Advancing the science and evidence

DTM™ SCS endurance therapy:
6-month clinical results and preclinical understanding

References:
8. Compared to average daily recharge of ~1 hour every day on higher dose therapies.

SPINAL CORD STIMULATION BRIEF SUMMARY

INDICATIONS: Spinal cord stimulation (SCS) is indicated as an aid in the management of chronic, intractable pain of the trunk and/or limbs-including unilateral or bilateral pain. CONTRAINDICATIONS: Diathermy - Energy from diathermy can be transferred through the implanted system and cause tissue damage resulting in severe injury or death. WARNINGS: Sources of electromagnetic interference (e.g., defibrillation, electrocautery, MRI, RF ablation, and therapeutic ultrasound) can interact with the system, resulting in unexpected changes in stimulation, serious patient injury or death. An implanted cardiac device (e.g., pacemaker, defibrillator) may damage a neurostimulator, and electrical pulses from the neurostimulator may cause inappropriate response of the cardiac device. Patient with diabetes may have more frequent and severe complications with surgery. A prospective assessment is advised for some patients with diabetes to confirm they are appropriate candidates for surgery. PRECAUTIONS: Safety and effectiveness has not been established for pediatric use, pregnancy, unborn fetus, or delivery. Avoid activities that put stress on the implanted neurostimulation system components. Recharging a rechargeable neurostimulator may result in skin irritation or redness near the implant site. ADVERSE EVENTS: May include: undesirable change in stimulation (uncomfortable, jolting or shocking), hematoma, epidural hemorrhage, paralysis, seroma, infection, erosion, device malfunction or migration, pain at implant site, loss of pain relief, and other surgical risks. Adverse events may result in fluctuations in blood glucose in patients with diabetes. Refer to www.medtronic.com for product manuals for complete indications, contraindications, warnings, precautions and potential adverse events. Rx only. Rev 0422

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DTM™ SCS therapy has shown superior back pain relief to traditional SCS. DTM™ SCS was inspired from preclinical research demonstrating that differential target multiplexed signals can differentially modulate neurons and glial cells to balance interactions perturbed by neuropathic pain.2,3,4 Expanding on the foundational DTM™ research, DTM™ SCS endurance therapy is an energy modified variation designed to offer additional treatment options to personalize care for more patients. Here, we summarize results presented at recent conferences.

**DTM™ SCS endurance therapy 6-month results**

**Primary purpose**
To evaluate the long-term efficacy and energy use of DTM™ SCS endurance therapy.

**Secondary purpose**
Further demonstrate the effectiveness of DTM™ SCS endurance therapy through 12 months by characterizing:
- Changes in pain intensity for overall, back and leg pain
- Programming parameters associated with energy use
- Changes in functional disability as measured by Oswestry Disability Index (ODI)
- Subject satisfaction
- Therapy safety data

**Design**
On-label, prospective, multicenter, single arm, de novo study with 3-, 6- and 12-month follow-up

**Centers**
- 12 sites in the United States

**Patient Population**
- Patients with chronic intractable overall pain (≥ 6) and moderate to severe back or leg pain (≥ 6)

**Sample size**
- 35 subjects implanted with a rechargeable device
- 30 subjects with 6-month follow-up (per protocol)

**6-month results**
- **Successful in trial**: 88% trial success rate (≥ 50% success)
- **Sustained, meaningful pain relief**: Patients were able to achieve a 4.1 reduction in VAS for overall pain from baseline to 6 months (Figure 1). Pain relief also sustained for back and leg pain
- **Therapy satisfaction**: 75% of patients were satisfied with DTM™ SCS endurance therapy at 3-months
- **Quality of life improvements**: 69% of patients improved in degree of disability from baseline to 3 months
- **Long-lasting recharge-free**: estimated 51%-71% years of longevity on Vanta INS based on real programming data (Figure 2)
- **Rapid recharge**: 5-minute daily recharge on Intellis INS
- **Consistent safety profile**: The frequency, type, seriousness and severity of adverse events demonstrated a risk profile in line with the commercial product

**Methods**
- **Sample size**
- **Centers**
- **Patient Impedance ranges (Ω)**
- **Baseline** (N = 32)
- **3 month** (N = 32)
- **6 month** (N = 30)
- **Mean VAS ± SE**

**Conclusions**
- **DTM derivatives** showed statistically significant reversal of pain behaviors when compared low-rate SCS stimulation in mechanical sensitivity testing
- **DTM derivatives** modulated neuro-inflammatory processes more than low-rate SCS
- **DTM derivatives** showed statistically significant reversal of gene expression in glial cells toward the naive state compared to low-rate stimulation

**Preclinical data**

**Objective**
To compare reduced-energy differential target multiplexed programming (DTMP) with low-rate programming in rodents after a spared nerve injury (SNI).

**Groups**
Rodents were randomized into five groups: Naive, No SCS, DTMP derivatives (DTMP E1, cycled 1:1; and DTMP E2, cycled 1:2) and low-rate (LR).

**Methods**
- **General**: Excluding the naive group, the rodents underwent SNI surgery.
- **SCS**: At 5 days post-surgery, DTMP E1, DTMP E2, or LR spinal cord stimulation (SCS) was delivered continuously for 48 hours.
- **Behavior**: Pain-related responses to mechanical (von Frey filaments) stimuli were collected preinjury and at 48 hours of stimulation.
- **Genetic analysis**: After the behavioral measures, the spinal cord (dorsal quadrant ipsilateral to injury) was removed for genetic analysis. RNA sequencing was used to determine changes in gene expression as a result of injury (No-SCS vs. Naïve) and as a result of SCS (SCS vs. No-SCS). Bioinformatics tools (Weighted Gene Co-expression Network Analysis [WGCNA] and Gene Ontology Enrichment Analysis [GOEA]) were used to analyze the results. WGCNA ranks the gene expression patterns into modules and then normalizes each module to an eigengene; whereas GOEA groups genes into modules based on relevant biological processes.

**Results**

**Behavioral studies**: All three therapies (DTMP E1, DTMP2, LR) significantly reduced mechanical hypersensitivity (p < 0.001 vs. No SCS), although DTMP E1 and DTMP E2 provided a statistically significant improvement as compared to LR (p < 0.05 vs. LR SCS) (Figure 3).

**Genetic analysis**: The injury significantly affected 25 WGCNA modules, consisting of over 8,000 individual gene transcripts. DTMP derivatives (E1 and E2) modulated neuro-inflammatory processes more than LR.