Randomized Crossover Study

The MuscleSCS Technique (4-8Hz BurstDR™ Octrode™): A Randomized Clinical Study of MuscleSCS Stimulation in the Treatment of Chronic Back Pain

Matthias Hubert Morgalla, MD, PhD, and Laura Olbrisch, MD

From: Department of Neurosurgery, Eberhard-Karls University, Tuebingen, Germany

Address Correspondence:
Matthias Hubert Morgalla, MD, PhD
Clinic of Neurosurgery, University of Tuebingen
Hoppe-Seyler-Str. 3
D-72076 Tuebingen, Germany
E-mail: matthias.morgalla@gmail.com

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Background: MuscleSCS is a new technique that combines spinal cord stimulation (SCS) with muscle stimulation to relieve pain.

Objectives: In this clinical study, we wanted to use rod electrodes to investigate the MuscleSCS method's effectiveness in the treatment of chronic lower back pain. One of our hypotheses was that the combined use of MuscleSCS and BurstDR™ would further improve the treatment.

Study Design: A prospective, single-center, single-blinded, randomized crossover study.

Setting: A university medical center.

Methods: Patients with chronic lower back pain had previously (one to 10 years ago) received an SCS system (Octrode™). In this study, they were randomly treated for 2 weeks each with BurstDR™ stimulation alone, MuscleSCS stimulation alone, or a combination of BurstDR™ stimulation and MuscleSCS stimulation. Thereafter, the patients were treated for another 6 weeks with one of the 3 methods (crossover possible). Pain ratings on the visual analog scale (VAS) were recorded and compared. A Pain Disability Index (PDI) questionnaire was used at the baseline and at 3 months.

Results: We included 24 patients in this study (11 women, mean age 62.3 yrs.) The values of the second week of the stimulation were the only ones used for the calculations. The first week of the stimulation was used as a wash-out period.

The combined application of BurstDR™ and MuscleSCS stimulation was associated with the best results (P = 0.032). PDI scores did not improve during this treatment. No serious adverse events occurred during this study. Seventy-one and a half percent of the patients experienced an improvement in their pain as a result of the additional MuscleSCS stimulation.

Limitations: In this study, only one fixed contact setting (3 & 4) was used to ensure uniform conditions for all patients and the ability to compare the different treatment modes.

Conclusion: This study showed that the combined application of SCS (BurstDR™) and additional MuscleSCS stimulation using a rod electrode could significantly improve outcomes for patients suffering from chronic back pain.

Key words: Spinal cord stimulation, muscle stimulation, chronic back pain, low-frequency stimulation, MuscleSCS

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Chronic lower back pain is difficult to treat (1). In many cases, conservative measures such as various medications, massages, physiotherapy, pain therapy, and interventional procedures cannot adequately relieve the pain. Insufficiency of the back muscles often leads to incorrect loading and, over

time, to structural changes in the muscles and their surrounding tissues, such as shortening and atrophy (2). Physiotherapy aims to use the trunk muscles to stabilize the spine and thus ensure the active protection of pain-sensitive structures in joints, intervertebral discs, and the surrounding tissue (3). If the pain persists despite these measures, a surgical procedure can often be carried out successfully. However, a significant number of patients do not benefit even from repeated surgical interventions.

Neuromodulative procedures may also be used to relieve chronic back pain. This type of technique targets the pain by stimulating the multifidus muscles (4-7). Stimulating the associated nerves that supply those muscles causes them to activate and regain strength over time. This then also leads to increased stability of the spine and subsequent pain relief (8,9).

Spinal cord stimulation (SCS), another option for treating back pain, is associated with good results when new-wave technologies such as BurstDR™ or high-frequency (HF) stimulation are used (10-12). However, if the patient's musculature is a pain factor, which is often the case, even these technqiues may be unable to relieve the pain. One of the main problems with SCS stimulation is that muscle receptors do not respond well to SCS therapy. Nonetheless, it is possible to stimulate alpha motoneurons in the anterior horn of the spinal cord by using lower-frequency SCS stimulation, which creates a massage-like effect for the muscles.

Previously, we conducted a pilot study showing that SCS stimulation could stimulate back muscles and thereby relieve pain (13). We named this new method the MuscleSCS technique. For the current study, we additionally stimulated motoneurons via SCS electrodes. By way of different electrode contact combinations and lower frequencies, various muscles in the back can be reached and stimulated. In the pilot study, we demonstrated that it was possible to stimulate muscles by using lower frequencies (2-8 Hz) of SCS electrodes, such as percutaneous plate electrodes (lamitrodes) or Octrodes™. This MuscleSCS stimulation was perceived by patients as pleasant and pain-relieving. Different stimulation parameters affected different muscle groups. From the many available options of stimulation parameters, an optimal stimulation setting could be determined for each patient.

For this study, we wanted to examine the MuscleSCS technique in clinical practice.

We had the following hypotheses:

1. Combining MuscleSCS stimulation with BurstDR™ stimulation can relieve back pain better than can BurstDR™ stimulation alone.
2. MuscleSCS stimulation alone can achieve similar pain relief to that effected by BurstDR™ stimulation alone.
3. Combined MuscleSCS stimulation and SCS stimulation can be performed with percutaneous rod electrodes (Octrodes™).
4. MuscleSCS stimulation is perceived as pleasant and pain-relieving by patients in clinical practice.
5. MuscleSCS stimulation does not cause serious side effects.

Methods

We studied patients who were suffering from lower back pain and had previously been treated with BurstDR™ stimulation via an Octrode™. We wanted to know if the addition of MuscleSCS stimulation would lead to better results than would BurstDR™ stimulation alone.

Inclusion Criteria

The study enrolled patients who suffered from chronic lower back pain, had undergone at least one instance of back surgery, and had also received unsuccessful pain management, physical therapy, and various analgesics. The patients were at least 18 years of age. They had experienced a successful SCS trial (> 50% pain relief) followed by the implantation of an internal pulse generator (IPG) with BurstDR™ stimulation. A rod electrode (Octrode™) had been used in that process. The patients were able to complete the questionnaires and willing to participate in the study.

Study Protocol

The patients, who suffered from lower back pain, had gone through a successful trial (> 50% pain reduction) and the subsequent implantation of an internal pulse generator in the past (one to 10 years ago). They had been treated with BurstDR™ stimulation up to that time. These patients were then contacted by telephone and offered MuscleSCS as an adjunct therapy to improve their current pain management. Patients who agreed to the additional MuscleSCS treatment and the participation in the study were invited to the outpatient clinic of the Department of Neurosurgery at the University of Tuebingen. The patients were again informed about the study and the procedure, which were explained in detail, and then agreed in writing to participate. Informed written consent was obtained

from each patient. The study was also approved by the local ethics committee (448/2020BO1). The questionnaire (F0) was filled out for the first time. Then the first phase of the study began.

Study Phase One (0-6 Weeks)

The stimulation was randomized for 6 weeks in the following manner:

2 weeks: only BurstDR™ (B)
2 weeks: only MuscleSCS stimulation (M)
2 weeks: BurstDR™ combined with MuscleSCS stimulation (BM)

The patients recorded their current pain sensations (visual analog scale [VAS] score of 0-10) in pain diaries once a day at lunchtime.

MuscleSCS stimulation was performed in the following way: it was done twice a day, for half an hour at 9 in the morning and at 8 in the evening. We used a stimulation frequency between 4 and 8 Hz. The patients could choose which frequency they preferred. A special program was developed for this purpose. The patients could switch the stimulation on and off independently. The BurstDR™ program was not continued during the MuscleSCS stimulation.

This completed the first phase of the study.

Study Phase 2 (6 Weeks-3 Months)

For another 6 weeks, the patients could use the form of stimulation from which they had benefited most in the first phase (crossover design). As before, the pain scores had to be documented daily in the pain diaries. Patients who wanted to change the stimulation again could do so. However, they had to note this alteration in their pain diaries so that an exact stimulation sequence was available later, thus allowing the researchers to see exactly which programs were used how often and how much the pain was reduced by the treatment at the same time.

After the completion of the second phase, 3 months had passed, and the questionnaire had to be completed again (F3M). This marked the end of the study.

The patients then continued to stimulate in the way that was best for them.

Statistical Evaluation

Phase One: The exclusive use of BurstDR™ stimulation was compared with the exclusive use of MuscleSCS stimulation. The Wilcoxon test and t-test were used for this comparison. In the same way, the sole use of BurstDR™ stimulation was compared with the combined use of BurstDR™ stimulation and MuscleSCS stimulation.

Phase 2: We used the repeated-measures ANOVA test for the PDI. In addition, the Bonferroni correction was used for multiple comparisons. The Wilcoxon test was used to measure patient satisfaction.

Results

This is a prospective, single-center, single-blinded, randomized crossover study.

From March 2018 to November 2020, 24 patients (11 women, 13 men, mean age 62.3 years, maximum age 85 years, minimum age 32 years) were enrolled in this study. All patients suffered from chronic back pain. A SCS system that used an Octrode™ as an electrode had been implanted at the Department of Neurosurgery of the University of Tuebingen in the past. Until now, the patients had been treated only by BurstDR™ stimulation. The period of the duration of the previous BurstDR™ stimulation is shown in Table 1. The Octrode™'s location in the spinal canal is shown in Table 2. Nearly half of the patients suffered from lower back pain (47.3%), and 45.8% of patients also had some form of leg pain. However, lower back pain was the dominant pain syndrome in these patients (Table 3). The demographic data of all patients are shown in Table 4. The values of the second week of the stimulation were the only ones used for the calculations. The first week of the stimulation was used as a washout period.

Comparison of the Different Stimulation Modes During the First 6-Week Stimulation Phase

Of the initial 24 patients, only 21 had complete data sets and could be used for the final analysis. We compared the group of patients who received only BurstDR™ stimulation to the group of patients who received only MuscleSCS stimulation. We then compared the group who received only BurstDR™ stimulation to the group who received the combination of the Burst-

Table 1. *Duration of the BurstDR™ stimulation prior to the use of additional MuscleSCS stimulation (n = 24).*

Duration of Stimulation	Number of Patients	Percentage
Less than one year	3	12.5
Between one and 5 years	16	70.8
Longer than 5 years	5	16.7
Total	24	100.0

DR™ and MuscleSCS stimulations. We used the VAS to measure the improvement in pain. There was no significant difference between the group who received only BurstDR™ stimulation and the group who received only MuscleSCS stimulation (P = 0.509) (Fig. 1). However, it should be noted that MuscleSCS stimulation by itself showed comparable results to BurstDR™ stimulation. The comparison between the group who received only BurstDR™ stimulation and the group who received the combination of the BurstDR™ and MuscleSCS stimula-

Table 2. *The Octrode™'s location in the spinal canal (n = 24).*

Location of Octrode™	Number of Patients	Percentage
T7-9	7	29.2
T7-10	1	4.1
T8-9	7	29.2
T8-10	2	8.4
T10-11	1	4.1
T10-12	2	8.4
T11-12	3	12.5
T11-L1	1	4.1
Total	24	100.0

Table 3. *Localization of pain in the patients (various locations possible in one patient) (n = 24).*

Localization of Different Pain Areas (Several Areas Possible)	Number of Patients	Percentage
Upper back	1	2.6
Middle back	1	2.6
Lower back	21	55.4
Whole back	1	2.6
Buttocks	2	5.2
One leg	7	18.4
Both legs	5	13.2
	38	100

Table 4. *Demographic data (n = 24).*

Patient Number	Gender	Age (Years)	Main Area of Pain	Number of Previous Back Operations	Duration of BurstDR™ Stimulation (Months)	Location of Electrode	Type of Electrode
1	Male	56	Back	3	32	T8/9	Octrode™
2	Male	59	Back	1	28	T7/8	Octrode™
3	Female	36	Back and leg	4	23	T11/12	Octrode™
4	Male	49	Back pain	4	32	T8/9	Octrode™
5	Female	69	Back pain	3	23	T8/9	Octrode™
6	Female	58	Back pain	3	35	T7/8	Octrode™
7	Female	82	Back and leg	3	38	T8/9	Octrode™
8	Male	65	Back pain	2	55	T8/9	Octrode™
9	Female	68	Back and leg	4	43	T10/11	Octrode™
10	Male	44	Back	4	123	T8/9	Octrode™
11	Female	72	Back	5	117	T8/9	Octrode™
12	Male	59	Back and leg	2	77	T11/12	Octrode™
13	Female	56	Back	2	44	T7/8	Octrode™
14	Female	74	Back	1	56	T7/10	Octrode ™
15	Male	76	Back and leg	1	53	T10/11	Octrode™
16	Female	85	Back	2	79	T7/8	Octrode™
17	Male	59	Back and leg	1	90	T10/11	Octrode™
18	Male	82	Back	5	59	T7/8	Octrode™
19	Male	63	Back and leg	2	35	T8/9	Octrode™
20	Male	62	Back	3	55	T7/8	Octrode™
21	Female	32	Back	2	4	T11/12	Octrode™
22	Male	80	Back	4	4	T8/9	Octrode™
23	Male	63	Back	3	53	T7/8	Octrode™
24	Male	68	Back	5	3	T11/12	Octrode™

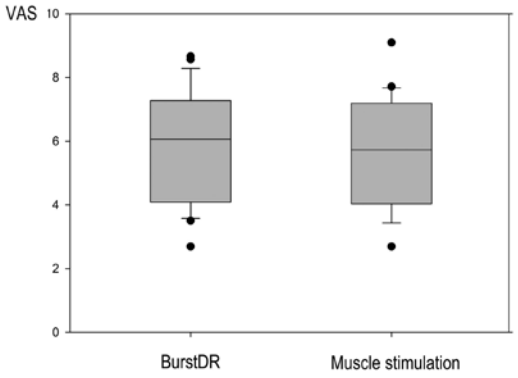

Fig. 1. *A boxplot graph compares BurstDR™ stimulation alone to MuscleSCS stimulation alone. There was no significant difference between the 2 different study groups (P = 0.509).*

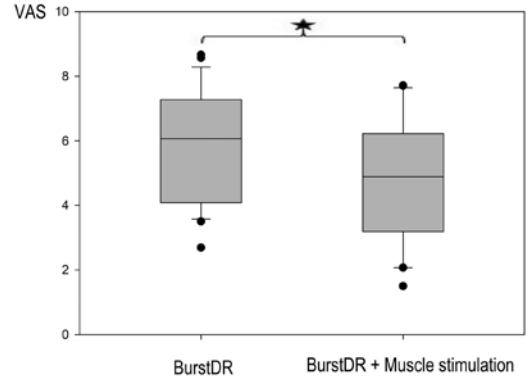

Fig. 2. *A boxplot graph compares BurstDR™ stimulation alone to a combination of MuscleSCS stimulation and BurstDR™ stimulation. Combining the 2 methods was associated with a significant improvement (P = 0.032).*

tions showed that a significant improvement was associated with the combined method ($P = 0.032$) (Fig. 2).

Adverse Events

We also investigated the possible side effects of MuscleSCS stimulation during the study period. An occasional uncomfortable sensation during stimulation was noted by 28.6% of patients. A brief burning sensation was reported by 14.3% of participants. Mild, short-lasting muscle cramps after the stimulation occurred in 14.3% of patients (Table 5). However, no serious adverse effects were noted.

Table 5. *Adverse effects (n = 21).*

Adverse Effect	Number of Patients	Percentage
Unpleasant feeling during stimulation	6	28.6
Stimulation not properly adjusted (too strong, too weak)	3	
Muscle cramps after the stimulation	3	14.3
Burning sensation during stimulation	3	14.3
Cold sensation	1	4.8
Short numbness in the area of the stimulation	1	4.8
Short imbalance after the stimulation	1	4.8

Pain Disability Index (PDI)

We examined the PDI at the beginning and at the end of the study. No statistical difference was found between the group who received only the BurstDR™ stimulation and the group who received only the MuscleSCS stimulation ($P = 0.715$). There was also no statistical difference between the group who received only the BurstDR™ stimulation and the group who received the combined BurstDR™ and MuscleSCS stimulations ($P = 0.61$).

Frequency Distribution of the Individually Selected Program During the Second Phrase

We also examined which of the 3 stimulation methods was chosen after the initial study phase. Most of the patients chose the combination of BurstDR™ and MuscleSCS (70.9%). Interestingly, 2 patients (8.3%) were satisfied with MuscleSCS stimulation alone (Table 6). Once patients selected their individual program, they did not change it during the second study phase.

Patient Satisfaction

We also evaluated patients' satisfaction with the MuscleSCS stimulation. More than 50% of the patients rated the MuscleSCS stimulation as good or very good (Table 7). Twenty-eight percent of the patients did not benefit from this additional treatment method. Overall, 71.5% of the patients in this study group benefited from the additional MuscleSCS stimulation.

Discussion

In this study, we demonstrated that MuscleSCS stimulation in combination with BurstDR™ stimulation

was associated with significantly better results in back pain relief than was BurstDR™ stimulation alone (hypothesis one met). MuscleSCS alone was able to achieve similar pain relief to that of BurstDR™ stimulation alone (hypothesis 2 met). A combination of MuscleSCS stimulation and SCS could be performed with percutaneous rod electrodes (Octrodes™) (hypothesis 3 met). Patients in clinical practice found MuscleSCS stimulation comfortable (hypothesis 4 met). MuscleSCS stimulation did not cause any serious side effects (hypothesis 5 met).

Additionally, MuscleSCS was shown to help 71.5% of participants with chronic low back pain in clinical practice. In a pilot study, we demonstrated that it was possible to produce pleasant, pain-relieving muscle stimulation using the MuscleSCS method. In this clinical study, we confirmed that rod electrodes (Octrodes™) were also capable of producing muscle stimulation that the participants perceived as pleasant and pain-relieving. We stimulated the Octrode's™ contact combination of 3 and 4 at 4-8 Hz. In our pilot study, we found this combination of parameters to be beneficial.

Musculature is an important factor in the etiology of chronic back pain. In the lumbar spine, the multifidus muscle, which belongs to the medial tract of the autochthonous back muscles, and the transversus abdominis muscle, which belongs to the abdominal muscles, provide the most effective segmental stability. The rectus abdominis muscle and the erector spinae muscles, along with the quadratus lumborum muscle, also stabilize posture (3).

Restoring functional stabilization to the multifidus muscles has been of great interest in the literature (4-7,14). These muscles have been considered tonic stabilizers of the spine (8). The concept of stimulating the medial branch of the ramus dorsalis to induce contractions of the multifidus muscle has been proposed. This treatment has been shown to relieve chronic low back pain (6,7,9,14).

However, until now, SCS has not been used to treat muscle pain. This is mainly because the pain signals sent to muscle pain receptors cannot be sufficiently influenced by current SCS techniques. Using an SCS electrode to provide low-frequency stimulation of alpha-motor neurons and cause direct muscle stimulation may have a massage-like effect on muscles, relieving pain like an ordinary massage. A 5-week, twice-weekly 30-minute massage has been shown to relieve pain, depression, and anxiety and even improve sleep in patients with chronic back pain (15).

Massage's ability to relieve muscle pain comes from specific mechanisms. When back pain occurs, the muscles of the back are activated to stabilize the spine and prevent movement, thus relieving pain. This subsequent constant activation may lead to tension and even spasms, and those effects in turn may cause damage to these muscles, which can be very painful and is a common cause of pain. The perceived pain that emanates from these muscles is related to the increase in the firing rate of nociceptors, which have different activation thresholds (16-18). Afferent nerve terminals have numerous receptor sites that respond to endogenous chemicals such as bradykinin, serotonin or 5-hydroxytryptamine, prostaglandin E2, adenosine triphosphate, and histamine (17-20). Both muscles and nerves are mechanosensitive structures that respond to a variety of mechanical stimuli. The conversion of a mechanical stimulus into a chemical signal, or the cellular signaling cascade that results from the external mechanical deformation of tissue, is known as mechanotransduction (17,18). This mechanotransduction may eventually lead to the transmission of signals throughout the cell, altering protein expression and initiating healing processes that relieve pain originally caused by muscle mechanisms and promote a restorative environment (21,22). Massage also increases serotonin levels, correlating with pain relief (23). Manual pressure relief (MPR) and

Table 6. *Frequency distribution of the individually selected program in phase 2 (n = 24).*

Type of Stimulation	Number of Patients	Percentage
MuscleSCS	2	8.3
BurstDR™	5	20.8
BurstDR™ and MuscleSCS	17	70.9
Total	24	100

Table 7. *Patient satisfaction with MuscleSCS stimulation.*

Patient Rating	No Satisfactory Improvement	Satisfactory Improvement	Good Improvement	Very Good Improvement	Total
Number of Patients	6	3	9	3	21
Percentage	28.5	14.3	42.9	14.3	100
Percentage		71.5%			

electrical neuromodulation (ENM) may successfully treat major trigger points in patients with lower back pain (24,25).

Our study also showed that MuscleSCS alone could reduce pain almost as much as BurstDR™ stimulation alone. This important finding emphasizes muscles' influence as contributors to pain. SCS has been shown to be a reliable technique for treating chronic lower back pain (26,27). The combination of SCS and MuscleSCS could further improve the treatment for this condition.

We have introduced a name for this new combined SCS method: the MuscleSCS technique. This method requires 3 components: the frequency of the MuscleSCS stimulation, a type of wave (e.g., BurstDR™, high-frequency), and a type of electrode (rod electrode, plate electrode). Depending on the 3 different components, various combinations of the subtechniques are possible (Table 8a-b). To achieve consistency when comparing results from different study groups, using the same labeling system is recommended for future research.

Limitations

In this study, only one fixed contact setting (3 & 4) of the electrode was used. The purposes of this choice were to establish uniform conditions for all patients and to allow us to compare the different treatment modes (M, BM, B). From our pilot study, we know that the different parameters' optimal settings can vary from one patient to another and that we could have achieved even better results if we had adjusted the settings for each patient.

Conclusion

This clinical study demonstrated that a combination of MuscleSCS and SCS achieved significantly better relief of chronic low back pain than did SCS alone. It was shown that MuscleSCS could also be performed with rod electrodes (Octrodes™). Further clinical studies are needed to confirm these results and to investigate other types of electrodes and waves in combination with MuscleSCS.

Table 8a. *Possible subtypes of the MuscleSCS technique.*

Components	Frequency of Muscle Stimulation	Type of Wave Used for SCS	Type of Electrode Used	Name
3	Frequency	BurstDR™	Percutaneous paddle lead	Frequency-BurstDR™-percutaneous paddle lead
3	Frequency	BurstDR™	Octrode	Frequency- BurstDR™-Octrode™
3	Frequency	Tonic	Quatrode	Frequency-Tonic-Quatrode
3	Frequency	10KHz	2 Octrodes	Frequency-10KHz, 2 Octrodes™

Table 8b. *Names of the combinations of MuscleSCS and some of its possible subtypes.*

Technique	Subtype	Final Name (Examples Using Different Frequencies)
MuscleSCS	Frequency-BurstDR™- percutaneous paddle lead	MuscleSCS (8Hz-BurstDR™-percutaneous paddle lead)
MuscleSCS	Frequency-BurstDR™-Octrode	Muscle SCS (6Hz-BurstDR™-Octrode™)
MuscleSCS	Frequency-Tonic-Quatrode	MuscleSCS (4Hz-Tonic-Quatrode)
MuscleSCS	Frequency-10KHz-2 Octrodes	Muscle SCS (8Hz-10KHz-2 Octrodes™)

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