed in the pain area to stimulate the region of the affected nerves: cutaneous afferents, or the dermatomal distribution of these nerves, which converge back on the spinal cord (19).

The successful use of SubQ also has been reported in FBSS patients with chronic low back pain (20–25). With the combination of SCS and SubQ it is possible to treat FBSS patients with chronic limb and back pain (26,27). We applied SubQ as an adjunct in FBSS patients receiving SCS for limb pain but had inadequate response to back pain. In so doing we investigated the short- and long-term efficacy of SubQ on low back pain.

Patient Selection

A prospective case series was performed in patients with chronic limb and/or low back pain. SCS is often the last option to treat patients with chronic limb and/or low back pain. That means that other pain treatments had been tried before SCS was considered. All patients had undergone several nerve blocks and medications were tried in an adequate doses and duration (nonsteroidal anti-inflammatory drugs, morphine, anti-epileptic, anti-depressive) and have had physical therapy and transcutaneous electrical nerve stimulation (TENS). Despite these treatments patients still had a severity of pain, which limited their daily life. All patients who are included in this pilot study had more than 12 months of chronic pain and as a consequence suffered major problems in their social and personal life. Patients included conformed the inclusion criteria for SCS, set by the Dutch Neuromodulation Association (VvNN). Screening a patient for SCS means they have to use the: Short Form Health Survey (SF-36, measuring functional health status), Hospital Anxiety and Depression Scale (HADS, scoring information on the potential presence as well as the severity of anxiety and/or depression disorders), McGill Pain Questionnaire (MPQ, measuring a quantitative profile of aspects of pain), visual analog scale (VAS, for accurately determining the level of pain), and a medication list. Patients also have to sign an informed consent. As well as a physical examination patients underwent a psychological screening.

The selection criteria used for this study were:

1. Diagnosis of FBSS with considerable disabling chronic limb and low back pain that is present for at least six months.
2. Mean intensity limb and low back pain score of 50 or higher measured on a 100-point VAS.
3. Failure to respond to other conservative treatments (including medications, psychological therapies, rehabilitation, and pain management programs).
4. Psychological clearance (including drug addictions, major depression, and similar severe disorders that might impact on successful treatment).
5. No coexisting chronic pain problems or neurologic diseases.
6. No coexisting conditions that would increase procedural risk (e.g. sepsis, coagulopathy).
7. Informed consent.

SCS and SubQ Implant Procedure

Patients received a SCS system targeted to relieve limb and back pain. If, after SCS trial stimulation, there was more than 50% pain relief in the limb but less than 50% back pain relief, patients received one or two subcutaneous leads in the region of back pain during implantation of the pulse generator (IPG).

SCS LEAD IMPLANTATION

Spinal cord stimulation was used primarily as a treatment for neuropathic pain in limb and lower back. The lead implantation was performed under local anesthetic beginning with a percutaneous technique with the patient in prone position. A pillow was placed under the abdomen to promote adequate forward flexion of the spine and to facilitate epidural lead placement. The entry level was determined using fluoroscopy and marking of the skin. The patient was prepared and draped. A Tuohy needle was inserted under fluoroscopy in a paraspinous approach with the beveled edge facing cephalad. The needle was inserted at the shallowest angle possible to allow atraumatic passage of the lead cephalad.

Entry into the epidural space was verified by using the loss of resistance technique to saline or air. The eight-polar lead (Octad® electrode, model 3877, Medtronic, Minneapolis, MN, USA) was slowly inserted through the needle under fluoroscopy. The stylet of the lead has a small bend at the tip, enabling the lead to be steered toward the target site. The Octad electrode reached as far as level T6 in the epidural space. A "snap lid" connector ENS (model 37022, Medtronic) was used to attach the epidural Octad electrode to the N'vision programmer (model 8840, Medtronic). During the perioperative test stimulation we tried to cover the whole pain area with paresthesias by changing the combination of the electrode points with the N'vision as well as repositioning the lead in the epidural space.

To find the maximum coverage of the pain area we searched from level T6 to T12. Unfortunately low back coverage was not adequate enough for pain suppression compared with the stimulation and pain suppression in the limb. Sometimes the effect of the stimulation in the low back disappeared over time. The position of the Octad lead was accepted if patient reported that 80% or more coverage of the pain area. Eventually the position of the tip of the Octad electrode was at T7 ($N = 1$), T8 ($N = 6$), T9 ($N = 2$). Then the open surgical part of the procedure began: The stylet and the Tuohy needle were removed and a minor incision made to allow fixation of the lead with a Titan anchor (model 3550–39, Medtronic), either at the paraspinal fascia or at the interspinous ligament, at the point where the lead entered the epidural space (T12–L1, L1–2). After anchoring the wound was closed and infiltrated with a local anesthetic.

Following the procedure, the patients were monitored in the recovery unit for two to four hours during which initial stimulation parameters were established using an external stimulator. Stimulation parameters (amplitude, pulse width, and frequency) were optimized by the pain nurse. In the week after the SCS trial, patients were reviewed on the effect of SCS on pain.

SUBCUTANEOUS LEAD IMPLANTATION

Following a successful SCS trial (>50% pain reduction in limb) the patient received an IPG. If after this test period there was inadequate relief of low back pain (<50%), one or two subcutaneous leads (Quad® Plus lead with an inline spacing of 12 mm, model 3888, Medtronic) were placed in the painful area in the back during the IPG implant surgery. If the low back pain was only located on one side of the spinal column, then one SubQ lead (Quad Plus lead) was used. If the lower back pain was on both sides of the dorsal column two SubQ leads were placed, one on each side of the dorsal column.

Prior to surgery the locations of the SubQ leads were precisely marked in the middle of the marked low back pain area with the patient standing. The wide space Quad lead would be placed in a

horizontal, vertical, or diagonal position depending on the location and course of the area of pain. In this study all patients suffered low back pain on both sides of the dorsal column. Therefore, two Quad Plus leads were used. The pain area in the lower back of all patients varied, radiating to the flank and the band of pain had a range from narrow (10–15 cm) to wide (15–20 cm). Because of the varying size of pain areas the leads were placed in different positions but always exactly in the middle of the severest pain area of the lower back.

Patients received preoperative intravenous antibiotics (2.2 Augmentin iv). The patient was placed in a prone position on the operating table with a pillow under the abdomen. The skin was infiltrated with Lidocaine 1% at the insertion point. A 14G Tuohy needle was inserted subcutaneously. Using the index finger on the surface of the skin the implanter guided the needle direction and estimated the depth of the SubQ lead. With the Tuohy needle correctly positioned the stylet was removed and the 4-contact Quad Plus lead with an inline spacing of 12 mm inserted into the Tuohy needle. As the last metallic area of the SubQ lead entered the skin, the needle was withdrawn leaving the SubQ lead in place. Once placed the leads should be superficial enough to be easily palpated through the skin. Position was confirmed using fluoroscopy (Fig. 1). The leads were secured with a Titan anchor (3550–39, Medtronic) in the subcutaneous fat using a 5-cm incision, while assuring that the proximal electrode on the lead did not come into contact with the anchor. Subsequently the wound at the middle of the back was reopened to disconnect the Octad lead from the temporary extension cable. The right and the left SubQ leads were tunneled to this wound using the Tuohy needle.

Before tunneling the extension leads, a pocket was created in the left lower abdominal wall. With an incision equal to the length of the implantable pulse generator the pocket was developed using normal dissection techniques. The implantable pulse generator should be placed no more than 2 cm deep and parallel to the skin surface.

One bifurcation extension lead (model 37082, Medtronic) in case of bilateral SubQ, or the stretch coil extension lead (model 37083, Medtronic) in case of unilateral SubQ, and one SCS extension lead (model 37081, Medtronic), were tunneled from the back wound to the left lower abdominal incision. After connecting the Quad leads to the connector cable the impedances of the implanted system were checked and the wounds closed. Care was taken not to place the connections above the spinal column but to place the connection of the extension lead (73081) on the left side of the dorsal column and the connection of the other extension (37082 or 37083) on the right sight.

For implantation of the IPG (Prime Advanced [model 37702, Medtronic] or Restore Advanced [model 37713, Medtronic]) the patient was placed in a lateral position. Both extensions were attached to the IPG, the impedance of the implanted system checked, and the wounds closed. This means that for the procedure of SCS with placement of subcutaneous leads both a percutaneous and open surgical technique were used.

After surgery, patients were monitored in hospital overnight and stimulation parameters established the following morning. Patients returned to hospital 10–12 days post surgery for removal of sutures. Stimulation parameters for SCS and SubQ were determined individually for each patient to provide settings with optimal coverage and pain suppression. Multiple programs were used for different positions, times of the day, or levels of activity when appropriate. In contrast to SCS the goal of lead selection and programming was to capture the broadest zone of coverage, directly in the region of pain.

Follow-Up

The patients returned to the clinic after 1, 3, 6, and 12 months. On every follow-up visit pain and disability, medication use, adverse events, and stimulation settings were noted.

All follow-up visits and data collection were done by I. Gültuna, MD, and T. Hamm, MA-ANP.

Pain relief was measured using a 100-point VAS scale. The patient has to place a mark on a 100-mm line, which corresponds to the pain level (three times a day). Zero means no pain at all and a VAS of

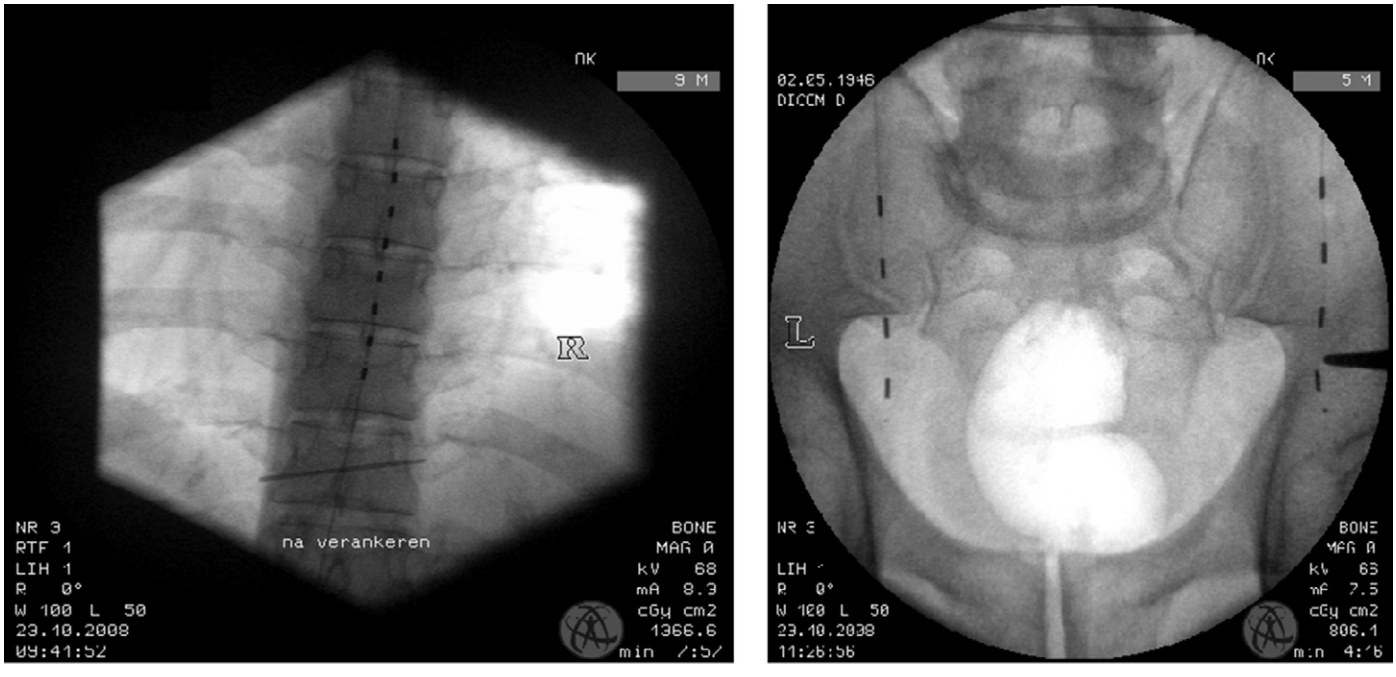

Figure 1. Fluoroscopic detail of spinal cord stimulation lead (left) and subcutaneous stimulation lead (right).

100 means the worst possible pain imaginable. From all these scores, an average was taken. Pain intensity for limb and lower back pain were scored separately.

Disability was rated using the Quebec Back Pain Disability Scale (QBPDS). With this questionnaire the patient indicates, on a scale from 0 to 5, how much effort it takes to complete 20 activities.

Patients also were asked to register their analgesic medication use in a diary.

Adverse events were collected over time and are represented in a descriptive manner.

The stimulation settings also were noted by every visit in the follow-up.

Statistical Analysis

Descriptive statistics were used to summarize study data. They were reported as percentages or using the arrhythmic mean (average) and the variance (standard deviation).

Student's *t*-test was used to compare for statistical significant differences. These tests were performed using Microsoft Office Excel (Redmond, WA, USA). The level of statistical significance (*p*-value) was set at 5%.

Pain and QBPDS after 12-month follow-up were compared with pain and QBPDS at baseline.

RESULTS

Demographics

Table 1 shows the patient characteristics. Eleven patients, five male and six female, with FBSS, in whom SCS alone was insufficient in treating low back pain, were included in the study. The mean age was 51 ± 8 years (range 38–62 years). Low back pain component was on average 65% of all pain (limb + low back pain together).

All patients underwent various interventional pain management procedures prior to neuromodulation. Surgical procedures included herniated disc surgery, laminectomy, and spondylodesis. Following surgery all patients had refractory chronic pain for which they received conventional pain therapies including oral analgesics, local injections, radiofrequency lesions, TENS, and physical therapy.

Pain Indices

In nine cases, SubQ was used in combination with SCS to treat chronic lower back and lower extremity pain. In two cases only SubQ was used to treat low back pain. One of the patients was included although she did not have significant limb pain. She had buttock pain with radiating to the back. SCS was tried but it was unsuccessful to cover the pain area. Her physical and psychological history was carefully evaluated. All previous treatments had failed, resulting in a poor quality of life. She was unable to sit because of pain she experienced 24 hours a day. With this in mind she was included in the pilot study despite the absence of significant limb pain (patient 5). The other patient started with SCS for limb pain and back pain. Percutaneous placement of epidural lead resolved limb pain completely but not back pain. During this procedure leads were placed subcutaneously for back pain trial stimulation instead (patient 4). Table 2 shows the pain scores of the limb at baseline, 1, 3, 6, and 12 months. Mean limb pain at baseline was 62 ± 14 ($N = 10$). SCS significantly reduced limb pain and the effect remained stable over time. Long-term outcome (12 months) limb pain VAS

Table 1. Patient Demographics.

Patient number	Sex	Age (years)	Pain indication/surgical background	Low back pain component* (%)
1	M	62	FBSS (2× herniated disc surgery + spondylodesis)	80
2	F	52	FBSS (stenosis + laminectomy L4–5)	60
3	M	55	FBSS (2× herniated disc surgery)	50
4	M	62	FBSS (herniated disc surgery and spondylodesis)	50†
5	F	50	FBSS (spondylodesis)	100
6	F	51	FBSS (herniated disc surgery and spondylodesis)	50
7	F	39	FBSS (2× herniated disc surgery)	60
8	M	58	FBSS (herniated disc surgery and laminectomy)	50
9	M	38	FBSS (herniated disc surgery)	80
10	F	51	FBSS (2× herniated disc surgery)	70
11	F	47	FBSS spondylodesis at three levels	70
Mean		51.4		65
SD		8.0		16

*Percentage of low back pain of total FBSS pain (limb + back pain).
†Patient 4 started with SCS for limb and back pain. Percutaneous placement of epidural lead resolved limb pain completely but not back pain.
FBSS, failed back surgery syndrome; SCS, spinal cord stimulation.

Table 2. Spinal Cord Stimulation: VAS Limb Pain (0–100).

Patient number	Baseline	SCS trial period	1 month	3 months	6 months	12 months
1	59	7	10	9	14	18
2	40	20		19	25	26
3	50	30	49	22	27	16
4	68*	—	—	—	—	—
5	—†		—	—	—	—
6	77	33	—	17	32	31
7	73	13	43	47	51	—‡
8	71	26	9	8	20	18
9	44	2	2	8	20	4
10	80	20	10	8	15	6
11	54	19	39	37	37§	37§
Mean	62	19	23	19	27	20
SD	14	10	20	14	12	11

*Patient 4 started with SCS for limb and back pain. Percutaneous placement of epidural lead resolved limb pain completely but not back pain. During this procedure leads were placed subcutaneously for back pain trial stimulation instead.
†Patient 5 started trial SCS for back pain only.
‡Patient 7 had neurostimulation device removed for magnetic resonance imaging scan.
§Patient has scored pain of trochantor major on VAS form. Limb pain due to FBSS unchanged from three months postoperative forward (oral communication patient).
FBSS, failed back surgery syndrome; SCS, spinal cord stimulation; VAS, visual analog scale.

Table 3. Subcutaneous Stimulation: VAS Low Back Pain (0–100).

Patient number	Baseline	SCS trial period	1 month	3 months	6 months	12 months
1	60	33	10	18	18	17
2	54	49	—	37	26	28
3	47	60	47	28	30	22
4	54	—*	—	16	32	34
5	51	—†	—	17	35	29
6	77	72	—	57	28	31
7	74	72	52	41	46	—‡
8	81	55	28	68	47	49
9	49	52	43	51	51	58
10	55	45	18	16	17	6
11	78	54	44	34	42	50
Mean	62	55	35	35	34	32
SD	13	12	16	18	12	16

*Patient 4 started with SCS for limb and back pain. Percutaneous placement of epidural lead resolved limb pain completely but not back pain. During this procedure leads were placed subcutaneously for back pain trial stimulation instead.
†Patient 5 started with SCS for back pain. Percutaneous placement of epidural lead resolved back pain only right-sided. Upon IPG placement patient received left-sided SubQ lead. After three months the SCS lead was placed subcutaneously on the right side.
‡Patient 7 had neurostimulation device removed for magnetic resonance imaging scan.
IPG, implantation of the pulse generator; SCS, spinal cord stimulation; SubQ, subcutaneous stimulation; VAS, visual analog scale.

was 20 ± 11 ($p = 0.001$, $N = 8$). Six out of eight patients (75%) had more than 50% limb pain reduction after 12 months of SCS.

Table 3 shows low back pain scores at baseline and at 1, 3, 6, and 12 months. The mean low back pain at baseline was 62 ± 13. During the SCS trial while radicular limb pain was relieved by the stimulation, buttock/lower back coverage was poor. The patients agreed to proceed with permanent implant including subcutaneous leads for low back pain. SubQ stimulation significantly reduced low back pain and the effect remained stable over time. Long-term (12 months) low back pain VAS was 32 ± 16 ($p = 0.0002$, $N = 10$). Four patients (40%) had more than 50% pain reduction after 12 months of SubQ. Figure 2 shows the overall VAS data of SCS and SubQ in these patients over time.

Disability

Table 4 shows the QBPDS scores at baseline and at 1, 3, 6, and 12 months. The mean QBPDS at baseline was 61 ± 15. SubQ stimulation significantly improved disability and the effect remained stable over time. Long-term (12 months) QBPDS was 49 ± 12 ($p = 0.046$, $N = 10$). Two patients who had been at home for up to a year, because of their illness, returned to work.

Medication

Table 5 shows the medication use of all patients at baseline and after 12-month follow-up. Two patients (patients 4 and 10) did not use any pain medication at the start of neuromodulation therapy.

All other patients (N = 9) showed a significant decrease and/or lighter pain medication use under optimal neurostimulation. Four patients (patients 1, 2, 3, and 7) stopped all pain medication.

Safety

A total of 14 adverse events were recorded over a one-year period of follow-up, of which nine required surgery (Table 6). These consisted of repositioning of the connector that had been placed too superficially under the skin (N = 2), repositioning of a SubQ lead after loss of paresthesias in the painful area (N = 3) and an IPG for patient comfort (N = 1), and battery replacement due to empty battery within one year (N = 2). One neurostimulation system was removed after 10 months for a magnetic resonance imaging to reassess a new spondylodesis.

Two patients reported that they were not entirely satisfied with neurostimulation. One patient did not have complete coverage of limb pain and one patient reported incomplete pain suppression of low back pain. These two patients both had one small area of pain remaining in the low back.

One patient reported two occasions of unexplained electrical shocks in the low back area when holding her electrical scoot mobile, early after onset of neuromodulation therapy. These effects have not reappeared since.

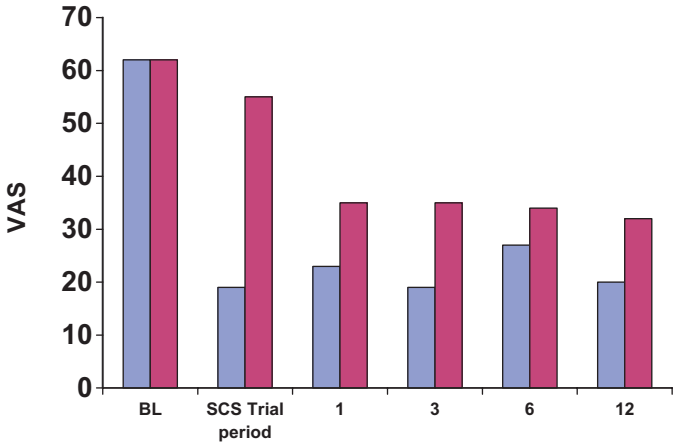

Figure 2. Pain cores (visual analog scale, VAS) for limb (blue) and back (purple). BL, baseline; SCS, spinal cord stimulation.

Stimulation Settings

Table 7 lists the stimulation settings of the SubQ leads for all patients. Preferred settings were: pulse duration 390–450 micros, stimulation frequency 30 Hz, and wide filed stimulation (use of the outer electrodes). Stimulation amplitude varied widely among patients. Nine patients (82%) used SubQ stimulation 24 hours per day.

DISCUSSION

In this prospective case series we investigated the effect of SubQ stimulation as an add-on therapy in FBSS patients with chronic limb and/or low back pain who had insufficient pain relief from SCS alone.

Spinal cord stimulation reduced limb pain significantly during trial stimulation and remained effective (more than 50% pain reduction) in 75% of patients during a 12-month follow-up. These results are in accordance with previous studies (2,28) and confirm that SCS is an effective treatment for limb pain due to FBSS. None of the patients, however, had sufficient pain relief with SCS for back pain and therefore were offered SubQ stimulation in addition. The overall reduction of low back pain using SubQ was 48%, four patients (40%) had more that 50% low back pain reduction. These results were consistent over time up to 12 months of stimulation. This study demonstrates that adding SubQ stimulation to SCS has a beneficial effect on suppressing low back pain.

Recent development shows us that axial back pain and limb pain can be treated by subcutaneous PNFS in combination with SCS (22). This might open a new way for treatment of axial low back pain.

There have been a number of publications on the use of SubQ or PNFS in low back pain, demonstrating adequate pain control. Others describe the use of peripheral field stimulation as a substitute for SCS (20,21,23–25).

In our study SubQ was used as an adjunct to SCS when SCS alone was insufficient in reducing low back pain. There are only a few studies that describe the simultaneous use of SCS and PNFS. One was a retrospective case study article in 20 patients with FBSS (22), another presented prospective patient outcomes (26,27). Ostensibly our study is the first prospective report on the combined use of SCS and SubQ with a follow-up period of 12 months.

Our results on low back pain suppression (48%) are less favorable than published by Mironer and collaborators (27), in which an overall success of 85–90% was demonstrated. Mironer investigated

Table 4. Quebec Back Pain Disability Scale.

Patient number	Baseline	1 month	3 months	6 months	12 months
1	76	45	47	35	61
2	60		48	45	40
3	62	50	66*	75*	55
4	36		22	23	27
5	50		37	34	42
6	84		62	62	54
7	66	53	52	58	—*
8	74	57	62	58	60
9	65	62	67	67	62
10	41	31	33	36	36
11	60	61	43	52	51
Mean	61	51	49	50	49
SD	15	11	15	16	12

*Patient had neurostimulation device removed for magnetic resonance imaging scan.

Table 5. Medication Use at Baseline and After 12-Month Follow-Up.

	1	2	3	4	5	6	7	8	9	10	11
Baseline medication											
Celebrix											
Diazepam						v					
Diclofenac							v				
Durogesic	v								v		
Fentanyl pleister						v					
Ibuprofen	v	v						v			
Lyrica			v			v		v			
Methotrexaat	v										
Morphine							v				
Oxycontin					v						
Paracetamol		v					v				
Temazepam	v										v
Tramal											
12 months											
Celebrix					v						
Diazepam											
Diclofenac											v
Durogesic											
Fentanyl pleister											
Ibuprofen								v			
Lyrica											
Methotrexaat											
Morphine											
Oxycontin											
Paracetamol						v					
Temazepam											
Tramal									v		

Table 6. Adverse Events.

Device	Description	Frequency
SCS lead	Incomplete coverage of pain in left lateral side lower limb requiring PRF sacro-iliacal joint block	1
SubQ stimulation lead	Repositioning of connector	2
	Repositioning lead	3
IPG	Repositioning	1
	Need for new battery within one year	2
Other	Unexplained electrical shocks while holding scoot mobile	2
	Entire neuromodulation system explanted for magnetic resonance imaging (for new spondylodesis)	1
	Not completely satisfied*	2

*Patients do not want have the neurostimulator system explanted. One of these patients is off pain medication.
IPG, implantation of the pulse generator; PRF, pulse radiofrequency; SCS, spinal cord stimulation; SubQ, subcutaneous stimulation.

the effect of coverage for axial back pain and the interaction between SCS and PNFS in two groups. In this study the patients had no limb pain. That is different from our study in which patients had both limb and back pain. The reason for this difference in relieving back pain is unclear, although the stimulation settings (anodal-cathodal programming) or analgesic medication may be contributing factors (29). The prospective study from Lipov et al. in 23 patients describes that the combination of PNFS as add on therapy to SCS is safe and effective for back and limb pain and is in accordance to our results (30). More research is needed to elucidate the difference in outcome.

Patient satisfaction was high in our patient group, which is demonstrated by the long daily use of SCS and SubQ. These results are in accordance with the findings by Mironer and collaborators, who found a patient satisfaction from 81% in 54 patients (27). Because follow-up in this pilot study was limited to one year, it is uncertain whether the pain relieving effect of SCS and SubQ persists over time. The long-term efficacy of SCS + SubQ treatment in patients with FBSS will be more thoroughly investigated in a randomized controlled trial, which is planned shortly.

The mechanism of PNFS has not been researched properly. The work of Krutsch et al. describes that large A-beta fibers modulate the smaller A-delta and C fibers in their afferent output (20). In another article it is proposed that the mechanism is based on anti-inflammatory and membrane depolarizing effect from the nerve, which ends in the skin, but he also describes the activation of the A-beta nerve fiber (18). More research is needed to understand the mechanism of the PNFS.

Table 7. Stimulation Settings.

Patient number	Placement		PW	Rate	Amplitude (V)		Contacts							
	Left	Right			Left	Right	Left				Right			
							0	1	2	3	0	1	2	3
1	V	V	210	80	9.5	9.7	−			+	−			+
2	V	V	420	65	3.2	2.2	−		+		−			+
3	H	H	390	30	7.9	8.5	+			−	−			+
4	V	V	390	30	2.3	2.9		+	+	−		+	+	−
5	V	V	450	30	4.2	2.1	+			−		−	+	
6	V	V	390	30	4.4	2.3		−	+			−	+	
7	H	H	390	60	8.5	8.1	−			+	−			+
8	H	H	390	30	6.9	6.4	−			+	−			+
9	H	H	450	30	6.0	3.3	−			+	−			+
10	H	H	390	30	5.3	6.0	+			−	−			+
11	D	D	390	30	4.7	3.8	+			−	−			+

D, diagonal; H, horizontal; V, vertical.

Pain suppression in limb and low back was accompanied by a significant (>70%) reduction in pain medication. The reduced consumption of analgesics with SCS treatment varies from 40% to 84% in published reports (31,32). The reduction in pain medication may result in less medication induced side-effects and cost savings (33). The SubQ electrode placement is a minimally invasive additive therapy, which has a major effect on the total pain outcome. It can be effectively placed subcutaneously with accuracy. The standard IPG (Prime Advanced) has 16 channels where two-sided Quad electrodes can easily be fitted to the IPG. There are two surgical drawbacks to this therapy. The first is the longer operation time, and the second the higher energy consumption when combining SCS and SubQ stimulation. In case the IPG longevity is less than a year this may be solved by replacing with a rechargeable pulse generator. At present it is therefore unclear if the combined use of SCS and SubQ is more cost-effective than SCS alone. The lifetime of the battery depends on the number of programs, the duration of the stimulation, and the settings of the electrodes, frequency, the pulse width, and the amplitude. The effect of frequency on outcome is evaluated by Reverberi et al. (18). In that article he describes that a lower frequency is more effective (<20 Hz). However, Bernstein et al. (22) had good results with a higher frequency. Note that a higher frequency with a broad pulse width and high amplitude can influence the battery consumption (17,18,21,24) More research is needed for optimization of the therapy settings in addition to energy consumption on battery life.

Because neuromodulation therapy is an invasive and expensive treatment careful selection of patients is important. The only reason to consider SCS, or PNFS, is when every other treatment, such as nerve blocks, medication, physical therapy, and TENS, have failed and patients are properly physically and psychologically screened. In this pilot study every patient used TENS with different programs for at least two weeks. Patients who had achieved major effect on pain relief obtained a TENS for personal use and were not candidate for SCS. All patients in the pilot study used a TENS, which eventually became less effective or the patient developed an allergy to the surface electrodes (34,35). The staged procedure as used in this study, i.e., applying SubQ only when SCS alone, is insufficient to treat back pain, may prove ideal for the optimal application of this therapy.

Apart from the above mentioned early battery replacements, seven surgical interventions were needed, of which six were neuromodulation therapy-related. Lead dislocation and technical repositioning surgery occurred more frequently. These consisted of repositioning of the connector ($N = 2$), the lead ($N = 3$), and an IPG ($N = 1$). The pilot study has provided insight into the positioning of the connections in the back. Two connections in the back of the patient have been replaced as they caused pain when leaning against the back of a chair or lying on his back. This was solved by positioning one connection to the right of the spine and the other to the left. The proceedings were well documented. As the anchor was not sufficiently fixed in the subcutaneous tissue, one SubQ sublead had to be repositioned three times. After the repositioning procedure, the pain disappeared and the patient claimed the return of normal sensory perception in the pain area. These numbers are in accordance with other reports (2,36–38). No SCS-related adverse events or infections were recorded.

Besides pain relief, SCS improved disability/function significantly, and 20% returned to work. These outcomes are in accordance with a previous report (7).

CONCLUSION

Peripheral nerve field stimulation may be considered as an additional treatment for chronic low back pain in patients with FBSS for whom SCS alone is insufficient in alleviating their symptoms. As many patients with FBSS have refractory limb and back pain, a larger number can be treated if standard SCS therapy is combined with SubQ stimulation.

Authorship Statements

The study was an initiative from all four authors who all recruit patients and analyze data. I. Gültuna, H. Aukes, and F. de Loos performed surgery. T. Hamm assisted with surgery and collected data. Drs. de Loos (MD), Gultuna (MD), Aukes (MD), and Hamm-Faber (MA-ANP) designed and conducted the study, including patient recruitment, data collection, and data analysis. Dr. Gultuna and Ms. Hamm-Faber prepared the manuscript draft with intellectual input from Dr. Aukes. All authors had complete access to the study data. All authors approved the final manuscript.

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COMMENTS

Contemporary neuromodulation faces the issue of inadequate axial back pain coverage with conventional spinal cord stimulation (SCS). One of the first corrective steps was to use subcutaneous peripheral nerve field stimulation (PNFS). However, more recent studies indicated clear advantage of using a combination of SCS and PNFS for the treatment of back pain.

The article by Hamm-Faber and others adds to our knowledge in this new field of neurostimulation. In their well designed, albeit small study, the authors demonstrated not only reduction in back pain but also a decrease in pain medication intake and improvement in disability.

Future studies on a significantly larger scale will hopefully help us with better understanding of the mechanisms and the most effective application of the combined use of SCS and PNFS.

Eugene Mironer, MD
Greenville, SC, USA

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Excellent prospective study. It clearly points out the respective roles of SCS and subcutaneous stimulation in the management of patients with FBSS. The results on low back pain seem to be very realistic, and of such a magnitude that the modality can seriously be considered as an additional tool in the management of these difficult pain conditions. In the US, there will probably be a larger percentage of trials performed, on a shorter basis, with simultaneous SCS and subcutaneous leads implanted. A larger prospective and randomized study will undoubtedly confirm the efficacy of the combined modalities.

Giancarlo Barolat, M.D.
Denver, CO, USA

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This study is an important contribution in subcutaneous field stimulation as an adjunct to spinal cord stimulation in the setting of failed back surgery. This is the first systematic set of observations longitudinally in the literature. At a time when healthcare resources are increasingly limited, this study provides further support for neuromodulation as a cost effective approach to back pain not amenable to operative intervention.

T. Stuart Meloy, MD
Winston-Salem, NC, USA

Comments not included in the Early View version of this paper.

