



# Effects of Low-Level Laser Therapy and Interferential Current Therapy in the Treatment of Complex Regional Pain Syndrome

## Kompleks Bölgesel Ağrı Sendromu Tedavisinde Düşük Doz Lazer Terapi ve Interferans Akım Terapisinin Etkileri

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### Abstract

**Objective:** The aim of this study is to estimate and compare the effects of low-level laser therapy and interferential current therapy in patients with complex regional pain syndrome type I.

**Material and Methods:** Prospective randomized clinical research, including 45 patients with post-traumatic unilateral complex regional pain syndrome type I, treated at the Clinical Center Nis from December 2004 to January 2007. Low-level laser therapy and kinesiotherapy were applied in group A (n=20), whereas group B (n=25) was treated with interferential current and kinesiotherapy. For assessment of the therapeutic effect, the following parameters were tested: pain intensity was determined by visual analog scale, figure-of-eight measurement was used to determine the circumference of the affected part of the extremity, and range of motion of the affected joint was measured by a standard goniometer.

**Results:** Statistically significant differences were obtained for all tested parameters in both groups, but the difference was greater in group A compared to group B (p<0.05).

**Conclusion:** The results of this study show that both physical procedures are effective in the treatment of complex regional pain syndrome type I, but the efficiency of laser therapy is statistically significantly higher compared to interferential current therapy.

**Key Words:** Complex regional pain syndrome, low-level laser therapy, interferential current

### Özet

**Amaç:** Bu çalışmanın amacı, kompleks bölgesel ağrı sendromu tip I hastalarında düşük doz lazer terapisi ve interferans akım terapisinin etkilerini değerlendirmek ve karşılaştırmaktır.

**Gereç ve Yöntemler:** Prospektif randomize klinik araştırmaya post-travmatik tek taraflı kompleks bölgesel ağrı sendromu tip I olan, Aralık 2004 ile Ocak 2007 arası Nis Klinik Merkezinde tedavi edilen 45 hasta dahil edildi. A grubuna (n=20) düşük doz lazer terapisi ve kineziterapi, B grubuna (n=25) interferans akım terapisi ve kineziterapi uygulandı. Terapötik etki, aşağıdaki parametreler ile test edildi; ağrı şiddeti visual analog skala ile ekstremitenin etkilenen kısmının çevresi sekizli figür ölçümü ile, etkilenen eklemde hareket genişliği standart açılışer ile ölçülerek değerlendirildi.

**Bulgular:** Her iki grupta da test edilen tüm parametreler için istatistiksel olarak anlamlı farklılıklar elde edildi, fakat fark B grubuna kıyasla A grubunda daha fazla idi (p<0,05).

**Sonuç:** Bu çalışmanın bulguları, her iki fiziksel yönteminde de kompleks bölgesel ağrı sendromu tip I tedavisinde etkili olduğunu gösterdi, ancak lazer terapisinin etkinliği interferans akım terapisine kıyasla istatistiksel olarak anlamlı derecede yüksekti.

**Anahtar Kelimeler:** Kompleks bölgesel ağrı sendromu, düşük doz lazer terapisi, interferans akım

## Introduction

Complex regional pain syndrome (CRPS) is a new term referring to reflex sympathetic dystrophy, and it is very frequent among pain syndromes (1). It has been estimated that 30% of the population suffers from chronic pain, and CRPS is present in 1/3 of this number (2). Its current incidence is unknown, as it often remains undiagnosed and disguised by the clinical picture of numerous pathological conditions (1,3). The most common cause is trauma that affects the extremities (2,4). CRPS type I is indicated by pathological sensory, motor, sudomotor, vasomotor, and/or trophic changes, most commonly localized to the distal part of the extremities (1,3). The syndrome is characterized by continuous regional pain, which is disproportionate according to duration and intensity, depending on the type of the initial damage (1). It has been observed that the progression of the disease induces spontaneous spread of symptoms along the affected extremity (5). CRPS type I is manifested in cases where pain is not limited to a dermatome or peripheral nerve distribution, while CRPS type II refers to cases where a nerve lesion is present (1,3).

The etiology and pathophysiological mechanisms of CRPS are still uncertain. It is believed that changes in the peripheral and central somatosensory and autonomous nervous system, as well as neurogenic inflammation, lead to the manifestation of CRPS I (3,5,6).

A unique therapeutic protocol has not been determined, even after two conferences of the International Association for the Study of Pain (IASP) dedicated to this disease (7,8). The primary aim of the treatment is to reduce pain and swelling, as well as to achieve full mobility and muscle strength, to improve function in the affected part of the extremity, and ultimately to achieve patient socialization (9). Considering the aims of the treatment, it is understandable why physical therapy represents the basis of every therapeutic protocol in the treatment of CRPS. Among the numerous physical procedures with analgesic and anti-edematous effects used in the treatment of CRPS, special emphasis is put on low-level laser therapy (LLLT) and interferential current (IFC) (9-11).

Despite the frequent application of IFC for pain management, there is a lack of experiment-based information about its clinical effectiveness (12). Theoretical mechanisms of the analgesic effects of IFC include potentially blocking the transmission of the pain signals, release of endorphins, increased circulation, and placebo mechanisms (13,14).

Low-level laser therapy has specific therapeutic effects, such as analgesia, anti-edematous and anti-inflammatory effects, and improvement of regenerative abilities (15-17). LLLT has a significant influence on the tone of the sympathetic nervous system, with the aim of its normalization, which justifies its application in the treatment of CRPS I (18).

Considering that LLLT is often used in the treatment of CRPS, this study was designed in order to determine whether the application of this therapy is more efficient than IFC.

The aim of this study is to estimate and compare the effects of LLLT and IFC in patients with complex regional pain syndrome type I.

## Material and Methods

### Patients

The study was conducted at the Clinic for Physical Medicine and Rehabilitation of the Clinical Center Nis (Serbia) from December 2004 to January 2007. During this period, 107 patients older than 18 years with CRPS I who had been diagnosed clinically on the basis of the modified research diagnostic criteria defined by the Budapest consensus group were referred to outpatient treatment. The modified research diagnostic criteria for CRPS were:

- 1) Continuing pain, disproportionate to any inciting event
- 2) At least one symptom in each of the four following categories:
  - a) Sensory: Reports of hyperesthesia and/or allodynia
  - b) Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
  - c) Sudomotor/edema: Reports of edema and/or sweating changes and/or sweating asymmetry
  - d) Motor/trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
- 3) At least one sign in two or more of the following categories:
  - a) Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)
  - b) Vasomotor: Evidence of temperature asymmetry and/or skin color changes and/or asymmetry
  - c) Sudomotor/edema: Evidence of edema and/or sweating changes and/or sweating asymmetry
  - d) Motor/trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
- 4) There is no other diagnosis that better explains the signs and symptoms (1)

The prospective randomized study included 50 patients with unilateral post-traumatic CRPS I in the first stage. Patients were instructed not to take any specific CRPS medication (corticosteroids, bisphosphonates, calcitonin, nifedipine, antiepileptic drugs, etc.) or analgesic medication. Exclusion criteria were: 1) anamnestic and clinical indicators that showed that patients suffered from diseases that were contraindicated for the application of the stated physical agents (acute and subacute thrombophlebitis, thrombosis, neoplastic disease, fever, etc.) and 2) pregnancy. During the study, 5 out of 50 patients dropped out. A total of 45 patients completed the study (Figure 1).

At the time of the start of this study, there was no ethics committee established at the Faculty of Medicine, University of Nis, but the study was approved by the postgraduate departmental committee. All patients gave informed written consent to participate in the study.

### Treatment

The examined patients were randomly selected and classified into two groups, using sequentially numbered, closed,

opaque envelopes that had been prepared earlier, using a computer-generated list of random numbers, and balanced to ensure equal numbers in each group.

Group A included 20 patients with CRPS I who were treated with LLLT and kinesitherapy. A GaAs laser diode was used with a low power of 70 mW, 810 nm wavelength, and 70 Hz, 640 Hz, and 5000 Hz frequency, depending on the dominant findings. Eight points along the joint line and painful points in the affected area were treated with 1.5 J/cm<sup>2</sup>.

Group B included 25 patients with CRPS I whose therapeutic protocol consisted of IFC and kinesitherapy. Bipolar IFC therapy was applied, with 90 Hz frequency, for 15 minutes with electrodes positioned locally on the painful and swollen part.

Individual kinesitherapy (active and active assisted exercises, strictly dosed up to pain threshold) was applied in patients from both groups for 30 minutes, twice a day.

The patients from both groups received the first 10 therapies every day for 5 days a week (2 weeks), and the next 10 therapies were received every other day.

### Outcome Measures

The following parameters were assessed in order to estimate the therapeutic effects: a) pain intensity at rest and during active movements, b) the circumference of the affected part of the extremity for assessing the edema, and c) range of motion of the affected joint.

Intensity of pain was measured by visual analog scale (VAS). VAS represents a 100-mm horizontal scale, graded from 0, which displays the condition without pain, to 100, which is the worst pain possible (19). Intensity of pain was separately measured at rest and during active movements of the wrist/ankle. VAS scores were taken as an average of what the patient suffered a few days before evaluation.

Hand/foot circumference was measured in order to quantify edema using a figure-of-eight measurement (20,21). Measurements of each patient's affected and unaffected hand/foot were performed. Hand/foot edema was expressed as the difference between hand/foot circumference of both hands/feet.

Active range of motion of the wrist/ankle was measured by a standard full-circle goniometer and recorded in degrees according to the method suggested by the American Academy of Orthopedic Surgeons in 1988 (22). Intraobserver bias was minimized by careful technique, and recordings were made in triplicate, and the mean of these measurements was noted. Range of motion of wrist/ankle was shown as a total range of motion of the affected joint in the sagittal plane.

All patients underwent evaluation of each separate parameter before treatment and after applying 20 therapeutic procedures.

Two types of comparison were made: 1) comparison of the monitored parameters before and after therapy for each separate group and 2) comparison of the obtained differences of the monitored parameters before and after therapy among groups.

### Statistical Analysis

The data obtained were analyzed using the Statistical Package for the Social Sciences (SPSS 10.0). For the examination of normal dispersion data, Kolmogorov-Smirnov test was used. The results of the statistical analysis were expressed as mean value (X) and standard deviation (SD). Statistical significance was tested by paired student t-test for repeated measurements in the same group and by independent student t-test for comparison between groups. The degree of statistical significance of  $p < 0.05$  was accepted for this study.

### Results

The demographic and basic characteristics of the patients are presented in Table 1. We did not find statistically significant differences among the tested groups in baseline characteristics ( $p > 0.05$ ). The tested groups were comparable with regard to all the parameters tested before therapy ( $p > 0.05$ ).

Mean values  $\pm$  SD ( $X \pm SD$ ) for both groups for each measured outcome at the beginning and at the end of therapy are presented in Table 2. After therapy, both groups showed a statistically significant reduction of pain and edema and increased range of motion of the affected joint, compared to basic values ( $p < 0.01$ ). The differences between the basic values and those obtained at the end of therapy for each measured outcome were compared between groups (Table 3). Statistical analyses showed more improvement in group A than in group B for all measured outcomes.

The application of laser therapy had a particularly beneficial effect in reducing pain intensity and edema, compared to IFC therapy ( $p < 0.001$ ).

No negative effects of the applied therapy were recorded in patients.

Figures 2 and 3 show the affected part of the extremity before and after the treatment in two patients from group A.

### Discussion

The choice of therapeutic procedures in the treatment of CRPS I is still an object of debate, since there is no unique therapeutic protocol (7,8,23,24). The multifactorial etiology of CRPS I and the complexity of the pathophysiological mechanisms influence the multidisciplinary therapeutic approach (25-30).

**Table 1. Baseline characteristics**

Characteristics	Group A (n=20)	Group B (n=25)	t	$\chi^2$	p value
Age (years)	53.90 $\pm$ 13.36	57.80 $\pm$ 10.75	1.08		>0.05
Gender (male/female)	8/12	8/17		0.31	>0.05
Duration (days)	33.75 $\pm$ 8.44	31.64 $\pm$ 7.79	0.87		>0.05
Localization of CRPS I* (hand/foot)	7/13	14/11		1.97	>0.05

\*CRPS I: Complex regional pain syndrome type I

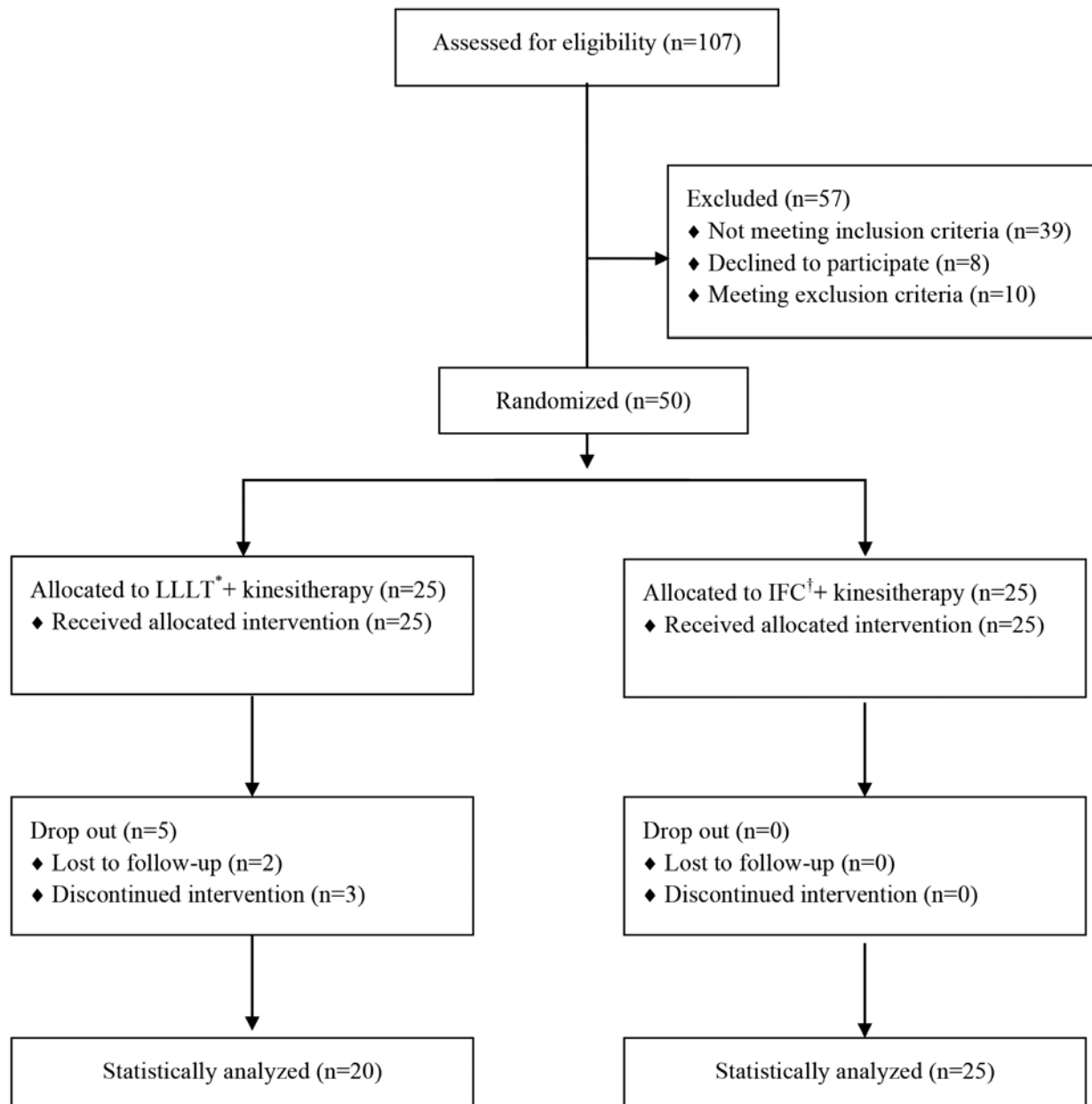


Figure 1. Flowchart of patient recruitment

\*LLL: low-level laser therapy; †IFC: interferential current

However, the application of a multidisciplinary approach does not provide the expected results, because a high percentage of patients still have dysfunction of the affected extremity after therapy (23,24).

The aim of our study was to compare the efficiency of LLLT and IFC in the treatment of CRPS I. The obtained results were better in the group with LLLT with regard to all measured out-

comes, especially to pain and edema. The available literature does not provide any studies comparing the clinical effects of these two physical agents.

Interferential currents are commonly used in CRPS I treatment. Their frequency is estimated at 44%, compared to other physical procedures used in the treatment of this syndrome (31). In the study by Nikolova (11), which compared the ef-

**Table 2. Assessment of pain, edema, and range of motion in both groups, before and after therapy**

Outcomes	Group A (n=20)			Group B (n=25)		
	Pre-therapy	Post-therapy	t	Pre-therapy	Post-therapy	t
VAS-rest <sup>‡</sup>	62.50±11.18	39.0±13.34	14.104 <sup>†</sup>	60.80±12.22	47.60±12.67	7.333 <sup>†</sup>
VAS-activity <sup>§</sup>	84.50±10.90	55.0±20.13	10.688 <sup>†</sup>	80.80 ±12.22	65.20±14.75	9.506 <sup>†</sup>
ΔO-hand <sup>¶</sup>	2.78±0.86	0.72±0.76	10.253 <sup>†</sup>	2.86±0.77	1.39±0.65	10.988 <sup>†</sup>
ΔO-foot <sup>**</sup>	3.35±1.12	1.04±0.75	10.023 <sup>†</sup>	3.18±1.12	1.77±0.82	10.696 <sup>†</sup>
ROM-wrist <sup>¶¶</sup>	39.86±31.81	86.43±15.47	4.999 <sup>*</sup>	43.21±25.01	63.21±18.14	6.273 <sup>†</sup>
ROM-ankle <sup>¶¶</sup>	17.69±8.32	38.08±5.60	11.132 <sup>†</sup>	19.54±5.68	30.45±6.10	7.372 <sup>†</sup>

\*p<0.01 statistically significant values;

†p<0.001 statistically significant values;

‡VAS-rest: visual analog scale at rest; §VAS-activity: visual analog scale during activity;

¶ΔO-hand= O-hand injured- O-hand uninjured; \*\*ΔO-foot= O-foot injured- O-foot uninjured;

¶¶ROM-wrist: range of motion wrist; \*\*ROM-ankle: range of motion ankle.

**Table 3. Statistical analysis of measured changes**

Outcomes	Group A (n=20)	Group B (n=25)	A-B	
	Mean±SD	Mean±SD	t	p
VAS-rest <sup>*</sup>	23.50±7.45	13.20±9.0	4.111	0.000
VAS-activity <sup>†</sup>	29.50±12.34	15.6±8.20	4.524	0.000
ΔO-hand <sup>‡</sup>	2.07±0.53	1.46±0.40	2.571	0.019
ΔO-foot <sup>§</sup>	2.31±0.83	1.41±0.44	3.225	0.004
ROM-wrist <sup>¶</sup>	46.57±24.65	20.00±11.93	3.375	0.003
ROM-ankle <sup>**</sup>	20.77±6.07	10.91±4.91	4.319	0.000

\*VAS-rest: visual analog scale at rest; †VAS-activity: visual analog scale during activity;

‡ΔO-hand: O-hand injured- O-hand uninjured; §ΔO-foot: O-foot injured- O-foot uninjured;

¶ROM-wrist: range of motion wrist; \*\*ROM-ankle: range of motion ankle.

iciency of IFC, ultrasound, and diadynamic current in the treatment of 400 patients with CRPS I, the best results were observed with the application of IFC in the early stage.

A small but double-blind and placebo-controlled study, performed at the Mayo Clinic, showed that the application of LLLT caused significant pain reduction (more than 50%) in 1/3 of examined patients with CRPS I (32).

Also, significantly higher pain and edema reduction was achieved by the application of LLLT in patients with shoulder-hand syndrome after cerebral ischemia, compared to the group in which electrotherapy (TENS, stabile galvanization) was applied (33).

Laser therapy was also effective in pain reduction in numerous musculoskeletal and neurological disorders (6,15,34-39). Analgesic effects of LLLT were shown in patients with both acute and chronic pain syndrome (17,40).

On the other hand, there are studies that state that LLLT does not achieve better therapeutic effects in musculoskeletal disorders, compared to placebo (41-43). The contradictory facts may be a result of imprecisely defined parameters related to the dosage and frequency of LLLT (15,34,42,43).

Despite that LLLT has been used in the clinical practice for decades, the mechanism of action is not completely clear (42).

Modulation of pain perception with the control gate theory and increased production of endogenous opioids are just some of the mechanisms of the analgesic effects of LLLT, considering that the analgesic effect of LLLT is explained as a synergic effect of several mechanisms (10,15,17,38,40,42). Laser therapy blocks the entrance of Na<sup>+</sup> into the cell, which is a stabilizing factor in cell membrane resting potential, and in that way, transmission of pain on the local level is impeded (10). Local reduction of pain is also achieved indirectly through anti-edematous and anti-inflammatory effects. By increasing local microcirculation, laser radiation reduces the edema, increases tissue oxygenation, and facilitates elimination of alogenic substances (38,40). It has also been demonstrated that laser therapy achieves its analgesic effect through inflammatory mediators-eg, reduction of the level of prostaglandin E-2 and inhibitory effects on cyclooxygenase 2 (34,36,38).

There is agreement that physical therapy is the most significant procedure in the treatment of CRPS. It represents a basis in a multidisciplinary therapeutic approach, considering that CRPS I is characterized by reduced function of the affected joint segment (2,25-30,44). Rho et al. (45) point out that CRPS therapy should primarily be initiated by the application of physical procedures. They even suggest that the treatment of patients with



Figure 2. a,b. A 54-year-old man with complex regional pain syndrome type I in the right foot (a) before treatment; (b) after treatment

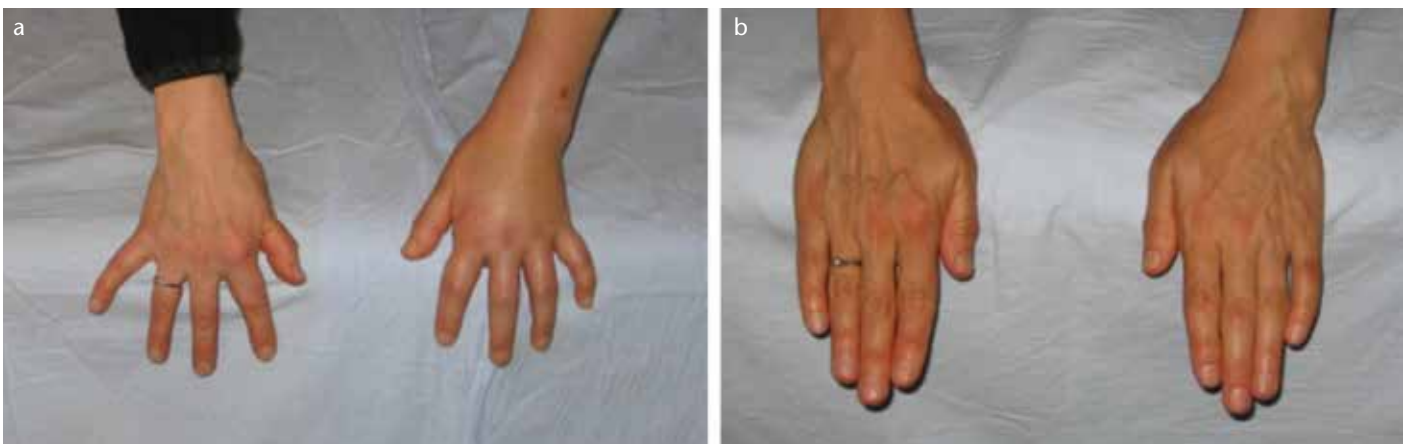


Figure 3. a,b. A 39-year-old man with complex regional pain syndrome type I in the left hand foot (a) before treatment; (b) after treatment

a mild form of CRPS should include only physical therapy. The American Physical Therapy Association shows that physical procedures may improve function in 80% of patients with CRPS I (7,24). Particular emphasis is put on the application of physical procedures in the early stages in order to prevent disease progression. It is possible that its timely use would prevent the development of muscular atrophy, contraction of adjacent joints and dysfunction of the affected extremity (7,8,44).

Numerous clinical studies often use the term "physical therapy" without defining the applied physical procedure. Lack of information on the efficiency of some physical procedures in CRPS treatment impedes the creation of a specific therapeutic protocol (2). Eccleston et al. (46) emphasize that the choice of

physical procedures should be adjusted to individual patients with regard to their clinical picture. It is also important to note that the application of aggressive physical therapy may lead to exacerbation of CRPS (30).

The results of our study should be considered in light of several limitations. The therapeutic effects of physical procedures were examined in a small population of patients and were monitored during a short time interval. In addition, the randomization of patients was not done on the basis of their psychosocial characteristics, which may influence the therapeutic response.

Future research is expected to aim at outlining the long-term therapeutic effects of LLLT in a wider population of patients. Besides, the plan is to direct future research at comparing the



therapeutic effects of LLLT with different frequencies and doses, as well as at comparing LLLT and placebo therapy.

## Conclusion

Our results show that the applied therapy causes statistically significant improvements in all measured outcomes in both groups but that this effect is considerably greater in the group of patients treated with LLLT. It has been observed that both physical procedures are efficient in CRPS I treatment, but LLLT provides better results, particularly with pain and edema reduction.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Faculty of Medicine, University of Nis.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - I.D., M.L., M.K.; Design - M.L., M.K., L.D.; Supervision - M.L., M.K.; Materials - M.K., L.D., A.S.; Data Collection and/or Processing - I.D., A.S.; Analysis and/or Interpretation - I.D., M.K., L.D., D.M.; Literature Review - I.D.; Writer - I.D.; Critical Review - I.D., M.K.; Other - A.S., D.M.

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