

E-book

Laser Therapy in Neuropathic Pain

ASV
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Research and Therapeutic Solutions

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NEUROPATHIC PAIN: AN UNDERRATED BURDEN

Neuropathic Pain is a chronic condition and represents a significant burden for patients and healthcare systems. The quality of life is worse in patients with Neuropathic Pain than in those with other types of chronic pain¹. Although the costs to healthcare systems are difficult to calculate, as they are fragmented based on the underlying disease, the overall expenditure on Neuropathic Pain is likely very high. Furthermore, Neuropathic Pain leads to psychosocial and emotional disorders that increase the burden on society².

The magnitude of the problem has been understood by all the stakeholders, both scientific investigators and the medical industry, as confirmed by the steep increase in the number of scientific publications and clinical trials reported after year 2000, indicating that a great amount of effort has been devoted to dealing with this problem.

Despite this attention, management of Neuropathic Pain continues to be a challenge and less than 50% of patients achieve pain relief of at least 50% with any drug or combination of drugs³. The current estimates are well below that number⁴. One of the reasons of this situation resides in the fact that there are multiple pathophysiological mechanisms of Neuropathic Pain, whereas most drugs have a mechanism of action that addresses only one pain mechanism. One patient may often suffer from different types of Neuropathic Pain, and no drug can effectively relieve all types of pain. This is clearly indicating the clinical need for new therapeutic solutions able to eliminate or decrease Neuropathic Pain and provide quality of life recovery.

- 1 Epidemiology of neuropathic pain and its impact on quality of life. Smith BH, Torrance N *Curr Pain Headache Rep.* 2012 Jun; 16(3):191-8
- 2 Healthcare utilization in people with postherpetic neuralgia and painful diabetic peripheral neuropathy. Dworkin RH, Panarites CJ, Armstrong EP, Malone DC, Pham SV *J Am Geriatr Soc.* 2011 May; 59(5):827-36.
- 3 Toward a definition of pharmacoresistant neuropathic pain. Hansson PT, Attal N, Baron R, Cruccu G *Eur J Pain.* 2009 May; 13(5):439-40
- 4 Neuropathy: A name for their pain. Eisenstein M *Nature.* 2016 Jul 14; 535(7611):S10-1

LASER THERAPY IN NEUROPATHIC PAIN

Laser therapy is a physical therapy that uses the laser beam to act on several human body mechanisms, such as:

- Heating the tissues, to provide an immediate relief from joint and muscle pain and stiffness;
- Promoting local microcirculation function, to decrease inflammation, edema and pain symptoms;
- Favouring cell metabolism, to enhance tissue repair processes and functional recovery.

Thanks to the effects on pain, edema and inflammation, laser therapy is a useful tool in many clinical specialties, such as pain management, rehabilitation, physiotherapy, etc.

Neuropathic Pain is a form of chronic pain resulting from damage to the nervous system. It is a painful condition that may comprise different types of pathologies: ranging from postherpetic neuralgia and painful diabetic polyneuropathy to post-surgery neuropathic pain, cord injury etc.

A portion of these patients is specifically affected by peripheral neuropathy and seeks medical treatment to alleviate the pain and improve the function associated to conditions that are localised at several body levels: spine, cervical area, elbow, wrist and hand, knee, ankle and foot, hip.

New therapeutic solutions are needed in this area, as Neuropathic Pain is characterised by poor outcomes with usual pharmacological treatments, often associated to side effects.

ASA is specialized in offering therapeutic solutions that are scientifically and clinically proven; in the last 15 years, ASA put a great effort in the application of laser therapy to Neuropathic Pain and related conditions.



→ 2.1

The biological effect on cells

In order to understand the mechanism of action of MLS® pulse, studies on cells have been performed (Monici et al). These scientific experiments conducted by ASAcampus, the joint laboratory between ASA and the Department of Experimental and Clinical Biomedical Sciences of the University of Florence, have shown that the treatment of muscle cells with MLS® Laser Therapy, not only induced cell differentiation, but was also promoting the synthesis of a large group of proteins. Some of those proteins are specifically related to defined biological mechanisms, involving among the others inflammation modulation, angiogenesis promotion, muscle contraction and, interestingly, nerve fibres regeneration.

The animal model studies

Preliminary investigation in peripheral nerve repair

Gigo Benato et al

After peripheral nerve transection, different surgery techniques are used to repair the nerve trunks. In addition to the surgical procedure itself, post-op rehabilitation is a key step to successful recovery.

The role of laser therapy in this field has been studied by a group of Italian and Brazilian experts (Gigo Benato et al) in a rat model. In this experiment, after complete nerve transection, the nerve has been repaired with a suture surgery and the animals were then divided into four groups: one placebo group, and three laser-treated groups (treated with continuous 808 nm laser, pulsed 905 nm laser, and with a combination of the two).

Results showed that laser therapy induces a statistically significant faster:

- Recovery of the lesioned function;
- Recovery of muscle mass;
- Myelination of the regenerated nerve fibres.

From comparison of the three different types of laser emissions, it turned out that the best functional outcome was obtained by the pulsed-continuous combined laser.

This led the way to the development of the concept of using MLS[®] Laser Therapy in the treatment of peripheral nerve problems, suggesting that early postoperative laser therapy should be considered as a very promising physiotherapeutic tool for rehabilitation after nerve suture surgery.

Experiments on Spinal Cord Injury

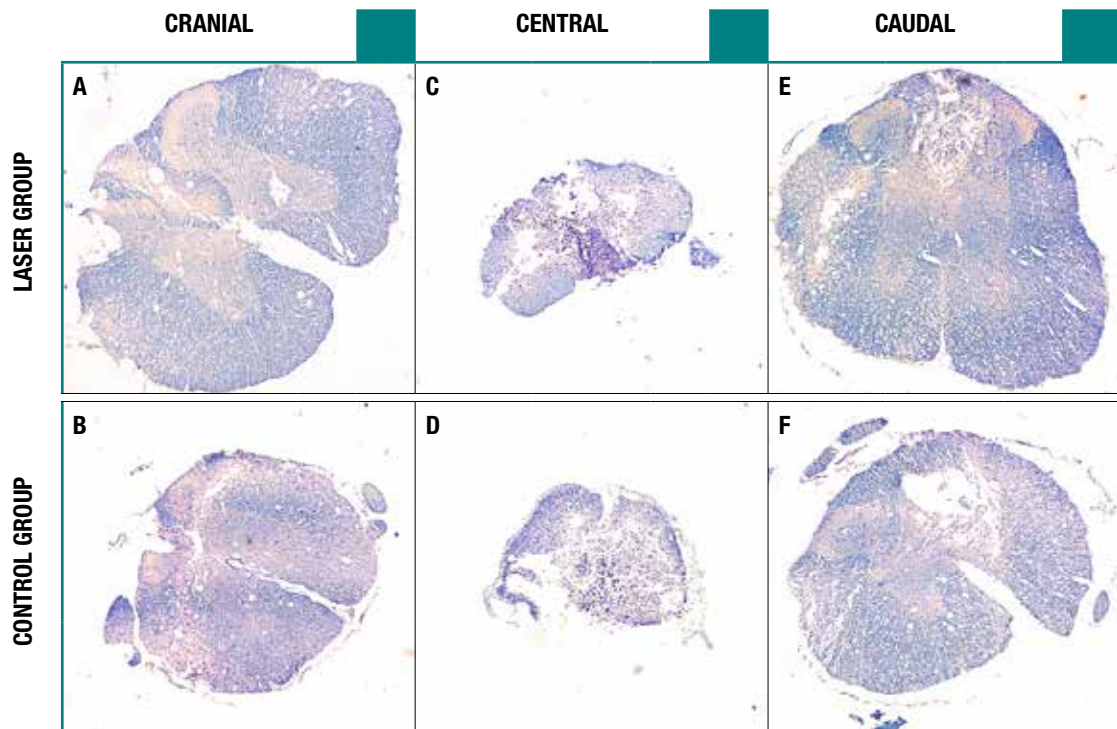
Svobodova et al

Recently, *Scientific Reports*, a prestigious magazine, has published a research on the effect of MLS[®] pulse on spinal cord injury (SCI) in the rat conducted by an interdisciplinary group of researchers from Czech Republic and United States. Spinal cord injury is a severe condition, for which effective treatments are currently lacking. After the injury, which is physically disrupting cells and tissues (primary injury), a strong inflammation is originated at the site of lesion (secondary injury), with the recruitment of specific cells called “macrophages”. Macrophages can be activated towards the inflammatory type (called “M1”) or the anti-inflammatory type (called “M2”). Following SCI, most macrophages are activated in the M1 type.

In this study, the injured animals were divided into two group, one of which has received laser therapy while the other hasn't. During a 9 week follow up period, all animals were periodically monitored and the results obtained by the two groups were compared highlighting that MLS[®] treated animals:

- Significantly improved in terms of functional recovery. Treated rats demonstrated better locomotor recovery of coordination and motor function respect to control. This result was confirmed by different complementary testing. MLS[®] Laser Therapy was also effective in reducing post-injury plantar hypersensitivity;
- Significantly counteracted muscle atrophy caused by decreased muscle activity;
- Showed a positive effect in terms of spinal cord grey and white matter sparing;
- When macrophage population was examined, a shift towards the M2 anti-inflammatory type has been observed.

Altogether those data suggest that MLS[®] Laser Therapy can be considered a promising therapeutic approach for improving functional recovery and tissue protection after spinal cord injury.



Svobodova B., Kloudova A., Ruzicka J., Kajtmanova L., Navratil L., Sedlacek R., Suchy T., Jhanwar-Uniyal M., Jendelova P., Machova Urdzikova L. (2019). The effect of 808nm and 905nm wavelength light on recovery after spinal cord injury. *Nature Scientific Report*, 9:7660

200 μ m

Histological analysis

(**A,B**) Representative images of Luxol-Fast Blue and Cresyl Violet stained cross sections 9 weeks after the SCI.

(**A**) – laser group, (**B**) – control group.

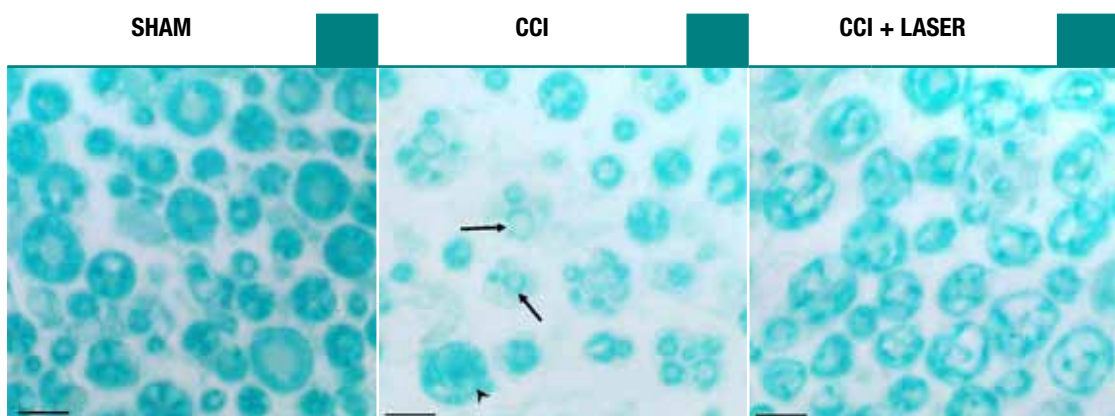
(**C**) Morphometric measurement of gray matter sparing showed a preservation of the tissue throughout the whole analyzed part of the spinal cord with significance 4–5 mm cranially and 3–7 mm caudally from the epicenter.

(**D**) White matter was also more spared with significance 3–6 mm cranially and 4–7 mm caudally from the lesion center.

Experiments on Neuropathic Pain

Micheli et al

Scientific Reports also reported the study conducted by ASAcampus and the University of Florence to investigate the effect of MLS[®]-MiS Laser Therapy in a model of sciatic nerve chronic constriction in the rat. This experimental model has been chosen as mimics the Neuropathic Pain experienced by patients with chronic degenerative nerve damage, and for which currently there is still the need for effective therapies. The study involved the creation of three groups: Sham (animals that received sham surgery, with nerve exposure without ligation), CCI (animals subjected to the ligation of the sciatic nerve, not treated with MLS[®]-MiS Laser Therapy), CCI + laser (animals subjected to the ligation of the sciatic nerve, treated with MLS[®]-MiS Laser Therapy). The results of the experiments demonstrated that the treatment with MLS[®]-MiS



Luxol Fast Blue staining. Representative micrographs of sciatic nerve axons in a sham, CCI and CCI + laser groups showing a partial laser-dependent neuroprotection of myelin thickness. Original magnification 400 X. Scale bar = 20 μ m.

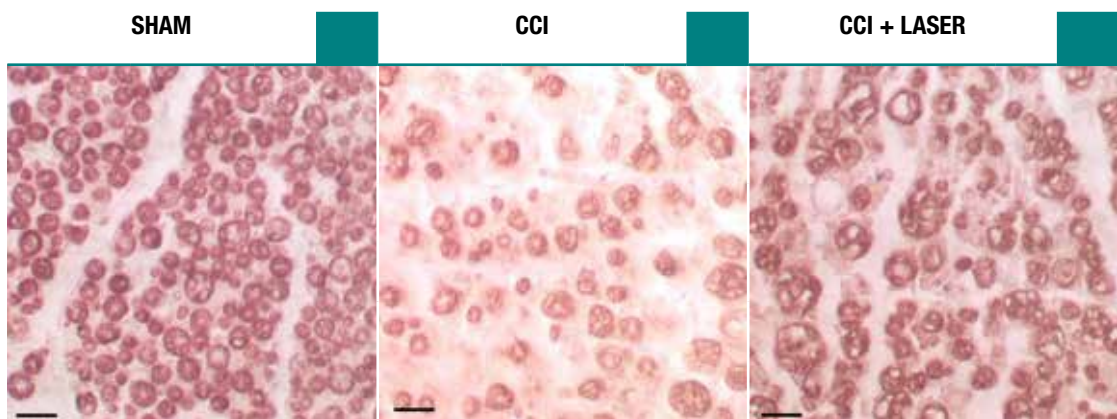
Laser Therapy reduced pain significantly and protected nerve structure. The mechanisms that have been observed include:

- Anti-inflammatory effect, by inhibition of enzymes involved in the inflammation process;
- Repair effect, involving myelin sheath restoration;
- Protective effect on central nervous system, modulating pain stimulation signalling.

Collected data suggest MLS[®]-MiS Laser Therapy can be considered a new promising therapeutic approach for the treatment of Neuropathic Pain after nerve lesion.

2.2.3 ←

Collected data suggest MLS[®]-MiS Laser Therapy can be considered a new promising therapeutic approach for the treatment of Neuropathic Pain after nerve lesion.



Myelin Basic Protein (MBP) expression. Protein expression of MBP was evaluated by immunohistochemistry in each experimental group. CCI group and CCI + laser group were compared to each other and with sham group. Original magnification 400X. Scale bar = 20 μ m.

The clinical experience on patients

Clinical experience in diabetic neuropathy

Khamseh et al

The number one cause of Peripheral Neuropathy is diabetes. According to the Foundation of Peripheral Neuropathy, 30 million American people suffer from some type of neuropathy and between 60-70% of those have diabetic peripheral neuropathy.

In other words, between 18 and 21 million Americans are dealing with diabetic neuropathy. This condition is heterogenous by its symptoms, pattern of neurologic involvement, progression, etc. Pharmacological treatment is what those patients has been proposed with limited success and many side effects⁵.

The effect of MLS[®] Laser Therapy in the treatment of diabetic neuropathic patients has been assessed by a team of the Tehran University.

In this study, nerve conduction has been measured before and after MLS[®] Laser Therapy treatment cycle. A nerve conduction study (NCS) is a medical diagnostic test commonly used to evaluate the function, especially the ability of electrical conduction, of the motor and sensory nerves.

At the end of the study, the subjects showed a significant increase in neural potential amplitudes, thus demonstrating a significant positive effect of MLS[®] Laser Therapy on improvement of nerve function in diabetic neuropathy. These results support the use of MLS[®] Laser Therapy in diabetic patients affected by peripheral neuropathy.

→ <https://www.foundationforpn.org/what-is-peripheral-neuropathy/types-risk-factors/>

Clinical experience in radiculopathies

Grennell, Perez et al

Back pain can occur from many sources and the associated pain can manifest in the area of injury and/or become radiating in nature, following the pathway of the affected nerve roots. Grennell reported the case of a 17 years old patient with severe lumbalgia and radiculopathy associated with a L4-L5 disc herniation that was treated with MLS® Laser Therapy. The results showed steady improvement of pain relief during the seven-month course of treatment. At nine months, the pain was not present. This first clinical experience suggested that MLS® Laser Therapy has beneficial effects on pain associated with disc herniation.

Some years later, Perez and colleagues reported the regression of a cervical radiculopathy following MLS® Laser Therapy treatment. In the reported case, not only MLS® Laser Therapy provided an effective non-invasive approach to treat cervical pain, but the remarkable result observed in this case is the successful outcome on the spinal cord narrowing. Regression of a herniated disk is thought to occur via an inflammatory reaction lead by macrophages. The Authors suggested that MLS® Laser Therapy could be a useful method to facilitate this process.

SAGITTAL MRI PRE-TREATMENT



SAGITTAL MRI AFTER MLS® TREATMENT



Clinical experience in lumbosacral sciatic pain

Guzman et al

Lumbosacral sciatic pain is a condition associated to spine degeneration which is affecting people daily life and activities. In fact, often pain is not only affecting the lumbar zone, but it is also irradiating down to the lower limb and can influence movement flexibility and general physical function. Conservative treatment involves the use of anti-inflammatory drugs and different physical therapy approaches. Nevertheless, most severe cases need to be treated with surgical intervention. A series of cases has been collected to reports on the use of MLS® Laser Therapy in lumbosacral sciatic pain. The goal was not only the management of the pain, but also the improvement in physical function with the aim of reaching a better quality of life for the treated patients. Patients improved not only in terms of pain management, but also in function and therefore in every day activity comfort, i.e. better sleep and better walk ability. The treatment was effective in keeping pain controlled between consecutive sessions. In conclusion, MLS® Laser Therapy resulted a useful approach for the treatment of lumbosacral sciatic pain.



Clinical experience in trigeminal neuralgia

Olmos

Regarding trigeminal neuralgia pain, an interesting case report has been collected by Olmos. The patient presented a typical neuralgia of the lingual nerve and the comorbidity of chronic pain and sleep related breathing disorders and he was found positive for obstructive sleep apnea (OSA). In the past, the patient had unsuccessfully tried drug therapy with anti-convulsant medication.

Treatment involved oral appliance therapy, MLS® Laser Therapy and Continuous Positive Airway Pressure (CPAP). After the treatment, the patient had complete elimination of his chronic pain and discontinued his medications. At 2 year follow up, he still continued to be free of pain. Overall results establish the efficacy of MLS® Laser Therapy in the treatment of neuropathy and, in combination with the treatment of OSA and bruxism, as a tool for long term cure.



Preliminary clinical results using MiS therapy in peripheral neuropathy

Mezzalana, D'Angelo

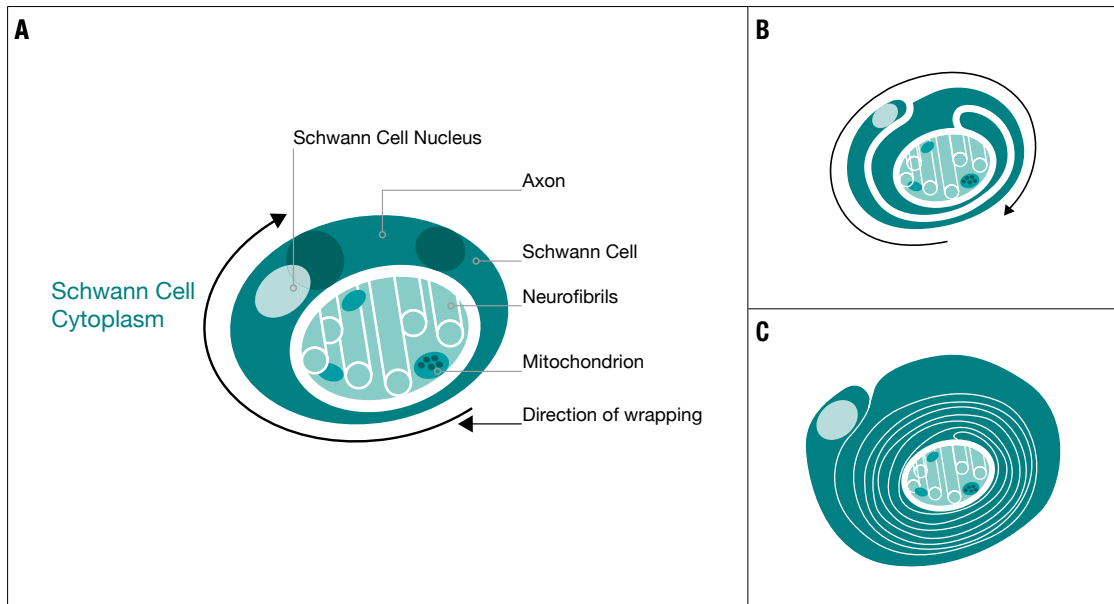
Recently, based on the encouraging results obtained so far in the field of Neuropathic Pain, ASA has designed and realized a new medical device solution based on MLS® pulse and specifically dedicated to the treatment of patient affected by peripheral neuropathy, named MiS. The preliminary clinical experience of two physiotherapy centers that have included MiS in their practice has been reported. Altogether, a total of 43 patients (mean age: 53 years, from 23 to 85 years) presenting Neuropathic Pain associated to different anatomical areas, were treated with MLS® pulse-based laser therapy, MiS. Pain (VAS score) and functionality (therapist evaluation) were evaluated at the end of treatment. The severity of pain decreased over time and was lower at the end of treatment. Based on the preliminary reported experience, the new MiS laser therapy demonstrated to be safe and effective in patients affected by Neuropathic Pain and therefore it is suggested that MiS represents a valuable and well-accepted tool for the management of peripheral neuropathies.

VAS PRE AND POST TREATMENT DIVIDED BY ANATOMICAL DISTRIBUTION OF THE TREATED AREAS

Area	Patient #	VAS Pre (mean)	VAS post (mean)	ΔVAS%
Spine	17	8,8	2,2	75%
Cervical area	3	8,3	3	63,9%
Elbow	4	9	0	100%
Knee	4	8	1,5	81,3%
Ankle / foot	3	7	2	71,4%
Hip (mainly pudendal nerve)	9	7	0	100%
Shoulder	1	9	0	100%
Wrist / Hand	2	7,5	2,5	66,7%
TOTAL	43	7,8	1,6	79,5%

MiS is the result of the deep knowledge of the therapeutic potential of the MLS® pulse, of which it inherits the wavelengths, the characteristic combined, synchronized and overlapped modulation of continuous and pulsed emissions, the safety of treatment, the proven efficacy, and the scientific evidence of the action mechanisms.

CONCLUSIONS



A. Schwann cell wraps around the axon. B. Schwann cell rotates around the axon forming layers. C. Myelin sheath is formed.

The scientific studies carried out have shown that the peculiarities of MiS are not limited to technological innovation and the enhancement of the biological effects already achieved with MLS® but, exceeding all expectations, have revealed new therapeutic effects that extend the possible applications of laser therapy towards pathologies with high social impact.

Based on the described evidences, ASA proposes MiS in the field of Neuropathic Pain: to see all device features [click here](#) and do not hesitate to contact us for any further request writing at marketing@asalaser.com.

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