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CASE REPORT

Novel spinal cord stimulation system with a Battery-Free micro-implantable pulse generator

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Abstract

Spinal cord stimulation (SCS) is effective for the treatment of chronic intractable pain of the trunk and limbs. The mechanism of action may be based, at least in part, upon the gate control theory; however, new waveforms may suggest other mechanisms. Although benefits of the SCS technology generally outweigh the complications associated with SCS, some complications such as infection and skin erosion over the implant can result in device removal. Additional reasons for device removal, such as pocket pain and battery depletion, have driven technological innovations including battery-free implants and device miniaturization. The neurostimulation system described here was specifically designed to address complications commonly associated with implantable batteries and/or larger implantable devices. The benefits of the small size are further augmented by a minimally invasive implant procedure. Usability data show that patients found this novel neurostimulation system to be easy to use and comfortable to wear. What is more, clinical data demonstrate that the use of this system provides statistically significant reduction in pain scores with responder rates (defined as ≥50% reduction in pain) of 78% in the low back and 83% in the leg(s). Advances in miniaturization technology arose from the considerable shrinkage of the integrated circuit, with an increase in performance, according to Moore's law (1965). However, commensurate improvements in battery technology have not maintained a similar pace. This has prompted some manufacturers to place the battery outside, against the skin, thereby allowing a massive reduction in the implant volume, with the hopes of fewer device-related complications.

KEYWORDS
implantable pulse generator, microstimulator, peripheral nerve stimulation, pulsed stimulation pattern, spinal cord stimulation, waveforms

INTRODUCTION

The earliest use of electrical modulation of the nervous system dates back several centuries.[1] During the past 50 years, neuromodulation of the spinal cord has become an established treatment for chronic, intractable, and neuropathic pain. The mechanism of action was initially theorized by Melzack and Wall and formulated as the "gate control theory".[2] However, newer theories are emerging, principally driven by novel waveforms that do not readily lend themselves to the gate control theory and do not take into account the burgeoning science regarding glia, and the biochemistry underlying chronic pain syndromes.[3] All SCS therapies, including the system described here (Figure 1), utilize mild electrical pulses to create an energy field that modulates the transmission of pain signals to the brain. SCS has been widely used for a variety of disease states including post-laminectomy syndrome, complex regional pain syndrome types I and II, ischemic pain, peripheral neuropathy, and visceral pain. The efficacy of SCS therapy is significant, sustainable, and superior to conventional medical management in the treatment of some chronic pain states.[4-8]

Despite the wide use of neuromodulation, this modality is not without complications, which are well documented[9,10] and remain a significant driving force behind the advances that have taken place over the last two decades.[11] These complications are categorized as hardware, technical issues, biological causes, and loss of efficacy.[12] Pain at the site of the implantable pulse generator (IPG) represents a significant portion of device-related complaints and can range from 12% to 64%[10,13] of SCS IPGs implanted in patients. In fact, in a recent retrospective study of 356 patients across 18 centers, the presence of technical/device-related complications was the reason for SCS device explant in 20% of patients.[14] The healthcare expenditure related to SCS replacements and explants looms as a significant threat to therapy access.[15]

Over the past 20 years, there have been a number of technological advances in conventional SCS systems, largely related to reductions in the IPG size, IPG power source (battery-free vs implanted battery; primary cell vs rechargeable), software innovations, telemetry and energy transfer, patient interface, stimulation paradigms, lead configurations, and anchoring mechanisms. The large decrease in the size of most IPGs has been motivated by the desire to reduce the invasiveness of the procedure, improve patient comfort and convenience, and ultimately decrease failure rate. Rechargeable battery technology can allow for smaller IPG volume. However, larger rechargeable IPGs are still required for certain stimulation paradigms that require higher power.[7,8] In addition, some of these large, rechargeable IPGs require strong commitment from the patient to charge the IPG daily.[7,8] Unfortunately, larger IPGs also increase the likelihood of IPG site irritation ("pocket pain").

In this article, we describe a novel microstimulator platform (Nalu Neurostimulation System, Nalu Medical, Inc.) that is indicated for both spinal cord stimulation and peripheral nerve stimulation. This device is externally powered and utilizes novel technology to treat chronic, intractable pain. We review the diagnostic indications, surgical technique, and early clinical data. We also provide a review of the system's significant advantages and limitations.

DEVICE DESCRIPTION

The neurostimulation system is composed of a microstimulator devoid of an implanted power source; rather, it is powered by an externally worn "Therapy Disk" (TD), which is radio frequency (RF) coupled to the IPG. The microstimulator or micro-implantable pulse generator (mIPG) allows for four lead configurations: (a) dual eight contact, (b) single eight contact, (c) dual four contact with tines, and (d) single four contact with tines (Figure 1). The neurostimulation system was initially FDA-cleared for commercial use in the United States through the 510(k)-review process for SCS (K183047) and for PNS (K183579), in March of 2019.

FIGURE 1 (Left) Micro-neurostimulation system implantables. Battery-free, micro-implantable pulse generator (mIPG) configurations with stimulation lead options (PNS & SCS). (Right) Micro-neurostimulation System Wearables & Patient Peripherals. Patient's smartphone, remote control app, and therapy disc with associated adhesive clip

The mIPG provides the electrical stimulation pulses that are transmitted, via the leads, to the desired epidural spinal cord site. The inductively coupled mIPG receives RF power and telemetry control data from the TD. The externally worn, rechargeable TD eliminates the need for an implanted battery and reduces implantable IPG volume that could possibly contribute to the well-documented issue with hardware-related, battery pocket pain.[14] In addition, a Bluetooth™-enabled smartphone interfaces with the device through an application and allows for both therapeutic programming and software updates.[16]

The mIPG contains microchip technology, which allows the generation of a family of complex pulsed stimulation patterns (PSP). The PSP family of waveforms are composite signals created by layering specific temporal patterns (pulse patterns, trains, and dosages) in a hierarchical structure. Each of these layers are independently configurable to offer and achieve optimal pain relief for each unique patient. In addition, a broad menu of other programmable therapy options is available. The unique system design allows the TD software to be upgraded externally, similar to smartphone software applications, delivering additional capabilities, parameters, and therapy options that are designed to meet evolving physician and patient preferences and unmet needs.[16] This upgradeability will enable patients and physicians to take advantage of certain technological advances made available through software upgrades in the therapy, without the risks and costs associated with additional surgeries.

Considerable speculation exists regarding the tolerability of an externally worn battery. In the case of the current neurostimulation system, the adhesive clip adheres to the skin and holds the TD in place over the mIPG (see Figure 2). This clip is unique to the neuromodulation space, as it uses an ostomy-grade, hydrocolloid adhesive that has a low incidence of allergic skin reaction (<0.6%)[17] and can be easily removed via a medical-grade adhesive remover. Typically, patients wear the clip, during routine activities including bathing, sleeping, and exercising, for an average of 3–4 days between clip changes.

While there are many diagnoses that constitute chronic, intractable pain, the most common and well-studied uses of SCS are failed back surgery syndrome (also known as, post-laminectomy syndrome or persistent spinal pain syndrome)[18] and complex regional pain syndrome.[5,6,19] The Centers for Medicare and Medicaid Services (CMS) National Coverage Determination indicates SCS as a choice of last resort when other treatment modalities (pharmacological, surgical, physical, or psychological) have been attempted but deemed unsuccessful, unsuitable, or contraindicated for the patient. Among other qualifying measures, the patient must be evaluated by a multidisciplinary team prior to implantation. The patient must undergo a psychological and physical examination. While many guidelines exist, risk mitigation and stratification must occur prior to and following implantation of the device. More recently, the Neurostimulation Appropriateness Consensus Committee (NACC) published guidelines for the appropriate approach to mitigation of adverse outcomes for neurostimulation devices.[20-22]

TECHNICAL APPROACH

The proper identification of a patient for therapy is paramount prior to surgical implantation of the system. Therefore, implanting physicians must follow prevailing medical standards and adhere to nationally recognized guidelines throughout the perioperative and postoperative continuum.

Prior to embarking on a SCS trial or permanent implant, it is strongly recommended that the patient undergoes an ergonomic "wear experience." A wear experience typically lasts 5 days, during which time the patient wears the adhesive clip and an inactive TD. The wear experience is critical because it ensures that the patient is comfortable using the adhesive clip and TD, has no skin reaction to the clip adhesive, and they are able to identify a comfortable site for future mIPG placement. Unlike other platforms, both the SCS trial phase and the wear experience allow the patient to fully experience life with the system, prior to implantation, thereby avoiding any surprises following mIPG implant. Once the patient identifies a comfortable TD location (Figure 2) during the wear experience, this area is outlined by the clinician onto the skin with a pen, prior to entering the operating room. The center of this ring (denoted by an "X") represents the targeted placement of the mIPG. In the surgical field, this predetermination is important, not only for surgical planning, but also to ensure the appropriate lead length is chosen.

The procedure employs familiar techniques affiliated with traditional implantation, with the major differences being a smaller pocket incision and the use of a custom tool for pocket creation.

The major steps include:

1. Insert and anchor leads as per common practice with conventional IPGs
2. Make an incision for a pocket, performing hemostasis if needed.
3. Create a subcutaneous pocket (using the custom "Pocket Tunneler")
4. Tunnel the electrodes to the pocket
5. Connect the leads to the mIPG
6. Insert the mIPG into the pocket and close*Lead Placement and Confirmation*: The lead placement is performed using standard SCS techniques. Once the leads are placed in the dorsal epidural space and normal impedances are confirmed, paresthesia mapping or anatomic placement may be used. A final

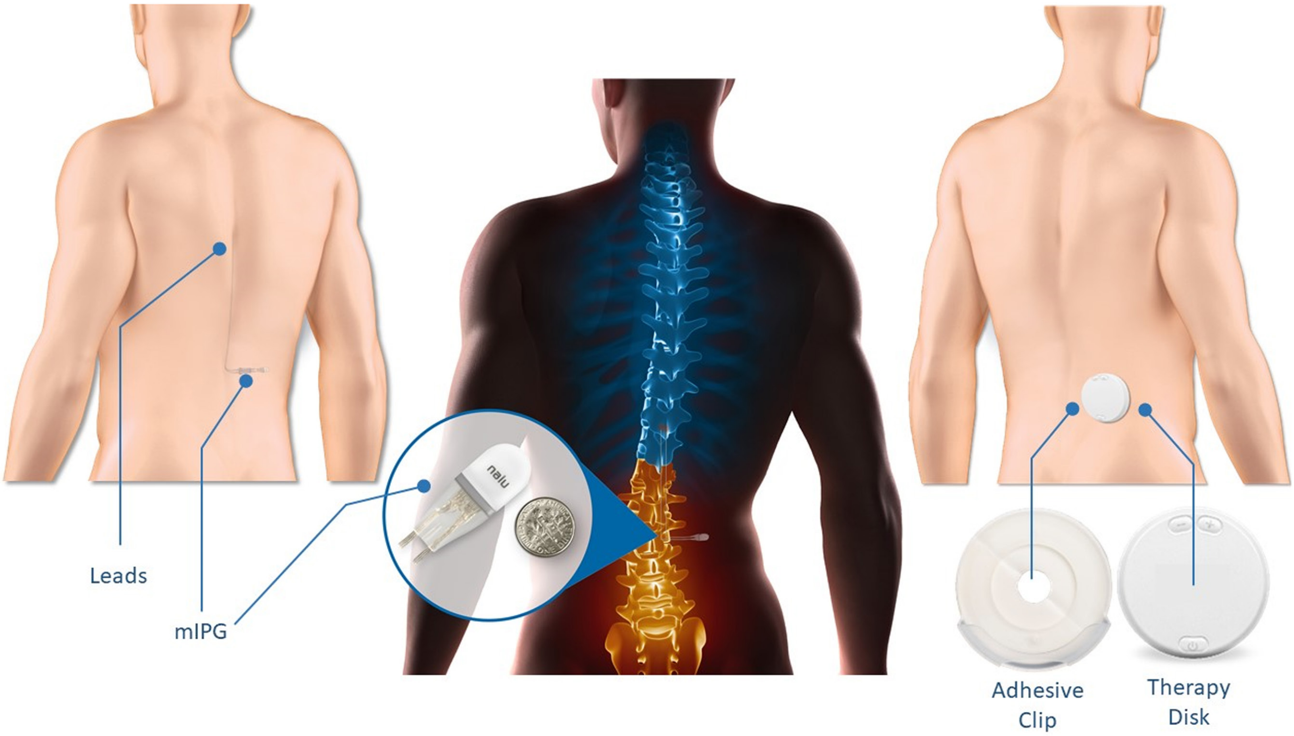
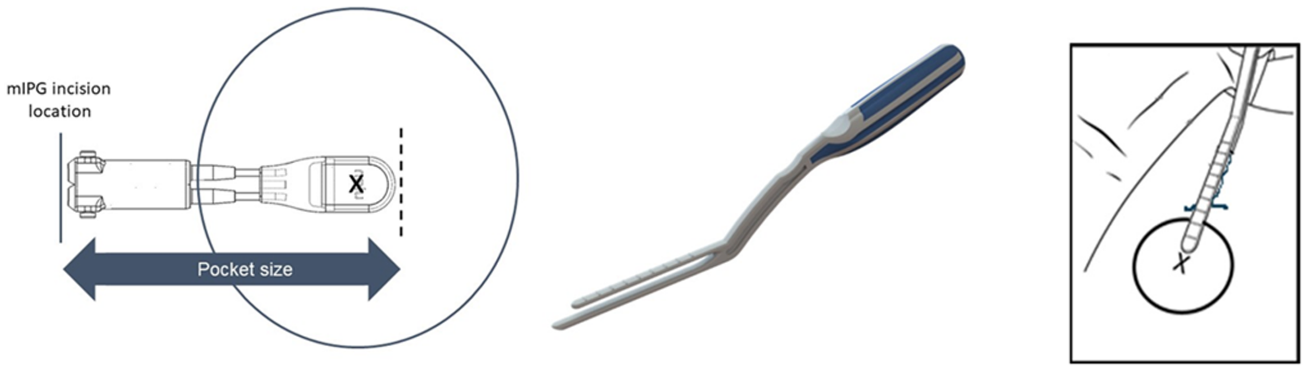


FIGURE 2 (Left) Micro-neurostimulation system implantables. (Center) Blown-up view of mIPG. (right) micro-neurostimulation system wearables



(A) (B) (C)

FIGURE 3 (A) mIPG and connectors are shown in relation to intended IPG location (X). The ring depicts the location of the therapy disc when worn by the patient. Vertical lines represent each end of the mIPG pocket. (B) Pocket Tunneler. The top prong remains above the skin during tunneling and ensures the pocket is made at a precise depth. The bottom prong is used for subcutaneous blunt dissection parallel to the skin while maintaining the proper pocket size. (C) Drawing of the Pocket Tunneler in use. The mIPG target location is denoted by the X. Note that the incision is made just outside the ring that defines where the therapy disc will be worn

fluoroscopic image should be captured to confirm final lead location.

IPG pocketing and placement: The mIPG should be unpackaged and placed onto the surgical field where it can be overlain on the center of the TD outline (Figure 3). The location of the second (lateral) incision should be marked based upon the size and orientation of the mIPG and pre-procedure planning derived from the wear experience (Figure 3). The second smaller incision is made lateral to the midline but medial to the intended TD location. The IPG pocket may then be made by first incising the tissue at an appropriate depth inside the ipsilateral, lateral aspect of the midline incision. The IPG pocket is created with a custom "Pocket Tunneler" supplied by the manufacturer (Figure 3), which ensures that the created pocket is tight fitting and at the appropriate depth, thereby minimizing mIPG movement and ensuring strong RF connectivity. (Figure 3). The pocket should terminate at the center of the TD outline ("X") on the skin. The SCS leads are tunneled from midline to the small, ipsilateral incision using standard technique. The mIPG is then connected to the SCS leads, and, following impedance checks, secured to the mIPG with a torque wrench. Once the leads are secured, the mIPG is inserted into the lateral pocket, utilizing a custom Insertion Tool (or common surgical tools), making sure to place the mIPG under the TD center mark ("X"), and the patient is then subject to proper surgical closure by primary intention. Any excess lead should be pulled to the midline and coiled as a strain relief. The final IPG location can be confirmed via palpation and fluoroscopy.

INITIAL CLINICAL EXPERIENCE AND OUTCOMES

A prospective, multi-center, open-label, clinical trial (nPower™ AUS), that was ethics committee approved (according to the Declaration of Helsinki) and sponsored by the manufacturer was initiated to confirm the safety and performance of the neurostimulation systems described herein for the treatment of intractable, chronic pain of the trunk and legs. Specifically, subjects with leg and/or back pain, meeting all of the inclusion and exclusion criteria, were recruited and consented for inclusion into the ethics-approved study (J. Salmon, D. Bates, N. Du Toit, P. Verrills, J. Yu, M. Taverner, V. Mohabbati, M. Green, G. Heit, R. Levy, P. Staats, J. Ruais, S. Kottalgi, J. Makous, B. Mitchell, unpublished observations). Subject cohort consisted of failed back surgery syndrome (FBSS) patients who failed to respond to conservative treatments. Subjects underwent a minimally invasive trial procedure to evaluate the new SCS system with multiple stimulation paradigms. Subjects who qualified continued on to the long-term implant phase of the study, were followed up at multiple, pre-defined time points, and will continue to be followed out to 2 years following implantation. Interim clinical outcome measures were captured, as well as comfort, usability, and compliance measures. A majority of the study subjects utilized a paresthesia-independent, novel, pulsed stimulation pattern as a part of the clinical study.

Thirty-one (31) intractable, chronic back, and/or leg pain subjects passed a screening and trial phase with ≥50% pain reduction from baseline (permanent to trial ratio of 31/35 = 89%) and moved into the long-term implant phase of the study. Three[3] of these subjects were withdrawn for study non-compliance; at the time of analysis, one subject had not yet received a permanent implant after a successful trial, due to COVID-19 restrictions. Of the remaining 27 subjects, 24 completed 90-day follow-up using either tonic (traditional, low-frequency stimulation; $n = 2$) or PSP therapy ($n = 22$). The average pain reduction was 79% ($n = 24$; $p < 0.0001$) in the leg and 73% ($n = 23$; $p < 0.0001$) in the back. The responder rate (≥50% pain relief) at 90 days was 83% in leg (20/24) and 78% in the back (18/23). In addition, at 90 days, 92% of subjects wore the TD at least 23 hours per day, and the average comfort score was 0.38 and ease-of-use score was 0.50, on an 11-point scale (0 is very comfortable/easy to use and 10 is Very uncomfortable/difficult to use). These interim efficacy data demonstrated robust connectivity between the TD and mIPG. Twenty-three non-serious adverse events (from 17 subjects), most of which are typical of SCS systems in general[9,23] and were determined to be device related, with the most common being mild skin irritation and unpleasant stimulation; all such events were resolved. There were no reports of pocket pain (0 of 35). Three subjects exhibited lead migration, two of which were revised via surgery. Five IPG migrations/rotations were reported and revised via surgery. Although a high revision rate was reported during this feasibility clinical study, the company worked to improve its physician training and education around these types of issues. Based on the company's current record of incident reports received from customers since commercial launch, the overall rate of reported incidents involving revision and device migration surgeries is <0.5%, which is markedly lower than the rate previously observed for subjects during this clinical study (J. Ruais, personal communication, data on file). Six serious adverse events were reported that were classified as anticipated and not device related. Of these, 4 were procedure related: one infection which reoccurred (2 infections in the same subject) led to an explant, CSF leak, and a bradycardia episode postoperatively. One patient had a cholecystectomy prior to implant, and one patient had sensitivity to the anesthetic administered. The rate of infection in the study was 2.8% (1/35).

DISCUSSION

The use of spinal cord stimulation for the management of chronic, intractable pain is a widely accepted and proven therapy. The long-term availability of this therapy will be driven not only by patient outcomes, but also through mitigation of complications and optimization of health care resource utilization. In addition, there have been a number of reviews that address the complication rate of spinal cord stimulation devices. While these rates vary by source, the loss of therapeutic efficacy and device-related complications represents a significant proportion of these issues.[14,24]

In the world of implantable neuromodulation devices, there is always room for advances in technology that minimize complications and maximize outcomes. By shrinking the IPG by a factor of up to 27 compared with conventional SCS IPGs, and increasing the programmable therapeutic options, the neurostimulation system described here helps to advance these two goals. The small size of the mIPG, which requires a smaller incision as compared to larger IPGs, along with the battery-free feature of the mIPG can help to decrease the rate of complications associated with IPG replacement or battery replacement surgeries. In terms of programming versatility, this neurostimulation system allows the delivery of multiple, novel pulsed stimulation patterns, and multiple therapy options that are comparable to and go beyond other commercial SCS systems. Wireless software upgrades for the delivery of future therapies developed by the manufacturer will also result in fewer replacement surgeries.

Global rising healthcare costs can apply a significant downward pressure on the availability of healthcare technology through insurance coverage and reimbursement policies. The utilization of spinal cord stimulation, when compared to lumbar reoperation, results in a lower healthcare dollar utilization in both the United States[24] and in the UK.[25] The initial cost of the system represents a sizable portion of the overall cost of treatment and may be subject to insurance preauthorization challenges or other restrictions imposed by insurers. Similarly, an increase in healthcare costs is often associated with patients who experience device explantation when compared to a cohort that continues therapy.[26] This is particularly striking when considering that unanticipated IPG explant rate, for any reason, is over 30% at 5 years.[27]

Innovations such as this neurostimulation system provide improvements that help to address certain complications in this therapy space, which, in turn, can help to increase the adoption of the SCS therapy. Given that the mIPG described here contains no implantable battery and that it has an expected service life of up to 18 years, the need for battery replacement surgeries is eliminated and the frequency of IPG replacement surgeries is considerably reduced compared with other available systems with implantable batteries.

Based on a 2017 multi-center retrospective study of then commercially available neurostimulation devices with the exit of therapy by explant, this study reported the following: From the date of conventional IPG implantation, a median time to unanticipated explant is 15 months for rechargeable IPGs and 36 months for primary cell IPGs.[14] The removal of the battery power source from the mIPG in the current neurostimulation system and placement of the power source in an external wearable component (TD) provide a significant advantage in three ways. First, by moving the bulk of the battery source ex vivo, a miniaturization of the implanted pulse generator is enabled. This small size helps to decrease the size of the surgical incision and pocket size needed to accommodate the mIPG, which can translate to better comfort for patients. In fact, Baranidharan et al. analyzed data from 764 SCS patients with conventional IPGs and found that 127 (17%) reported pocket pain and that 41% of pocket pain patients (7% overall) required revision surgery due to the pocket pain.[28] Second, patient satisfaction cannot be understated when considering the burden of IPG charging.[29] When 35 SCS patients who received a conventional IPG consisting of an implanted battery were asked about discomfort during IPG charging, 31% said it was slightly or very uncomfortable.[29] The remaining 69% of patients reported the charging as comfortable or tolerable. The recharge burden of the current system is nearly non-existent, as the TD can be removed from the body and is recharged by placing it on a charging station. Third, given the programmability of the external TD, software upgrades to this neurostimulation system can be accomplished in a non-invasive, wireless manner, whereas in the past, oftentimes software upgrades to implantable battery-powered devices required replacement surgeries.

There are a number of advantages to having an RF-powered IPG (system described here) verses a pure RF system of the past (eg, Ref. 30). A pure RF system converts the received energy directly into stimulation pulses. This has the significant drawback that the stimulation delivered is dependent on the RF coupling between the implanted receiver and the externally worn pulse generator antenna. In other words, if the external device is well coupled, the stimulation may be stronger than if poorly coupled. Coupling strength may vary with the relative position between the external antenna and the implanted receiver. Some pure RF systems limit the current output from the receiver to cap the stimulation delivered to the target tissue. Although such a feature can ensure safety and/or comfort, it does not ensure that proper stimulation levels are delivered independent of the RF coupling. By contrast, an internal IPG rectifies and stores the RF energy and has independent stimulation (current) generation circuits that utilize the stored energy. In this way, the system achieves coupling-independent stimulation. In summary, pure RF systems may allow for a smaller implant size but come at the potentially significant cost of compromised therapy delivery.

There are some limitations regarding the current system that are affiliated with the external wearable aspect of the device. Some patients may find the adhesive clip and/or TD uncomfortable or may show sensitivity to the adhesive on the clip. Fortunately, patients have the opportunity to wear the clip and TD during the wear experience, prior to mIPG implantation, which mitigates this concern. In an ongoing study (J. Salmon, D. Bates, N. Du Toit, P. Verrills, J. Yu, M. Taverner, V. Mohabbati, M. Green, G. Heit, R. Levy, P. Staats, J. Ruais, S. Kottalgi, J. Makous, B. Mitchell, unpublished observations), 96% of patients had successful wear experiences that typically lasted 2 weeks prior to implant. However, in commercial wear experiences, the TD is worn an average of 5 days (J. Ruais, personal communication, data on file).

CONCLUSION

A novel, fully capable spinal cord neurostimulation system is described in which a battery-free mIPG is implanted using standard SCS techniques. Due to the substantially smaller size of this mIPG (<1.5 cm^3), the rate of IPG-related complications commonly attributed to larger IPGs and the commensurate larger incisions and pockets, are likely reduced. Preliminary results from an ongoing first-in-human study demonstrated favorable clinical outcomes comparable to conventional SCS, with no reports of IPG pocket pain in 35 patients (J. Salmon, D. Bates, N. Du Toit, P. Verrills, J. Yu, M. Taverner, V. Mohabbati, M. Green, G. Heit, R. Levy, P. Staats, J. Ruais, S. Kottalgi, J. Makous, B. Mitchell, unpublished observations). Additionally, the preliminary results demonstrated favorable comfort and ease-of-use outcomes, which underscore the viability of this system. Further clinical studies are needed to confirm these initial findings.

AUTHOR CONTRIBUTIONS

Mark N. Malinowski: Primarily responsible for the content and drafting the manuscript; Reviewed, edited, and approved the final draft. Gary Heit: Primarily responsible for developing the implant technique for this novel device. Reviewed, edited, and approved the final draft. Lawrence R. Poree: Primarily responsible for developing the implant technique for this novel device. Reviewed, edited, and approved the final draft. James Makous: Primarily responsible for the content, drafting the manuscript, and developing the implant technique. Reviewed, edited, and approved final draft. Kasra Amirdelfan: Primarily responsible for developing the implant technique for this novel device. Reviewed, edited, and approved the final draft.

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CONFLICT OF INTEREST

Mark N. Malinowski: Consulting agreements – Nalu Medical, SI Bone, Inc; Equity – PrescribeFIT LLC; Research – Abbott Laboratories; Medical Advisory Board and Consulting – Biotronik. Gary Heit: Nalu Medical – Equity Holder and Hourly consulting contract; Nesos Inc. – Co-Founder; Human Exploratorium – VP of Research and Development. Lawrence R. Poree: Consultant – Medtronic, Saluda, Nalu. James Makous: Consultant and Shareholder – Nalu Medical, ReStalsis Health; Consultant – EBT Medical. Kasra Amirdelfan: Consultant – Medtronic, Nevro, Boston Scientific, Nalu, Presidio, Biotronik, Mesoblast, Vivex Laboratories.

DATA AVAILABILITY STATEMENT

Due to its proprietary nature, supporting data cannot be made openly available. Further information about the data and conditions for access are available from Nalu Medical (www.nalumed.com).

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REFERENCES

1. Nahm FS. From the torpedo fish to the spinal cord stimulator. Korean J Pain. 2020;33(2):97–8.
2. Melzack R, Wall PD. Pain mechanisms: a new theory. Science. 1965;150(699):971–9.
3. Chakravarthy K, Fishman MA, Zuidema X, Hunter CW, Levy R. Mechanism of action in burst spinal cord stimulation: *review and recent advances*. Pain Med. 2019;20(Suppl. 1):S13–22.
4. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. Neurosurgery. 2005;56(1):98–106.
5. Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. Pain. 2007;132(1–2):179–88.
6. Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, et al. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24-month follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. Neurosurgery. 2008;63(4):762–70.
7. Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, et al. Novel 10-kHz high-frequency therapy (HF10 therapy) is superior to traditional low-frequency spinal cord stimulation for the treatment of chronic Back and leg PainThe SENZA-RCT randomized controlled trial. Anesthesiology. 2015;123(4):851–60.
8. Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, et al. Comparison of 10-kHz high-frequency and traditional low-frequency spinal cord stimulation for the treatment of chronic Back and leg pain: 24-month results from a multicenter, randomized, Controlled Pivotal Trial. Neurosurgery. 2016;79(5):667–77.
9. Cameron T. Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: a 20-year literature review. J Neurosurg. 2004;100(3 Suppl Spine):254–67.
10. Mekhail NA, Mathews M, Nageeb F, Guirguis M, Mekhail MN, Cheng J. Retrospective review of 707 cases of spinal cord stimulation: indications and complications. Pain Pract. 2011;11(2):148–53.
11. Fishman MA, Antony A, Esposito M, Deer T, Levy R. The evolution of neuromodulation in the treatment of chronic pain: forward-looking perspectives. Pain Med. 2019;20(Suppl. 1):S58–68.
12. Taylor RS, Van Buyten J-P, Buchser E, et al. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. Spine. 2005;30(1):152–60.
13. Dietvorst S, Decramer T, Lemmens R, Morlion B, Nuttin B, Theys T. Pocket pain and neuromodulation: negligible or neglected? Neuromodulation. 2017;20(6):600–5.
14. Pope JE, Deer TR, Falowski S, Provenzano D, Hanes M, Hayek SM, et al. Multicenter retrospective study of neurostimulation with exit of therapy by explant. Neuromodulation. 2017;20(6):543–52.
15. Kumar K, Rizvi S. Cost-effectiveness of spinal cord stimulation therapy in management of chronic pain. Pain Med. 2013;14(11):1631–49.

16. Physician Resources Content – Nalu. https://nalumed.com/physician-resources-content/
17. Nybaek H, Jemec GBE. Skin problems in stoma patients. J Eur Acad Dermatol Venereol. 2010;24(3):249–57.
18. Christelis N, Simpson B, Russo M, Stanton-Hicks M, Barolat G, Thomson S, et al. Persistent spinal pain syndrome: a proposal for failed Back surgery syndrome and ICD-11. Pain Med. 2021;22(4):807–18.
19. Centers for Medicare & Medicaid Services | CMS: https://www.cms.gov/
20. Deer TR, Lamer TJ, Pope JE, Falowski SM, Provenzano DA, Slavin K, et al. The neurostimulation appropriateness consensus committee (NACC) safety guidelines for the reduction of severe neurological injury. Neuromodulation. 2017;20(1):15–30.
21. Deer TR, Provenzano DA, Hanes M, Pope JE, Thomson SJ, Russo MA, et al. The neurostimulation appropriateness consensus committee (NACC) recommendations for infection prevention and management. Neuromodulation. 2017;20(1):31–50.
22. Deer TR, Narouze S, Provenzano DA, Pope JE, Falowski SM, Russo MA, et al. The neurostimulation appropriateness consensus committee (NACC): recommendations on bleeding and coagulation Management in Neurostimulation Devices. Neuromodulation. 2017;20(1):51–62.
23. Deer T, Skaribas I, McJunkin T, Nelson C, Salmon J, Darnule A, et al. Results from the Partnership for Advancement in neuromodulation registry: a 24-month follow-up. Neuromodulation. 2016;19(2):179–87.
24. Lad SP, Babu R, Bagley JH, Choi J, Bagley CA, Huh BK, et al. Utilization of spinal cord stimulation in patients with failed back surgery syndrome. Spine. 2014;39(12):E719–27.
25. Taylor RS, Ryan J, O'Donnell R, Eldabe S, Kumar K, North RB. The cost-effectiveness of spinal cord stimulation in the treatment of failed back surgery syndrome. Clin J Pain. 2010;26(6):463–9.
26. Han JL, Murphy KR, Qasim Hussaini SM, Yang S, Parente B, Xie J, et al. Explantation rates and healthcare resource utilization in spinal cord stimulation. Neuromodulation. 2017;20(4):331–9.
27. Van Buyten J-P, Wille F, Smet I, Wensing C, Breel J, Karst E, et al. Therapy-related explants after spinal cord stimulation: results of an international retrospective chart review study. Neuromodulation. 2017;20(7):642–9.
28. Baranidharan G, Bretherton B, Richert G, Kay T, Marsh N, Roberts B, et al. Pocket pain, does location matter: a single-Centre retrospective study of patients implanted with a spinal cord stimulator. Reg Anesth Pain Med. 2020;45(11):891–7.
29. Lam CK, Rosenow JM. Patient perspectives on the efficacy and ergonomics of rechargeable spinal cord stimulators. Neuromodulation. 2010;13(3):218–23.
30. North RB, Calodney A, Bolash R, Slavin KV, Creamer M, Rauck R, et al. Redefining spinal cord stimulation "trials": a randomized controlled trial using single-stage wireless permanent implantable devices. Neuromodulation. 2020;23:96–101.