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Clinical Studies

Surgical treatment of refractory low back pain using implanted BurstDR spinal cord stimulation (SCS) in a cohort of patients without options for corrective surgery: Findings and results from the DISTINCT study, a prospective randomized multi-center-controlled trial

James J. Yue, MD, DABPM[a,*], Christopher J. Gilligan, MD, MBA[b], Steven Falowski, MD[c], Jessica Jameson, MD[d], Mehul J. Desai, MD, MPH[e], Susan Moeschler, MD[f], Julie Pilitsis, MD, PhD[g], Robert Heros, MD[h], Edward Tavel, MD[i], Sayed Wahezi, MD[j], Robert Funk, MD[k], Patrick Buchanan, MD[l], Anne Christopher, MD[m], Jacqueline Weisbein, DO[n], Denis Patterson, DO[o], Robert Levy, MD, PhD[p], Ajay Antony, MD[q], Nathan Miller, MD[r], Keith Scarfo, DO[s], Scott Kreiner, MD[t], Derron Wilson, MD[u], Chi Lim, MD[v], Edward Braun, MD[w], David Dickerson, MD[x], Jonathan Duncan, MD[y], Jijun Xu, MD[z], Kenneth Candido, MD[aa], Ibrahim Mohab, MD[bb], Fishell Michael, MD[cc], Bram Blomme, PhD[dd], Udoka Okaro, PhD[dd], Timothy Deer, MD[ee]

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* Corresponding author: Frank H. Netter School of Medicine, Department of Orthopaedic Surgery, Connecticut Orthopaedics, 800 Howard Ave, New Haven, CT 06519, USA.

E-mail address: JYue@ct-ortho.com (J.J. Yue).

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[a] Connecticut Orthopaedics, Hamden, CT, United States
[b] Brigham and Women's Hospital, Boston, MA, United States
[c] Center for Interventional Pain and Spine, Lancaster, PA, United States
[d] Axis Spine Center, Coeur d'Alene, ID, United States
[e] International Spine, Pain and Performance Center, Washington, DC, United States
[f] Mayo Clinic, Rochester, NY, United States
[g] Florida Atlantic University, Boca Raton, FL, United States
[h] Spinal Diagnostics, Tualatin, OR, United States
[i] Clinical Trials of South Carolina, Charleston, SC, United States
[j] Montefiore Montefiore Medical Center, Bronx, NY, United States
[k] Indiana Spine Group, Indianapolis, IN United States
[l] Spanish Hills Interventional Pain Specialists, Camarillo, CA United States
[m] Saint Louis Pain Consultants, Chesterfield, MO United States
[n] Napa Valley Orthopedic Medical Group, Napa, CA United States
[o] Nevada Advanced Pain Specialists, Reno, NV United States
[p] Anesthesia Pain Care Consultants, Tamarac, FL United States
[q] The Orthopaedic Institute, Gainesville, FL United States
[r] Coastal Pain & Spinal Diagnostics Medical Group, Carlsbad, CA United States
[s] Rhode Island Hospital, Providence, RI United States
[t] Barrow Brain and Spine—Ahwatukee, Phoenix, AZ United States
[u] Goodman Campbell Brain and Spine, Greenwood, IN United States
[v] Carolina Orthopaedic and Neurosurgical Associates, Spartanburg, SC United States
[w] Kansas University Medical Center, Kansas City, KS United States
[x] Endeavor Health, Chicago, IL United States
[y] Burkhart Research Institute for Orthopaedics, San Antonio, TX United States
[z] The Cleveland Clinic Foundation, Cleveland, OH United States
[aa] Chicago Anesthesia Associates, SC, Chicago, IL United States
[bb] Banner University Medical Center, Tucson, AZ United States
[cc] Advanced Pain Care, Henderson, NV United States
[dd] Abbott Labs, Austin, TX United States
[ee] The Spine and Nerve Center of the Virginias, Charleston, WV United States

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ABSTRACT

Background: Low back pain (LBP) is a highly prevalent, disabling condition affecting millions of people. Patients with an identifiable anatomic pain generator and resulting neuropathic lower extremity symptoms often undergo spine surgery, but many patients lack identifiable and/or surgically corrective pathology. Nonoperative treatment options often fail to provide sustained relief. Spinal cord stimulation (SCS) is sometimes used to treat these patients, but the lack of level 1 evidence limits its widespread use and insurance coverage. The DISTINCT RCT study evaluates the efficacy of passive recharge burst SCS compared to conventional medical treatment (CMM) in alleviating chronic, refractory axial low back pain.

Methods: This prospective, multicenter, randomized, study with an optional 6-month crossover involved patients who were not candidates for lumbar spine surgery. The primary and secondary endpoints evaluated improvements in low back pain intensity (NRS), back pain-related disability (ODI), pain catastrophizing (PCS), and healthcare utilization. Patients were randomized to SCS therapy or CMM at 30 US study sites.

Results: The SCS arm reported an 85.3% NRS responder rate (≥ 50% reduction) compared to 6.2% (5/81) in the CMM arm. After the 6M primary endpoint, SCS patients elected to remain on assigned therapy and 66.2% (49/74) of CMM patients chose to trial SCS (crossover). At the 12M follow-up, SCS and crossover patients reported 78.6% and 71.4% NRS responder rates. Secondary outcomes indicated significant improvements in ODI, PCS, and reduced healthcare utilization. Six serious adverse events were reported and resolved without sequelae.

Conclusion: DISTINCT chronic low back pain patients with no indication for corrective surgery experienced a significant and sustained response to burst SCS therapy for up to 12 months. CMM patients who crossed over to the SCS arm reported profound improvements after 6 months. This data advocates for a timely consideration of SCS therapy in patients unresponsive to conservative therapy.

Background

Low back pain (LBP) is a leading cause of long-term disability and pain worldwide and often results in chronic opioid use [1–4]. Unlike other costly global health problems, such as diabetes and ischemic heart disease, LBP has a greater impact on the working-age demographic, including indirect costs such as disability benefits and lost labor productivity which are estimated to amount to $84.1 to $624.8 billion per year [1–5]. LBP is associated with psychological and sociological problems [6–8]. As such, LBP is widely recognized as a complex biopsychosocial disease requiring a multidisciplinary approach and holistic assessment of treatment outcomes [9–11].

As LBP transitions into a chronic state, more than six months after onset, patients will seek relief beyond primary care. Typically, these patients lack clear identification of pain generators through imaging, other than generalized degenerative changes in the intervertebral disc, vertebral body, zygapophysial joint, ligaments, or sacral iliac joint, complicating diagnosis, and targeted treatment. In addition, most patients presenting for treatment will have more than 1 pain generator [9,12,13]. This subset of non-specific LBP patients is underserved, and in the absence of effective and sustainable interventions, conservative management of these patients remains the main course of care [14].

Spinal cord stimulation (SCS) is a relatively safe and reversible non-pharmacological therapy for chronic neuropathic pain. Persistent or recurrent pain following spinal surgery is common affecting 20% or more patients; this has recently been termed persistent spinal pain syndrome type 2. Previously this has been termed failed back surgery syndrome and has been the subject of much work validating the use of SCS in this population [15].

High-level evidence of SCS for refractory low back pain without corrective surgery options has historically been limited, but recently growing [16]. For most of the 5 and a half decades of its history, the only

available SCS treatment modality was low-frequency pulses (40-60 Hz) applied to the spinal cord to induce continuous paresthesia over the painful area (tonic stimulation). Passive recharge burst SCS is a newer paradigm that uses a waveform that mimics natural neural patterns and can deliver pain relief in the sensory free range (the paresthesia free range/amplitude is adjusted to 60% of the sensory threshold level, typically below 1.3 mA). It has been found to modulate the medial and lateral pathways in the brain, offering statistically superior pain relief compared to tonic SCS [17,18].

The 6-month results from this study revealed marked improvements in pain, function, pain-related emotional distress, daily pain interference, and greater perception of change were noted in LBP patients receiving passive recharge burst SCS therapy in addition to conventional medical management (CMM) [19]. This contrasted with patients assigned to CMM only who reported negligible to 0 change after 6 months. Here, we report the 12-month follow-up, including efficacy and safety data from the same patients with optional crossover at 6 months for both arms.

Methods

Patient population

This study was registered with ClinicalTrials.gov (NCT04479787) and conducted according to the United States Code of Federal Regulations. At enrollment, an independent medical monitor (Orthopedic spine surgeon) validated informed consent and eligibility criteria, including a complete case and imaging review.

DISTINCT enrolled 270 adults with chronic axial low back pain without underlying pathology amenable to surgical intervention and who had not previously undergone lumbar spine surgery. Magnetic resonance imaging (MRI) and/or computed tomography (CT) images of the spine obtained within 12 months prior to screening were reviewed prior to enrollment to confirm a lack of an identifiable pathology that could effectively be treated with surgery. All investigators are spine surgeons (orthopedic or neurosurgical) and interventional pain specialists (anesthesiology or physical medicine and rehabilitation) in the United States leveraging their expertise in the diagnosis and treatment of spinal pain. Patients met all eligibility criteria (see Table S1) and provided written informed consent before any non-standard care study-specific procedures.

The DISTINCT study was designed to investigate the primary efficacy endpoint with 200 recruited patients (ITT). However, 270 patients were enrolled to increase understanding of the nonsurgical back pain population. The study includes data from 269 randomized participants. One patient was enrolled but withdrawn prior to being randomized and therefore not included in the data analysis. See Deer et al (2023) for study design and statistical calculations [19].

Spinal Cord Stimulation (interventional arm): Patients were randomized (3:2 ratio to account for SCS trial failures) to the SCS or the CMM arm, stratified by study site. An electronic data collection system was used for randomization assignments. Patients randomized to the SCS arm underwent a trial procedure with temporary implanted electrode leads and an external pulse generator (Abbott, Plano, TX, USA) for a minimum of 4 days. Patients with a successful study outcome, defined as at least a 50% reduction in pain intensity on the Numerical Rating Scale (NRS), received a permanent implant. Patients who did not achieve ≥50% pain relief during the trial period (SCS trial failures) were not eligible for a permanent implant. A rechargeable or non-rechargeable implantable pulse generator (Prodigy or Proclaim, Abbott, Plano, TX, USA) and percutaneous or paddle leads (Abbott, Plano, TX, USA) were used per surgeon preference. BurstDR (paresthesia-free) stimulation was delivered intermittently using burst SCS in a 1:3 ratio (30 sec on, 90 sec off) or 1:12 ratio per standard burst programming guidance (30 sec on, 360 sec off) [20].

Conventional Medical Management (CMM arm): Patients in the CMM arm received active, supervised medical care, including medication optimization, noninterventional and interventional therapy. Medication optimization included dose titration, initiation, and discontinuation of prescription medication when clinically appropriate. Supervised non-interventional therapy was administered, including but not limited to physical therapy, chiropractic care, cognitive behavioral therapy, and acupuncture. Interventional therapy such as injections and radiofrequency ablation were also included. Patient-reported outcomes were assessed after each patient interaction and, if necessary, therapy adjustment(s) were made to optimize pain management.

Outcomes Assessment

The primary endpoint evaluated the difference in NRS responder rates between the randomized SCS and CMM arms at 6 months. Responders were defined as having at least a 50% reduction in pain. An intention-to-treat (ITT) analysis included patients who failed the SCS trial. An “as treated” evaluation (PTE) analysis was also performed for all SCS-implanted patients with complete six-month data. Hypothesis testing for superiority used a two-sided Z-test with unpooled variance at $\alpha = 0.05$. Per the statistical analysis plan, a primary endpoint analysis with 90% power was achieved if at least 200 patients attended the 6-month follow-up visit.

Secondary study outcomes included the difference in both arms for patients reporting a ≥ 13-point improvement in the Oswestry Disability (ODI) and the change in NRS from baseline compared between the two treatment arms. Descriptive outcomes included the proportion of patients electing to cross-over after the primary endpoint and the proportion of patients within 1 SD of the population norm or achieving a minimal clinical difference of interest (MCID) on PROMIS-29 domains, the proportion of patients who either be clinically catastrophizing at baseline (PCS score ≥ 30) and report a score of < 30 at follow-up, or report a 40% score decrease at follow-up compared to baseline, pain condition-related medication use, healthcare resource use, patient satisfaction with therapy and Patient Global Impression of Change (PGIC). Outcome data were collected at baseline/enrollment, 1M, 3M, 6M, 9M, and 12 months by the study site coordinators.

Adverse events were collected and reported throughout the study. All serious device-related adverse events (SADE) leading to death or a significant decline in subject health during the study were reported. Adverse device effects (ADEs) were also collected.

Crossover

Upon completion of the 6-month primary endpoint visit, patients were allowed to crossover to the other arm. For patients randomized to the CMM arm wishing to crossover, the permanent implant was performed prior to the 12-month follow-up visit. Patients transitioning to the SCS arm followed the trial and permanent SCS procedures as per the standard of care. After receiving a permanent implant, the patients continued to participate in the study.

Statistical methods

This study was designed to enroll a maximum of 270 patients in a randomization ratio of 3:2 (SCS: CMM). The enrollment accounted for an attrition rate of up to 25% in both arms up to 6 months for a power of 90%. Sample size calculation was performed using PASS 15 (NCSS LLC).

Appropriate statistical methods were applied based on the data types. Continuous variables were analyzed using the 2-sample t-test or the test comparing cumulative distribution functions. Binary variables were analyzed using the Z test.

Descriptive summary statistics were presented for the descriptive endpoints within each treatment arm. Continuous variables were sum-

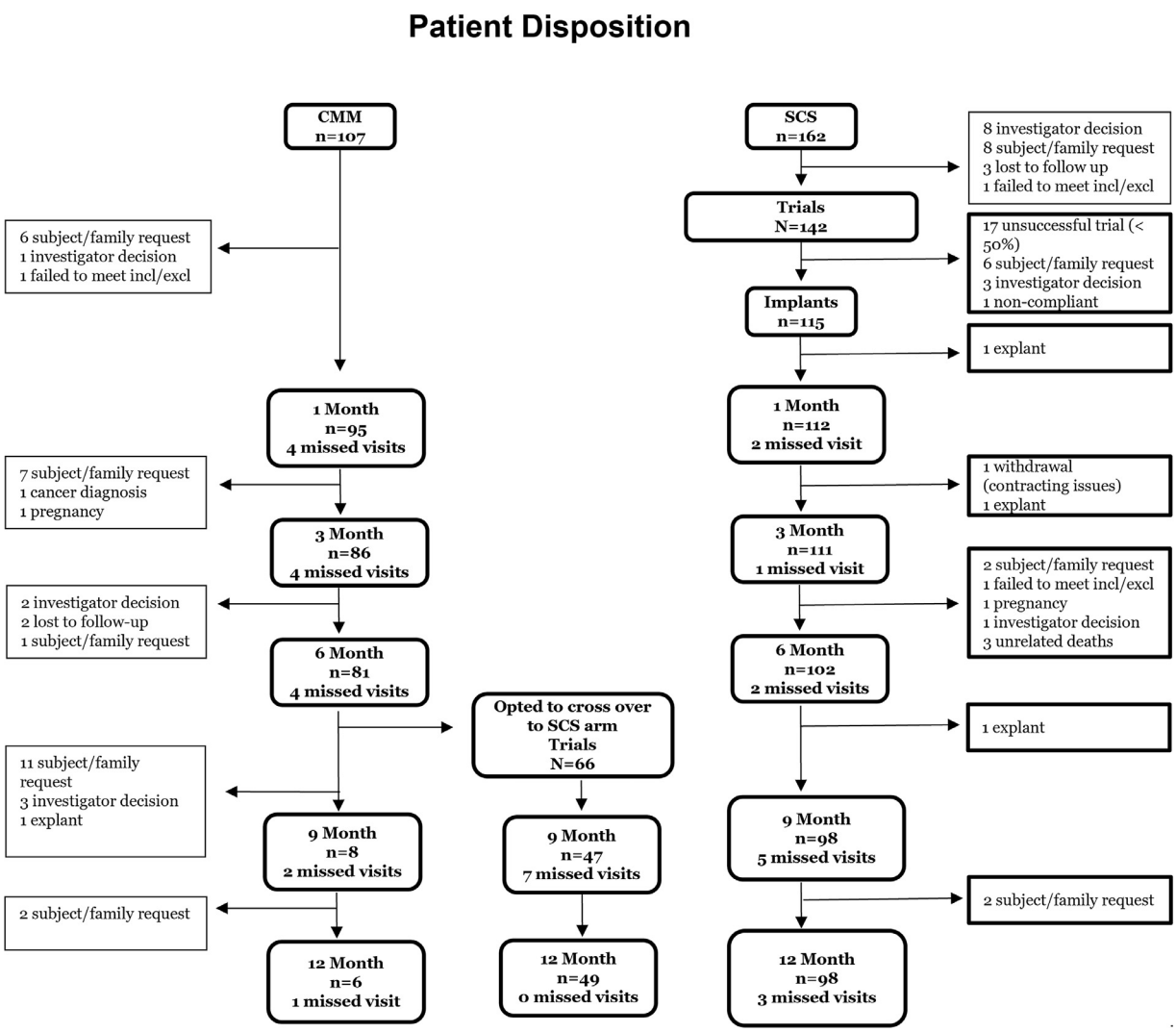

Fig. 1. Consort diagram showing subject disposition from enrollment through 12 months.

marized using mean, standard deviation, median, minimum, and maximum. Categorical variables are summarized using counts and percentages. The 95% confidence intervals for each type of data are listed where applicable. Arm differences are summarized using descriptive statistics and 95% confidence intervals. Statisticians analyzed the randomized cohort without access to data combining outcomes with treatment allocation.

Results

Patient demographics

Figure 1 shows the patient consort diagram throughout the study. A total of 270 patients were enrolled at 30 study sites in the United States (US). The mean ± SD age of patients at the time of enrollment was 58.5 ± 12.8, with female patients comprising 44.3% of the total population (Table 1). There were no significant differences in age, gender, weight, height, or body mass index. Similarly, there was no significant difference (p=.1685) between the study arms for baseline pain measured by NRS. Patients had multiple diagnoses (average of 3, range 2-5) and according to the inclusion criteria, 60.8% (161/265) of patients were diagnosed with chronic nonspecific LBP with 34 and 93 diagnosed with 2 and 3 indications respectively. Lumbar spondylosis accounted for 52.1% of diagnosis, 33.2% diagnosed with degenerative disc disease, and 38% with lumbar radiculopathy. The DISTINCT patients reported a mean ± SD pain score of 7.8±1.2 and were living with pain for approximately 12.32±11.33 years. The patients were moderately disabled at study entry due to back pain with an average ODI of 52. During this period of back pain, patients exhausted several conventional pain management treatments. Nearly all patients had received physical therapy (97.2%) and injections (95.1%). Other types of treatments included chiropractic therapy (53.0%), radiofrequency ablation/rhizotomy (44.9%), massage therapy (38.7%), acupuncture (29.2%), and/or occupational therapy (14.2%). Medication (use of opioids) was utilized by 44.7% of patients for pain management (SCS- 46.1, CMM- 43,1). During the trial period, a non-implanted temporary trial system was used for randomized patients, with a trial success rate of 88% (SCS; n=115, and crossover; n=66). Most permanent implant physicians (56% pain management and rehab, 44% Ortho/Neurosurgeon) implanted a Proclaim (recharge free IPG (98%); 2 patients received a Prodigy (rechargeable) IPG. Percutaneous (56.5%) or paddle leads (43.5%) were implanted, with spinal levels T7 (45.2%) and T8 (52.2%) representing the most implanted level location of the cephaled aspect of the lead or paddle (Table 2). Most patients with percutaneous leads were implanted with 2 leads. Outcome data were collected according to the consort diagram (Fig. 1).

Pain reduction

The primary endpoint was the proportion of responders (≥ 50% reduction in NRS) between the 2 arms at 6 months. The SCS arm reported

Table 1
Subject demographics at enrollment.

	SCS (N=162)	CMM (N=107)	Total (N=269)
Age (year)			
Mean ± SD (n)	58.1 ± 13.0 (162)	59.1 ± 12.4 (103)	58.5 ± 12.8 (265)
Median (Q1, Q3)	59.0 (49.0, 67.0)	58.0 (50.0, 69.0)	58.0 (50.0, 68.0)
Gender, n(%)			
Female	59.3% (96/162)	50.5% (52/103)	55.8% (148/265)
Male	40.7% (66/162)	49.5% (51/103)	44.2% (117/265)
Race, n(%)			
White	81.5% (132/162)	82.5% (85/103)	81.9% (217/265)
Black or African American	8.0% (13/162)	2.9% (3/103)	6.0% (16/265)
Asian	1.2% (2/162)	7.8% (8/103)	3.8% (10/265)
American Indian or Alaska Native	0.6% (1/162)	1.9% (2/103)	1.1% (3/265)
Declined / Unable to Disclose	8.0% (13/162)	5.8% (6/103)	7.2% (19/265)
Native Hawaiian or Other Pacific Islander	0.6% (1/162)	0.0% (0/103)	0.4% (1/265)
Pain Numeric Rating Scale (NRS)			
Mean ± SD (n)	7.8 ± 1.2 (162)	7.9 ± 1.1 (107)	7.8 ± 1.2 (269)
Median (Q1, Q3)	8.0 (7.0, 9.0)	8.0 (7.0, 9.0)	8.0 (7.0, 9.0)
Duration of subject's pain on subject's life (year)			
Mean ± SD (n)	11.85 ± 10.58 (162)	13.06 ± 12.44 (103)	12.32 ± 11.33 (265)
Median (Q1, Q3)	10.00 (4.00, 15.00)	10.00 (4.00, 16.00)	10.00 (4.00, 15.00)
Pain Diagnosis*			
Chronic, non-specific, low back pain	60.5% (98/162)	61.2% (63/103)	60.8% (161/265)
Discogenic pain	6.8% (11/162)	7.8% (8/103)	7.2% (19/265)
Degenerative disc disease	30.9% (50/162)	36.9% (38/103)	33.2% (88/265)
Lumbar disc herniation	4.3% (7/162)	3.9% (4/103)	4.2% (11/265)
Lumbar facet arthropathy	21.6% (35/162)	25.2% (26/103)	23.0% (61/265)
Lumbar radiculopathy	34.6% (56/162)	43.7% (45/103)	38.1% (101/265)
Lumbar spinal stenosis	22.2% (36/162)	23.3% (24/103)	22.6% (60/265)
Lumbar spondylosis	48.1% (78/162)	58.3% (60/103)	52.1% (138/265)
Mechanical low back pain	7.4% (12/162)	3.9% (4/103)	6.0% (16/265)
Spondylolisthesis	6.2% (10/162)	4.9% (5/103)	5.7% (15/265)
Scoliosis	3.7% (6/162)	3.9% (4/103)	3.8% (10/265)
Other	7.4% (12/162)	15.5% (16/103)	10.6% (28/265)
Treatment for current condition*			
Physical Therapy	96.1% (148/154)	99.0% (98/99)	97.2% (246/253)
Occupational Therapy	13.0% (20/154)	16.2% (16/99)	14.2% (36/253)
Massage Therapy	38.3% (59/154)	39.4% (39/99)	38.7% (98/253)
Chiropractic Therapy	54.5% (84/154)	50.5% (50/99)	53.0% (134/253)
Acupuncture	33.8% (52/154)	22.2% (22/99)	29.2% (74/253)
Subject undergone any injections or interventions to treat their low back pain*	97.4% (148/152)	91.4% (85/93)	95.1% (233/245)
Injection	42.1% (64/152)	49.5% (46/93)	44.9% (110/245)
Radiofrequency ablation/ rhizotomy	18.4% (28/152)	10.8% (10/93)	15.5% (38/245)
Medication Use			
Opioid Usage	46.1% (53/115) 24.8	43.1% (44/102)	44.7% (97/217)
Opioid Dosage	± 22.5 (47)	44.4 ± 79.9 (37)	32.6 ± 50.2 (84)

* Patients may be diagnosed with more than one indication

Table 2
Device Characteristics for Permanent Implant.

	SCS (N=115)	Crossover (55)
IPG Model		
3660 (Proclaim XR5)	97.4% (112/115)	98.2% (54/55)
3662 (Proclaim XR7)	0.9% (1/115)	1.8% (1/55)
3772 (Prodigy)	1.7% (2/115)	0.0% (0/55)
Lead Model		
Percutaneous lead	55.7% (46/115)	58.2% (32/55)
Paddle Lead	43.5% (50/115)	41.8% (23/55)
Implant Location		
T5	0.9% (1/115)	1.8% (1/55)
T6	3.5% (4/115)	5.5% (3/55)
T7	45.2% (52/115)	43.6% (24/55)
T8	52.2% (60/115)	43.6% (24/55)
T9	10.4% (12/115)	10.9% (6/55)
T10	0% (0/115)	1.8% (1/55)

a responder rate of 85.3% (87/102), compared to 6.2% (5/81) in the CMM arm. Thirty-one CMM patients reported an unchanged baseline pain score, compared to two patients in the SCS arm. Further analysis shows that 49% of SCS responders (43/87) reported a substantial pain reduction of ≥80% [95% CI; 32.4%, 52.3%] [19].

After the 6M primary endpoint, all SCS patients elected to remain on therapy. In contrast, 66.2% (49/74) of patients randomized to CMM chose to cross over and trial SCS. The mean NRS change ± SD for the 49 patients who chose to crossover was 0.3 ± 1.5 (95% CI, [-0.1, 0.7]) indicating a nominal response to CMM. At the 12M follow-up, after 6M and 12 months of passive recharge burst therapy for the crossover and the SCS arm, both arms reported 71.4% (35/49, CMM crossover) and 78.6% (77/98, SCS) responder rates for ≥ 50% reduction in NRS, respectively. The CMM crossover arm reported a 12-month NRS score of 3.1 ± 2.2, which represents a decrease of 4.8±2.4 from a 6M score of 7.6±1.6 (SCS arm at 12M=2.5±2.2). A substantial reduction (≥80%) in NRS was reported by 40.8% of the SCS arm and 24.5% of the crossover arm. Only 6 patients chose not to switch to the SCS arm and continued with CMM. Efficacy results from this group are not presented because the remaining CMM group has insufficient statistical power to allow meaningful comparisons with the SCS/crossover groups (Fig. 2).

Disability improvement

Secondary endpoints for change from baseline on the Oswestry disability index (ODI) were calculated. At enrollment, both arms reported moderate to bed-bound disability with a mean±SD ODI score

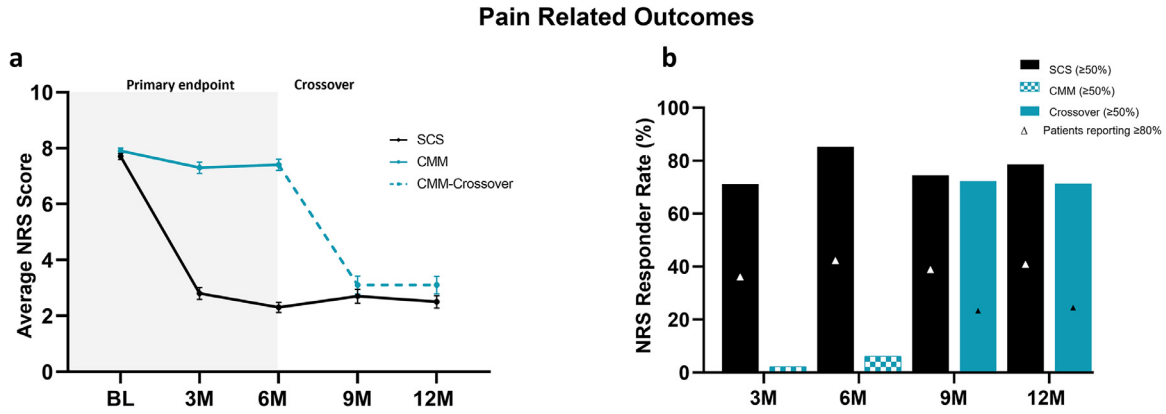

Fig. 2. Reduction in NRS score. (A) The average ± SD NRS score for SCS decreased from 7.7±1.2 at baseline to 2.3±1.8 at 6M and sustained at 2.5±2.2 at 12 months. Patients randomized to the CMM did not report a significant decrease at baseline (7.9±1.1) or at 6M (7.4±1.8). Post crossover, the 6M scores decreased to 3.1±2.2. (B) 78.6% of SCS patients reported a 50% decrease in NRS at 12M with 40.8% reporting an 80% substantial decrease. In contrast, only 6.2% of the CMM group reported a 50% decrease in NRS at 6M with 71% reporting a 50% decrease in NRS after crossover. About 21.4% reported an 80% substantial decrease at 12M.

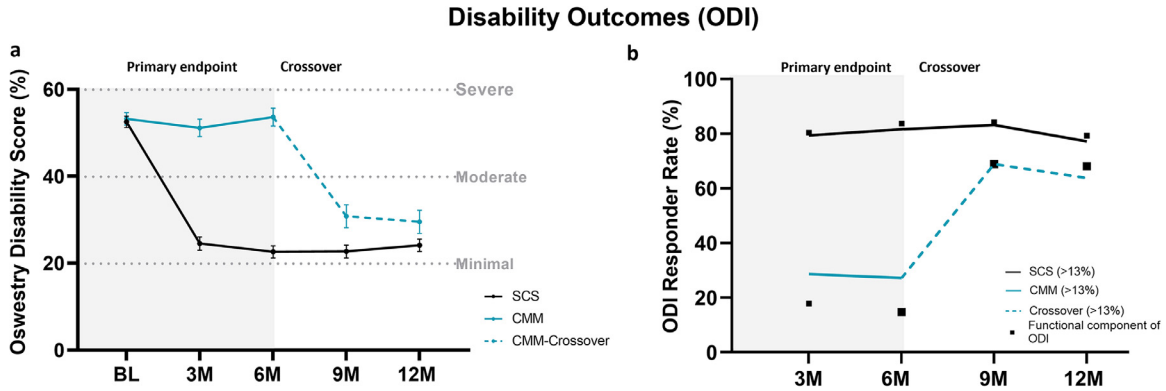

Fig. 3. Backpain disability changes. (A) The percent ± SD ODI score for SCS decreased from severe-moderate disability to moderate-minimal disability after 3M. The effect was sustained through 12M (Average score: 52.5±13.8 at baseline to 24.1±13.6 at 12 months). Patients randomized to the CMM reported severe-moderate disability at 6M (53.6±18.1). Post crossover, patients reported moderate-minimal disability with an average ± SD ODI score of 29.5±18.2. (B) 77.2% of SCS patients reported a ≥13 decrease in ODI at 12M in line with the improvement observed from the functional component (79.3%). In contrast, only 27.2% of the CMM group reported a ≥13 decrease in ODI at 6M with 69% reporting a ≥13 decrease in ODI after crossover. 69% reported functional improvement at 12M.

of 52.5±13.8 (SCS) and 53.2±14.6 (CMM). At 6 months, 86.7% (85/98) of the SCS arm reported a ≥13-point decrease in ODI score compared to 27.2% (22/81) in the CMM arm. The mean ODI score for the SCS arm decreased by 29.4±18.8 and 27.6±17.0 at 6 and 12 months, respectively. Within the CMM arm, the same comparison shows a 6M decrease of 0.7±13.0, which is less than the 13-point decrease required for an MCID. After crossover, 74.5% (35/47) of responders reported a decrease of ≥13 points in ODI score (6M post-crossover score =29.5±18.2). Both groups reported similar response rates (77.2% SCS vs. 74.5% CMM crossover) at 12 months. In addition, 66.3% (61/92) of the SCS arm and 55.3% (26/47) of the CMM crossover reported a substantial (≥20-point) improvement in disability scores. The functional domain for disability is similar to the reduction in disability (Fig. 3).

Pain catastrophizing score (PCS)

The mean ± SD PCS score for SCS decreased from 27.6±13.6 at baseline to 7.7±10.2 at 12 months, indicating a return to normality. There was no change at 6M for the CMM arm prior to passive recharge burst treatment. However, patients reported improvements (mean score at 12M of 12.0±11.0) after receiving passive recharge burst SCS, which represented a level of catastrophizing similar to a nonpain population (13.9) (Fig. 4).

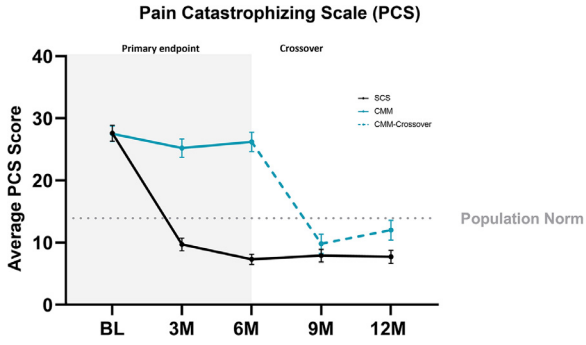

Fig. 4. Catastrophizing changes. The average ± SD PCS score for SCS decreased from 27.6±13.6 at baseline to 7.7±10.2 after 12 months. The CMM group did not observe a significant change within the first 6 months. After cross-over, the average±SD PCS score decreased from 27.5±12.5 at baseline to 12.0±11.0 at 12 M. Both groups reported scores below the population norm (13.9).

Improvement in health-related quality of life (HQoL)

The Promis-29 questionnaire was used to assess health-related quality of life. Overall, SCS patients improved in all seven domains. Physical (5a), social function (5b), and pain interference (5c), improved

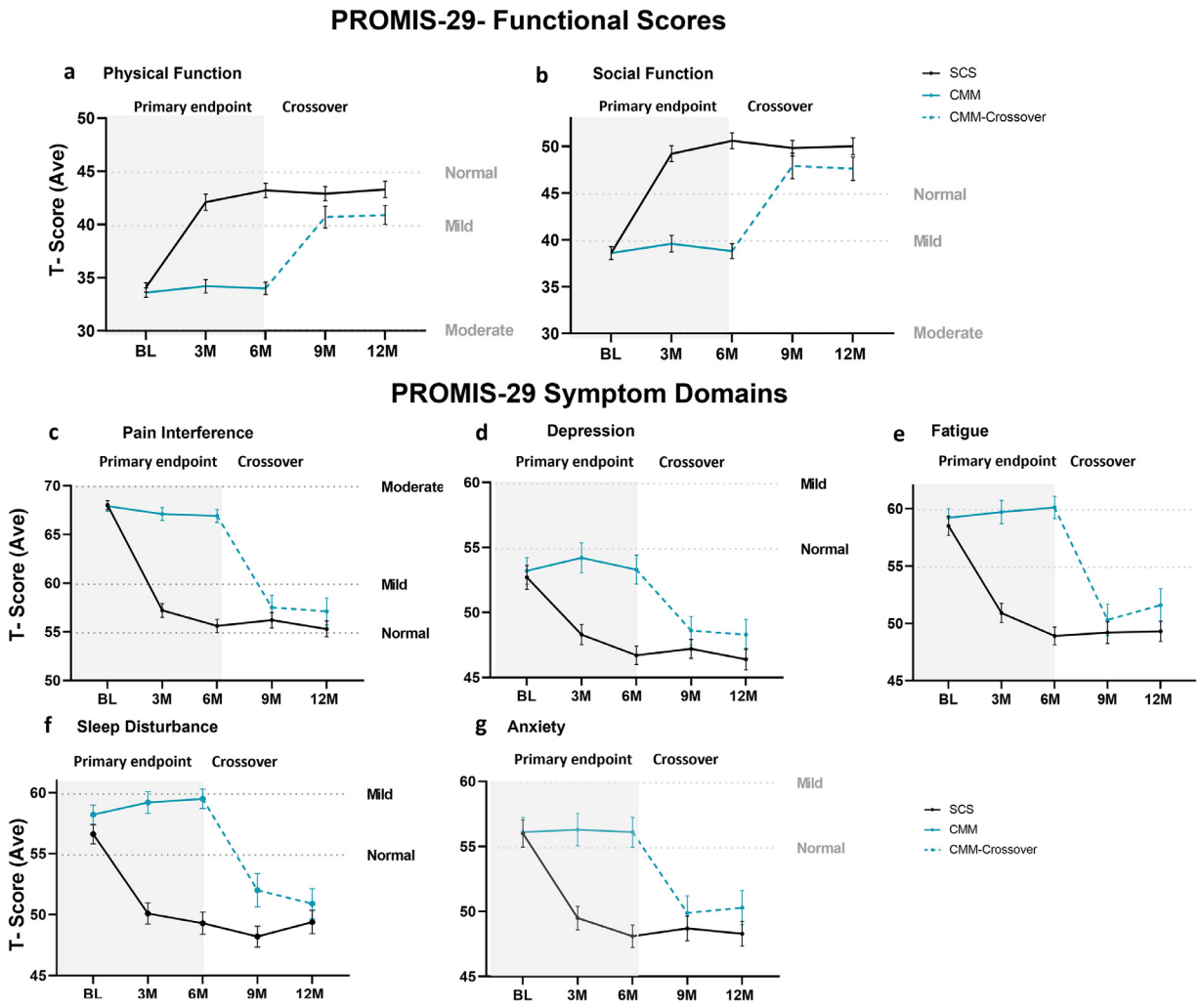

Fig. 5. Quality of Life/Activities of Daily Living. Improvement in functional ability is denoted by an increase in score. Improvements in symptoms are denoted by a reduction in score. Patients reported improvements from mild to normal levels for physical function (A) and social function (B). Patients reported a reduction to normal limits for pain interference (C), depression (D), fatigue (E), sleep disturbance (F), and anxiety (F). Patients originally reported baseline levels within mild-moderate symptoms.

from moderate disability to mild-normal range. Symptoms of, depression (5d), fatigue (5e), sleep disturbance (5f), and anxiety (5g) improved from mild symptoms to normal range within 6 months of treatment and were sustained at 12 months. CMM patients saw no improvement in functional or symptomatic domains during the first 6 months of comparator therapy. Patients reported improvements over baseline scores after crossover, with improvements in the moderate- normal range for functional domains. Similar improvements were also observed in the symptomatic domains (Fig. 5).

Healthcare utilization

SCS group reported a decrease in injection and ablation therapy. At 6M, the CMM group reported physical therapy (8.8%) and injections (18.8%). Other types of treatments included chiropractic therapy (5.0%), radiofrequency ablation/rhizotomy (5.0%), massage therapy (11.3%), acupuncture (3.8%), and other therapy (10.0%). The post-6M crossover group (CMM crossover) reported using fewer healthcare resources on passive recharge burst SCS therapy. Three patients each received physical therapy and injections (6%, 3/49). No other care was reported.

Opioid reduction was significant for within-group comparison when baseline MME dosage is compared to 12M dosage for both SCS and crossover group ($p<.001$). There was no significant difference in the CMM group or between groups (SCS vs CMM vs CMM crossover, $p>.05$). At 6 months, 20% of patients discontinued/reduced opioid use (17.1%) during treatment with SCS (Mean ± SD MME change from baseline to 12m - 20.3±32.9, $p>.05$). At 12 months, a higher percentage of patients discontinued (25.6%)/reduced opioid use (25.6%) (Mean ± SD MME change from baseline to 12m - 6.9 ± 27.8, $p<.001$). at 12 months.

For the CMM arm, 13.8% of patients reported opioid discontinuation with 10.3% reducing opioid usage (Mean ± SD MME change from baseline to 6M - 0.9 ± 12.1; Mean ± SD MME change from 6M to 12M - 5.1 ± 14.9, $p>.05$). At 6M, 17.2% of CMM patients also reported initiating opioids or increasing dosage, compared to 9.7% in the SCS arm. After crossover, 42% of CMM-crossover patients discontinued (15.8%) /reduced opioid use (26.3%, Mean ± SD MME change from 6M to 12M - 18.2 ± 19.4, $p<.001$).

Similarly, anticonvulsant data were descriptively collected. About 27.9% of SCS patients discontinued (18.6%)/reduced use (9.3%) and 20% of crossover patients discontinued usage. No crossover patient reported reduction.

Across the groups, there was no difference in the use of physical or chiropractic therapies, but these were applied sparingly as most had failed these patients before the study.

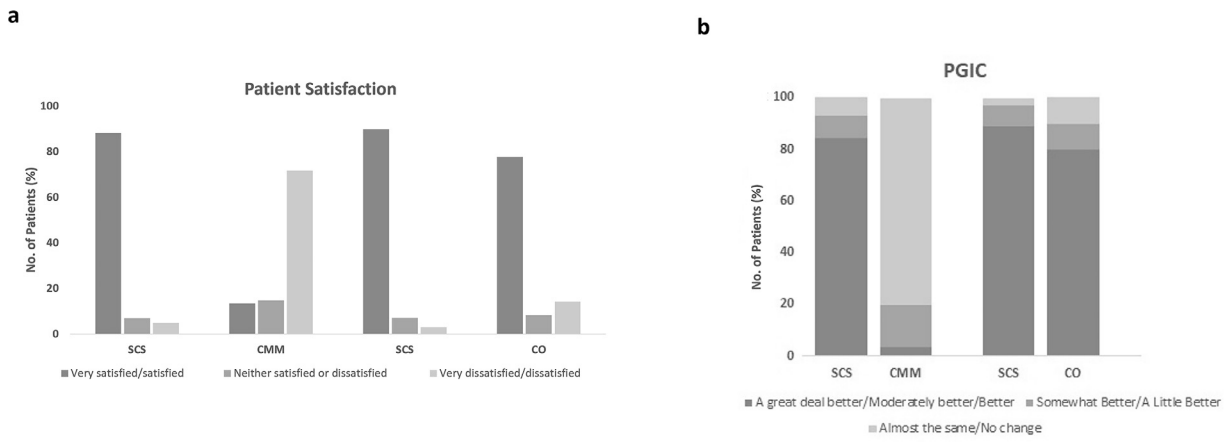

Fig. 6. (A) At 6M, 88.2 of SCS patients were very satisfied/satisfied with assigned therapy. About 71% of CMM patients reported dissatisfaction with their conservative therapy however, 6M after cross-over, 77% indicated they were very satisfied/satisfied with the new treatment (B). SCS (88.8%) and crossover patients (79.6%) indicated their conditions significantly improved with therapy at 12 M.

Patient satisfaction

Overall, 88% of SCS patients reported being very satisfied/satisfied with their therapy and indicated that their condition had improved by a great deal, better, or moderately. A high proportion of CMM patients reported dissatisfaction with their therapy (71%), and 80% stated that there was no change in their condition. After crossing over, 77% of the CMM-crossover group reported that they were very satisfied with their therapy, and 79.6% agreed that their condition had improved significantly at the 12M visit (Fig. 6).

Complications

Sixteen subjects randomized to the SCS arm reported 22 events for an overall adverse event rate of 9.8% (16/162). Infection (2), numbness (1), and postoperative pain (1) were reported as serious events related to the SCS devices or the procedure (SADE). Pain at the IPG site (4) and decreased pain relief (4) were the most common nonserious events (ADE). Two lead migrations were reported for this group, which were resolved surgically. About 86% (19/22) of all reported events occurred before the 6-month time point. No adverse events were reported by the CMM group within the first 6 months of the study. After crossover, 2 (2.9%) patients reported infection as a serious device-related adverse event (SADE). Five ADEs were reported for lead migration (2), infection (2), and seroma (1). The crossover adverse event rate was 8.6% (6/70).

Overall, 3% (7) patients required an explant (4 infections, 1 IPG damage, and 2 IPG site pain). All reported lead migrations were surgically revised (4 patients, 1.7% event rate). Table 3 summarizes the device-related events.

Discussion

This study shows the long-term improvements in overall pain, function, psychological distress, well-being, medication use, and healthcare utilization in the SCS group and the CMM group opting to cross over to SCS treatment. Our group previously reported the 6-month outcomes from this prospective, multicenter trial comparing the effectiveness of SCS+CMM with that of CMM alone in a population of chronic back pain patients without options for corrective surgery [19].

After 12 months of burst SCS, 79% and 41% of randomized SCS patients reported ≥50% and ≥80% pain relief respectively. The overall average pain score was sustained at 2.5 on the NRS. Notably, all patients originally assigned to SCS treatment chose to continue in this randomization arm. These results are in line with the responder rates at 12 months observed for high-frequency spinal cord stimulation treatment in a similar population [16]. More than 81% of the CMM group elected to crossover to the SCS arm. These patients reported significant improvements after 6 months of passive recharge burst SCS treatment with 71% and 21% reporting 50% and 80% pain relief and an overall average NRS pain score of 3.

Given the complex nature of treatment-refractory back pain without corrective options, this study utilized a selective, yet broad array of validated patient-reported outcomes encompassing the multidimensional impact of low back pain. Disability decreased to minimal-moderate severity with more than twice the MCID improvement on this scale [21]. Pain catastrophizing, combining feelings of rumination, magnification, and helplessness, reduced below the level expected in a non-diseased population [22]. Similarly, functional and symptom domains of the PROMIS-29 profile normalized or improved to a mild severity at 12 months corresponding to levels reported by 80% of the general population [23–25]. These results were corroborated by a satisfaction rate of almost 90% in the SCS and 80% in the crossover group. Furthermore, overall healthcare utilization was substantially reduced within groups for SCS (compared to baseline) and implanted crossover (compared to 6 months of CMM therapy) participants.

SCS had a substantial impact on opioid use, with over 40% and 50% of patients discontinuing or reducing dosage, respectively after 6 months for the CMM-crossover participants, and 12 months for the SCS group. SCS also affected anticonvulsant medication use with over 20% of both cohorts stopping, or reducing their intake. The effect on other medication classes evaluated, including topical medications, antidepressants, and anti-inflammatory medications, was less profound, with most patients continuing their baseline dosage.

The results of the CMM-crossover group are particularly significant; eliminating inter-individual variability from the between-group comparison and reducing the effect of covariates [26]. Interestingly, CMM-crossover patients showed similar profound improvements although always slightly below the 6-month level observed in the group originally assigned to SCS. This suggests a small carry-over effect possibly due to the prolonged use of ineffective therapies, although the datasets of the SCS and crossover groups substantially overlap. It has been suggested that a longer delay in SCS implantation after the onset of pain influences efficacy, and the treatment effect was more noticeable in patients with a shorter time with pain (≤10 years) originally assigned to the CMM group [27,28]. No statistical test was performed to assess the carryover effect. Further, the study protocol did not specify a washout period to minimize any potential confounding effects of carryover. Washout periods in SCS studies for chronic pain are typically used when comparing different stimulation designs or programming features [16,29,30].

Table 3
Device-related Adverse event.

Event Description	SCS			Cross Over		
	# of Events	Subjects with Events n/N (%)	Event Description	# of Events	Subjects with Events n/N (%)	Event Description
SADE	4	4/162 (2.5%)	Infection (2)[a] Numbness (1)[b] Post surgical pain (1)[c]	2	2/70 (2.9%)	Infection(2)[a]
ADE	18	15/162 (9.3%)	Pain at IPG (4)[d] Reduced pain relief (4)[e] Infection (2)[f] CSF leakage (1)[g] Damaged IPG (2)[h] Dermatitis and Desquamation (1)[i] Lead migration (2)[j] Pain/ Loss of Analgesia (1)[k]	5	5/70 (7.1%)	Lead Migration (2)[j] Infection (2)[f] Seroma at incision site (1)[i]
Total	22	16/162 (9.8%)*	7	6/70 (8.6%)**		

* 3 patients reported two events each
** 1 patient reported two events
[a] Infections resolved with IPG explants
[b] Leg Numbness resolved with trial lead removal
[c] Severe post-surgical pain resolved with analgesic therapy in ER
[d] IPG site discomfort (revision needed in 1/4 subjects, explant in 2/4, medication in 1/4)
[e] Reduced pain relief (revision needed in 3/4 subjects, reprogramming in 1/4)
[f] Infection (Medication in 3/4 subjects, explant in 1/4)
[g] CSF leakage (noted and resolved with conservative care during lead implant)
[h] Damaged IPG resolved with replacement
[i] Resolved with conservative care
[j] Resolved by 2X reprogramming, 2x revision
[k] Same patient explanted in [f]

Both SCS and crossover groups reported a low frequency of device- and procedure-related adverse events (AEs), 9.8% and 8.6%, respectively. The higher AE rate in the SCS group is attributed to the longer follow-up with an implanted device and a higher number of non-serious events. The rates of serious events requiring hospital admission were similar at 2.5% and 2.9% and consisted mainly of infections that usually manifest after the implant procedure. Pain at the IPG site and decreased pain relief were the most common nonserious adverse events at 12 months, although no safety events occurred with a frequency above 3%. No explants were performed due to loss of efficacy. These safety results compare favorably with the AE rate of HF-10 treatment in the same patient population which reached 28% [16]. Most of these events occurred within 6 months of an implant with 14% reported between months 6-12 underscoring the belief that adverse events are usually observed within the first year of SCS therapy [16].

Multidisciplinary pain rehabilitation is considered the gold standard for low back pain patients [10,31]. Burst SCS not only reduced pain, but also improved disability and emotional distress facilitating, and in some patients even obviating, further therapy aimed at improving physical, cognitive, and emotional functions. Furthermore, pain catastrophizing and depressive symptoms have been associated with a lack of recovery, and it has been suggested that beliefs about pain are more important than pain intensity in determining the quality of life of LBP patients [32–35]. Our previous research demonstrated that burst SCS appears to be as effective in a chronic pain population with high psychological distress as in patients without distress [36]. Passive recharge burst SCS is also accessible and optimized through remote programming to reduce barriers to care and provide cost savings [37]. Finally, SCS is a non-pharmacological treatment option that may help reduce a reliance on opioid therapy and the resultant potential for misuse, abuse, and accidental overdose all of which contribute to multiple public health crises [38,39].

Although adverse events were limited in this study, complications have been reported in up to 40% of SCS patients, with lead migration and infection being of particular concern [40–42].

The LBP patients in this study were ineligible for surgery mainly due to significant imaging changes (often multiple) without a definitive causal connection to the patient's symptoms. Even in LBP patients with a clear and defined pain generator and structural pathology that warrants surgical intervention, long-term outcomes can be unfavorable. The evidence supporting spine surgery for the treatment of nonspecific LBP contrasts with the frequency of surgery [43–46]. There appears to be conflicting consensus regarding the role that spine surgery plays in relieving radicular pain and disability due to neural compression [47,48]. This observation rationalizes considering SCS therapy earlier in the treatment continuum for a significant number of LBP patients as corroborated by our results.

Study limitations

Most of the participants had received multiple therapies for many years in attempts to treat their lower back pain and when assigned to the study arm continuing this previously ineffective treatment, the perception of a poor outcome is likely to be amplified. The CMM arm in our study nonetheless followed the current recommended and reasonable course of care for this patient population and revisited many previously tried conservative options as directed by our spine experts. The poor results in the CMM arm at 6 months reflect the limited efficacy of those treatment options in a large segment of this LBP population. Furthermore, the DISTINCT study boasts a strong study design with the option to crossover, ensuring internal validity, and includes a large number of patients from 30 sites across the US. Our study had a balanced, diverse steering committee including specialists from orthopedic spine surgery, neurosurgery, and interventional pain who ensured that all domains and aspects of care were addressed. Observational bias is another limitation of the study, as it was not possible to blind the researchers to the presence of an implantable generator. Finally, the placebo effect influences clinical trials. To mitigate this effect, the primary endpoint was set at 6 months instead of 3 months. The magnitude and duration of the response are indicative of the effect of the treatment. During the study execution, an adjudication committee assessed all adverse events.

Conclusions

In this randomized controlled trial, patients with chronic predominately axial low back pain without options for corrective surgery showed a significant and sustained response to passive recharge burst SCS therapy up to 12 months after implant. The results in the implanted crossover participants (who received burst SCS therapy after 6 months of CMM) support the timely consideration of passive recharge burst in patients not responding to conservative therapy. None of the SCS patients switched to the CMM group. Together, these results strongly favor the addition of passive recharge burst SCS for patients with non-surgical low back pain.

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Declaration of competing interest

One or more of the authors declare financial or professional relationships on ICMJE-NASSJ disclosure forms.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.xnsj.2024.100508.

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