

Retrospective Analysis of Real-World Outcomes of 10 kHz SCS in Patients with Upper Limb and Neck Pain

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Background: Patients living with chronic upper limb and neck (ULN) pain are reliant on often ineffective therapies as they face limited options for effective long-term treatment.

Objective: Prospective clinical studies have demonstrated that high-frequency spinal cord stimulation at 10 kHz (10 kHz SCS) is effective in treating chronic pain in multiple etiologies including ULN pain. This study aimed at validating the findings from clinical studies on ULN in a real-world cohort.

Study Design: A retrospective, observational review.

Setting: A multicenter review between April 2016 and August 2019.

Patients and Methods: Anonymized data were extracted from a real-world database of 47 consecutive patients aged ≥ 18 years of age with chronic upper limb and/or neck pain who were trialed and permanently implanted with 10 kHz SCS. Patient-reported pain relief, quality of life, function, sleep and medication use were extracted from anonymised patient records where available. Responder rates, defined as the proportion of patients with at least 50% pain relief at the end of trial and the last visit after implantation, were calculated.

Results: All patients reported successful response ($\geq 50\%$ pain relief) at the end of trial and $>75\%$ patients continued to respond to the therapy at the last follow-up period. Majority (72%) of patients reported improvement in function, about half of the patients (53%) reported improvement in sleep and one-third of the patients (36%) reported reducing their medication at last follow-up.

Conclusion: 10 kHz SCS provides durable pain relief to patients with chronic upper limb and neck pain.

Keywords: 10 kHz SCS, upper limb, neck, pain

Introduction

Pain arising in the upper limb(s) and neck (ULN) is a significant contributor of discomfort, disability and depression worldwide.¹⁻⁵ It becomes chronic in up to a third of patients,⁶⁻⁹ yet there are limited effective long-term treatment options.¹ Hence, chronic opioid use remains unacceptably high in this group.¹⁰

Spinal cord stimulation (SCS) is an established treatment for chronic, intractable, neuropathic pain conditions.¹¹ However, as traditional SCS uses sensory paresthesia to determine lead placement, it had comparatively limited applications in the neck region due to difficulties in achieving paraesthesia coverage.^{5,12-17} Improvements in the stimulation waveform have offered the ability to enhance pain relief, coverage and comfort.^{11,18-20} Unlike traditional SCS, high-frequency

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SCS at 10 kHz (10 kHz SCS) provides pain relief without any paresthesia,^{11,18-20} and has an established body of clinical trial evidence in back, lower limb and upper limb and neck pain.^{18,21-25} Subjects implanted with 10 kHz SCS devices demonstrated improvements in disability compared to baseline with almost 2.5 times the minimum clinically important difference in pain disability index (PDI) scores at 12 months.^{23,26}

While randomized, controlled trials determine a causal effect of an intervention, it is becoming increasingly common to externally validate their results in the real-world via observational studies.²⁷ A retrospective real-world study in patients with chronic back and leg pain treated with 10-kHz SCS confirmed consistent pain relief, functional improvement and reduction in pain medication use observed in a prospective randomized, control trial.^{28,29} Similar studies are needed to show the benefits of 10 kHz SCS in ULN pain patients in a clinical setting. The aim of this study was to perform a real-world, multicentre, retrospective review of efficacy and safety of 10 kHz SCS in patients with chronic upper limb and neck pain.

Patients and Methods

Study Design

This study was a retrospective analysis of anonymised data extracted from the commercial real-world database (NevroCloud™) of consecutive patients aged ≥ 18 years of age with chronic upper limb and/or neck pain who were trialed and permanently implanted with 10 kHz SCS between April 2016 and August 2019.²⁸ Trial and permanent implantation followed procedures described previously.²³ Briefly, patients who were candidates for the treatment were trialed with 10 kHz SCS (Senza System, Nevro Corp., Redwood City, CA, USA) by placing the leads anatomically at vertebral levels ranging from C2 to C6. Given the paraesthesia-independent nature of the 10 kHz SCS therapy,³⁰ on-table paraesthesia mapping was not required. Patients who reported at least 50% pain relief during the trial period were eligible to receive permanent implantation with a 10 kHz SCS device. Stimulation was delivered at a frequency of 10 kHz, pulse width of 30 μ s, and amplitudes adjusted to maximize the patient's pain relief. Based on the patient's feedback on pain relief, standard programming strategies were used to optimize the therapy, which included an electrode bipole search to determine the optimal stimulation site within the vertebral column and if needed additional programs including pulse dosing and multi-area pain

sequencing (MAPS)/bipole interlacing were used. Due to the retrospective nature of the analyses and use of anonymized data listings, ethical committee approval was not required for this study.

Assessments

Only patients achieving $\geq 50\%$ pain relief during their 10 kHz SCS device trial and subsequently proceeding to permanent implantation were included in the data collection. All patients were assessed at baseline prior to 10 kHz SCS trial, at the end of the trial (EoT) and at the last visit after implantation before the data collection in August 2019. Data were entered into the global commercial database after each follow-up. At the time of analysis, patient records were extracted from the database and data on pain intensity, distribution, history of previous spine surgery, pain relief with therapy, change in medication, function and sleep and programme of choice were analysed. Pain intensity was assessed using the 11-point verbal rating scale (VRS) where 0 = no pain and 10 = worst possible pain and percentage pain relief obtained from the therapy as reported by the patient (0% = no pain relief, 100% = complete pain relief). Response to 10 kHz SCS was defined as at least 50% patient-reported pain relief from baseline (measured on a scale of 0% to 100%). Improvement in function and sleep were assessed as "yes" or "no" and change in medication was assessed as "decrease", "same", "increase" and "no details". Programming details were recorded as "pulse dosing", "MAPS/Bipole interlacing", "therapy optimization" and "no details".

At the time of report, complaints from the patients that were related to therapy (therapy-related events) were extracted from the complaints database and included in the analysis.

Statistical Analyses

All outcomes were analysed as observed. Continuous variables were reported descriptively, using the median \pm SD, or mean as appropriate. Categorical variables were calculated as percentages where possible and statistical significance calculated using a 2-tailed, paired *t*-test. A *P*-value less than 0.05 was considered statistically significant.

Results

Patient Characteristics

Over the 40-month period, a total of 47 consecutive patients were included in the analysis. As the data were anonymized,

longitudinal follow-up of patients was not possible, therefore outcomes were assessed at the last visit. Overall, the median time between implantation and the last visit was 19.4 months (SD \pm 12.4). Nearly half (53%) of patients had previous spine surgery, 38% were surgery naïve and details were not available in 9% patients. Prior to 10 kHz SCS trial, the mean pain intensity score (VRS) was 7.9 (\pm 1.4). Baseline data on medication use were not available for analysis.

Pain Relief and Responder Rate

VRS score at baseline was not found to be associated with pain relief achieved during the trial with 10 kHz SCS device ([Supplementary Figure S1](#)). At the EoT, mean pain intensity score reduced by 70% (VRS score 7.9 at

baseline to 2.3 at EoT; $p < 0.001$; [Figure 1A](#)). Given the permanent implant requirement of achieving $\geq 50\%$ pain relief during the 10 kHz SCS device trial phase, all patients (100%) in this dataset achieved a response (at least 50% pain relief) during the trial (mean patient-reported pain relief 70% \pm 3%; [Figure 1B](#)) and proceeded to receive permanent implants.

At last follow-up, the VRS score was 2.9 ($p < 0.001$; [Figure 2A](#)), with 76% of patients maintaining a response to treatment (mean patient-reported pain relief 58% \pm 4%; [Figure 2B](#)).

A comparison of pain relief and responder rates by previous spine surgery is shown in [Figure 3](#). Regardless of previous spine surgery status, similar reductions were

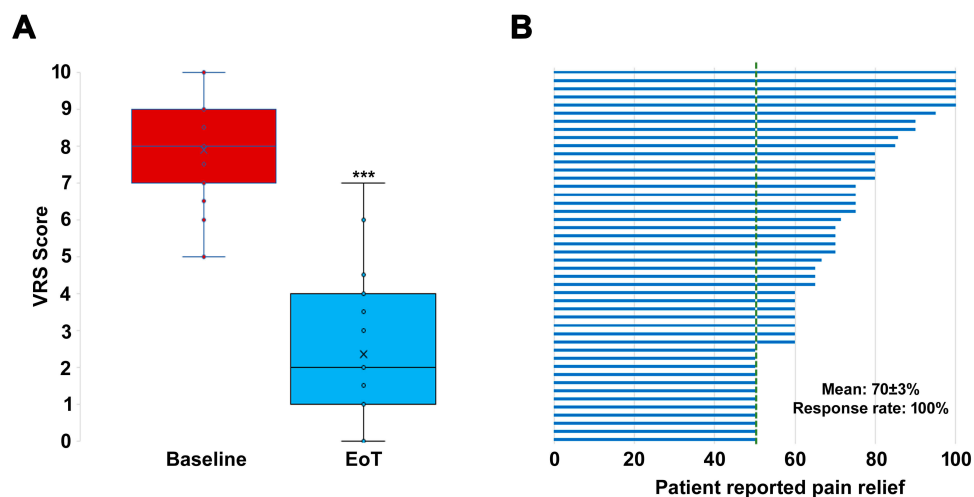


Figure 1 Pain relief and responder rate at End of Trial (EoT). (A) VRS score and (B) patient-reported percentage pain relief. VRS, 11-point verbal numeric rating scale (0=no pain to 10=worst possible pain). *** $p < 0.001$ compared to baseline; 2-tailed paired *T*-test.

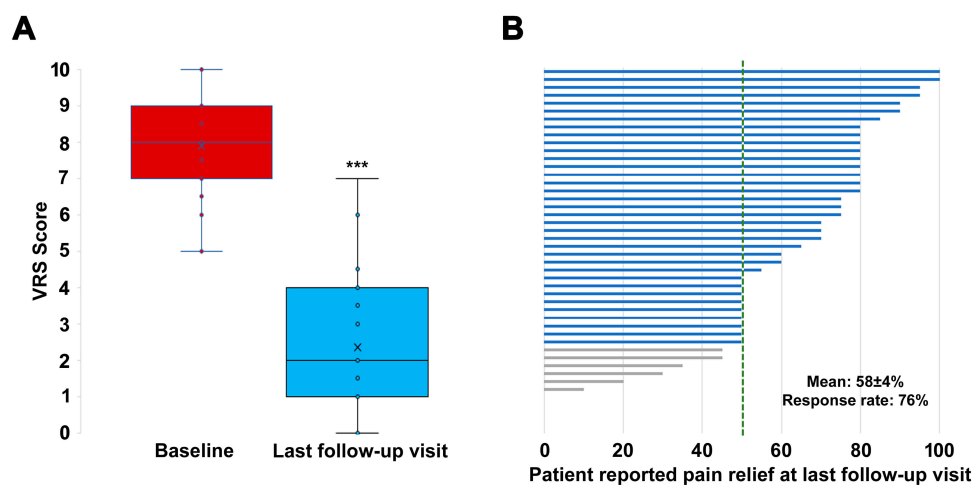


Figure 2 Pain relief and responder rate at last visit. (A) VRS score and (B) patient-reported percentage pain relief. VRS, 11-point verbal numeric rating scale (0=no pain to 10=worst possible pain). *** $p < 0.001$ compared to baseline; 2-tailed paired *T*-test.

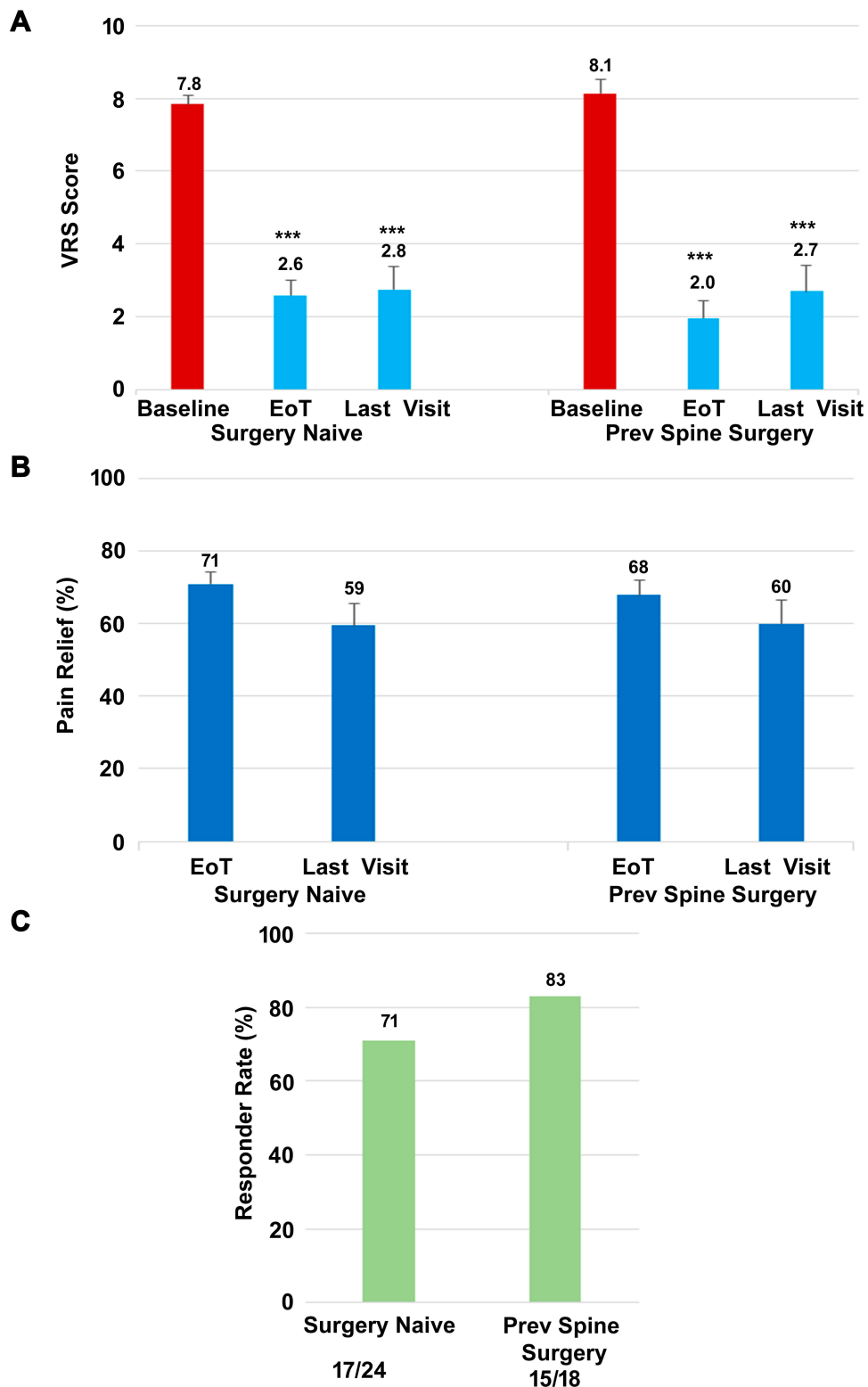


Figure 3 Mean pain intensity scores (A), mean patient reported percentage pain relief (B) and responder rate (C) at EoT and last follow-up in patients with previous spine surgery and patients who are surgery naïve. ***p<0.001 compared to baseline; 2-tailed paired T-test.

seen in VRS score at EoT (67% reduction in pain intensity in surgery naïve and 75% reduction in pain intensity in patients with previous spine surgery) and

last follow-up (64% and 66%, respectively; Figure 3A). Mean patient-reported pain relief was also similar between surgery naïve patients and patients with

previous spine surgery at EoT and last visit (Figure 3B). At last follow-up, 71% of surgery naïve and 83% of patients with previous spine surgery reported a response (Figure 3C).

Quality of Life and Functional Outcomes

Consistent with findings from large multicentre retrospective review in chronic trunk and/or limb pain patients, at last follow-up visit, 72% patients reported improvement in function (Figure 4A). Similarly, 53% patients in this study reported improvement in sleep (Figure 4B).

Medication Change

In response to question on change in medication following 10 kHz SCS therapy, 36% patients reported decrease in medication use, which was also comparable to the findings from multicentre retrospective review in chronic trunk and/or limb pain patients (Figure 4C).

Program of Choice

Majority of patients in this study utilised pulse dosing (53%), while 17% patients used multi-area pain sequencing (MAPS)/bipole interlacing and 15% used therapy optimization (Figure 4D).

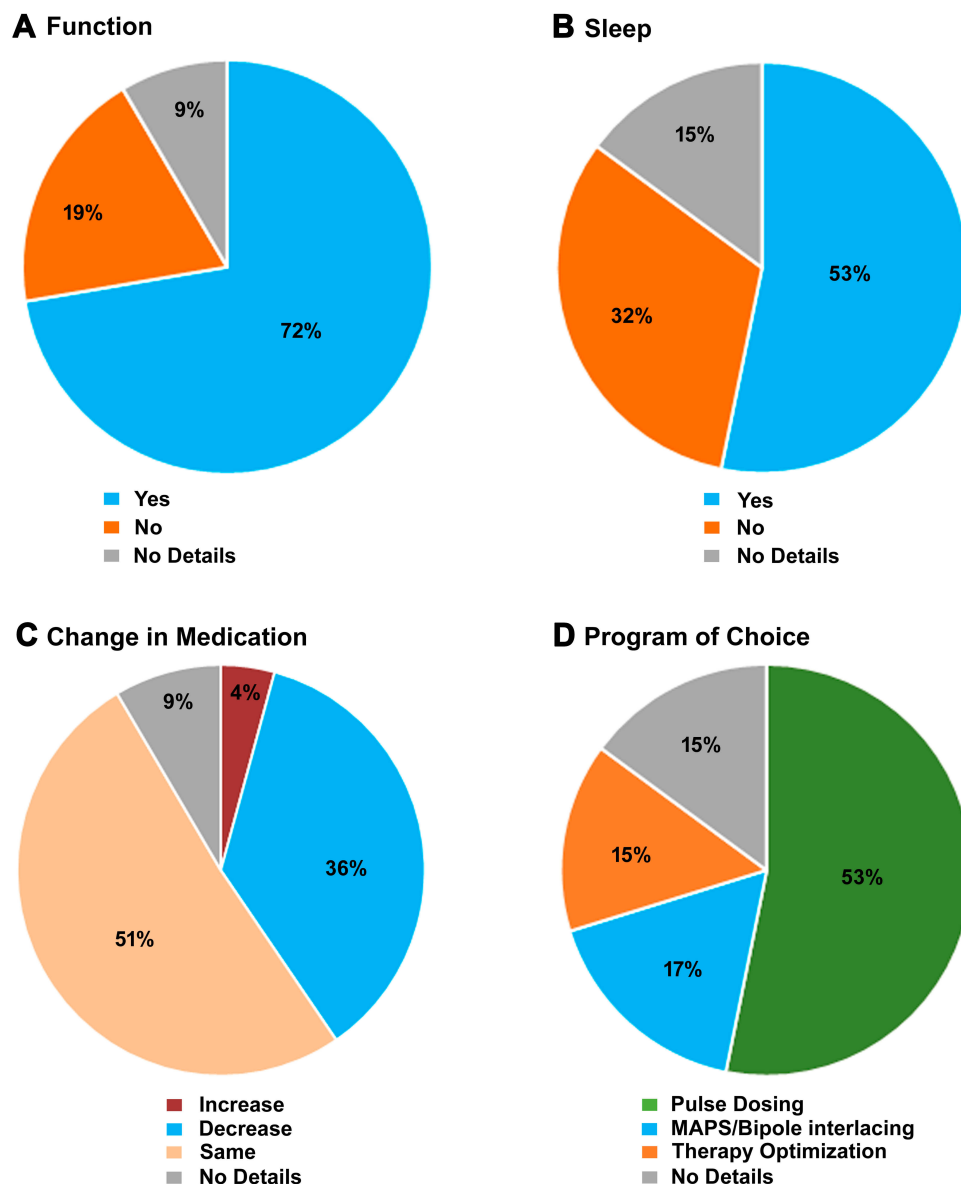


Figure 4 Evaluation at the last visit of (A) overall changes in function (B), sleep (C) medication and (D) efficacious programming options following 10 kHz SCS treatment. MAPS: multi-area pain sequencing.

Table 1 Therapy-Related Events

	Number of Events, n (%)	Status
Implant site pain	1 (2.1%)	Resolved
Overstimulation	2 (4.3%)	Resolved
Ineffective therapy	2 (4.3%)	Resolved

Therapy-Related Complaints

Details of therapy-related complaints or events reported in patients included in this study are listed in Table 1. The frequency of therapy-related events was less than 5% and all of the events were resolved with programming and none required explant of device.

Discussion

The current study reports on patients with ULN pain, building on the body of evidence for the efficacy of 10 kHz SCS. Median follow-up time in this study and the patient characteristics were comparable to the previous prospective, single-arm clinical trials with 12-month follow-up assessments.^{23–25}

Due to the retrospective nature of the study, separate pain scores were not available for neck and upper limb pain. Nevertheless, reduction in pain intensity scores (63–76%) seen in this study are comparable to findings from previous prospective^{23–25} and retrospective studies.²⁸ At last follow-up, over three-fourths (76%) of the patients reported at least 50% reduction in pain relief. Responder rate seen in this study is also comparable (74–90%) to the findings from single-arm studies in subjects with ULN pain^{23–25} and similar to the responder rate reported in a retrospective review of patients with chronic trunk and/or limb pain.²⁸ Interestingly, pain relief and responder rate were comparable between patients with prior spine surgery and those who were surgery naïve. The findings indicate pain relief seen with 10 kHz SCS was consistent across different study settings.

In addition to pain relief, 10 kHz SCS conferred functional benefits for patients with chronic upper limb and neck pain. More than 70% of the patients reported improvement in function following 10 kHz SCS therapy. The results are similar to the findings from multicentre retrospective review in patients with chronic trunk and/or upper limb pain (improvement in 72% patients).²⁸

Sleep disturbance is a common complaint for patients with chronic pain and may be aggravated by opioid use, due to their drowsiness side effects. In the current study, nearly

half of the patients reported improvement in sleep following 10 kHz SCS treatment, results comparable to multicentre retrospective review in chronic trunk and/or limb pain patients (improvement in 68% patients) and to findings from single-arm clinical studies (65–72% reduction in pain and sleep questionnaire-3 scores).^{23,24,28} Similar to previous reports, the current study also demonstrated concurrent decrease in medication use in 36% of patients. Although specific medication use was not captured, the findings were similar to the chronic trunk and/or limb pain real-world study (32% reduced medication use),²⁸ which was similar to the 30% of patients in the upper limb and neck pain prospective, single-arm trial,²³ and the 36% of patients in the SENZA-RCT trial who reported reducing or stopping opioid pain medication at 12 months.^{18,31,32} Although the data lacked granular details, these results suggest the improvements reported in the trials (disability measures, general functioning, mental health and patient satisfaction with treatment) may be generalized to the real-world.

Given device-related complications are reportedly commonly encountered in SCS for upper limb and neck pain,³³ the incidence of therapy-related AEs was included in this analysis. The incidence of therapy-related AEs seen in this study was relatively low and comparable to study-related AEs seen in prospective clinical studies.^{23,24} More importantly, all the events were resolved with programming and did not require explant of device.

This review had limitations due to its real-world setting. The retrospective nature of this study limited the collection of patient-specific characteristics, including pain aetiology, medication use and implantation details. It is important to note that medication use does not and could not include types or dose of medication. Lack of in-depth reporting limited analysis of quality of life, function and sleep measures and non-standardised measures makes comparisons between studies a challenge. Furthermore, it is not common to see 100% success during a temporary trial with SCS device. The results reported in the study should be interpreted with caution.

In conclusion, the current study shows pain relief, quality of life, function and medication use with 10 kHz SCS achieved in multiple prospective clinical trials in patients with chronic upper limb and neck pain and to other chronic pain states can be extrapolated to regular clinical practice.^{18,23,24,34,35} This study adds to the growing body of evidence for the utility of 10 kHz SCS for chronic pain states.

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Disclosure

Dr. Sayed is a consultant for Nevro Corp. Drs. Barnard and Rotte are employees of Nevro Corp. The authors report no other conflicts of interest in this work.

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