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Mini Review Open Access

# Low-Level Laser Therapy (LLLT) Improves the Repair Process of Peripheral Nerve Injuries: A Mini Review

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## Abstract

**Purpose:** The aim of this study was to perform a mini-review on the effects of low-level laser therapy on nerve regeneration.

**Methods:** In this study, the authors associated the new fibrin sealant derived from snake venom as a method of nerve repair end-to-side.

**Results and conclusion:** The use of fibrin sealant effectively provided an axonal regeneration, and the association with low-level laser therapy elevated this regenerative process, as demonstrated in the morphometric and morphological analyzes.

**Keywords:** Fibrin sealant; Low level laser therapy; Nerve regeneration; Snake venom

## Introduction

Nerve damage occurs due to innumerable factors, such as gunshot wounds, knife injuries, trauma and a greater number of automobile accidents. Therefore, the nerve can be injured by neuropraxia, axonotmosis or neurotmesis, the latter being more severe, which can lead to motor, sensory and functional losses, significantly interfering with the individual's daily, employment, social and emotional activities [1-3]. The incidence rate in the population compared to those of peripheral nerve damage is about 2% to 2.8%, reaching 5% when involving nerve plexuses and root nerves [4-6].

In the search to repair such lesions, the end-to-side neurorrhaphy technique was described in the literature as an alternative when it is impractical to apply direct grafts [7,8]. The sural nerve can be used as a donor of fibers and applied in the end-to-side neurorrhaphy technique, since its morphology and growth in symmetry would be a suitable model for experimental studies in neuropathies [9].

The use of the sural nerve in neurotmesis was reported in the experiment by Buchaim et al. [10] with a differential: the use of this spinal nerve (sensory) being a donor to the vagus nerve (cranial and mixed), electing the end-to-side technique without an epineural window, also inserting two other components that are gaining prominence in the literature as a repair model in peripheral nerve regeneration, fibrin sealant derived from snake venom and the aid of photobiomodulatory effects of low-level laser therapy.

Fibrin sealant derived from snake venom (*Crotalus durissus terrificus*) has been highlighted in the international literature [10-13]. Produced by the research group of the Center for the Study of Venoms and Venomous Animals (CEVAP, UNESP/Botucatu-SP, Brazil), it presents three individual solutions that must be homogenized before application: fibrinogen originated from buffalo blood; calcium chloride and a thrombin-like fraction.

Its differential characteristics as being a biological and biodegradable compound, not producing adverse reactions since there are no remnants of human blood components and thus do not transmit infectious diseases, in addition to good adhesive quality that gives it the function of replacing the suture conventional [13].

The second differential of the study by Buchaim et al. [10] was the use of low-level laser therapy (LLLT) or currently titrated as photo modulation therapy (PBMT), which stands out as a focus of interest in the literature in the area of peripheral nerve regeneration.

The PBMT presents its characteristics related to the reduction of the time of repair of the tissues, besides the capacity to raise the cellular proliferation. Its wavelength, as an infrared irradiation, is easily absorbed by the tissues and loss of intensity is minimal, affecting metabolic changes, DNA activity, adenosine triphosphate (ATP) formation and mitochondrial chain. ATP from injured or impaired regions of blood perfusion can reactivate injured cells and metabolic disorders [14]. PBMT is still related to pain relief and inflammation, prevention of tissue death in order to avoid neurological degeneration [15,16].

## Application of LLLT

The laser used in the study by Buchaim et al. [10] was the gallium-aluminum-arsenide laser (GaAlAs, Laserpulse IBRAMED®, Brazil), applied at three different points in the surgical area, wavelength of 830 nm, with 30mW optical power output of potency, total energy per session 1.44 J, energy density of 4.1 J/cm$^2$, beam area of 0.116 cm$^2$, cumulative dose 23.04 J and exposure time of 16s per point. The equipment was tested so that the applied dose was adequate. The beginning of the application occurred in the first postoperative period and followed for 5 weeks with 3 applications per week [10,17-21].

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## Morphometric Results

It was observed in the morphometry that the control group presented all dimensions evaluated (area and diameter of the fibers, area and diameter of the axon, and area and thickness of the myelin sheath) with greater measurements and significant difference with the fibrin sealant group and the laser associated fibrin sealant group, except for the thickness of the myelin sheath, which showed a significant difference only with the fibrin sealant group [10]. In the group that received PBMT, there were larger measurements in all dimensions, besides a significant difference, except for the area and thickness of the myelin sheath, with a group not treated with laser [10].

## Morphological Results (Optical and Electron Microscopy)

Optical microscopy revealed in the control group a sural nerve (graft) with prevalence of myelin fibers in relation to the unmyelinated fibers, grouped homogeneously. On the other hand, the sural nerve adhered to the intact vagus nerve obtained a greater amount of regenerated myelinated nerve fibers and unmyelinated fibers originating from the donor nerve (vagus nerve), evidenced irregularly in relation to the control group. Regenerated myelin axons in the graft segments originated by the donor nerve were confirmed by transmission electron microscopy [10].

## Biopharmaceuticals (Fibrin Glue Derived from Snake Venom)

During the experimental surgery, it was observed that fibrin sealant derived from snake venom can be applied in a simple way and obtained good tissue fixation, clearly characterizing its benefit when compared to neurorrhaphy, in addition to its easy application with lesser skill requirement of the surgeon [22-25].

## Laser Photomodulation Therapy (PBMT)

In the analyzed samples, a blood vessel neoformation was evidenced in the grafts of the experimental groups. This new vascularization aids in the process of tissue regeneration [26]. The PBMT is classified as a differential in the process of tissue regeneration and recovery, also relating its anti-inflammatory and anti-edematous effects, besides providing analgesia and circulatory normalization [17-21,27]. The literature also demonstrates the relation of the laser in the morphological and functional recovery of the nervous system, but there is still no consolidation of the PBMT application protocols [28-30].

The PBMT can provide a decrease in the migration of mononuclear cells, and consequently edema absorption, besides providing an increase in the cellular respiration and an inference in the process of Schwann cells proliferation, allowing a better myelin production [31,32]. As evidenced in the present study, the PBMT increased the diameter of the nerve fibers, offering an increase in the regeneration of the peripheral nerve, being able to favor the elevation in the metabolism of the neurons [33,34].

## Other Applications of PBMT

The literature evidences the application of PBMT in other tissues or regions, such as bone [12,35], cartilage and orthopedic disorders [36], cells *in vitro* culture [37], Central Nervous System [38,39] and also in cases such as cerebral palsy in children [40]. In addition to PBMT, there are other physical agents that can be used in clinical practice as auxiliary methods in the treatment of tissue repair, such as low-intensity pulsed ultrasound [41].

## Conclusion

In view of the results obtained, this research showed that the use of fibrin sealant derived from snake venom was of good resolution against the recovery of peripheral nerve lesions, with improvement of the process of nerve regeneration aided by PBMT. The method approached with the use of the end-to-side neurorrhaphy caused the growth of donor nerve axons to the graft, and regeneration occurred even without the need for an opening in the epineurium.

Thus, fibrin sealant allowed for axonal regeneration, being an effective alternative in nerve recovery and the approach together with the low-level laser therapy created a treatment that increased nerve regeneration.

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