



Clinical pain research

A novel miniature, wireless neurostimulator in the management of chronic craniofacial pain: Preliminary results from a prospective pilot study[☆]



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HIGHLIGHTS

- Technological and cosmetic limitations inhibit use of PNS for craniofacial pain.
- Management of craniofacial pain with a wirelessly powered PNS system.
- 10 patients implanted with wireless stimulators, powered by an external transmitter.
- Patients monitored for pain relief and AE's for 4 weeks.
- All patients reported pain relief over primary pain areas with no reported AE's.

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ABSTRACT

Objective: To report a novel wireless neuromodulation system for treatment of refractory craniofacial pain.

Background: Previous studies utilizing peripheral nerve stimulation (PNS) of the occipital and trigeminal nerves reported positive outcomes for alleviating neuropathic pain localized to the craniofacial and occipital areas. However several technological limitations and cosmetic concerns inhibited a more widespread acceptance and use of neuromodulation. Also, a relatively high incidence of adverse events like electrode erosions, dislocation, wire fracture and/or infection at the surgical site mandates a change in our approach to neuromodulation technology and implant techniques in the craniofacial region.

Methods: We report a novel approach for the management of craniofacial pain with a wirelessly powered, minimally invasive PNS system. The system is percutaneously implanted and placed subcutaneously adjacent to affected facial nerves via visual guidance by the clinician. In this feasibility study, pilot evidence was gathered in a cohort of ten subjects suffering from a combination of chronic headaches, facial pain for at least 15 days per month and for at least 4 h/day.

Results: At four weeks post-implant follow up, all patients reported sustained pain relief of the primary pain area. Electrode location and total number of electrodes used per subject varied across the cohort. The average pain reduction using the visual analog scale was $\geq 82\%$. The procedure had no adverse events or side effects.

Conclusion: Percutaneous placement of a wireless neurostimulation device directly adjacent to affected craniofacial nerve(s) is a minimally invasive and reversible method of pain control in patients with craniofacial pain refractory to conventional medical managements. Preliminary results are encouraging and further larger scale studies are required for improved applications.

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1. Introduction

Chronic craniofacial pain (CCFP) or atypical facial pain or persistent idiopathic facial pain or atypical trigeminal neuralgia are a few of the names applied for the debilitating/refractory painful conditions with a varied lifetime prevalence [1,2]. Facial pain affects nearly 26% of people during their lifetime [3] while typical trigeminal neuralgia in population occurs in 0.3% [1].

CCFP arises from abnormal peripheral activation of cranial nerves that convey pain information to the brain and can result from events including but not limited to, infection, trauma, surgery, or invasive dental procedures. It is characteristically similar to pain due to trigeminal neuralgia and these disorders possibly are located on the same spectrum in a temporal sequence [2,4,5]. Intractable headache and/or migraine affect nearly 40 million Americans and in spite of various treatment protocols 3–5% of these patients does not improve but suffer from overwhelming despair in dark quiet rooms consuming high doses of narcotics [6–8].

Opioids are the most commonly prescribed for treatment of CCP along with anticonvulsants and anti depressants. Longstanding usage of opioids is associated with tolerance and dependence while opioid dose escalation over time to maintain analgesic effects become regular events. Additionally, chronic opioid use has the potential for increased risks of diversion, abuse, addiction, and can cause opioid induced side effects including nausea, sedation, constipation and hyperalgesia. A recent FDA recommendation for opioid use calling for reductions in chronic opioid prescription is another reason to consider neurostimulation treatment for pain control [9].

Lack of effective medical management resulting in persistent pain and significant decrease in quality of life has led to the development of destructive procedures including hot or cold radiofrequency nerve ablation. Surgical/chemical neurectomy or decompressive neurotomies were common treatments [10]. These, however, may result in irreversible side effects including sensory or motor loss and subsequent differentiation pain along the ablated nerve [11]. Neither radiosurgery nor sphenopalatine ganglion ablation or neurectomy yielded successful results in CCFP conditions [12,13].

Peripheral nerve stimulation (PNS) for craniofacial pain has proven to be a viable therapeutic option in the treatment of chronic disabling pain because of its non-destructive and reversible nature [14,15].

The Neuromodulation Appropriateness Consensus Committee (NACC) after evaluation of peer reviewed literature, current research and clinical experience found evidence to support extracranial stimulation for treatment of facial pain and migraine [16]. Advancements in wireless energy transmission and micro-processor technology have recently enabled development of miniature, percutaneous neurostimulation hardware and software to help control these pain syndromes involving craniofacial peripheral nerves [19]. Several studies have shown encouraging results [17,18].

However, widespread use of PNS neuromodulation has been limited by multiple technological issues/concerns and remains underutilized [18–20]. Available neurostimulation systems have not been designed for use in the peripheral nerve space, especially in and about the craniofacial region and are associated with complications including electrode migrations and procedural complications due to cumbersome equipment as well as stimulation systems. Not only cosmetic concerns, but relatively high adverse event rates including such events as device erosion, fracture, and infection have also played a discouraging role [11,18–21]. Our experience with a novel wireless, minimally invasive design in the treatment of occipital neuralgia yielded good results [22]. We report this alternative approach for the management of CCFP. A

Table 1

Demographics and target nerves.

Sub	Sex	Age	Location of pain	Target nerve(s)
1	F	67	Right V3	Mental nerve
2	M	55	Left V3	Mental nerve
3	F	58	Left V3	Mental nerve
4	F	64	Right V2	Infraorbital nerve
5	F	76	Left V1, V3	Supraorbital, mental nerves
6	F	62	Right V2, V3	Infraorbital, mental nerves
7	F	42	Right V1, V3	Supraorbital, mental nerves
8	M	74	Left V2, V3	Infraorbital, mental nerves
9	M	75	Left V2, V3	Infraorbital, mental nerves
10	F	63	Right V2	Infraorbital nerve

minimally invasive, wireless stimulation system is percutaneously implanted and placed subcutaneously adjacent to affected facial and/or occipital nerves involved in intractable craniofacial pain. Initial data were gathered in a cohort of ten subjects suffering from chronic headaches, facial pain for at least 15 days per month and at least 4 h/day. The primary objective of this study was to determine the analgesic effect of wireless neuromodulation in controlling chronic pain as applied to various nerve distributions within the CCFP.

2. Methods

Inclusion criteria: Patients of at least 22 years of age at the time of signing the informed consent and without anatomical defects that would compromise or complicate the study were included. The Subjects were on stable doses of pain medications for at least 4 weeks prior to screening. Subjects were willing to undergo the surgical implant procedure, attend visits as scheduled and comply with the study requirements. Patients were willing and able to operate the programmer, recharge the equipment and properly fill out the electronic diary. Subjects were good surgical candidates for the implant procedure and had a life expectancy greater than 12 months beyond the study period. Subjects had a decreased pain intensity of at least 50% from baseline after local anesthetic block of the targeted craniofacial nerves in the past.

Exclusion criteria: Patients with migraine, cluster headache, trigeminal autonomic cephalgia, other types of craniofacial pain considered to be of central origin and those who failed psychological evaluation were excluded. Subjects on anticoagulation therapy and/or unfit for surgical procedures were also excluded.

Demographics: Ten patients (7 female, 3 male) were enrolled (mean age of 60 years). All patients were selected based on a history of CCFP (Table 1) manifesting as chronic headache, facial or occipital pain for at least 15 days per month and at least 4 h/day. Pain was of neuropathic origin from direct or indirect neural injury to the trigeminal, supraorbital, infraorbital nerves. Root causes of CCFP included trauma, surgery, infection, congenital defects, and trigeminal neuropathy.

Device description: Subjects were implanted with one or more wireless stimulator systems (StimRelieve LLC, Miami Beach, FL, USA) each containing four or eight contacts (3 mm in diameter with 4 mm spacing). The stimulator system utilizes an implantable electrode contact array, microprocessor receiver and antenna embedded within the electrode wire that couples to an external transmitting antenna and pulse generator (Figs. 1 and 2) The implanted stimulator is 100% passive (i.e., no implanted power source). The external transmitting antenna was worn in a baseball cap (Fig. 3) and is wirelessly coupled to provide energy to the implanted stimulator. Subjects would have to wear the baseball cap on a daily base for at least 8 h/day. The antenna component would cover the location of the inbedded receiver, externally powering the electrode array and thus providing therapeutic stimulation

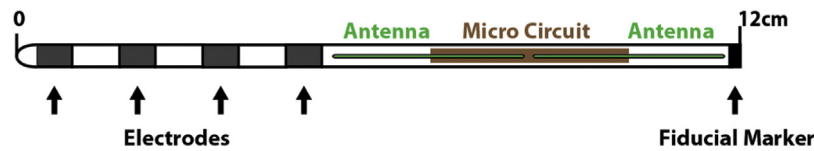


Fig. 1. Neuro-stimulator electrode, MRI compatible, for both 1.5 and 3 T.

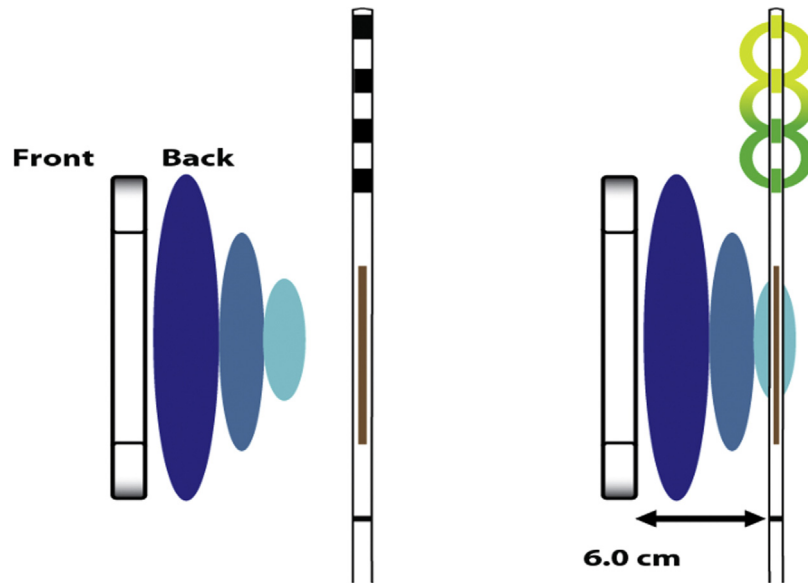


Fig. 2. Neurostimulator receiver.

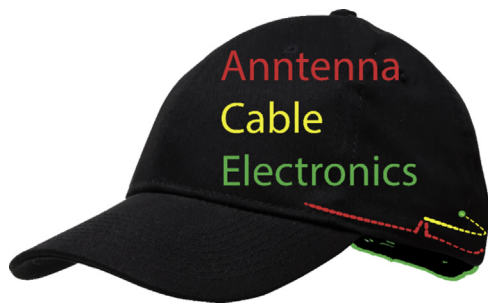


Fig. 3. External pulse generator in a baseball cap.

infraorbital, and/or auriculotemporal nerve targets was used for stimulator insertion. Doppler ultrasound was used to map out arterial vasculature around the target stimulator path and the stimulating electrodes were placed adjacent to nerves previously identified as pain generators by successful diagnostic nerve blocks using local anesthetic injections.

AP and lateral fluoroscopic images were used to document final electrode positioning (Figs. 4 and 5). The stimulator system was subsequently activated wirelessly to confirm electrode positioning while the patient reported comfortable paresthesia along the distribution of the targeted nerve, after retraction of the needle tip exposing electrode contacts. The device was anchored via a subdermal suture located at the skin entry point. Distal tubing was cut

to the enervated nerves. The external pulse generator is programmed by the clinician to send desired stimulation parameters through a direct electric coupling RF transmitting antenna to the electrode receiver, thereby wirelessly transferring stimulation commands and power to the implanted stimulator. The system uses radiofrequency energy at 915 MHz to transfer power and selected parameters to the implanted stimulator. The implanted stimulator and power source are coupled at such a short distance that the energy emitted from the antenna is relatively low. Wavelengths and product specifications have been designed to decrease risk related to the wireless transmission of energy¹² and reliably transfer the clinician's desired stimulation parameters [23].

The stimulation parameter spectrum available for clinical use and evaluation include: amplitude: 1–24 mA, pulse width: 10–1000 ms, frequency: 5–20,000 Hz.

Surgical procedure: Under strict aseptic precautions, the skin and subcutaneous tissues were infiltrated with local 1% lidocaine. A small skin incision was made for needle insertion, which was shaped by hand to match the skull contour to achieve appropriate device placement. A 14-gauge Tuohy needle at supraorbital,



Fig. 4. Skull X-ray anterior–posterior view showing the supraorbital and infraorbital location of the electrode.



Fig. 5. Skull X-ray lateral view showing the supraorbital and infraorbital placement of the electrodes.

at the insertion site and buried subcutaneously. The skin entry site was closed with suture/steristrip.

Stimulation protocol: Stimulation parameters were set at pulse widths of 100–200 ms and frequency of 60 Hz. (This is not to be confused with the device communication frequency between the external generator and electrode microprocessor of 915 MHz.) Amplitudes were set at patient preference, which was typically between 1 and 3 mA. A therapeutic stimulation regimen was applied for up to 30 days followed by removal of the devices utilizing fluoroscopy and a small incision at the electrode insertion site. During stimulation sessions, when therapy was needed to alleviate pain, patients wore a special baseball cap that housed the external pulse generator within the fabric lining (Fig. 3).

Metrics for evaluating pain: Patients were monitored for ongoing pain relief and adverse events at 2 weeks and 4 weeks post-implant. Subjects were asked to describe their pain relief using the visual analog scale (VAS). Subjects were asked to report on medication usage at each assessment.

3. Results

All patients reported sustained pain relief over primary pain areas with various electrode placements and number of electrode contacts (Table 2). Patients were uniformly pleased with results in terms of pain relief and post-implant cosmetics. Average pain reduction across all subjects using the Visual Analog Scale (VAS) was $\geq 82\%$. The average baseline VAS pain score for the patient population was 8.44 with a median of 9.17 ± 1.77 STD. The post stimulation average VAS pain score was 1.61 ± 0.35 STD (Fig. 6).

There were no reported or observed adverse events. All patients reported reduced pain medication dosage by at least 50%. Over 40% of the patients were able to stop taking pain medication completely

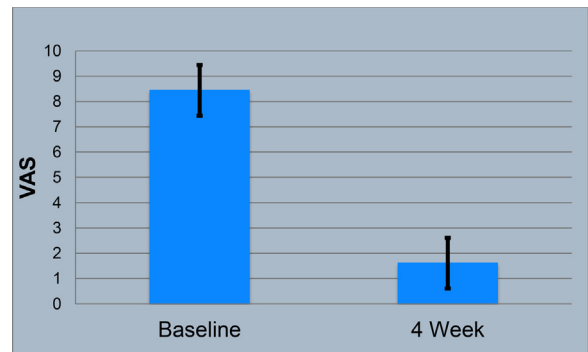


Fig. 6. Average pain reduction as measured by VAS STD ($n = 10$).

during the four-week period. After the end of the trial period, subjects had to restart medication.

4. Discussion

PNS has been a valuable therapeutic option in the management of chronic disabling facial pain since it is non-destructive and reversible [6,11,15]. Extracranial stimulation of nerves supplying craniofacial region has been recommended by the NACC for the treatment of chronic facial pain (and migraine) backed up by evaluation of published literature on current research and clinical experience. The committee did not find support for intracranial nerve stimulation [16].

Nevertheless the delivery systems utilized for PNS have not been designed for the peripheral nerve space, anatomically, especially in the craniofacial region. Thus these neurostimulation devices suffer from complications resulting from the bulk of the equipment, implantable nature of the batteries and lengthy surgical procedure [11,18–21].

The adverse events and side effects also make an effective treatment method such a PNS, an unacceptable one. FDA approval and insurance coverage are also lacking/limited at this time [21,24,25].

Wireless neuromodulation, on the other hand, mitigates the complications related to the conventional PNS devices and shows promise while expanding the number of indications for the treatment of chronic pain conditions [26]. There is a significant reduction in hardware components. A simple percutaneous placement of the electrode without the need to tunnel and attach an implanted pulse generator can be advantageous to the patient and the surgeon in reducing costs, procedure time, postoperative pain, and adverse events while achieving the desired pain control. It also adds to the cosmetic results and the positive emotional appeal.

The application and advantages with this minimally invasive wireless modality has been reported earlier for occipital neuralgia. Both patients tolerated the procedure very well and no complications related to the device or the stimulation procedure was reported [22].

In the present series also, we did not encounter any complications related to the surgery or the stimulation protocol. During the trial period the pain relief was sustainable in all the patients.

However, at the present time, the experience has been limited to fewer patients. Future studies will focus on larger patient populations with expanding metrics beyond the VAS and medication log usage, to include the Short-Form McGill Pain Questionnaire (MPQ-SF), Quality of Life (SF-36), European Quality of Life – Five Dimensions (EQ-5D), Patient Global Impression of Change (PGIC) and long term adverse events.

Table 2
Patient responses and type of stimulator.

Sub	VAS baseline	VAS week 4	Mandibular	Infraorbital	Supraorbital
1	10.0	0.0		8 contact	8 contact
2	10.0	0.7	8 contact		
3	10.0	0.0	8 contact		
4	6.0	0.5		8 contact	
5	9.6	0.6	4 contact		
6	6.5	3.4		4 contact	
7	9.7	0.8		8 contact	8 contact
8	9.3	0.9	4 contact		
9	8.6	0.1		4 contact	
10	9.1	0.0			8 contact

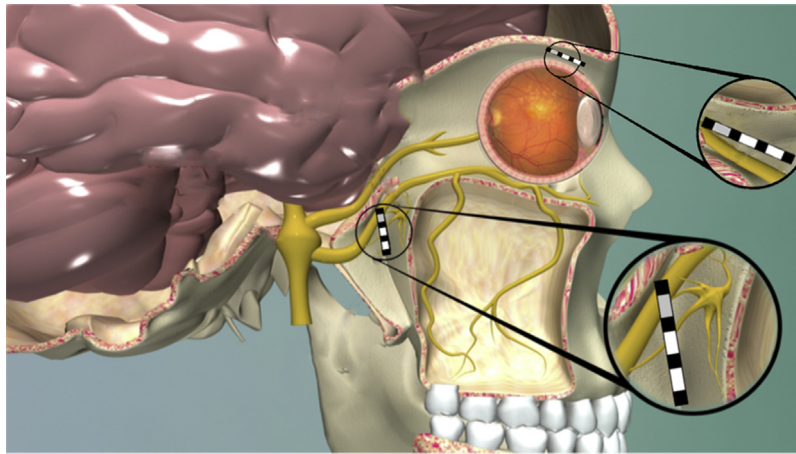


Fig. 7. Targeted subcutaneous percutaneous placement of four electrode array neurostimulators through an introducer catheter is placed in various targeted craniofacial nerve locations (trigeminal and supraorbital shown in this illustration).

5. Conclusion

Percutaneous placement of a novel, wirelessly powered, neurostimulation system adjacent to affected craniofacial nerves for the treatment of craniofacial pain appears to be a safe and effective option while avoiding significant adverse events associated with conventional devices of PNS. Further studies are necessary to better understand long-term results, expanded indications and placement techniques for a variety of pain conditions referable to the peripheral nervous system (Fig. 7).

Ethical issues

Ethics committee approval was secured and 10 patients were consented and subsequently recruited for this pilot study.

Authorship statement

Dr. Weiner designed the study. All physicians treated patients at the study site. Dr. Weiner and Dr. Montes recruited patients, collected and analyzed the data. Niek Vanquathem prepared the manuscript. All authors reviewed the manuscript critically and approved the final version.

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Conflict of interest statement

Dr. Richard L. Weiner: Consultant for StimRelieve LLC.
Dr. Carlos Montes Garcia: Nothing to disclose.
Mr. Vanquathem: Employee of the sponsor.

References

- [1] Mueller D, Obermann M, Yoon MS, Poitz F, Hansen N, Slomke MA, Dommes P, Gizewski, Diener HC, Katsarava Z. Prevalence of trigeminal neuralgia and persistent idiopathic facial pain: a population bases study. *Cephalgia* 2011;31:1542–8.
- [2] Weiss AL, Ehrhardt KP, Tolba R. Atypical facial pain: a comprehensive, evidence-based review. *Curr Pain Headache Rep* 2017;21:8.
- [3] Macfarlane TV, Blinkhorn AS, Davies RM, Kincey J, Wothington HV. Oro-facial pain in the community: prevalence and associated impact. *Community Dent Oral Epidemiol* 2002;30:52–60.
- [4] Forsell H, Jaaskelainen S, List T, Svensson P, Baad-Hansen L. An update on pathophysiological mechanisms related to idiopathic orofacial pain conditions with implications for management. *J Oral Rehabil* 2015;42:300–22.
- [5] Cornelissen P, van Kleef M, Mekhail N, Day M, van Zundert J. World Institute of Medicine. 3. Persistent idiopathic facial pain. *Pain Pract* 2009;9:443–8.
- [6] Weiner RL. Occipital neurostimulation for treatment of intractable headache syndromes. *Acta Neurochir Suppl* 2007;97:129–33.
- [7] National Headache Foundation; 2007. www.headaches.org.
- [8] Kaniecki R. Headache assessment and management. *JAMA* 2003;289:1430–3.
- [9] Torrance N, Smith BH, Bennett M, Lee AJ. The epidemiology of chronic neuropathic pain in the community. Results from a general population survey. *J Pain* 2006;7:281–9.
- [10] Vorenkamp KE. Interventional procedures for facial pain. *Curr Pain Headache Rep* 2013;17:308.
- [11] Slavin KV. Peripheral nerve stimulation for neuropathic pain. *Neurotherapeutics* 2008;5:100–6.
- [12] Cepero R, Miller RH, Bressler KL. Long-term results of sphenopalatine ganglionectomy for facial pain. *Am J Otolaryngol* 1987;8:171–4.
- [13] De Salles AA, Gorgulho A, Golish SR, Medin PM, Malkasian D, Solberg TD, Selch MT. Technical and anatomical aspects of novalis stereotactic radiosurgery sphenopalatine ganglionectomy. *Int J Radiat Oncol Biol Phys* 2006;66:53–7.
- [14] Popeney CA, Alo KM. Peripheral neurostimulation for the treatment of chronic, disabling transformed migraine. *Headache* 2003;43:369–75.
- [15] Johnson MD, Burchiel KJ. Peripheral stimulation for treatment of trigeminal postherpetic neuralgia and trigeminal posttraumatic neuropathic pain: a pilot study. *Neurosurgery* 2004;55:135–41.
- [16] Deer TR, Mekhail N, Petersen E, Krames E, Staats P, Pope J, Saweris Y, Lad SP, Diwan S, Falowski S, Feler C, Slavin K, Narouze S, Merabet L, Buvaendran A, Fregni F, Wellington J, Levy RM. The appropriate use of neurostimulation: stimulation of the intracranial and extracranial space and head for chronic pain. *Neuromodulation Appropriateness Consensus Committee. Neuromodulation* 2014;17:551–70.
- [17] Lee PB, Horazek C, Nahm FS, Huh BK. Peripheral nerve stimulation for the treatment of chronic intractable headaches: long-term efficacy and safety study. *Pain Physician* 2015;18:505–16.
- [18] Schwedt TJ, Dodick DW, Hentz J, Trentman TL, Zimmerman RS. Occipital nerve stimulation for chronic headache—long-term safety and efficacy. *Cephalalgia* 2007;27:153–7.
- [19] Slavin KV. Technical aspects of peripheral nerve stimulation: hardware and complications. *Prog Neurol Surg* 2011;24:189–202.
- [20] Slavin KV, Vannemreddy PS. Repositioning of supraorbital nerve stimulation electrode using retrograde needle insertion: a technical note. *Neuromodulation* 2011;14:160–3.
- [21] Parker JL, Cameron T. Technology for peripheral nerve stimulation. *Prog Neurol Surg* 2015;29:1–19.
- [22] Perryman LT, Speck B, Weiner RL. A novel wireless minimally invasive neuro-modulation device for the treatment of chronic intractable occipital neuralgia: case illustrations. *J Neurol Stroke* 2017;6:00213.
- [23] Tyler Perryman L, Larson P, Glaser J. Tissue depth study for a fully implantable, remotely powered and programmable wireless neural stimulator. *Int J Nano Stud Technol* 2016;(S2:001):1–6.
- [24] Birk DM, Yin D, Slavin KV. Regulation of peripheral nerve stimulation technology. *Prog Neurol Surg* 2015;29:225–37.
- [25] Thimineur M, De Ridder D. C2 area neurostimulation: a surgical treatment for fibromyalgia. *Pain Med* 2007;8:639–46.
- [26] Yearwood TL, Perryman LT. Peripheral neurostimulation with a microsize wireless stimulator. *Prog Neurol Surg* 2015;29:168–91.