# Successful Management of Diabetic Peripheral Neuropathic Pain Using MiS MLS® Laser Therapy: A Case Report.

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## INTRODUCTION

Neuropathic pain (NP) is a particularly severe form of chronic pain, arising as a direct consequence of a lesion or disease affecting the somatosensory nervous system[1]. This condition is the result of a series of different pathological mechanisms, and it is usually described based on the anatomic localization or etiology. The conditions and the pathophysiological states that determine the onset of neuropathic pain mostly involved are metabolic disorders (e.g. peripheral diabetic neuropathy), neuropathies associated with viral infections (e.g. post-herpetic neuralgia, HIV, leprosy), autoimmune disorders affecting the central nervous system (e.g. multiple sclerosis and Guillain–Barre syndrome), chemotherapy-induced peripheral neuropathies, damage to the nervous system of traumatic origin (e.g. spinal cord injury and amputation), inflammatory disorders, hereditary neuropathies, and channelopathies[2].

Estimates of NP in the general population suggest the prevalence is 7% to 10%[3], increasing to around 20% to 30% in people with diabetes[4]. Studies have also reported greater prevalence of neuropathic pain, as with chronic pain overall, in older people, women, and people from areas of high social deprivation[5].

The principal clinical signs associated to NP are allodynia (pain due to a stimulus that does not normally provoke pain), hyperalgesia (an increase in the perception of pain generated by a stimulus that causes pain) and paresthesia (a condition that determines the perception of anomalous sensations comparable to needle bites, tingling, itching, reduced, or even loss of sensitivity). In patients suffering from NP, the perceived pain is usually spontaneous, manifesting itself without needing a stimulus. This pathological condition substantially affects the quality of life of patients, compromising their psychological state[6].

It is important to distinguish NP from other forms of pain which arises from actual or threatened damage to non-neural peripheral tissue. NP is generally unresponsive to analgesics such as nonsteroidal anti-inflammatory drugs (NSAID) or opioids. Rather, gabapentinoids, tricyclic antidepressants, and serotonin–norepinephrine reuptake inhibitors are recommended as first- and second line treatments[7].

Nonetheless, these medications for NP provide greater than 50% pain relief in less than half of people treated. Furthermore, analgesics in general, particularly opioids and gabapentinoids, can potentially cause harm, providing an even greater emphasis on appropriate use[8].

Peripheral neuropathic pain (PNP) is a direct consequence of a lesion or disease affecting the peripheral nerves. There are two main types of PNP. The pain experienced in the nerve trunk is a result of chemical or mechanical insults to sensitized nociceptors in the nervi nervorum. This pain can have a deep aching quality and often approximates the course of the involved nerve. Dysesthetic pain, on the other hand, is a consequence of damaged or regenerating neuronal fibers. It can have an electrical, burning, or launching quality. Finally, a combination of both types could occur.

PNP is typically worsened by activities that compress or stretch the involved nerves. The signs of PNP include pain with active and passive range of motion of the involved limb; tenderness to palpation of the involved nerve; tenderness or inflammation of the tissue innervated by the involved nerve[9].

The management of PNP mostly require a multidisciplinary approach

based on medication[10]; cognitive-behavioral therapy[11] to reduce distress and worrying thoughts; education regarding peripheral nerve physiology; gentle movement without undue tension on the nerve bed to help restore the endoneurial circulation; treatment of the local dysfunction affecting the nerve / manual therapy; physical agents that gate the sensation of pain such as electric stimulation, cold or heat[12].

Among physical therapies, laser therapy has emerged as a promising approach for the management of peripheral neuropathies. However, the efficacy of laser therapy in treating peripheral neuropathies remains a subject of ongoing study and debate. Some studies have suggested that laser therapy may be beneficial in improving the symptoms of peripheral neuropathies, primarily through its anti-inflammatory, analgesic, and tissue healing-promoting effects. The theory proposes that laser light may stimulate cellular metabolism, increase local blood flow, and reduce inflammation, thereby contributing to the alleviation of neuropathic symptoms. Nevertheless, the results of studies on laser therapy for peripheral neuropathies are inconclusive, with some studies demonstrating significant benefits while others have not. Factors influencing the efficacy of laser therapy include the duration of treatment, the power of the laser used, the type of neuropathy, and the severity of symptoms.

The following clinical case presents the use of a particular type of therapeutic laser, the multiwave-locked system (MLS®) laser, at high power ($P_{average}$>500mW). This system spatially and temporally combines two wavelengths, 808nm and 905nm, with programmable emission in continuous/frequency-modulated mode for 808nm and pulsed mode for 905nm.

Previous clinical evidence indicates that lasers belonging to the MLS® family have been effective in the treatment of diabetic polyneuropathies[14-17].

In this case report, the MiS laser device was utilized. This laser belongs to the MLS® family of devices, and it is distinguished by a maximum peak power of 1 kW and maximum average power of 6W± 20%, which enables the safe targeting of deeper tissue layers, a common site of neuropathic pain onset.

In a pre-clinical study, Micheli et al.[18], through a model of sciatic nerve chronic constriction in the rat, that mimics the neuropathic pain, demonstrated that the treatment with MLS®-MiS laser therapy reduced pain significantly and protected nerve structure through different mechanisms. This included inhibition of the enzymes involved in the inflammation process, myelin sheath restoration, and modulation of pain-stimulating signaling at the central nervous system level.

In a preliminary clinical experience, Mezzalira et al.[19] tested the safety and efficacy of MiS laser in a group of patients suffering of peripheral neuropathy of different origins, obtaining an average pain reduction of 79.5%.

Based on its characteristics and the previous evidence on mechanism of action and clinical effects, the MiS laser was considered a valid device to treat neuropathic pain in diabetic polyneuropathies.

## CLINICAL CASE

The patient is a 67-year-old female with a diagnosis of type II diabetes mellitus in 2008 and ongoing insulin therapy since 2014. She also has bilateral coxarthrosis and gonarthrosis on the right side. The patient was suffering of pain, numbness and burning feeling in the legs and feet since 2019 for the right side and since 2020 for the left side. In October 2022 a distal sensorimotor polyneuropathy of the lower extremities was diagnosed. The EMG exam presented an axonal degeneration and a partial segmental demyelination, more pronounced for sensory fibers. The patient reported a loss of skin sensibility at the lateral aspect of the left thigh.

In November 2023, the patient decided to undergo a cycle of laser therapy due to the persistence of severe pain despite the previous uneffective medical treatment (NSAIDs, analgesics and rest).

## MATERIALS AND METHODS

The patient was evaluated through the Neuropathic Pain Symptom Inventory (NPSI) which is a scale approved for valuating both peripheral and central neuropathic pain[13]. NPSI is used to aid in the diagnosis of certain subcategories of neuropathic pain syndromes and to help determine beneficial treatments. The scale ranges from zero to 10, with zero being no pain at all and 10 being the worst imaginable pain. The total scores of all ten descriptors are added to find the total pain intensity. Each descriptor may be observed separately to evaluate different types of pain in isolation. Sections of the scale include the evaluation of the severity of spontaneous pain, painful attacks, provoked pains, and abnormal sensations.

The patient underwent to a cycle of MLS® laser treatments, with MiS device: 3 sessions per week, every other day, for two weeks. The handpiece was equipped with a lens of 2 cm of diameter and spot area of 3.14 $cm^2$.

During each session, the laser was initially applied in scan mode along the dorsal and the plantar aspects of both feet (total area treated per foot ≈ 200 $cm^2$) - Fig. 1.

Subsequently, during the same session, each lower limb was treated in fixed mode. The following areas were treated for each limb: four along the posterior aspect of the foot, four along the plantar aspect of the foot, and two along the deep fibular nerve - Fig 2.

The parameters used in the two stages, depending on the method of application, are reported in Table 1.

The selection of parameters and the application methodology are based on a synthesis of literature data, the setting proposed by the device, and previous experience.

## RESULTS AND CONCLUSION

The patient reported no pain, numbness and burning feeling in the legs for the left leg after the fourth session while for the right leg after the fifth session.

At the end of laser therapy cycle the loss of skin sensibility at the lateral aspect of the left thigh was improved and the zone has diminished in size.

After the last treatment session, the patient's pain sensations were evaluated through the NPSI score. The total NPSI score resulted decreased of 70%, from 67/100 to 20/100 after 6 laser sessions in two weeks. NPSI scores, before and after MLS® laser treatment, are reported in Table 2.

At the follow-up examination one month later, the improvement remained.

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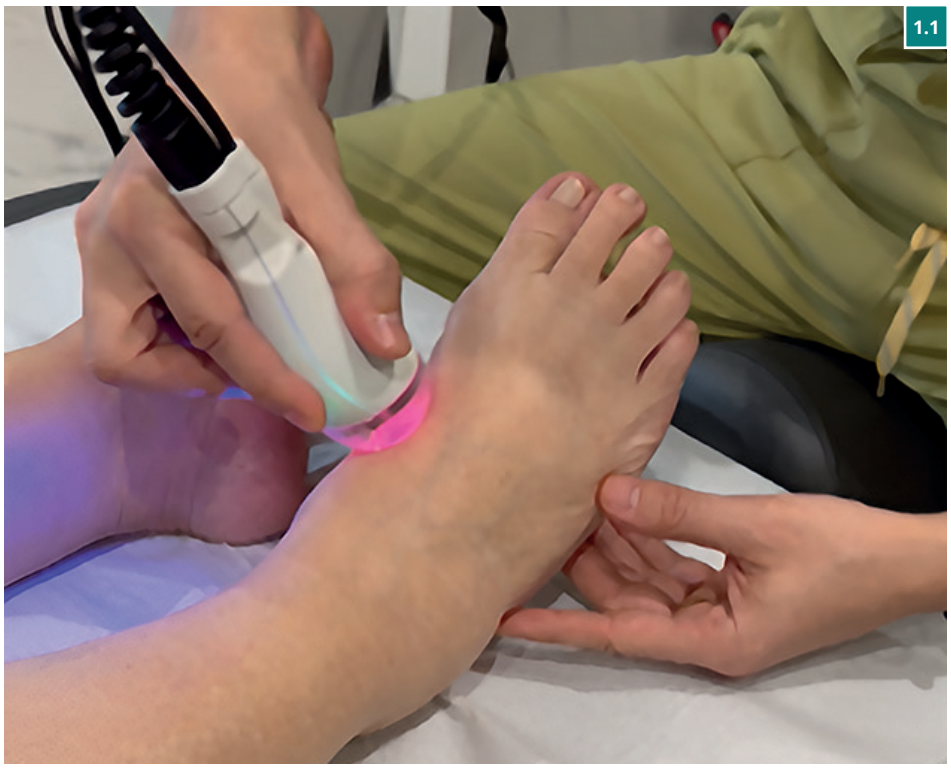
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**Figures 1.1, 1.2**
First Phase - Scanning of the dorsal and the plantar aspects.

| MODALITY | FREQUENCY (Hz) | INTENSITY (%) | ENERGY (J) | DOSE (J/cm²) | DURATION (min:sec) |
|---|---|---|---|---|---|
| Scan mode | 30 | 60 | 999.68 | ~ 5.0 | 08:06 |
| Fixed mode | 10 | 30 | 6.74 | 2.25 | 00:07 (per point) |

**Table 1**
Different settings used during each treatment session.

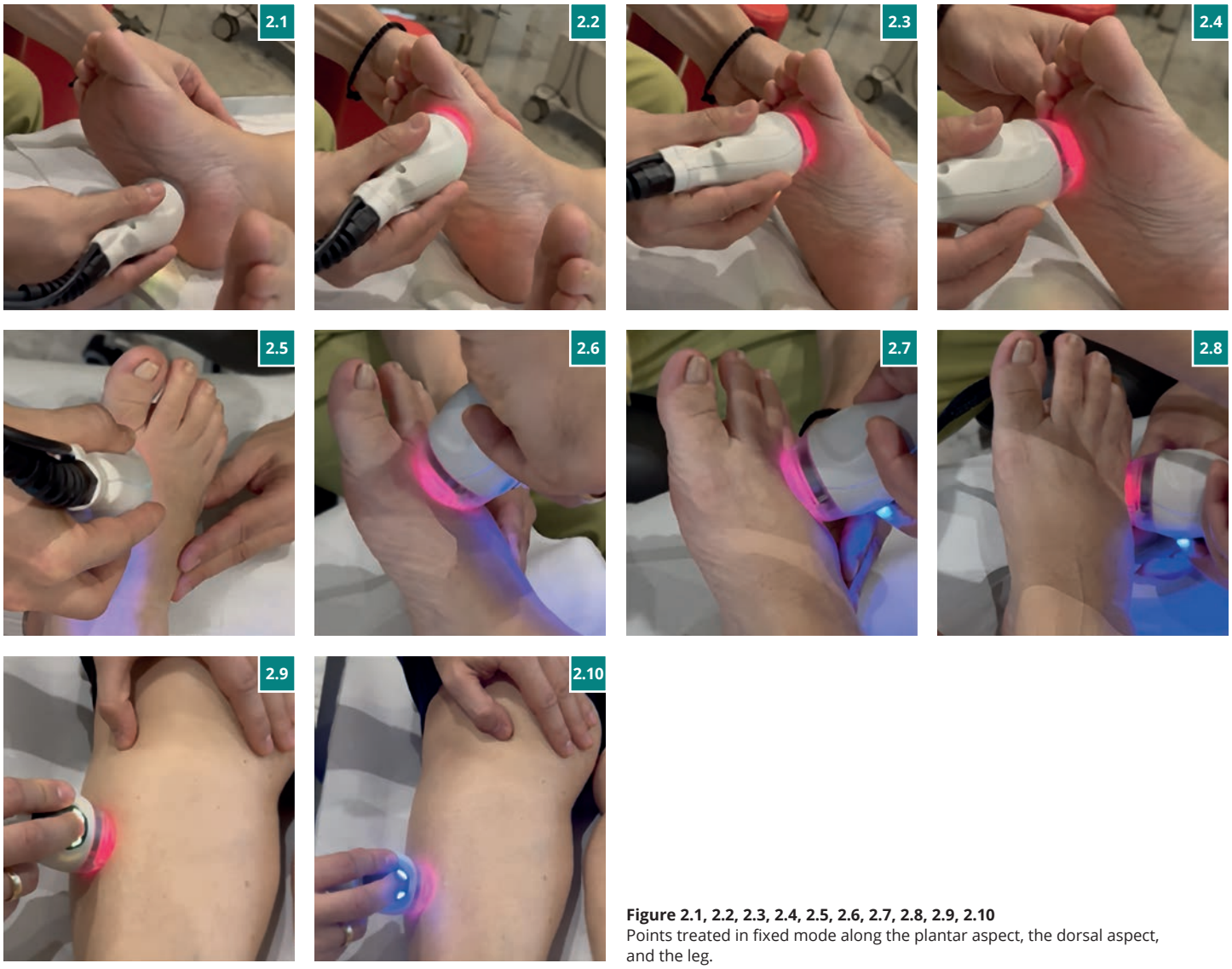


**Figure 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 2.10**
Points treated in fixed mode along the plantar aspect, the dorsal aspect, and the leg.

| NEUROPATHIC PAIN SYMPTOM INVENTORY (NPSI) | BEFORE | AFTER | REDUCTION (%) |
|---|---|---|---|
| **Severity of the Spontaneous Pain** | | | |
| Q1. Does your pain feel like burning? | 10 | 4 | 60% |
| Q2. Does your pain feel like squeezing? | 7 | 3 | 57% |
| Q3. Does your pain feel like pressure? | 9 | 3 | 66% |
| Q4. During the past 24h, your spontaneous pain has been present: permanently / 8 to 12 h / 4 to 7 h / 1 to 3 h / < 1h | permanently | 4 to 7 h | |
| **Severity of the Painful Attacks** | | | |
| Q5. Does your pain feel like electric shocks? | 0 | 0 | - |
| Q6. Does your pain feel like stabbing? | 8 | 0 | 100% |
| Q7. In the past 24 h how many of these pain attacks have you had? >20h/11 to 20/ 6 to 10/ 1 to 5/ none | 1 to 5 | None | |
| **Severity of your Provoked Pains** | | | |
| Q8. Is your pain provoked or increased by brushing on the painful area? | 8 | 3 | 62.5% |
| Q9. Is your pain provoked or increased by pressure on the painful area? | 5 | 3 | 40% |
| Q10. Is your pain provoked or increased by contact with something cold on the painful area? | 0 | 0 | - |
| **Severity of Abnormal Sensations** | | | |
| Q11. Do you feel pins and needles? | 10 | 2 | 80% |
| Q12. Do you feel tingling? | 10 | 2 | 80% |
| **Subscores** | | | |
| 1. Burning (superficial) spontaneous pain: Q1 | 10 | 4 | 60% |
| 2. Pressing (deep) spontaneous pain: (Q2+Q3)/2 | 8 | 3 | 62.5% |
| 3. Paroxysmal pain: (Q5+Q6)/2 | 4 | 0 | 100% |
| 4. Evoked pain: (Q8+Q9+Q10)/3 | 6.5 | 2 | 69% |
| 5. Paresthesia/Dysesthesia: (Q11+Q12)/2 | 10 | 2 | 80% |
| **Total intensity score** | | | |
| 1. Q1 | 10 | 4 | 60% |
| 2. (Q2+Q3) | 16 | 6 | 62.5% |
| 3. (Q5+Q6) | 8 | 0 | 100% |
| 4. (Q8+Q9+Q10) | 13 | 6 | 54% |
| 5. (Q11+Q12) | 20 | 4 | 80% |
| Total: (1+2+3+4+5) /100 | 67 / 100 | 20 / 100 | **70%** |

**Table 2**
NPSI scores before and after the treatment.