

Novel Minimally Invasive Wireless Nanotechnology Neuromodulation System in the Management of Chronic Pain Syndromes

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ABSTRACT

Chronic back pain has been reported to plague over 90 million Americans, with a large percentage of inflicted forced to manage their pain with addictive and dangerous opioid therapies as their only long-term remedy. Spinal cord stimulation (SCS) has been proven to be a reliable adjunctive therapy for over 40 years to assist in pain management for those with failed back surgery syndrome (FBSS), however limitations in waveforms to prevent plasticity as well as the need for expensive and highly invasive surgery have limited the adoption of neurostimulation. Recent advancements in nanotechnology enabled minimally invasive procedural approaches that both lower tissue trauma for the patient, and provide a lower cost option for the combination management of pain.

Wireless neuromodulation leveraging advancements in nanotechnology for the relief of chronic pain in multiple trials and case studies. A miniature stimulator device with microelectronics is placed by percutaneous methods at targeted nerves and controlled by a wireless power generator outside the patients' body providing pain relief for a number of conditions like chronic back pain secondary to failed back surgery, facial pain, and post-herpes zoster neuralgia. Device migrations occurred in a small number of patients and securing the device in-situ has been a topic for further refinements.

Devices with nanotechnology materials and wireless control have better efficiency because of improved neural-electric interface (replacing the more popular term, the brain-machine-interface). These techniques offer less invasive, less expensive and yet improved outcomes with better cosmetic results and safety profiles. Wider applications of the technology, however, require further studies on more patients and metrics for outcome evaluations.

INTRODUCTION

Spinal cord stimulation has been utilized for over 40 years and has been proven to provide therapeutically effective pain relief from chronic conditions like failed back surgery, regional pain syndromes and neuralgias. Several measurable outcomes in VAS 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 were shown to have superior results as 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 health care facilities ^[4,5]. At the same time, historically SCS has not been devoid of complications and limitations in the conventional form utilizing an implantable battery, since patients have been shown to fail the therapy and the device options have had a long history of severe adverse events primarily related to the implantable pulse generator (IPG) battery units ^[6,7]. A large percentage of patients reportedly have failed the trial period utilizing

conventional SCS devices, with reported outcomes as high as 50% failures^[6-8], while additional failures have been due to equipment complications contributed by the migration/fracture of the electrodes as well as implanted power generator (IPG) failures and complications in re-charging. Post-surgical complications like infection, hemorrhage and painful operative wound remain inherent to all open surgical procedures. Additionally, SCS in its conventional form is incapable of reaching some anatomical locations to provide targeted therapeutic localized pain relief^[6,8-12].

Several advancements have been introduced in to the SCS equipment over the past few years which have reduced adverse events while promoting the efficacy of the modality thereby increasing the indications for its applications^[13]. Percutaneous techniques, smaller batteries, rechargeable batteries, increased life of power generators and improved anchoring methods are some of these advancements. Part of the refinement also comes from the advancements in the technology of nanomaterial and wireless power transfer techniques.

NANO-ELECTRODES AND WIRELESS TECHNOLOGY FOR NEUROMODULATION

The conventional SCS system has electrodes in a catheter enclosure attached to a long extension cable(s) that connects the electrodes to an implantable pulse generator (IPG) that is placed inside the patient's body and inherits 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 this SCS equipment requires implantation of electrodes, extension cables and the battery inside the body requiring multiple incisions along with long segment tunnels under the skin.

An advancement in this field is the new external wireless power generator (WPG) utilizing a dipole antenna for electric field coupling accomplished with 'microwaves' which are very short length pulsed electromagnetic waves at Giga Hertz frequencies (GHz). This device (Stimwave), instead of lower frequencies of 100-500 kHz of the inductive range for most of the implanted medical devices, is powered by radiative electric field coupling through tissue at microwave frequencies, which enables smaller sized implants which can be placed significantly deep in tissue through a needle. It also affords minimal power loss because of the higher frequency and allows a much better transfer of energy to smaller implants^[14]. This principle behind the frequency changes in relation to the wavelength were pointed by Feynman long back. "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]."

The requirements for dorsal root ganglion (DRG) stimulation are much lower compared to epidural SCS or muscle stimulation in terms of current amperage and the micro-implant WPG is capable of delivering the range of 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 includes the nanoelectronics on the device itself. It can be incorporated in to a variety of lead types carrying 4 or 8 contacts either in a percutaneous or a paddle type electrode and the receiver wire is mated to the device internally also transferring power wirelessly (**Figure 1**).

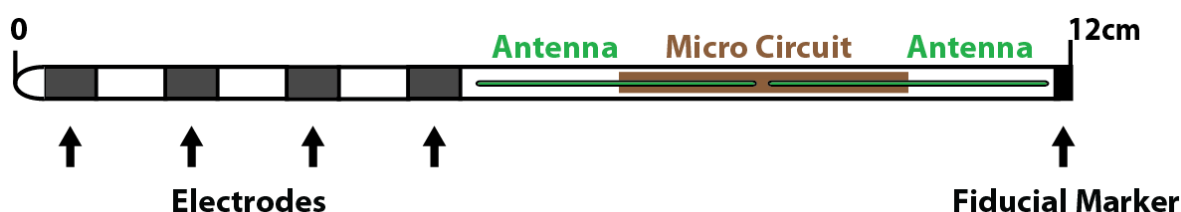


Figure 1. Neuro-stimulator electrode, MRI compatible, for both 1.5 and 3 Tesla.

A dipole antenna receiver intercepts the high frequency microwave electromagnetic energy coming from outside the body to produce an oscillating electric field. Frequency in the range of GHz was found to be more energy efficient^[16]. Typically the antenna within the device lumen can be anywhere from 2 cm to 8 cm long, and can be modified depending upon the indications and the depth at which the device is implanted, since the EMF (electrode magnetic field) energy is dissipated across the tissue layers (of skin, fat, muscle, blood vessels and bone). 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, as the embedded circuitry within the device enables production of charge-balanced waveforms. This is managed by internalized addressing systems within the device (**Figure 2**). It is important to note that microwave fields are safe since the high frequencies fail to activate to cell membranes and thus nervous tissue damage is unlikely.

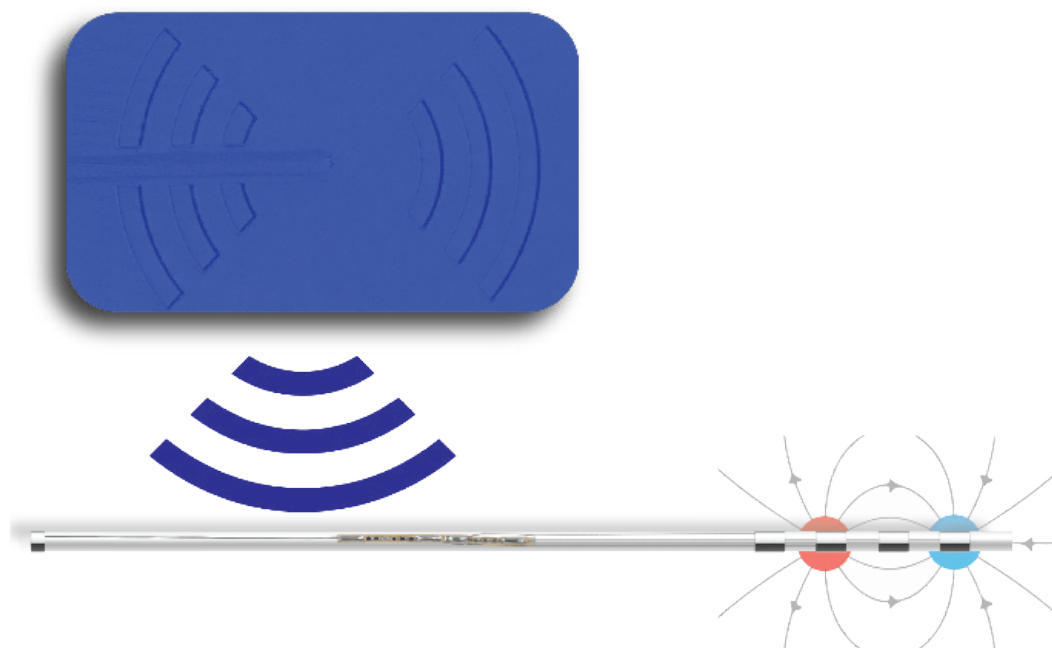


Figure 2. Neurostimulator receiver. The contacts on the stimulator leads are managed by independent integrated, application specific circuits. The embedded circuit system within the device provides charge-balanced waveforms.

WIRELESS POWER GENERATOR (WPG)

The WPG employs standard cellular phone technology, with an average pulse output power of up to 1 Watt, 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 (**Figure 3**). Clinicians as well as patients communicate with the WPG via a controller that uses Bluetooth technology and also can be accessed by a software application (app) on a mobile phone ^[14].

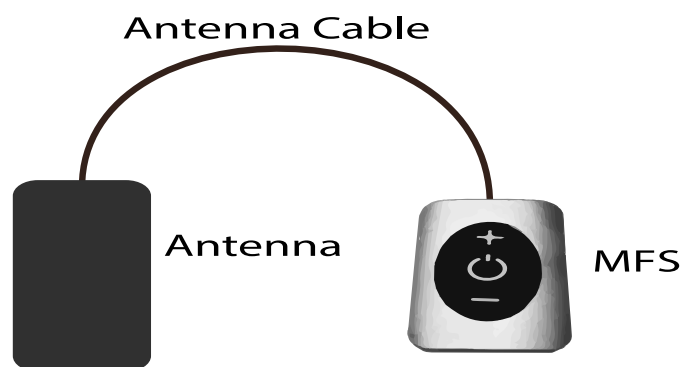


Figure 3. Freedom SCS external device

DISCUSSION

The wireless SCS system with nanotechnology has been clinically applied for SCS, DRG and PNS throughout Europe and in the USA for several years and multiple trials have shown encouraging results. The capabilities of this system however, enabled its utility to be tested in a variety of chronic pain syndromes. Poon et al. demonstrated that in a biological media the operating frequency for wireless powered devices was in GHz range as opposed to the MHz could have potential advantages ^[16,17]. At this frequency range, the size reduction of the receiver has been demonstrated in their 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. Notwithstanding the study parameters in the animal study, successful

stimulation was observed in providing significant pain relief in patients with back and leg pain following FBSS^[19,20], post herpetic neuralgia^[21], refractory craniofacial pain^[22] and occipital neuralgia^[23]. These patients require implantation of electrode(s) only while the wireless power generator excludes surgical implantation of the battery inside the body. Hence, there were no complications related to extensive surgical procedure, multiple incisions and interventions for battery failure in this group of patients treated with WPG. As a result there was reduced operating time, consumables and increased comfort to the patient.

CONCLUSION

Conventional SCS, due to its bulky implantable equipment, has been reported to have significant complications and failures, although the technique has proven to be useful in the management of chronic pain syndromes. The minimally invasive procedures of neuromodulation aim to reduce the equipment related adverse events while the symptomatic relief is provided proportionate to the upgrades to the technology. One part deals with the prospects of improvements in the patients' symptoms while the other part deals with the technology refinements to the equipment. The former would take multiple variables in to account as the targets of stimulation and the clinical presentations in their myriad forms attempt to balance with each other.

The latter has shown significant changes over the past decade owing to the improved understanding of nanotechnology and wireless navigation. Delivery of higher frequency stimulation with the WPG, instead of lower frequencies (100-500 kHz), the inductive range for the conventional implanted devices, enables miniature implants, to be placed deeper in tissue through a needle, percutaneously, also affording minimal power loss and a much better transfer of energy to these nanomaterial implants. Stimwave systems have matched these developments to improve clinical outcomes with reduced adverse events in their clinical experience so far, though limited in numbers. Further experience with patients and modifications in the apparatus would demand larger patient populations to be studied with a wide variety of instruments for outcome measurements.

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