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Research Article

A Comparison of the Clinical Effectiveness of Specific Neurostimulation and Photobiomodulation Modalities with Therapeutic Nutrition in the Treatment of Peripheral Neuropathy

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Abstract

Peripheral neuropathy (PN) is a severe condition with numerous comorbidities. Approximately 4% of adults and the elderly develop polyneuropathy of various etiologies. The incidence of PN likely increases with age and multiple facets of declining health. Many pharmacological agents are inadequate in treating PN, and some have significant side effects. Thus, other treatment options, methods, and modalities to treat PN should be advanced and explored. This retrospective study reports a comparison of the clinical effectiveness of specific neurostimulation and photomodulation (low-level laser therapy) modalities with therapeutic nutrition in the treatment of the symptoms of PN. Most participants reported some level of symptom relief with each of the treatment components, while neurostimulation provided nearly universal relief of all PN symptoms in the participants surveyed.

Keywords: *Low-Level Laser; Neurostimulation; Peripheral Neuropathy; Photobiomodulation; Therapeutic Nutrition*

Abbreviations

LLLT: Low-level Laser Therapy; PBM: Photobiomodulation; PN: Peripheral Neuropathy; QoL: Quality of Life

Introduction

Approximately 4% of adults and the elderly will develop peripheral neuropathy (PN) of various etiologies, the most common being metabolic syndrome, diabetes, and post-chemotherapy-related toxicity, by recent estimates [1]. Pharmacotherapy is often limited to symptom reduction, rarely treating the underlying pathology, and has limited effectiveness and utilization due to side effect profiles and patient costs. This study evaluated the clinical effectiveness of three nonpharmacologic modalities for the management of the most common forms and symptoms of PN. Neurostimulation, photomodulation (low-level laser), and a specific nutrition plan were tested concurrently and independently. One thousand two hundred surveys were extracted and evaluated for data. The 52 respondents who answered all survey questions thoroughly were chosen for this study.

PN is a relentless condition with numerous comorbidities [2]: some causal and others from the direct effects of PN (falls, risks associated with immobility, depression, narcotic dependency, and more). Recent estimates indicated that up to 4% of adults and the elderly develop polyneuropathy of various etiologies [3]. The incidence of PN likely increases with age and multiple facets of declining health [4].

Pharmacotherapy may be limited in effectiveness and by costs, particularly for the most common symptoms of PN due to diabetes mellitus [5,6]. Many pharmacological agents also have significant side effect profiles [7] but are rarely sufficient for treating underlying pathologies of most types, all of which create additional patient care issues as well as frequent patient discontinuation of treatment [8].

The most common causes of PN are well-documented and include diabetes, chemotherapy, toxicities, and compression neuropathies [9]. Diabetes remains a significant cause of not only neuropathy but also multisystem pathologies [10]. Potentially more significant causes of PN in contemporary societies are the critical increases in the prevalence of obesity, metabolic syndrome, and poor overall health [11]. A delay in diagnosis and its relationship to the actual onset of the metabolic stage poses significant risks for the eventual development of PN.

With advances in drug therapy come improved methods of care for many illnesses, but also adverse reactions. Some of the most well-documented drug-related neuropathies include those related to the use of statins [12], anticancer regimens [13], and common quinolone class antibiotics [14,15] as well as metronidazole [16,17].

Methods

This study is the first of its kind. This retrospective study was designed and performed using a secured internet platform and new multiple-choice questions specific to the usage of each treatment component as well as specific reporting of each patient's symptom. Over 60 days, beginning October 2015, approximately 1200 responses were received after sending approximately 5000 email invitations to patients.

The respondents were previously treated in the primary and affiliated clinics or received treatment at home with the same three study treatment components. The in-facility group and at-home group received identical support and direction for neuropathic pain and or PN. At-home care lacked direct clinician oversight, although phone and web forum support was offered. Of the 1200 patients, 52 completed the survey in its entirety, not skipping a single question.

In this initial study, data were extrapolated only from the fully completed surveys to be reasonably sure that all three treatment components were assessed. However, other valid data regarding single component usage that markedly stood out regarding neurostimulation are noted in the "Findings" section that follows.

Fifty-two cases were summarized in the final study; however, most of the 1200 respondents reported some level of symptom relief with the use of one or more of the treatment components, and no worsening or exacerbation of symptoms. The primary outcomes were assessed according to the study design.

As a retrospective study, data on the type of disease treated for each patient were ascertained by patient declaration. A survey was developed based on the range of the three treatments offered to these patients. The reported results were extracted and placed in tables by one reviewer and checked by another. The quality of the study design was assessed accordingly.

Any disagreements among researchers were resolved by consensus. When the number of patients assigned was the same as the number analyzed, it was assumed that withdrawals did not occur. Where units were not equal—which can result from missing data or withdrawal—or resolved by the textual context, it was concluded that withdrawals did not occur.

This study was controlled to estimate the extent to which the observed outcomes were the results of each treatment offered. Observational data were only gathered from those patients who participated in the self-directed treatment regimen or received at-home treatment combined with in-office, physician-supervised treatment.

Of the 52 selected patients in this study, 14 were in-clinic and received physician-directed and at-home applications of the three primary modalities. As such, the researchers had more control over patient compliance with the prescribed courses of treatment.

The study results suggest that all prescribed modalities offered some degree of benefit, with the most significant benefit achieved from all three components (neuromodulation, photobiomodulation, and the nutrition plan) that were physician-directed in-clinic and at-home. Each patient was monitored and supported by a staff member at all times during the treatment period. Patients often reported a considerable improvement in symptoms in as little as 2 weeks with maximum benefits at 36–52 weeks after beginning the combined treatment regimen.

Findings

The study results consistently demonstrated improvements in several different groups of the surveyed symptoms of PN (i.e., pain, tingling, numbness, and burning sensations). Each measurement category, excluding numbness sensations and one instance of pain sensation, fell within reasonable standards for meaningful change across chronic pain conditions and, therefore, was considered a clinically significant change. Also, most measures trended towards symptom improvement in most patients after the initial course of treatment. Refer to functional rating indices (Figure 1–12).

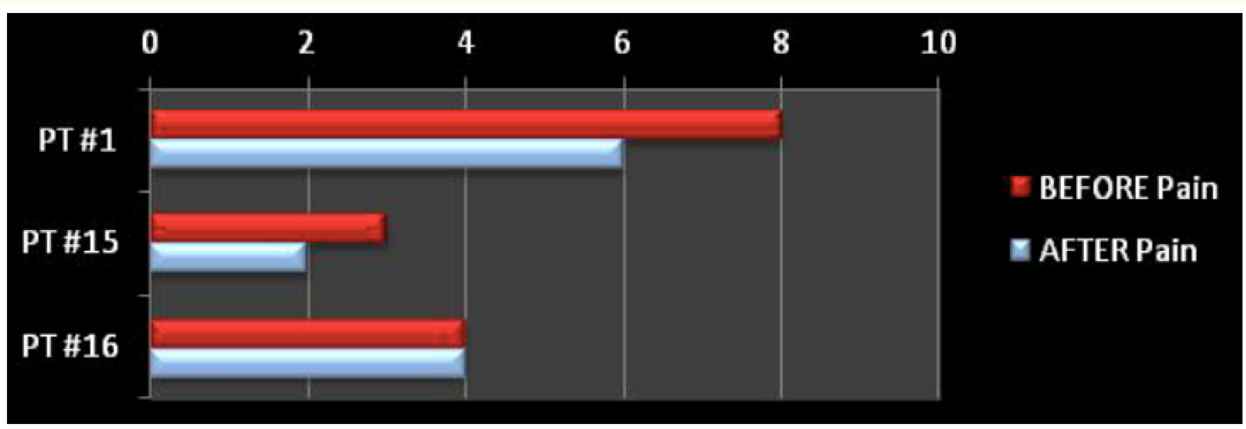

Figure 1: *Pain. Three patients were treated in-office but did not receive neurostimulation as part of the treatment regimen.*

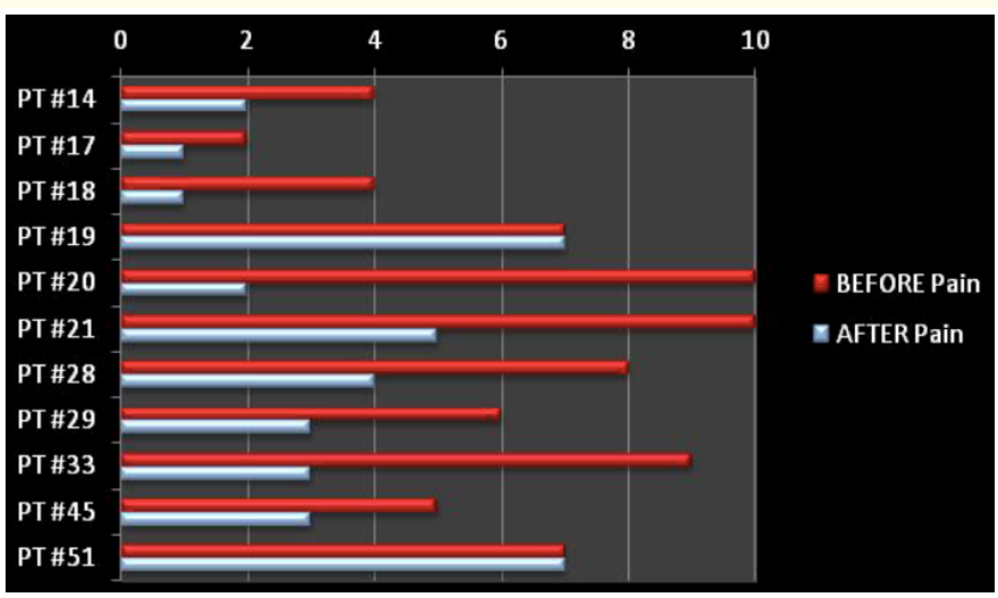

Figure 2: *Pain. Eleven patients were treated in-office with neurostimulation as part of the treatment regimen.*

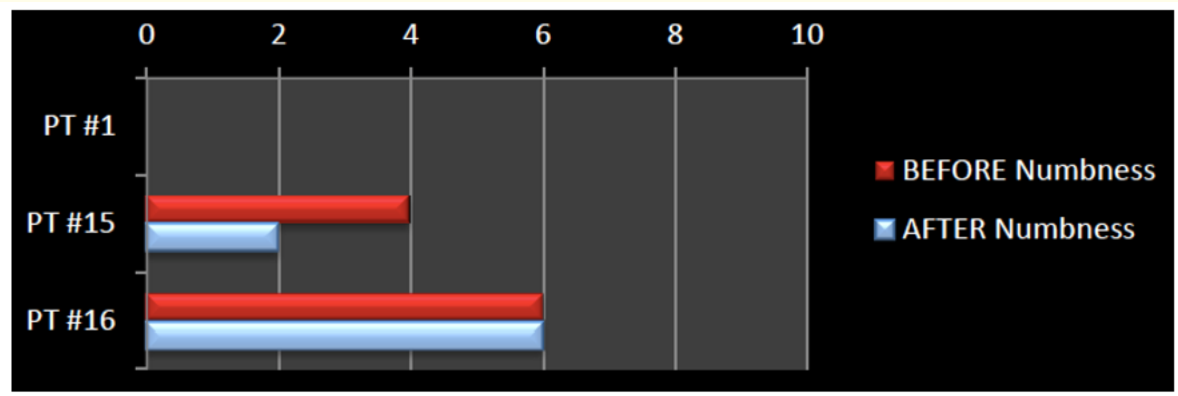

Figure 3: *Numbness. Three patients were treated in-office but did not receive neurostimulation as part of the treatment regimen.*

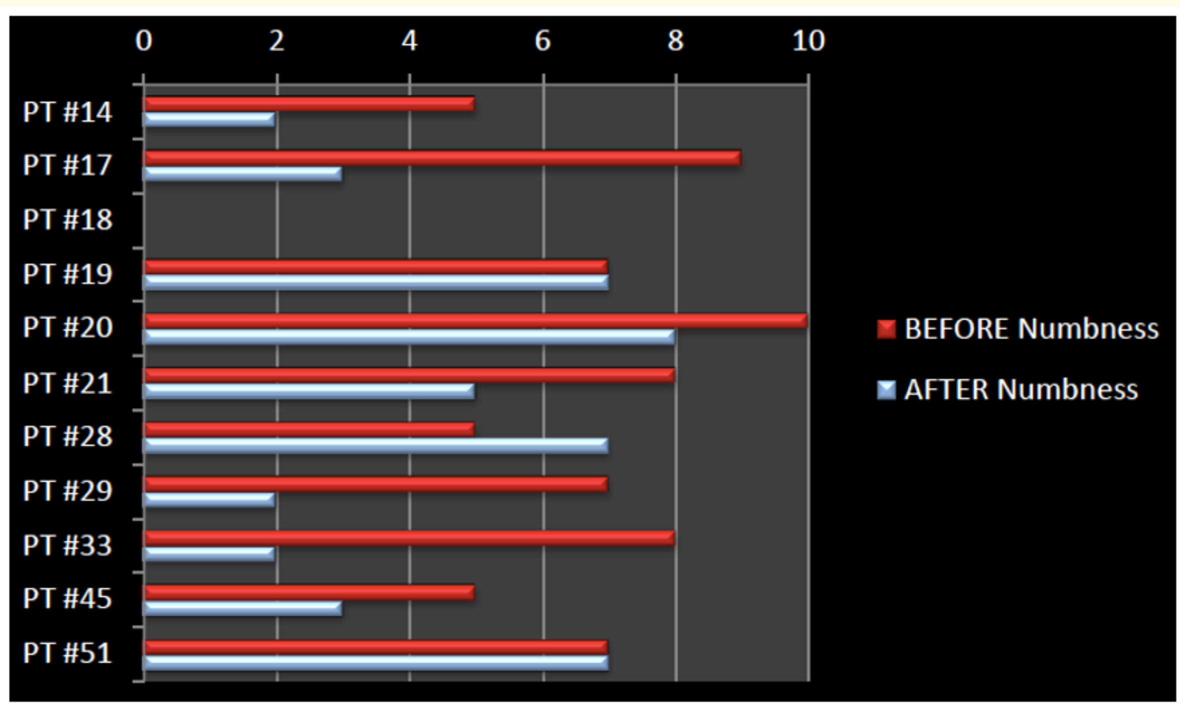

Figure 4: *Numbness. Eleven patients were treated in-office with neurostimulation as part of the treatment regimen.*

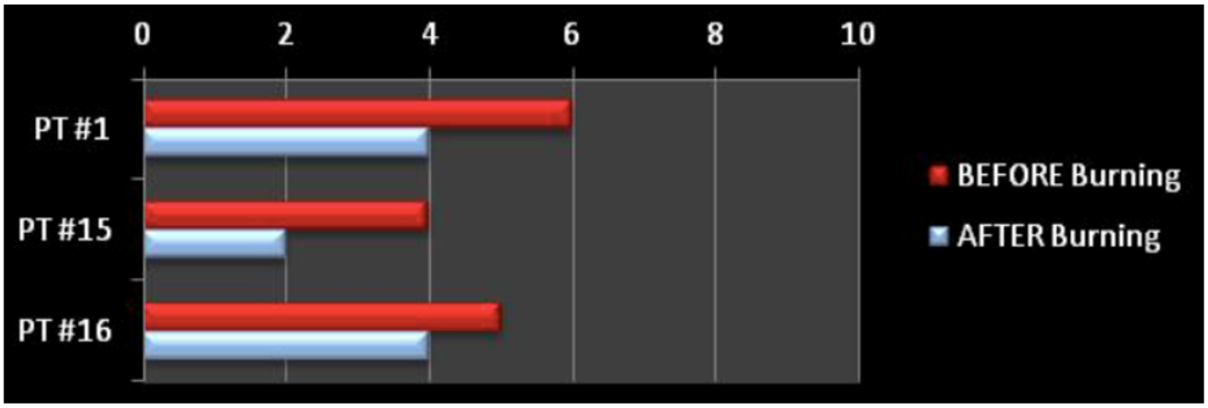

Figure 5: *Burning. Three patients were treated in-office but did not receive neurostimulation as part of the treatment regimen.*

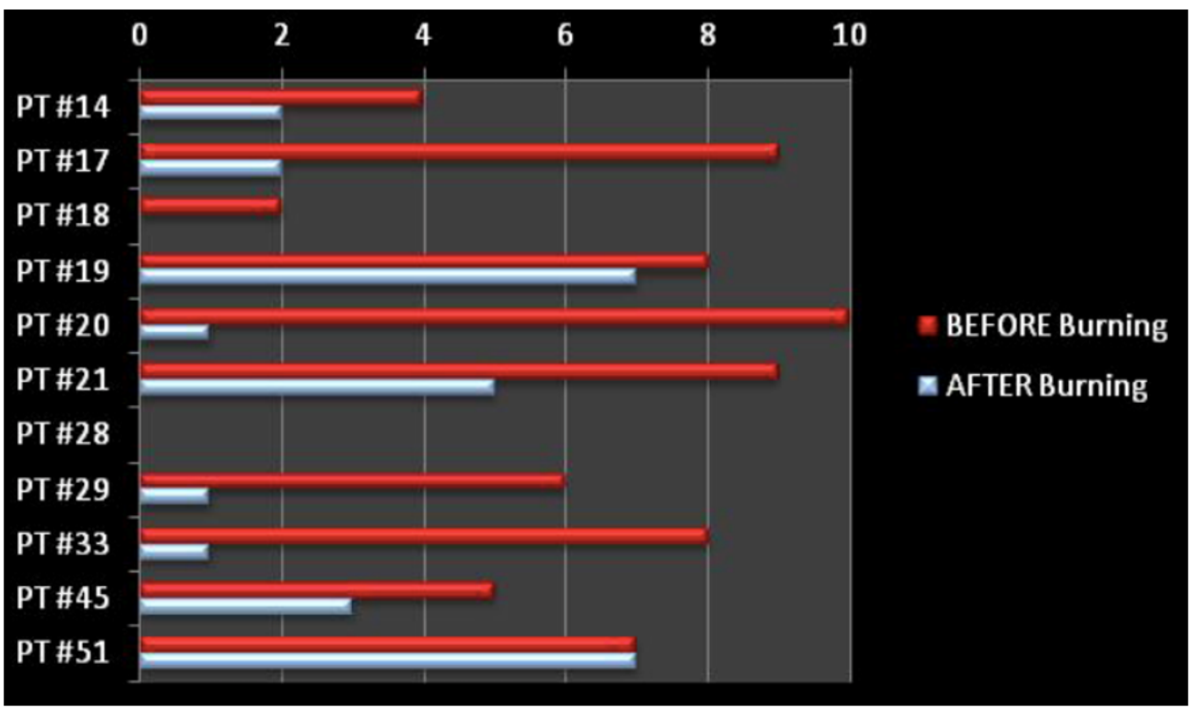

Figure 6: *Burning. Eleven patients were treated in-office with neurostimulation as part of the treatment regimen.*

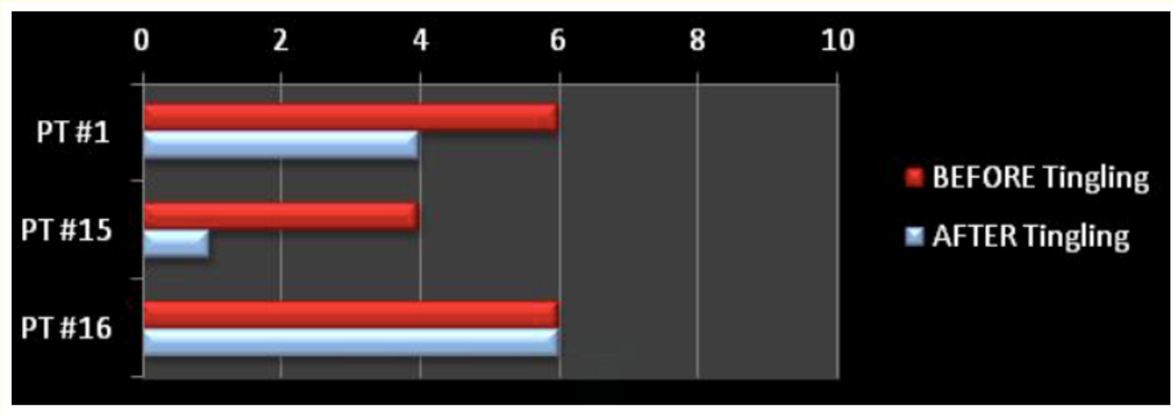

Figure 7: *Tingling. Three patients were treated in-office but did not receive neurostimulation as part of the treatment regimen.*

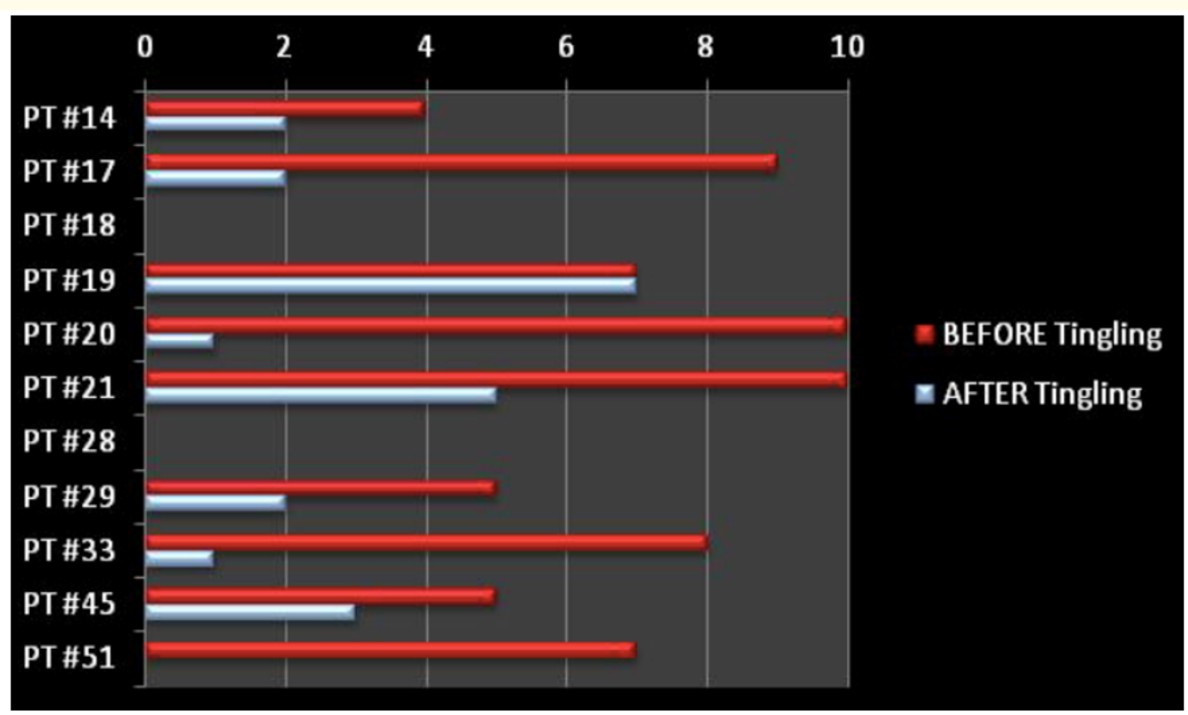

Figure 8: *Tingling. Eleven patients were treated in-office with neurostimulation as part of the treatment regimen.*

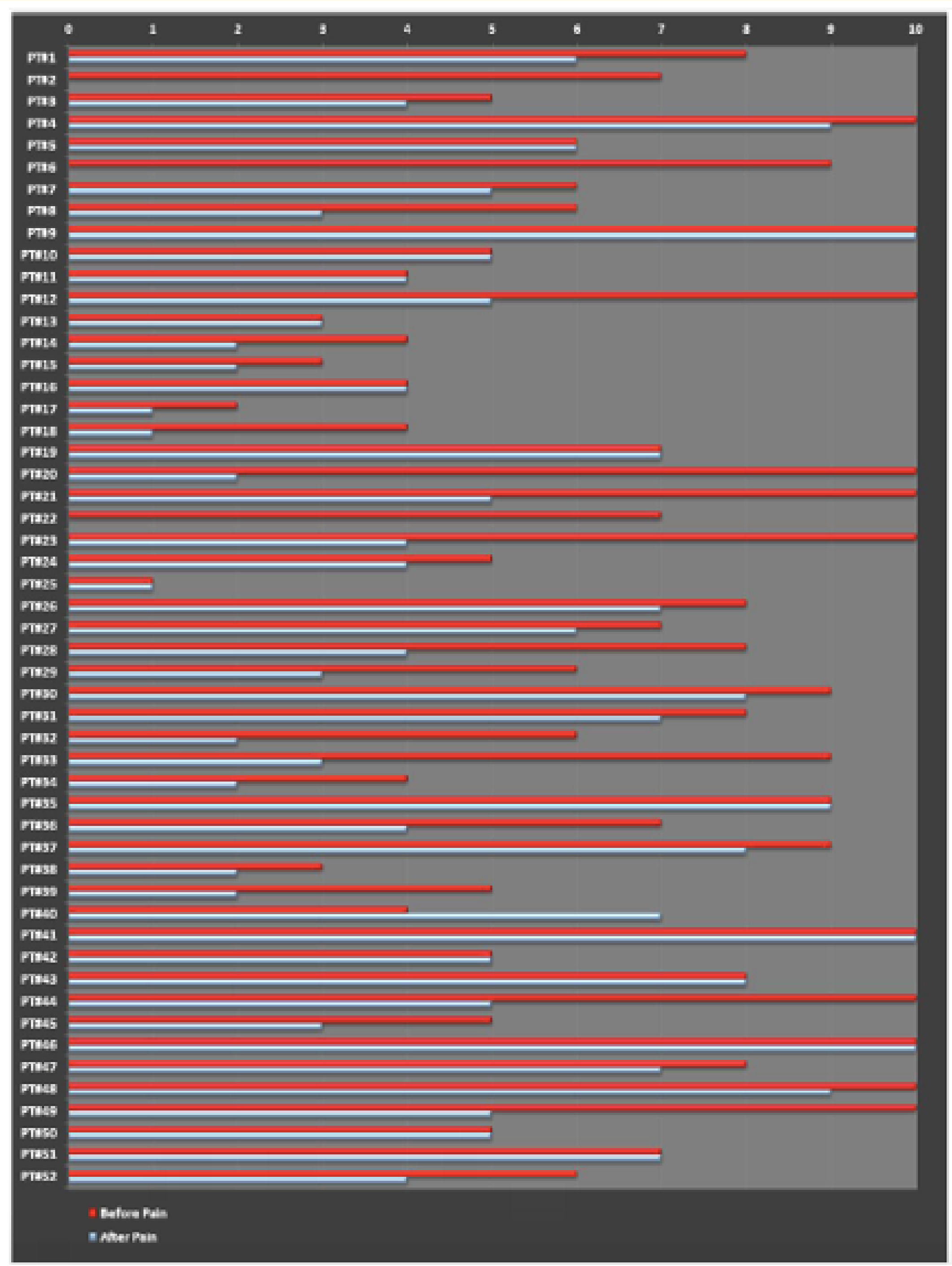

Figure 9: *Pain (before and after treatment) with neurostimulation as part of the treatment regimen.*

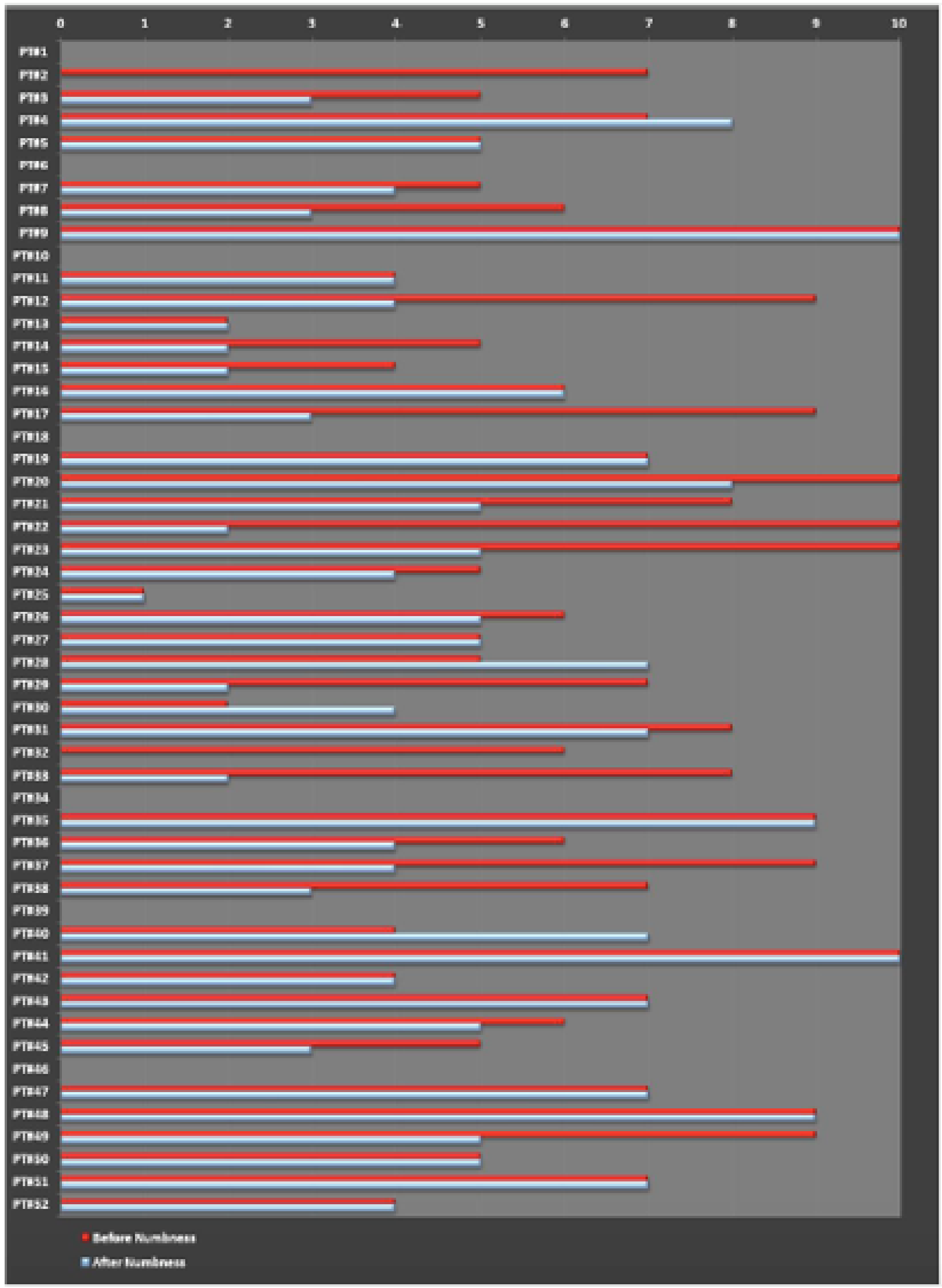

Figure 10: *Numbness (before and after treatment) with neurostimulation as part of the treatment regimen.*

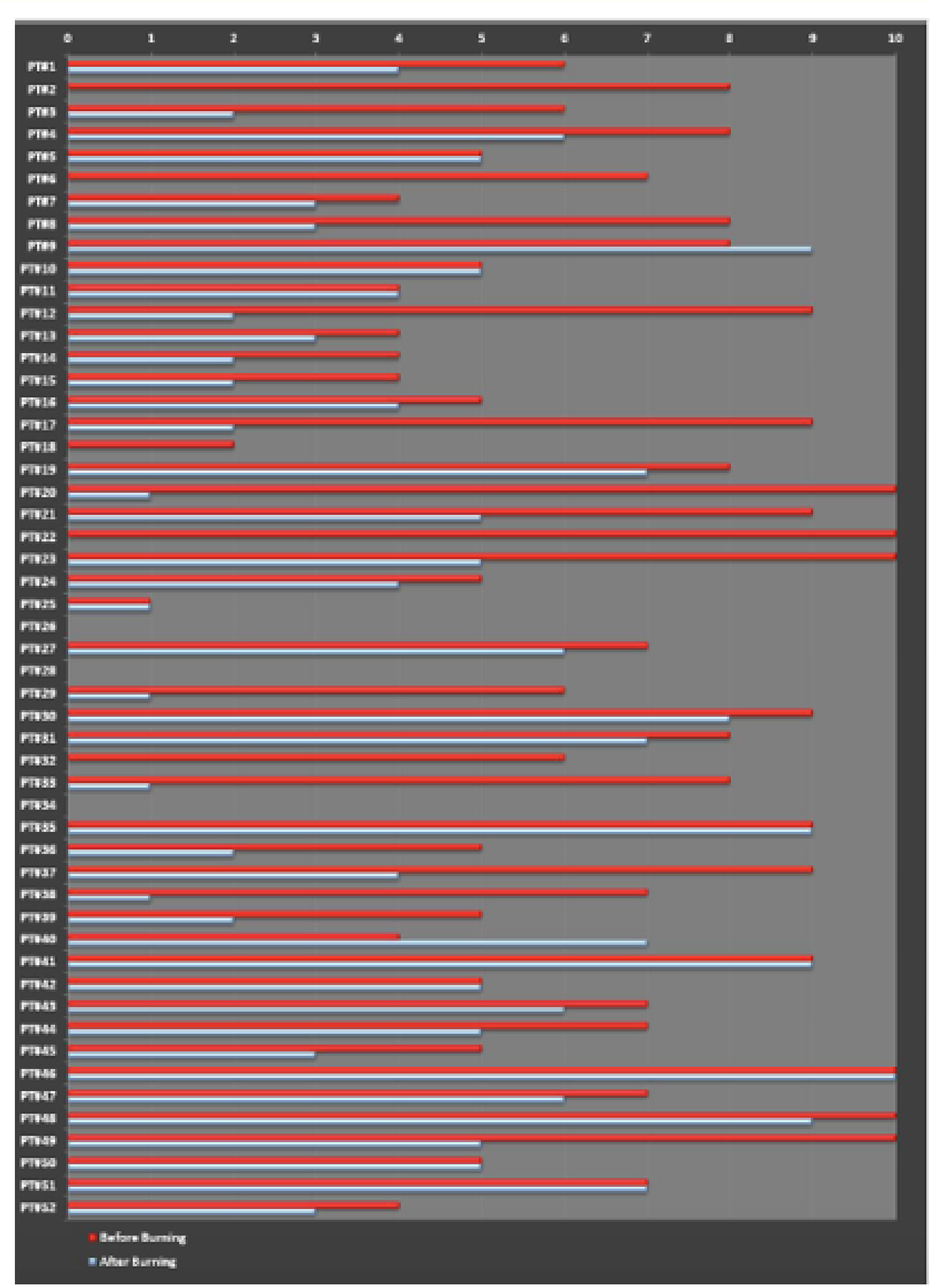

Figure 11: *Burning (before and after treatment) with neurostimulation as part of the treatment regimen.*

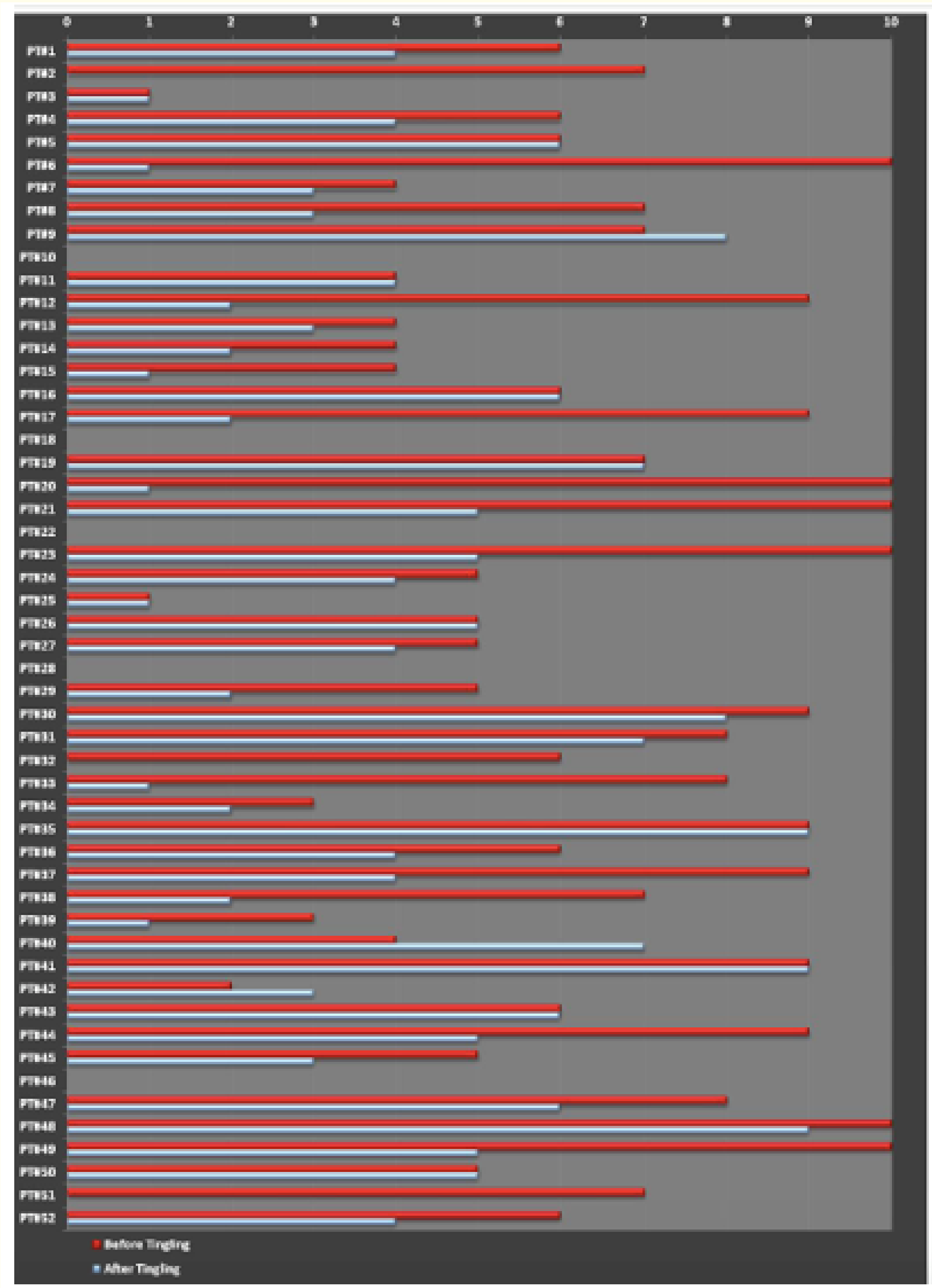

Figure 12: *Tingling (before and after treatment) with neurostimulation as part of the treatment regimen.*

For each measurement category, the rates and extent of responses were higher when treatment included the most consistent application of the neurostimulation. Most survey respondents reported significant relief via the application of the neurostimulation treatment alone. There was no other single component when used as stand-alone in the 1200 surveys reviewed that demonstrated almost universal relief of PN symptoms.

Using a visual analog scale of 11, of the 14 in-clinic respondents who were treated with all three components, 8 (73%) reported at least a 33% decrease in pain, 5 (45%) reported at least a 33% decrease in numbness sensations, 7 (64%) reported at least a 33% decrease in burning sensations, and 6 (54%) reported at least a 33% decrease in tingling sensations. Each measurement category fell within reasonable standards for meaningful change across chronic pain conditions and, therefore, constituted a clinically significant change.

Of the three patients who did not use neurostimulation but received low-level laser therapy (LLLT) and declared that they followed the prescribed nutrition plan, 2 (66%) reported at least a 33% decrease in pain, 1 (25%) reported at least a 33% decrease in numbness sensations, 2 (50%) reported at least a 33% decrease in burning sensations, and all 3 (100%) reported at least a 33% decrease in tingling sensations. Each measurement, excluding the numbness sensations category, fell within reasonable standards for meaningful change across chronic pain conditions and, therefore, constituted a clinically significant change.

Of the in-clinic respondents who were treated with all three critical components cited herein, 73% reported at least a 33% decrease in pain, 45% reported at least a 33% decrease in numbness sensations, 64% reported at least a 33% decrease in burning sensations, and 54% reported at least a 33% decrease in tingling sensations. Each measurement category fell within reasonable standards for meaningful change across chronic pain conditions and, therefore, constituted a clinically significant change.

The combination of the neurostimulation, LLLT, and the recommended clinical diet demonstrated a clinically significant improvement in health-related quality of life (QoL). In the experience of twelve clinicians regularly administering these treatment components, QoL improvements with prolonged neurostimulation have been reported consistently by most patients treated in-clinic or at-home for PN and related pain.

Costs of treatment

The mean cost per out-patient treatment was approximately $750.00, while the average in-clinic treatment cost for 2–3 months was about $3500. The treatment cost per patient varied by the type and length of the regimen provided.

Discussion

The three modalities tested in this study were neurostimulation (using the FDA-approved NDGen® neurostimulator), photobiomodulation (using class 1 and 3B, medical-grade, low-level laser therapy units), and a specific, proprietary nutrition plan (using the NeuropathyDR® Nutrition Therapy Plan). See the Supplementary Information section at the end of this paper for further information on the NDGen® neurostimulator and NeuropathyDR® Nutrition Therapy Plan.

In this study, photobiomodulation (PBM) consisted of direct, in-clinic and at-home applications of LLLT using primarily class 1 and 3B devices, and infrared therapy at various wavelengths. The administration of LLLT is comfortable (since no significant heat is produced) and is extremely safe when administered by trained professionals. The primary effect of LLLT is stimulating and enhancing mitochondrial and intracellular functions and reducing pain and concurrent inflammatory reactions [18,19]. Furthermore, laser therapies are safe for use in patients with pacemakers and metallic implants, including prosthetic joints and limbs.

The propriety nutrition plan utilized was a carbohydrate-controlled, plant-based [20], low-allergenicity diet combined with broad-spectrum and neurotropic-targeted oral and topical nutrient supplementation. Upon performing the initial patient evaluation, dietary supplements are frequently recommended. It has been noted that appropriate, supervised dietary supplementation in unique combinations seems to greatly enhance the nutritional component of a patient's treatment program [21]. Some of the 1200 respondents showed improvement in symptoms and significant weight loss following the nutrition component alone.

Limitations of the research

The researchers had no control over patient compliance with the at-home treatment regimen being investigated beyond the patients' declarations. Furthermore, the relevance of the patients' declarations regarding the effectiveness of prior treatments sought outside of this study was assessed. The evidence for effectiveness was generally limited to subjective self-reported findings, as patients tend to understate or overstate their level of discomfort (in this case, self-reported feelings of pain, tingling, numbness, and or burning sensations). When considering self-reported findings, a patient may be unable to articulate the level of discomfort for many reasons accurately.

Recommendations for future research

The design of future studies should include larger groups for enhanced comparative analysis. Future studies should be designed to analyze further and compare controlled and independent groups to determine the effectiveness of these modalities for the treatment of PN and related chronic pain. Regarding the positive self-reported findings and limitations to self-reporting, further research could clarify any remaining uncertainties.

According to Wager., *et al*. (2013), brain imaging may be clinically useful to visualize and objectively quantify the degree of pain. Also, skin punch biopsy, electromyography, and nerve conduction velocity testing might, in some cases, be useful to quantitatively, accurately, and objectively assess an underlying diagnosis of tingling and numbness sensations (e.g., small fiber neuropathy) [22].

Future studies should include brain imaging, electromyography, and nerve conduction velocity testing at the onset of treatment and after the completion of treatment. These tests, in conjunction with the self-reported findings, should provide a more accurate measure of the overall effectiveness of treatment modalities for chronic neuropathic pain, paresthesia, and related symptoms.

Summary

This study aimed to determine and compare the clinical effectiveness of several nonpharmacologic modalities for treating PN of various etiologies and related chronic neuropathic pain, numbness, and paresthesia. Also, it evaluated the overall level of relief of each category of patient symptoms for three independent treatment components as well as the effectiveness of physician-directed treatments combining all three components. Nonpharmacologic interventions were exclusively assessed as clinical and patient experiences with drug-only therapy are accompanied frequently by adverse reactions and limited effectiveness, particularly in the long-term [1].

Conclusion

Most participants reported some level of symptom relief with one of the treatment components with no significant worsening of symptoms or side effects. In-clinic patients who received the three modalities simultaneously and were firmly supervised fared best, whereas the neurostimulator provided nearly universal relief of all PN symptoms surveyed. Each component tested resulted in statistically significant symptom relief, with the best results obtained via the simultaneous application of all three modalities when supervised in-clinic.

Conflict of Interest Statement

John Hayes, Jr., MD is co-founder of NeuropathyDR® and co-designer of the NDGen® neurostimulator used in this study. Sources of support for the work: self-funded by NeuropathyDR®. Shannon Boyce, J.D. acknowledges a proprietary interest in the NDGen® neurostimulator used in this study. Nicholas A. Kerna, PhD, MD, MPH, DNBCE, declares that his contribution to this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

Supplementary Information

The NDGen® neurostimilator is an advanced FDA-approved electrotherapy neurostimulator that combines adjustable waveforms (shape, pulse width, and duration) with unique physician-determined programming. It is wearable, portable, and utilizable for both neuropathic pain control and neuropathy treatment. The development of the NDGen® neurostimulator was the result of research findings and best practices in electrotherapy as well as multi-treatment clinical testing and reporting [23,24]. The NDGen® neurostimilator was co-designed by John Hayes, Jr., MD of the United States.

The NeuropathyDR® Nutrition Plan is a carbohydrate-controlled plant-based [20], low-allergenicity diet combined with broad-spectrum and neurotropic-targeted oral and topical nutrient supplementation. The NeuropathyDR® Nutrition Plan was co-developed by John Hayes, Jr., MD of the United States.

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