

830 nm light-emitting diode low level light therapy (LED-LLLT) enhances wound healing: a preliminary study

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Background and aims: The application of light-emitting diodes in a number of clinical fields is expanding rapidly since the development in the late 1990s of the NASA LED. Wound healing is one field where low level light therapy with LEDs (LED-LLLT) has attracted attention for both accelerating wound healing and controlling sequelae. The present study evaluated LED-LLLT in 5 wounds of various etiologies.

Subjects and methods: There were 5 patients with ages ranging from 7 to 54 years, comprising 2 males and 3 females. The study followed 5 wounds, namely 2 acute excoriation wounds; 1 acute/subacute dog bite with infection; 1 subacute post-filler ulcerated wound with necrotic ischemic tissue and secondary infection; and 1 subacute case of edema and infection of the lips with herpes simplex involvement after an illegal cosmetic tattoo operation. All patients were in varying degrees of pain. All wounds were treated with multiple sessions (daily, every other day or twice weekly) using an LED-LLLT system (830 nm, CW, irradiance of 100 mW/cm² and fluence of 60 J/cm²) till improvement was achieved.

Results: Full wound healing and control of infection and discomfort were achieved in all patients, with wound condition-mediated treatment periods ranging from 1 to 8 weeks. No recurrence of the herpes simplex case was seen in a 4-month follow-up.

Conclusions: 830 nm LED-LLLT successfully brought about accelerated healing in wounds of different etiologies and at different stages, and successfully controlled secondary infection. LED-LLLT was easy and pain-free to apply, and was well-tolerated by all patients. The good results warrant the design of controlled studies with a larger patient population.

Key words: LED-LLLT · Excoriation wounds · Scar prophylaxis · Secondary infection · Herpes simplex · Ischemic necrosis

Introduction

A meta-analysis from Woodruff and colleagues demonstrated that phototherapy has had a good track record in the treatment of wounds, both iatrogenic and traumatic. ¹⁾ This appeared to be particularly true for the 830 nm GaAlAs-based therapeutic laser. ^{2,3)} Up until the late 1990's, light-emitting diodes (LEDs) had not

achieved the same degree of acceptance as laser diode-based systems, because of low and unstable output powers, high angles of divergence with poor photon intensities and the lack of wavelength specificity: it was easy to source a red LED with a waveband from 600 to 680 nm or so, but almost impossible to find a 633 nm LED. Even the very much more expensive superluminescent LEDs (sLEDs) were significantly less effective in inducing neovascularization in a rat model compared with a laser diode at the same 830 nm wavelength and similar dose. ⁴⁾ However, Whelan and colleagues introduced the NASA LED in 1998 as the

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result of work on a new generation of LEDs to provide light for growing plants on the Space Station,⁵⁾ and this new, many orders of magnitude more powerful and quasimonochromatic light source became available to phototherapists and researchers. Whelan's group quickly proved that the near-infrared (near-IR) NASA LED was very effective for wound healing.⁶⁾ More recently, Trelles and colleagues showed that LED-LLLT cut the healing time after full face ablative laser resurfacing by more than half and significantly and swiftly reduced the postoperative sequelae of erythema, edema, pain and bruising.⁷⁾ The systemic effect of 830 nm LED phototherapy, also known as low level light therapy (LED-LLLT) was proved to accelerate wound healing in indirectly-irradiated dorsal wounds in an animal model, compared with unirradiated but identically-handled controls.⁸⁾ With such expanding bodies of evidence, the author planned this preliminary trial in his clinic to assess the efficacy of an 830 nm LED-LLLT system for a variety of wound types and stages.

Subjects and methods

Five patients with wounds were enrolled in the trial, with ages ranging from 7 to 54 years, 2 males and 3 females. All patients had the treatment protocol explained to them, and signed written forms of informed consent to undergo the treatment, participate in the trial and to permit the use of their clinical photography. The study followed the precepts of the World Medical Association (WMA) Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" as amended at the 59th WMA congress in Seoul, Korea, 2008.

The study followed the effect of LED-LLLT on 5 wounds, namely 2 acute excoriation wounds; 1 acute/subacute dog bite with infection; 1 subacute/chronic post-filler wound with necrotic ischemic tissue and secondary infection; and 1 subacute case of edema and secondary infection of the lips with herpes simplex involvement after an illegal tattoo. All patients were in varying degrees of pain. Details of the patients and their treatment are given in the following section.

The LED-LLLT system used was the HEALITE II® (Lutronic Corporation, Goyang, South Korea). This system consists of a treatment head with a 5-panel articulated treatment array comprising 1800 new-generation LEDs. The articulated panels can be adjusted to fit the contour of the treated area, in this case the face of the patient, to ensure even distribution of the light energy. The recommended distance between the head and the

target tissue is from 10 – 17 cm within which the near-field irradiance remains virtually identical. The head is mounted on a hinged arm with place-and-stay friction hinges, and fitted to the stand and base of the system (**Figure 1**). The LEDs deliver 830 nm \pm 3 nm in continuous wave (CW), giving 4 preselectable irradiances (power densities) at the recommended distance from the tissue as follows: 100 mW/cm² when set to intensity 4, 80 mW/cm² at intensity 3, 60 mW/cm² at intensity 2 and 40 mW/cm² at intensity 1. The manufacturer's recommended dose, based on dosimetry from the LED literature, was 60 J/cm² which was delivered in the present study over 11 minutes at intensity 4.

In addition to the 830 nm wavelength, each panel is equipped with two rows of dual wavelength LEDs, delivering both near-IR 830 nm and visible yellow light at 590 nm (<200 μ J/cm²). According to the manufacturers, this yellow light energy has a dual function and is unique to this system. During the first one minute of any irradiation session, only the yellow LEDs are activated panel by panel, sequentially delivering ultra-low levels of light energy in what the manufacturers term photosequencing technology. After the first minute, the 830 nm LEDs are activated with many orders of magnitude more power than the 590 nm energy, so the yellow LEDs then lose any clinical effect and simply become a visible indicator of the emission of the invisible near IR 830 nm energy. The photosequencing technology is further examined in the Discussion section.

At each treatment, the entire face was treated, and not just the wounded area. Patients wore small opaque occlusive safety goggles during treatment and the operator and all staff in the treatment room wore approved safety glasses for the 830 nm wavelength. All wounds were treated with multiple sessions (daily, every other day or twice weekly), following the manufacturer's recommended protocol as described above. Treatment was continued until wound healing was complete or until the patient and clinician were satisfied with the result.

Case reports and results

Case 1: A 7-year-old boy sustained 2 excoriation injuries to his face: a small one across the bridge of his nose and long and deep injury to his left face, extending from the upper eyelid down to the white lip (**Figure 2a**). He was in some pain and the larger wound was beginning to itch, leading to the possibility of further damage through self-excoriation, particularly a problem with children. His parents were extremely anxious about the potential for scar formation, particu-

larly for the larger of the wounds, and brought him to the author's clinic the day after he sustained the wounds. The patient was treated with 830 nm LED-LLLT daily for 7 days, at the parameters described in the Methods section. After the first session, the pain and itching were totally controlled and an excellent result for both wounds at one week post-baseline is seen in **Figure 2b**.

Case 2: A 7-year-old girl tripped and fell heavily against the edge of a set of stairs in her kindergarten and sustained a deep scratch with mild bruising and some pain. She was treated elsewhere for some days, but the wound did not improve and her parents were extremely anxious about potential scarring because the injury appeared recalcitrant to treatment, and brought the patient to the author's clinic (**Figure 3a**). She received 16 LED-LLLT treatment sessions over some 8 weeks at the described parameters and finally achieved the good result seen in **Figure 3b** 10 weeks post-baseline and 2 weeks after the final treatment.

Case 3: When playing with her pet dog, a 25-year-old female was bitten deeply on her nose. Plastic surgery was ruled out at another clinic because of the difficulty associated with suturing the wounds. The patient came to the author's clinic 3 days after the incident when it appeared that the wound was mildly infected (**Figure 4a**). She was in considerable pain. Fortunately the dog had had its rabies shots, so rabies infection was not a problem, but two areas of the wound were rather deep and the author considered suturing. Controlling the infection was the priority however, and the patient underwent daily LED-LLLT treatments at the usual parameters, with a course of oral antibiotics, and without suturing. After 4 sessions the inflammation had almost totally resolved (**Figure 4b**), and the pain had been totally relieved. From the advanced degree of healing of even the deep puncture wounds, the author decided that sutures were not required and continued with the LED-LLLT only. The final result after 18 days and 13 sessions was excellent (**Figure 4c**).

Case 4: A 52-year-old male underwent a filler procedure (JUVÉDERM®, Allergan Inc, Irvine, CA, USA) elsewhere, but developed ulcerative tissue necrosis due to ischemia from obstructed blood flow and clear signs of severe secondary infection were noted when he presented at the author's clinic in considerable pain, 3 days after the treatment in another clinic (**Figure 5a**). The author performed an escharotomy without any skin flap, started the patient on antibiotics and anti-inflammatory agents, and treated the wound with 830 nm LED-LLLT (same parameters as above) for 29 treatment sessions over 5 weeks with the wound healing

by secondary intention. Pain was fully controlled after the 3rd treatment session. After 2 weeks the wound was clearly closing with good granulation tissue formation and much less infection (**Figure 5b**), further improvement was achieved at 3 weeks post-baseline (**Figure 5c**) and full closure with highly acceptable cosmesis was obtained as seen in **Figure 5d**, 6 weeks from baseline and 1 week after the final treatment. Further improvement of the final result can be expected due to the remodeling process.

Case 5: A 54-year-old female had an illegal lip tattoo performed at a hair salon unauthorized to perform tattoos. Within a week she suffered from an attack of herpes simplex on both lips, a bacterial infection with swelling of the lips and a fever. She went elsewhere for treatment, but after three days her condition became worse, and she came to the author's clinic (**Figure 6a**). She had a fever, herpes simplex lesions, her lips were swollen and infected and she complained of pain around the mouth when eating or drinking with numbness and mild paralysis of the left-hand side of her mouth. She was treated almost daily with 830 nm LED-LLLT for three weeks. The pain improved after the first session and was alleviated completely after the third session. Improvement in the infection was seen at one week after starting treatment (**Figure 6b**), almost complete improvement was noted at 2 weeks (**Figure 6c**), and total clearance of all problems including the numbness and paralysis was achieved at 3 weeks after starting treatment (**Figure 6d**). There has been no recurrence of the herpes simplex or other symptoms during a 4-month follow-up. The patient also pointed out a marked improvement in her overall skin condition, especially the skin tone and her pore size.

Discussion

The author would first of all like to acknowledge that the small patient population and the lack of any control subjects are limitations to the study, but this was a preliminary trial to assess the potential efficacy of the LED-LLLT system used in accelerating wound healing. Despite the small population, the range of wound types and stages was interesting, and all responded well to 830 nm LED-LLLT.

The photosequencing technology associated with the HEALITE II system comprising the addition of the 590 nm to the 830 nm main treatment beam is very interesting, and deserves some discussion. According to the manufacturers, the targets for the very low-energy yellow light (<200 $\mu\text{J}/\text{cm}^2$) are the epidermal keratinocytes and Merkel cells in the stratum basale, both



Fig. 1: The HEALITE II® LED phototherapy system (Lutronic Corp., Goyang, South Korea). The articulated planar arrays can be adjusted to fit the contour of any part of the body, and the ‘place and stay’ hinged arm allows adjustment for height and reach.



Fig. 2: A 7-year-old boy with 2 excoriation injuries to the left face (a) at baseline and (b) after 1 week of daily 830 nm LED treatments



Fig. 3: A 7-year-old girl who injured her face at kindergarten with (a) a scratch and bruising at baseline, and (b) 10 weeks from baseline and 2 weeks after the final treatment session (16 sessions over 8 weeks)



Fig. 4: A 25-year-old female with an infected dog bite injury on her nose. (a) The findings at baseline. Infection-related erythema is clearly visible around the puncture wounds, some quite deep with a little laceration. (b) 6 days later after 5 LED-LLLT sessions, the infection has resolved and the dog bite marks are repairing well, even the deeper ones. (c): The final result at 18 days (13 sessions) from baseline.

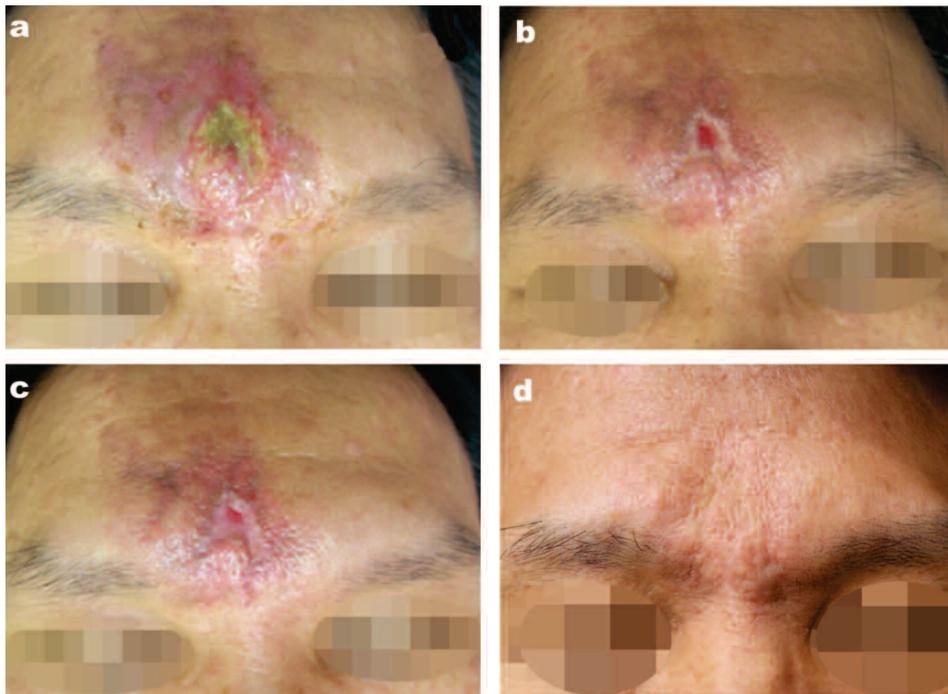


Fig. 5: Post-filler ulceration. (a) A 52-year-old male underwent a filler procedure elsewhere, but developed ischemic tissue necrosis with severe secondary infection at baseline. (b) After 2 weeks the wound is clearly closing with good granulation tissue formation and much less infection. (c): The further improvement at 3 weeks post-baseline with almost complete closure of the ulcerous wound. (d): Full closure with very acceptable cosmesis has been obtained 6 weeks from baseline and 1 week after the final treatment (29 sessions).



Fig. 6: An adverse reaction was seen in a 54-year-old female following an illegal cosmetic lip tattoo. (a) at baseline, swelling of the lips with secondary bacterial infection and herpes zoster can be seen. (b) Findings 1 week after start of treatment (4 sessions). (c) 2 weeks post-baseline, improvement is noted. (d) The final excellent results 3 weeks from baseline after 12 LED-LLLT treatment sessions. Improvement in the overall skin condition should also be noted.

of which are rich in mitochondria that are known to respond very well to yellow light at around 590 nm,⁹⁾ thereby enhancing ATP production, increasing calcium ion signaling and inducing cytokine synthesis from the keratinocytes, well known for their ability to synthesize cytokines very swiftly with visible light.¹⁰⁾ In addition to stimulating epidermal cellular metabolism and cell-cell signaling, these cytokines can then drop down into the dermis to act as signaling agents for dermal matrix cells, preconditioning the cells before the 830 nm irradiation occurs. In addition, epidermal cells have been proven to respond very well to ultra-low incident levels of visible light energy with enhanced mitochondrial activity:^{11,12)} in the system used in the present study, the manufacturers have termed this “micro-LLLT”, and this ensures strong activation of epidermal cellular metabolism, ensuring that the epidermis is not neglected during any phototherapeutic intervention. The Merkel cells are components of the neuroendocrine system, and are also intriguing as a target for 830 nm energy, playing roles in both cell to cell signaling and neuropeptide production,¹³⁾ and enhancing the stimulatory effect of the activated keratinocytes in the epidermis.

As noted in the Introduction section, a large body of evidence already exists about the efficacy of 830 nm in enhancing wound healing. Beyond wound healing, in a recent review in this journal on 830 nm LED-LLLT, Kim and Calderhead made a convincing argument for the solid efficacy of this wavelength.¹⁴⁾ In addition to discussing wound healing the authors also showed good examples of 830 nm LED-LLLT for infection control, dermatitis and suppurative diseases. Certainly in the present study, inflammation was controlled very effectively in the 3 affected cases (cases 3, 4 and 5), in combination with oral antibiotics. This raises the question of whether it was the antibiotics or the LED-LLLT which controlled the inflammation, but from the author’s experience, inflammation control occurred much sooner with the 830 nm LED therapy than has been the case with many similar infective wounds treated only with antibiotics in the past. A controlled trial would of course be required to confirm this, but the author is convinced that the combination had a

clear synergistic effect.

The larger scar in Case 1 took only a week to heal. It was a deep injury with erythema and a little edema: it was also painful and had started to itch. The pain and the itching were attenuated after the very first LED session, which meant that the patient was not tempted to keep scratching the healing wound. Furthermore, deep and comparatively wide partial thickness wounds such as this one have been associated with hypertrophic scar formation which even in mild scars can lead to pruritis and the possibility of further damage through self-excoriation,¹⁵⁾ especially in children.

In Case 2, although the wound appeared macroscopically to be much less serious than in Case 1, it proved resistant to conventional treatment in the first clinic visited by the patient and her parents, and took a surprisingly long time to heal even with 830 nm LED-LLLT (8 weeks, 2 sessions/week). Based on the author’s experience with the other patients in this study who received treatment more frequently, perhaps 3 treatments a week or more would have given a faster result, but the patient was only able to attend twice weekly and this is something a future controlled trial can address.

Conclusions:

In the 5 cases treated with 830 nm LED-LLLT in the present study, effective wound healing was achieved in all 5 with no visible scar formation in 4 out of the 5. In the most serious case (Case 4, ischemic necrosis following a filler injection), the cosmesis was very acceptable, and would very probably have been much more serious without the application of LED-LLLT. All patients were extremely satisfied, and discomfort was swiftly ameliorated in the first 1 or 2 sessions, which helped patient (and parent) compliance. 830 nm LED-LLLT with the system used in the present study was very easy to apply, was pain- and side-effect free, and was appreciated by the patients. The results of this small preliminary assessment certainly warrant future controlled and blinded random clinical trials with statistically meaningful populations.

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