Long-Term Clinical Outcomes of a Low-Energy Derivative Study of Differential Target Multiplexed™ Spinal Cord Stimulation

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INTRODUCTION

Differential Target Multiplexed™ spinal cord stimulation (also known as DTM™ SCS) is a unique programming approach where electrical signals are multiplexed spatially and temporally. DTM™ SCS was inspired from pre-clinical research demonstrating that multiplexed signals can differentially modulate neurons and glial cells to balance interactions perturbed by neuropathic pain.[1] DTM™ SCS is an established therapy that has shown superior back pain relief to traditional SCS.[2] Derivatives of the DTM™ waveform are now being investigated to understand opportunities to tailor therapy delivery based on different patient profiles. A recent feasibility study (n=12) investigating a reduced-energy DTM™ SCS derivative (DTM™ SCS endurance therapy) demonstrated:

- Subjects achieved a similar degree of pain relief and patient satisfaction to baseline (≥200 Hz) therapy[3]
- An 82% reduction in charge delivered per second[3]

Here we present results from a recently completed study of subjects trialed using the same DTM™ SCS derivative with a modified energy profile (DTM™ SCS endurance) and followed through 12-month follow-up post-device activation.

MATERIALS & METHODS

This was a prospective, multicenter, open-label, post-market study. This study was IRB approved and registered on clinicaltrials.gov (NCT04601454). Subjects that reported an overall pain Visual Analog Score (VAS) of ≥6 at Baseline with moderate to severe back and leg pain were enrolled. Subjects that were a candidate for SCS and met eligibility criteria underwent a SCS trial, per labeling. Subjects that reported ≥50% improvement in overall pain relief while programmed to DTM™ SCS endurance therapy were eligible for implant with a rechargeable neurostimulator. Evaluation visits occurred at 1-, 3-, 6-, and 12-months post-device activation.

The primary outcome was change in overall (back and leg) pain intensity, as measured by VAS, from baseline to 3-Month visit in per-protocol subjects. Additional outcomes included changes in overall pain at 6- and 12-Months, changes in back pain, and leg pain, programming parameters associated with energy use, and safety data at 3-, 6- and 12-Months. Patient satisfaction, Oswestry Disability Index (ODI), and EQ-5D-5L health questionnaires were collected at 3- and 12-Months. Programming parameters were reported through 12-Months and details are provided on the corresponding poster.[4]

Per protocol analysis (cycling “on”) and a DTM™ SCS endurance completers analysis (cycling “On” or “Off”) are presented for the primary outcome. The DTM™ SCS endurance completers analysis is reported for all other outcomes and includes all subjects programmed to DTM™ SCS endurance therapy for over 90% of their study duration.

RESULTS

Demographics

57 subjects were enrolled at 12 US sites from November 2020 through June 2021. Demographics for all enrolled subjects are detailed in Table 1. The most common primary indications for enrolled subjects were:

- post-laminectomy pain/failed back surgery syndrome (61.4%)
- radiculopathy (29.8%)
- degenerative disc disease (8.8%)

Forty-nine subjects started a device trial, and 43 completed a trial end visit. Out of 38 (88.3%) subjects with trial success (self-reported ≥50% improvement in overall pain relief), 35 were implanted with a rechargeable neurostimulator, and 29 completed the 12-Month visit and were included in the DTM™ SCS endurance completers analysis set.

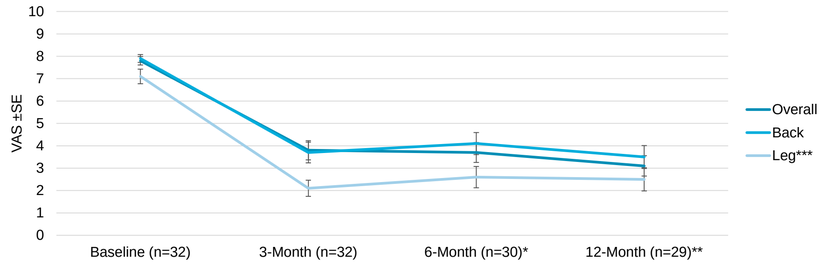
Table 1. Baseline Demographics (n=57)

Mean (SD) Age (Years)	63.2 (11.9)
Female	57.9%
Mean (SD) Years Since Pain Onset	13.4 (13.3)
Mean (SD) Number of Surgeries	1.7 (1.5)
No Surgical History	12.3%

Mean Pain Scores

At the 3-, 6-, and 12-Month visits, the reduction in pain, as measured by VAS, in overall pain, back pain, and leg pain is shown in Figure 1.

Figure 1. Mean VAS (Overall, Back & Leg Pain)



*Subjects were excluded from analysis at 6-Months due to programming changes from DTM™ SCS endurance therapy (N=1) and due to study exit (N=1)
**Subjects were excluded from analysis at 12-Months due to programming changes from DTM™ SCS endurance therapy (N=2) and due to study exit (N=1)
***n for leg pain is 31 at baseline and 3-Months, 29 at 6-Months, and 28 at 12-Months due to a missing value at baseline for one subject

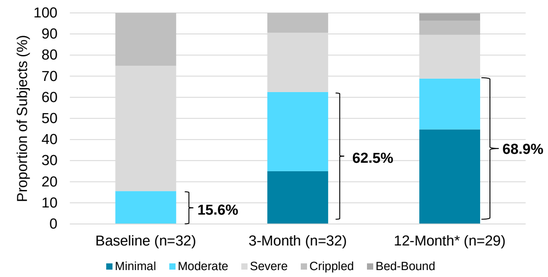
The mean reduction from baseline in overall pain VAS score was 3.9cm at the 3-Month follow-up, 4.1cm at the 6-Month follow-up, and 4.6cm at the 12-Month follow-up. For per-protocol analysis the mean reduction from baseline in overall pain VAS score was 3.9cm at the 3-Month follow-up, 4.0cm at the 6-Month follow-up, and 4.4cm at the 12-Month follow-up.

The mean reduction from baseline in back pain VAS score was 4.3cm at the 3-Month follow-up, 3.9cm at the 6-Month follow-up, and 4.4cm at the 12-Month follow-up. The mean reduction from baseline in leg pain VAS score was 5.0cm at the 3-Month follow-up, 4.8cm at the 6-Month follow-up, and 4.8cm at the 12-Month follow-up.

Mean Oswestry Disability Index (ODI) Scores

From Baseline, 68.8% of subjects at 3-Months and 75.9% of subjects at 12-Months improved to a less disabled category. The mean change in ODI from Baseline to 3-Months was -17.0, and from Baseline to 12-Months was -22.0. The proportion of subjects in the minimal/moderate disability categories increased from 15.6% at Baseline to 62.5% at 3-Months and 68.9% at 12-Months (Figure 2). ODI scores were not collected at the 6-Month visit.

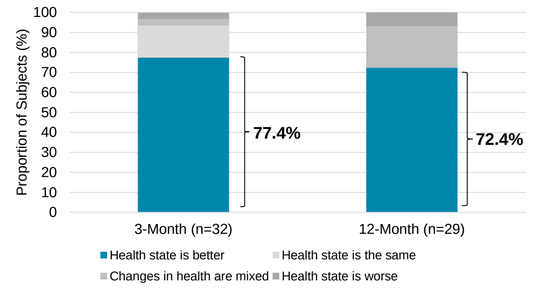
Figure 2. Mean ODI Scores



Change in EQ-5D

Compared to Baseline, 77.4% of subjects were in a better health state at 3-Months and 72.4% were in a better state at 12-Months (Figure 3). The mean change in EQ-5D Index from baseline to 3-months was 0.29, and from baseline to 12-Months was 0.30. EQ-5D was not surveyed at the 6-month visit.

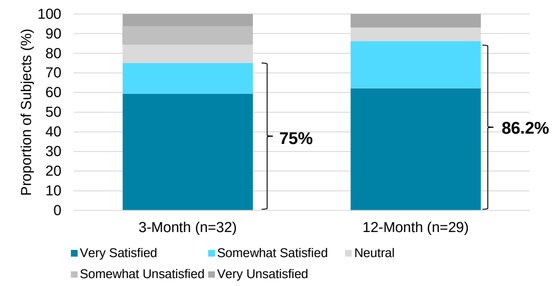
Figure 3. Changes in EQ-5D Domains



Subject Satisfaction

75% of subjects at the 3-Month visit and 86.2% of subjects at the 12-Month visit reported that they were “very satisfied” or “somewhat satisfied” with their (Figure 4). Subject satisfaction was not reported at 6-Months.

Figure 4. Subject Satisfaction



Adverse Events

Only Adverse Events (AEs) related to the device, therapy, or procedure were collected for this study. A total of 12 AEs were reported in 28.6% (10/35) of the implanted subjects. 1 total serious adverse event (SAE; device- and procedure-related implant site infection), considered a serious adverse device effect (SADE), was reported in 1 implanted subject. No deaths have occurred.

DISCUSSION

Advanced SCS patterns can employ energy-conserving programming approaches through therapy cycling as well as manipulations of amplitude, frequency, and pulse width. The use of DTM™ SCS endurance therapy with a modified energy profile in this study resulted in clinically meaningful pain relief as well as improved function and a high degree of therapy satisfaction. In current research, it is important to consider the additional benefits of SCS as a therapy related to quality of life, function, and individual patient experience. This study suggests that a DTM™ SCS derivative therapy with a modified-energy profile could impact patient experience with rechargeable devices and may benefit those patients best suited for recharge-free devices.

DISCLOSURE

This study was sponsored by Medtronic.

REFERENCES

1. Vallejo R, Kelley CA, Gupta A, Smith WJ, Vallejo A, Cedeño DL. Modulation of neuroglial interactions using differential target multiplexed spinal cord stimulation in an animal model of neuropathic pain. Mol Pain. 2020 Jan-Dec;16:1744806920918057.

2. Fishman M, Cordner H, Justiz R, et al. 12-Month Results from Multicenter, Open-Label, Randomized Controlled Clinical Trial Comparing Differential Target Multiplexed Spinal Cord Stimulation and Traditional Spinal Cord Stimulation in Subjects with Chronic Intractable Back Pain and Leg Pain. Pain Pract. 2021; 00: 1– 12. doi: 10.1111/papr.13066. Epub ahead of print.

3. Fishman M, Hatheway J, Will A, et al. Utilization of Different Energy Profiles of Differential Target Multiplexed™ Spinal Cord Stimulation. American Society of Pain & Neuroscience (ASPN); July 22-25, 2021; Miami, FL. Abstract.

4. Provenzano D, Amirdelfan K, Grewal P, et al. Modeling Energy Demands of a Reduced-Energy Derivative of DTM™ Stimulation on Rechargeable and Recharge-Free SCS Systems. American Society of Regional Anesthesia and Pain Medicine (ASRA); November 17-18, 2022; Orlando, FL. Poster.

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