Chapter

Wireless Neuromodulation: From Bench to Bedside

Laura Tyler Perryman

Abstract

Spinal cord stimulation (SCS), as a neuromodulation therapy, has rapidly evolved over the past few decades to become the treatment of choice for many chronic pain syndromes. However, many equipment-related limitations such as the bulk of the equipment, an implantable pulse generator (IPG), the limited therapeutic stimulation frequency utilized, and the potential adverse events have restricted SCS applications. Recently, advanced nanotechnology and minimally invasive surgical techniques have shown promising options to expand the indications due to reduced surgical trauma/hospital time/costs. We describe the basis for nanotechnology neuromodulation and the preliminary experience with wireless SCS in the treatment of chronic pain conditions. The equipment utilizes a miniature stimulator with microelectronics, percutaneously placed at the appropriate stimulation target, with wireless control to provide the desired stimulation, and then moderated by the clinician and the patient. The wireless device reduces the bulk of the SCS equipment to a single electrode (with embedded sensors), using the new improved neural-electric interface. This wireless neuromodulation (WNM) has been clinically used in several chronic pain conditions, including failed back surgery syndrome, facial pain, chronic regional pain syndrome, and postherpetic neuralgia, with encouraging outcome, without the complications of a traditional SCS resulting from the IPG or its accessories.

Keywords: neuromodulation, wireless, nanotechnology, chronic pain, spinal cord stimulation

1. Introduction

Therapeutic modulation of excitable neural tissues in the body by electrical stimulation has become an important intervention to manage chronic disabling conditions like pain, involuntary movements, extrapyramidal syndromes, chronic peripheral vascular disease, and cardiac arrhythmias [1–9]. Devices are being implanted to deliver stimulatory signals to the target tissue, record vital signs or action potentials, perform electric cardiac pacing, and control drug release, as well as interface with auditory systems for assisted hearing or even image formation for visual prosthesis. All these systems utilize a subcutaneous battery-operated implanted pulse generator (IPG) to provide power.

Spinal cord stimulation (SCS) has been utilized for over five decades to provide therapeutically effective pain relief from chronic conditions like failed back surgery syndrome (FBSS), regional pain syndromes, and neuralgias, reducing the need for opioids. Several measurable outcomes like pain scores, disability scores, and quality of life scales have shown consistent improvement with SCS in patients with back pain and leg pain [1–3].

Outcomes following SCS therapy have demonstrated superior results compared to conservative medical treatment for patients with FBSS in several studies [2, 4], and SCS was also shown to be more cost-effective over the long term due to a decrease in follow-up visits, diagnostic tests, and overall consumption of healthcare facilities [4, 5]. Historically, on the other hand, SCS has not been devoid of complications and limitations in its conventional form utilizing an IPG, since the device options have had a long history of severe adverse events primarily related to the IPG [6, 7]. A large percentage of patients, reportedly as high as 50%, have failed the trial period utilizing conventional SCS devices [6–8], while additional failures came from equipment complications caused by the migration/fracture of the electrodes as well as IPG failures and complications in recharging or reimplantation. Postsurgical complications like infection, hemorrhage, and painful operative wounds were frequently seen associated with IPG and its extension wires. Additionally, SCS in its conventional form is incapable of reaching some anatomical locations to provide targeted therapeutic localized pain relief [6, 8–12].

Several modifications have been introduced to the SCS equipment over the past few years, which have reduced adverse events while promoting the efficacy of the modality, thereby increasing the number of clinical indications [13]. Percutaneous techniques, smaller compact batteries, rechargeable batteries, increased life of the IPG, and improved anchoring methods are some of these modifications currently in use. Part of the refinement also comes from the advancements in the technology of nanomaterials and wireless power transfer techniques.

2. Nanoelectrodes and wireless technology for neuromodulation

An advancement in this field is the new miniature pulse generator (mini PG) with wireless access (WPG) utilizing a dipole antenna for electric field coupling. This is accomplished with "microwaves", which are very short wavelength pulsed electromagnetic waves at gigahertz (GHz) frequencies. This device (Stimwave Technologies, Florida, USA), instead of using lower frequencies of 100 – 500 kHz of the inductive range operational in most of the present-day implanted medical devices, is powered by a radiative electric field coupling through tissues at microwave frequencies that enable smaller-sized implants to be placed at a significant tissue depth through a percutaneous technique. It also affords minimal power loss, since the higher frequency allows a much better energy transfer to a smaller implant [14]. The principle behind the frequency changes in relation to the wavelength was elaborated earlier by Feynman: "If you build a corresponding circuit on a small scale, its natural frequency goes up, since the wave length goes down as the scale; but the skin depth only decreases with the square root of the scale ratio, and so resistive problems are of increasing difficulty. Possibly we can beat resistance through the use of superconductivity if the frequency is not too high, or by other tricks [15]."

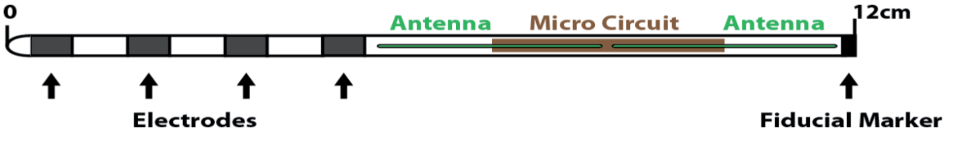

Figure 1.
MRI compatible electrode with nanostimulator and microcircuit to contact wireless pulse generator. This is the only implantable component required for WSCS.

The micro-implant WPG is capable of delivering clinically appropriate stimulation with dimensions of 800–1350 μm diameter, a significantly miniature size compared to the conventional SCS-IPG. This is equal to the size of a standard lead body that also incorporates the nanoelectronics within the device itself. It also can be integrated with a variety of lead types carrying four or eight contacts, either in a percutaneous or a paddle-type electrode, and the receiver wire has circuits in the stimulator device internally with wireless access (**Figure 1**).

3. The implantable wireless lead or the implantable neural stimulator (INS)

The INS has an enclosure housing the stimulating electrode array, designed to apply electrical pulses to the target tissue and antenna-1 and configured to receive electric energy input from an external antenna-2 through electrical radiative coupling. The antenna-2, physically separated from the INS lead, is connected to the antenna-1 by electric circuits configured to generate electrical pulses for stimulating the neural tissue (**Figure 1**).

4. The nanoelectronic substrate of the miniature wireless pulse generator

The INS is without any power source and stays in contact with the excitable neural tissue with passive components capable of receiving an external input signal at a frequency between 300 MHz and 8 GHz. A controller module, positioned in proximity to the patient body, to generate the input signals, sends them to the antenna-2; the latter transmits the input signal to the first dipole antenna placed within the INS through electrical radiative coupling, and antenna-1 extracts the stimulus feedback signal from signals received by the antenna-2 to adjust the parameters of the input signals based on the stimulus feedback.

The electrical pulses from the activated stimulating electrode, however, result in zero net charge within the patient's body. The electrodes can be selectively marked as a stimulating return electrode or an inactive one. It can have one capacitor in series with one or more electrodes.

At present, several therapeutic intra-body electrical stimulation techniques are available to manage neuropathic pain. However, they utilize a bulky, heavy, subcutaneous IPG connected to the implantable wired leads and have many failures or adverse events like mechanical dislodgement, impingement of the lead extension cables, and infection, along with IPG-related discomfort, pain, and irritation. The lead configuration includes cylindrical percutaneous or paddle leads. Cylinders are usually 1.3 mm in diameter and contain several circular electrodes, which are used for trial testing, later followed by permanent placement by minimally invasive, percutaneous approach. Paddles contain electrodes with a wider surface area directionally targeted for control over neural excitation and require invasive surgical procedures like laminectomy or laminotomy.

INS is designed to be placed in the patient through an introducer or a needle with electrodes (**Figure 2**) that include a semicylindrical array of electrodes/contacts made up of platinum, or platinum-iridium, or gallium-nitride, or titanium-nitride, or iridium-oxide or similar combinations. The contacts can be 2–16 in number having a length of 1 to 6 mm and 0.4 to 3 mm in width. They are spaced 1 to 6 mm apart with a combined surface area of 0.8 to 60 mm^2. The lead can also be a paddle type, deliverable through a 14-gauge needle. The enclosure has an external

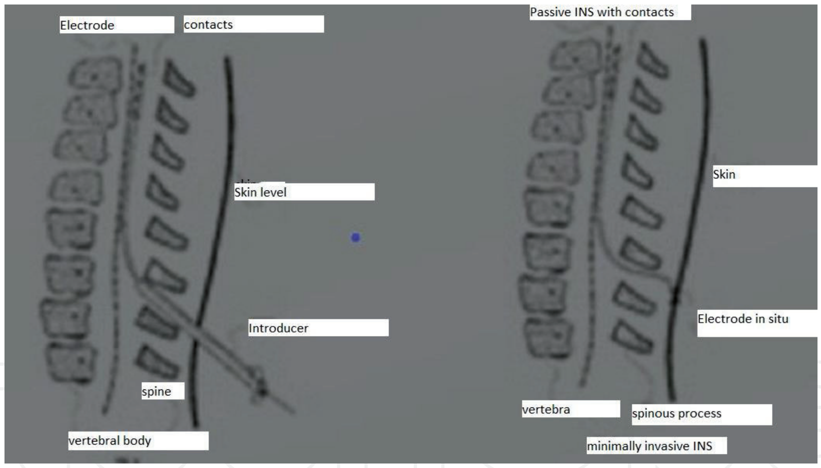

Figure 2.
Minimally invasive approach to place the wireless implantable neural stimulator in the spinal epidural space.

biocompatible coating of polymethyl methacrylate (PMMA), polydimethylsiloxane (PDMS), perylene, polyurethane, polytetrafluoroethylene (PTFE), polycarbonate, or a silicone elastomer.

The antenna-1 within the INS enclosure has 2 to 8 contacts, configured to couple with each other as well as the circuit, and these contacts are located proximally relative to the electrode inside the enclosure. These contacts are 1 to 6 mm in length, 1 to 2.5 mm in width, and spaced 30 to 80 mm apart. One antenna is constructed as a conductive trace contained on the circuits and can be fabricated as a conductive wire connected to the circuits, which are flexible with a bend radius of 0.5 mm and located proximal in the enclosure with a waveform conditioning circuit.

5. Remote control of power or polarity selection for a neural stimulator

The dipole antenna receives input signals containing polarity assignment information and electrical energy, the former designating the polarities for the electrode contacts. The circuits are configured to control an electrode interface so that these electrode contacts have polarities designed by the polarity assignment information to create electrical pulses from the electrical energy contained in the input signal. These electrical pulses reach the contacts according to the polarities assigned.

6. The remote radiofrequency power system with a low-profile transmitting antenna

The antenna for this wireless system includes a metal signal layer with radiating surface, a feed port, a wave guide surrounding the antenna, and a configuration to guide electromagnetic (EM) energy transmitted from the radiating surface in a direction away from the antenna. It also has a controller module connected to the feed port to drive the antenna to transmit EM energy from the radiating surface, while the antenna, wave guide, and controller module are configured to match a reception characteristic of an implantable device, so that the latter can produce electrical pulses of sufficient amplitude to stimulate the target neural tissue utilizing the EM energy received from the antenna-2, located up to 10 cm away.

Adverse events related to the IPG, due to excessive absorption of EM energy, include burning of tissue, creation of undesirable blood clots, and skin irritation

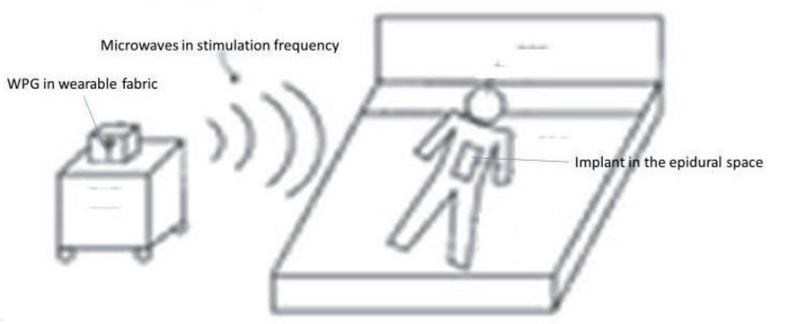

Figure 3.
Remote access by wireless antenna (experimental setting).

Figure 4.
Neurostimulator receiver. The contacts on the electrodes are managed by independently integrated, circuits that are application specific. The circuitry system within the device produces charge-balanced waveforms.

because of adhesions between the implant and tissues. A wireless device, on the other hand, has the antenna located outside the body with a controller module connecting the implantable device with the antenna (**Figures 3** and **4**).

The antenna has a dielectric lens filling the wave guide, protruding outward from an opening of the wave guide to narrow the transmitted EM energy and direct it away from the transmitting surface. It also has a return loss cutoff frequency associated with the wave guide; the dielectric lens lowers the return loss of cutoff frequency. The antenna operates within 500 MHz to 4 GHz frequency band.

7. Wireless energy supply

The INS receives energy by a wireless method, which includes radiating EM energy from the surface on an antenna located up to 10 cm away, inside the patient, so that the implanted device creates appropriate electrical pulses to stimulate the target neural tissue, using the received EM energy, even during sleep. The radiating surface of the antenna can be placed 1 to 6 feet away from the INS and can be adjusted to increase the EM energy provided to the latter (**Figure 3**). The interface is facilitated by a link between the programmable module and the controller module so that the stimulation pulses created at the implantable device are transmitted as data-encoded parameters from the programming module to the controller module, thus effectively stimulating the neural tissue.

A dipole antenna receiver intercepts the high-frequency microwave EM energy coming from outside the body to produce an oscillating electric field. Frequencies in the range of GHz were found to be more energy efficient [16]. Typically, the antenna within the device lumen can be anywhere from 2 to 8cm long and can be modified depending upon the indications and the depth at which the device is implanted, since the EM field energy is dissipated across the tissue layers of the skin, fat, muscle, blood vessels, and bone. The deeper the placement, the longer the antenna should be to receive adequate power. Each contact on the electrodes is provided with independent power, a part of an "application-specific" integrated circuit; the embedded circuitry within the device enables production of charge-balanced waveforms. This is managed by internalized addressing systems within the device (**Figure 4**). It is important to note that microwave fields are safe, since these high frequencies fail to activate cell membranes and thus nervous tissue damage is unlikely.

8. Wireless pulse generator (WPG)

The WPG employs standard cellular phone technology, with an average pulse output power of up to 1 W, depending upon the stimulation parameters and according to the requirements of the target tissue. A radiofrequency (RF) transmitter placed inside the WPG encodes stimulus waveforms into the signal according to the program settings. A microprocessor inside this transmitter controls the data communications and settings (**Figures 3** and **4**). Clinicians as well as patients communicate with the WPG via a controller that uses Bluetooth technology (**Figure 5**) and also can be accessed by a software application (app) on a mobile phone [14].

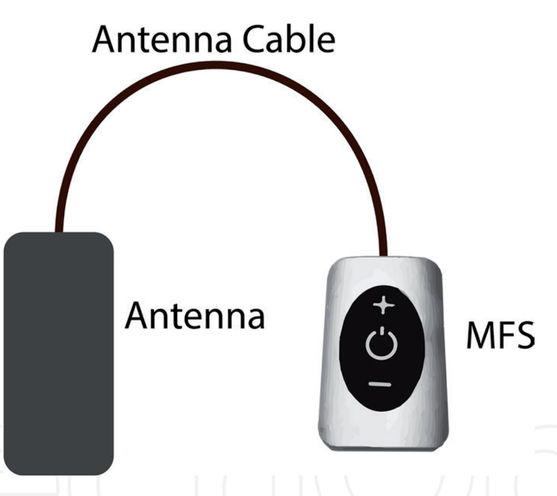

Figure 5.
External wireless pulse generator.

9. Discussion

The traditional SCS (TSCS) system has electrodes in a catheter enclosure attached to a long extension cable(s) that connects the electrodes to an IPG that is placed inside the patient's body, inheriting the complications due to failure or malfunction of any of these components. Efforts have been ongoing to reduce the bulk of the implanted material and yet improve the efficiency of the system. Reduction in size has a challenge from the battery life expectancy with the conventional energy settings. Thus, TSCS equipment requires implantation of electrodes, extension cables, and the battery inside the body, requiring multiple incisions along with long segment tunnels under the skin, producing considerable tissue trauma with pain and hemorrhage.

The wireless SCS system with nanotechnology has been clinically used for SCS, dorsal root ganglia (DRG) stimulation, and peripheral nerve stimulation (PNS) throughout Europe and the USA for several years, and multiple trials have shown encouraging results. The capabilities of this system enabled its utility to be tested in a variety of chronic pain syndromes. Poon et al. [16, 17] demonstrated that in a biological media, the operating frequency for wireless-powered devices was in GHz range as opposed to the MHz, which could have potential advantages. At this frequency range, the size reduction of the receiver has been demonstrated in the subsequent studies by Tyler Perryman et al., while the tissue depth relationship to the energy transmission were further elaborated [17, 18]. Tyler Perryman et al. conducted studies in animals and verified the tissue depths at which the wireless stimulation could achieve effective current density [18]. The dipole antenna of the wireless system (at 915 MHz) could energize the stimulators implanted at a depth of 12 cm in porcine models, especially efficient with a 4.3 cm antenna. Successful stimulation has been observed to provide significant pain relief in patients with back and leg pain with FBSS [19, 20], post herpetic neuralgia [21], refractory craniofacial pain [22], occipital neuralgia [23], and CRPS [24]. Patients undergo implantation of the INS with integrated microcircuits enabling coupling with a pulse generator, while the wireless pulse generator circuit excludes surgical implantation of the IPG, thus eliminating complications related to multiple surgical incisions and interventions for failed IPG or its extension cables. Consequently, there is reduced operating time, minimal consumables, and increased comfort to the patient. In the long run, this should decrease the costs of SCS and reduce overall healthcare budget in neuromodulation.

10. Financial implications and economic benefits with the wireless neuromodulation technology

Every innovation carries financial burden, and there are economic repercussions as the inventions arrive into the clinical practice. For easy understanding, traditional SCS has a structure as follows:

1. Electrodes + connection cables + implantable pulse generator inside the patient body
2. External controller (for the patient as well as the clinician)

Conversely, wireless neuromodulation with nanotechnology utilizes only implantable stimulating electrodes and an implantable receiver placed in a micro-incision pocket. Because of the reduced bulk of the implants, wireless technology has much more to offer other than the costs alone. It reduces surgical trauma, operating time, con-sumables, anesthesia, complications secondary to multiple incisions/tissue trauma, and hospital visits.

11. Costs involved with nanotechnology wireless SCS

The initial implantation of the wireless stimulator	18,000 Euros
IPG costs:	Zero (0)
Annual maintenance of the neuromodulation cost	1500 Euros/3

Compared to the wireless neuromodulation, TSCS was reported to be more expensive (**Table 1**). There have been limited reports on the costs and long-term maintenance

	Author	Journal	Year	No. of patients	Cost
1.	Manca et al. [25]	European J Pain	2008	52	CAD 19,486, Euro 12,653
2.	Kumar et al. [10]	J Neurosurg Spine	2006	160	CAD 23,205
3.	Kumar and Bishop [26]	J Neurosurg Spine	2009	197	CAD 21,595, USD 32,882
4.	Hornberger et al. [27]	Clin J Pain	2008	NA	USD 26,005 (nonrechargeable)
					USD 35,109 (rechargeable)
5.	Babu et al. [28]	Neuromodulation	2013	4536	USD 30,200 (percutaneous)
				4536	USD 29,963 (paddle electrodes)
6.	Annemans et al. [29]	J LTE Med Implants	2014	Model	UK£ 15,056 (HF SCS)

Table 1.
Literature on TSCS cost.

Procedure	TSCS USD*	TSCS CAD*	TSCS UKS*	Stimwave WSCS
Implantation	32,882	21,595	15,081	€18,000
Complication cost	9649	5191	576	NA
Revision cost	5450		5339 (lead)	€2500
IPG cost	**13,150**	**10,591**	**7243**	**0**
Maintenance	**5071 (4 years)**	**3539 (4 years)**	**NA**	**1500 (3 years)**

HF SCS therapy was similar to TSCS in its costs and complications. USD, US dollar; CAD*, Canadian dollar; UKS*, United Kingdom Sterling Pound.*

Table 2.
Reported costs of traditional SCS (TSCS) and the wireless SCS (WSCS).

		European experience [30]	American experience [31]
1.	Repositioning of electrode	€360	$2700
2.	Replacement	€1530	$5450
3.	Reimplantation following infection	€6192	$19,600

Table 3.
Costs for lead revision/repositioning in TSCS.

of TSCS in the literature. Detailed report on follow-up costs, complications, and replacement charges for reimplantation has not been forthcoming. However, the natural course of TSCS with its multiple implant components leading to their inherent complications could be expected as reported in a few of the studies (**Tables 1–3**). Wireless neuromodulation is evolving, and only limited experience has been reported so far. However, large-scale multicenter studies have been initiated to improve our understanding about the efficacy and acceptable long-term results in the form of improved quality of life, reduced complications, reduction in healthcare costs, and better cosmetic results.

12. Conclusions

Nanoelectronics have contributed to the development of miniature implants for therapeutic purposes, and wireless technology coupled with mini WPG appears to enhance the quality of neuromodulation in the field of functional neurosurgery and pain management therapies. Wireless neuromodulation, so far applied as SCS, DRG, and PNS, has provided efficient pain relief in cases of FBSS, neuralgic pain, CRPS, and facial pain syndromes. The results observed in small case series or case illustrations are comparable to traditional SCS methods and devoid of many of the complications of TSCS, primarily related to IPG/battery accessories. Further wireless neuromodulation experience may demonstrate improved quality of life associated with significant reduction in cost as well as reduction in complications, with improved cosmetic and functional results.

Copyright information

Authors hold the following patents. Information in the chapter includes material from the patent applications.

1. US9409029B2. Remote RF power system with low profile transmitting antenna
2. US9254393B2. Wearable antenna assembly
3. US9220897B2. Implantable lead
4. US9199089B2. Remote control of power or polarity selection for a neural stimulator
5. US8849412B2. Microwave field stimulator
6. US8903502B2. Methods and devices for modulating excitable tissue of the exiting spinal nerves
7. US9409030B2. Neural stimulator system
8. US15228715. Remote rf power system with low profile transmitting antenna
9. US9522270B2. Circuit for an implantable device

Author has copyrights on the publications referenced [18, 19, 22, 23].

Author details

Laura Tyler Perryman
Stimwave Technologies, Inc., Pompano Beach, Florida, USA

*Address all correspondence to: laura@stimwave.com

References

[1] Turner JA, Loeser JD, Bell KG. Spinal cord stimulation for chronic low back pain: A systematic literature synthesis. Neurosurgery. 1995;**37**:1088-1096

[2] Kumar K, Taylor RS, Jacques L, 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**:762-770

[3] Kapural L, Yu C, Doust M, 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 pain the SENZA-RCT randomized controlled trial. Anesthesiology. 2015;**123**:851-860

[4] Deer TR, Mekhail N, Provenzano D, et al. The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: The neuromodulation appropriateness consensus committee. Neuromodulation. 2014;**17**:515-550

[5] Mekhail NA, Aeschbach A, Stanton-Hicks M. Cost benefit analysis of neurostimulation for chronic pain. The Clinical Journal of Pain. 2004;**20**:462-468

[6] Turner JA, Loeser JD, Deyo RA, Sanders SB. Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: A systematic review of effectiveness and complications. Pain. 2004;**108**:137-147

[7] Mekhail NA, Mathews M, Nageeb F, Guirguis M, et al. Retrospective review of 707 cases of spinal cord stimulation: Indications and complications. Pain Practice. 2011;**11**:148-153

[8] Cameron T. Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: A 20-year literature review. Journal of Neurosurgery. 2004;**100**:254-267

[9] Krishna K, Jefferson RW, Gupta S. Complications of spinal cord stimulation, suggestions to improve outcome, and financial impact. Journal of Neurosurgery. 2006;**5**:191-203

[10] Kumar K, Hunter G, Demeria D. Spinal cord stimulation in treatment of chronic benign pain: Challenges in treatment planning and present status, a 22-year experience. Neurosurgery. 2006;**58**:481-496

[11] North RB, Kidd DH, Zahurak M, et al. Spinal cord stimulation for chronic, intractable pain: Experience over two decades. Neurosurgery 1993;**32**:384-394; discussion 394-395.

[12] Pineda A. Complications of dorsal column stimulation. Journal of Neurosurgery. 1978;**48**:64-68

[13] Slavin KV. Spinal stimulations for pain: Future applications. Neurotherapeutics. 2014;**11**:535-542

[14] Yearwood TL, Perryman LT. Peripheral neurostimulation with a microsize wireless stimulator. In: Slavin KV, editor. Stimulation of the Peripheral Nervous System. The Neuromodulation Frontier. Progress in Neurological Surgery. Basel, Switzerland: Karger Publishing; 2016. pp. 168-191

[15] Feynman RP. There's plenty of room at the bottom. CalTech, Pasedena CA: Presentation to the American Physical Society; 1959

[16] Poon AS, O'Driscoll S, Meng TH. Optimal operating frequency in wireless power transmission for implantable devices. In: Conf Proc IEEE Eng Med

Biol Soc; Lyon, France. 2007. pp. 5674-5679

[17] Poon A, O'Driscoll, Meng TH. Optimal frequency for wireless power transmission into dispersive tissue. IEEE Transactions on Antennas and Propagation. 2010;**58**:1739-1750

[18] Tyler Perryman L, Larson P, Glaser J. Tissue depth study for a fully implantable, remotely powered and programmable wireless neural stimulator. International Journal of Nano Studies and Technology. 2016;**S2**(001):1-6

[19] Weiner RL, Yeung A, Garcia CM, Perryman LT, Speck B. Treatment of FBSS low back pain with a novel percutaneous DRG wireless stimulator: Pilot and feasibility study. Pain Medicine. 2016;**17**:1911-1916

[20] Billet B, Wynendaele R, Vanquathem N. Wireless neuromodulation by a minimally invasive technique for chronic refractory pain. Report of preliminary observations. Medical Research Archives. 2017;**5**:1-8

[21] Billet B, Wynendaele R, Vanquathem N. A novel minimally invasive wireless technology for neuromodulation via percutaneous intercostal nerve stimulation (PNS) for post-herpetic neuralgia: A case report with short term follow up. Pain Practice. 2018;**3**:374-379

[22] Weiner RL, Garcia CM, Vanquathem N. A novel miniature wireless neurostimulator in the management of chronic craniofacial pain: Preliminary results from a prospective pilot study. Scandinavian Journal of Pain. 2017:350-354

[23] Perryman LT, Speck B, Weiner RL. A novel wireless minimally invasive neuromodulation device for the treatment of chronic intractable occipital neuralgia: Case illustrations. Journal of Neurology & Stroke. 2017;**6**:00213

[24] Herschkowitz D, Kubias J. Wireless peripheral nerve stimulation for complex regional pain syndrome type I of the upper extremity: A case illustration introducing a novel technology. Scandinavian Journal of Pain. July 2018:555-560

[25] Manca A, Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, et al. Quality of life, resource consumption and costs of spinal cord stimulation versus conventional medical management in neuropathic pain patients with failed back surgery syndrome (PROCESS trial). European Journal of Pain. 2008;**12**:1047-1058

[26] Kumar K, Bishop S. Financial impact of spinal cord stimulation on the health care budget: A comparative analysis of costs in Canada and the United States. Journal of Neurosurgery: Spine. 2009;**10**:564-573

[27] Hornberger J, Kumar K, Verhulst E, Clark MA, Hernandez J. Rechargeable spinal cord stimulation versus non-rechargeable system for patient with failed back surgery syndrome: A cost consequences analysis. The Clinical Journal of Pain. 2008;**24**:244-252

[28] Babu R, Hazzard MA, Huang KT, Ugiliweneza B, Patil CG, Boakye M, et al. Outcomes of percutaneous and paddle lead implantation for spinal cord stimulation: A comparative analysis of complications, reoperation rates, and health-care costs. Neuromodulation. 2013;**16**:418-427

[29] Annemans L, Van Buyten JP, Smith T, Al-Kaisy A. Cost effectiveness of a novel 10 kHz high-frequency spinal cord stimulation system in patients with failed back surgery syndrome (FBSS). Journal of Long-Term Effects of Medical Implants. 2014;**24**:173-183

[30] Kemler MA, Furnee CA. Economic evaluation of spinal cord stimulation for chronic reflex sympathetic dystrophy. Neurology. 2002;**59**:1203-1209

[31] Bell GK, Kidd D, North RB. Cost-effectiveness analysis of spinal cord stimulation in treatment of failed back surgery syndrome. Journal of Pain and Symptom Management. 1997;**13**:286-295