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PNS CLINICAL EVIDENCE

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Short Communication

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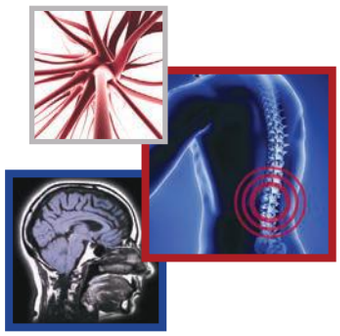
Pain Management



Prospective case series on the use of peripheral nerve stimulation for focal mononeuropathy treatment

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Practise points

- Over 10 million adults in USA experience chronic pain yet current treatment options are limited.
- Peripheral nerve stimulation, possibly through the release of inflammatory neurotransmitters and endorphins directly involved in the pain pathway, shows potential in increasing pain threshold for certain populations.
- Our 39 patient case series supports the use of neuromodulation treatment for mononeuropathy through improvement in visual analog scale pain scores and a decrease in opiate use and improvement in daily function.
- Further studies are necessary to support our conclusion that peripheral nerve stimulation may be a viable treatment option for focal mononeuropathy.

Aim: This case series looks at outcomes in 39 patients implanted using the Bioness Stimrouter system on various isolated mononeuropathies. **Patients & methods:** A case series of 39 patients with a total of 42 implants were enrolled starting August 2017 at various pain management centers. **Results:** Of 39 patients studied, 78% of the participants noticed an improvement in their pain. There was a 71% reduction in pain scores with the average preprocedure score of 8 improving to 2 post-implant. Participants noted on average a 72% improvement in activity with the greatest observed in the brachial plexus (80%) and suprascapular nerve (80%) and smallest in the intercostal nerve (40%). Approximately 89% of those implanted with a peripheral nerve stimulator experienced a greater than 50% reduction in opioid consumption. **Conclusion:** Peripheral nerve stimulators are a new, minimally invasive neuromodulation modality that shows promising early results in our 39-patient case series.

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Keywords: case series chronic pain focal mononeuropathy opioids peripheral nerve stimulation

Approximately 10% of the US population experiences chronic neuropathic pain [1]. Despite its widespread prevalence, nerve pain remains difficult to treat. Current conservative treatments with anticonvulsants, capsaicin and antidepressants are marginally effective with less than 50% of the population experiencing a greater than 50% reduction in pain [2]. Short courses of opioids are effective in treating neuropathy and neuralgia in the intermediate treatment period (8 days to 8 weeks) but its long-term efficacy is unknown [3]. Long-standing use of opioids for chronic pain is associated with hyperalgesia [4,5], increased tolerance [6] and increased addiction potential [7]. With the push to move away from prescribing opiate therapy for chronic pain, researchers are developing alternative nonopioid modalities.

The emerging field of neuromodulation has been successful in treating neuropathic pain [8–10]. Neuropathy remains a common indication to place a spinal cord [11] or dorsal root ganglion (DRG) stimulator [8]. Peripheral nerve stimulation (PNS), first described in 1967 [12], has a similar mechanism of action to traditional spinal cord stimulation (SCS). It is theorized that overactivation of large sensory afferent nerve fibers decrease transmission of painful stimuli [13]. Despite evidence supporting PNS's efficacy in treating neuropathic pain [14–18], traditional SCS has been a more popular treatment modality. Other proposed mechanisms utilize the Frankenhauser–Huxley

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Table 1. Implant facility and total number of implants.

Implant facility	Number of implants
Stanford	8
Johns Hopkins Health System	1
Kerlan–Jobe Orthopaedic Clinic	2
Oklahoma Heath	1
The Surgical Center of Connecticut	8
Duke Pain Medicine	2
Spine Institute Northwest	3
The Premier Surgical Center New Jersey	1
Surgery Center Camelback	1
HolyCross	1
Surgery Center of Des Moines – East	1
Potomac View Surgery Center	1
Brigham and Women's Hospital	2
VCU Virginia Commonwealth University Health System	1
Mount Sinai	1
University of Michigan	1
Alliance Surgery Center	1
Emory Acute Surgery Center	2

model suggesting the therapeutic mechanism of action is the association between the activation of potassium and inactivation of sodium channels involved in neuronal conduction block [19].

Up until recently, PNS implantation required surgical dissection with the direct placement of a multi-contact electrode (paddle) along or immediately adjacent to the nerve [20]. The open surgery was complicated by iatrogenic nerve injury [21,22] and a greater than 85% revision rate [23]. In 1999, Weiner *et al.* published favorable results of a percutaneously implanted PNS system for treatment of occipital neuralgia [24]. Subsequent work continued to support PNS percutaneous implantation as a safe and efficacious treatment for craniofacial [18] and extremity neuropathic pain [25]. One observed limitation with the first PNS devices was the size of the implantable pulse generator (IPG). It was difficult to find a peripheral pocket large enough for implantation and installation on the trunk requiring a long tunneling course.

Subsequently, a new peripheral nerve stimulator was designed for percutaneous placement with an external IPG. In their manuscript, Deer *et al.* describes a PNS system that is subcutaneously implanted with either fluoroscopy or ultrasound that uses a three-electrode contact with a four-pronged anchoring system. The device is powered and controlled by an external pulse generator that is mounted with adhesives to the skin adjacent to the PNS [26]. In his prospective, multicenter, randomized, double-blind, partial crossover study of 94 patients, Deer *et al.* demonstrated improvement of neuropathic pain pre- and postimplant of the novel PNS device [26].

With this new minimally invasive, percutaneous implantation technique, it seems logical to consider a potentially less invasive, peripheral neuromodulation device that directly targets the affected nerve. Since the published study by Deer *et al.,* there has been a shortage of recent evidence on the validation of PNS on treating focal mononeuropathy. The purpose of this study is to show the results from a 39-patient case series using a peripheral nerve stimulator in treating mononeuropathy. To our knowledge, this is one of the first studies of its kind describing the exact nerve location of a PNS implantation with an external pulse generator and its efficacy as well as length of time the disposable user patch was applied.

Patients & methods

A case series of 39 patients with a total of 42 implants were enrolled in a Bioness postimplant survey study starting in August 2017 at various pain management centers in USA. The centers that participated in the study are provided in Table 1, the nerve location, technique, number of implants and target nerve are provided in Table 2. There was a total of 39 participants and 42 PNS evaluated. One participant had a bilateral tibial nerve implant and two subjects had two PNS implanted on different nerves. Not all participants answered every question on the survey (see n-values on charts for responders). Patients were surveyed by Bioness before and approximately 3–6 months

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Table 2. Summary of methodological parameters.

Implanted nerve	Indication	Number of responders	Diagnostic block prior to implant total responders	Sedation used	Imaging technique	Single- or dual-incision closure
Axillary	Poststroke shoulder pain (6 13)	13	2 5	MAC with local (6 6)	US: 6; Fluoroscopy and US: 1; Unknown: 5	Dual: 8; Unknown: 5
Genital femoral	Genital femoral neuralgia	1	1 1	Unknown	US and paresthesia	Dual
Intercostal	Unknown	1	1 1	MAC	US	Dual
Ilioinguinal	Unknown	1	1 1	Unknown	US and paresthesia	Dual
Lateral femoral cutaneous	Unknown	3	2 3	Unknown	US and paresthesia: 2 Unknown: 1	Dual: 2; Unknown: 1
Peroneal	Unknown	2	1 2	MAC: 1; Unknown: 1	US: 1; Unknown 1	Dual: 1; Unknown: 1
Intercostal	Unknown	1	0 1	General	US	Dual
Saphenous	Unknown	2	1 2	Local: 1; MAC: 1	US: 2	Dual
Suprascapular	Unknown	1	1 1	Unknown	Paresthesia and US	Dual
Sural	Unknown	1	1 1	Unknown	Paresthesia and US	Dual
Tibial	Unknown	5	4 4	Local: 3; Unknown: 2	Paresthesia and US: 2 US: 3	Dual: 5

MAC: Monitored anesthesia care; US: Ultrasound.

after device implantation. A total of 54% of the patients surveyed were female and 46% were male. Data obtained from survey were analyzed and presented in this paper.

All patients who received a Bioness StimRouter PNS were included in the study with no exclusions. Indication for implantation was chronic mononeuropathic pain. Many of the patients in our survey failed conventional SCS, DRG and nerve ablative procedures. Due to our inability to present each individual technique used for each target nerve (>17 peripheral nerves targeted with Bioness Stimrouter), we have attempted to summarize the key elements of the procedural technique in Table 2 for the nerves targeted in our study. We recommend providers consult Bioness with regard to recommendations on specific techniques and reference guides for more detailed methodology. The majority of patients in our study received a preprocedure test block along the suspected nerve with a greater than 50% reduction in pain. Most peripheral nerves were accessed using ultrasound using an in-plane technique (Table 2). Implants were performed using light sedation and or local anesthetic. After placement and before implantation, the device was stimulated at least three-times between 0.5 and 1.5 mA, and patient feedback was obtained to ensure the detected paresthesia mapped the distribution of pain. A dual incision technique was performed to secure and permanently bury the lead. All implants were adjusted using the following ranges, intensity: 1–30 mA; frequency: 0–200 Hz; phase duration: 70–500 ms. Adverse events were not directly evaluated in this study but no serious events including infection and lead migration were reported. Bioness had obtained patient consents for all survey participants in all of the centers as part of standard of care.

Results

Summary of patient demographic

The study demographic mainly consisted of US patients in pain centers nationally that participated in a postimplant survey without any exclusion criteria. The minimum age of implantation was 18, with 54% of study subjects being females and 46% of study subjects being males. The average age of female patients was 59, and the average age of the male patient was 61. There were 24 different peripheral nerve locations that were involved in our study, and all subjects were asked the same postimplant questions with regard to change in visual analog scale (VAS) score, activity and postoperative opioid consumption.

Changes in VAS score

The average percent reduction of VAS pain scores ranged from 29 to 100%, differing by the peripheral nerve stimulated. The average VAS prior to implantation was 8 compared with 2 after PNS implantation with a noted reduction of 71% (see Table 3). The greatest reduction in pain scores were seen in the lateral femoral cutaneous nerve with preimplant pain scores improving from an average of 8 to 0 (100% reduction in pain score) post

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Table 3. Average change in visual analog scale score by peripheral nerve stimulated.

Location	N	Visual analog scale prior to implant	Visual analog scale after implant	Change (%)
Total	39	8.2	2.4	70.8
Lateral femoral cutaneous	3	8.3	0.0	100.0
Genitofemoral	1	10.0	1.0	90.0
Ilioinguinal	1	10.0	1.0	90.0
Sural	1	8.0	2.0	75.0
Peroneal	3	9.0	2.3	74.1
Axillary nerve	18	8.0	2.4	70.1
Suprascapular	1	9.0	3.0	66.7
Saphenous	3	7.7	2.7	65.2
Tibial	5	7.8	2.6	66.7
Brachial plexus	2	9.5	4.5	52.6
Intercostal	1	7.0	5.0	28.6

Table 4. Percent improvement in activity by peripheral nerve stimulated.

Nerve location	n	Improvement in activity (%)
Total	27	72.0
Axillary	14	73.5
Brachial plexus	1	80.0
Genitofemoral	1	75.0
Ilioinguinal	1	75.0
Intercostal	1	40.0
Lateral femoral cutaneous	2	70.0
Peroneal	2	75.0
Suprascapular	1	80.0
Sural	1	60.0
Tibial	3	73.3

implantation. The smallest pain score improvement (29%) was seen when PNS was implanted into the intercostal nerve with (n = 1).

Effect on activity

Data from all 27 participants who responded to the survey referring to improvement in activity stratified by the peripheral nerve involved are indicated in Table 4. Participants were asked to estimate their percent improvement in activity. All (100%) of the questionnaire responders noted improvement in activity with the quantification of their improvement ranging from 40 to 80%. Participants noted on average a 72% improvement in activity with the greatest noted in the brachial plexus (80%) and suprascapular nerve (80%) and smallest in the intercostal nerve (40%).

Table 5 indicates the duration in days the external pulse transmitter and disposable patch were applied prior to replacement. From the 34 total responders, the PNS was turned on 6.0 days per week requiring patch replacement every 5.2 days. Most of the data were available for responders with an axillary PNS who indicated using the PNS on average of 6.2 days per week requiring patch replacement every 4.4 days.

Effect of opioid consumption

Approximately 65% of the participants (11 of the 34 responders) were on opiates prior to PNS implantation. After implantation, participants noted an average reduction in opioid use by 68%. Figure 1 demonstrates that 89% of those implanted with a peripheral nerve stimulator observed a greater than 50% reduction in opioid consumption.

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Table 5. Duration in days of external pulse transmitter and disposable patch application prior to replacement with new patch by peripheral nerve stimulated.

Nerve location	n	Average days Pt used device	Frequency of disposable patch replacement (in days)
Total	34	6.0	5.2
Axillary	16	6.2	4.4
Brachial plexus	2	5.3	2
Genitofemoral	1	7	3
Ilioinguinal	1	7	7
Intercostal	1	7	7
Lateral femoral cutaneous	3	7	7
Saphenous	1	7	7
Peroneal	2	7	7
Suprascapular	1	4.5	4.5
Sural	1	2.5	2.5
Tibial	5	5.9	6

Pt: Patient.

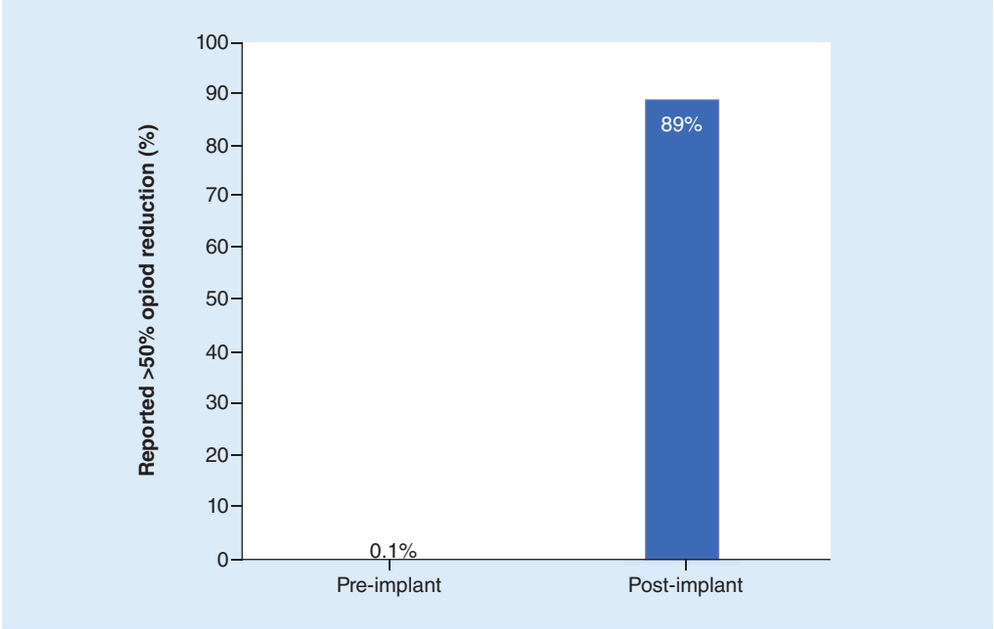

Figure 1. Percent of patients reporting greater than 50% opioid reduction post-implant.

Discussion

Chronic pain currently impacts more than 100 million adults in USA [27–29]. It is estimated that approximately 10% of the US population experiences chronic neuropathic pain [1]. Traditional SCS has been a good treatment option for neuropathic pain but its ability to target specific focal regions is difficult.

The pathophysiology of pain and the mechanism behind neuromodulation is complex. Peripheral nociceptive pain is mediated by the small free nerve endings of Aδ and C fibers. Upon painful stimulation, these small nerves transmit signals to the interneurons of gray matter on the dorsal horn and stimulate second-order neurons to send pain signals to the brain. Upon chronic painful stimulation, nociceptors mediate pain transmission via release of inflammatory neuropeptides (substance P, calcitonin gene-related peptide) at the dorsal horn, stimulating inflammatory cascades that magnify pain responses [30].

Several mechanisms of action for PNS have been proposed, it has been suggested that PNS works via both the Gate Control Theory and via inhibition of neurogenic inflammation [31,32]. The Gate Control Theory was first

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described in 1965 by Malzack and Wall and provides the foundation for current understanding of the therapeutic mechanism behind SCS. Through direct nonpainful orthodromic stimulation by PNS of non-nociceptive Aβ fibers, the dorsal horn interneurons are activated and inhibit the transmission of pain signals from the nociceptive Aδ and C fibers [13,31,33].

It has been postulated that PNS modulates the release of inflammatory neurotransmitters and endorphins directly involved in the pain pathway [31]. Nerve fiber damage during peripheral nerve injury leads to firing and transmission of ectopic discharges through low-threshold Aβ and high-threshold Aδ and C fibers [31]. Studies performed in healthy human volunteers have seen increased pain thresholds in patients undergoing PNS likely attributed to modifications of local inflammatory mediators.

Our case series suggest PNS is effective in controlling pain. Approximately 56% of the participants received upper extremity peripheral nerve stimulators. These regions have historically been considered at higher risk and technically difficult to target with traditional dorsal column SCS. Early PNS symptoms required open surgical implantation and were associated with high levels of iatrogenic nerve [21,22] injury and lead migration [23]. The new PNS system as described previously by Deer *et al.* in his large randomized controlled trial (RCT) study, observed zero device-related severe adverse events and a response rate of 38% [26]. For isolated peripheral mononeuropathies, early evidence suggests peripheral nerve stimulators are less invasive, safer and more effective than traditional SCS. Our results showed that 100% of the patients noted an improvement in their activity and an average VAS reduction score of 71%. Adverse events were not directly evaluated in this study but none were reported to the manufacturer. In contrast, the severe device-related complications for dorsal column SCS or DRG is 18% in refractory neuropathic back and leg pain [34], 11.1% in patients with recurrent radicular pain undergoing SCS after lumbosacral spine surgery [35] and 14% in newer studies on SCS in failed back surgery syndrome [36] compared with 0% severe device-related complications as seen in Deer *et al.* study.

Our data confirm findings seen in Deer *et al.* with overall improvement in self-reported pain scores and increase in functional activity in patients receiving PNS [26]. Notable was a self-reported reduction of opiates by 68%. Additionally, 89% of those implanted with a peripheral nerve stimulator observed a greater than 50% reduction in opioid consumption. As dependence and tolerance to prescription opioid medication continues to rise with increase in morbidity and mortality secondary to opioid use [27,37,38], PNS offers one treatment modality for patients refractory to medical management who continue to suffer from chronic neuropathic pain of peripheral origin.

All (100%) of the questionnaire responders noted improvement in activity with an average of 72% improvement, the greatest being among patients with axillary nerve implantation. The axillary nerve is commonly affected in patients with poststroke shoulder pain. The sensory and motor fibers of the axillary nerve are stimulated as it exits the quadrangular space. The motor portion can be stimulated to reduce subluxation and improve functional activity. Though more randomized controlled trials with PNS are necessary to reaffirm findings seen in our study, the use of PNS may lead to improvement in activity and ultimately quality of life. Studies have shown that chronic pain leads to significant debilitation and depression [39–41]. Thus, PNS may not only help alleviate pain but also provide significant improvement in an individual's overall wellbeing.

With PNS, it is difficult to decide where to place the IPG. If implanting an upper extremity or distal nerve, implantation will have long tunneled leads. The system evaluated in our case series used an IPG secured with adhesive table superficial to the lead's contact points. On average, patients changed their patch every 5 days. From our data, it appears that the more proximal peripheral nerves required more frequent IPG changes while the more distal nerves were changed less frequently. On average, patients used their device 6 out of 7 days of the week. Sustained relief experienced longer than the devices' use is an expected outcome with peripheral neuromodulation.

Our study is limited by its retrospective nature and small sample size making it difficult to draw definitive conclusions. This is a self-reported survey collected by Bioness that is subject to participant response and collection bias. The follow-up time period was limited to 6 months, conclusions on long-term efficacy are unable to be drawn. While we attempted to obtain data from multiple centers, for unclear reasons some locations contributed more to the dataset than others. The data were raw and independently analyzed with no influence by the manufacturer. Adverse events and lead migration was not measured. This is one of the first studies describing the exact nerve location of a PNS implantation and its efficacy. Finch *et al.* published a double-blind crossover trial of 11 PNS patients showing decreased pain response in patients undergoing PNS [25,42]. Our study adds to the literature and supports the conclusions published by Finch *et al.* Further randomized control studies with long-term follow-up are needed to confirm the utility of PNS in alleviating chronic pain.

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Early results support the use of PNS as a neuromodulation treatment for mononeuropathy. Our patients experienced improvement in VAS pain scores, reported a decrease in opiate use and improvement in daily function, suggesting that this may be a very viable treatment option for focal mononeuropathy.

Financial & competing interests disclosure

KV Chakravarthy is a consultant to Abbott, Bioness, Medincell, SPR Therapeutics, Nalu Medical, Medtronic, Oska Wellness. He has stock options in Nalu Medical and Oska Wellness. He is the founder of Douleur Therapeutics, NanoAxis and Newrom Biomedical. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that Bioness had obtained patient consents for all survey participants in all of the centers as part of standard of care.

Data sharing statement

The authors certify that this manuscript reports the secondary analysis of clinical trial data that have been shared with them, and that the use of these shared data is in accordance with the terms (if any) agreed upon their receipt. The source of these data are: Bioness Stimulator Survey Data.

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    Crossover trial of PNS patients.

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StimRouter®

STIMROUTER PATIENT SURVEY RESULTS

As the market leader in Peripheral Nerve Stimulation, Bioness is the only company to survey our own implanted patients to learn about the performance of our chronic pain solution. Through better understanding how patients use the **StimRouter** each day, we can learn from them how to improve our products and support materials. As part of our continuous improvement effort, the **StimRouter** Team surveyed nearly 500 patients about their experience with **StimRouter**. 133 patients responded representing 17 different nerves. Here is what they had to say about how the **StimRouter** helps them manage their chronic pain:

- **88% of patients surveyed report actively using their StimRouter to treat their chronic pain**
- **79% of patients who have had their StimRouter for one year or longer still actively use their device**
- **76% of patients surveyed reported that they are satisfied with their device, and almost 40% reported that they are extremely satisfied**
- **A majority of patients surveyed reported that their activity level increased by at least 50% after receiving their StimRouter**

StimRouter patients continue using their device because it helps them significantly reduce their pain, become more active, and get back parts of their lives that they feared they had lost. In their own words:

- *Awesome product that provides a non narcotic solution*
- *I wish I had gotten it sooner*
- *The StimRouter has significantly reduced pain in my paralyzed arm and helped return some function*
- *I love my StimRouter device!*
- *Because of the StimRouter, I got my life back!*

FOR MORE INFORMATION ABOUT STIMROUTER OR TO SPEAK WITH OUR LOCAL STIMROUTER REPRESENTATIVE, CALL 800.211.9136.

Individual results vary. Patients are advised to consult with a qualified physician to determine if this product is right for them.

Important Safety Information and Risks: For Indications for Use, Contraindications, Warnings, Adverse Reactions, Precautions and other safety information please refer to www.stimrouter.com/risks (also available in the StimRouter Clinician s Guide).

Bioness®

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A Comparison of the use of PNS to SCS and DRG for Lower Extremity Pain

Einar Ottestad MD[1], Ofer M Wellisch MD MPH[2], David Spinner DO[3], Andy Veldkamp[4]

[1] Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University, Palo Alto CA
[2] Department of Anesthesiology, Columbia University Vagelos College of Physicians and Surgeons at Stamford Health, Stamford, CT
[3]Department of Rehabilitation and Human Performance, Icahn School of Medicine at Mount Sinai, New York, NY
[4] Bioness Inc, Valencia, CA

Introduction

Chronic neuropathic pain of the lower extremity (LE) can be challenging to treat. Beyond physical therapy, nerve blocks, and medication management, spinal cord stimulation has been frequently utilized with inconsistent results, particularly when targeting the sole of the foot. Dorsal root ganglion (DRG) stimulation was introduced in 2016 as a viable alternative to target leg pain; however, the procedure involves complex neuraxial intervention. Advances in peripheral nerve stimulation (PNS) addresses the challenges in treating chronic LE pain conditions inadequately treated with SCS and DRG stimulation. The Bioness StimRouter PNS System is indicated for chronic pain of peripheral nerve origin in the upper extremity, trunk, and LE. The system allows placement of a compact, flexible percutaneous lead on the target peripheral nerve guided by ultrasound, fluoroscopy or surface anatomy. The procedure is generally performed in 30-minutes or less. No existing literature could be found comparing PNS to other forms of neuromodulation in treatment of chronic LE pain.

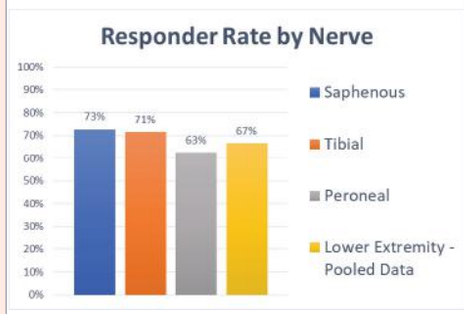
Methods

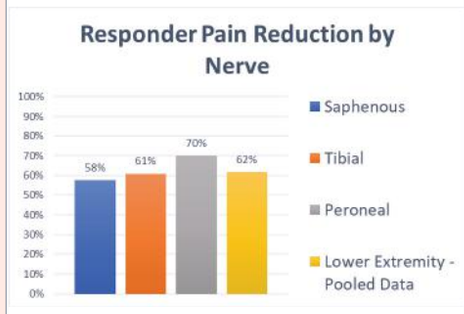
A 27-patient case series is presented to study PNS efficacy (responder rate & pain reduction), safety (adverse events) and efficiency (procedure time) for chronic pain of the LE with no exclusion for participation. 63% of the patients surveyed were female and 37% were male.

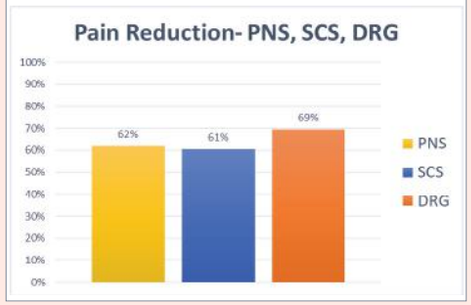
Results

There was an average responder rate of 67% for lower extremity pain using pooled data for the saphenous, peroneal, and tibial nerves. The average pain reduction in responders was 62%, with an average implant duration of 0.9 years. Saphenous nerve stimulation exhibited the highest responder rate (73%), where 58% of patients suffered from persistent post-surgical pain s/p TKA. 94% of patients who were taking prescription opioids prior to their PNS implant reported opioid sparing effects post-implant. 47% of patients who were taking prescription opioid pain medication prior to implant reported at least a 50% reduction in their opioid use. Average procedure time across all implant locations was 32 minutes. Of note, in a larger multicenter, RCT by Deer et al* there were no reported serious adverse events, infections, or lead migration. Of the 27 patient respondents, 96% would recommend permanent PNS to other patients with chronic pain.

Results (continued)







Discussion

Event description	Nerve root incidence rate*	Published SCS incidence rates	SCS incidence rate	DRG incidence rate	PNS incidence rate
CSF leaks	12%	0.3%-7%	0.30%	0.54%	N/A
Infection	12%	2.5%-14%	1.12%	1.08%	0%
Persistent pain at the implant site	N/A	0.9%-12%	0.56%	0.18%	0%

Table 1: Comparison between events reported in current analysis and published rates with SCS and DRG stimulation.

Table 1 compares the available neuromodulation treatment modalities for lower extremity chronic pain taking into consideration procedure length, invasiveness, adverse events, responder rate, and pain reduction. PNS is a safe and viable tool that may be integrated into treatment algorithms for chronic lower extremity pain of peripheral nerve origin.

Conclusion

Permanent PNS systems like the StimRouter represent a minimally invasive neuromodulation modality that continues to show promise. Taken together, integration of PNS into existing algorithms for the treatment of chronic neuropathic pain of the lower extremity should be considered.

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Authorship Statement

Einar Ottestad MD, Ofer Wellisch MD, and David Spinner DO are consultants of Bioness Inc. Andy Veldkamp is an employee of Bioness Inc.

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Peripheral Nerve Stimulation (PNS) for Chronic Joint Pain in Patients Who Are Not Candidates for Joint Replacement Surgery

Einar Ottestad, MD, Andy Veldkamp MBA

Introduction: Approximately 1 in 4 adults in the US with arthritis have severe, chronic joint pain.1 The typical treatment algorithm includes conservative treatments like physical therapy, medications and steroid injections. Patients who fail conservative management are often presented with surgical treatment which may include joint replacement surgery (JRS). For some patients who are not candidates for surgical procedures because of comorbidities, pain treatment is limited primarily to oral analgesics. Recent advances in medical device technology and imaging have made Peripheral Nerve Stimulation (PNS) minimally invasive, fast to implant under local anesthesia, and simple to control.

Methods: A survey was conducted of US patients with chronic joint pain of the shoulder and knee who received the first FDA cleared PNS System, the StimRouter® (Bioness Inc., Valencia, CA), approved to treat chronic pain of a peripheral nerve origin excluding pain in the craniofacial region. The selection criteria for the database was the nerve stimulated corresponding to the shoulder and knee. Patients who received the implant for Hemiplegic Shoulder Pain were excluded. The PNS implant consists of a small, thin implanted lead powered by an External Pulse Transmitter and controlled with a Patient Programmer (**Figure 1**). The percutaneous procedure is ≈15-30 minutes long and performed using ultrasound guidance while the patient is awake. "Trial" stimulation is integrated into the permanent lead placement, combining two procedures.

Results: 10 patients responded to the survey: 5 Saphenous nerve and 5 Axillary nerve implants. Responder Rates are summarized in **Table 1** and **Table 2**. The combined responder rate for all nerves is 60% and average pain reduction for "responders" is 68%. Responders were classified as those patients who experienced a 50% or more reduction in their pain post-implant. Average implant time was 1.2 years.

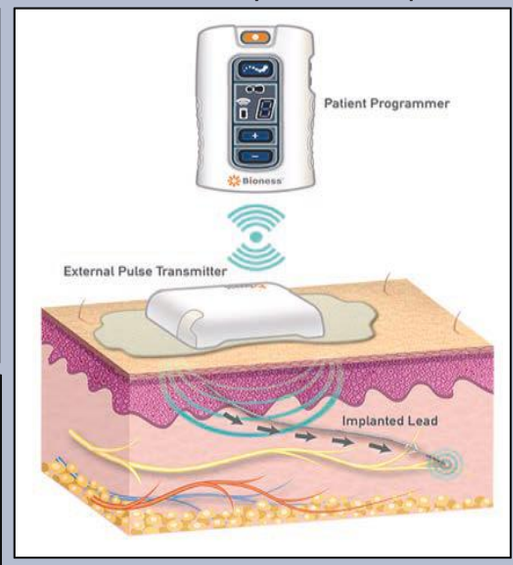

Figure 1

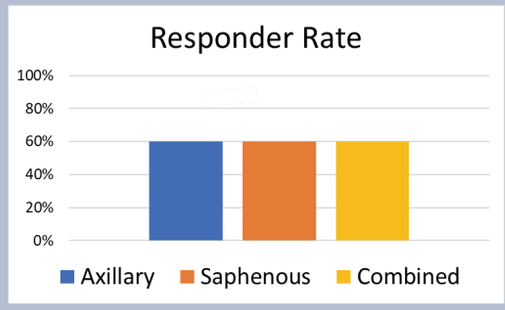

Table 1

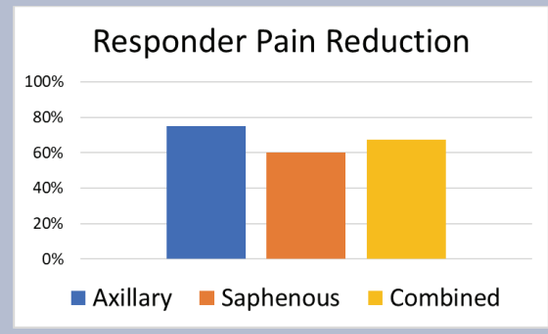

Table 2

Discussion: PNS targeting chronic joint pain is a promising therapy that has benefits for patients who are not candidates for JRS and have responded favorably to diagnostic nerve blocks without durable benefit. Visualization of the target peripheral nerve with ultrasound makes it easy to percutaneously place the small lead. Although additional data and high-quality studies are needed, complications associated with older technology including lead migration, fracture, and skin erosion are likely reduced with this system given its simplicity, ease of use, and minimally invasive implant procedure.

References:

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Disclosures:

1. E. Ottestad, MD is on the Scientific Advisory Board for Bioness Inc.
2. Andy Veldkamp is an employee of Bioness Inc.

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Fluoroscopic Assisted Placement of Suprascapular Nerve Stimulation with Stimrouter

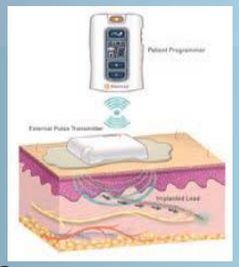
Mayo Mitsuya DO, Martin Quiroga DO, Alexis Escobar MD
Interventional Pain Management, General Surgery

Introduction

Peripheral nerve stimulation is a proven method of treating chronic musculoskeletal and nerve related pain. Previous approaches focused on sole use of Ultrasound to facilitate placement of leads requiring high skill with the Ultrasound probe. With the use of Fluoroscopic assistance and application of musculoskeletal anatomy, we demonstrate a new novel lead placement technique for peripheral nerve stimulation for the Suprascapular Nerve.

Images

1



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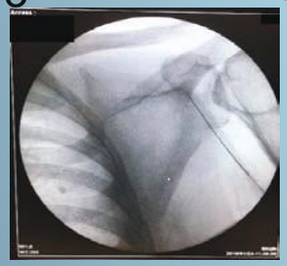

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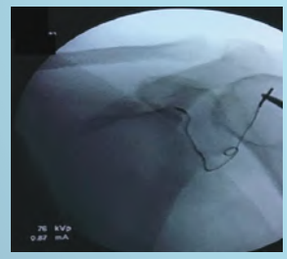


1. Bioness-StimRouter
2. Anatomy of Suprascapular Nerve at Spinoglenoid Notch
3. Inferior Suprascapular Nerve Block Approach
4. Post Stimrouter Implant (Medial: Lead; Lateral: Receiver tunneled to deltoid for additional coverage shoulder coverage with EPT)

Methods of Integration focus

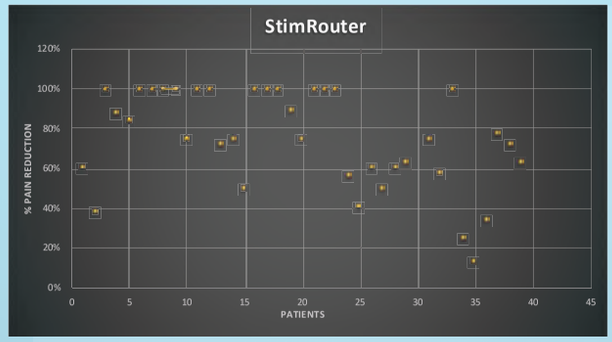
Suprascapular Nerve approach – the nerve is approached in a similar manner as applied by Dr. Sulindro, Dr. Spinner and Dr. Gofeld. The Spinoglenoid notch is entered from an inferior anatomical entry point. The Scapula is fluoroscopically placed in a neutral position and the Acromion and Coracoid process are aligned to provide a consistent view. The neck of the Glenoid process is also elongated to fully identify the Glenohumeral joint to avoid joint penetration. This approach allows parallel access to the Suprascapular nerve. The electrode can be placed strategically parallel to the nerve for maximized surface area of stimulation.

Results

Demographics	
Gender	Male: 7 ; Female: 20
Age	Mean: 55 years ; Range: 29-82 years

Nerve	# of Patients	Average Pain Relief
Suprascapular	27	76%

Response Rate (> than **50% pain reduction**)	**24/27 Patients**	**89%**



Discussion

Fluoroscopy was integrated into our approach to peripheral nerve stimulation for various reasons. First, fluoroscopy allows us to integrate musculoskeletal anatomy in adjunct with Ultrasound anatomy to provide a multi-modal approach in approaching our target nerve. Secondly, fluoroscopy allows us to visualize boney land marks which provide us with safety and a means to quantify the AP trajectory of the needle. This allows us to provide more consistency in our approach. Thirdly, fluoroscopy allows us to provide a new dimension in the set up of the trajectory of the needle placement to the destination. Approaching the peripheral nerve in a parallel fashion allows for improved contact with stimulation.

As we learned from SCS, accuracy in the location of the implantation affects the results of the pain relief. With saved fluoroscopic images of the nerve blocks, the physician can, with confidence, approach the nerve in a consistent and standardized manner. This approach not only increases the accuracy and potency of the treatment, but it additionally allows the physician to improve their skill set and shorten the duration required to complete the procedure. This is achieved by using technology (Fluoroscopy) with which we are comfortable as Interventionalists.

As the results show, the previously difficult Suprascapular stimulation has become technically feasible with outstanding pain relief scores. Intraoperative time was reduced significantly as the Ultrasound probe placement was assisted with the use of Fluoroscopic anatomy. Using this technique for the initial nerve block and subsequent implantation allows the physician to quantify the location of the block and able to reproduce the exact location for stimulation.

Furthermore, the use of Fluoroscopy in combination with Ultrasound provides direct Fluoroscopic visualization of the lead post anchor deployment to identify immediate migration. Post-op migration concerns are easily identified with Fluoroscopy in office. EPT placement troubleshooting is also assisted with use of Fluoroscopy.

Conclusion

With the combined use of Fluoroscopy and Ultrasound guidance in our approach to Suprascapular Nerve stimulation, accuracy of stimulation and consistency in obtaining pain relief were both achieved. This approach can be reproduced in a consistent manner, which will allow for further discussion on the standardization of lead placement in the future.

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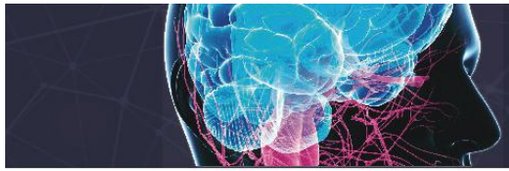

DRIVING INNOVATION THROUGH
SCIENCE & EVIDENCE

North American Neuromodulation Society
est 1994

Novel Placement Technique for Suprascapular Nerve Stimulation

Mayo Mitsuya DO

Alexander Escobar MD

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Disclosures

- Consultant – Nuvectra
- Consultant – Bioness/Stimrouter

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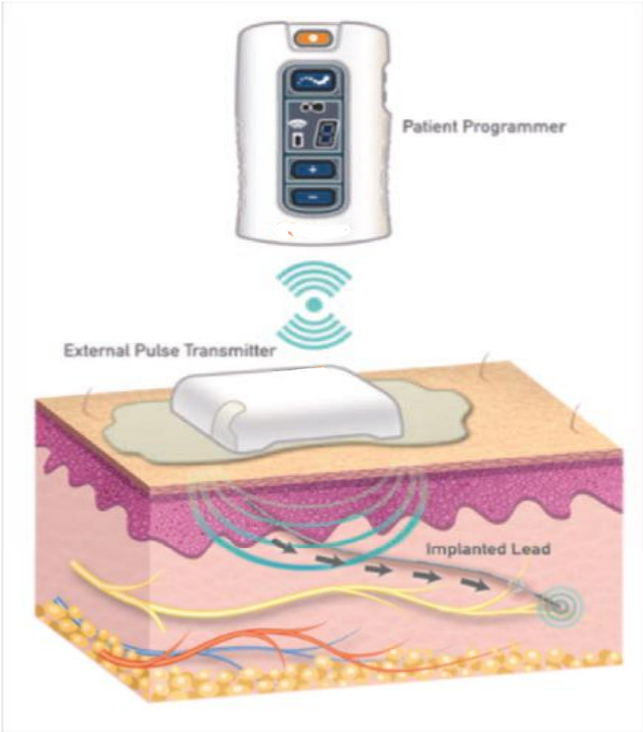
Introduction



- Peripheral nerve stimulation is an established modality used for treatment of chronic musculoskeletal and neuropathic pain.
- Techniques have focused primarily on the use of ultrasound guidance.
- We demonstrate a novel lead placement technique targeting the suprascapular nerve using an inferior to superior spinoglenoid technique under fluoroscopic guidance.

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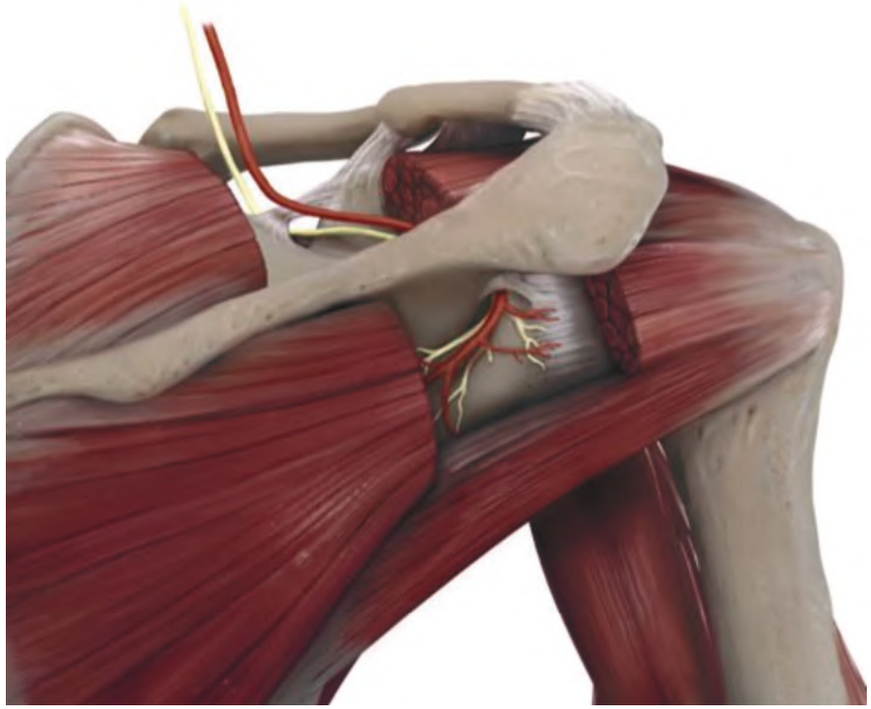
Methods



- Suprascapular nerve is approached in a similar technique reported by Drs. Sulindro, Spinner, and Gofeld.
- The spinoglenoid notch is positioned under the fluoroscope.
- The spinoglenoid notch is entered from an inferior anatomical entry point.
- Goals:
  - Parallel access to suprascapular nerve
  - Avoid injury – lung apex, brachioplexus
- The electrode can be placed strategically parallel to the nerve for maximized surface area of stimulation.

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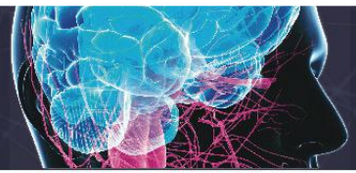

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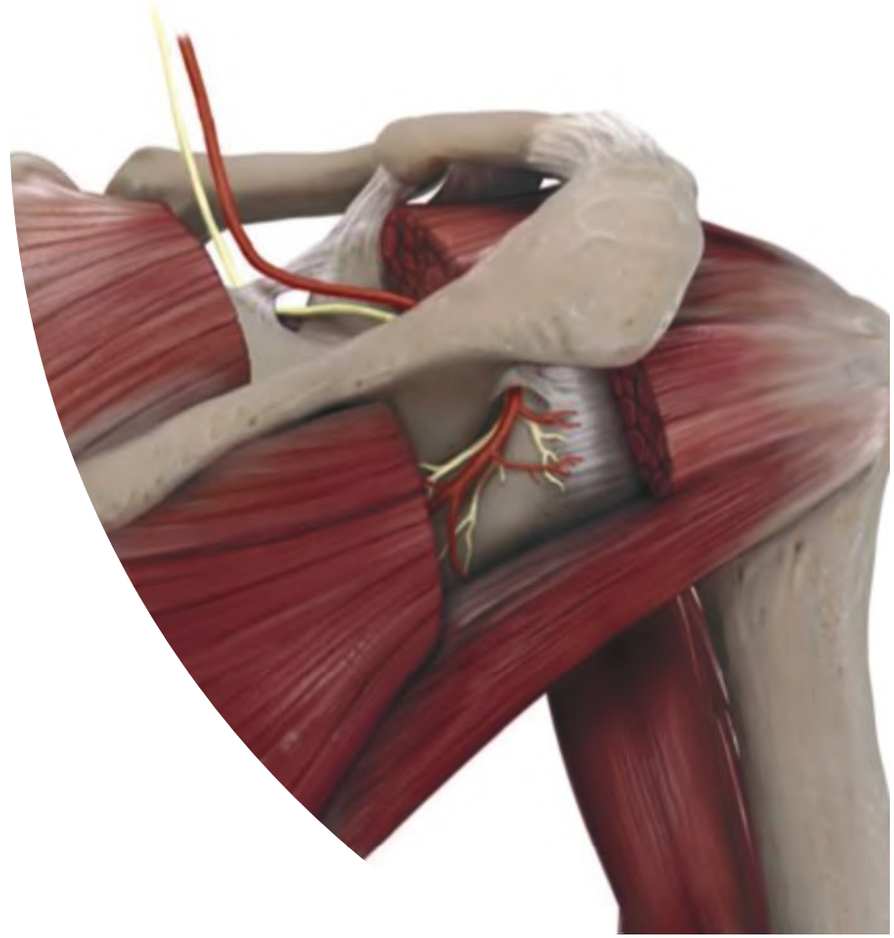

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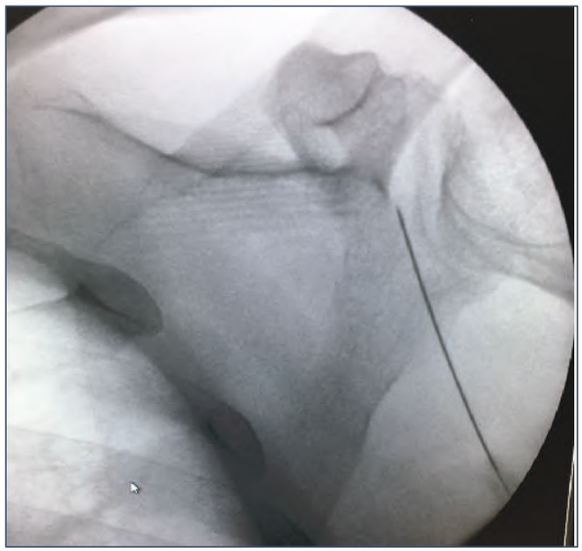
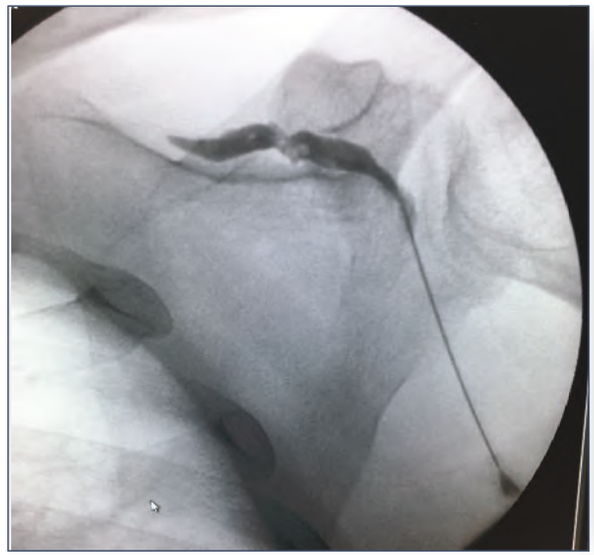
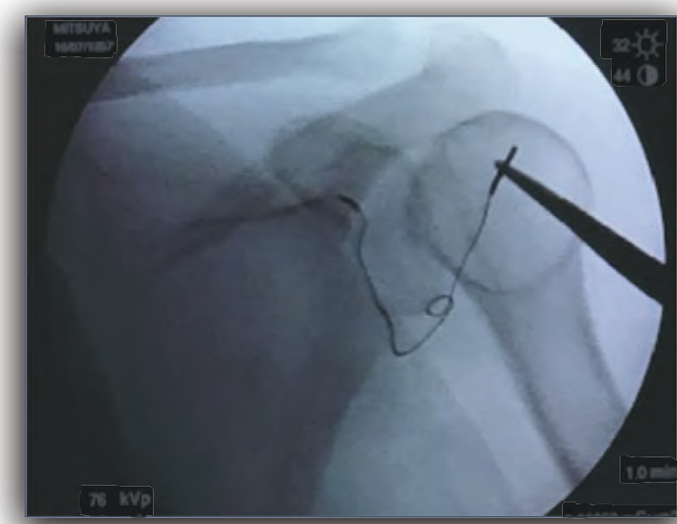
Technique







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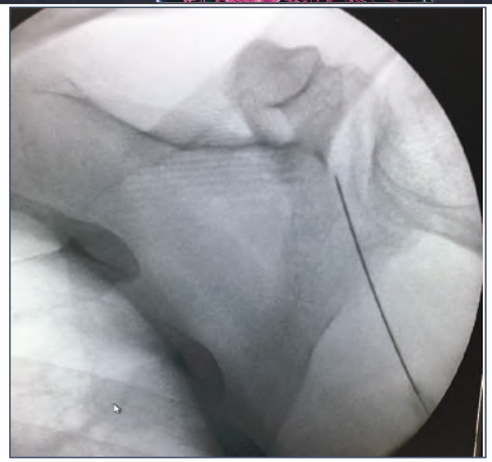

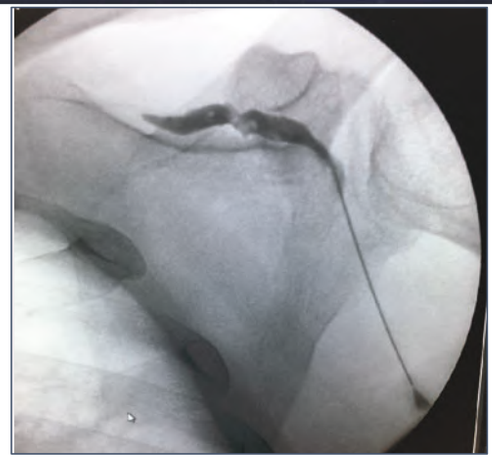

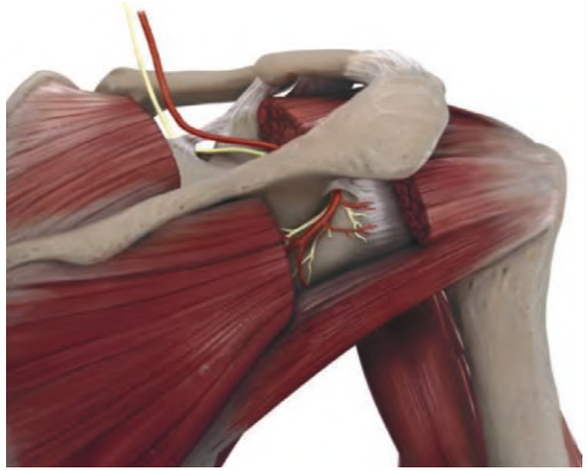

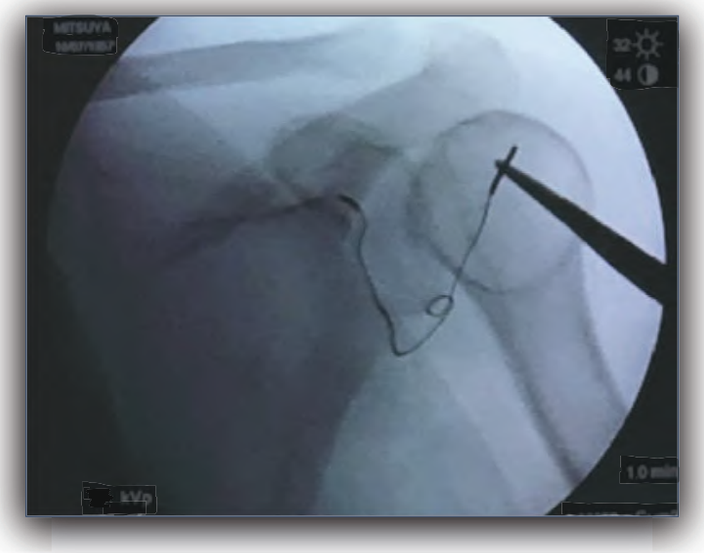

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Results

Demographics	
Gender	Male: n=8 ; Female: n=22
Age	Mean: 55.6 years ; Range: 29-82 years

Operative Time		
0 min – 10 mins	10 mins – 15 mins	15 mins – 30 mins
7	16	7

Nerve	# of Patients	Average Pain Relief
Suprascapular	30	75%

Response Rate (> than **50% pain reduction**)	**27/30 Patients**	**90%**

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Discussion

- Fluoroscopy was integrated into our approach to peripheral nerve stimulation for the suprascapular nerve for various reasons. The use of fluoroscopy allows us to integrate musculoskeletal anatomy in combination with ultrasound anatomy to provide a multi-dimensional approach. The use of fluoroscopy also allows us to visualize bony landmarks that provide critical safety views to quantify the AP trajectory of the needle for consistent reproducible placement. Lastly, fluoroscopy allows the electrodes to stimulate the peripheral nerve in a parallel fashion for what we feel allows for improved pain relief.
- As we learned from spinal cord stimulation, accuracy and reproducibility in the location of the implantation effects the efficacy and compliance of the therapy. With documented fluoroscopic images the clinician can facilitate consistency and standardization for a variety of pathological shoulder changes that can affect ultrasonic views. We feel that this approach increases the accuracy of lead placement, avoiding vital surrounding structures, enhances the ergonomics of lead location, and ultimately improves the use of PNS therapy for both patient and physician.
- Our data demonstrates that peripheral nerve stimulation using the inferior to superior spinoglenoid technique as described is a reproducible and effective strategy for the treatment of chronic shoulder pain. Intraoperative time was also significantly reduced despite the use of both ultrasonography and fluoroscopy. Using the technique described in our methods for the initial nerve block and subsequent implantation allows the physician to quantify the location of the block and reproduce the exact location for stimulation.
- Furthermore, the use of fluoroscopy in combination with ultrasonography provides direct visualization of the lead post anchor deployment to identify immediate migration. Post operative troubleshooting concerns are easily identifiable with the use of fluoroscopy in office. External pulse transmitter placement location is also optimized with the use of fluoroscopy that can be compared to previous saved images that are reproducible and less reliant on provider variability.

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Conclusion

- With the combined use of fluoroscopy and ultrasound guidance using our inferior to superior spinoglenoid technique to suprascapular nerve stimulation, we feel the accuracy of stimulation leads to improved patient compliance and reproducible sustained pain relief. This approach not only reduces chance of injury to the apex of the lung but can be reproduced in a consistent manner, which will allow for further discussion on the standardization of lead placement in the future.

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CLINICAL REPORT

Ultrasound-Guided Percutaneous Peripheral Nerve Stimulation for the Treatment of Lower Extremity Pain: A Rare Case Report

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■ **Abstract**

Objective: This case report presents an application of percutaneous peripheral nerve stimulation to the right superficial peroneal nerve to treat a patient with chronic intractable L5–S1 radiculopathy pain that conventional treatment failed to ameliorate.

Methods: The patient underwent an uneventful implantation of a percutaneous peripheral nerve stimulator. The implanted lead (15 cm in length and 1.2 mm in diameter) containing the receiver coil and 3 stimulation electrodes (Bioness Stimrouter®, Valencia, CA, U.S.A.) was implanted parallel with the trajectory of the right superficial peroneal nerve.

Results: Two weeks after implantation of the percutaneous peripheral nerve stimulator, the patient experienced excellent pain relief and reported a significant increase in mobility. At the 3-month follow-up consultation, the patient reported maintenance of the reduction of pain in his right lower extremity as well as improved performance in his daily activities.

Conclusion: Percutaneous peripheral nerve stimulation offers an alternative treatment option for intractable pain associated with chronic radiculopathy, especially for patients in whom conventional treatment options have been exhausted. Further clinical series involving larger numbers of patients are warranted in order to assess the definitive role of percutaneous peripheral nerve stimulation for the treatment of chronic intractable radiculopathy pain. ■

Key Words: chronic pain, neuropathic pain, lumbosacral radiculopathy, percutaneous nerve stimulation, peripheral nerve stimulation, case report

BACKGROUND

Lumbosacral radiculopathy (LSR), like other forms of radiculopathy, results from nerve root impingement and/or inflammation that has progressed enough to cause neurologic symptoms in the dermatome and myotome that are supplied by the affected nerve root (s). In the United States it is believed to occur in approximately 3% to 5% of the population, with men and women being affected in equal proportion, although men are most likely to develop symptoms in their 40s, whereas women are affected most commonly between the ages of 50 and 60 years. Of the patients who suffer

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from this condition, 10% to 25% develop symptoms that persist for more than 6 weeks.[1]

The pain associated with LSR usually arises from damage caused to the sinuvertebral nerve and/or the nerve root, the 2 structures capable of transmitting neuronal impulses that result in the experience of pain. The impingement of these structures, most commonly the nerve root by herniation of the intervertebral disc into the epidural space, is thought to initially result in direct toxic injury to the nerve root by chemical mediation (eg, phospholipase A2, thromboxanes, metalloproteinases, among other agents) and then exacerbation of the ensuing intramural and extraneural swelling, which results in venous congestion and conduction block.[1,2] Treatment options include lifestyle modifications, medications, physical therapy, corticosteroid injections, and decompressive surgery. Additionally, in carefully selected patients with chronic LSR, previously unresponsive to medical and surgical treatment, spinal cord stimulation (SCS) has been used, with moderate to high success rates.[3,4]

Chronic radicular pain in the extremities, presumably the most commonly occurring form of neuropathic pain, may present a challenge in terms of long-term management.[1] Over the past 2 decades, electrical neuromodulation techniques have re-emerged as a viable technical approach in the surgical treatment of medically refractory neuropathic pain, eclipsing several other available procedures. For instance, in an extensive review and meta-analysis of conventional SCS by Taylor et al., more than half of all patients with chronic back and leg pain experienced significant pain relief. The researchers observed that this was maintained for a mean follow-up period of 24 months. This review is one of several demonstrating that electrical neuromodulation is an effective treatment option for a cohort that is notoriously difficult to treat.[4,5]

Despite their growing popularity, electrical neuromodulation techniques do not come without shortcomings.[3,4,6] One of the issues in the use of spinal cord neuromodulation for pain in the extremities is the frequently encountered inability to keep the stimulation field steady enough to match the area of paresthesia with the area of pain.[3] Furthermore, central neuraxial stimulation approaches often fail to discretely provide sustained therapeutic paresthesia over the patient's painful area.[3,4,6] Among different types of neuromodulation, percutaneous peripheral nerve stimulation (PNS) holds the unique position of being the least invasive and at the same time the least established in terms of scientific evidence and regulatory approvals. However, it is now gaining tremendous momentum in terms of accumulation of clinical experience and development of new indications, and may be particularly effective, either as a stand-alone therapy or as an adjuvant to SCS, when the pain is localized to a part of a single extremity.[3,4,6]

It has been hypothesized that pain relief from PNS, as sensed through paresthesia, is mediated by antegrade (orthodromic) stimulation of non-nociceptive Aβ fibers present in the free nerve endings of the peripheral nervous system, which results in the activation of the same interneurons that are involved in the processing and transmission of nociceptive information by peripheral Aβ and C nerve fibers in the superficial layers of the dorsal horn of the spinal cord.[4,6,7]

This case report presents the story of an elderly male patient who underwent implantation of a percutaneous PNS along the trajectory of the right superficial peroneal nerve to treat a chronic L5 radicular pain, previously unresponsive to SCS. To our knowledge, this is the first English-language literature description of a case where a percutaneous PNS was successfully implanted distally to the site of pain generation (in this case the L5–S1 neural foramen) for the treatment of chronic lumbosacral radiculopathy pain.

CASE DESCRIPTION

A 73-year-old male patient with a medical history significant for multiple lumbar surgeries complicated by methicillin-resistant *Staphylococcus aureus,* epidural abscess, post-laminectomy syndrome, and SCS implantation/explantation presented at our pain medicine outpatient clinic for further evaluation of chronic, intractable, right lower extremity pain. He characterized the pain as shooting and shock-like, located predominantly in his right lateral leg and dorsal foot, with corresponding ambulatory limitation.

Prior to presenting at our pain medicine outpatient clinic, the patient had undergone implantation of an SCS at a different institution. SCS leads had been implanted at the level of T10 and paresthesia obtained at the heel and arch of the right foot, which was partially successful in decreasing the pain intensity. However, the SCS was inconsistent in regards to ameliorating the symptoms in the right lateral leg, the area where the patient complained the pain was most intense.

Physical examination was notable for significant weakness with great toe extension, toe flexion, foot

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eversion, and inability to rise up onto his toes or heels. MRI revealed extensive scar tissue in the right L5–S1 lateral recess and neural foramen (Figures 1 and 2). Electromyography (EMG) revealed chronic L5 and S1 radiculopathies and length-dependent sensorimotor peripheral neuropathy, primarily axonal in nature.

While multiple lines of evidence congruently identified a right L5 radiculopathy and a length-dependent sensorimotor peripheral neuropathy, the patient predominantly experienced pain distally in the right superficial peroneal nerve distribution. Therefore, a diagnostic ultrasound-guided superficial peroneal nerve block was performed using 2 mL of 0.25% bupivacaine. This block provided 80% reduction in pain for 2 days. Within a few months, after informed decision making, he underwent placement of a percutaneous PNS (Bioness StimRouter®, Valencia, CA, U.S.A.) along the trajectory of the right superficial peroneal nerve. Ultrasound (US) guidance was used to identify the superficial peroneal nerve between the anterior and lateral leg compartments (Figure 3). Intraoperative stimulation of the nerve was obtained at 1.5 milliamps.

Two weeks after implantation of the percutaneous PNS, the patient reported he was walking 5 times farther than his typical morning walk and experienced a reduction of pain from 8 out of 10 to 1 out of 10 on the numeric rating scale (NRS). At the 3-month follow-up consultation, the patient reported maintenance of the reduction of pain in his right lower extremity with the implanted percutaneous PNS and improved performance in his daily activities.

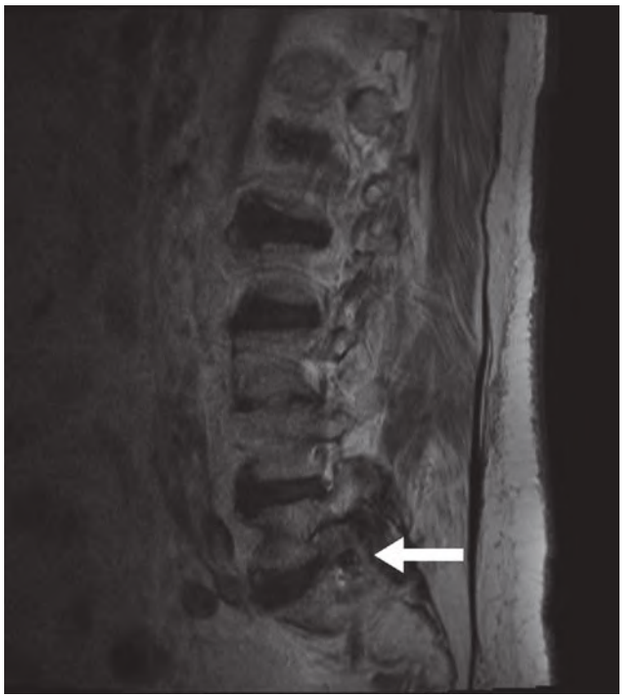

Figure 1. MRI revealing extensive scar tissue in the right L5–S1 lateral recess and neural foramen (sagittal view). White arrow points to the L5–S1 neural foramen.

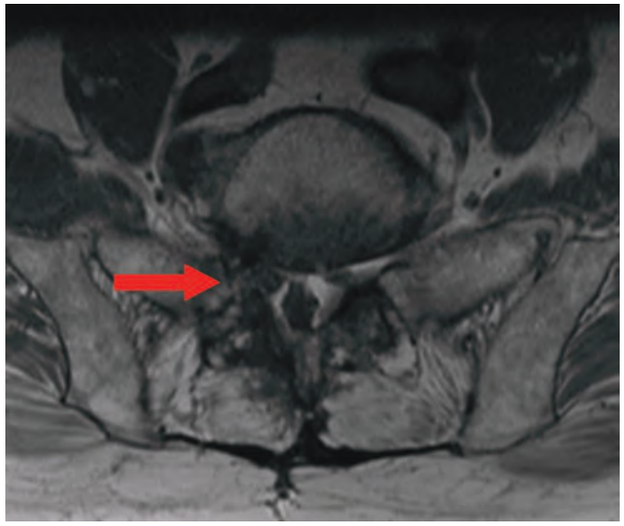

Figure 2. MRI revealing extensive scar tissue in the right L5–S1 lateral recess and neural foramen (axial view). Red arrow points to the L5–S1 neural foramen.

DISCUSSION

Pain modulation in the peripheral nervous system is mainly controlled by the nociceptive system. Primary nociceptive neurons in the periphery contain free nerve endings (Aδ and C fibers) that respond to noxious stimuli or tissue injury (eg, thermal or chemical). These stimuli originate nociceptive signals that travel into the spinal cord, where they synapse with second-order neurons in the grey matter of the dorsal horn. Some of these second-order neurons contain axons that ascend the spinal cord and project to the brainstem or thalamocortical system, where the conscious pain response is generated.[6,7] Another way through which nociceptors can mediate pain signaling is by the release of neuropeptides (eg, substance P, calcitonin gene-related peptide) at the terminal end of peripheral nerve fibers, leading to an increased inflammatory response, also known as neurogenic inflammation, and causing further local changes that magnify the pain response (eg, vasodilation, plasma extravasation, attraction of macrophages, degranulation of mast cells).[6]

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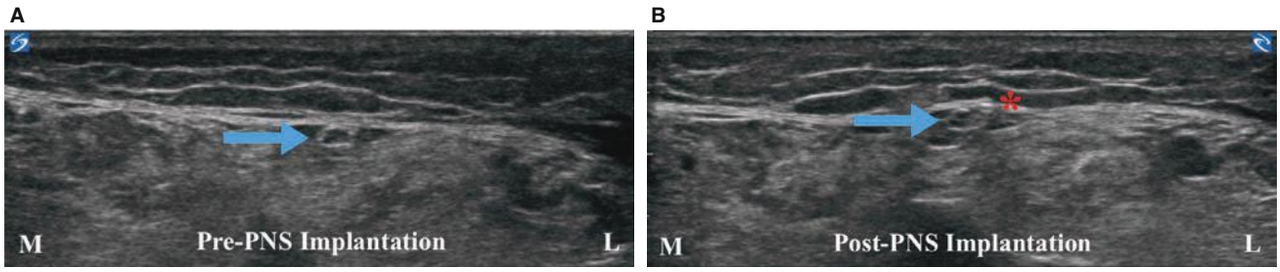

Figure 3. A, Intraoperative ultrasound imaging showcasing the trajectory of the superficial peroneal nerve between the anterior and lateral leg compartments (before stimulator implantation). Blue arrow points to the superficial peroneal nerve (fascicular bundle to the right of the arrow). L, lateral; M, medial; PNS, peripheral nerve stimulator. B, Intraoperative ultrasound imaging showcasing the percutaneous PNS placement along the trajectory of the superficial peroneal nerve between the anterior and lateral leg compartments (after stimulator implantation). *Peripheral nerve stimulator (bright white spot to the left of the asterisk. Blue arrow points to the superficial peroneal nerve (fascicular bundle to the right of the arrow).

The original explanation for the mechanism of action of PNS, based on the Gate Control Theory by Wall and Melzack (1965)[7,8], postulates that orthodromic stimulation of non-nociceptive Aβ nerve fibers results in the activation of the interneurons of the superficial layers of the dorsal horn of the spinal cord, the same interneurons that are involved in the processing and transmission of nociceptive information by peripheral Aβ and C nerve fibers. This nonpainful stimulation provided by PNS inhibits these interneurons, therefore decreasing or interrupting the transmission of pain signals.[7] Furthermore, some studies have suggested that PNS may also directly change the excitability of peripheral nerve fibers, increasing the threshold for nociceptive stimulation to occur.[6,7] It is possible that this direct peripheral inhibition happens through an alteration in the local concentrations of biochemical mediators that enhance pain response. By altering the local concentrations of neurotransmitters and endorphins, it is possible that PNS directly inhibits some of the mechanisms responsible for peripheral neurogenic inflammation.[6,7]

In this case, an elderly male patient underwent a successful implantation of a percutaneous PNS along the trajectory of the right superficial peroneal nerve to treat a chronic lumbosacral radiculopathy pain, which had previously been unresponsive to SCS.

Considering the patient's medical history strongly in favor of chronic L5 radiculopathy pain, as noted by leg pain in the context of previous multiple lumbar surgeries, post-laminectomy syndrome, and asymmetric leg muscle weakness on physical examination, associated with the findings of extensive scar tissue in the right L5–S1 lateral recess and neural foramen in the MRI, some controversy might arise when discussing the utilization of EMG in this case. Although a lot is debatable in regards to the usage of EMG for the diagnosis of extremity pain, in this case in specific the patient underwent the examination taking the following into consideration:

1. EMG may be used to effectively exclude other conditions that might mimic radiculopathy, such as an entrapment neuropathy or other forms of peripheral neuropathy. As demonstrated by Haig et al.,[8] the diagnostic impression may often be altered after electrodiagnostic testing.
2. Electrodiagnostic testing can to some extent suggest severity, or extent of the disorder beyond the clinical symptoms. Involvement of other extremities can be delineated or the involvement of multiple roots may be demonstrated.
3. There is utility in solidifying a diagnosis. An unequivocal radiculopathy on EMG helps in reducing diagnostic uncertainty and may identify avenues of management previously not considered.[9]

When analyzing this case in detail, it is also important to consider the hypothesis of a double crush syndrome (DCS) as a possible etiology for the patient's complaints. Considering the lower limb, currently available literature on DCS is sparse, and although a few investigators have established a possible overlap of distal peripheral entrapment in the lower extremities in patients with lumbar neural compression,[9] at this time a complete understanding of the disease process remains elusive.[10,11] Recently, US has been proposed as a useful adjuvant tool to improve electrodiagnostic testing for the diagnosis of peripheral nerve conditions. Given the inexpensive, noninvasive nature of US, its use is likely to become more common in the future. However, at this

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time there is still no absolute confirmatory test, and thus no method for an accurate diagnosis of DCS.[11] In this case, we find the hypothesis of DCS unlikely when compared to an isolated L5 radiculopathy pain based on the following: (1) no evidence of entrapment neuropathy in the electrodiagnostic testing; (2) no evidence of peripheral nerve injury to the superficial peroneal nerve during the pre-procedural US scan, namely, no evidence of nerve swelling/neuroma or pain during sonopalpation of the emergence of the superficial peroneal nerve at the lateral side of the fibular head/neck; and (3) right L5–S1 nerve root impingement at the lateral recess and neural foramen, confirmed by both MRI and EMG.

This case report is unique in the sense that the stimulator was implanted proximally to the area where the pain was the most intense, instead of proximally to the area where the pain stimulus was being generated (right L5–S1 nerve root impingement at the lateral recess and neural foramen, confirmed by both MRI and EMG).

This case report raises new important questions concerning our understanding of the physiology of pain signaling and the mechanism of action of PNS. Specifically, it is likely that the mechanism of pain suppression with PNS is far more complex than simple peripheral and spinal inhibition. This question has been addressed in recent neuroimaging studies of patients with chronic migraine, which convincingly indicate the presence of central mechanisms of PNS action. These may include both suppression of activity in pain-processing cerebral circuits and activation of areas that are involved in the descending system of pain control and modulation.[6,7]

CONCLUSIONS

Chronic lumbar radiculopathy pain is often treated with lifestyle modifications, physical therapy, medications, epidural steroid injections, surgeries, and SCS. The volume and diversity of therapeutic approaches are a testament to the challenging nature of providing lasting pain relief for this condition.

This case report suggests that for patients experiencing chronic radicular pain predominantly confined to the superficial peroneal nerve distribution, implantation of a percutaneous PNS may provide pain relief where other options have failed.

Further clinical series involving larger numbers of patients are warranted in order to assess the definitive role of percutaneous PNS for the treatment of chronic intractable radiculopathy pain.

ACKNOWLEDGEMENTS

The authors would like to thank Jeff Cara, DO, and Michael Osborne, MD, from the Department of Pain Medicine at Mayo Clinic for their contributions to this work.

CONFLICTS OF INTEREST

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Ultrasound-Guided Percutaneous Peripheral Nerve Stimulation for the Treatment of Chronic Intractable Pain Following a Lipofibromatous Hamartoma of the Median Nerve - A Rare Case Report.

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(1) - Department of PM&R, Central Lisbon University Hospital Center. Lisbon, Portugal; (2) - Department of Pain Medicine, Mayo Clinic. Jacksonville, USA; (3) - Department of Orthopedic Surgery, Mayo Clinic. Jacksonville, USA; (4) - Department of Anesthesiology and Perioperative Medicine, Mayo Clinic. Jacksonville, USA.

CASE DESCRIPTION

A 50-year-old woman presented at our Pain Medicine outpatient clinic for further evaluation of a chronic, severe, intractable pain of the left upper extremity after being diagnosed with a Lipofibromatous Hamartoma (LFH) of the left median nerve (MN) during surgical release of the carpal tunnel. At observation the patient described left upper extremity pain that she rated as an 8-9/10 on the numeric rating scale (NRS). She also described sharp, shooting, squeezing, throbbing pain that worsened with using her left hand as well as loss of sensation and weakness in the distal part of the hand and fingers. To quote her directly she noted, "I want to cut off my hand".

Using ultra high frequency (UHF) ultrasound (US) (at 50MHz) the boundaries of the LFH to the unaffected MN were determined (Figures 1 and 2) and an US-guided block of the MN was performed, which proved to be successful in ameliorating the pain in the patient's forearm and hand. After the success of the block was established the patient was submitted to an US-guided placement of a percutaneous peripheral nerve stimulator (PNS) (Bioness Stimrouter®, Valencia, CA) in the trajectory of the left MN. Two stimulator electrodes were implanted longitudinally just distal to the elbow but proximal to the LFH with excellent stimulation coverage of the nerve achieved at 1.2 and 1.4 milliamp, respectively (Figures 3 and 4).

After an uneventful procedure, the pain score immediately decreased from 8-9/10 to <6 on the NRS. Two weeks after the procedure the patient reported continued significant pain relief, with an average pain level of 6/10, located mainly in the distal part of the hand. At the six-month follow-up consultation the patient maintained continued pain relief and reported no adverse events of any kind with the implanted PNS.

FIGURES

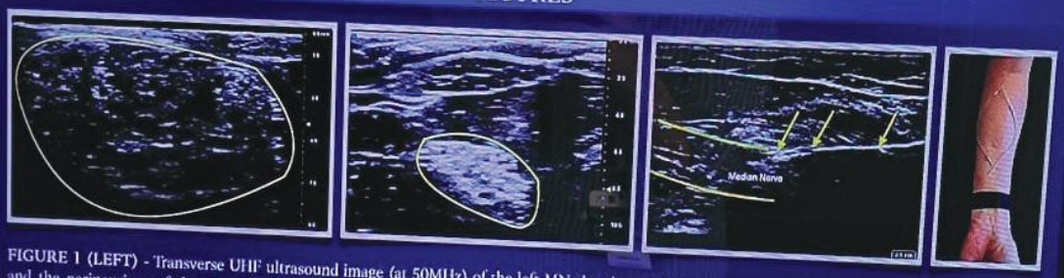

FIGURE 1 (LEFT) - Transverse UHF ultrasound image (at 50MHz) of the left MN showing proliferation of mature adipocytes within the epineurium and the perineurium of the nerve; **FIGURE 2 (CENTER LEFT)** - Transverse UHF ultrasound image (at 50MHz) of the normal appearing MN proximal to the LFH; **FIGURE 3 (CENTER RIGHT)** - Longitudinal UHF ultrasound image (at 50MHz) of the stimulator electrode implanted along the trajectory of the MN just distal to the elbow; **FIGURE 4 (RIGHT)** - Peripheral nerve stimulator placed over a volunteer's forearm skin, showcasing the trajectory of the leads implanted in the patient.

DISCUSSION

The original explanation for the mechanism of action of PNS, based on the Gate Control Theory by Wall and Melzack (1965), postulates that orthodromic stimulation of non-nociceptive Aβ nerve fibers results in the activation of the interneurons of the superficial layers of the dorsal horn of the spinal cord, the same interneurons that are involved in the processing and transmission of nociceptive information by peripheral Aβ and C nerve fibers. This non-painful stimulation provided by PNS inhibits these interneurons, therefore decreasing or interrupting the transmission of pain signals [1]. Furthermore, some studies have suggested that PNS may also directly change the excitability of peripheral nerve fibers, increasing the threshold for nociceptive stimulation to occur [1,2]. It is possible that this direct peripheral inhibition happens through an alteration in the local concentrations of biochemical mediators that enhance pain response. By altering the local concentrations of neurotransmitters and endorphins, it is possible that PNS directly inhibits some of the mechanisms responsible for peripheral neurogenic inflammation [1,2].

In this case, a 50-year-old female patient underwent a successful implantation of a percutaneous PNS along the trajectory of the left MN to treat a chronic, severe, intractable left upper extremity pain. This is unique and innovative in regards that to our knowledge this is the first description in the English literature of a case where a LFH was successfully treated by way of implantation of a percutaneous PNS.

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Early Intervention with Peripheral Nerve Stimulation for Complex Regional Pain Syndrome

Bryce Cole Holmgren MD, Scott Pritzlaff MD, Micheal Leong MD, Einar Ottestad MD

Introduction

Complex regional pain syndrome (CRPS) is a debilitating condition that is frequently refractory to treatment.

Until recently, **peripheral nerve stimulation (PNS)** was a treatment option that has largely been ignored due to lack of user-friendly, commercially available systems.

We present a case of a patient who with CRPS who underwent successful treatment with PNS.

Methods

Informed consent was obtained for this case presentation. A **single lead percutaneous PNS system (StimRouter, Bioness Inc)** was used (FIGURE 1).

The **median nerve was targeted in mid forearm** due to ease of placement, patient ergonomics, and decreased risk of migration.

Peripheral Nerve Stimulator (PNS) System

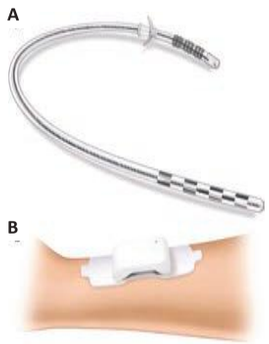

FIGURE 1:
A) Implantable electrode. A barbed end anchors the electrode within 1-2 mm of the target nerve.

B) External Pulse Transmitter (EPT) generates electrical impulses via transcutaneous induction

PNS Implantation

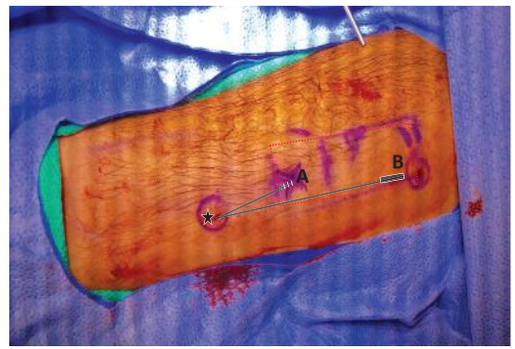

FIGURE 2: Lead placement targeting the median nerve in the forearm. The lead entry site incision (✯) was marked ahead of time. Ideally, 5cm of lead exists between the electrode contacts (A) at the nerve target and the skin to minimize migration. The lead is then tunneled proximally to the antecubital fossa. The receiver (B) and contacts (A) will be covered by the external pulse transmitter (red dotted rectangle).

Ultrasound Approach for PNS

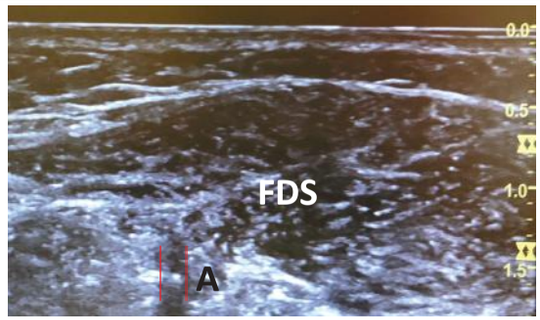

FIGURE 3: Short axis view of the median nerve (A) at the mid-forearm. The introducer (red double lines) used for placing the 3-contact lead is adjacent to the nerve. FDS = flexor digitorum superficialis.

Case Report

A 52-year-old man presented for pain management after suffering a forearm laceration. He underwent **complex surgical median nerve repair but had escalating, diffuse, non-dermatomal pain in the arm and hand and was diagnosed with CRPS type II**. He failed numerous medications and was unable to participate in desensitization therapy. **An ultrasound-guided right median nerve block at the mid-forearm provided a 90% reduction in pain**.

We then proceeded with placement of an implantable median nerve PNS system (FIGURE 2). An **out-of-plane approach was employed in order to place the lead parallel with the median nerve** (FIGURE 3).

Results

- The patient had immediate **70-80% improvement** in his pain when the device was turned on.
- At his most recent follow up 6 months after implantation he continues to report significant (70-80%) reduction in his pain.
- Additionally the patient has had improvement in the grip strength of his right had at 6 months.

Discussion

Percutaneous stimulation is a viable alternative to other therapies in the **treatment of CRPS especially early in the treatment course**. Careful consideration during the placement of these devices is critical to the success of the intervention.

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A case series on the use of peripheral nerve stimulation for focal mono-neuropathy treatment

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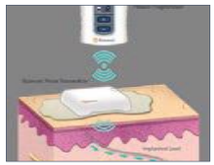
Introduction

Peripheral mono-neuropathy can be debilitating for the patient and difficult to treat. Current neuromodulation treatment systems have relied more heavily on dorsal column spinal cord and dorsal root ganglion stimulators. With the localizing source of pain usually being a peripheral nerve, it is reasonable to consider a more focally targeted neuromodulation device that uses less overall energy and more selective targeting of current.

In peripheral nerve stimulation (PNS) using the Bioness Stimrouter system, intradermal leads are placed along the peripheral nerve sheath and secured via a deployable anchoring system. One prior study has evaluated the efficacy of the Bioness Stimrouter system[1], but there are no studies describing the specific nerves innervated, or the system's effects on opioid use and functional activity. We present a 39 patient case series looking at peripheral nerve stimulation on various isolated mono neuropathies in reducing VAS score, opioid consumption, and increased functional activity post stimulation.



Methods

A case-series of 39 patients with a total of 42 implants were enrolled starting in August 2017 at various pain management centers in the United States with no exclusion for participation. Patients were surveyed before and after device implantation. 54% of the patients surveyed were female and 46% were male.

Results

Of the 39 patients studied, 78% of the participants noticed an improvement in their pain. There was a 71% reduction in pain scores with the average pre-procedure score of 8 improving to 2 post-implant. The greatest reduction in pain scores were seen in the lateral femoral cutaneous nerve with pre-implant pain scores improving from an average of 8 to 0 (100% reduction in pain score) post implantation. The smallest pain score improvement (29%) was seen when PNS was implanted into the intercostal nerve with (n=1).The axillary (47%) and tibial nerves (11.9%) were the most commonly implanted and achieved an average pain reduction score of 69% and 64% respectively. The lateral femoral cutaneous implants had the highest pain reduction of 100%. Participants noted on average a 72% improvement in activity with the greatest noted in the brachial plexus (80%) and suprascapular nerve (80%) and smallest in the intercoastal nerve (40%).

Results (continued)

Of the nineteen patients on opiates prior to their procedure, 94% of them have noticed a 50% or greater reduction in opiate consumption. Self-reported activity levels improved in 100% of the patients after peripheral nerve stimulator implantation.

Table 1.

Location	N	VAS Prior to Implant	VAS After Implant	Change (%)
Total	39	8.2	2.4	0.7
Lateral Femoral Cutaneous	3	8.3	0.0	100.0
Genitofemoral	1	10.0	1.0	90.0
Illeoinguinal	1	10.0	1.0	90.0
Sural	1	8.0	2.0	75.0
Peroneal	3	9.0	2.3	74.1
Axillary Nerve	18	8.0	2.4	70.1
Suprascapular	1	9.0	3.0	66.7
Saphenous	3	7.7	2.7	65.2
Tibial	5	7.8	2.6	66.7
Brachial Plexus	2	9.5	4.5	52.6
Intercostal	1	7.0	5.0	28.6

Results (continued)

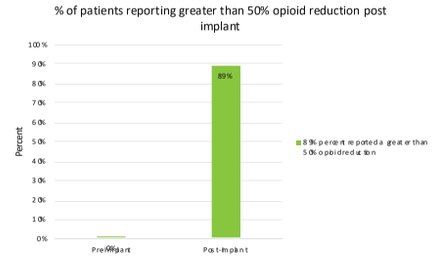


Figure 1: Percent of patients reporting greater than 50% opioid reduction pre- and post- implant with Bioness Peripheral Nerve Stimulator

Conclusion

Peripheral nerve stimulators are a new, minimally invasive neuromodulation modality that shows promising early results in our 39-patient case-series. Further exploration of use of peripheral nerve stimulation should be encouraged in our pain management treatment algorithm.

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1.Deer T, Pope J, Benyamin R, et al. Prospective, Multicenter, Randomized, Double-Blinded, Partial Crossover Study to Assess the Safety and Efficacy of the Novel Neuromodulation System in the Treatment of Patients With Chronic Pain of Peripheral Nerve Origin. *Neuromodulation*. 2016;19(1):91-100.

Authorship Statement

Krishnan Chakravarthy MD, PhD is a consultant to Abbott, Medincell, and Bioness Inc. He is a founder of Newrom Biomedical and Douleur Therapeutics

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Use of Ultrasound for Placement of a Novel Peripheral Nerve Stimulator for Chronic Neuropathic Pain: Single Institution Results

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Department of Anesthesiology, Perioperative and Pain Medicine, Stanford School of Medicine

Introduction

Management of neuropathic pain continues to remain challenging and current available treatments are often insufficient which has resulted in a renewed interest in the use of neuromodulation for the treatment of peripheral neuropathic pain. However, treatment of peripheral neuropathies via neuromodulation has been hindered by lack of devices designed specifically for this purpose secondary to adapting device size for pulse generators designed for spinal cord stimulation.

The StimRouter System features a novel fully implanted one-piece lead with an inductively powered system designed specifically for the treatment of mononeuropathies of lower and upper extremities, pelvis, and trunk. Various techniques for placing this device, including both fluoroscopic guidance and ultrasound guidance have been used, both allowing quick recovery times. With ultrasound guidance, precise anatomical localization is possible. Once programmed, the unit can be turned on and off, titrated, and variables modified by the patient per their function level as an adjunct for the management of chronic neuropathic pain.

The StimRouter System offers a new avenue for directed treatment of mononeuropathies with customizable treatment per patient needs.

Figures

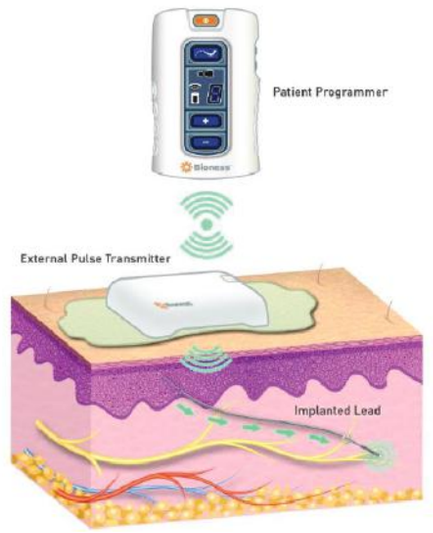

Figure 1 StimRouter System showing implanted lead with external pulse transmitter which is applied via adhesive device with patient programmer to control device. (Courtesy Bioness)

Figure 2 Implantable Lead showing anchor system, receiver to be oriented with external pulse transmitter and stimulation electrode to be placed by targeted nerve.

Results

Demographics	
Gender	8 Male, 13 Females
Age	56.2 y (19-85)

Mononeuropathies	
Nerve	# of Systems
Lateral femoral cutaneous	5
Tibial	4
Saphenous	3
Sural	3
Ilioinguinal	2
Suprascapular	2
Axillary	1
Genitofemoral	1
Pudendal	1
Radial	1

Follow Up	
Available for 19 of 21 patients	
50% of Greater Relief	Less than 50% Relief
11 patients	8 patients
Avg: 85.12% relief	Avg: 16.25% relief

Complications
1 removed secondary to complication
1 secondary to skin breakdown at site from overuse

Methods

At our institution 21 patients had 23 StimRouter Systems implanted for various mononeuropathies under ultrasound guidance from January 2017 to November 2017. We describe the patients' follow up, experience, and response of peripheral nerve stimulation for the treatment of various mononeuropathies. IRB approval was obtained.

Discussion

StimRouter systems marks the first dedicated minimally invasive device for peripheral nerve stimulation. Unique is the ease of placement with ultrasound and minimally invasive nature of the device. Our experience shows ease of placement and significant improvement in several patients and reinforces an expanded role for peripheral nerve stimulation. However, high comparative variability of patients with peripheral neuropathy has implications on treatment and continued experience with peripheral nerve stimulation for the treatment of chronic neuropathic pain is needed to further refine techniques and more accurately identify patients who may benefit the most from such interventions as identified by our results.

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StimRouter®

Clinical Study Summary

Bioness®

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Clinical Study Results

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With

luigbo, MD†;
ortocarrero, PhD‡;
erberg, PhD§;

Prospective, Multicenter, Randomized, Double-Blinded, Partial Crossover Study to Assess the Safety and Efficacy of the Novel Neuromodulation System in the Treatment of Patients With Chronic Pain of Peripheral Nerve Origin

Timothy Deer, MD*; Jason Pope, MD†; Ramsin Benyamin, MD‡; Ricardo Vallejo, MD, PhD§; Andrew Friedman, MD¶; David Caraway, MD, PhD**; Peter Staats, MD††; Eric Grigsby, MD, MBA‡‡; W. Porter McRoberts, MD§§; Tory McJunkin, MD¶¶; Richard Shubin, MD***; Payam Vahedifar, MD†††; Daryoush Tavanaiepour, MD‡‡‡; Robert Levy, MD, PhD§§§; Leonardo Kapural, MD, PhD¶¶¶; Nagy Mekhail, MD, PhD****

Primary Efficacy

At 3-months the group receiving StimRouter treatment demonstrated a **statistically significant improvement** in pain as compared to the control group ($p<0.0001$).

Primary Safety

No serious adverse events related to the device were reported during the duration of the study (12-months).

Secondary Outcomes

The treatment group had significantly more **favorable outcomes related to quality of life** and satisfaction as compared to those in the control group.

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Clinical Study Results

50% of the treatment group rated their **satisfaction 8 or higher** on a 10 point scale

53% of the treatment group rated their global impression of change in activity limitations, symptoms, emotions and **overall quality of life** related to their painful condition between 5-7 on a 7-point scale

31% of the treatment group rated their **satisfaction at a 10** on a 10-point scale

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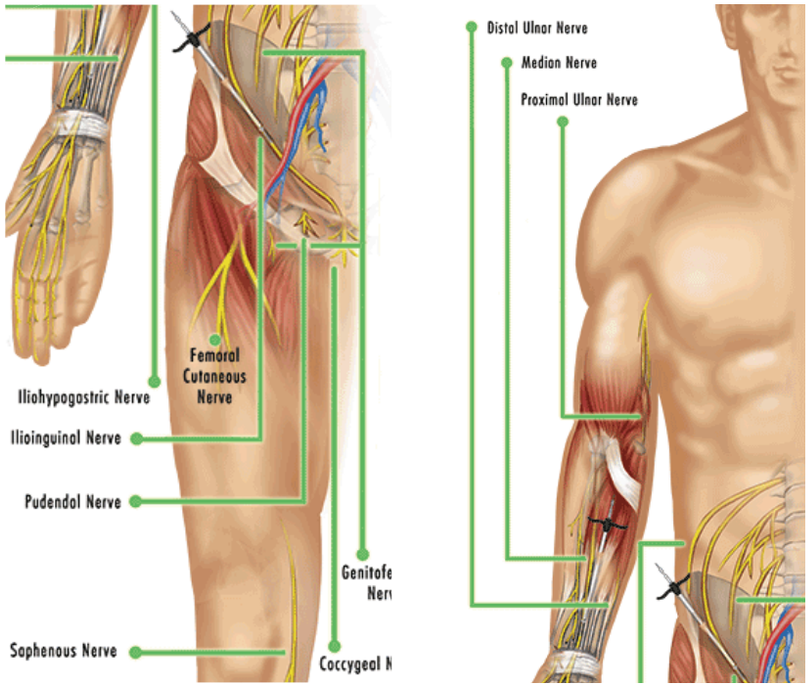
Clinical Trial Peripheral Nerve Sites



Arm

Ulnar (15), Median (8), Radial (2), Axillary (1), Suprascapular (1)

Leg

Peroneal (8), Saphenous (7), Tibial (4), Femoral cutaneous (4), Femoral (3), Sural (1), Genitofemoral (1)

Trunk

Ilioinguinal (13), Intercostal (12), Suprascapular (6), Pudendal (3), Iliohypogastric (2), Coccygeal (1), Genitofemoral (1) Superior cluneal (1)

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(onlinelibrary.wiley.com) DOI: 10.1111/ner.12381

Prospective, Multicenter, Randomized, Double-Blinded, Partial Crossover Study to Assess the Safety and Efficacy of the Novel Neuromodulation System in the Treatment of Patients With Chronic Pain of Peripheral Nerve Origin

Timothy Deer, MD*; Jason Pope, MD†; Ramsin Benyamin, MD‡; Ricardo Vallejo, MD, PhD§; Andrew Friedman, MD¶; David Caraway, MD, PhD; Peter Staats, MD††; Eric Grigsby, MD, MBA‡‡; W. Porter McRoberts, MD§§; Tory McJunkin, MD¶¶; Richard Shubin, MD***; Payam Vahedifar, MD†††; Daryoush Tavanaiepour, MD‡‡‡; Robert Levy, MD, PhD§§§; Leonardo Kapural, MD, PhD¶¶¶; Nagy Mekhail, MD, PhD****

Introduction: Currently available central nervous system treatment strategies are often insufficient in management of peripheral neuropathic pain, prompting a resurgence of neuromodulation focused on peripheral pain. A new peripheral nerve stimulation device was investigated in a prospective, randomized, double blind, crossover study, looking specifically at efficacy and safety, with Food and Drug Administration oversight.

Methods: Prospective, multicenter, randomized, double-blind, partial crossover study to assess safety and efficacy. After IRB approval, patients were enrolled, implanted, and then followed for three months to assess efficacy and one year for safety based on Food and Drug Administration guidance.

Results: One hundred forty-seven patients were consented and screened for the study. Thirty-five did not meet inclusion or exclusion criteria. Ninety-four patients were implanted and then randomized to the treatment (45) or the Control group (49). The primary efficacy endpoint, three months after randomization to treatment, demonstrated that patients receiving active stimulation achieved a statistically significantly higher response rate of 38% vs. the 10% rate found in the Control group ($p = 0.0048$). Improvement in pain was statistically significant between the randomized groups, with the Treatment group achieving a mean pain reduction of 27.2% from Baseline to Month 3 compared to a 2.3% reduction in the Control group ($p < 0.0001$). During the partial crossover period, patients again demonstrated statistically significant improvement in pain relief with active stimulation compared to baseline. Further, the Treatment group had significantly better improvement than the Control group in secondary measures including but not limited to quality of life and satisfaction. Safety, assessed throughout the trial and with follow-up to one year, demonstrated no serious adverse events related to the device. All device-related adverse events were minor and self-limiting.

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For more information on author guidelines, an explanation of our peer review process, and conflict of interest informed consent policies, please go to http://www.wiley.com/WileyCDA/Section/id-301854.html

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Conclusion: The novel peripheral nerve stimulation device is a safe and effective treatment strategy to address neuropathic pain of peripheral nerve origin.

Keywords: Bioness, chronic pain, peripheral nerve, StimRouter, study

Conflict of Interest: David Caraway serves as a consultant to Medtronic, Stimwave, and Nevro. David Caraway is currently employed by Nevro. Eric Grigsby is the CEO of Neurovations. Tory McJunkin serves as a consultant to St. Jude Medical, Medtronic, and Axonics Modulation. Tory McJunkin owns stock in St. Jude Medical and Nevro. Peter Staats has no conflicts of interest to report, other than being an investigator for Bioness. W Porter McRoberts has no conflicts of interest to disclose. Robert Levy serves as a consultant to Bioness, Inc., Nevro, Inc., Medtronic, Inc., Spinal Modulation, Inc., St. Jude Medical, Inc., and Vertos, Inc. Dr. Levy has been awarded stock options from Bioness, Inc., Nevro, Inc., Spinal Modulation, Inc., and Vertos, Inc. Ricardo Vallejo serves on the advisory board of Halyard and serves as a consultant speaker for St. Jude Medical and Boston Scientific. Dr. Vallejo receives grants for research through Boston Scientific and Nevro. He is also involved in clinical trials with Nevro, Medtronic, St. Jude Medical, and Halyard. Leonardo Kapural serves on the advisory board for SPR Therapeutics and Neuros. Dr. Kapural also serves as a consultant for St. Jude Medical. Ramsin Benyamin serves on Advisory boards for Medtronic, Halyard, and Integral Spine Solutions. He also is a minor shareholder for Integral Spine Solutions. Jason Pope is a consultant for Medtronic and St Jude Medical. Dr. Pope serve as a consultant to Bioness in the past. Payam Vahedifar, Daryoush Tavanaiepour, Nagy Mekhail, Richard Shubin, and Andrew Friedman have no conflicts of interest to disclose. All authors except Jason Pope were investigators paid by the sponsor, Bioness.

INTRODUCTION

Neuromodulation has recently experienced a steep climb in innovation, with advances in new targets, waveforms, and implantable leads (1,2). Although these new innovations may improve pain coverage not historically captured with traditional spinal cord stimulation (SCS), they may fail to cover discrete mononeuropathies, or the pain pattern simply may not merit central nervous system access. Peripheral nerve stimulation (PNS) offers a possible solution, but has been hindered by the lack of devices designed specifically for the periphery (3). One limitation to adapting current SCS style devices for peripheral use is the size of the required implanted pulse generators. Whether radio-frequency (RF) coupled or fully implantable placement in the proximity of the peripheral lead is often difficult requiring lead extension tunneling and less than optimal siting of the implanted pulse generators. A design-specific PNS system offers an alternate choice (3), by providing a less invasive, less expensive, and energy efficient treatment (3,4).

The investigative device is specifically designed for the treatment of peripheral nerve pain in the lower and upper extremities, pelvis, and trunk. Craniofacial pain was not studied. The Food and Drug Administration (FDA) recommended avoidance of stimulation of the craniofacial region. The system requires implantation of a specially crafted lead that is powered by an external pulse transmitter (EPT). This pivotal study follows after a successful feasibility study with the purpose of demonstrating safety and efficacy in the treatment of peripheral nerve-related neuropathic pain.

The prevalence of neuropathic pain of peripheral origin is difficult to estimate, but contributes to nearly 8–10% of adults with neuropathic pain (5). As opioids continue to come under fire for lack of safety and efficacy (6–8), pain providers are looking to advanced techniques to manage pain more safely and cost effectively (9).

The features of this novel lead and inductively powered system is a significant innovation in the field of PNS. The fully implanted one-piece StimRouter lead (Fig. 1) containing the receiver, electrodes, and anchoring mechanism, is implanted using nerve stimulation via a test probe with the option of image guidance. Once implanted, the EPT is then utilized to power the system. The patient employs the Patient Programmer (Fig. 2) and EPT (Fig. 3) utilizing RF signals for communication.

The implanted lead is 15 cm in length and 1.2 mm in diameter, containing the receiver coil and three stimulation electrodes. The silicone anchor employed in the StimRouter System is four pronged in design, and ensures that the lead is adequately secured to the tissue.

As with other neuromodulation therapies for the central axis, the patient has a programmer to select desirable settings and the clinician/representative has a device programmer. For programming and daily use, the EPT is positioned directly over the receiver of the implanted lead by mounting it on a disposable electrode patch placed on the skin. Customization of the patient's waveform, intensity, pulse rate, phase duration, and treatment time, among other parameters, can be programmed and wirelessly downloaded to the EPT and Patient Programmer to allow for optimal, repeatable delivery of stimulation. Once programmed by the clinician, the patient can turn the unit on and off, change programs, and titrate intensity at an in-home environment. A rechargeable, lithium battery powers the EPT, under which lies the disposable electrode that is designed to be replaced every two to three days.

METHODOLOGY

Study Design, Patient Selection, and Randomization

The purpose of this study was to evaluate the safety and efficacy of the StimRouter System for use in the treatment of severe, intractable pain of peripheral nerve origin associated with posttraumatic or post-surgical neuralgia, exclusive of the craniofacial region. The study design is a prospective, multicenter, randomized, double-blind, partial crossover, three stage group (upper extremities, lower extremities, trunk) sequential study. Primary outcomes included pain relief and safety, measured by average pain at rest using a numerical rating scale (NRS) followed for three months (10), and safety, determined by assessment of adverse events (AEs) during the one-year study period. Analysis of primary and secondary measures was compared to baseline pre-implant values. A Responder was defined as having at least a 30% decrease in the NRS with no upward titration in the patient's pain medicine regimen. Secondary outcome measures included changes in medication dose, type, and frequency; quality of life using the Brief Pain Inventory (BPI) and Quality of Life SF-12v2 Health Survey (QoLSF-12v2); patient impression of improvement with treatment

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Figure 1. StimRouter lead illustration.

using the patient global impression of change scale (PGIC); change in worst pain using the NRS; change in interference of pain with physical and emotional functioning; patient satisfaction; and long-term safety at one year. The trial was performed at 13 independent study sites (Table 2) and Internal Review Board (IRB) approval was obtained by each site. The study was conducted with approval from the FDA and served as a pivotal study for clearance of the StimRouter Neuromodulation System in the United States.

Inclusion criteria:

- adults ($\geq$22 years) suitable for an implanted electrode for pain relief
- severe intractable chronic pain of peripheral nerve origin associated with posttraumatic/postsurgical neuralgia for $\geq$3 months
- worst chronic pain level in the last 24 hours $\geq$5/10 (on 0–10 NRS), where such pain is attributable to a lesion or disease of the somatosensory nervous system
- stable regimen of pain medications for at least four weeks prior to screening and willing and able to maintain an equivalent dosage of their current pain medications from randomization to three-month follow-up
- tolerate skin surface stimulation when using transcutaneous electrical nerve stimulation
- complete all required visits.

Exclusion criteria:

- decline to provide written consent or follow-up
- pregnant, plan on becoming pregnant, or are breastfeeding
- presence of active systemic infection

Figure 2. StimRouter patient programmer.

Figure 3. StimRouter EPT and disposable electrode patch.

- immunocompromised
- may need diathermy or therapeutic ultrasound at the implant site
- have an implanted medical device within 15 cm of the intended target for placement of the StimRouter System
- allergy to components of the device
- have bleeding disorders or active anticoagulation that cannot tolerate cessation for device placement.

Once the inclusion and exclusion criteria were met, patients were then implanted with the StimRouter Device and postoperative stabilization occurred, allowing 14–24 days postimplant for healing and recovery. The patient was then randomized using a centralized web-based system in a 1:1 fashion to either the Treatment or Control group. Randomization used the Pocock–Simon covariate adaptive randomization procedure so that approximately an equal number of patients were assigned to the Treatment and Control groups within each anatomical subgroup and within each study center. Please refer to Table 1. Both groups are well matched, demonstrating successful randomization, noting the lack of statistical difference by *p*-value comparison. The Treatment group received electrical stimulation from the StimRouter System and stable dosing of pain medications, while the Control group received no therapeutic stimulation and a stable dose of pain medications, both for 90 days. Patients had planned visits at 30, 60, and 90 days following the randomization, with continued follow-up for safety and secondary measures at 6 and 12 months. After the 90 day period, crossover to the Treatment group was offered to the Control group, and medications were then titrated as needed (Fig. 4).

At crossover, Control patients that began stimulation using the device were then followed over a 90-day treatment period for a secondary efficacy analysis. All participating patients were monitored for safety at each visit through 12 months (Fig. 5).

Intent to treat analysis and power justification was used to detect a difference in safety and efficacy outcomes. This required a minimum 90 patient enrollment with at least 70 patients completing three-month follow-up after receiving treatment with the StimRouter device for at least three months: 45 from the Treatment group, 25 from the Control group who crossed over to treatment and received electrical stimulation for three months. Using this sample size, the treatment could be claimed to be significantly better ($p \leq 0.05$) than the control when the Cochran–Mantel–Haenszel test statistic, adjusting for anatomic location and study center, is larger than 2.17.

Implant Procedure

The implant procedure has been described previously (3). After informed consent and appropriate preoperative comorbidity

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Table 1. Comparison of Baseline Characteristics Between Randomization Groups.

Variable	Demographics	All	Treatment ($N = 45$)	Control ($N = 49$)	p value
Gender	Male	39 (41.5%)	20 (44.4%)	19 (38.8%)	0.577
	Female	55 (58.5%)	25 (55.6%)	30 (61.2%)	
Age (years)	Mean ± SD	53.0 ± 11.1	52.8 ± 10.0	53.2 ± 12.1	0.875
Ethnicity	Caucasian	86 (91.5%)	40 (88.9%)	46 (93.9%)	0.571
	African-American	3 (3.2%)	2 (4.4%)	1 (2.0%)	
	Native American	1 (1.1%)	1 (2.2%)		
	Hispanic	3 (3.2%)	1 (2.2%)	2 (4.1%)	
	Other	1 (1.1%)	1 (2.2%)		
Work status	Employed	40 (42.6%)	18 (40.0%)	22 (44.9%)	0.749
	Worker's compensation	1 (1.1%)		1 (2.0%)	
	Unemployed	19 (20.2%)	11 (24.4%)	8 (16.3%)	
	Retired	18 (19.1%)	8 (17.8%)	10 (20.4%)	
	Other	16 (17.0%)	8 (17.8%)	8 (16.3%)	
Pain subgroup	LE	27 (28.7%)	13 (28.9%)	14 (28.6%)	0.978
	Trunk	41 (43.6%)	20 (44.4%)	21 (42.9%)	
	UE	26 (27.7%)	12 (26.7%)	14 (28.6%)	

LE, lower extremity; UE, upper extremity; SD, standard deviation.

management, the region of the body overlying the peripheral nerve is sterilely prepped and draped. Fluoroscopic or ultrasound imaging may be used to aid lead placement of the stimulation probe. A 1.0–1.5 cm incision is created approximately 7–10 cm from the desired stimulation target nerve. The distal end of the stimulation probe is placed in the desired location, near identified nerve, and evidence of target PNS is obtained via test stimulation through the probe. Once confirmed, the introducer set is placed over the stimulation probe and the probe is subsequently removed, allowing introduction of the lead. Stimulation is again confirmed by testing using the lead, and once reconfirmed; the introducer sheath is removed, deploying the four-pronged-anchor system (Fig. 3). A lead adapter is then connected to the lead for another confirmation of lead placement by test stimulation. The stylet in needle assembly is then utilized to tunnel the proximal end of the lead subcutaneously. Care needs to be taken to ensure the external electrode patch (Fig. 6) can be easily placed over the proximal end of the lead (Fig. 7), overlying the receiving electrode. The incisions are then closed in standard fashion based on the surgeon's preference. A radiograph of the implanted system is subsequently performed to document location. Importantly, no additional sutures, strain relief loops, or tunneling around major joints was performed in this study, as the novel device eliminates the need for altering the surgical technique.

The EPT is designed for two to three days of continuous use, however, subjects were instructed to charge it daily to assure uninterrupted treatment. A second EPT would be assigned and registered to same Patient Programmer if the subject required constant stimulation. Parameters varied with Phase duration 70–500 μ/sec, Pulse rate 1–200 Hz, time on ranging from 10 min

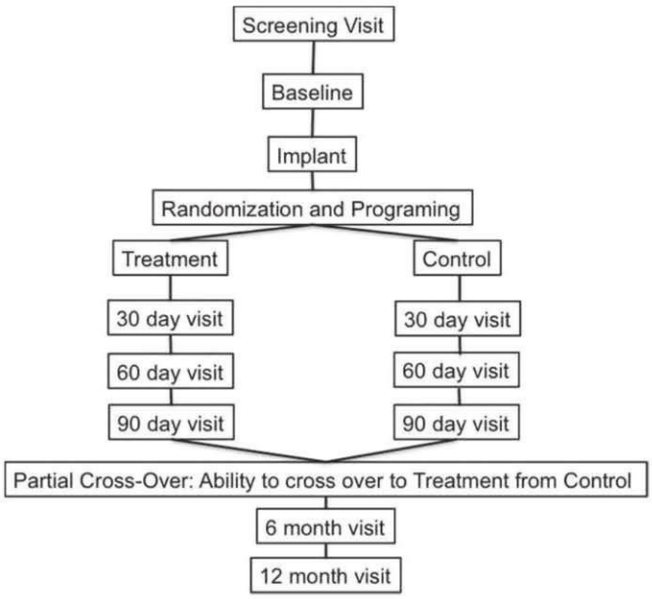

Figure 4. Trial design.

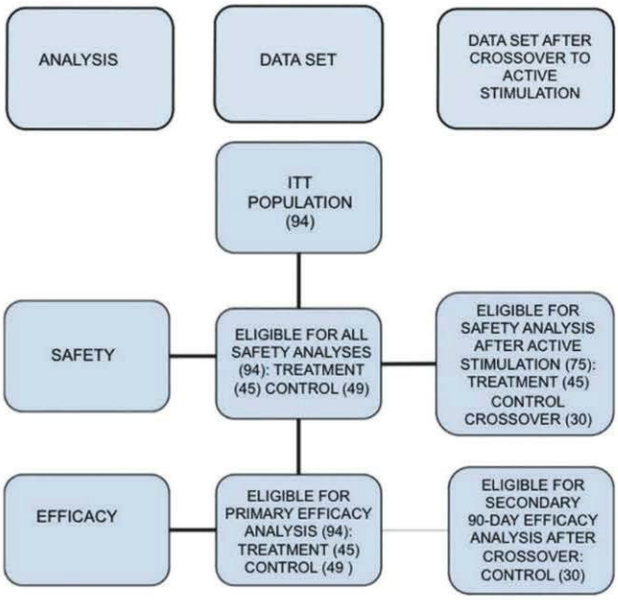

Figure 5. Study design and outcome assessment.

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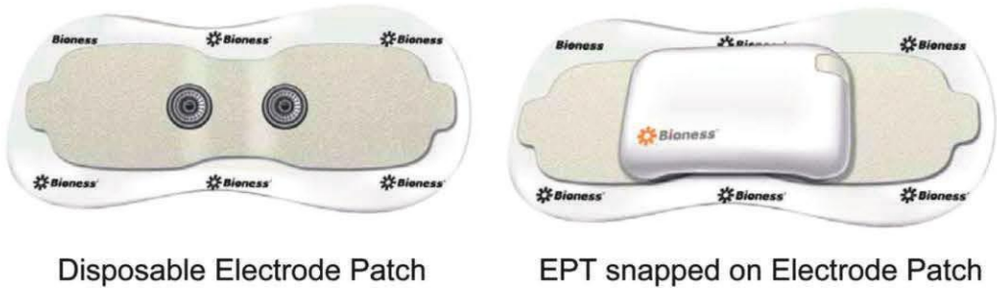

Figure 6. External user device components.

Figure 7. Implant (lead).

Table 2. Enrollment Site.

Site	Patients recruited	Treatment ($N = 45$)	Control ($N = 49$)
1	12	3/5 (60%)	0 (0%)
2	10	0 (0%)	2/5 (40%)
3	4	0 (0%)	1/2 (50%)
4	4	2/2 (100%)	0 (0%)
5	3	0 (0%)	0 (0%)
6	11	4/6 (67%)	0 (0%)
7	11	3/6 (50%)	0 (0%)
8	22	3/10 (30%)	2/12 (17%)
9	7	1/3 (33%)	0 (0%)
10	2	0 (0%)	0 (0%)
11	4	0 (0%)	0 (0%)
12	2	1/2 (50%)	0 (0%)
13	2	0 (0%)	0 (0%)
Total	94	17/45 (38%)	5/49 (10%)

Table 3. Mean Reduction in Pain From Baseline to Month Three, by Randomization Group.

Study participants	Treatment ($N = 45$)	Control ($N = 49$)	Difference	*t*-test
94	27.2%	2.3%	24.9%	$p < 0.0001$

to 12 hours (mean six hours per day at three-month study visit). Typical settings were 200 μ/sec; 100 Hz; with amplitude set for paresthesia. Multiple programs were loaded (different parameters) on Patient Programmer if subject reported attenuation of response. Subjects were able to select program and control amplitude as subjectively required.

RESULTS

After IRB approval, 147 patients were consented and screened for the study. Fifty-three patients did not meet either the inclusion or exclusion criteria or elected not to participate. Ninety-four patients were then implanted and randomized to either the Treatment ($N = 45$) or the Control group ($N = 49$). Demographics of the patients enrolled in the study are described in Table 1.

The patients were recruited for participation in the trial from 13 centers. All centers recruited at least 2 patients, an average of 7 per site and a median of 11. Please see the following table on site recruitment.

Efficacy

Table 3 describes summary information for the primary outcome regarding efficacy. Forty-five patients were randomized to the Treatment arm following the implant. The primary outcome of the study was to determine pain relief achieved using the new peripheral lead system, where at least a 30% decrease in pain without an increase in pain medicine use defined the Responders. The difference between overall mean reduction in average pain from Baseline to three-month follow-up in the Treatment group vs. the Control group was statistically significant ($p < 0.0001$ by *t*-test) with 27.2% improvement in the Treatment group vs. 2.3% in the Control group.

Table 4 presents primary endpoint results with the Responder rate statistically significantly higher ($p = 0.0048$) for the Treatment group compared to the Control group. Employing the Cochran–Mantel–Haenszel one-sided test as described in Methodology, the primary endpoint was achieved at planned interim analysis. This analysis resulted in a corresponding test statistic of 2.59 which exceeded the prespecified study stop

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Table 4. Primary Efficacy Outcome; Responders by Randomization Group.

Total number of patients	Treatment ($N = 45$)	Control ($N = 49$)	Difference	Cochran-Mantel-Haenszel one-sided test
94	17/45 (38%)	5/49 (10%)	28%	$p = 0.0048$

Table 5. Comparison of Randomization Groups on Number (Percent) of Responders by Anatomic Location.

Anatomic location of the implanted lead	# of patients	Treatment ($N = 45$)	Control ($N = 49$)	Difference
UE	26	4/12 (33%)	0 (0%)	33%
LE	27	5/13 (38%)	2/14 (14%)	24%
Trunk	41	8/20 (40%)	3/21 (14%)	26%
Total	94	17/45 (38%)	5/49 (10%)	28%

LE, lower extremity; UE, upper extremity.

Table 6. Comparison of Randomization Groups on Average Pain Reduction by Anatomic Location.

Anatomic location of the implanted lead	Treatment			Control			Difference	
	N	Mean	SD	*N*	Mean	SD	Mean	SD
UE	12	29.2	33.3	14	6.5	20.0	22.7	26.9
LE	13	21.0	30.8	14	1.2	31.8	19.8	31.3
Trunk	20	30.1	30.6	21	0.2	26.3	29.9	28.4
Total	45	27.2	30.9	49	2.3	26.0	25.0	28.5

LE, lower extremity; UE, upper extremity; SD, standard deviation.

Table 7. Crossover Data at Day 90.

Study participants in control group	Control group that crossed over	Rate of responders
45	30	30% (9/30)

cutoff of 2.17. Once this endpoint was verified, safety follow-up was completed and the study was stopped.

Anatomic location of implant is defined in Table 1. Of the total number of patients in the Treatment group, 12 were in the upper extremity, 13 in the lower extremity, and 20 in the trunk which is comparable to that of the Control group. The Responder rate was statistically higher for the Treatment group as compared to the Control group for all anatomical areas (Tables 5 and 6).

Efficacy of the device was measured again during the partial crossover period. The Control group was allowed to cross over to the stimulation (Treatment) group and they were followed for 90 days for efficacy. Nine (9/30) were classified as Responders (30% reduction in pain without upward titration of pain medicine) (Table 7).

Secondary outcomes are described in Table 8 at day 90. The Treatment group had better improvement than did the Control group, including worst pain score, BPI score for general activity, mood, walking, normal work, relations to other people, sleep, and enjoyment in life. The Treatment group also had significantly better improvement than the Control group in quality of life; PGIC in activity limitations, symptoms, emotions, and overall quality of life related to the painful condition; patient global impression of degree of change since beginning care at the study clinic; and patient satisfaction.

Safety

Ninety-four (94) patients underwent implantation with mean follow-up of 320 days postimplantation. No serious device-related AEs were reported. No unanticipated device-related events were reported. All available patients were followed up to one year. Overall, the rate of AEs was equal in both groups. One hundred forty-seven patients were consented and screened for the study. Thirty-five did not meet inclusion or exclusion criteria. Ninety-four patients were implanted and then randomized to the treatment (45) or the Control group (49).

Table 8 describes the patient satisfaction with the device. The study did not capture the reason for the dissatisfaction in the Patient Satisfaction Scale (poor coverage or for other concerns).

Table 9 demonstrates the number of patients that experienced AEs. There were a total of 55 subjects, out of the implanted 94 that had an AE. Twenty-eight patients experienced AEs in the Treatment group and 27 patients experienced AEs in the Control group. No device related serious adverse events (SAEs) occurred in either group. Nine patients experienced SAEs, nondevice related, in the Treatment group while 11 patients had SAEs, nondevice related, in the Control group, totaling 20 SAE patients.

Table 10 lists the total number of events that occurred out of those 55 patients described in Table 9. Seventy-four AEs occurred in 28 patients in the Treatment group. Seventy-two AEs occurred in 27 patients in the control group. Fourteen patients experienced 28 device-related AEs in the Treatment group, while 13 patients experienced 23 related AEs in the Control group, totaling 51 device-related AEs in 27 patients.

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Table 8. Secondary Efficacy Measures at Three Month Follow-Up.

Variable	Label	All	Treatment	Control	*p*-value
BPI worst pain score	Baseline (V1)	8.1 ± 1.1	8.1 ± 1.1	8.0 ± 1.1	0.562
	Three months (V6)	6.7 ± 2.3	5.7 ± 2.2	7.6 ± 2.0	0.000
	Change (V6–V1)	−1.3 ± 2.2	−2.4 ± 2.3	−0.3 ± 1.6	<0.0001
BPI average score for general activity	Baseline (V1)	6.6 ± 2.0	6.6 ± 2.2	6.5 ± 1.8	0.748
	Three months (V6)	5.1 ± 2.7	4.2 ± 2.6	6.0 ± 2.5	0.003
	Change (V6–V1)	−1.3 ± 2.5	−2.3 ± 2.7	−0.4 ± 2.0	0.001
BPI average score for mood	Baseline (V1)	6.3 ± 2.2	6.6 ± 2.3	6.0 ± 2.1	0.134
	Three months (V6)	4.8 ± 3.0	4.3 ± 3.1	5.3 ± 2.9	0.148
	Change (V6–V1)	−1.4 ± 2.7	−2.2 ± 3.1	−0.6 ± 2.1	0.012
BPI average score for walking ability	Baseline (V1)	5.1 ± 3.2	5.2 ± 3.3	5.1 ± 3.2	0.930
	Three months (V6)	3.7 ± 3.3	2.7 ± 2.7	4.7 ± 3.5	0.008
	Change (V6–V1)	−1.2 ± 2.7	−2.4 ± 3.0	−0.1 ± 1.9	<0.0001
BPI average score for normal work	Baseline (V1)	6.6 ± 2.1	6.6 ± 2.3	6.6 ± 1.9	0.898
	Three months (V6)	5.2 ± 2.7	4.2 ± 2.6	6.2 ± 2.5	0.001
	Change (V6–V1)	−1.3 ± 2.6	−2.4 ± 2.6	−0.3 ± 2.1	<0.0001
BPI average score for relations with other people	Baseline (V1)	5.7 ± 2.4	5.9 ± 2.5	5.4 ± 2.2	0.263
	Three months (V6)	4.5 ± 3.0	4.0 ± 2.9	4.9 ± 2.9	0.179
	Change (V6–V1)	−1.1 ± 2.7	−2.0 ± 3.1	−0.3 ± 2.0	0.007
BPI average score for sleep	Baseline (V1)	6.3 ± 2.5	6.4 ± 2.7	6.2 ± 2.3	0.568
	Three months (V6)	5.2 ± 3.1	4.1 ± 3.1	6.3 ± 2.8	0.001
	Change (V6–V1)	−0.8 ± 2.8	−2.1 ± 2.8	0.3 ± 2.2	<0.0001
BPI average score for enjoyment of life	Baseline (V1)	6.7 ± 2.2	7.0 ± 2.2	6.4 ± 2.2	0.184
	Three months (V6)	5.4 ± 3.1	4.5 ± 3.1	6.2 ± 2.8	0.009
	Change (V6–V1)	−1.3 ± 2.8	−2.5 ± 2.9	−0.1 ± 2.0	<0.0001
Pain medication (at three-month)	Not Increased	91	44 (97.8%)	47 (95.9%)	0.608
	Increased	3	1 (2.2%)	2 (4.1%)	
Quality of life	Baseline (V1)	35.7 ± 4.6	35.5 ± 4.9	36.0 ± 4.3	0.389
	Three months (V6)	36.3 ± 4.4	36.9 ± 4.5	35.8 ± 4.3	0.250
	Change (V6–V1)	0.6 ± 4.8	1.4 ± 5.9	−0.2 ± 3.4	0.037
Patient global impression of change in activity limitations, symptoms, emotions, and overall quality of life related to your painful condition (range 1–7, with 1 indicating no change and 7 indicating a great deal better/considerable improvement)	1	22	1 (2.2%)	21 (42.9%)	<0.0001
	2	10	1 (2.2%)	9 (18.4%)	
	3	11	6 (13.3%)	5 (10.2%)	
	4	12	9 (20.0%)	3 (6.1%)	
	5	10	10 (22.2%)		
	6	13	9 (20.0%)	4 (8.2%)	
	7	8	5 (11.1%)	3 (6.1%)	
	Missing	8	4 (8.9%)	4 (8.2%)	
	Mean ± SD	3.6 ± 2.1	4.8 ± 1.5	2.5 ± 1.9	<0.0001
Patient global impression of degree of change since beginning care at this clinic (range 0–10, with 0 indicating much better, 5 indicating no change, and 10 indicating much worse)	0	8	5 (11.1%)	3 (6.1%)	0.002
	1	3	3 (6.7%)		
	2	10	7 (15.6%)	3 (6.1%)	
	3	16	13 (28.9%)	3 (6.1%)	
	4	14	7 (15.6%)	7 (14.3%)	
	5	22	5 (11.1%)	17 (34.7%)	
	6	4	1 (2.2%)	3 (6.1%)	
	8	4		4 (8.2%)	
	9	3		3 (6.1%)	
	10	2		2 (4.1%)	
	Missing	8	4 (8.9%)	4 (8.2%)	
	Mean ± SD	4.0 ± 2.3	2.8 ± 1.6	5.0 ± 2.4	<0.0001
Patient satisfaction (range 0–10, with 0 indicating not satisfied at all and 10 indicating completely satisfied)	0	24	2 (4.4%)	22 (44.9%)	<0.0001
	1	1		1 (2.0%)	
	2	4		4 (8.2%)	
	3	4	3 (6.7%)	1 (2.0%)	
	4	6	3 (6.7%)	3 (6.1%)	
	5	4	1 (2.2%)	3 (6.1%)	
	6	6	5 (11.1%)	1 (2.0%)	
	7	4	4 (8.9%)		
	8	9	4 (8.9%)	5 (10.2%)	

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Table 8. *Continued*

Variable	Label	All	Treatment	Control	*p*-value
	9	7	5 (11.1%)	2 (4.1%)	
	10	17	14 (31.1%)	3 (6.1%)	
	Missing	8	4 (8.9%)	4 (8.2%)	
	Mean ± SD	5.0 ± 3.9	7.3 ± 2.9	3.0 ± 3.6	<0.0001

Plus–minus values are means ± SD. All BPI scores range from 0 to 10, with 0 indicating no pain and 10 indicating "Pain as bad as you can imagine." Quality of Life was assessed by using the SF-12v2 Health Survey, and a higher score is better for the outcome.
BPI, Brief Pain Inventory; SD, standard deviation.

Table 9. Adverse Events by Number of Patients.

Event		Randomization group		Total patients
		Treatment (*N* = 45)	Control (*N* = 49)	
Serious adverse events	Device related SAE(s)	0	0	0
	Nondevice-related SAE(s)	9	11	20
	Total SAE patients	9	11	20
Adverse events (not serious)	Device related AE(s)	14	13	27
	Nondevice-related AE(s)	5	3	8
	Total AE patients	19	16	35
Either SAE or AE		28	27	55

Table 10. Adverse Event Finding by Type and Number of Events.

Event		Randomization group		Total number of adverse events
		Treatment (*N* = 45)	Control (*N* = 49)	
Serious adverse events	Device-related SAE(s)	0	0	0
	Nondevice-related SAE(s)	14	11	25
	Total SAE(s)	14	11	25
Adverse events (not serious)	Device-related AE(s)	28	23	51
	Nondevice-related AE(s)	32	38	70
	Total AE(s)	60	61	121
Either SAE or AE		74	72	146

Twenty patients experienced 25 SAEs, nondevice related (9 patients experienced 14 SAEs in the treatment arm and 11 patients experienced 11 SAEs in the control arm). Table 11 demonstrates the SAEs by category. Table 12 demonstrates the number overview of AEs by the number of patients.

Fifty-five total patients experienced an AE, 25 of which were SAEs. Of note, there were no SAEs that were study device related (Tables 10–12). Thirty-five total subjects experienced non-SAEs, which were similar in number and nature for both the Treatment and Control groups.

Fifty-one device-related AEs were reported in this 94-subject population none of which were serious, with a similar occurrence for both the Treatment and Control groups. These events typically occurred and resolved early within the first three months of the study, and were largely localized to the stimulation area or site of surgery and were superficial in nature (e.g., skin rash, redness, soreness). The investigators reported that of the 51 related events, 41 (80.4%) were mild in intensity.

Transient skin irritations were reported in 13 subjects. Two subjects were eventually discontinued after experiencing prolonged skin sensitivity to the electrode patch.

Of the 94 subjects implanted, 15 did not participate in the 6- and 12-month follow-up and 33 patients lack follow-up at the 12 month visit, representing an attrition of 51% (48/94). Despite this, the safety data are compelling, both at the 6- and 12-month endpoints demonstrating no serious device-related events and treatment success. Ten patients exited the study before the 12 month visit. Seven patients had the device explanted, five of which were related to dissatisfaction with the pain relief, one patient developed chronic dermatitis/sensitivity to the electrode patch and elected to exit the study at the six month visit, and another rejected the lead after picking at the initial implant site, creating a dehiscence near the knee. All explants were performed without complication. Because of encapsulation tissue around the device, one patient elected to retain a portion of the lead *in situ* (Table 12). No SAEs occurred related to the device.

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Table 11. Number of Serious Adverse Events by Category.

SAE category	Treatment	Control	Total
Resulting in death	0	0	0
Life-threatening	1	0	1
Inpatient hospitalization or prolongation of hospitalization	10	7	17
Resulting in persistent or significant disability/incapacity	0	0	0
Congenital anomaly/birth defect	0	0	0
Required intervention to avoid permanent damage/impairment	3	4	7
Total SAEs	14	11	25
Related to study treatment	0 (0%)	0 (0%)	0 (0%)
Not related to study treatment	14 (100%)	11 (100%)	25 (100%)

Table 12. Overview of Adverse Events by Number of Patients.

	Severity of AE	Treatment ($N = 45$)	Control ($N = 49$)	Total ($N = 94$)
No. of patients with no SAE(s)	Mild	13 (28.9%)	11 (22.4%)	24 (25.5%)
	Moderate	6 (13.3%)	5 (10.2%)	11 (11.7%)
	Severe	0 (0%)	0 (0%)	0 (0%)
	Total	19 (42.2%)	16 (32.7%)	35 (37.2%)
No. of patients with no SAE(s), with at least one device-related AE		14 (31.1%)	13 (26.5%	27 (28.7%)
No. of patients with at least one SAE	Mild	1 (2.2%)	3 (6.1%)	4 (4.3%)
	Moderate	7 (15.6%)	7 (14.3%)	14 (14.9%)
	Severe	1 (2.2%)	1 (2.0%)	2 (2.1%)
	Total	9 (20.0%)	11 (22.4%)	20 (21.3%)
No. of patients with at least one device-related SAE		0 (0%)	0 (0%)	0 (0%)
No. of patients with at least one device-related AE leading to withdrawal from the study		1 (2.2%)	1 (2.0%)	2 (2.1%)
Treatment related mortality rate		0 (0%)	0 (0%)	0 (0%)

DISCUSSION

Treatment innovation to adequately address chronic pain patients requires intensive study, specifically to determine efficacy and patient safety. Interest in neuromodulation of the periphery, and the development of a device suited for treatment of distal extremity peripheral nerve neuropathic pain challenges, drove the innovation and interest in this clinical study. The study, focused on a novel stimulation system and method, achieved a statistically significant extent of pain relief with at least 30% pain reduction in the afflicted area, as compared to the Control, based on the Cochran–Mantel–Haenszel test. Seventeen of the forty-five (37.5%) patients were defined as Responders, as compared to the Control group (5/49 or 10.2%) at three months.

Until this paper, there is no well-designed PNS study and all claims of 50% reduction have been anecdotal or based on limited evidence. The FDA felt the previous RF PNS delivery-based approvals were no longer valid and based on minimal data. This is not an SCS device so an SCS reduction rate was not considered. It is also important to note, that the comparative variability in the patient populations indicated for SCS vs. PNS is arguably much higher for the latter given the diverse etiologies/mechanisms of pathology and subsequent variety of implant locations. With that being said, the FDA gave guidance that a prospective study was needed with patients serving as their own control.

Interestingly, 13 patients had a six-point change in the PGIC. On further review, these patients' dramatic response was not readily explained, even though they may represent optimized disease indication and implementation of the therapy.

No device-related SAEs occurred during the implantation or tenure of the device placement in patients implanted with this therapy. The safety profile is unparalleled and demonstrates that of the 75 patients that received stimulation, comprised of the original Treatment group and the crossed-over group from the Control, no patient experienced serious or unanticipated device related adverse reactions.

Not only is pain reduction and safety important, but so too is a closer examination of the secondary outcomes. Outcomes in reductions or lack of increase in baseline pain medication, improvement in the quality of life, patient satisfaction, and global impression of change were more favorable in the Treatment group beyond those found in the nonstimulation Control group.

The device was designed for treatment of mononeuropathies excluding the face. The study criteria and population was based on the agreed targets with the FDA collaboration. Notwithstanding, future studies are warranted to illuminate the potential cranio-facial use of the device on efficacy and safety. Although in the present study efficacy divided into the regional analysis of the trunk, upper extremity, and lower extremity all produced meaningful statistical change as defined, future studies focused on specific nerve pathologies or locations may be beneficial to further profile patients and optimize outcomes. The attrition rate reported does not predict failure with the device, and 33 patients lack data at the 12 month visit. Only seven patients had the device explanted out of the 94 implanted.

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CONCLUSION

The data satisfied the primary efficacy and safety outcome measures of the study: patients reported significant pain reduction at three months and safety follow-up to one year demonstrating this tested system to be a safe and viable tool in the pain treatment algorithm. Innovation in neuromodulation therapies have recently been focused on the central neural axis. Peripheral nerve targets and neuromodulation techniques directed to the periphery will continue to improve patient safety and treatment outcomes. The StimRouter Neuromodulation System is FDA cleared for adults who have severe intractable chronic pain of peripheral origin, as an adjunct to other modes of therapy (e.g., medications) and is therefore accessible to patients, allowing for additional larger scale use.

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Authorship Statements

Timothy Deer participated in the design of the study, data analysis, and along with all other authors except Jason Pope, participated in patient recruitment, device implantation and data collection. Timothy Deer prepared the manuscript draft with important intellectual input from Jason Pope and Leonardo Kapural. All authors edited and accepted the final version of the manuscript. Timothy Deer served as Medical Monitor for the study and had completed access to the study data.

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COMMENTS

The authors are to be commended for this work. With limited predicate peripheral nerve stimulation (PNS) data, they had to satisfy rigorous FDA design and monitoring criteria, and overcome system limitations and adverse events. In that context, they have now laid seminal groundwork for both larger studies, and future research and development. As such, efficacy and cross over rates will improve; benchmarking both the historic challenges, and future successes of PNS in the management of chronic peripheral pain syndromes.

Kenneth M. Alo', MD
Houston, TX, USA

***

Peripheral nerve stimulation for selected intractable pain syndromes is undergoing a resurgence as new technologies are applied to specific mononeuropathic conditions. This paper demonstrates one method of reducing peripherally mediated pain, which can be considered as additional armamentarium for the pain treatment physician.

Richard Weiner, MD
Dallas, TX, USA

***

Methods of performing peripheral nerve stimulation continue to evolve. This particular study focuses on a device that is a hybrid between the fully implantable and the partially external. In many cases, it would appear to provide very suitable therapy for the more simple and classic cases of neuralgia. As a viable alternative to more expensive approaches capable of small, region specific coverage (i.e., fully implantable DRG systems), this concept could have significant economic impact. The authors have done a credible job of presenting the findings of their sponsored research. It remains for the attending physician to decide appropriate patient selection for application of this therapy.

Thomas Yearwood, MD, PhD
Pascagoula, MS, USA

Comments not included in the Early View version of this paper.

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Peripheral Nerve Stimulation for Chronic Idiopathic Orchialgia

Adrian Darryll Sulindro MD, David Spinner DO

Department of Rehabilitation Medicine, Affiliate of the Icahn School of Medicine at Mount Sinai, New York, NY

Icahn School of Medicine at Mount Sinai

Introduction

Orchialgia is pain in the testes and often considered chronic if occurring over three months. Although it can be caused by infection and inflammation, often times the causes are idiopathic.(1) Peripheral nerve stimulation is commonly used for chronic musculoskeletal and nerve related pains but in this case we demonstrate the effective use of if for chronic idiopathic orchialgia

Images

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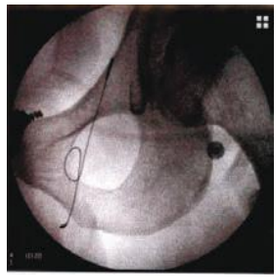

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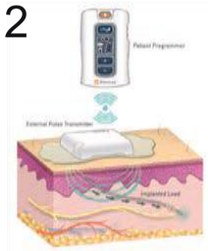

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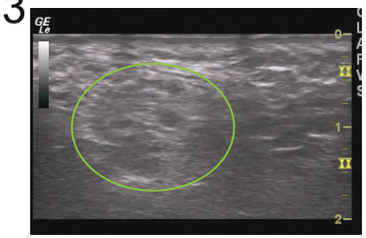

1. Fluoroscopic picture of peripheral nerve lead
2. Bioness Peripheral nerve stimulator
3. Spermatic cord in cross section

Case Description

A 35 year old male presented with left groin pain which started 2 years prior after a fall. Pain was described as mild to severe tugging and pulling in the left groin, as well as radiation to the left abdomen. Patient denies any exacerbating factors. Pain is slightly alleviated with stretching, and has mild tingling of the left groin but no weakness or radiation to the lower extremities. Physical therapy and NSAIDs have not given relief, and pain has not improved over time. Lower back, abdominal and groin imaging, as well as urologic workup has been negative for any pathology and orchialgia is so far idiopathic in nature. An ilioinguinal nerve block had definite pain relief into the abdomen, but not the testicle, so a genital branch of the genitofemoral nerve block was performed, with successful testicular pain relief and therefore was scheduled for peripheral nerve stimulator leads for implantation into the left ilioinguinal and genitofemoral nerves

With the patient supine, the left lower groin was evaluated with ultrasound using a 12 mHz linear array transducer. The genital branch of the genitofemoral nerve is very challenging to visualize with ultrasound and often not seen. We were able to clearly visualize the spermatic cord which contains the vas deferens, pampiniform plexus, lymphatic vessels, arteries and nerves in cross section. Using a proximal to distal and out of plane approach, a 18 gauge spinal needle was placed into the spermatic cord. A blunt tip guidewire was then passes thru and the spinal needle removed. Stimulation into the spermatic cord was achieved and the introducer sheath was placed into the spermatic cord. Then the Bioness StimRouter lead was guided into the cord. Repeat stimulation into the testicle was achieved. The introducer sheath was removed leading the electrodes adjacent to the structures of the cord. The receiver was then tunneled proximally towards the abdomen.

A two week post-procedure programing was performed with the patient reporting good tingling into his pain distribution and nerve response to the stimulation, furthermore the patient returned for follow up appointment and continued to feel relief post implantation of the peripheral nerve stimulator.

Discussion

Peripheral nerve stimulation (PNS) is one of the methods of electroanalgesia for patients with pain syndromes. It has most commonly been used for treatment of neuropathic pain, often when the nerve lesion is distal to stimulation site (2). Orchialgia is a chronic pain occurring in the testes and the pain is often described as dull and aching, or may be exacerbated by exercise. Although it is often caused by infection and inflammation, often times the causes are idiopathic. (1). A full workup of to rule out any infectious causes are necessary as well as any other pathological causes before one should label it as idiopathic orchialgia. The testicles receive multiple innervations; the testis mainly from the superior spermatic plexus via nerve fibers accompanying the internal spermatic vessels, and the parietal/visceral layers of the tunica vagnialis and cremaster muscle carried by the genital branch of the genitofemoral nerve. (3). There has been multiple described treatments including minimally invasive options such as spermatic cord blocks and pelvic plexus blocks (4,5) as well as surgical options including microsurgical denervation of spermatic cord, testicular denervation and orchiectomy (6,7).

In our case, there was a documented 2 year workup with multiple specialists including various musculoskeletal as well as urology specialists, conservative management and medical management has all failed to give effective pain relief. Our case demonstrates a novel use and approach for complete coverage of testicular pain, with the insertion of the lead towards the testicle overlying the spermatic cord likely blocking both the testis and overlying parietal/visceral layers of the tunica vaginalis as they receive innervation over the spermatic cord and genital branch of genitofemoral nerve.

Conclusion

Using peripheral nerve stimulation to treat chronic idiopathic orchialgia may provide a patient longer lasting relief than nerve blocks and give a less invasive option than surgery for those with intractable idiopathic orchialgia and can help reduce reliance on pain medication.

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Greater Occipital Nerve Stimulation: A New Approach to an Old Problem

Scott Pritzlaff, MD, CIPS, FIPP; Michael Leong, MD; Einar Ottestad, MD, CIPS, FIPP

INTRODUCTION

Occipital neuralgia (ON) may occur in the **distributions of the greater, lesser, or third occipital nerves** and patients frequently describe sharp, severe, lancinating pain. The **greater occipital nerve (GON)** is strongly implicated in ON due to its circuitous course as it emerges from the suboccipital triangle.

Until recently, stimulation of the GON was limited to placement of large, cumbersome systems with mixed results. In most cases, landmark or fluoroscopic techniques were employed making it difficult to ensure consistency of lead placement.

With the introduction of StimRouter (Bioness Inc, Valencia, CA), a new peripheral nerve stimulation (PNS) option for targeting the GON is now available **(FIGURE 1)**.

PNS SYSTEM

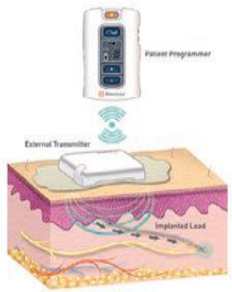

FIGURE 1. The StimRouter PNS system is FDA-approved for severe, intractable chronic pain of peripheral nerve origin. None of the new percutaneous PNS systems have approval for craniofacial pain.

METHODS

The ultrasound transducer is initially placed at the external occipital protuberance and then moved caudally until the first bifid spinous process is visualized representing C2. The GON nerve can be identified as it runs in **an oblique fashion between the semispinalis capitis (SSC) and obliquus capitis inferior (OCI) muscles (FIGURE 2)**.

The probe is then rotated with the lateral edge of the ultrasound transducer angled toward the C1 transverse process. The 15cm lead is placed in the typical fashion using an out-of-plane approach **(FIGURE 3). This technique places the lead parallel to the nerve and allows for easy tunneling toward the shoulder area.**

The lead is tunneled inferiorly toward the shoulder blade first and then laterally, allowing for the external pulse transmitter (EPT) to rest comfortably on the upper shoulder **(FIGURE 4)**.

ULTRASOUND TECHNIQUE

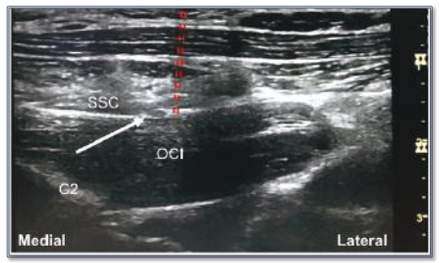

FIGURE 2. The GON (arrow) runs in an oblique fashion between the semispinalis capitis (SSC) and obliquus capitis inferior (OCI) muscles at C2. The red line denotes the desired trajectory for lead insertion, just lateral and parallel to the nerve.

LEAD AND DEVICE PLACEMENT

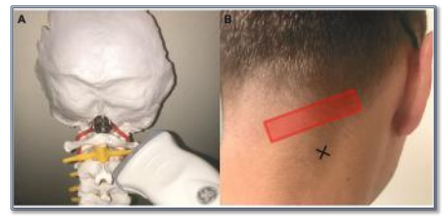

FIGURE 3. (A, B) Orientation of the ultrasound probe with respect to C1 and C2. The GON can be visualized at C2 with the lateral edge of the ultrasound transducer angled toward the C1 transverse process. It can be targeted via an out-of-plane approach with the entry point (X) inferior and lateral to the path of the nerve.

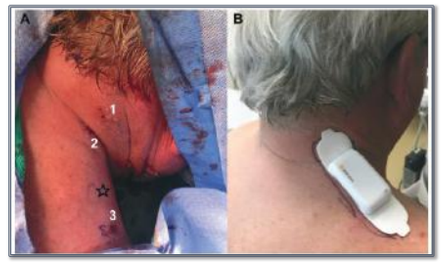

FIGURE 4. (A) Intraoperative photo showing the double-tunnel technique. The initial needle entry point is shown (1). The lead was then tunneled inferiorly (2) and laterally across the shoulder (3). The receiver position was also marked (☆). (B) The patient several weeks later showing the positioning of the external pulse transmitter over the receiver.

RESULTS

Stimulation of the GON with StimRouter is feasible with this approach to the nerve at C2. One of the biggest considerations is the final location of the receiver, as this dictates where the patient wears the EPT.

Proper pre-surgical scanning and marking are essential to ensure an optimal result.

DISCUSSION

StimRouter is a consideration for patients with ON who have responded favorably to diagnostic nerve blocks but have not had a durable benefit.

Because of its predictable course and easy visualization with high-resolution ultrasound, the GON is an ideal target for this new PNS system.

Although additional data and high-quality studies are needed, complications associated with older systems including **lead migration, fracture, and skin erosion are likely reduced with this system given its simplicity and ease of use.**

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The Science Behind Successful Outcomes

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The Use of Peripheral Nerve Stimulation for the Treatment of Tibial Neuralgia: Description of the Use of Ultrasound Guidance Technique for Percutaneous StimRouter Lead Placement with Anatomical Considerations

Josephson, Youssef DO, Ottestad, Einar MD, Spinner, David DO

Introduction

Tibial neuralgia is a common source of foot and ankle pain. The primary etiologies include: compression (tarsal tunnel syndrome), crush injuries, or trauma.

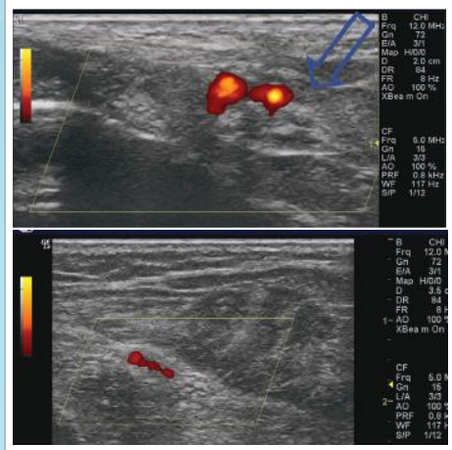
Patients commonly present with numbness, tingling, and neuropathic pain in the distribution of the tibial nerve with or without weakness. If traditional conservative care fails, the use of peripheral nerve stimulation may be a reasonable and effective treatment option. The StimRouter® is a novel, fully implanted peripheral nerve stimulation system that is powered by a small, External Pulse Transmitter (EPT) and battery external power source worn by the patient. Placement of the lead can be performed using paresthesia mapping which can be difficult, painful, and lead to sub-optimal placement. We describe the use of ultrasound (US) guidance with US landmarks and pearls to ensure proper lead placement directly adjacent to the nerve using two techniques.

Methods:

At 3 separate institutions, 10 patients had StimRouter implants for tibial neuralgia using US guidance from 1/17 to 5/17.

1. **In-Plane technique:** Tibial nerve is identified in tarsal tunnel in short-axis view then traced proximal 5-7 cm where nerve lies deep to soleus. A lateral to medial approach is used placing the lead through the facial plane to lie over tibial nerve and under soleus. The receiver is tunneled cephalad and medial which allows EPG to be placed over medial leg.
2. **Out-of-Plane Technique:** The tarsal tunnel is identified short axis adjacent to the medial malleolus. The Tibial nerve is visualized adjacent to the tibial artery and veins. The nerve is traced proximally about 5-7 cm. The nerve is kept short axis while utilizing a distal to proximal out-of-plane needle approach. The guidewire targets first the superficial side so the lead can be placed 'long' on the nerve. The receiver is then tunneled cephalad away from the medial malleolus.

Figure 1



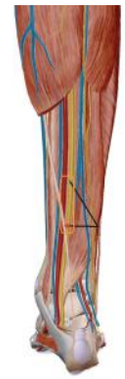
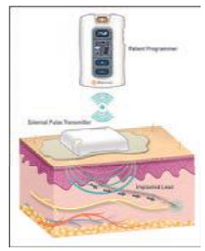


Fig 1 top left: Tarsal tunnel short axis view, big arrow is tibial nerve.
Fig 2 middle left: 7cm proximal of tarsal tunnel, tibial nerve to the right and adjacent to tibial artery deep to soleus.
Fig 3 top right: posterior view of leg showing technique 1 position of lead and battery, soleus removed.



Results

With the StimRouter the "trial" is integrated into the implant procedure. The use of US guidance combined with patient feedback throughout stimulation and percutaneous placement of the permanent lead delivers additional confidence of the proper location of the lead electrodes adjacent to the target nerve.

Discussion

Classically, electrode placement involves an open procedure under general anesthesia with dissections for nerve visualization, electrode placement, tunneling, and placement of a implantable pulse generator (IPG) with battery. The StimRouter is a novel percutaneously placed electrode with an external "wearable" worn by the patient controlled by a small "Patient Programmer" that resembles a small remote control, allowing the patient to be in charge of their pain management. Because there is no IPG it allows for a minimally invasive treatment option. The use of ultrasound provides a fast, easy, effective, safe, and reliable method of lead placement adjacent to the target nerve with local anesthesia while the patient is awake. We describe two novel US guided techniques for lead placement with consideration for patch location. Proper patch (EPT) placement allows for a better patient experience with day-to-day use and better treatment compliance.

Conclusion

Recent advances in PNS technology allow for permanent, non-opioid, reversible, minimally invasive solutions for the management of chronic pain on the responsible peripheral nerve. Multiple visualization techniques can be employed to place the lead percutaneously using only local anesthesia with patient feedback, obviating the need for a separate trial lead procedure.

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Peripheral Nerve Stimulation for Chronic Shoulder Pain: A Proof of Concept Anatomy Study

Michael Gofeld, MD; Anne Agur, PhD

Objectives: Although spinal cord and dorsal root ganglia stimulation may be effective for managing regional pain syndromes, a more targeted approach is perhaps more appealing for discrete anatomical structures. Chronic shoulder pain is a common musculoskeletal problem with significant socioeconomic impact. A peripheral nerve stimulation of the axillary and suprascapular nerves may prove to be effective as a long-term solution for this indication. In anticipation of the future experimental research and clinical utilization, a sound methodology for the lead placement was developed, and its feasibility is tested in a cadaveric study.

Materials and Methods: Normal anatomy was corroborated with ultrasound scans of live models and cadaver specimens. A step-by-step ultrasound-guided implantation technique was designed. The procedure was completed targeting both the axillary and suprascapular nerves. The accuracy of the lead placement was confirmed by dissections.

Results: The implanted devices were found adjacent to the target nerves within 0.5–1 cm distance.

Conclusions: The anatomical dissections confirmed the accuracy of ultrasound-guided placement of the lead. The described method is based on normal anatomy and appeared to be reproducible by following the outlined procedural steps.

Keywords: Anatomy, implantation, peripheral nerve stimulation, shoulder pain, technical report

Conflict of Interest: Michael Gofeld is a member of the Surgical Advisory Board of Bioness Inc. Anne Agur reports no conflicts of interest.

INTRODUCTION

Chronic shoulder pain is the second most common musculoskeletal complaint after the knee (1). Diagnoses are different and include relatively manageable problems, such as the rotator cuff pathology and osteoarthritis, and more convoluted conditions poorly responding to conventional conservative and surgical remedies. Examples of latter are frozen shoulder (FS) and hemiplegic shoulder pain (HSP). While the prevalence of FS among the general population is 2%–4%, it affects up to 59% of patients with long-term diabetes mellitus (2). HSP is a frequent unfortunate stroke sequel with the reported incidence of shoulder pain of 47% at 12 months (3). HSP has significant adverse effect on functional recovery and quality of life and proven to be challenging to control by conventional methods (4). Both, FS and HSP, may become debilitating and recalcitrant to local and systemic therapies. One of the explanations of such persistence may be related to the neurobiological transformation and modulation of a nociceptive pain. A long-standing chronic pain, regardless of the initial anatomical cause, may become neuropathic. Thus, peripheral and central modulation may play a more significant role in seemingly obvious musculoskeletal disorders, such as osteoarthritis and rotator cuff syndrome (5–8). The premise of a neuropathic component presents an opportunity for managing shoulder pain by neuromodulation.

Although, spinal cord and dorsal root ganglia stimulation may be effective for the regional pain syndromes, a more targeted approach might be considered for discrete peripheral nerves or anatomical structures. Chronic shoulder pain may be treated by either surface or internalized peripheral nerve stimulation (PNS). Published studies were focused on an intramuscular stimulation of terminal axillary nerve (AN) branches (9–11). Conversely, Kurt et al. successfully managed chronic shoulder pain by a fully implanted spinal cord stimulator-type lead onto the suprascapular nerve (SSN) (12).

In anticipation of future experimental research and clinical utilization, a sound methodology for PNS lead placement needs to be developed, and its feasibility challenged in a cadaveric study. Because peripheral nerves' location is variable, and they are surrounded by blood vessels, muscles, and tendons, precise imaging guidance is desirable. Ultrasonography is a proper imaging tool to localize the target nerve and to guide PNS lead placement. The objective of this cadaveric study was to assess SSN and AN ultrasound-guided PNS lead placement and confirm the procedural accuracy by anatomical dissections.

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For more information on author guidelines, an explanation of our peer review process, and conflict of interest informed consent policies, please go to http://www.wiley.com/WileyCDA/Section/id-301854.html

Source(s) of financial support: none; Bioness Inc. provided StimRouter leads.

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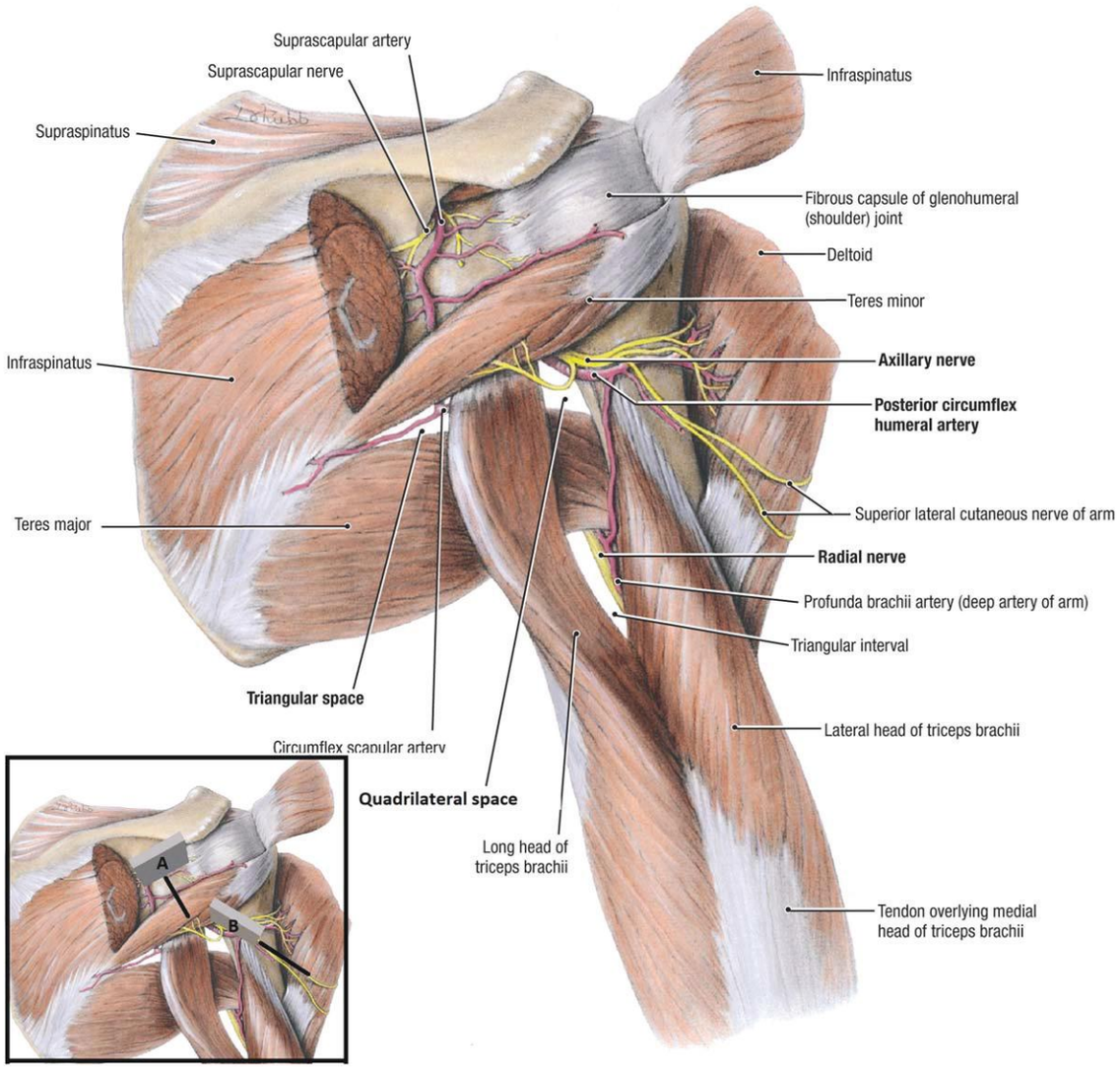

Figure 1. Gross anatomy of the axillary and SSN s (adapted from the *Grant's atlas of anatomy*, 14th ed, with permission). In the inset: a, ultrasound transducer orientation for the access to the SSN; b, ultrasound transducer orientation for the access to the AN; black lines, the direction of insertion. [Color figure can be viewed at wileyonlinelibrary.com]

MATERIALS AND METHODS

Approval was received from the University of Toronto Health Sciences Research Ethics Board.

Aix llary Nerve

The detailed topography of the AN and quadrangular space was reviewed using anatomy textbooks (13) and embalmed dissected specimens. The AN is a terminal branch of the C5 and C6 nerve roots. It stems from the posterior cord of the brachial plexus at the level of axilla and courses inferior to the border of the subscapularis muscle. The nerve exits the axilla posteriorly via the quadrangular space along with the posterior circumflex humeral artery. After leaving the quadrangular space, the main nerve trunk gives off two branches. The posterior branch provides motor innervation to the teres minor muscle and innervates the skin over the inferior part of the deltoid. The anterior branch provides motor innervation to the deltoid muscle and sends articular branches to the shoulder joint. The quadrangular space is a square-shaped hiatus in the muscles of the posterior scapular region (Fig. 1). The borders of this space are: superiorly the teres minor, inferiorly the teres major, laterally the surgical neck of the humerus, and medially the long head of triceps brachii. The posterior circumflex humeral artery lies adjacent and typically distal to the nerve.

The topographic anatomy was corroborated with anonymized ultrasound images obtained in clinical practice. The anterior branch of the AN can be easily identified when the ultrasound transducer is placed longitudinally on the postero-lateral aspect of the proximal humerus (Fig. 2). Since an ideal lead position requires placement of the lead so it lies in contact and parallel to the main trunk of the AN, a long-axis view of the artery was obtained as shown in Figure 1 (inset) and Figure 3. The nerve itself cannot be easily found in its long axis; however, shifting the transducer cephalad keeping with the same orientation would inevitably result in determining the anatomically correct trajectory for the lead placement. Additional topographic anchors were identified. In a more proximal position, the

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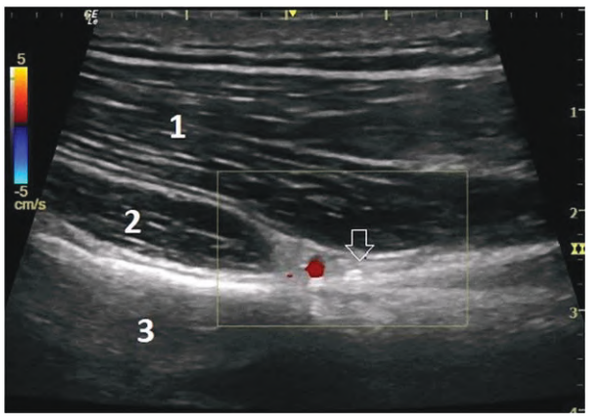

Figure 2. Distal AN sonoanatomy. Arrow, the AN (short axis); red, posterior circumflex artery (short axis); 1, deltoid muscle; 2, teres minor muscle; 3, humerus. [Color figure can be viewed at wileyonlinelibrary.com]

belly of the teres minor was seen, whereas more inferiorly. The tendinous part of the lateral head of triceps brachii (adjacent to the bone surface) and the teres major (deep plane) were visualized.

The implantation was performed in lightly embalmed anatomic specimens. A commercially available device (StimRouter, Bioness, Valencia, CA, USA) labeled for PNS was used. The specimen was retained in a lateral decubitus position. A linear high-frequency ultrasound transducer (LogicE, GE, Milwaukee, WI, USA) was placed in a long-axis to the AN view (Fig. 1). After obtaining the desired orientation and visual localization of the quadrangular space, a stab incision was done. The implantation was performed per the manufacturer guideline as the following. The deltoid muscle was penetrated with an 18-gauge Crawford needle. Next, a guide probe was inserted and placed in the quadrangular space under in-plane ultrasound guidance (Fig. 4). The needle was removed and a plastic dilator was placed over the probe. After reaching the desired position, the probe and internal component of the dilator were removed leaving only a plastic sheath. A metallic lead holder with the electrode was placed through the sheath and after the tines were deployed, both the sheath and lead holder were removed. In a clinical case, the lead tunneling is needed to keep the receiver (proximal end of the lead) under the skin at the posterolateral deltoid area. This step was omitted. The dissection of the specimen was performed exposing the quadrangular space and the lead. The distance between the lead to the AN was measured.

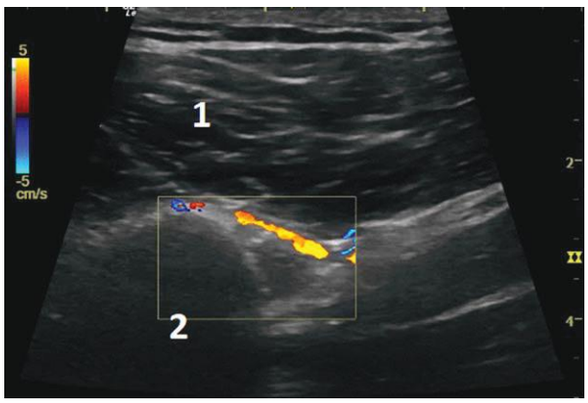

Figure 3. Sonoanatomy of the quadrangular space. Color, posterior circumflex artery (long axis); 1, deltoid muscle; 2, humerus (short axis). [Color figure can be viewed at wileyonlinelibrary.com]

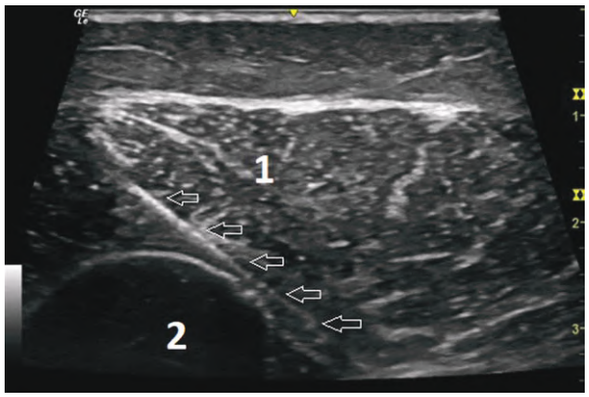

Figure 4. StimRouter guidewire (arrows) is inserted into the quadrangular space. 1, deltoid muscle; 2, humerus (short axis). [Color figure can be viewed at wileyonlinelibrary.com]

Suprascapular Nerve

The SSN, a branch of the superior trunk of the brachial plexus (C5 and C6), innervates the supraspinatus and infraspinatus muscles, as well as the shoulder joint (13). It does not have cutaneous branches. After passing through the suprascapular notch, inferior to the superior transverse scapular ligament, the SSN courses inferolaterally in the supraspinous fossa at the periosteal level to reach the lateral border of the spine of the scapula. The nerve course around the spinoglenoid notch to reach the infraspinous fossa where if gives off terminal muscular branches to infraspinatus. At the level of the suprascapular notch, the nerve has a fixed position in the fibro-osseous tunnel roofed by the superior transverse scapular ligament. The suprascapular artery most commonly passes superficial to the ligament. The majority of sensory branches to the shoulder joint and capsule are leaving the main trunk proximally to the suprascapular notch.

The nerve can be accessed at the suprascapular notch using fluoroscopy. The nerve block and PNS lead placement can be done by using this method. However, it would require a prone position that may be uncomfortable. Ultrasound-guided SSN block is a routinely practiced technique. Usually, an in-plane injection is performed. Nevertheless, a PNS lead placement using this technique is suboptimal due to a risk of migration—the only tip of the lead would be placed close enough to the nerve, and any subsequent traction created by overlaying trapezius and supraspinatus muscles may result in its dislodgement. An out-of-plane, identical to the fluoroscopy-based method is theoretically possible. However, the spine of scapulae may limit the feasibility of such approach.

Therefore, we have developed and tested a unique approach. A linear high-frequency ultrasound transducer (LogiqE, GE Healthcare, Milwaukee, WI, USA) was placed in the short-axis view (Fig. 1, inset). The SSN was localized at the infraspinous fossa as it coursed around the spinoglenoid notch (Fig. 5). The specimen was retained in a lateral decubitus position. After obtaining the desired short-axis orientation to the SSN, a stab incision was done 2–3 cm distally to the transducer. The skin and infraspinatus muscle was penetrated with 18-gauge Crawford needle. A guide probe was inserted and placed adjacent to the SSN under out-of-plane ultrasound guidance. The needle was removed and the guide was advanced in the cephaladmedial direction. The transducer was shifted to the supraspinatus fossa. The guide was advanced parallel to the nerve and its tip was identified as a bright hyperechoic signal at the supraspinous fossa. The rest of the implantation was performed following the same steps as described above. The dissection of the specimen was

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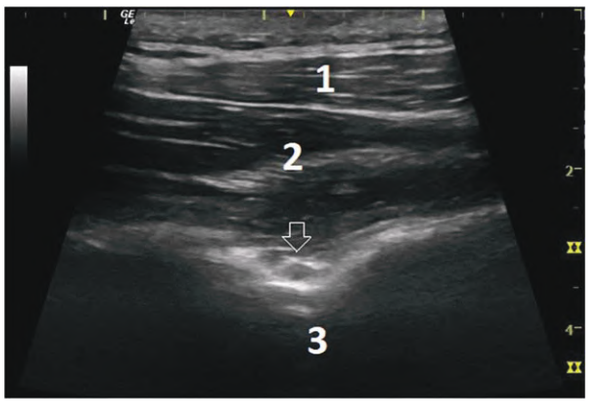

Figure 5. The SSN in the spinoglenoid fossa. Arrow, SSN (short axis); 1, deltoid muscle; 2, infraspinatus muscle; 3, scapula. [Color figure can be viewed at wileyonlinelibrary.com]

performed by exposing the supraspinous fossa and the lead. The distance between the lead and the SSN was measured.

RESULTS

The dissections confirmed PNS lead placements adjacent to the target nerves within 0.5 cm distance (Figs. 6 and 7). The contacts and the tines were found in the connective adipose tissues surrounding each nerve. No visible damage to the nerves or corresponding blood vessels was identified.

DISCUSSION

PNS is entering a new era of technological renaissance that predictably relaunched following the Food and Drug Administration

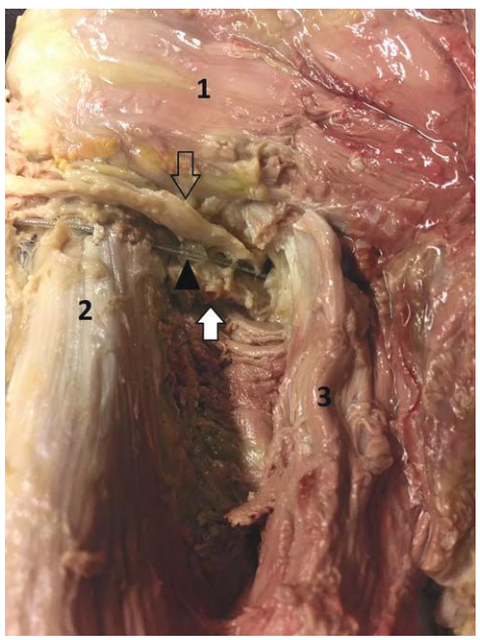

Figure 6. The lead (black arrowhead) is placed adjacent to the AN (open arrow). White arrow, posterior circumflex humeral artery (cut); 1, teres minor muscle; 2, lateral head of triceps brahii; 3, long head of triceps brahii. [Color figure can be viewed at wileyonlinelibrary.com]

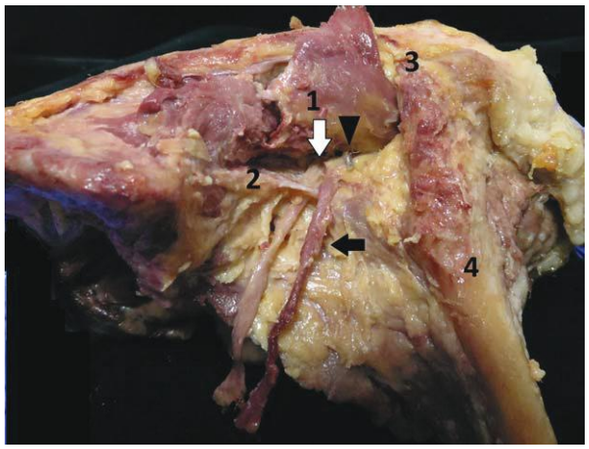

Figure 7. The lead (black arrowhead) is placed adjacent to the SSN (white arrow). Black arrow, suprascapular artery; 1, supraspinatus muscle; 2, transverse ligament; 3, acromion process; 4, humerus. The specimen is in a ventral superior view. [Color figure can be viewed at wileyonlinelibrary.com]

(FDA) approval of novel devices (14–16). These devices are designed to address the evident problems of off-labeled PNS systems, that is, a long-term stability, complexity, and effectiveness. The new miniaturized wireless technologies make possible to stimulate discrete peripheral and autonomic nerves and manage chronic neuropathic pain and functional disorders by electrical stimulation outside of the central nervous system. Among these new indications, the HSP deserves special consideration. HSP affects up to 84% of the survivors at an early poststroke period (4) and up to 47% after one year (3). Traditionally, a poststroke loss of muscle tonus and subluxation were considered the main reason for the development of HSP (17). More recently, HSP was found to be multifactorial and rather related to spasticity than to subluxation (18). Both motor function and subluxation may be partially improved with surface stimulation; however, it was not as beneficial at reducing pain (19). Neuromuscular electrical stimulation of the AN branches was initially thought to be effective for management of the shoulder joint subluxation and pain. However, clinical studies demonstrated only pain reduction without changes in the objective status (10,20). Moreover, the most recent paper provided compelling evidence for the successful alleviation of HSP independently to the anatomic status of the glenohumeral joint (10). The results are not surprising considering the mechanism of action: surface stimulation at the motor points activates the deltoid muscle, whereas stimulation of the distal branches of the AN would be predominantly sensory. The anatomically sound approach is to access the main trunk of the AN to be able to activate both motor and sensory functions.

Because the SSN is stemming from the same C5, C6 nerve roots, its stimulation may provide results similar to the axillary neuromodulation. Excluding the case report of Kurt et al., there were no publications related to PNS of SSN (11). Stimulation of the terminal branches of the SSN in case of a neuropathic postsurgical shoulder pain was suggested by Theodosiadis et al. (21). In both publications, the shoulder pain was successfully managed by the implantation of an off-labeled system that included a four-contact lead and an internal pulse generator (IPG). Conceivably, this method may be used for the treatment of other chronic shoulder pain conditions.

The current trends in the PNS technology are focusing on the lead miniaturization, adding stability by adding tines, and utilization of a wireless induction models, thus eliminating the need for an IPG. All recently approved by FDA devices are following the same principles

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(13–15). We utilized the leads provided by the Bioness Inc. (StimRouter, Bioness Inc., Valencia, CA, USA). It is a monopolar stretchable lead that maintains stability by deployable silicone tines. It is activated percutaneously via simple electric induction mechanism. This unique design allows elimination of IPG and simultaneous transcutaneous activation of both the lead and the deltoid muscle motor points. The implantation process is facilitated by a special lead holder to deliver the lead to a predetermined depth and position adjacent to the AN. The nerve must be contacted at the quadrilateral space to assure optimal stimulation of the main trunk.

The described method should help practicing physicians to perform anatomically sound image-guided PNS implantation. Other commercially available leads can be inserted using this approach. Review of the device clinical efficacy is beyond the scope of this article. Nevertheless, a precise implantation is a *sine qua non* for a clinically effective long-term stimulation.

Although a fluoroscopy-guided procedure aimed at the medial aspect of the surgical neck of the humerus (axillary PNS) or the suprascapular notch (suprascapular PNS) is possible, theoretical and practical disadvantages should be considered, such as the prone position, inability to control depth, potential risks of vascular damage, and intramuscular placement.

Conceivably, ultrasound guidance is the best imaging method to facilitate an accurate placement of percutaneous PNS leads. Most of the current and future PNS targets are readily sonographically conspicuous and implantations can be accomplished using either a short- or long-axis views. Moreover, pertinent regional anatomy can be learned, and the implantation can be carefully planned and executed. Ultrasonography is immeasurably helpful in localization the desired segment of the nerve, thus circumventing implantation adjacent to an injured part. A large nerve can be tested intraoperatively under vision to find a better sensory zone and to avoid an unwanted motor stimulation. Ultrasonography may improve procedural safety preventing damage to blood vessels and tendons.

Presently, PNS practice is repeating the developmental stages of regional anesthesia: from landmark-based to electric stimulation to ultrasound-guided methods. Educational publications and hands-on practical sessions are needed to increase competency and assure the safety of PNS. The described method is based on normal anatomy and appeared to be reproducible by following the outlined procedural steps.

Acknowledgement

The authors wish to commemorate the deceased individuals who donated their bodies for the advancement of education and research.

Authorship Statements

Dr. Michael Gofeld designed and conducted the study and prepared the manuscript with important intellectual input from Prof. Agur. Prof. Agur performed dissections and collected data.

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Healthcare Economic Impact of PNS for Chronic Pain, a New Treatment Algorithm

Einar Ottestad, MD, Mark Geiger

Introduction: The overall treatment algorithm for chronic pain patients has not changed significantly in the last several decades, resulting in a burden on patients and the healthcare system. Patients experience months to years of medication trials, temporary nerve blocks, repeated ablation procedures, and surgery without obtaining durable pain relief. As a result some resort to alternative solutions to manage their pain, legal or otherwise, exacerbating the opioid crisis. Medicare and private payers bear the financial burden of poor chronic pain outcomes in the treatment algorithm since many therapy options provide only temporary relief. Peripheral Nerve Stimulation (PNS) has had a resurgence in recent years with new, easy to deploy systems that deliver a targeted, effective, permanent, yet reversible solution that shows promise in improving the chronic pain treatment algorithm and delivering savings to the health care system.

Methods: The cost of routine chronic pain treatment algorithms prior to and after PNS were compared, including blocks, ablations and ultimately spinal cord stimulation (SCS). The new treatment algorithm has been shortened to include one diagnostic nerve block to confirm the target peripheral nerve causing the chronic pain. If that is successful in temporary pain relief then patients are implanted with a PNS implant which consists of a small, thin implanted lead powered by an external pulse transmitter, and controlled with a patient programmer (**Figure 1**). The percutaneous procedure is ≈15 minutes long and performed using ultrasound guidance while the patient is awake. "Trial" stimulation is integrated into the lead placement, combining two procedures. The average cost to the healthcare system for one chronic pain patient in 2016 before and after PNS were analyzed to compare total cost and time to durable relief.

Results: The cost using the old treatment algorithm compared to the new process with PNS illustrates a significantly higher cost and duration until analgesia with the old pathway. The cost and time to receive adequate pain reduction for an average chronic pain patient is described in **Table 1**. An estimated 81% reduction in cost to the healthcare system is realized with a 53% reduction in the time to effective chronic pain treatment.

Figure 1

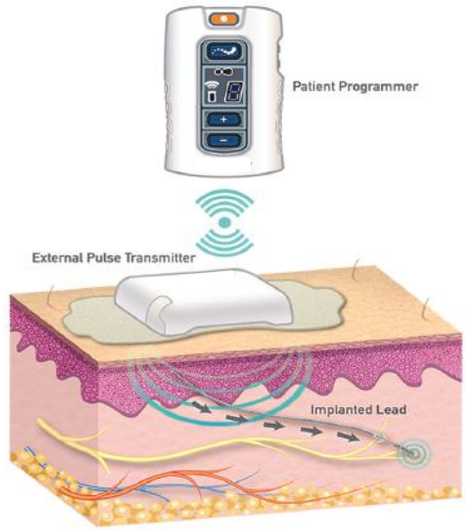

Table 1 - Chronic Pain Cost/Patient			
2016 Treatment Algorithm W/O PNS	**Avg Cost**	**Total**	**Time (months)**
Prescription Opioids	$ 6,162	$ 6,162	6
Nerve Blocks (2)	$ 372	$ 744	6
Nerve Ablation (2)	$ 5,200	$ 10,400	12
Spinal Cord Stimulation*	$ 44,500	$ 44,500	0.5
Total:	**$ 56,234**	**$ 61,806**	**24.5**
2017 Treatment Algorithm, PNS	**Avg Cost**	**Total**	**Time (months)**
Prescription Opioids	$ 6,162	$ 6,162	6
Diagnostic Nerve Block	$ 372	$ 372	3
StimRouter PNS	$ 5,500	$ 5,500	0.5
Rehabilitation			2
Total:	**$ 12,034**	**$ 12,034**	**11.5**

* Average between Medicare and BCBS payments

Conclusion: PNS targeting chronic, mono-neuropathic pain of a peripheral nerve origin is a promising therapy that has the benefits of simplifying/shortening the treatment algorithm, providing significant pain reduction without side effects, and reducing the overall cost to the healthcare system by potentially eliminating more invasive/destructive steps in the process.

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2. Table 1:
   - www.goodrx.com
   - www.healthcarebluebook.com
   - www.mdsave.com

Disclosures:

1. E. Ottestad, MD is on the Scientific Advisory Board for Bioness Inc.
2. Mark Geiger is an employee of Bioness Inc.

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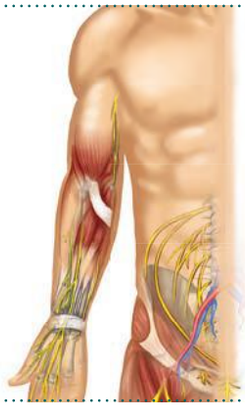

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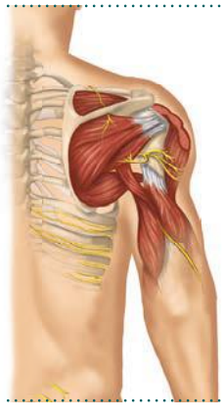

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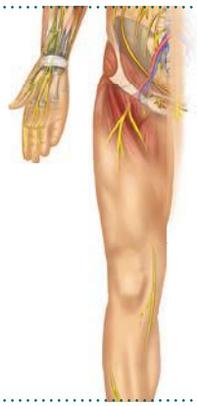

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Orthopedic Surgery	TKR
Radiation Oncology	Sarcoma
Family Medicine	Osteoarthritis
Surgery	Post Herniorrhaphy
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Thoracic Surgery	Intercostal Neuralgia
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*Oswald, J., & Chakravarthy, K. (2019, January). A case series on the use of peripheral nerve stimulation for focal mono neuropathy treatment. Poster session presented at the North American Neuromodulation Society annual convention, Las Vegas, NV.

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