Retrospective Study

BURST(able): A Retrospective, Multicenter Study Examining the Impact of Spinal Cord Stimulation with Burst on Pain and Opioid Consumption in the Setting of Salvage Treatment and "Upgrade"

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Background: Loss of efficacy (LOE) is a well-known phenomenon associated with spinal cord stimulation (SCS) and is the leading cause of explant. Although recent advances in neuromodulation have resulted in a decreased incidence of LOE, it still occurs. Intuition suggests that when LOE ensues, switching to a different SCS therapy/platform could potentially be a viable clinical option; however, there are no data presently available to validate this theory.

Objectives: The primary objective was to evaluate the efficacy of SCS therapy rotation with DeRidder Burst on reversing LOE. A subobjective was to evaluate the hypothesis that the body will treat a novel waveform as a "different therapy" when introduced for the first time, regardless of the setting.

Study Design: Multicenter, retrospective.

Setting: Private practice.

Methods: A total of 307 patients with ongoing SCS therapy had a de novo therapy conversion to DeRidder Burst via surgical revision or software upgrade. Each cohort was split into 2 additional arms/subcohorts: those who were failing their SCS (salvage) versus those who were reporting success with their SCS system but were looking for increased pain relief (upgrade). This study was physician-directed and not commercially funded.

Results: There were statistically significant reductions in Numeric Rating Scale, percent pain relief in both surgical revision and software upgrade arms. A statistical reduction in opioid dosing was seen in the overall population and the salvage group. Larger reductions in pain/opioid consumption were observed in the surgically revised group when the revision was performed earlier. Subgroup analysis showed both salvage and upgrade groups restored treatment efficacy irrespective of time or the previous frequency/waveform.

Limitations: The retrospective nature of the study and the inability to eliminate potential confounding variables when evaluating the use of opioids in the study population.

Conclusions: LOE is an unfortunate occurrence with few evidence-based solutions presently available to reverse it. Our findings suggest that implementing D-Burst stimulation may be an effective option for treating LOE, as well as potentially reducing opioid consumption, regardless of the prior SCS system.

Key words: Spinl cord stimulation, loss of efficacy, salvage, burst

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Although traditional spinal cord stimulation (SCS) (tonic stimulation at frequencies below 1500 Hz [t-SCS]) has been shown to be an effective treatment option for a variety of chronic pain conditions, historically it has been plagued by the "50/50 phenomenon": roughly 50% of patients who undergo the treatment will report 50% or more reduction in pain (1-3). This disparity sparked the desire to improve on t-SCS therapy and narrow the gap between successes and failures. Recent innovations in the field have improved on the overall success of SCS by increasing the percentage of responders to the therapy (≥ 50% reduction in pain), as well as decreasing the overall incidence of loss of efficacy (LOE). Despite these advances, there are still those patients who fail SCS over time due to LOE and are left in search of options. With nearly 50,000 neurostimulators implanted annually around the globe, it is estimated that the cost for this therapy will reach $7 billion dollars per year by 2020 (4,5); consequently, one could argue the financial implications of LOE on health care, at any level, are at least as relevant as the direct impact it has to the patients who experience failure.

The incidence of LOE with SCS has been estimated at roughly 34.5% (6-8), with approximately 44% of patients undergoing explant of their system (9). In a systematic review, Turner et al (10) demonstrated that 62% of patients treated with SCS had satisfactory pain reduction at 1 year; however, efficacy fell to 53% at 5 years, and further reduced to 35% at 10 years. If one were to examine the efficacy of SCS strictly for the treatment of complex regional pain syndrome, evidence suggests that it is no better than conventional medical management at 2 years (11). Although device-related complications are certainly a contributing factor in many reported cases of "failure" (1.6%–13.2%), LOE can still occur in the absence of any known hardware-related malfunction, thus making it challenging to avoid in some instances.

Historically, there are limited evidence-based options for patients when LOE occurs. Typically, the first step in the algorithm involves attempts to reverse LOE through programming changes or intermittently switching the SCS device off for several weeks or months at a time (aka "SCS holiday") (12). Invariably, these options rarely succeed at a meaningful level, thus leaving only targeted drug delivery (TDD) or chronic oral opioids as the only remaining options for treatment (13). With respect to the former, TDD is an accepted therapy with known efficacy for the treatment of axial low back pain, failed back surgery syndrome (FBSS), and many other recalcitrant chronic pain conditions (14-16). However, TDD is at a disadvantage owing to the palpable risk of overdose from medication pocket fill or device malfunction (17), thus making it a less desirable option for many patients and practitioners. Chronic oral opioids are even less suitable as a long-term treatment option for LOE given the scant evidence to support their use in the treatment of chronic pain, as well as the number of deaths that have resulted from the abuse and misuse of these medications (18,19). Ergo, pain management providers should be searching for more reasonable and safer solutions.

Recent advances in SCS have increased the overall "responder rate" and decreases in LOE when utilizing their respective platforms (3,20-22). Although these advances have not totally eliminated LOE, their existence does present a potentially viable treatment alternative should LOE with t-SCS occur. The existence of these different stimulation modalities has led to the concept of potentially rotating one SCS platform for another in the event of LOE to see if one therapy could succeed in which another failed. To date, the only evidence describing this concept is limited to 2 separate case series: (1) burst stimulation to treat failures with traditional low-frequency SCS; and (2) the use of dorsal root ganglion stimulation for 2 patients with complex regional pain syndrome who failed DC-SCS (23,24).

We present the findings of a multicenter, retrospective study examining the use of burst stimulation as a means of salvaging SCS failures due to LOE or as a way to increase pain relief in patients already responding to SCS.

Defining the Burst Waveform

It is important to clearly define what the authors consider to be "burst" stimulation for 2 fundamental reasons: (1) highlighting the stark differences between this particular waveform and conventional stimulation patterns supports the authors' hypothesis/premise that burst could be considered a "different" treatment option as compared with tonic and variants of tonic; and (2) reproducibility—there are other stimulation patterns that have been referred to as "burst" and may not yield the same results as claimed. The term "burst" should not be used interchangeably as the authors would contend that the efficacy of one type may not be generalized to another.

In 2010, De Ridder et al (25,26) reported on the creation of a novel waveform referred to as "burst." In the years since, it was patented/rebranded as Burst-DR (Abbott, Plano, TX) and is predominantly used in SCS for the treatment of back and leg pain (19,25).

Fundamentally speaking, the term "burst" refers to stimulation impulses that are grouped together into small packets and then spaced apart by periods of dormancy. Burst as defined by De Ridder (D-Burst) refers to packets consisting of 5 individual 1000 μs spikes separated by 4 to 1000 μs passive recharge resting intervals. This particular version is unique in that each spike has a synergistic effect with the one immediately prior, which results in a slow plateau of calcium influx and ultimately creates a charge accumulation. This charge accumulation will dissipate passively, leading to a nonlinear "super action potential" that is larger than the summation of each of the individual spikes followed by a quiescent phase or dormancy before the next packet begins (27-30). It has been proposed that this waveform leads to intermittent "bursts" of synaptic stimulation followed by periods of dormancy that could potentially protect against synaptic habituation, which in turn may decrease LOE (31). This waveform is fundamentally different than "rate-cycling," a form of t-SCS that was rebranded as "burst," whereby tonic impulses are simply grouped and spaced to suggest a burst packet.

An important consequence of D-Burst is its ability to recruit neurons that naturally fire in the same manner and would otherwise be unaffected by tonic stimulation patterns. This subset of neurons has 3 distinct functions (32):

- Supply augmented postsynaptic responses to presynaptic action potentials
- Create enhanced strength in synaptic connectivity
- Create contrasting activation of parallel, integrated anatomic pathways.

Collectively, these changes on the cellular level are believed to be the reason why D-Burst achieves distinctive changes on a macro level (i.e., its ability to act on the medial pain pathway of the thalamus [medial thalamus to the anterior cingulate and insular cortices]) to manipulate the descending inhibitory system for controlling pain, as well as the motivational/affective component of pain, which influence one's attention to their pain (22,33).

Does D-Burst SCS Have "Different" Treatment Implications?

In 2019, Falowski (34) published the findings of a small case series that compared/contrasted the measurable physiologic responses of various stimulation patterns using intraoperative neuromonitoring and electromyography (EMG) (Fig. 1). When D-Burst was examined, the morphology of the electrophysiologic

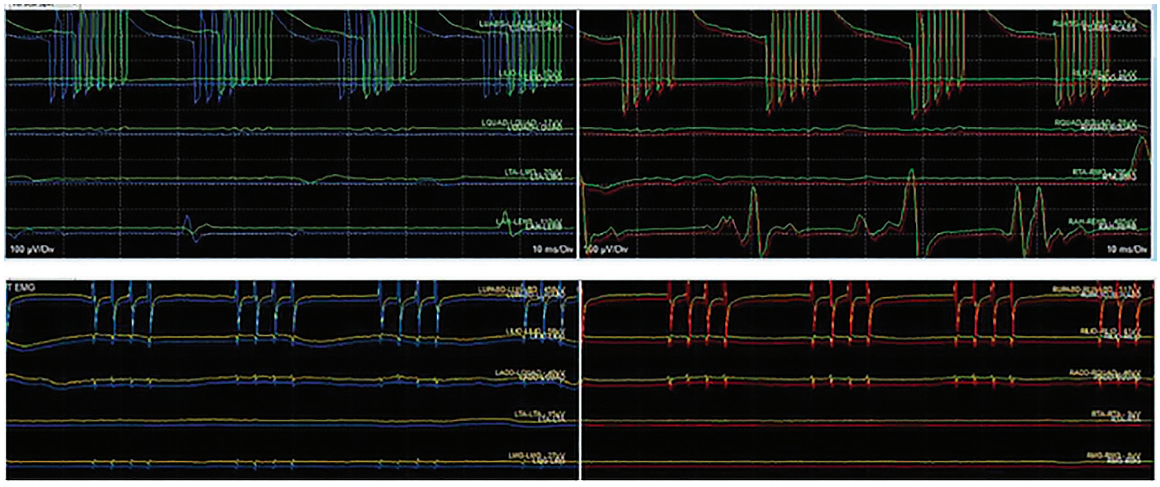

Fig. 1,: *Intraoperative neuromonitoring with EMG recording (A) D-Burst stimulation demonstrating temporal summation with associated propagated EMG response; (B) Rate-Cycling "burst" stimulation demonstrating linear, one-to-one response with each pulse (29).*

responses elicited in the extremities showed: (1) a temporal summation of EMG recruitment noted after each burst complex indicating a charge accumulation of calcium; and (2) subsequent passive discharge suggestive of a "super" action potential (34). These findings support the notion that D-Burst is a significant departure from t-SCS and could, in fact, be considered a "different" type of therapy on the physiologic level as compared with traditional methods (as well as rate-cycling) for stimulating the dorsal columns.

Methods

Study Design

This is a physician-initiated study using data from patients treated at 7 independent pain practices across the United States. No industry funding/sponsorship or industry manuscript or data guidance were received for this study. Data were obtained retrospectively using previously treated patients and garnered strictly through existing medical records. As such, no study-specific changes relating to the study patients or their care were made; institutional review board waivers were obtained where indicated.

There were 2 main patient cohorts in the study (Fig. 2):

DR-S: Those patients who had their existing SCS platform surgically revised to one that was capable of transmitting the D-Burst waveform (internal pulse generator [IPG] only with adaptors or IPG and leads)

DR-ON: Patient with a currently implanted SCS system that was already capable of transmitting D-Burst waveform but was not yet enabled to deliver it—change was made via programming to enable the device to begin transmitting D-Burst (D-Burst On)

Each of these cohorts were then divided into 2 additional subcohorts:

Salvage group: Patients reporting less than 50% pain relief (partial or total treatment decay) with their current SCS system despite exhaustive reprogramming and a change was made to the current SCS system in an attempt to "salvage" the patient and return them to being a responder with 50% or more pain relief.

Upgrade group: Patients reporting 50% or more pain relief and opted to have a change made to their existing SCS system in an effort to achieve even greater pain relief.

Data Collection

The data collected were as follows:

1. Age and gender
2. Primary diagnoses
3. Original SCS device information: device manufacturer, date of implant, and lead position(s) in relation to the spinal level
4. Reason for revision:
   a. Salvage: therapy was failing with existing SCS system (providing < 50% pain relief) and a change was being made in an effort to return the patient to 50% or more pain relief

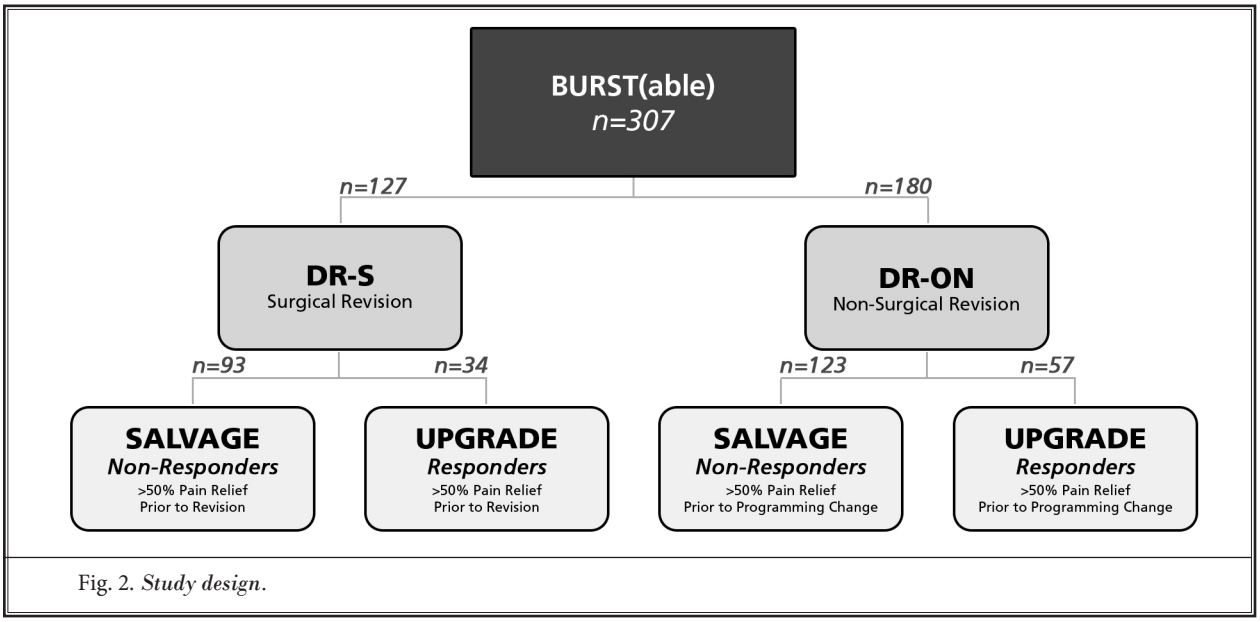

Fig. 2. *Study design.*

b. Upgrade: therapy was succeeding with existing SCS system (providing ≥ 50% pain relief) and a change was being made in an effort to achieve more pain relief
5. Method of device revision: surgical revision (IPG changed) versus programming change (device was capable of transmitting D-Burst but was not utilizing it).
6. Reason for device failure (i.e., inadequate relief, insufficient coverage, etc.)
7. Date of revision
8. Numeric Rating Scale (NRS) scores before and after change
9. Percentage of pain relief before and after
10. Was the failure (if device was failing) rectified?
11. If the IPG was changed, were adaptors used or were the leads changed as well?
12. How the revision was performed (e.g., if the original IPG was surgically exchanged for a D-Burst IPG)? If the leads were changed, what was the new location?
13. Medication regimen before and after change
14. Date and NRS score at most recent patient encounter.

The entire database was stored on a password protected, encrypted, web-based database. Neither the individual result nor the aggregated results could be viewed by the site investigators after each entry.

Statistical Analysis

Data preparation was performed using Microsoft Excel (Microsoft Corp., Redmond, WA). Statistical analysis was performed using XLSTAT version 2018.5 software (Addinsoft, New York City, NY, USA) by an independent, nonindustry funded or sponsored third-party statistician. The individual tests used to calculate *P* values for statistical significance are outlined in the Results section later.

Results

There were 307 total patient entries across the 7 sites: 187 women and 120 men with an overall average age of 60 years (Table 1). There were 13 different diagnoses noted with "mixed" pain (pain reported from a combination of body parts/regions [e.g., low back, leg, buttock and radiating down the leg(s) or neck, shoulders and shooting down the arm(s)], FBSS and radiculopathy being the 3 most commonly reported diagnoses (Table 2).

Of the 307 patients, 127 were surgically revised (DR-S) with the remaining 180 having their existing IPG programmed to become D-Burst-capable (DR-ON). Within the DR-S cohort, 93 were failing their current SCS platforms and were in need of "salvage," whereas 34 reported adequate relief but elected to have their system surgically revised to a D-Burst capable system in an attempt to "upgrade" their device with the hopes that even more pain relief would be obtained. Conversely, 123 of the DR-ON cohort were failing their then-current

Table 1: *Breakdown of subjects in study*

Criteria	n	%
Mean Age	60	
Gender		
Male	187	60.9%
Female	120	39.1%
DR-S	127	41.4%
Salvage	93	30.3%
Upgrade	34	11.1%
DR-ON	180	58.6%
Salvage	123	40.1%
Upgrade	57	18.5%

Table 2: *Statistical Analysis by diagnosis.*

Diagnosis	n	NRS		% Relief	
		Δ	*P* values	Δ	*P* values
Axial Neck Pain	3	1.00	0.44	23.33%	0.70
Axial Mid Back	3	-3.00	0.028	28.33%	0.36
Axial LBP	58	-1.74	0.0001	23.93%	< 0.00001
CRPS	15	-2.53	0.005	24.00%	0.009
FBSS	63	-2.75	< 0.00001	33.41%	< 0.00001
LSS	1	-6.00	NA	70.00%	NA
*Mixed	102	-1.81	< 0.00001	16.25%	< 0.00001
MS	1	-1.00	NA	30.00%	NA
Neuropathy	9	-2.44	0.035	22.78%	0.029
PAP	1	-1.00	NA	20.00%	NA
PHN	1	1.00	NA	20.00%	NA
Radiculopathy	49	-2.35	<0.00001	28.27%	<0.00001
Sacroiliitis	1	0.00	NA	0.00%	NA

Paired sample t-tests were used to calculate statistical significance. NRS Δ: change in NRS score, negative scores reflect decrease in pain as rated by NRS. % Relief Δ: change in percentage of pain relief, positive scores reflect increase in percent of pain relief reported. (* Refers to patients who identified their pain as a mix of back/neck pain and radicular symptoms) suggestive

Table 3. *Statistical analysis by cohort and subgroup at during initial post-operative period. Paired t-test was used to calculate statistical significance.*

GROUP	n	NRS				% Relief			
		Pre	Post	Δ	*P*	Pre	Post	Δ	*P*
Total	307	6.62	4.51	-2.11	< 0.00001	34.32%	58.41%	24.09%	< 0.00001
DR-S	127	6.88	4.28	-2.60	< 0.00001	29.21%	62.56%	33.35%	< 0.00001
Salvage	93	7.44	4.32	-3.12	< 0.00001	25.75%	60.27%	34.52%	< 0.00001
Upgrade	34	5.35	4.18	-1.18	0.036	38.68%	68.82%	30.15%	< 0.00001
DR-ON	180	6.43	4.67	-1.76	< 0.00001	37.93%	55.49%	17.56%	< 0.00001
Salvage	123	7.43	5.33	-2.10	< 0.00001	31.24%	49.21%	17.98%	< 0.00001
Upgrade	57	4.26	3.23	-1.04	0.0006	52.37%	69.04%	16.67%	< 0.00001
BSX	15	7.73	4.07	-3.67	< 0.00001	24.00%	61.67%	37.67%	< 0.00001
Medtronic	22	6.68	3.82	-2.86	< 0.00001	25.91%	66.82%	40.91%	< 0.00001
Nevro	22	7.27	3.68	-3.59	< 0.00001	24.55%	70.91%	46.36%	< 0.00001

Table 4. *Distribution SCS platforms.*

SYSTEM	n
Abbott	248
BSX	15
Medtronic	22
Nevro	22

SCS systems, and 57 were reporting adequate relief and being switched to D-Burst in an attempt to "upgrade" their device to potentially provide even more relief.

Of the 127 who were surgically revised (DR-S), 22 were switched from devices capable of 10,000 Hz; the remaining 105 were patients with devices only capable of tonic waveforms in conventionally lower frequencies (Table 3). The most common previous SCS system recorded in the study were those belonging to Abbott (previously St. Jude and ANS)—this was owing to the fact that all 180 of the DR-ON cohort were patients with Abbott devices that were capable of D-Burst but implanted prior to the US Food and Drug Administration (FDA) approval that allowed D-Burst to be used clinically in the United States (Table 4).

The average amount of time that elapsed from the point of initial implant to the time of conversion/revision was 2.81 years across the entire cohort (4.53 years for the DR-S group, and 1.6 years for the DR-ON group). Of the 307 subjects, 293 had long-term follow-up visits (354.4 average days) with NRS scores captured (DR-S: 302.7 days and DR-ON: 388.8 days). There was a statistically significant difference in elapsed time between the DR-S and DR-ON groups (1650.4–583.4, respectively). The likely explanation for this difference is owing to the commercialization process of D-Burst, which became available in the United States in the fall of 2016. For a short period of time prior to the formal release, Abbott began releasing IPGs that were preembedded with software that would make the device capable of producing the D-Burst waveform via a wireless programming change once FDA approval was obtained; thus why the elapsed time for the DR-ON group is so much shorter than DR-S. This difference did not impact the analysis, however, as the impact on LOE is comparable between the groups.

There were statistically significant reductions in NRS (Fig. 3) scores and percentage pain relief (PPR) (Fig. 4) in the postoperative period (~1 month postrevision/programming change) across the entire population of patients, each cohort (DR-S and DR-ON), as well as each subcohort (salvage and upgrade); *P* values were calculated using paired sample t-tests (Table 3). At long-term follow-up, these improvements held up in all groups analyzed except for the "upgrade" subcohort of DR-ON (Table 5). Statistical significance was also calculated by diagnosis using paired sample t-tests (Table 2).

Of the 127 patients who were surgically revised (DR-S), 21 had their entire system replaced (leads and IPG); the remaining 106 had only the IPG replaced and utilized adaptors to connect to the existing leads (Table 6). There were no statistically significant differences between the 2 groups (analysis of variance test).

Opioid usage was recorded immediately prior to the revision/programming change and after to assess for any changes in usage (Fig. 4; Table 7). There was a statistically significant decrease in opioid usage across the entire cohort of patients after being exposed the D-Burst (paired sample t-test), as well as in the DR-S salvage subcohort. Although the decrease in the DR-S

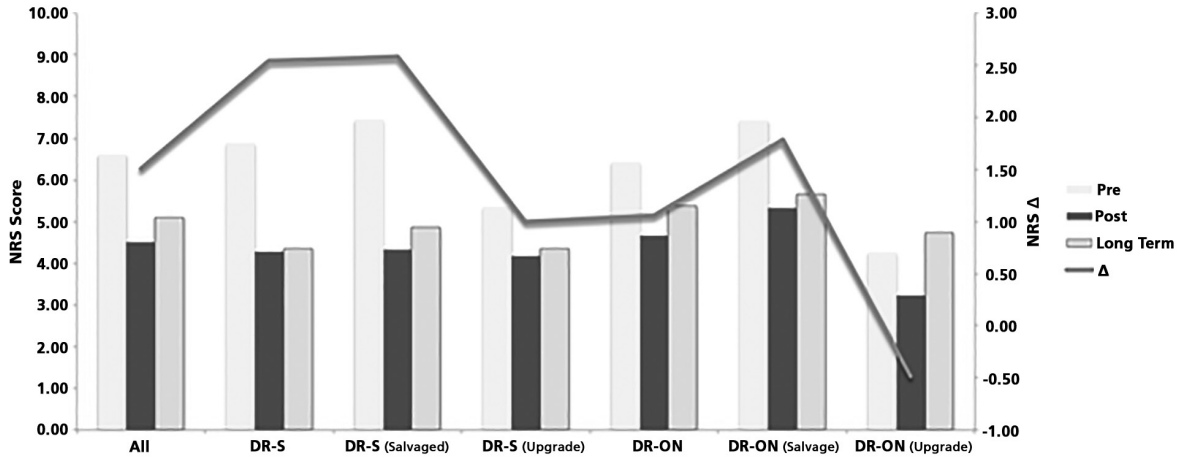

Fig. 3. *Numeric Rating Scale (NRS) Reductions: Pre – baseline, Post – post-operative, Long Term – scores at "long-term" follow-up (average time points varied for each cohort and subcohort (see Table 5), Δ – delta between pre and post*

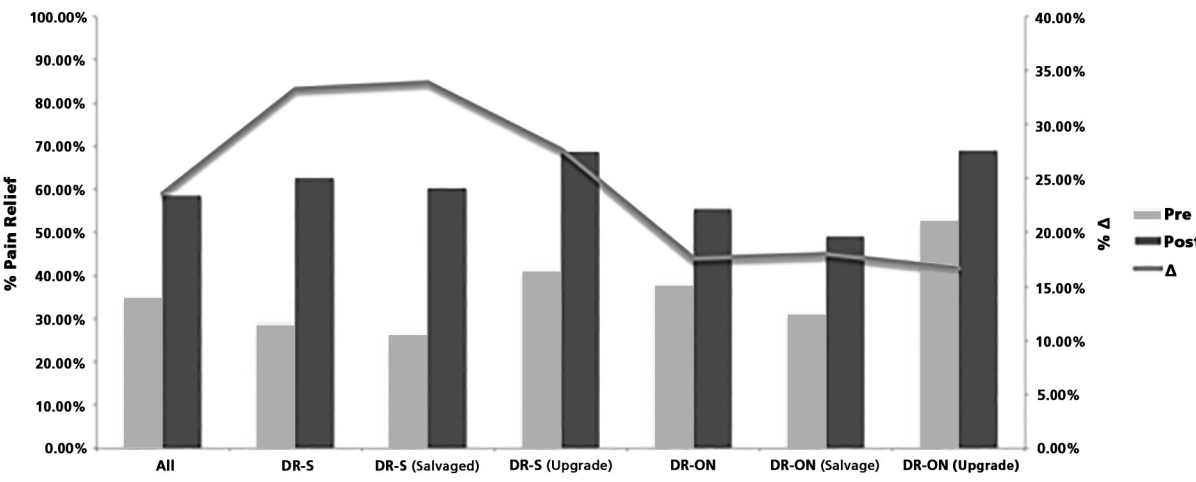

Fig. 4. *Percentage Pain Relief (PPR): Pre – baseline, Post – post-operative, Δ – delta between pre and post*

upgrade subcohort was not statistically significant, there were no patients who increased their daily usage (Fig. 6).

The average length of time between the initial implant and the revision/programming change across the entire study was 1026.4 days (Table 5). There was a greater degree of improvement in NRS (Fig. 7) score and PPR (Fig. 8) if the revision or programming changes took place within the first 2 years; after 2 years, there was little difference in the improvement achievable between the time points. Opioid usage, however, seemed to respond differently over time as there appeared to be negative correlation between opioid consumption and time—in the DR-S cohort, the more time that elapsed, the less of a decrease in opioids was noted (Fig. 9).

The most commonly cited reason among salvage patients for failure with their former SCS platform was "inadequate pain relief" (DR-S = 65, DR-ON = 92), followed by "insufficient coverage," "unwanted

Table 5. *Longevity data*.

GROUP	n*	Elapsed Time (days)		NRS			
		Implant to Change	Change to Present*	Pre	LT*	Δ	*P*
TOTAL	293	1024.8	366.9	6.62	5.11	-1.51	< 0.00001
DR-S	117	1650.4	305.9	6.88	4.34	-2.54	< 0.00001
Salvage	83	1534.7	302.8	7.44	4.86	-2.58	< 0.00001
Upgrade	34	1967.2	313.4	5.35	4.35	-1.00	0.0113
DR-ON	176	583.4	407.4	6.43	5.37	-1.06	< 0.00001
Salvage	121	747.6	406.6	7.43	5.65	-1.78	< 0.00001
Upgrade	55	546.8	409.4	4.26	4.75	0.48	0.076
BSX	14	1767.20	222.64	7.73	3.93	-3.80	< 0.00001
Medtronic	21	2330.41	162.57	6.68	3.27	-3.41	< 0.00001
Nevro	20	670.32	250.30	7.27	4.60	-2.67	0.0004

Pain scores measured at long term follow up or "present" are labeled "LT," Not all subjects were available for long term follow up, * refers to actual number reporting NRS scores

Table 6. *Direct comparison between revising the entire system with new leads and new IPG ("Whole System") versus keeping the existing leads in place, replacing only the IPG and using an adaptor to connect ("Adaptor") support.*

GROUP	N	NRS				% Relief			
		Pre	Post	Δ	*P*	Pre	Post	Δ	*P*
Adaptors	106	6.92	4.30	2.61	0.872	29.34%	61.89%	32.55%	0.309
Whole System	21	6.71	4.19	2.52		28.57%	65.95%	37.38%	

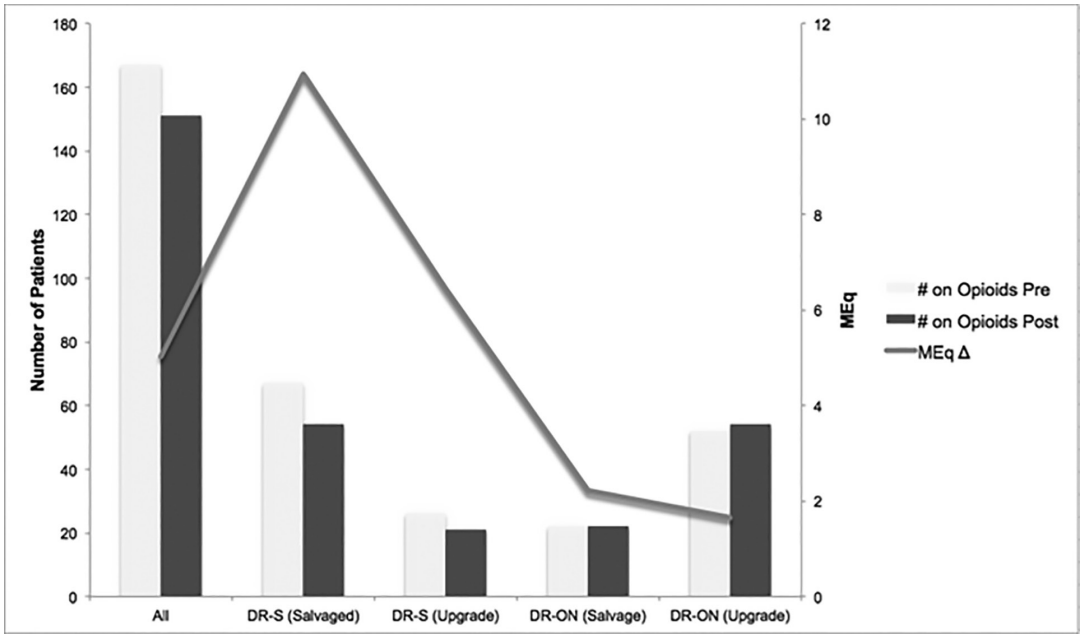

Fig. 5. *Changes in morphine equivalent dosing (MEq) and number of opioid users per cohort: # on Opioids Pre – number of patients on opioids at baseline, # on Opioids Post – number of patients on opioids after exposure to D-Burst, MEq Δ – changes in MEq from baseline.*

Table 7. *Opioids*.

	TOTAL	DR-S		DR-ON	
		Salvage	Upgrade	Salvage	Upgrade
MEq's					
Pre	19.36	33.24	21.79	12.05	9.74
Δ	14.58	22.28	15.81	10.63	8.09
% Change	-24.69%	-32.95%	-27.46%	-11.79%	-16.93%
# of Patients on Opioids					
Pre	167	67	26	22	52
Post	151	54	21	22	54
# that stopped Opioids	34	16	5	4	9
# that started Opioids	18	3	0	4	11
# with MEq decreased	78	37	15	9	17
# with MEq increased	21	4	0	4	13

(Morphine Equivalents = MEq; Number = #). * denotes statistical significance

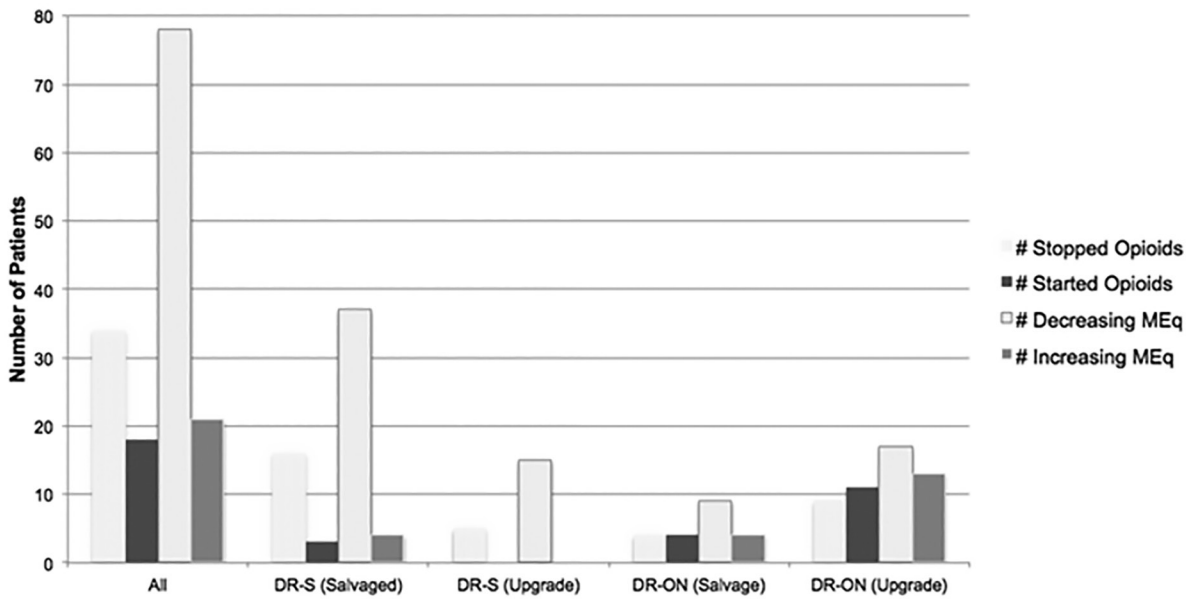

Fig. 6. *Changes in opioid usage by cohort: # Stopped Opioids – number of patients who stopped all opioid usage, # Started Opioids – number of patients that started using opioids, # Decreasing MEq – the number of patients who were able to decrease their daily MEq intake, # Increasing MEq, the number of patients who increased their daily MEq intake.*

paresthesia overflow," and "system not working" (Table 8). Calculations were performed to analyze the impact D-Burst had on potentially rectifying the reported failures/deficiencies. Patients who reported "Dead IPG/Malfunctioning" were removed from consideration in this calculation as these patients did not fail their therapy but rather experienced a hardware issue. Patients who reported "SCS System Was Not Failing—Upgrade Candidate" were also removed from calculation as there was no failure/

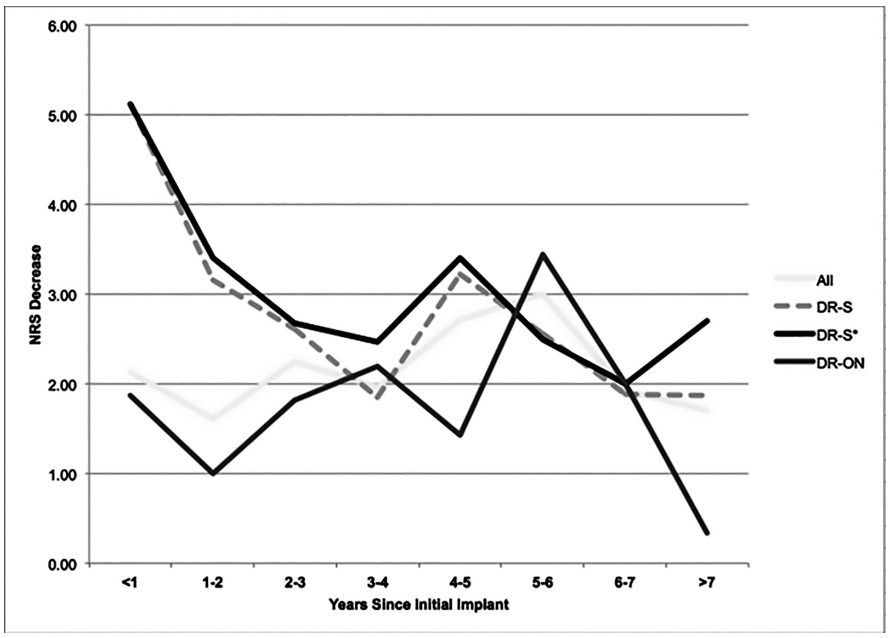

Fig. 7. *NRS over time: All – entire study population, DR-S – Surgical Revision, DR-S* – DR-S cohort adjusted to remove those IPG's that were dead and not failing, DR-ON – Non-Surgical Revision.*

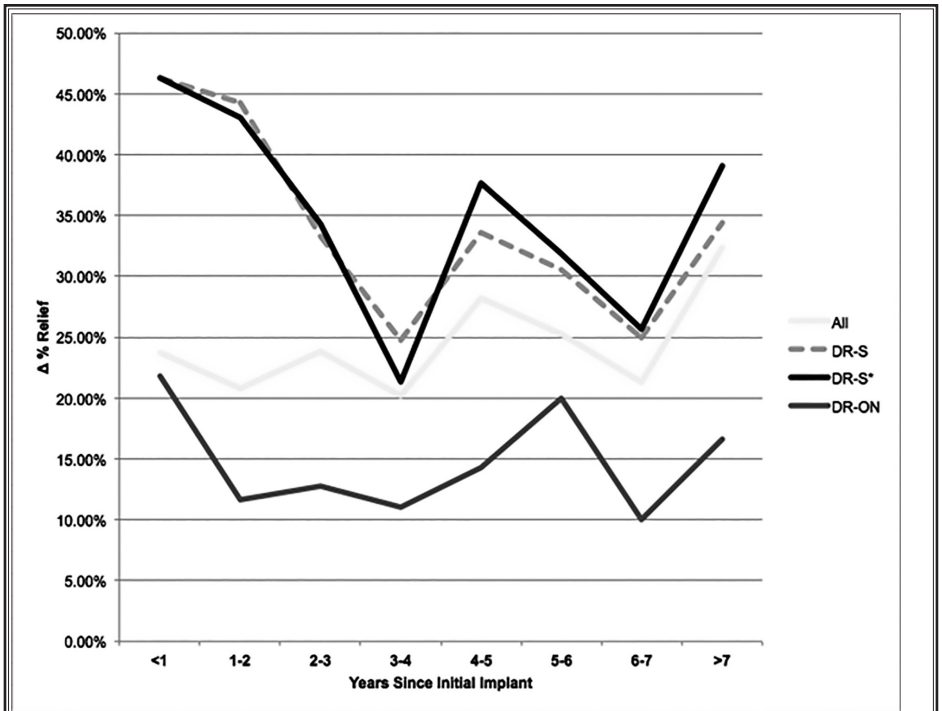

Fig. 8. *Percentage (%) pain relief over time: All – entire study population, DR-S – Surgical Revision, DR-S* – DR-S cohort adjusted to remove those IPG's that were dead and not failing, DR-ON – Non-Surgical Revision*

deficiency perceived that would need rectification. After adjusting both cohorts (DR-S = 103, DR-ON = 123), it was found that the majority of patients in the study reported rectification of their former complaints when switched to D-Burst (DR-S = 89.3%, DR-ON = 72.4%).

Discussion

The SUNBURST study showed that the D-Burst waveform was superior to traditional low-frequency tonic stimulation in individuals who were naive to SCS (19). Given that the study excluded individuals with any prior experience with SCS (trial failure or LOE previous SCS system), no recommendations could be made based on the data collected regarding the superiority, or even the overall efficacy, of D-Burst in the setting of LOE. Moreover, there has yet to be a head-to-head study comparing D-Burst to other forms of "burst" insofar as determining superiority, comparing longevity, or even efficacy. It should be noted that this study does not aim to make any claims of superiority for D-Burst over any other SCS therapy options in the setting of LOE or otherwise; the findings presented herein merely offer data to support the notion of utilizing D-Burst secondarily to other stimulation alternatives.

This study examines the use of D-Burst as either a salvage therapy in patients with LOE or as an "upgrade" to patients experiencing only partial relief. Our data showed D-Burst resulted in statistically significant reductions in pain and NRS scores at just over 1 year, regardless of the prior SCS therapy (tonic, rate-cycling, or 10 kHz). In those patients who had their SCS devices surgically revised to become D-Burst-capable due to insufficient coverage or inadequate pain relief, NRS pain scores were reduced by 1.74 and 3.51 points, respectively. Patients in the "salvage" groups of both cohorts (those reporting failures and/or LOE with their prior SCS devices) showed statistically significant improvements in their pain when exposed to D-Burst. Surprisingly, the DR-S upgrade group also showed a statistically significant reduction in pain that was sustained for over 10 months. These findings suggest that switching to D-Burst is a valid option for treating LOE, as well as in patients who are responders but unsatisfied with their current level of pain relief.

Of the patients who required surgical revisions (DR-S), 89.4% reported their complaint with the previous platform (e.g., inadequate relief, insufficient coverage, unwanted paresthesia overflow) was rectified with D-Burst. Unexpectedly, there were no statistically significant differences in pain relief between patients who had their entire system changed (leads and IPG) compared with those who simply changed the IPG and used adaptors to preserve the preexisting leads already in place. This was a constructive finding as future patients wishing to undergo a change in their SCS therapy may opt for a less invasive option and expect to have the same degree of pain relief.

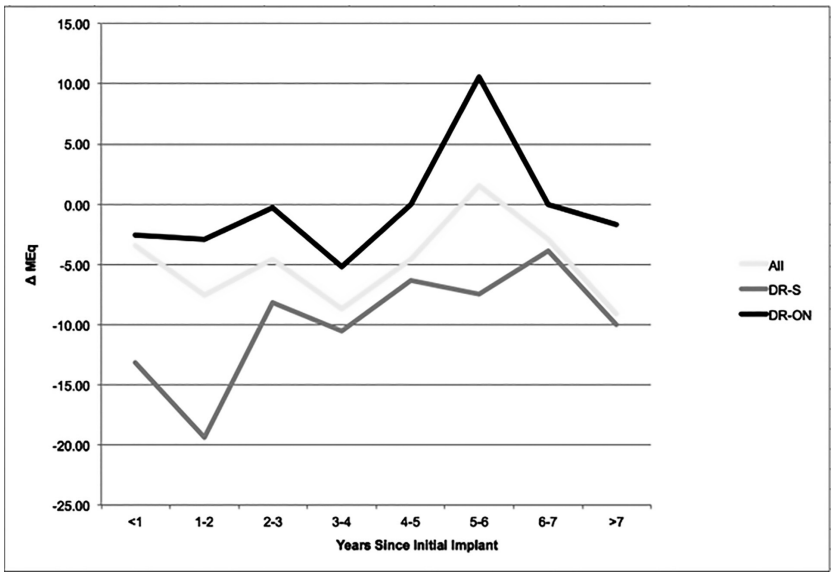

Fig. 9. *Change in opioid dosing over time: All – entire study population, DR-S – Surgical Revision, DR-ON – Non-Surgical Revision.*

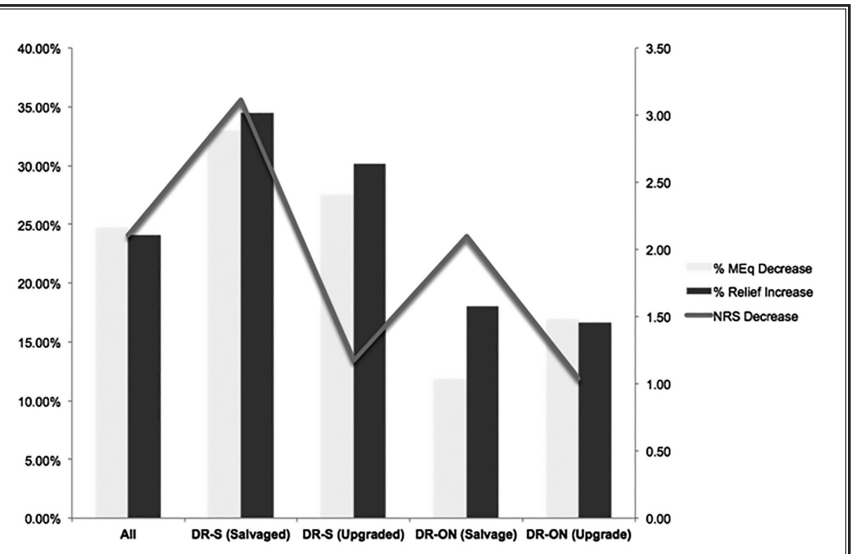

Fig. 10. *Chart illustrating the lack of concordance between NRS, % pain relief and opioid usage: % MEq Decrease – percentage decrease in MEq's, % Relief Increase – increase in percentage of pain relief, NRS Decrease – Numeric Rating Scale Decrease.*

The reduction in opioids was encouraging. The DR-S salvage group reported statistically significant reductions in daily opioid usage despite

Table 8. *Reported reasons for dissatisfaction and/or failure with previous SCS platform and rate of rectification per cohort.*

Failures/Deficiencies	n	Fixed	%
DR-S	103*	92	89.3%
Inadequate Relief	65	61	93.8%
Insufficient Coverage	31	24	77.4%
Unwanted Paresthesia Overflow	4	4	100%
System Not "Working"	3	3	100%
DR-ON	123*	89	72.4%
Inadequate Relief	92	75	81.5%
Insufficient Coverage	30	13	43.4%
Unwanted Paresthesia Overflow	1	1	100%
System Not "Working"	0	0	NA

having both the highest starting NRS scores and baseline opioid requirements. It is not clear if the simple introduction of D-Burst was responsible for the reduction in morphine equivalents or rather the fact that the pain was reduced to the point that patients found themselves less dependent on opioids as a means of treating their pain on a daily basis. Given the ever-present problem of prescription drug abuse and addiction, these results suggest a means of treating patients with LOE that are on elevated amounts of chronic opioids.

Implications

In previous years, if a patient reported LOE, there was little sense in attempting to revise the system with a competing platform to solve the issue as there was little-to-no difference between SCS platforms at the time. It was only logical to classify that patient as having "failed neurostimulation," as a whole, and move on to a different treatment modality entirely; at that point in the treatment continuum, options are quite limited.

Currently, there are 3 different methods for stimulating the dorsal columns: traditional tonic stimulation at frequencies ≤ 1500 Hz (t-SCS), high frequency tonic stimulation at 10 kHz, and D-Burst (20,35). Despite improvements and innovation, there are still those patients who fail SCS. If habituation to previously effective levels of stimulation is thought to be the chief cause of LOE, it would seem reasonable to "rotate" SCS therapy to one that the body has not yet been habituated to. In other words, if a patient fails SCS-"Option A," the intuitive answer is to switch the patient to SCS-"Option B." This would be akin to a commonly employed technique used throughout the practice of medicine as it pertains to the use of medications: when a patient fails to respond to one particular class of medication (i.e., a ACE inhibitor for hypertension), the patient is not simply labeled a "treatment failure" and their condition assumed to be untreatable—the next step is to try a different class of medications (i.e., switching to a calcium channel blocker). In this concept, different classes of medications have different mechanisms of action, thus the rationale for rotating therapies is based on the concept that one medication may succeed in which another failed owing to the fact that they act on different parts of a cell, different tissue, or even a different part of the body.

Using this analogy and applying it to dorsal column stimulation, one could deduce that the mechanism of action of these therapies is likely to be fundamentally different with respect to their neurophysiologic effects on the body; further studies need to be done to further elucidate and verify this concept. As described earlier, the D-Burst waveform works differently from t-SCS on both the cellular and macro levels. The results of our study show that D-Burst behaves differently in the face of LOE, and does not appear to be subject to the same limitations of time as proposed by Kumar et al (2). When all of these points are considered, it would appear that the concept of rotating SCS options (D-Burst in this case), similar to the way one would rotate medication classes, may hold merit and should be considered a viable option.

More importantly, the results of this study now suggest that a failure of SCS is not necessarily a failure of neuromodulation or the therapy as a whole, merely a failure of that one particular type of stimulation, and perhaps other options may succeed in which another failed. In theory, this concept may also apply to high-frequency stimulation, however, that was not evaluated in this study.

Correlating Pain Scores and Opioid Usage

Treatment success can be measured in a number of ways that do not rely solely on subjective measures of pain, such as NRS or PPR (i.e., quality of life, Oswestry Disability Index, etc.). A statistically significant reduction in pain means little if a patient is unable to decrease their reliance on chronic opioids or improve their ability to participate in the activities of daily living. A challenge that neuromodulators have faced for decades is the patient that reports improved pain but is unable or unwilling to come down from their opioids. Although many of the innovative therapies in neuromodulation advertise impressive reductions in Visual Analog Scale (VAS) scores, opioid reduction

is typically an afterthought when it should be held in even higher regard than any subjective measure of pain.

The findings of this study not only showed improvements in pain, but a reduction in opioid usage. Although it is unclear if these reductions were the result of the noted improvements in pain or if the waveform itself was somehow responsible due to its ability to act on the medial thalamic pathway, it should be noted that more than 70% of the patients in this study were using opioids on a chronic basis in the setting of LOE — a patient population anecdotally known for their reliance on opioids and historically not inclined to decrease. The authors are not suggesting that D-Burst is a means for reducing opioid consumption, however, it should not be overlooked as a potential contributor based on the findings presented earlier.

Perhaps the most intriguing piece of datum was the lack of correlation between the degree of improvement in pain (NRS and PPR) and the percent reduction of opioids. The DR-S salvage group had the largest change in NRS scores, PPR, as well as decrease in opioid consumption as measured by daily morphine equivalents. In comparison to the DR-S upgrade group, the NRS reduction was less than half of what was observed in the DR-S salvage group; however, the opioid reduction was only marginally decreased (Fig. 10). In comparison to the DR-ON salvage group, the NRS score reduction was only 32.7% less that what was observed in the DR-S salvage group and almost double that of the DR-S upgrade group, however, the reduction in opioid consumption was less than both groups (one-third of what was noted in DR-S salvage and less than half of that in DR-S upgrade). This lack of correlation highlights the very important fact that reductions in pain do not necessarily correlate to reduction in opioids. At a time when the medical profession is so centered on reducing patient reliance on opioids by finding treatments that could be deemed "opioid alternatives," the results presented herein support the notion that for a treatment to be labeled as such, its impact on opioid consumption should be specifically studied (as shown here) and not inferred from changes in VAS scores.

Limitations

Although the subject number in this study is substantial, data were obtained retrospectively, which limited some of the analyses that could be performed. A prospective study with longer time points is suggested to further validate this concept and the conclusions made. Confounders such as the wide-spread push within the pain management community to curtail opioid prescribing patterns for chronic, noncancer pain and the wide-spread public health care initiative to further decrease opioids could be a factor in explaining the opioid reduction; however, the direct cause-and-effect of change in SCS therapy linked to opioid reduction within the study patient populations should not be overlooked. It should also be noted that this study was not designed to promote the superiority of D-Burst over other SCS treatment options or suggest it may succeed where others failed. This manuscript merely explores the idea of rotating SCS therapies and the potential for reducing pain in the settings described earlier.

Conclusions

In this physician-initiated, multicentered, retrospective study, D-Burst was shown to be a viable option for treating, and potentially reversing, LOE with SCS. Additionally, the findings presented here support the notion that a failure with one particular type of DC-SCS system is not a failure of neuromodulation therapy as a whole, rather it may be merely a failure of one particular type of stimulation platform. As such, introducing a different "type" of stimulation to the dorsal columns (in this case D-Burst) similar to the concept of "therapy rotation," is a valid option to overcome the consequence of LOE and may be a valuable tool in the treatment of chronic pain.

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