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Original Article

The Effect of Low-Level Laser in Knee Osteoarthritis: A Double-Blind, Randomized, Placebo-Controlled Trial

Béla Hegedűs, M.D.,[1] László Viharos, Ph.D.,[2] Mihály Gervain, Ph.D.,[3] and Márta Gálfi, Ph.D.[4]

Abstract

Introduction: Low-level laser therapy (LLLT) is thought to have an analgesic effect as well as a biomodulatory effect on microcirculation. This study was designed to examine the pain-relieving effect of LLLT and possible microcirculatory changes measured by thermography in patients with knee osteoarthritis (KOA). ***Materials and Methods:*** Patients with mild or moderate KOA were randomized to receive either LLLT or placebo LLLT. Treatments were delivered twice a week over a period of 4 wk with a diode laser (wavelength 830 nm, continuous wave, power 50 mW) in skin contact at a dose of 6 J/point. The placebo control group was treated with an ineffective probe (power 0.5 mW) of the same appearance. Before examinations and immediately, 2 wk, and 2 mo after completing the therapy, thermography was performed (bilateral comparative thermograph by AGA infrared camera); joint flexion, circumference, and pressure sensitivity were measured; and the visual analogue scale was recorded. ***Results:*** In the group treated with active LLLT, a significant improvement was found in pain (before treatment [BT]: 5.75; 2 mo after treatment : 1.18); circumference (BT: 40.45; AT: 39.86); pressure sensitivity (BT: 2.33; AT: 0.77); and flexion (BT: 105.83; AT: 122.94). In the placebo group, changes in joint flexion and pain were not significant. Thermographic measurements showed at least a 0.5°C increase in temperature—and thus an improvement in circulation compared to the initial values. In the placebo group, these changes did not occur. ***Conclusion:*** Our results show that LLLT reduces pain in KOA and improves microcirculation in the irradiated area.

Introduction

Since Endre Mester began his pioneering investigations, numerous clinical and basic research studies have demonstrated the physiological effects and medical applicability of low-level laser therapy (LLLT). Its application was initiated based on previous work that demonstrated properties of low-level laser that exert a positive influence on fibroblast[1] and osteoblast[2] proliferation, collagen synthesis,[3] and bone regeneration.[4] In vivo examinations have also shown that LLLT significantly stimulates the activity of alcalic phosphatase and calcium accumulation.[5] In addition to cartilage damage and bone metabolism, pathological alterations are also known to exhibit reduced circulation in the vessels of the joint parallel to the degenerative changes. Numerous authors have reported increased microvascularization as a histological effect of the laser beam.[6,7] While examining revascularization—a phase of wound healing—Mester found a significant increase in the number of vascularized areas in laser-treated patients.[8] In light of the domestic and international literature, the aim of this study is to gather evidence of the analgesic effect of low-level laser as well as its possible effect in increasing microcirculation. In order to obtain objective data, thermographic measurements were taken, and follow-up examinations were performed to control for the permanency of the effects obtained.

Patients and Methods

Both female and male patients with mild to moderate knee osteoarthritis (KOA) were recruited to the study. Reasons for exclusion included considerable deformity of the varus or valgus, ankylosis, intense synovitis, or gonitis observed during physical examination; erosive or destructive alterations detected by radiograph (Kellgren-Lawrence stage 4); and the usual contraindications for laser therapy (Table 1).

Thirty-five patients were selected for the examinations, but only 27 patients (22 women and 5 men) completed the

[1]Physio- and Balneotherapy Center, Orosháza-Gyopáros, Hungary.
[2]Bolyai Institute, University of Szeged, Szeged, Hungary.
[3]County Hospital, Laboratory for Thermography, Orosháza, Hungary.
[4]Department of Biology, Juhász Gyula Teacher Training College, University of Szeged, Szeged, Hungary.

Table 1. Participation in the Study

Inclusion criteria	*Exclusion criteria*
Men or women between the ages of 30 and 65 with: 1) Knee pain intensity above 40 mm on VAS 2) Mild to moderate knee osteoarthritis confirmed by x-ray	1) Lab results abnormal (inflammatory and infectious disease, malignant tumor). 2) Arterial circulatory blockage in lower limbs. 3) Observed during physical examination: – considerable deformity of the varus and valgus – ankylosis – intense synovitis – gonitis 4) Detected in radiograph: – erosive, destructive alteration 5) Usual contraindications for laser therapy

study, 18 of whom were in the active LLLT group and 9 in the placebo LLLT group. Eight patients from the placebo group who left the experiment provided no reasons for doing so, nor did they return to the institute. The demographic data on the patients included in the study are summarized in Table 2.

During the study patients received no steroids, antidepressants, or sedatives. A detailed case history and physical status were recorded. Various examinations were conducted prior to treatment in order to rule out other diseases and to attain patient homogeneity (Table 3). Those who underwent treatment were given full disclosure and signed an agreement form on participation in the study.

Permission was granted for this study by the Institute's Research Ethics Committee. The patients received no other therapies or pain medication.

Treatments were administered on the same days twice a week over a period of 4 wk with an OPTIKOP KLS GaAlAs diode laser (power 50 mW, continuous wave, wavelength 830 nm) or with a placebo probe (power 0.5 mW) of the same appearance and display. The probes were numbered 1 (active) and 2 (placebo). Randomization was ensured by having patients randomly choose sealed envelopes from a bowl containing an equal number of slips with either number 1 or 2, which corresponded to one of the laser probe numbers. Neither the patients nor the operator knew which was the active or placebo LLLT probe. Treatment was administered in skin contact only over the joint which caused the most explicit complaints. The dose delivered was 6 J/point.

In one session, a patient was given a total dose of 48 J/cm^2. The size of the point in the focus of the laser light was nearly 0.5 mm^2; that is to say, the power density was approximately 50 $mW/0.5\,mm^2$, i.e., 10 W/cm^2. The laser has European certificate no. CE 0120. The device is self-checked in accordance with European Standards (CE) and requires no special staff. Treatment was administered over the femoral and tibial condyles in every case since enthesis is often responsible for the complaints mentioned by the patients. Laser irradiation was aimed at the synovia and cartilage in the joint line. The points that were irradiated were the medial and lateral epicondyle of the tibia and femur, the medial and lateral knee joint gap, and the medial edge of the tendon of the biceps femoris muscle and semitendinosus muscle in the popliteal ditch (Fig. 1).

Valgization was carefully performed on the knee joint when the medial knee joint gap was being treated, and varization was carried out when treatment was administered to the lateral knee joint gap. The knee joint was flexed on treating the popliteal ditch. In order to judge the efficacy of the treatment, subjective (pain on a 10-cm scale), semi-objective (pressure sensitivity on the Ritchie index scale), and objective (flexion in degrees, circumference in centimeters, and thermography with temperature [°C]) parameters were measured (Table 4). Thermographic measurements were used to observe microcirculatory changes during the treatment period, and a computer system enabled us to digitize the image.[9,10]

Considering that thermographic measurement is very sensitive but that its specificity is low, an attempt was made to set appropriate standard examination conditions. The examination room was therefore kept at a constant temperature (21–23°C) and free from drafts at a humidity of 70–80%. Prior to measurement, patients rested for 15 min and then the affected part of the body was washed with alcohol.

Table 2. Demographic Data

Distribution of patients			*Kellgren-Lawrence stage*				
	Men	*Women*		*Men*	*Women*	*Comorbidities*	
						Diabetes mellitus	2
No. of patients	5	22	I	2	3	Hypertonia	9
						Hypothyreosis	1
Age of patients	37–44	32–65	II	10	9	Ulcus ventriculi	1
Average age	41.00	51.40				Hyperlipidemia	1
Overall average	49.48		III	—	3	Arteriosclerosis universalis	2
						Myoma uteri	2

Table 3. Examinations Before Treatment

Dexascan	
X-ray (comparative image of bilateral knee joints)	
Doppler (arteries of the lower limbs: a. femoralis; a. poplitea)	
Laboratory	
Blood	WBC, RBC, HBG, HTC, sedimentation rate, CBC, BUN, Se creatinin, glucose, Se bilirubin , K, Na, Se ALP, SGOT, SGPT, gamma-GT, Se Ca, Se P, ELFO, Se protein, RF, Se urea, Se cholesterol, Se triglyceride
Urine	protein, pus, glucose, UBG, pH, ketone, bilirubin, blood, specific gravity, sediment

Patients were told to avoid coffee, alcohol, and cigarettes prior to measurement since these can influence circulatory conditions. In every case, medial and lateral comparative measurements were performed from anterior–posterior and posterior–anterior angles.

A basic (or zero) examination was performed prior to treatment; all other measurements were carried out weekly after the second treatment at the same time each week. In order to control for the permanency of the effect obtained, control measurements were performed 2 wk and 2 mo after completing the therapy.

Results

The graph shows changes in the four parameters examined, plotted against time, for treatment with active and

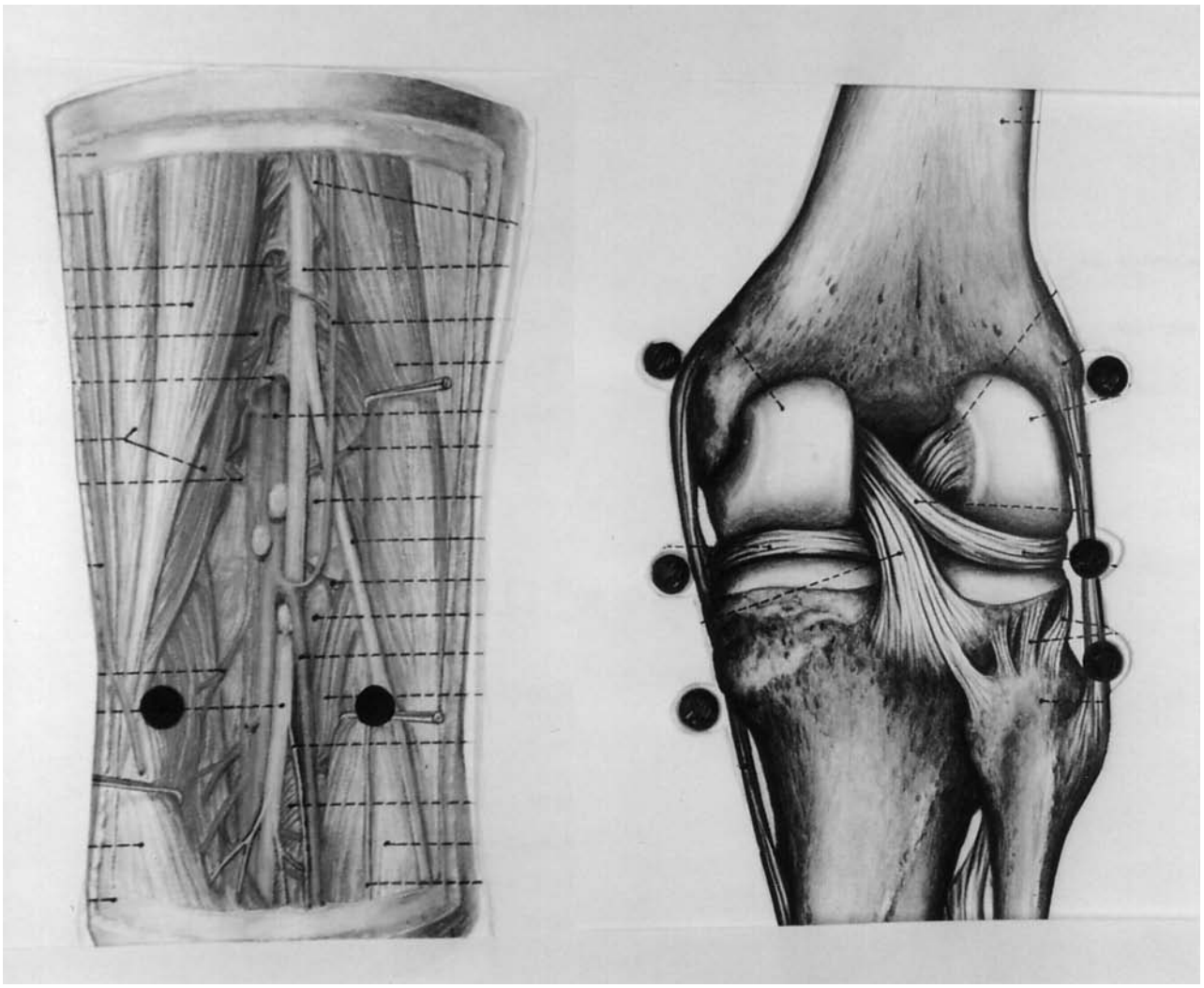

FIG. 1. Irradiated points.

Table 4. Outcome Measures

Pressure sensitivity (Ritchie index)	
0	Not sensitive
1	Pressure sensitive
2	Pressure sensitive, which patients also demonstrate through facial expressions
3	Pressure sensitive, which patients also demonstrate through facial expressions and by retraction of limb)
Pain (10 cm visual analogue scale)	
Flexion (Domján-Bálint mobimet: degree)	
Circumference (cm)	
Thermography (°C)	

placebo LLLT probes. Certain examination times were compared to the initial data; a comparison was also made between the two groups for the time of examination. For statistical analysis, *t*-tests were used for within-group differences and ANOVA for between-group comparison over time.

Joint flexion was 105.83° before treatment (BT) in the active laser group (Fig. 2a), and 122.27° immediately after the last treatment session (AT); 124.33° 2 wk AT; and 122.94° 2 mo AT. For treatment with the placebo probe (Fig. 2b), joint flexion was 107.22° BT, 115.22° AT, 116.11° 2 wk AT, and 112.11° 2 mo AT. For the active LLLT group, a significant

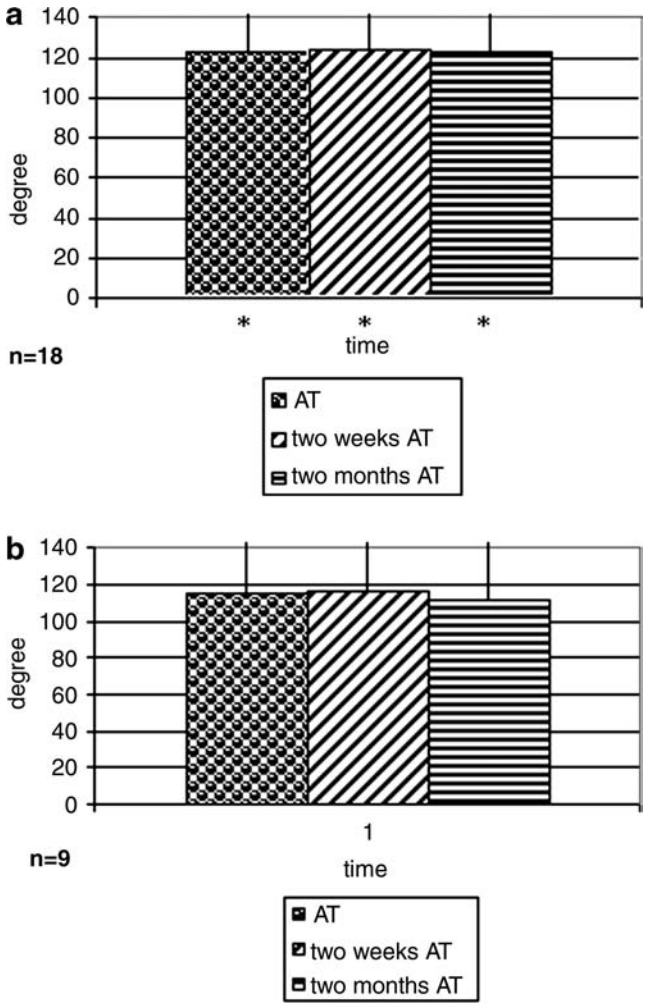

FIG. 2. (**a**) The effect of laser treatment on joint flexion. Treatment resulted in significant improvement in joint flexion at all times examined. (**b**) The effect of placebo laser treatment on joint flexion. We observed no significant change from treatment at any of the times examined. AT, after treatment.

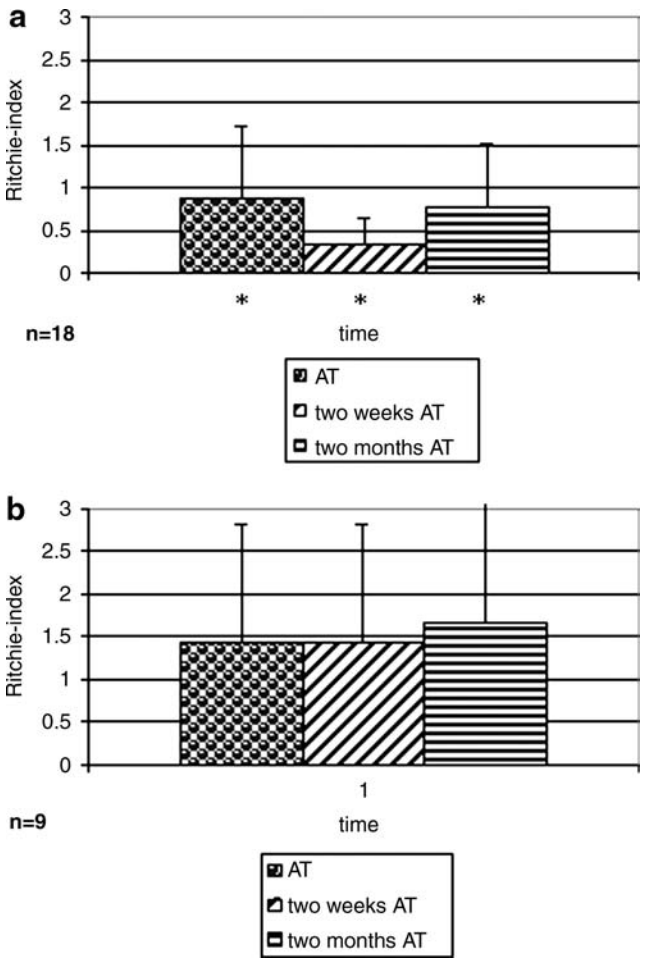

FIG. 3. (**a**) The effect of laser treatment on pressure sensitivity of the joint. Treatment resulted in significant improvement in joint flexion at all the times examined. (**b**) The effect of placebo laser treatment on pressure sensitivity of the joint. We observed no significant change from treatment at any of the times examined.

change could be detected compared to the initial value at every time examined. This trend could not be observed for the placebo group ($p < 0.05$).

Pressure sensitivity of the joint for treatment with the active probe (Fig. 3a) was 2.33 BT, 0.83 immediately AT, 0.33 2 wk AT, and 0.77 2 mo AT as measured using the Ritchie index. For treatment with the placebo probe (Fig. 3b), pressure sensitivity was 2.11 BT, 1.44 directly AT, 1.44 2 wk AT, and 1.66 2 mo AT. There was only a significant change at all the times examined for the active LLLT group compared to the initial value, whereas none was detected for the placebo LLLT group ($p < 0.05$).

Pain in the joint for treatment with the active probe (Fig. 4a) was 5.75 BT, 1.71 immediately AT, 1.05 2 wk AT, and 1.18 2 mo AT on a 10-cm scale. For treatment with the placebo LLLT probe (Fig. 4b), pain was 5.62 BT, 4.13 immediately AT, 4.07 2 wk AT, and 4.12 2 mo AT. A significant change could be detected at all times examined for the active LLLT group compared to the initial value, whereas this trend could not be observed for the placebo LLLT group ($p < 0.05$).

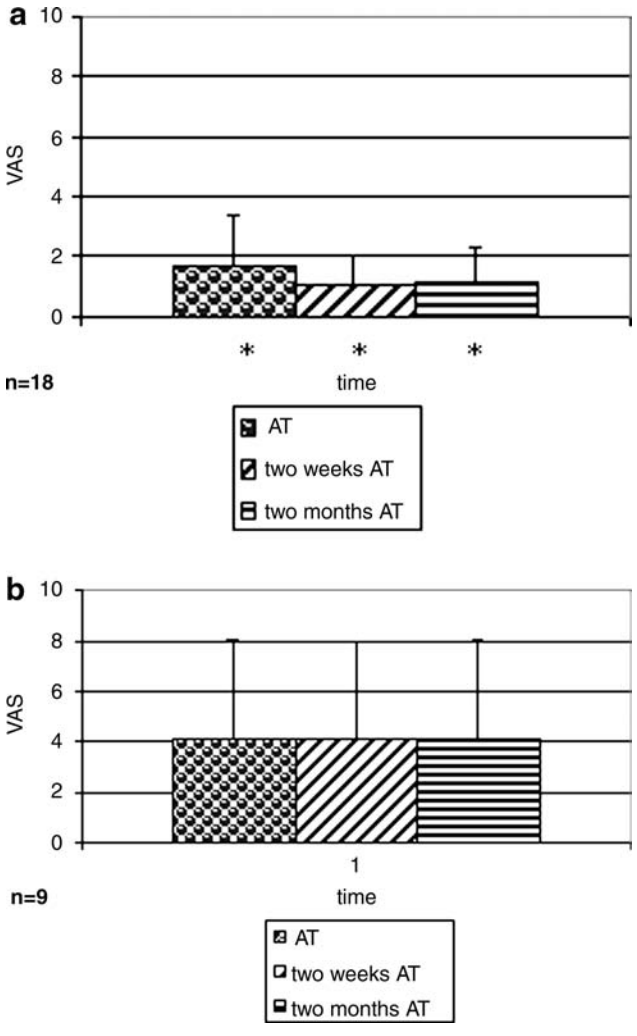

FIG. 4. (**a**) The effect of laser treatment on pain in the joint. Treatment resulted in significant improvement in joint flexion at all the times examined. (**b**) The effect of placebo laser treatment on pain in the joint. We observed no significant change from treatment at any of the times examined.

The circumference of the joint was 40.45 cm BT for treatment with the active probe, 39.61 cm immediately AT, 39.58 cm 2 wk AT, and 39.86 cm 2 mo AT. For the group treated with the placebo LLLT probe, circumference was 40.44 cm BT, 39.86 cm immediately AT, 39.87 cm 2 wk AT, and 40.05 cm 2 mo AT. With regard to the examined parameters, no significant changes appeared for the effective or placebo group under the effect of the treatment ($p \geq 0.05$).

Increased metabolism and a richer blood supply to tissues beneath the surface represented important factors in the thermographic results. Where tissues have a higher metabolism and there is a richer blood supply beneath the surface skin, more infrared rays are emitted. The opposite also holds true.

During the treatment period, weekly thermograms showed increasing temperature in previously cold areas and an extension of the warmer area (Fig. 5a and 5b). There was no increase in skin temperature in the placebo LLLT group (Fig. 6a and 6b).

At follow-up measurements 2 mo after probe (Fig. 7a and 7b) therapy, the thermographic changes remained elevated by at least a 0.5°C in patients who experienced pain relief. An increased temperature was even observed in the nontreated control side in all patients who were treated with the active LLLT.

Discussion

Our measurement results provide evidence that treatment with the active LLLT probe resulted in significant improvement for all evaluated parameters. In the placebo LLLT group, we found nonsignificant changes in joint flexion and pain. In the active LLLT group, we found significant improvement with regard to joint flexion, pain, and pressure sensitivity in the active group in comparison with the placebo group at the times examined. The positive effects obtained from active LLLT still persisted 2 mo after treatment. The lack of effect on knee circumference was expected and has not been demonstrated with other therapies. In the placebo LLLT group, three patients gave an account of an explicit reduction in their complaints, which is in line with placebo improvement in studies of other KOA therapies.

It is a weakness of the study that we did not use other validated tools for measurement of KOA pain and disability such as the WOMAC questionnaire or the Lequesne index. However, there is a high correlation between pain scores and these tools, and there is little reason to believe that incorporation of these tools would have altered our results.

Over the years more than 100 double-blind, placebo-controlled studies have been published on the effects of LLLT. These articles also showed the favorable anti-inflammatory effect of LLLT.[11–13] Based on the objective, semi-objective, and subjective measurements after laser and placebo treatments in patients with seropositive rheumatoid arthritis, Barabás came to the conclusion that laser treatment exerts a positive influence on the clinical signs and laboratory parameters of this disease.[14] Ohshiro also demonstrated a positive effect on microcirculation and verified changes by thermography in parallel with the reduction of pain.[15]

In studies where the temperature of the skin was measured, it was reported to have risen in the irradiated site.[15–18]

Mester noticed an increase in the migration index of T lymphocytes after laser irradiation. He observed that this

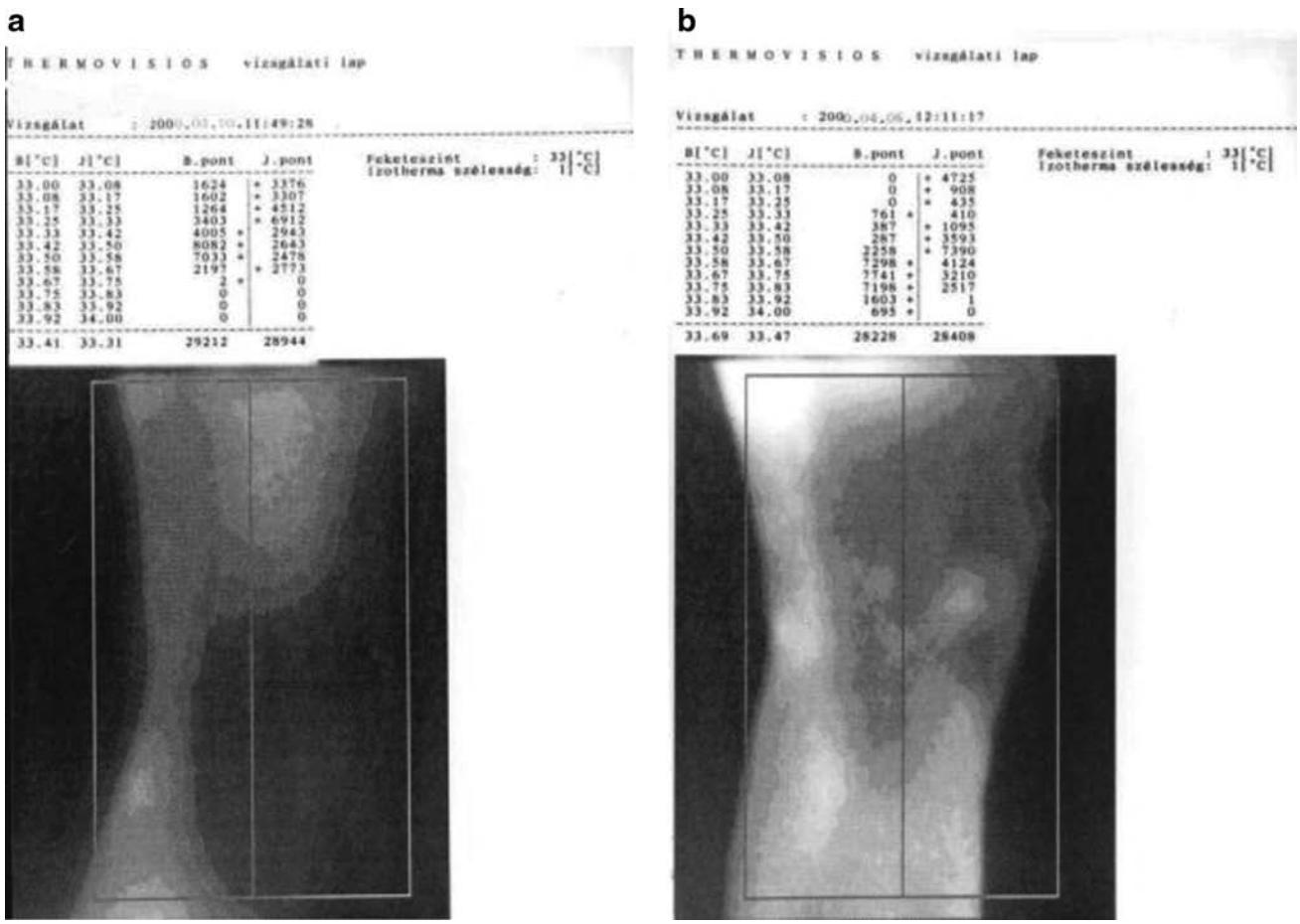

FIG. 5. (**a**) Lateral image of a right knee before eight active low-level laser therapy (LLLT) treatments. White and grey colors represent higher temperatures, greyer and black colors represent colder temperatures. (**b**) Lateral image of a right knee after eight active LLLT treatments.

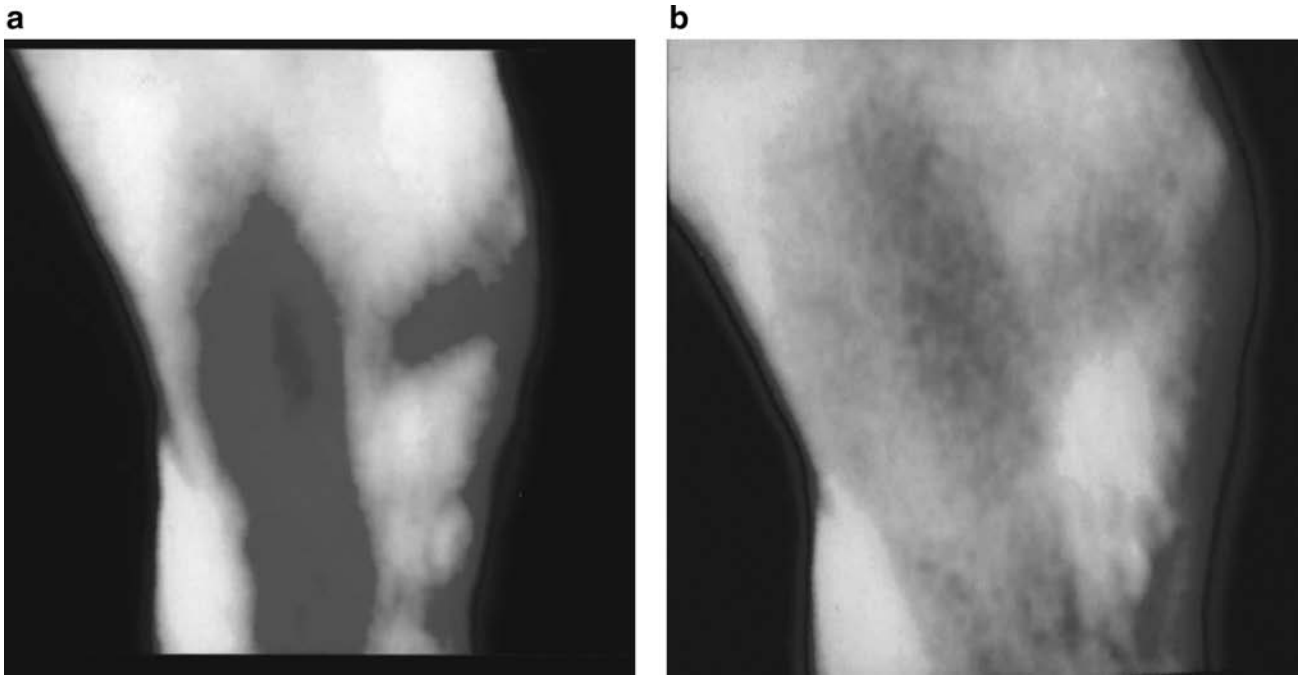

FIG. 6. (**a**) Medial thermogram of the left knee before eight placebo LLLT treatments. (**b**) Medial thermogram of the left knee after eight placebo LLLT treatments.

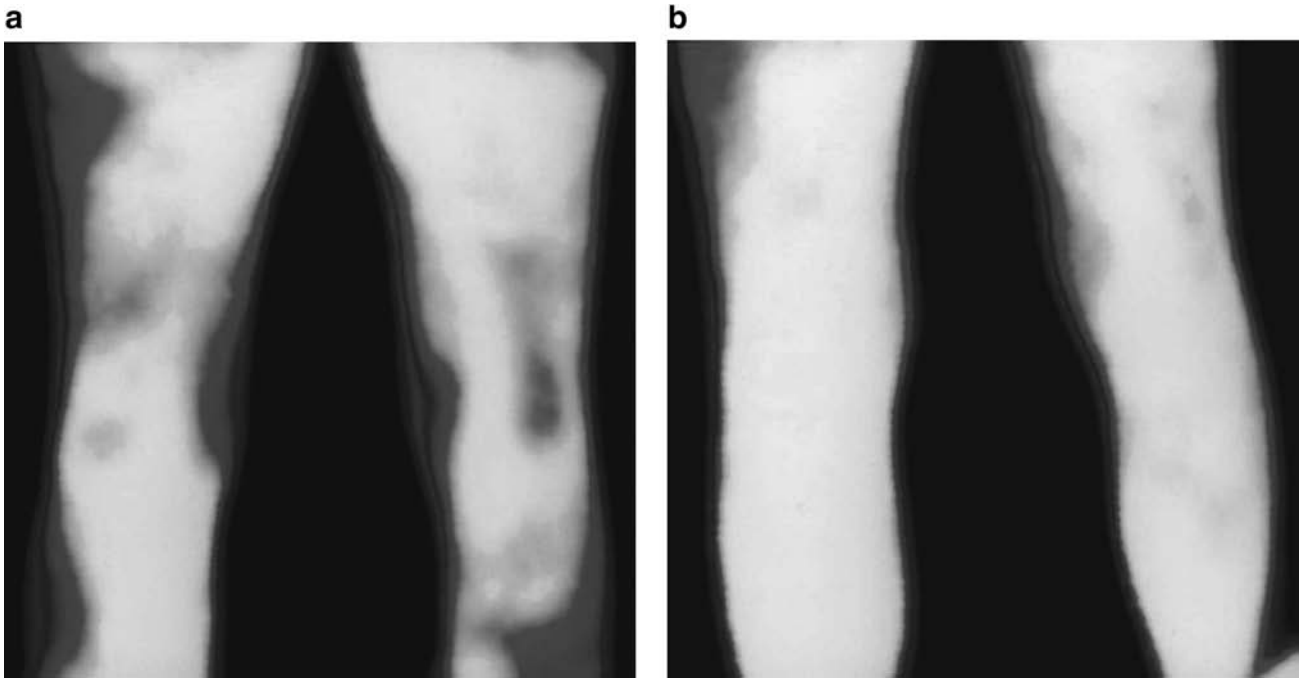

FIG. 7. (**a**) Image from posterior–anterior angle before eight treatments of the right knee joint. (**b**) Image from posterior–anterior angle after eight treatments of the right knee joint.

change can be transmitted by pouring the medium of treated cells on nontreated lymphocytes. In patients with bilateral leg ulcer that failed to respond to conservative treatment, while treating the wound of one limb he also noticed slower but unambiguous wound healing on the other side.[8] Other authors have reported effects proximal and distal from the irradiated area.[19–21]

With qualitative evaluation of the results obtained, we noticed an increase in temperature, suggesting circulatory changes at a good distance from the treated points and on the untreated side. On the other hand, we did not find this clear change in the control group.

In summary, low-level laser represents an effective treatment for short-term improvement in patients suffering from painful KOA.

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Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Béla Hegedűs, M.D.
Physio- and Balneotherapy Center
Fasor Str. 3
Orosháza-Gyopáros
Hungary

E-mail: arthrodent@freemail.hu