Retrospective Review

High Frequency Spinal Cord Stimulation at 10 kHz for the Treatment of Chronic Pain: 6-Month Australian Clinical Experience

Marc Russo, MBBS[1], Paul Verrills, MBBS[2], Bruce Mitchell, MBBS[2], John Salmon, MBBS[3], Adele Barnard, PhD[2], and Danielle Santarelli, PhD[1]

From: [1]Hunter Pain Clinic, Broadmeadow, NSW, Australia; [2]Metro Spinal Clinic, South Caulfield, Victoria, Australia; [3]PainCare Multidisciplinary Group, Cottesloe, WA, Australia

Address Correspondence:
Dr Marc A. Russo, MBBS, DA (UK), FANZCA, FFPMANZCA
Director, Specialist Pain Medicine Physician
Hunter Pain Clinic
91 Chatham Street
Broadmeadow, NSW, 2292, Australia
E-mail: algoguy@gmail.com

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Background: High frequency spinal cord stimulation at 10 kHz (HF10 therapy) represents a prominent advance in spinal cord stimulation (SCS) therapy, having demonstrated enhanced efficacy in patients with back and leg pain and pain relief without paresthesia that is sustained at 24 months post implant.

Objective: To report on the effectiveness HF10 SCS therapy for a wide range of intractable pain conditions in clinical practice.

Study Design: Retrospective investigation of 256 patients who trialed HF10 SCS for chronic intractable pain of various etiologies.

Setting: Three Australian pain clinics.

Methods: Two hundred fifty-six patients trialed HF10 SCS with view of a permanent implant if successful. Pain distributions included back + leg, back only, head ± neck, and neck ± arm/shoulder. About 30% of patients had previously failed traditional low-frequency paresthesia-based stimulation, while the remaining cohort were either highly refractory to treatment or not recommended by the pain physician for traditional SCS. Pain scores (numerical pain rating scale – NPRS) and functional outcome measures (Oswestry Disability Index – ODI; and activity tolerance times) were assessed at baseline, post-trial, and at 3 and 6 months post-implant as available in the medical records.

Results: Of the 256 patients, 189 (73%) reported a positive trial and were implanted. Patients with back + leg pain demonstrated the highest trial success rate (81%). A mean reduction in pain, among those for whom data were available, of 50% was sustained up to 6 months post-implant across the entire patient population. Sixty-eight percent of patients who failed traditional SCS reported a positive trial and mean pain relief at 6 months was 49% ($P < 0.001$). An 8.6 point reduction in ODI (21%) at 6 months and improved sitting, standing, and walking tolerances were also reported.

Limitations: As data was collected retrospectively, missing data points were unavoidable; this was primarily due to inconsistent data collection and patients being lost to follow-up. Patient populations were diverse and a control group was not appropriate in this setting.

Conclusions: These retrospective results demonstrate a significant advancement for patients suffering with chronic intractable pain and are consistent with recently published clinical results for HF10 SCS. HF10 SCS appears to be a viable, paresthesia-free alternative to traditional SCS, with high trial success rates, demonstrated effectiveness in a range of pain distributions including those typically difficult to treat with traditional SCS, and the possibility to restore pain control in patients who have previously failed traditional SCS.

Key words: Spinal cord stimulation, high frequency stimulation, HF10, paresthesia-free stimulation, back pain, leg pain, cervical pain, neuromodulation

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Low back pain has been ranked as the greatest contributor to overall burden in Australia and the sixth greatest worldwide, with immense economic burden placed on patients and their families, communities, health care systems, industries, and governments (1). In an Australian "cost-of-illness" study, the total cost associated with low back pain has been estimated at over AUD 9 billion (2). Providing relief for chronic predominant back pain can be a challenge. Spinal cord stimulation (SCS) has become a viable treatment option for patients with chronic pain and is commonly indicated for patients with failed back surgery syndrome (FBSS) (3-5). SCS patients report greater improvements to pain, quality of life, and activity levels, and have a higher return-to-work rate than those receiving conservative treatment (6-8). The success of SCS has also been correlated to decreased analgesic medication use and is particularly apparent for patients with predominant lower extremity pain (9).

A recent systematic review and meta-analysis has reported the mean SCS responder rate among patients with chronic back and leg pain (although not including patients who had previously failed SCS and primarily those with predominant leg pain) achieving the "equivalent of 50% more pain relief" to be 53%, at a mean follow-up time of 24 months. Although more than 50% of the included studies did not report the specific location of pain, the authors conclude that the effectiveness of SCS in relieving predominant back pain is debatable (9). It has also been noted that the rate of success is not correlated to the year of the study, an indication that despite an extensive history of clinical application and changes to the clinical methods or technology, significant clinical improvement is lacking (9-11). The efficacy of SCS for axial back pain has been suggested in observational studies to be improved by utilizing hybrid neurostimulation therapies, such as a SCS paddle style leads placed with a percutaneous introducer (12) and combined spinal-peripheral neurostimulation (13). New generation multicolumn lead approaches aimed at increasing paresthesia-pain coverage may improve success (14). However, these technologies still pose limitations owing to the side effects of paresthesia, such as unintended, unwanted, or painful stimulation, loss of effective paresthesias, or stimulation shocks as a result of change in body position (3,15-17).

High frequency spinal cord stimulation at 10 kHz (HF10™ Therapy) represents novel neurostimulation therapy. HF10 therapy received CE Mark for use in Europe in 2010 and was approved by the Therapeutic Goods Administration (TGA) for use in Australia in June 2011. The mechanism of action likely includes attenuation of wide dynamic range (WDR) neuron activity (18). WDR neurons are hyperactive in chronic pain; they take on a wide range of stimuli from primary afferent neurons, and when repeatedly stimulated, exhibit a progressive increase in responsiveness and pain signaling, known as "wind-up" (19,20). High frequency stimulation may suppress WDR responsiveness and thus modify chronic spinal pain signaling (21).

HF10 therapy offers the possibility of enhanced effectiveness in patients with predominant back pain, back pain with or without leg pain, and also in those with leg pain only, and provides pain relief without paresthesia mapping or therapeutic paresthesias (15,18,22,23). The first in-human HF10 study, a short 4-day trial performed by Tiede et al (15) in 24 patients with predominant back pain across 5 US centers, reported greater reductions in overall pain and higher responder rates than traditional SCS, without paresthesia or any serious adverse effects. A subsequent prospective open-label European multicenter study by Van Buyten et al (18) trialed HF10 SCS in a larger cohort of 83 patients with low back pain, following patients after implantation for 6 months. They reported an 88% trial successful rate, and significant improvements in both back and leg pain (> 50% back pain reduction in 74% of patients) and functional measures (Oswestry Disability Index [ODI] and sleep) at 6 months, as well as a reduction in the use of analgesic medications. Follow-up of these patients was extended to 24 months, and a subsequent paper reported sustained, clinically significant results, providing support for long-term efficacy of HF10 SCS in chronic intractable back and leg pain (22). A large randomized control, active comparator trial of Senza® HF10 SCS system developed by Nevro Corp. (Menlo Park, CA, USA) has recently demonstrated superior results to traditional stimulation in patients with back and leg pain (23).

These studies also provided evidence that HF10 SCS exhibits a similar safety profile to traditional SCS. Adverse effects were predominantly non-severe, and no adverse effects related to paresthesia, such as those commonly seen in traditional SCS patients, were reported (18,22). Furthermore, advantages to the HF10 SCS surgical procedure are the result of switching from paresthesia mapping to anatomical lead placement, which translates to more predictable procedure times and reduced patient discomfort and anxiety (15,24).

The objective of this study was to report on the

Australian experience of HF10 SCS therapy for the management of various distributions of chronic intractable pain among patients refractory to previous treatments in routine clinical practice.

Methods

The experience of 3 Australian centers (Hunter Pain Clinic, NSW; Metro Spinal Clinic, VIC; PainCare Multidisciplinary Group, WA) that have been applying HF10 SCS since the technology received regulatory approval in Australia was pooled together and analyzed.

Device Description

The Senza™ rechargeable HF10 SCS system is a product of Nevro Corp. (Menlo Park, CA, USA) and was approved by the Australian authorities (TGA) in June 2011 for use in the management of chronic intractable pain of the trunk and/or limbs. The device delivers electrical stimulation, with frequencies of up to 10 kHz, via a pulse generator and dual leads into the epidural space. Stimulation at 10 kHz at amplitudes of 0.1 – 3.0 mA is typically paresthesia-free.

Patients

A combined total of 256 patients underwent the trial procedure between June 2011 and December 2013 (Fig. 1A). As this is a retrospective data collection study, without formal inclusion and exclusion criteria, patients presented to clinics with a range of chronic intractable pain distributions, including back only, leg only, back + leg, head ± neck pain, neck ± shoulder/arm pain, and other complex pain patterns (16.8% either different location or not recorded, Table 1). The patients studied were not candidates for, or responders to, traditional SCS therapy. Patients were deemed suitable for trial of HF10 SCS as per physicians' opinion and psychologi-

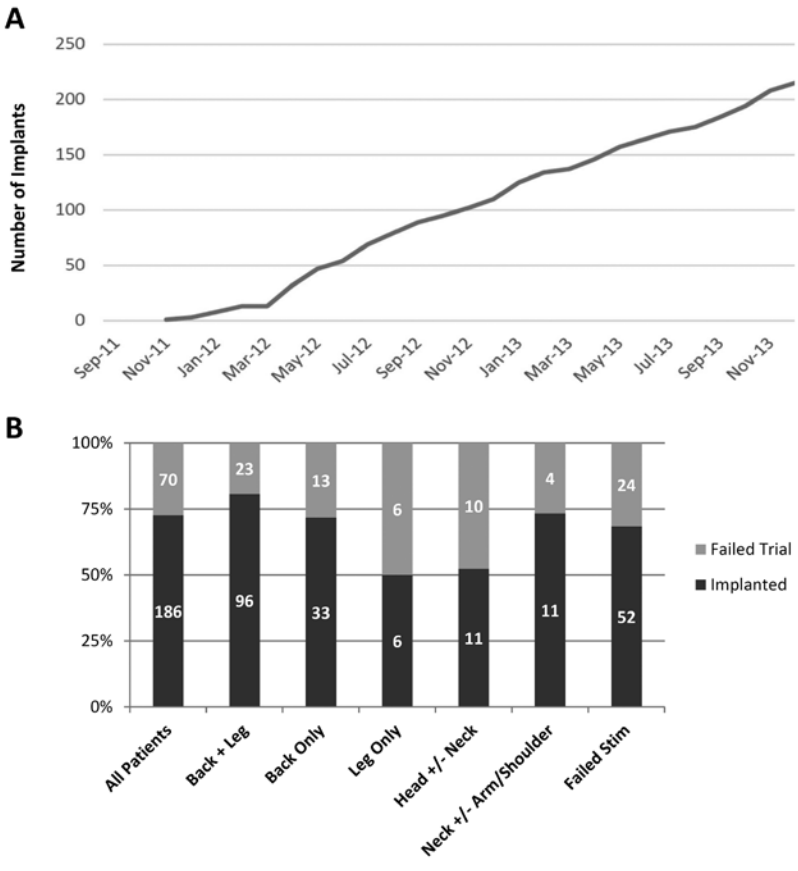

Fig. 1. *A. Cumulative number of implants between all 3 centers. B. Trial to implant procedure rates grouped by common pain distributions.*

cal evaluation. Data were extracted from clinic medical records after consent for the use of data was obtained from each patient.

Trial Procedure

Under fluoroscopic guidance, 2 temporary electrodes were placed in the midline dorsal epidural space with a staggered offset to cover the target areas in a contiguous fashion. For low back and or leg pain leads were typically placed from T8 to T11 with the primary anatomic target at the T9/10 disc as per the manufacturer's recommendations. For neck and arm pain the anatomic targets were the C2/3 disc and C3 and C4 vertebral bodies per the physician's empirical clinical choice. Impedance was checked and the leads were secured to the skin and connected to the external trial system. Intraoperative paresthesia testing was not performed. Patients were discharged and typically trialed HF10 SCS for 7 – 14 days. Each patient received an initial set of programs and underwent reprogramming during the trial period as needed if analgesia was insufficient.

Table 1. *Patient baseline characteristics*.

Patient Baseline Characteristics	N	%
Total	256	
Male	88	34.4%
Female	168	65.6%
Age (Mean ± SD)	54.8 ± 16.2	
Pain Indication		
Back + Leg	119	46.5%
Back only	46	18.0%
Head ± Neck	21	8.2%
Neck ± Arm/Shoulder	15	5.9%
Leg only	12	4.7%
Other/Unrecorded	43	16.8%
Previous Stimulation		
Failed traditional stimulation	76	29.7%
Stimulation naive	84	32.8%
Not recorded	96	37.5%
Pre-Trial Statistics		
Mean NPRS	7.45 ± 1.54	
Mean ODI (%)	41.42 ± 14.3	
Median Sitting Tolerance (minutes)	20	
Median Standing Tolerance (minutes)	15	
Median Walking Tolerance (minutes)	15	

NPRS = Numerical Pain Rating Scale; ODI = Oswestry Disability Index.

Most, but not all, centers arranged for plain film imaging of the thoracic or cervical spine to document lead position at time of removal of the leads. Typically, the trial was deemed successful if overall pain reduction was ≥ 50% from baseline, an outcome criterion widely used in the Australian environment and the SCS community at large. However, unlike clinical trials, patients may also proceed to implant if they experienced a level of analgesia which they deemed was significant, and/or experienced a significant improvement in functional capacity, and/or were able to significantly reduce medication intake during the trial period or some other measure of success that was deemed clinically appropriate. Patients who did not experience any significant benefits were regarded as having a failed trial and did not proceed to implant.

Implant Procedure

Patients who had a successful trial underwent surgical implantation of the Senza™ Implanted Pulse Generator. Via similar epidural entry technique as used in the trial implant, percutaneous leads were placed into the final trial position. Impedance was checked and correct position of the leads was confirmed on both the anteroposterior and lateral x-ray images. Leads were anchored to the spinous process fascia and tunneled to the IPG pocket, which was placed at the physician's discretion either over the lateral flank posteriorly or in the subcutaneous tissue of the anterior abdominal wall. The leads were connected to the IPG and the surgical site was irrigated and closed in multiple layers. No intraoperative paresthesia testing was performed. Patients were typically discharged over the next 1 – 2 days and asked not to engage in significant physical activity over the next 6 weeks in order to minimize of the possibility of lead migration.

Data Collection and Analysis

Patient baseline, post-trial, and 3 and 6 month post-implant data were collected by clinic personnel retrieved retrospectively from each site's medical records. Information collected at all sites included pain distribution, previous stimulator treatments, and overall pain (numerical pain rating scale [NPRS]; 0 – 10: where 0 = no pain and 10 = the worst pain imaginable). Additional functional outcome measures were collected at 2 of the 3 sites: ODI, and sitting, standing, and walking tolerance times.

Statistical analysis of data was conducted with the SPSS statistical software package (IBM, Armonk,

NY, USA). Statistical significance was determined by a paired samples t-test with a P-value of < 0.05 considered significant. Means were calculated for more complete datasets, such as NPRS and ODI, while medians were reported for functional outcome measures in order to counteract large variances and outliers.

Results

Baseline Statistics

A total of 256 patients underwent the trial procedure: 34% men and 66% women. The mean age was 55 ± 16, with ages ranging from 19 to 91 years. The most common pain distributions were back + leg (47%), back only (18%), head ± neck (8%), neck ± arm/shoulder (6%), and leg only (5%). Sixteen percent either had pain in another area or the information was unavailable in the chart. At least 30% of patients had previously failed traditional SCS or peripheral nerve field stimulation (PNFS) although in 37.5% this was not recorded. The mean pre-trial pain score (NPRS) was 7.5 ± 1.5. The mean pre-trial ODI (%), where available, was 41.4 ± 14.3. Median pre-trial activity tolerances (minutes) were 20 sitting, 15 standing, and 15 walking. A summary of baseline information is presented in Table 1.

Trial Pain Score Outcomes

Of the 256 patients who underwent a trial of HF10 SCS, 186 patients (73%) reported a positive trial and proceeded to permanent implant. Patients presenting with back and concomitant leg pain demonstrated the highest trial success rate (81%), followed by patients with back pain only (72%) (Fig. 1B). Of those patients that had previously failed traditional SCS and/or PNFS, 68% had a positive trial. Overall, mean NPRS was reduced by 60% post-trial (7.5 ± 1.6 vs 3.0 ± 1.5; $P \leq 0.001$).

Post-Implant Pain Score Outcomes

Clinically significant reductions in pain scores were observed among all patient groups with around 50% reduction from baseline at 3 and 6 months post-implant ($P \leq 0.001$) (Fig. 2A). Despite relatively small sample sizes, statistically significant reductions in pain were observed in patients with neck ± arm/shoulder pain or head ± neck pain over the course of 6 months post-implant ($P \leq 0.05$) (Fig. 2C). Patients that were known to have previously failed traditional stimulation also reported significant reductions in pain (Fig. 3). At 6 months post-implant, 55% of previously failed stimulator patients reported 50% pain reduction and 8% reported ≥ 80% pain reduction (n = 38). Irrespective of the baseline pain score, a similar reduction in pain was observed at 6 months (Supplement 1A; pre NPRS ≥ 7: 3.9 ± 1.6 vs pre NPRS < 7: 3.4 ± 2.5).

Functionality Outcomes

Improvements to functionality across the entire patient population were also observed. A mean 7 point reduction in ODI was observed at 3 months post-implant and an 8.6 point reduction (21%) was observed at 6 months post-implant (Fig. 4A) and this was significantly positively correlated to NPRS at 6 months (r = 0.503, $P < 0.001$) (Supplement 1B). A trend for improvements in sitting, standing, and walking tolerances was also observed (Fig. 4B). Median sitting tolerance was improved by 40 minutes at 6 months and median standing and walking tolerances were improved by 15 minutes at 6 months. NPRS was also significantly negatively correlated to standing (r = -0.346, $P < 0.05$) and walking tolerances (r = -0.261, $P < 0.05$) at 6 months post-implant (Supplement 1B).

Discussion

This large multicenter retrospective investigation of HF10 SCS therapy in standard Australian clinical practice provides clinical results that signify a promising therapeutic option for patients suffering with a range of chronic intractable pain complaints and who failed or were not suitable candidates for traditional SCS therapy. This study demonstrates the effectiveness of HF10 SCS therapy in a challenging patient cohort and demonstrates significant improvements in pain and daily function.

In line with previous HF10 clinical studies (15,18,22), a high trial success rate in patients with back pain was also observed, in contrast to traditional SCS, in which efficacy is questionable in patients with predominant back pain (4,14,25). Pain intensity remained significantly reduced by around 50% at 3 and 6 months post-implant, whether observing all patients or patients grouped by specific pain distributions. Improvements to functional measures were also observed; an 8.7 point reduction in ODI at 6 months, along with improvements to sitting, standing, and walking tolerances. Significant correlations between pain score and functional measures (ODI, and standing and walking tolerances) were found. Similar to the European clinical study (18), the current study also included a large number of patients that had previously failed traditional SCS and/or PNFS

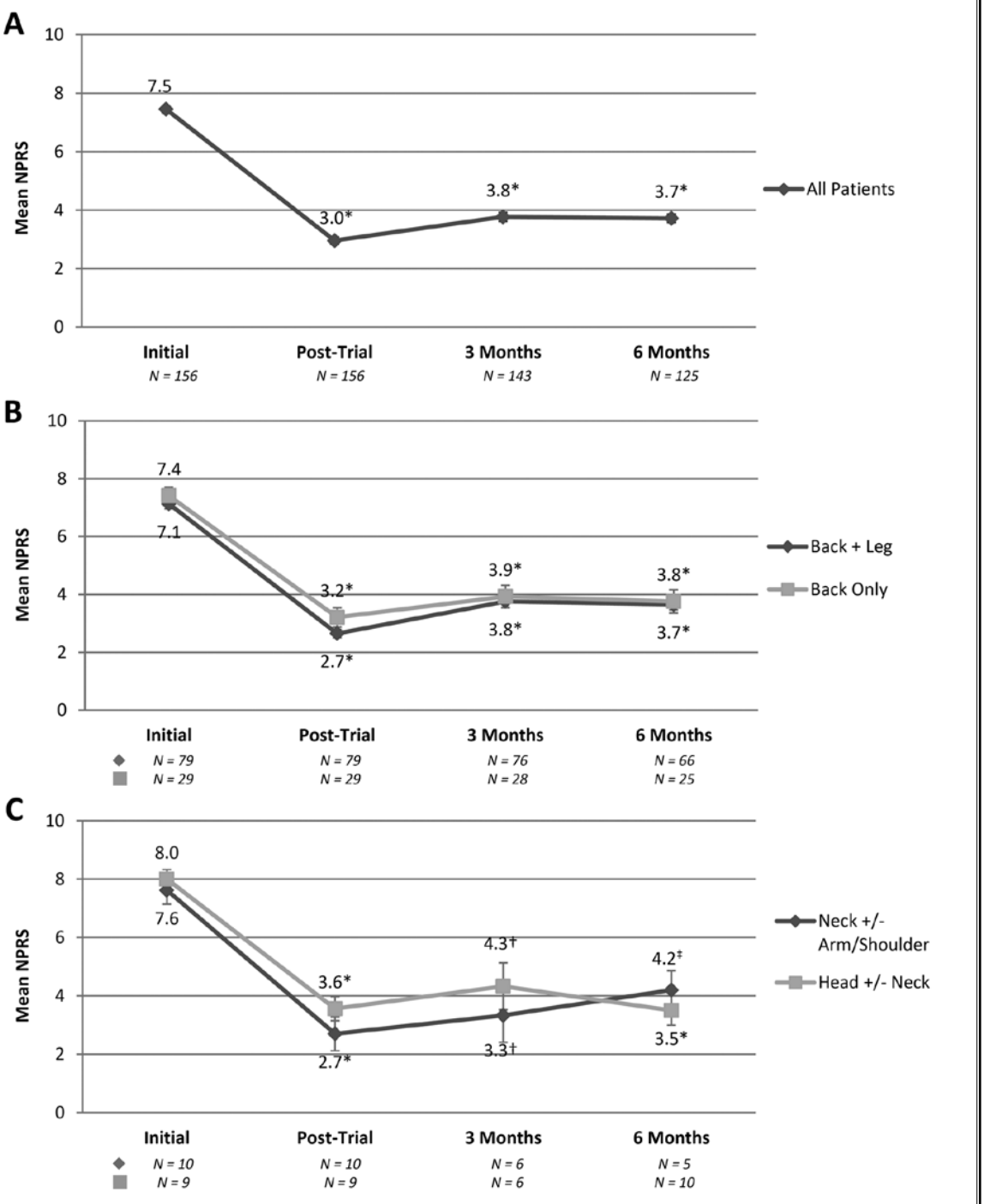

Fig. 2. *Mean overall pain (NPRS) scores for patients: pre-trial, post-trial, and 3 and 6 months post-implant. A. All patients. B. Back + Leg and Back only patients. C. Neck ± Arm/Shoulder and Head ± Neck patients. (± standard error of the mean; *P < 0.001; †P < 0.01; ‡P < 0.05).*

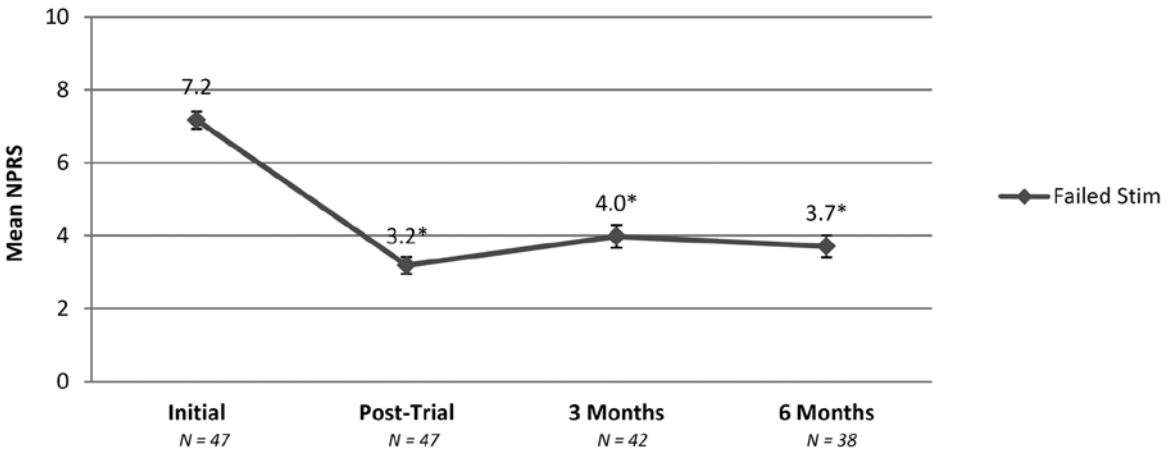

Fig. 3. *Mean overall pain (NPRS) for patients who had previously failed traditional stimulator treatment (SCS/PNFS): pre-trial, post-trial, and 3 and 6 months post-implant (± standard error of the mean; *P < 0.001).*

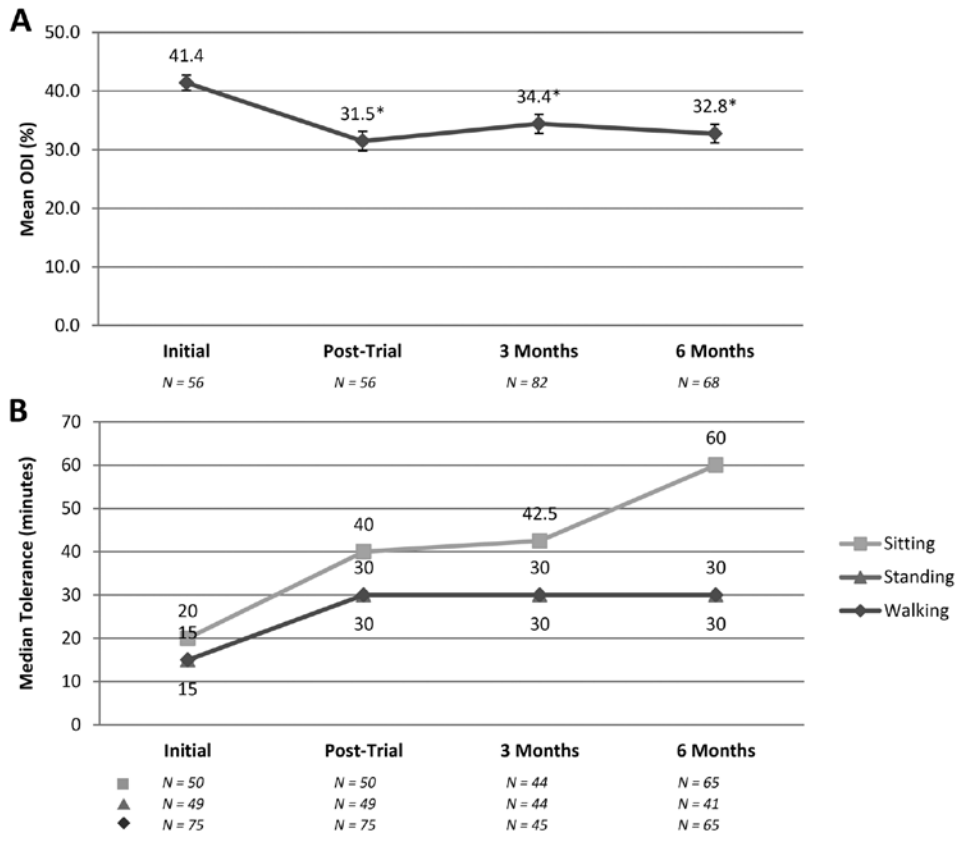

Fig. 4. *Functional outcome results for all patients: pre-trial, post-trial, and 3 and 6 months post-implant. A. Mean ODI (%) (± standard error of the mean; *P < 0.001; Note: only one site collected post-trial ODI data, hence the lower N for initial–post-trial). B. Median activity tolerances (minutes).*

(n = 78), and 68% of these patients experienced a successful trial and proceeded to implant. Pain reductions for these patients were statistically significant at 3 and 6 months post-implant, with over 55% of patients having reported > 50% pain relief at 6 months.

One major advantage of HF10 therapy is that it is paresthesia free. As such, it overcomes side effects such as unintended, non-concordant, overwhelming, and/or painful stimulation, and stimulation shocks as a result of change in body position (3,15,17). Additionally, the safety profile of HF10 SCS has been previously assessed by Al-Kaisy et al (22), who reported similar occurrence of adverse effects compared to traditional SCS and no signs of neurological deficit or dysfunction attributable to the therapy after 24 months.

The results of this study reflect the results of the European clinical trial study, in which HF10 SCS outcomes were assessed in back pain patients (18) (Fig. 5). Improvements to pain and ODI were significant although not as marked as in the clinical study, however. There are several possible reasons for this that may be considered as limitations of this study and these will be discussed below.

As a retrospective investigation of standard clinical practice, this study has several limitations. Documentation of outcomes and patient follow-up is less rigorous than in clinical trials; for example, patient reviews, questionnaire completion, and programming sessions were sometimes inconsistent. Also, as a result of retrospective pooling of data between the sites and disparity in routine recording of outcome measures, few patients had a full set of pain, disability, and activity tolerance scores (not all sites reported pre-trial pain scores and only one site collected post-trial ODI data). A portion of patients were lost to follow-up, which, together with data pooling, can hide a sub-cohort of non-responders and potentially bias the outcome. However, this may have a 2-way effect; for example, if a patient is doing well, they may not feel the need to attend follow-up sessions, thus there is a significant potential for under reporting successful clinical outcomes.

Another limitation relates to the heterogeneity of the patient population, such as the wide range of pain distributions (including cervical pain), the presence of co-morbidities, and the inclusion of a large number of patients who had previously failed traditional SCS, all of which were excluded in the clinical studies. In the clinical trials, trial success was strictly determined by the percentage of pain relief, however, in this investigation, numerous factors such as patient satisfaction, changes in analgesic medication intake and functionality determine trial success rather than a strict > 50% pain relief cut-off. If the trial clinical measure for success is not also the reported measure of clinical outcomes success (here greater than 50% pain relief) then conclusions are negatively biased. We produced box and whisker plots to identify potential outliers (Supplement 2A, B) and further investigated those patients to create a list of reasons for lack of significant pain relief (Supplement 2C). The major reasons were confounding pathology (new and/or old), low pre-trial NPRS scores, trial success based on benefits other than pain, pocket/anchor site pain, lead migration, recharging issues (post-injury), and infection. A more detailed discussion of device programming and device troubleshooting is outside the scope of this documentation of "real world" study results and the reader is referred to review the clinical summary paper (26) and the Senza physician's operating manual.

This commentary is not to suggest that there are not patients who do achieve back pain relief with traditional SCS, nor that there are not patients who find the paresthesia sensation a soothing, pleasing sensation. One can imagine that some patients are reassured by the fact that experiencing paresthesia reinforces to them that the device is delivering therapy, just as some patients may find paresthesia distracting to engagement in everyday activities of daily living and may prefer a paresthesia-free therapy. Until such time as there was a study in which each individual patient experienced both chronic paresthesia therapy delivery and chronic paresthesia-free therapy delivery, one can only use pain score relief as a de-facto proxy of patient most desired therapeutic approach.

Nonetheless, this is a large study of high frequency SCS, with statistical analysis confirming clinically important, sustained pain relief even in this group of highly refractory and diverse patient etiologies. While this study lacks the level of scientific vigor of a prospective controlled study, it serves the purpose of assessing the post-market effectiveness of HF10 SCS therapy in the most difficult patients seen in a general practice ("real world") setting, as a follow-up to the previous prospective long-term clinical study (18,22). In the opinion of the authors, it is important to analyze efficacy for domains and in addition, document that efficacy though multiple study types which includes not only randomized controlled trials, but also includes mechanism of action studies and in addition post market "real world" studies. This data set fulfills a pre-existing gap in the

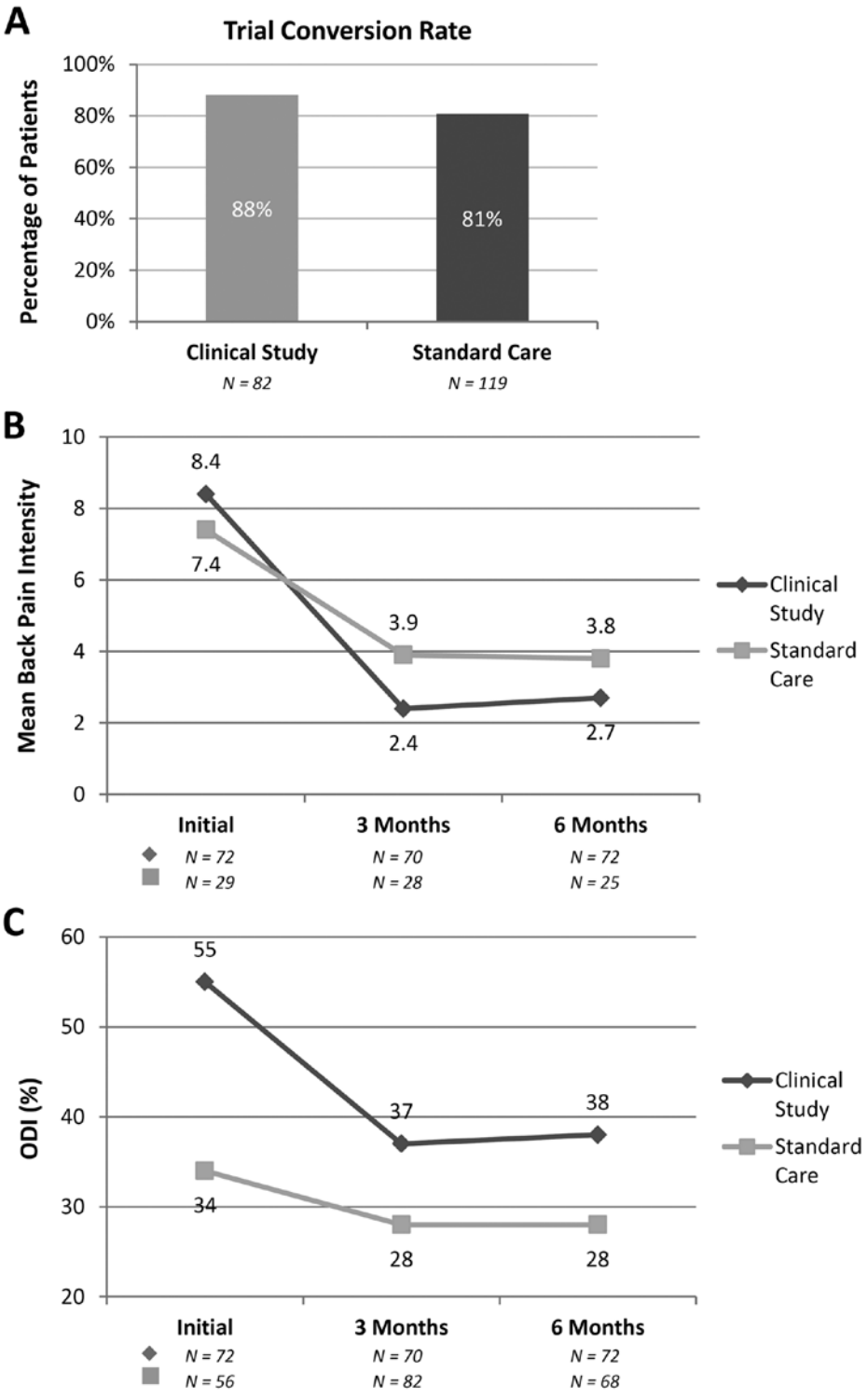

Fig. 5. *Clinical (Van Buyten et al / Al-Kaisy et al 2013) versus standard care (Australian data) outcomes (n = 82 vs 119; this figure compares back +/- leg pain patients as patients with other pain distributions were not included in the clinical study). A. Trial conversion rates. B. Mean back pain intensity (NPRS). C. ODI (%).*

clinical studies related to HF10 therapy. Fig. 5 illustrates how the current data from the Australian general practice setting ("Standard Care") are consistent with the results of the prior European prospective clinical trial study ("Clinical Study"). It is important to note that the results reported here include outcomes achieved when HF10 SCS was novel to Australian practice. The widespread, growing use and familiarity of HF10 SCS therapy has led to further improved patient outcomes compared to the results presented here which are more consistent with the clinical trial results. We are confident that ongoing studies will confirm this and with continuing patient follow-up and a solid dataset of long-term results, we aim to report on the long-term outcomes in the future.

Conclusion

The results of this retrospective investigation of HF10 therapy in routine clinical practice demonstrate that HF10 SCS is effective in a widely heterogeneous and highly refractory patient population who were not suitable candidates for traditional SCS. Additionally, this study provides particularly promising evidence that HF10 SCS is a viable alternative for patients who have previously failed traditional SCS and can be implemented in standard "real world" practice settings while offering a high trial-to-implant conversion rate and significant pain relief.

Author Contributions

Drs. Marc Russo (MBBS, DA (UK), FANZCA, FFPMANZCA), Paul Verrills (MBBS FAFMM GDMM (Hons) MPainMed FIPP), Bruce Mitchell (MBBS FACSM FACSP FASMF MPainMed FIPP), and John Salmon (MBBS) conducted the study, including patient consultation and data collection. Adele Bernard (PhD) and Danielle Santarelli (PhD) performed data analysis, interpreted the data, and prepared the manuscript. All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of Interest

The authors have not received any reimbursement or honorarium in any other manner. Dr Marc Russo and Dr Paul Verrills are members of the Nevro Scientific Advisory Board. Drs. Marc Russo, Paul Verrills, Bruce Mitchell, and John Salmon are all practicing interventional pain physicians and are consultants for Nevro Corp. and other neuromodulation companies. Adele Bernard and Danielle Santarelli have no conflicts of interest to report.

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Supplement 1.

A. Paired samples test for patients grouped by pre NPRS. The mean NPRS at 6 months is similar for patients with severe initial pain (NPRS>7: mean 6m NPRS = 3.86) and moderate initial pain (NPRS≤6: mean 6m NPRS = 3.37). The mean differences in pain relief (PRE NPRS – 6m NPRS) are significantly different (p>0.001).

B. Pearson's correlation coefficients for recorded 6 month outcomes. ODI and NPRS at 6 months are significantly positively correlated (r=0.503, p<0.001). Walking tolerance is significantly positively correlated to sitting tolerance at 6 months (r=0.614, p<0.001), and also to standing tolerance (r=0.890, p<0.001). Sitting and standing tolerances at 6 months are also significantly positively correlated (r=0.614, p<0.001). NPRS and walking and standing tolerances at 6 months are significantly negatively correlated (r=-0.261; p<0.05; and, r=-0.346, p<0.05, respectively).

A

Paired Samples Statistics

PRE NPRS (Binned) Grouped			Mean	N	SD	SEM
<= 6	Pair 1	PRE NPRS	5.34	35	.802	.136
		6m NPRS	**3.37**	35	1.536	.260
7+	Pair 1	PRE NPRS	8.08	90	.939	.099
		6m NPRS	**3.86**	90	1.590	.168

Paired Samples Test[a]

PRE NPRS (Binned) Grouped			Paired Differences					t	df	Sig. (2-tailed)
			Mean	SD	SEM	95% CI of the Difference Lower	95% CI of the Difference Upper			
<= 6	Pair 1	PRE NPRS - 6m NPRS	**1.971**	1.790	.303	1.356	2.586	6.515	34	**.000**
7+	Pair 1	PRE NPRS - 6m NPRS	**4.222**	1.853	.195	3.834	4.610	21.618	89	**.000**

B

Correlations

		6m ODI	6m NPRS	6m Walking tolerance	6m Sitting tolerance	6m Standing tolerance
6m ODI	Pearson Correlation	1	**.503****	-.088	**-.335***	-.163
	Sig. (2-tailed)		**.000**	.590	**.034**	.314
	N	68	**63**	40	**40**	40
6m NPRS	Pearson Correlation	.503**	1	**-.261***	-.108	**-.346***
	Sig. (2-tailed)	.000		**.048**	.418	**.031**
	N	63	125	**58**	58	**39**
6m Walking tolerance	Pearson Correlation	-.088	-.261*	1	**.602****	**.890****
	Sig. (2-tailed)	.590	.048		**.000**	**.000**
	N	40	58	65	**65**	**41**
6m Sitting tolerance	Pearson Correlation	-.335*	-.108	.602**	1	**.614****
	Sig. (2-tailed)	.034	.418	.000		**.000**
	N	40	58	65	65	**41**
6m Standing tolerance	Pearson Correlation	-.163	-.346*	.890**	.614**	1
	Sig. (2-tailed)	.314	.031	.000	.000	
	N	40	39	41	41	41

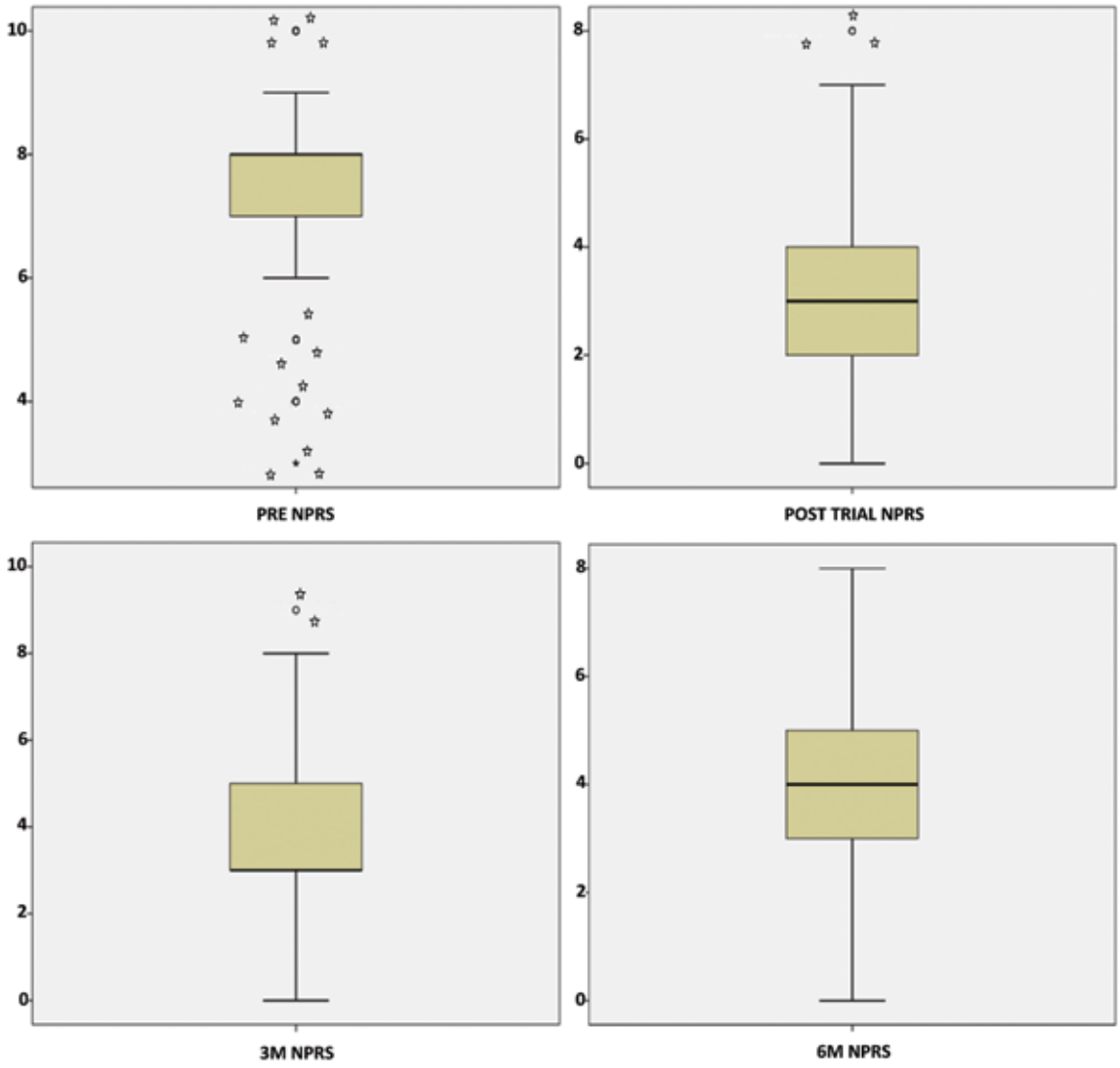
**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Supplement 2.

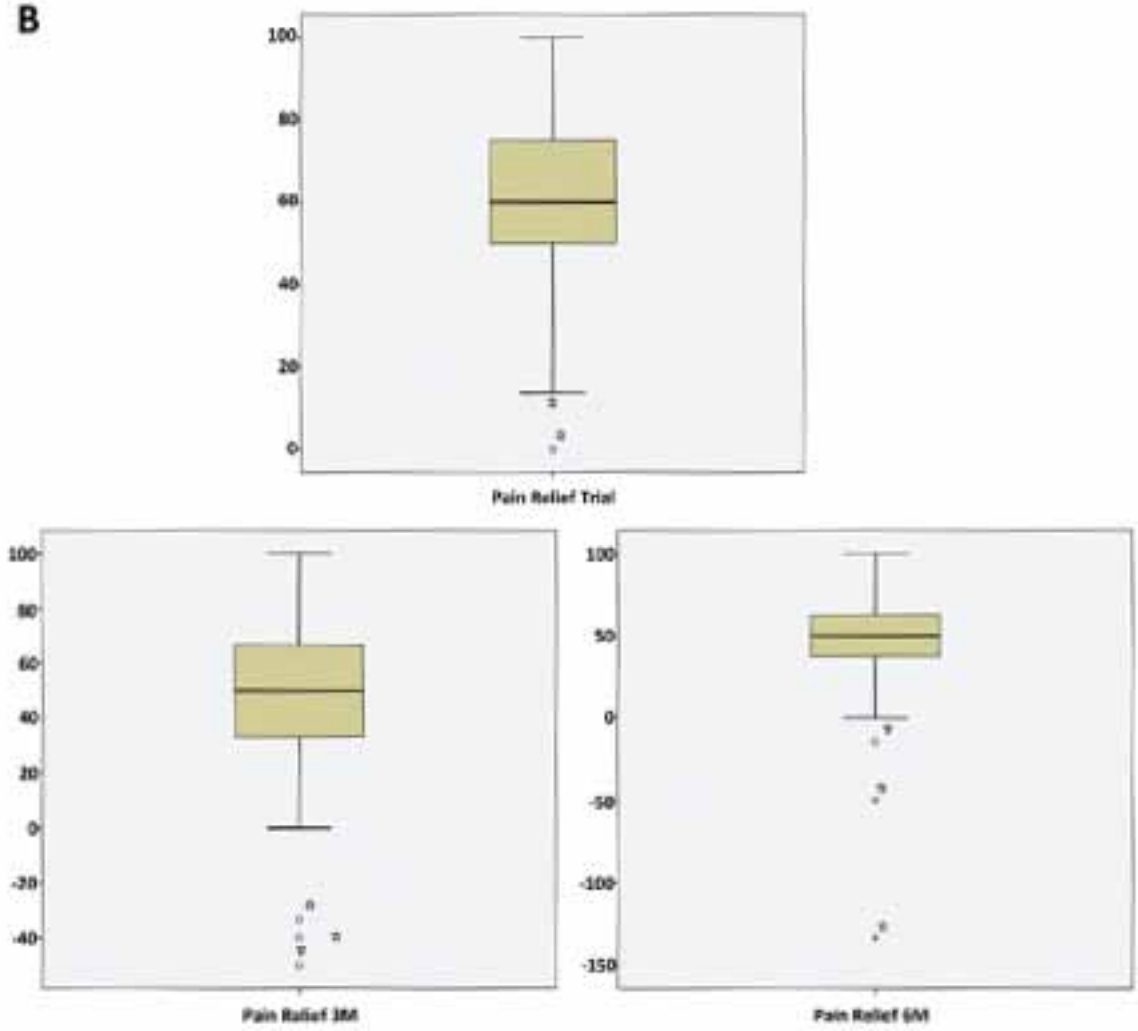
A. Box and whisker plots to identify outlier patient data points – Pain Score (NPRS: 0 - 10). Outliers are indicated by star symbols.
B. Box and whisker plots to identify outlier patient data points – Pain Relief (%). Outliers are indicated by star symbols.
C. Reasons for lack of significant pain relief for outlier patients.

A



Supplement 2

B



C

Reason for lack of significant pain relief	N
Confounding pathology (new and/or old)	3
Low pre-trial NRS scores	3
Lead migration	3
Trial success based on benefits other than pain	2
Pocket/anchor site pain	2
Recharging issues (i.e. post-injury)	1
Infection	1
Loss of therapy efficacy	1
Unknown	2

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