Realief Therapy for Peripheral Neuropathy: Experience with 100 Patients

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Background: Peripheral neuropathy is a common disorder resulting from damage to peripheral nerves. Symptoms, which can include pain, abnormal sensations, numbness, muscle weakness, and problems with balance, frequently become more extensive and severe over time and can interfere with quality of life. Most existing treatments have limited effectiveness and are often associated with troubling side effects. Laser therapy is noninvasive and may be as effective as other treatment options.

Objective: To describe the effects of Realief Therapy, a protocol using high-power laser therapy combined with individualized treatment plans, in patients with neuropathy due to any cause.

Methods: One hundred patients were seen in a private clinic. History, symptoms, medications, and other variables were collected at the initial consult. At each treatment visit, patients reported symptom intensity for pain, numbness, and burning on numeric rating scales (from 1 [least severe] to 10 [worst]). The ability to detect pain and vibration was tested using a pinwheel and a tuning fork, respectively; scores were assigned that corresponded to the highest position on the limb where the sensation was not detected.

Results: Of the 100 patients, 63 were male and 37 were female. Ages ranged from 15 to 89 years (mean 66.7 years). Neuropathic symptoms had lasted for more than 2 years in 70% of patients. Diabetes was the most commonly reported cause of neuropathy (n = 26).

Data were analyzed for 80 patients with symptoms in the lower extremities. The mean percent reductions were 52% for pain, 55% for numbness, and 44% for burning; 69% of patients experienced a reduction of 50% or more on at least one symptom. Areas insensitive to pinprick and vibration decreased dramatically in most patients, retreating from above the ankle, calf, or thigh to a limited region on the bottom of the foot.

Conclusion: Realief Therapy greatly reduced symptoms in a majority of patients and is therefore a promising approach to the treatment of peripheral neuropathy.

Introduction

The peripheral nervous system is made up of nerves that extend beyond the brain and spinal cord, which together form the central nervous system, to innervate (communicate with) the organs of the body, including the muscles, skin, and internal organs. Nerves are made up of bundles of long fibers that extend from individual nerve cells located in or near the spinal cord to the body part they innervate.[1] Thus, a nerve fiber may be very long, reaching from the back to the fingers or toes (**Figure 1**). The fibers vary in thickness and in whether they are insulated with myelin, which increases the speed at which information can travel along the nerve (**Figure 2**).[1, 2]

Two major classes of peripheral nerves are the motor nerves and sensory nerves, which respectively control the muscles and convey sensory information such as pain, temperature, and body position to the central nervous system (**Figure 2**). The sensory nerves are further divided into groups of nerves that process particular types of information. For example, large-fiber sensory nerves sense vibration, touch, and body position, whereas small-fiber nerves sense pain and temperature.[1, 2] Autonomic nerves, another class of peripheral nerves, control involuntary bodily functions such as digestion and blood pressure.

Peripheral neuropathy

Peripheral neuropathy refers to a wide range of disorders that involve damage to the peripheral nerves. Damage can result from a variety of causes,[2] which include injury; compression, such as in carpal tunnel syndrome; chronic diseases such as diabetes,

which interferes with the nutritional support of nerves; vitamin deficiencies due to poor nutrition or alcoholism; infections, such as HIV or herpes zoster, the virus that causes shingles; and some cancers and treatments for cancer, among others. In addition, some neuropathies are inherited. However, often neuropathy is idiopathic, meaning that its cause is not known. The damage can both disrupt normal nerve function, leading to numbness, balance problems, or muscle weakness, and cause inappropriate nerve signaling, resulting in muscle spasms, pain, oversensitivity to touch, or other abnormal sensations.

The symptoms of peripheral neuropathy can vary substantially from patient to patient depending on the cause and which nerves are affected,[3] but pain, abnormal sensations (dysesthesias or paresthesias) such as tingling or burning, loss of sensation (numbness), and trouble with balance are common. Often these symptoms begin at the ends of the nerves, such as in the feet or the hands, and gradually expand as damage to the nerve increases along its length[2, 3]; for example, symptoms may spread from the foot to the calf and up into the thigh. Because the damage occurs first in longer nerves, feet are usually affected before hands.[1] Some patients do not even realize that they have lost nerve function in their extremities ("asymptomatic" neuropathy), whereas pain and other symptoms can be quite severe for others and can worsen over time. Our experience has been that, in many patients, a loss of sensation that can be detected clinically with a pinprick or vibrating tuning fork will extend higher on the limb than the overt symptoms of pain or burning, suggesting that loss of sensory transmission occurs before the inappropriate signaling that causes the characteristic symptoms of neuropathy (**Figure 3**).

Because of the many possible causes of peripheral neuropathy, the different patterns of symptoms, and the different ways of measuring the signs and symptoms, it is difficult to know exactly how prevalent the disorder is. As part of the National Health and Nutrition Examination Survey in the United States, Gregg et al. estimated the prevalence of peripheral neuropathy in the general population by using a combination of self-report of symptoms and the presence of at least one region of the foot that was insensitive to stimulation with a filament.[4] Of those over 40 years old, 14.8% were estimated to have peripheral neuropathy; in individuals over 40 with diabetes, the

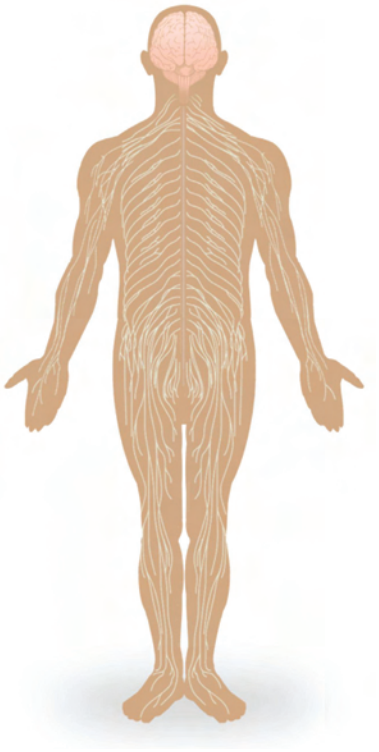

Figure 1. The peripheral nervous system. Peripheral nerves originate in or near the spinal cord and can extend all the way to the fingers or toes.

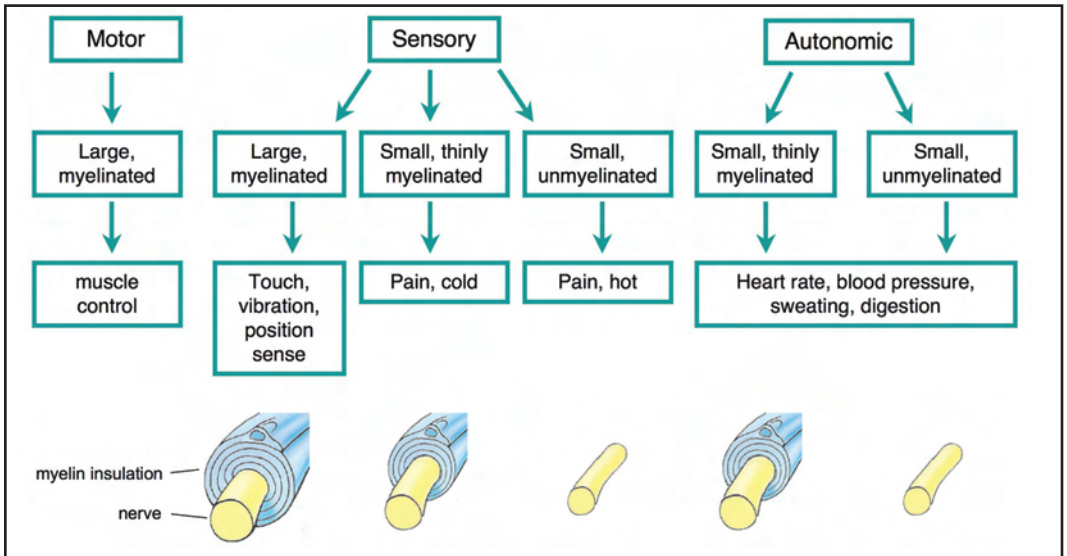

Figure 2. Types of nerves in the peripheral nervous system and their functions. Nerves can vary by size (large or small) and amount of myelin insulation (fully insulated, thinly insulated, or uninsulated). Large nerves transmit signals more quickly than small nerves, and myelinated nerves more quickly than unmyelinated nerves. Motor nerves are large and myelinated and control muscle function. Sensory nerves can be large or small, with different amounts of myelin; each type transmits a different type of sensory information to the central nervous system. Autonomic nerves are small and myelinated only thinly if at all; these nerves control involuntary body functions, such as heart rate and digestion.

rate was estimated to be 28.5%. However, many of these individuals were asymptomatic. A systematic review[5] reported the prevalence of neuropathic pain at 0.9% to 8% of the overall population, but this included pain of central as well as peripheral origin; however, this is consistent with another estimate for neuropathic pain that was also derived from multiple reports of 3% of the population.[6] Diabetes is a frequent cause of neuropathy and one of the best studied; although, as with other forms of neuropathy, estimates of its prevalence range widely, it is likely that diabetic neuropathy affects millions of individuals in the United States.[7]

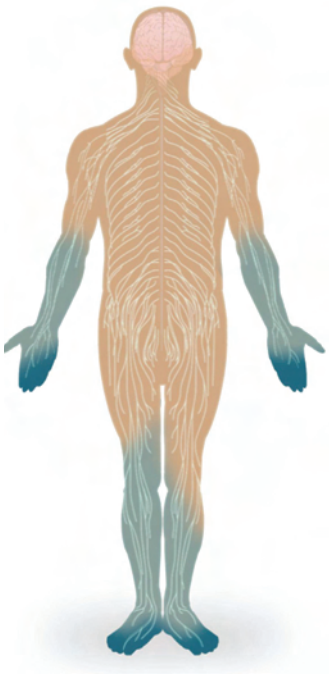

Figure 3. Distribution of affected areas. Symptoms are often distributed in a "stocking and glove" pattern, first appearing on the toes or feet and then expanding up the leg before repeating the pattern in the hands and arms. In many cases, the area that has lost sensation (as tested with pinprick or vibration; pale blue) is much larger than the area with overt symptoms such as pain, burning, or noticeable numbness (dark blue).

For many patients, the symptoms of peripheral neuropathy, particularly pain, can result in substantial decreases in quality of life, including problems with sleep, emotional disturbances, and limited mobility that can lead to social isolation.[5, 6, 8-10] The costs to the patient and to society can also be quite extensive. Patients with neuropathic pain use health care more frequently and have much higher expenditures than patients without neuropathic pain, although some of this utilization may be due to coexisting medical conditions, which are frequent in patients with neuropathy.[5] Patients with diabetic neuropathy incur direct medical costs many times higher than patients with diabetes but no neuropathy[11]; a 2003 article estimated that the annual costs of diabetic peripheral neuropathy and its complications (including amputations) were almost US$11 billion and accounted for up to 27% of the total costs of diabetes.[12] In addition, neuropathy can affect the ability of the patient or a caregiver to work, adding loss of income to the substantial direct medical costs.[5]

Drug treatments for peripheral neuropathy

Treatment for neuropathy should start with addressing the underlying cause, if it is known.[13, 14] However, once neuropathy is established, addressing the cause, such as glycemic control in patients with diabetes, may not be sufficient to relieve the neuropathy.[15]

The most common approach to the treatment of neuropathy itself is the use of medications. The drugs recommended for first-line use are certain types of antidepressants (tricyclics such as amitriptyline, and serotonin/norepinephrine reuptake inhibitors such as duloxetine and venlafaxine) and the anticonvulsants gabapentin and pregabalin.[16-18] These treatments are aimed almost exclusively at neuropathic pain; while they may improve mood and quality of life,[19] they do not specifically address other symptoms such as numbness, nor do they resolve the underlying damage to the nerves. They are also, to greater or lesser degrees, associated with unpleasant side effects, such as sedation, cardiac block, and urinary retention for the tricyclic antidepressants, and sedation, dizziness, and vision problems for the anticonvulsants.[6, 17]

Although these medicines can provide symptom relief, they do not usually abolish symptoms altogether, and the goal may be to make the pain more tolerable rather than to eliminate it.[17] Furthermore, not all patients respond, and several may need to be treated for one patient to achieve a 50% reduction in pain.[6, 17] This "number needed to treat" is about 2.5 for tricyclic antidepressants and about 4 for anticonvulsants[17]; however, the antidepressants are associated with more adverse effects.[6]

In clinical trials of pregabalin for patients with diabetic neuropathy, about 40% to 50% of patients experienced a 50% decrease in pain from baseline.[20] The percentages achieving this level of pain reduction were even lower for patients with postherpetic neuralgia, ranging from about 22% to about 40%, for both pregabalin and gabapentin.[20, 21] Thus, many patients obtain only limited benefit from these drugs and few are free from pain. Although pain medications are frequently underprescribed,[5] there is a clear need for additional safe and effective treatments for peripheral neuropathy.

Other types of treatments

A variety of nonpharmaceutical approaches have also been used to treat the symptoms of peripheral

neuropathy, including topical treatment with capsaicin,[22] electrical stimulation at the skin surface[23] or to the nerves with needles,[24] acupuncture,[25] and magnetic therapy.[26] Although these treatment methods have shown some success at relieving neuropathic symptoms, particularly pain, and improving quality of life, most have not been extensively studied.[27] Furthermore, the relief provided by some modalities may not be lasting, requiring sustained treatments over time.[23, 24]

More recently, various types of light therapy have been used to treat neuropathy. Light is part of a continuum of electromagnetic energy that ranges from radio waves, which have very long wavelengths, to gamma waves, which have very short wavelengths. Visible light is one slice of this spectrum, with wavelengths ranging from 400 nm to 800 nm, between the shorter wavelengths of ultraviolet light and the longer wavelengths of infrared light. In addition to wavelength, light waves can vary in their amount of energy, or their power, often reported in watts (W).

One form of light therapy, monochromatic infrared energy (MIRE, also known as anodyne light therapy), uses an array of diodes to provide low-level light. MIRE has shown conflicting results in randomized trials, and although some positive results have been reported (see, for example, ref. 28), many studies have been poorly designed, and more rigorous examination has shown no benefit of MIRE over placebo.[29]

Laser therapy

Therapeutic lasers work by delivering energy of a specific type and wavelength to tissues. Depending on the wavelength used and the tissue it is applied to, the energy in the light can be absorbed by molecules within the cells and tissues, thus affecting cellular activities. For example, hemoglobin in red blood cells and the mitochondrial enzyme cytochrome c oxidase can absorb the wavelengths of light produced by therapeutic lasers, resulting in the stimulation of cellular metabolism and leading to the production of ATP, the energy source for cells.[30] This additional energy, in turn, helps the healing process. The interaction of laser light with cells can also prompt the release of pain-reducing compounds or the removal of pain-producing substances, decrease inflammation, and affect communication between cells.[31] Thus, laser therapy works with the body's own resources to heal injuries, and the healing process continues after the laser has been turned off. Lasers are also effective at reducing pain,[31] possibly by inhibiting the ability of neurons to send painful signals.[32, 33]

Lasers are classified by how much power they can produce. Class III lasers have a maximum power output of 500 mW (0.5 W). These lasers have been used for decades in so-called "low-level laser therapy" (LLLT) to treat a variety of medical conditions,[34] including neuropathy. However, the low power of these devices limits how far the laser energy can penetrate into tissues, and therefore limits their potential to heal deep structures. In one study, LLLT was not significantly better than placebo at relieving the pain of diabetic neuropathy, although symptoms did improve somewhat from baseline.[35]

In 2003, the FDA approved the use of class IV lasers for therapeutic applications. These lasers are much more powerful than the class III lasers used for LLLT, with output of up to 12 W. This enables the light to penetrate more deeply into affected tissues and allows for much greater power density in the tissues.[34]

Here, we describe the use of a high-power, 980-nm gallium arsenide diode laser combined with individualized, dynamic treatment plans to treat 100 patients with neuropathy of any cause.

Methods

Subjects

All patients were seen in a private clinic by TK. One hundred consecutive patients with any type of neuropathy who gave consent to participate in the study and received at least one treatment were enrolled in the study.

History and patient-reported symptoms

The patient's peripheral neuropathy was assessed at the initial consult. Information obtained from the patient included diagnosis (if available); history of the onset, duration, and progression of symptoms, and the surface areas affected; the qualitative characteristics of the symptoms (eg, burning, pain, numbness), including any radiation along dermatomal patterns; and factors affecting symptom severity, such as time of day, activity level, medications, rest, ice, or splinting. Information on current medications taken for the neuropathy and the presence or absence of balance problems were also solicited from the patients. The patient's general medical history was assessed for any contraindications to high-power laser therapy, such as the presence of a tumor or an implanted device in the areas to be treated, or current treatment with drugs that increase sensitivity to light, including tetracycline and antifungals.

At each visit, the patient completed numeric

rating scales (symptom scales) to indicate the current level of pain, numbness, and burning. The scales ranged from 1 (least severe) to 10 (worst). Patients also indicated on a diagram which areas of the body were affected by these sensations, as well as by tingling and stiffness. The patients were asked if the sensations were new, increasing, or decreasing from the levels reported at the previous visit.

Sensory evaluation

Patients were evaluated with sensory and reflex testing, and any soft tissue contracture or losses in joint motion were noted. The extent of sensory loss was determined with a 512-Hz tuning fork to determine the subjective vibration threshold and a Wartenburg pinwheel to determine subjective pinprick sensitivity. These assessments were repeated every 2 to 3 weeks and at the end of the treatment plan. After the initial evaluation, vibration was assessed with either a 512-Hz or 256-Hz tuning fork, which have been reported to give similar results.[36]

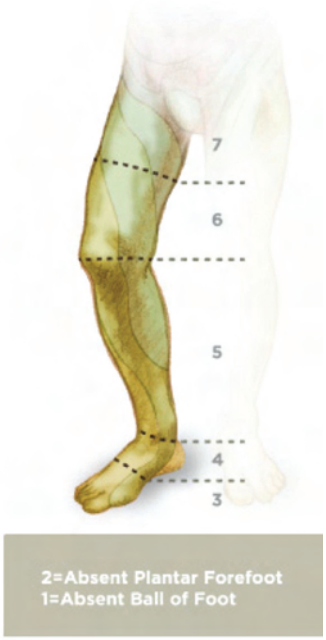

Figure 4. Measurement of sensitivity. The lower extremities were divided into 7 "zones" for recording sensitivity to vibration and pinprick. The highest zone in each limb with loss of sensation was recorded as the score. A score of 0 represents normal sensation.

Use of the tuning fork and pinwheel were first demonstrated for the patient on an area with normal sensation. Sensation in the affected areas was then tested, and responses were binned into zones according to the affected area of the limb, as illustrated in **Figure 4**. The highest value from the most-affected limb was taken as the initial score for the analysis, and the highest value obtained from the same limb at the last treatment session was used as the final score.

The tuning fork was placed on the dorsum (top) of the first toe, on the dorsum of the foot at midfoot, at the anterior ankle, and then up the anterior (front) of the leg and thigh. The pinwheel was placed on the dorsum of the first toe and then was run up the dorsum of the foot at midfoot, up to the anterior ankle, and up the anterior of the leg and thigh.

Treatment

Treatment was performed with a 980-nm class IV therapeutic laser (AVI-HCLL 12, Avicenna Laser Technology, West Palm Beach, FL) with output strength ranging from 1 W to 12 W. Power density into the treated areas was achieved with a combination of wattage setting and exposure time.

The proprietary Realief Therapy protocol was used to create customized treatment programs for each patient, including number, duration, and intensity of treatments. The findings in the initial exam (surface areas with sensory deficits) were the primary factor taken into consideration and the specific presentation of symptoms was secondary. The treatment parameters were varied as necessary in subsequent sessions with the goal of reaching a "therapeutic window" that provided symptom relief. During the treatment sessions, the laser was held approximately 0.5–1 inch above the skin surface and moved at approximately 1 inch/second in areas where vibratory or pinprick sensory loss was noted. Surface areas of both nerve roots supplying the affected areas were stimulated as well. In preclinical research, treating the spinal roots with laser irradiation dramatically expedited the healing of crushed peripheral nerves.[37]

In addition to the laser therapy, joint mobilization and cryotherapy were performed if needed, and some patients were given stretching exercises to perform at home.

Analysis

Information from all 100 patients is included in the summaries of patient characteristics. Only data from patients who completed the entire treatment plan or whose symptoms had resolved before the end of the planned treatment were included in the detailed analyses. In addition, only treatments on lower extremities were analyzed because a minority of patients presented only with neuropathy of the upper extremity or torso. Descriptive statistics were calculated using Excel software (Microsoft Corporation, Redmond, WA).

Results

As planned, 100 patients were enrolled in the

Table 1. Patient characteristics

Characteristic	Distribution[a]
Sex (M/F)	63/37
Age (y; mean ± SD)	66.7 ± 13.0
Males	65.8 ± 11.0
Females	68.4 ± 15.8
Range	15–89
Cause of neuropathy	
Diabetes	26
Chemotherapy	4
Alcoholism	3
Car accident	2
Bells Palsy	1
Diabetes + Alcoholism	1
Diverticulitis	1
Drop foot	1
Multiple Sclerosis	1
Pulled Hamstring	1
Restless Leg Syndrome	1
Not available	58
Diagnosed by	
Neurologist	57
Family practictioner	25
Podiatrist	6
Oncologist	3
Neurosurgeon	1
Orthopedist	1
Not available	7
Duration (y)[b]	
mean ± SD	6.4 ± 6.0
range	0.5–40
Duration	
≥10 y	30
>2–9 y	39
≤2 y	30
Medications	
Gabapentin (Neurontin)	33
Pregabalin (Lyrica)	7
Amytriptyline (Elavil)	1
Nortriptyline (Pamelor)	1
Gabapentin + Pregabalin	3
Gabapentin + Amytriptyline	2
Not available	39

[a] Values are numbers of patients, unless otherwise specified
[b] One patient did not report duration

study (63 male, 37 female; age range 15 to 89 years; **Table 1**). About one-third reported having symptoms for more than 10 years, one-third for 2 to 9 years, and one-third for less than 2 years (**Table 1**). The most frequently reported cause of neuropathy was diabetes (26 patients; **Table 1**).

Neuropathy was present in the lower extremities (legs and feet) in 94 of the 100 patients and in the hands in 28 patients; 23 of the patients with hand symptoms also had symptoms in the lower extremities. One patient had neuropathy of the pudendal nerve in the pelvis. In 97 patients, the symptoms were progressing in severity and area affected.

Treatment programs and exclusion of data

Individualized treatment plans were developed for each patient. The number of treatments in the plans ranged from 4 to 15, usually given twice per week. The planned laser therapy sessions ranged from 10 to 30 minutes in duration, with 30 minutes being the session length set for most patients (83 of 100). After the first session, treatments were adjusted as needed for each patient on the basis of the response to the previous treatment session and the results of new examinations. Some patients also received cryotherapy or joint mobilization as part of their ongoing treatment, and some were given stretching exercises to perform at home.

Sixteen patients did not complete the established number of treatments. In 2 patients, the symptoms had dissipated sufficiently that the patient and practitioner jointly agreed that no additional treatments were needed; the data from these patients were included in further analyses. The remaining 14 patients either interrupted the treatment for extended vacations (n = 4) or stopped treatment for unknown reasons (n = 10); these patients were excluded from the analyses. In addition, 6 patients did not have symptoms in the lower extremities, and their data were not included in the analyses of the symptom scales and sensory evaluations. Thus, data from 80 patients were analyzed.

Patient-reported symptoms

Of the 80 patients with analyzable data, 77 had pain at baseline, 78 had numbness, and 62 had burning sensations in the affected limb (**Table 2**). The levels of these 3 symptoms were reported by the patients at each visit using a numeric rating scale from 1 (least severe) to 10 (worst). At the initial visit, the median value on the pain scale was 5 (interquartile range [IQR], 3 to 8; **Figure 5**). At the final visit, the median

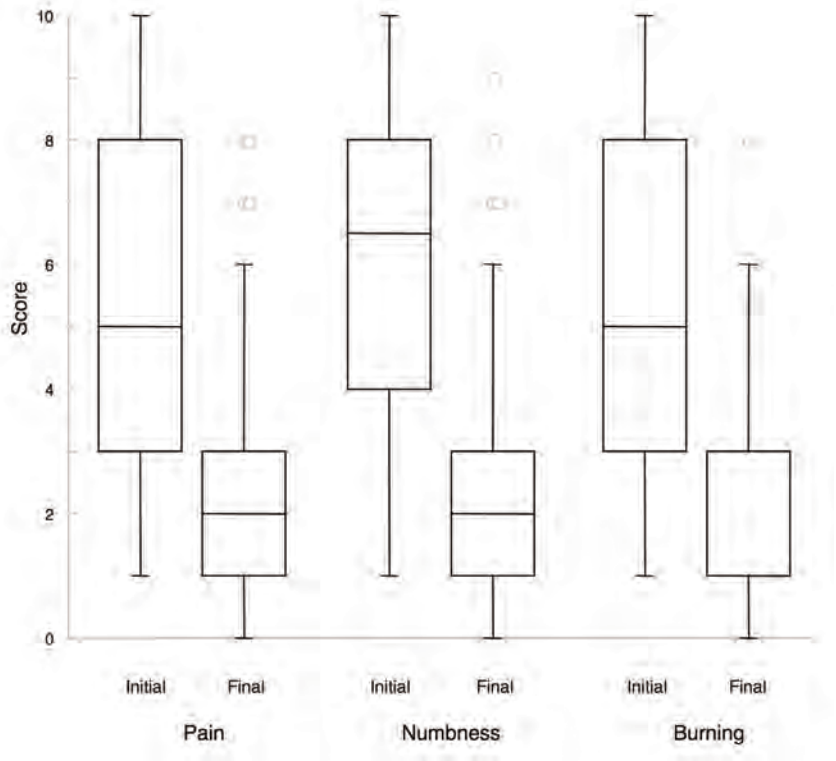

Figure 5. Change in symptom scores from initial to final treatment visit. Box plots representing the distribution of scores on the Pain (n = 77), Numbness (n = 78), and Burning (n = 62) numeric rating scales at the initial and final treatment visits. The line through each box is the median, the top of the box is the 75th percentile (3rd quartile), the top of the "whisker" is the 95th percentile, the bottom of the box is the 25th percentile (1st quartile), and the bottom of the "whisker" is the 5th percentile. Circles represent individual responses above the 95th percentile. For the final burning score, the median = the 25th percentile = 1.

pain score was 2 (IQR, 1 to 3; **Figure 5**). Similarly, the median numbness score decreased from 6.5 (IQR, 4 to 8) to 2 (IQR, 1 to 3), and the median burning score decreased from 5 (IQR, 3 to 8) to 1 (IQR, 1 to 3) (**Figure 5**). Symptoms either did not improve or worsened for some patients (**Table 2**), including 1 patient who had no burning symptoms at baseline and reported a burning score of 1 at the final visit. The mean percent reductions in score were 52% for pain, 55% for numbness, and 44% for burning. The median time to first symptom relief, as reported by the patients, was 3 treatments (range 2 to 7). Of patients with symptoms at baseline, symptom score improved by at least 50% in 53 (69%) of those with pain, 53 (68%) of those with numbness, and 36 (58%) of those with burning.

Twenty-nine of the eighty patients whose data were analyzed reported problems with balance at baseline. Among these patients, balance had improved by the final visit in 17 (59%).

Sensory evaluations

Sensation in the affected limbs was measured using the ability to detect pinpricks and vibration. The lower limbs were divided into 7 zones, from the ball of the foot (zone 1) to the upper thigh (zone 7; **Figure 4**). The highest zone with a loss of sensation was recorded as a score; a score of 0 indicated normal sensation in all areas.

Two patients had normal pinprick and vibration sensation at the initial visit, and in neither case did abnormal sensation develop over the course of treatment. In those with loss of pinprick sensation, most had loss up to zones 4 (ankle) through 6 (knee) at baseline (**Figures 3, 6a**); after treatment, the loss of pinprick sensation retreated in most patients to zones 1 (ball of foot) through 3 (top of foot). Similarly, the majority of patients with deficits in the ability to detect vibration had lost this sense up to zones 5 (shin) to 7 (thigh), but normal sensation returned to all but zones 1 to 2 (base of foot) in most patients after treatment (**Figure 6b**).

One patient with a score of 1 at baseline had a loss of pinprick sensation in zones 2 and 3 after completion of treatment; however, this same patient experienced an improvement in vibration sensation

Table 2. Changes in numeric rating scales from initial to final treatment visits

	Symptom present at baseline, n (%)[a]	Reduction[b] n (%)[c]	No change n (%)[c]	Increase n (%)[c]
Pain	77 (96%)	67 (87%)	8 (10%)	2 (3%)
Numbness	78 (98%)	68 (87%)	7 (9%)	3 (4%)
Burning	62 (78%)	46 (74%)	13 (21%)	3 (5%)

[a] Percentage of patients relative to total number analyzed (n = 80).
[b] Reduction in score represents an improvement in symptoms.
[c] Percentage of patients relative to those who had symptom at baseline.

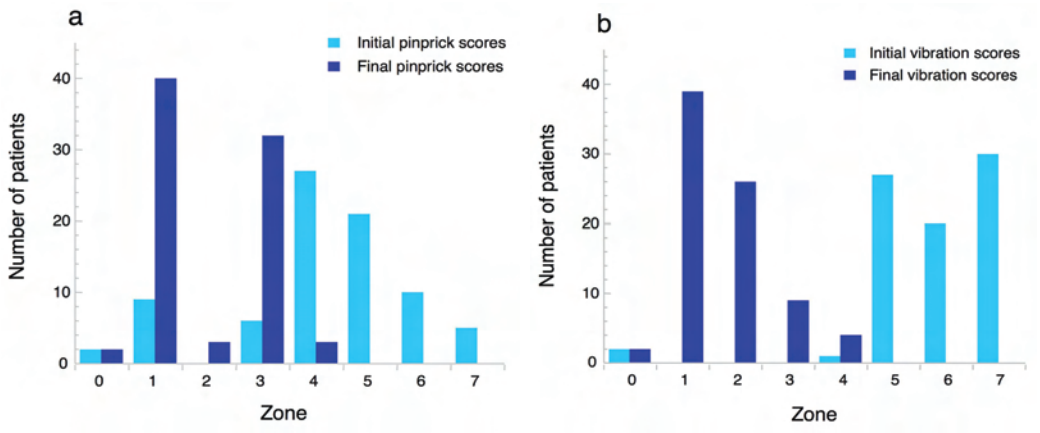

Figure 6. Change in response to stimulation from the initial visit to the final visit. The lower limbs were divided into 7 "zones" from 1 (ball of foot) to 7 (upper thigh). See Figure 4 for reference. The scores reflect the highest zone with disturbed ability to detect pinprick (**a**) or vibration (**b**). A score of 0 indicates no disturbance. In most patients, sensation returned to most of the leg and foot after treatment.

(a reduction in score from 6 to 2). Eight patients (7 of whom had a score of 1 at baseline) showed no change in pinprick response but a reduced vibratory score reflecting improvement in vibration sensation. All other patients improved on both measures.

Additional treatments

Thirty-eight of the 86 patients who completed their original treatment plan subsequently received additional treatments. Of these, 18 extended their initial care (continuing treatments within 30 days of completing the initial program) by 2 to 9 treatment sessions. All but 1 of these patients had experienced substantial symptom relief during the initial treatment program. The remaining 20 patients each returned after more than 30 days for a single "maintenance" treatment.

Discussion

This study enrolled 100 consecutive patients with peripheral neuropathy of any cause and examined their responses to treatment with Realief Therapy. The patients had, on average, had symptoms of peripheral neuropathy for 6.4 years, and 30 had experienced symptoms for 10 years or more. In many, the symptoms had been progressing despite the use of drug therapies, yet the majority experienced symptom relief after Realief Therapy (**Figure 7**), regardless of the duration of symptoms.

We analyzed subjective (symptom scales) and semi-objective (sensory testing) scores for the 80 patients who had symptoms in the legs and who completed their individualized treatment plan. Of these 80 patients, the clear majority experienced substantial symptom relief by the end of the treatment period, and most experienced some relief within just a few sessions (range, 2 to 7 sessions). The average decreases in score were 52% for pain, 55% for numbness, and 44% for burning, values associated with a high degree of clinical improvement and well above the threshold of 30% for clinically meaningful changes.[38]

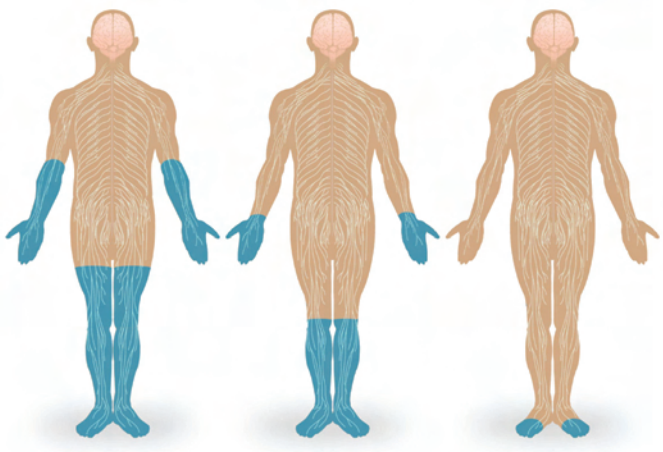

Figure 7. Return of sensation after therapy. Typical extent of areas affected by active symptoms and loss of sensation before (left), during (middle), and after (right) the Realief Therapy treatment program are illustrated in blue.

Sensation was measured by the ability to detect both pinprick and vibration. Pinprick is used to measure the function of small-fiber nerves, which sense pain and temperature, and vibration is used to measure the function of large-fiber, usually myelinated, nerves, which also sense light touch and proprioception (position sense). In all of the patients, the extent of the limb that had abnormal responses to vibration (that is, evidence of damage to the large-fiber nerves) became much smaller after treatment; in half of the patients with abnormal sensation at baseline, the disturbance was limited to the sole of the

foot by the final treatment session. In contrast, only 71 patients (89%) showed improvement in the area sensitive to pinprick. Small- and large-fiber nerves may be differently affected by the disease process,[3] and function may return to them at separate rates.

In 6 (8%) of the 80 patients, some (but not all) symptoms became more severe (5 patients reported worsening on one or more of the symptom scales, and in 1 patient the area insensitive to pinprick expanded). This may, paradoxically, be partially due to an improvement in nerve function. For example, a nerve that had provided no sensation (numbness) in a particular area may send aberrant signals interpreted as pain or burning as its function recovers. In addition, most patients who worsened on one measure (such as pinprick) showed clear improvement on others (such as vibration). However, we cannot rule out the possibility that some patients did not benefit from or indeed had their symptoms exacerbated by the treatment.

Nonetheless, on the basis of this small sample, the Realief therapeutic protocol appears to provide at least as much if not more benefit as many of the traditional—primarily pharmaceutical—treatments for neuropathy. Realief provided at least a 50% reduction in pain score in 53 of 77 (69%) of the patients with pain at baseline; this compares favorably with the 40% to 50% of patients achieving a 50% reduction in pain in studies of pregabalin for diabetic neuropathy.[20] Although the measurements used in the studies are not directly comparable, Realief therapy also appears to decrease pain scores as much as high doses of gabapentin.[19] Realief Therapy also provided relief of symptoms not usually tracked in studies of other therapies, including numbness and burning. Furthermore, laser therapy is associated with fewer side effects than medications: these are usually limited to temporary increases in pain in the day following treatment, mild bruising, temporary dizziness, or skin reactions.[34]

This pilot study of Realief therapy was limited in its scope. By design, the number of patients was small, and certain types of information, such as changes in concomitant medications as symptoms improved, was not collected. Furthermore, some symptoms, such as problems with balance, were noted but not quantified. We are currently designing a much larger study that will capture this and additional information to give a clearer view of the benefit provided by Realief therapy, including the impact on quality of life. We also hope to analyze whether the response to treatment varies with the type of neuropathy, which should be possible with a larger group of patients.

Although most patients in this study had symptoms that were progressing at the start of treatment, in the vast majority the symptoms regressed during 2 to 8 weeks of Realief Therapy, both in spatial extent and in severity. Realief Therapy is therefore a promising noninvasive approach for improving the symptoms of peripheral neuropathy.

Case Study 1

For a little over a year, Mr. F, a 79-year-old man, had symptoms of numbness, pain (including shooting pains), 'pins and needles', and increased sensitivity to touch below the knees of both legs. The symptoms had begun in his toes and then progressed up towards his knees; the symptoms had also gotten worse over time. Mr. F is retired, but the symptoms limited his activities and ability to exercise and interfered with his balance and sleep. An electromyelogram (EMG) performed by a neurologist confirmed the presence of peripheral neuropathy. Although the cause was not known, Tinel's tests were positive for nerve compression at the tarsal tunnels (ankles). He was not taking any medications for the neuropathy.

When Mr. F first came to the clinic he rated his symptoms at 9/10 for pain, 8/10 for numbness, and 9/10 for burning, a level he described as "moderate". Tuning fork tests showed a loss of vibration sensation from the waist down, and pinprick tests confirmed increased sensitivity below the knee. He also had loss of joint motion in his ankles.

Mr. F was treated with physical manipulations to restore motion to his ankles. Laser therapy, 3 minutes each side at the lumbar nerve roots and 12 minutes per leg, was used to treat the neuropathy symptoms.

By the third visit, Mr. F's ability to detect vibration had returned between the waist and the lower quarter of the leg on the right and lower third of the leg on the left. The increased sensitivity to the pinwheel was also now limited to the bottom third of the leg. Mr. F rated his pain at 5/10 (present only in his feet), numbness at 4/10, and burning at 3/10 (present only in his toes) and reported that his symptoms were better overall.

At visit 15, Mr. F's vibration sensation was abnormal only on the balls of his feet, although he still had hypersensitivity to pinprick. Mr. F reported that his pain, numbness, and burning were all now at 2/10 and were present only in the front part of the soles of his feet.

Case Study 2

Ms. Y is a 65-year-old woman whose symptoms of numbness, pain (including shooting pains), pins and needles, and increased sensitivity to touch began 2 years ago, about the same time she was diagnosed with type 2 diabetes. Her symptoms started in the toes and spread to the lower third of each leg, getting more intense as they spread; she also had abnormal feeling in her hands and fingers. The symptoms interfered with her daily activities and her balance also deteriorated, so she had to be very careful as she walked. EMG and nerve conduction velocity studies performed by a neurologist confirmed the presence of peripheral nerve dysfunction. She was prescribed gabapentin, which helped her to sleep.

When Ms. Y came to the clinic, we noted loss of vibration sensation in her lower legs. Pinprick sensation was absent in the lower part of her right leg and up to the middle of her left thigh, but she was hypersensitive to the pinwheel in the region just below her knee. She also had reduced reflexes at the knees and heels and loss of motion in her wrists, ankles, and toes. She rated her pain at 9/10, numbness at 6/10, and burning at 4/10.

Ms. Y was treated with physical manipulations to restore motion to her ankles. Laser therapy, 3 minutes each side at the lumbar nerve roots and 12 minutes per leg, was used to treat the neuropathy symptoms.

At her third visit, sensitivity to vibration had returned except to the lowest third of her right leg and lowest quarter of her left leg. Abnormal pinprick responses were limited to her feet, ankles, and—on the left side only—the lowest quarter of the leg; these regions were divided into areas of no sensation on the farthest parts of the limb with hypersensitivity on the back of the foot, ankle, or leg. Her range of motion had improved in the wrists and ankles, and her self-rated symptoms were 4/10 for pain, numbness, and burning, with all symptoms confined to the lower portions of the leg.

At visit 16, sensitivity to vibration was fully present in both legs and the abnormal response to pinprick was limited to a small area of increased sensitivity on the first left toe. Ms. Y rated her symptoms at 1/10 for pain, numbness, and burning present mostly at the very front of the soles, and reported that the only bothersome symptom remaining was a stiff feeling at the fronts of her feet.

References

1. Shy ME. Peripheral neuropathies. In: Goldman L, Ausiello D, editors. Cecil Medicine. 23 ed. Philadelphia: Saunders Elsevier; 2007.
2. National Institute of Neurological Disorders and Stroke. Peripheal Neuropathy Fact Sheet. 2011. Available at: http://www.ninds.nih.gov/disorders/peripheralneuropathy/detail_peripheralneuropathy.htm?css=print. Accessed on April 8, 2011.
3. Ziegler D, Mayer P, Wiefels K, Gries FA. Assessment of small and large fiber function in long-term type 1 (insulin-dependent) diabetic patients with and without painful neuropathy. Pain. 1988;34(1):1-10.
4. Gregg EW, Sorlie P, Paulose-Ram R, Gu Q, Eberhardt MS, Wolz M, et al. Prevalence of lower-extremity disease in the US adult population >=40 years of age with and without diabetes: 1999-2000 national health and nutrition examination survey. Diabetes Care. 2004;27(7):1591-1597.
5. O'Connor AB. Neuropathic pain: quality-of-life impact, costs and cost effectiveness of therapy. Pharmacoeconomics. 2009;27(2):95-112.
6. Gilron I, Watson CP, Cahill CM, Moulin DE. Neuropathic pain: a practical guide for the clinician. Cmaj. 2006;175(3):265-275.
7. Kronenberg H, Melmed S, Polonsky K, Larsen P. Diabetic Neuropathies. Williams Textbook of Endocrinology. 11th ed. Philadelphia: Saunders Elsevier; 2008.
8. Benbow SJ, Wallymahmed ME, MacFarlane IA. Diabetic peripheral neuropathy and quality of life. Qjm. 1998;91(11):733-737.
9. Davies M, Brophy S, Williams R, Taylor A. The prevalence, severity, and impact of painful diabetic peripheral neuropathy in type 2 diabetes. Diabetes Care. 2006;29(7):1518-1522.
10. Van Acker K, Bouhassira D, De Bacquer D, Weiss S, Matthys K, Raemen H, et al. Prevalence and impact on quality of life of peripheral

neuropathy with or without neuropathic pain in type 1 and type 2 diabetic patients attending hospital outpatients clinics. Diabetes Metab. 2009;35(3):206-213.

11. Le TK, Able SL, Lage MJ. Resource use among patients with diabetes, diabetic neuropathy, or diabetes with depression. Cost Eff Resour Alloc. 2006;4:18.

12. Gordois A, Scuffham P, Shearer A, Oglesby A, Tobian JA. The health care costs of diabetic peripheral neuropathy in the US. Diabetes Care. 2003;26(6):1790-1795.

13. Dworkin RH, O'Connor AB, Backonja M, Farrar JT, Finnerup NB, Jensen TS, et al. Pharmacologic management of neuropathic pain: evidence-based recommendations. Pain. 2007;132(3):237-251.

14. Dworkin RH, O'Connor AB, Audette J, Baron R, Gourlay GK, Haanpaa ML, et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. Mayo Clin Proc. 2010;85(3 Suppl):S3-14.

15. Kirby M. Painful diabetic neuropathy -- current understanding and management for the primary care team. British Journal of Diabetes & Vascular Disease. 2003;3:138-144.

16. Attal N, Cruccu G, Haanpaa M, Hansson P, Jensen TS, Nurmikko T, et al. EFNS guidelines on pharmacological treatment of neuropathic pain. Eur J Neurol. 2006;13(11):1153-1169.

17. Moulin DE, Clark AJ, Gilron I, Ware MA, Watson CP, Sessle BJ, et al. Pharmacological management of chronic neuropathic pain - consensus statement and guidelines from the Canadian Pain Society. Pain Res Manag. 2007;12(1):13-21.

18. Pai S. Peripheral Neuropathy. In: Rakel D, editor. Integrative Medicine. 2 ed. Philadelphia: Saunders Elsevier; 2007.

19. Backonja M, Beydoun A, Edwards KR, Schwartz SL, Fonseca V, Hes M, et al. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. JAMA. 1998;280(21):1831-1836.

20. Lyrica (pregabalin) [package insert]. New York, NY: Parke-Davis; 2010.

21. Neurontin (gabapentin) [package insert]. New York, NY: Parke-Davis; 2010.

22. McCleane G. Topical application of doxepin hydrochloride, capsaicin and a combination of both produces analgesia in chronic human neuropathic pain: a randomized, double-blind, placebo-controlled study. Br J Clin Pharmacol. 2000;49(6):574-579.

23. Kumar D, Alvaro MS, Julka IS, Marshall HJ. Diabetic peripheral neuropathy. Effectiveness of electrotherapy and amitriptyline for symptomatic relief. Diabetes Care. 1998;21(8):1322-1325.

24. Hamza MA, White PF, Craig WF, Ghoname ES, Ahmed HE, Proctor TJ, et al. Percutaneous electrical nerve stimulation: a novel analgesic therapy for diabetic neuropathic pain. Diabetes Care. 2000;23(3):365-370.

25. Abuaisha BB, Costanzi JB, Boulton AJ. Acupuncture for the treatment of chronic painful peripheral diabetic neuropathy: a long-term study. Diabetes Res Clin Pract. 1998;39(2):115-121.

26. Weintraub MI, Wolfe GI, Barohn RA, Cole SP, Parry GJ, Hayat G, et al. Static magnetic field therapy for symptomatic diabetic neuropathy: a randomized, double-blind, placebo-controlled trial. Arch Phys Med Rehabil. 2003;84(5):736-746.

27. Cruccu G, Aziz TZ, Garcia-Larrea L, Hansson P, Jensen TS, Lefaucheur JP, et al. EFNS guidelines on neurostimulation therapy for neuropathic pain. Eur J Neurol. 2007;14(9):952-970.

28. Leonard DR, Farooqi MH, Myers S. Restoration of sensation, reduced pain, and improved balance in subjects with diabetic peripheral neuropathy: a double-blind, randomized, placebo-controlled study with monochromatic near-infrared treatment. Diabetes Care. 2004;27(1):168-172.

29. Lavery LA, Murdoch DP, Williams J, Lavery DC. Does anodyne light therapy improve peripheral neuropathy in diabetes? A double-blind, sham-controlled, randomized trial to evaluate monochromatic infrared photoenergy. Diabetes Care. 2008;31(2):316-321.

30. Tata DB, Waynant RW. Laser therapy: A review of its mechanism of action and potential medical applications. Laser & Photonics Reviews. 2011;5(1):1-12.

31. Fulop AM, Dhimmer S, Deluca JR, Johanson DD, Lenz RV, Patel KB, et al. A meta-analysis of the efficacy of laser phototherapy on pain relief. Clin J Pain. 2010;26(8):729-736.

32. Chow R, Armati P, Laakso EL, Bjordal JM, Baxter GD. Inhibitory Effects of Laser Irradiation on Peripheral Mammalian Nerves and Relevance to Analgesic Effects: A Systematic Review. Photomed Laser Surg. 2011;[epub ahead of print].

33. Chow RT, David MA, Armati PJ. 830 nm laser irradiation induces varicosity formation, reduces mitochondrial membrane potential and blocks fast axonal flow in small and medium diameter rat dorsal root ganglion neurons: implications for the analgesic effects of 830 nm laser. J Peripher Nerv Syst. 2007;12(1):28-39.

34. Tunér J, Hode L. The New Laser Therapy Handbook. Grängesburg, Sweden: Prima Books; 2010.

35. Zinman LH, Ngo M, Ng ET, Nwe KT, Gogov S, Bril V. Low-intensity laser therapy for painful symptoms of diabetic sensorimotor polyneuropathy: a controlled trial. Diabetes Care. 2004;27(4):921-924.

36. Juma A, Mandal A. Vibration sensitivity testing with tuning fork—256 Hz or 512 Hz? European Journal of Plastic Surgery. 2007;30(1):5-6.

37. Rochkind S, Nissan M, Alon M, Shamir M, Salame K. Effects of laser irradiation on the spinal cord for the regeneration of crushed peripheral nerve in rats. Lasers Surg Med. 2001;28(3):216-219.

38. Farrar JT, Young JP, Jr., LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain. 2001;94(2):149-158.