

Low Level Light Therapy with Light-Emitting Diodes for the Aging Face

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KEYWORDS

• Low level light therapy • LED • Light-emitting diodes • Aging face

KEY POINTS

- Light-emitting diodes–low level laser therapy (LED-LLLT) does not deliver coherent energy as do lasers and laser diodes, but it does deliver highly narrow-band quasimonochromatic light with more than 95% of the photons at the rated wavelength allowing for precise chromophore targeting.
- LED-LLLT need not be delivered by a clinician, but can be given by a trained nurse or therapist under clinician supervision thereby freeing up the clinician for other duties.
- LED-LLLT is easy to deliver, is safe, effective, pain and side-effect free, and is well tolerated by patients of all ages from infants to centenarians.

LOW LEVEL LIGHT THERAPY

The acronym *LLLT* originally stood for *low level laser therapy*, which was first coined by Ohshiro and Calderhead in 1988.¹ It is a term that has come in for a fair amount of misinterpretation and abuse, with investigators often talking about “low level lasers,” for example. The original concept of LLLT was focused on the *therapeutic effect* induced in the target tissue by the incident photons, irrespective of the system generating these photons.

Photons and Photon Intensity

Photons are discrete particles of pure light energy without mass. The first law of photobiology states that without absorption, there can be no reaction, so the incident photon must be absorbed by the target cells for any reaction to occur. When a photon is absorbed by a cell, it passes on its energy to the cell. The degree of the photon density determines what sort of

energy transfer occurs. In parallel with the Ohshiro-Calderhead Arndt-Schultz curve, which illustrates the level of biological activity depending on the strength of the stimulus (**Fig. 1**),^{2,3} low photon intensities excite the cell, moderate ones sustain the cell, strong intensities will damage the cell through the generation of a photo-thermal reaction, retarding cellular activities, and very strong ones will kill the cell.

Photoactivation Versus Photodestruction

If we think of a cell, as shown schematically in **Fig. 2**, we can assign to each cell 2 thresholds based on the aforementioned concept: the damage threshold and the survival threshold. As the level of stimulus increases, the level of the reaction in the cell increases. If the level of reaction is below the damage threshold of the cell (see **Fig. 2A**), the thermal reaction, if any, is negligible and the photo-biomodulation or photoactivation of the cell and its activity occurs. This activity takes 3 forms: if photoactivated cells are damaged or

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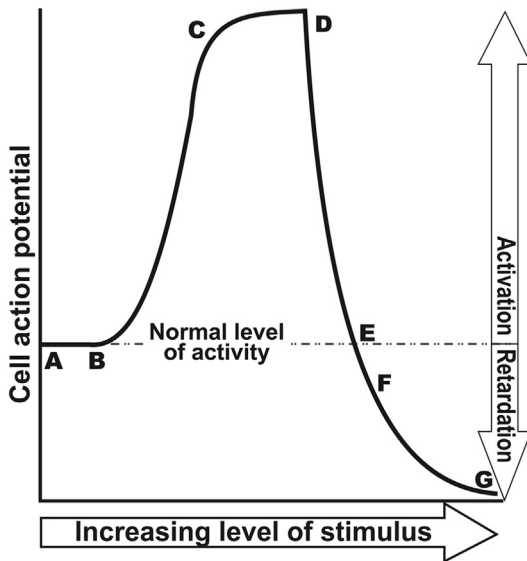


Fig. 1. Ohshiro and Calderhead's LLLT-adapted version of the Arndt-Schultz curve. From point A to B there is very little change in the cell action spectrum, but there is a rapid increase from point B to C concomitant with the increasing stimulus level. The activity plateaus out at C to D and after D drops sharply back down to normal levels at point E. As the strength of the stimulus increases beyond point E to point F, activity drops below the normal level with mild retardation and cell damage, which further drops until cell death at point G. The highest increase in cell activity, and most effective LLLT treatment, would, therefore, be induced by the parameters that could achieve section C to D on the curve. HLLT, high-level light therapy.

compromised in some way, they will be repaired; if they have a function to do, for example, fibroblast synthesis of collagen and elastin, they will perform that function better and faster; if there are not enough cells, then more will be recruited or the existing cells will proliferate.^{4,5} These actions can happen singly or in combination. The above concepts explain the level of low level laser therapy: it refers to the *level of the reaction* induced in the cell by the incident light energy. This level of reaction can be classed as phototherapy, whereby some form of clinical effect is achieved through photo-biomodulation of the cell actions but without heat or damage.

What Systems Can Deliver Low Level Light Therapy?

In the late 1980s, the only clinically appropriate sources available for true phototherapy were low-powered laser diodes or defocused surgical lasers. Light-emitting diodes (LEDs) were

available; but they were totally inappropriate for clinical indications, having low and unstable output powers, large angles of divergence, and wide wavebands. It may come as somewhat of a surprise to see that surgical lasers could, and still can, be used for phototherapy. As **Table 1** illustrates, a high-level laser can be used for LLLT and a low-level laser can be used to deliver high-level light therapy with powerful thermal damage. *Terminology, therefore, matters* because it is the *level of the tissue reaction* that is important and not the level of the laser or light source delivering the beam.

THE LIGHT-EMITTING DIODE

In the past decade and a half, LEDs have become accepted sources for therapeutic systems. The year 1988 was the pivotal year for LEDs, when Professor Harry Whelan and his team at the Space Medicine Laboratory of the National Aeronautic and Space Administration (NASA) developed the first of a new generation of LEDs, the so-called NASA LED.⁶ The same group quickly went on to demonstrate the clinical efficacy of near-infrared LEDs for wound healing,⁷ and the new-generation LED was available to researchers and clinicians as a valid therapeutic light source. In fact, at the time of writing, LEDs are now supplanting laser diode-based systems for many applications; it was suggested some 10 years ago by Kendrick C Smith, Emeritus Professor at Stanford University and a leading photobiologist, that *low level laser therapy* should become *low level light therapy* but share the same acronym of LLLT.⁸ That is now the case.

What Is a Light-Emitting Diode?

At the heart of LEDs are tiny semiconductor chips. When a DC current is applied to an LED, light (photons) is emitted in an uninterrupted elliptical cone with divergence usually in the range of 60° to 110° across the larger diameter of the beam. **Fig. 3** illustrates the construction of the older and current form of LEDs. The light from LEDs is completely noncoherent, but in high-grade LEDs a very high percentage of the photons are at the rated wavelength. The higher the grade of the LED, the narrower the bandwidth of the emitted photons and is defined as *quasimonochromaticity*, allowing LEDs to emit the rated wavelength plus or minus a very few nanometers.

Despite being noncoherent, LEDs emit photons with some sort of directionality thanks to the parabolic reflector mentioned earlier; but because the photons are totally out of phase, it is impossible to collimate an LED beam completely and,

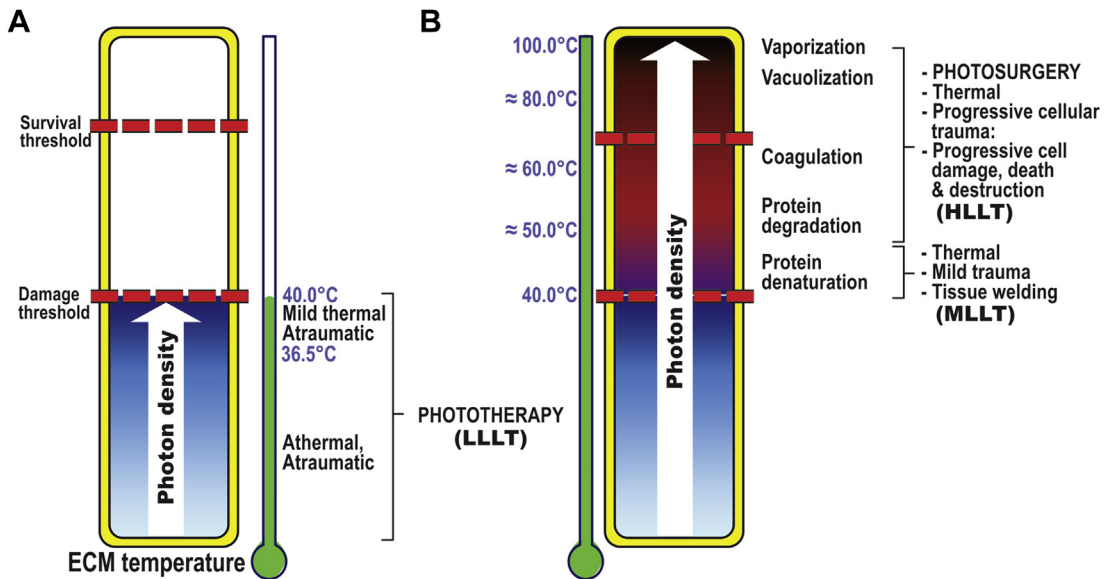


Fig. 2. A cell with its damage and survival thresholds indicated, together with the classification of the level of cellular reaction (Ohshiro's classification⁵) and changes in extracellular matrix (ECM) temperature. In (A), as the level of the absorbed incident photon energy increases, cell activity is enhanced and is characterized as athermal and atraumatic LLLT. A slight increase in the tissue temperature would then be seen, adding mild thermal activation to the photoactivation process, although by this stage the peak in the level of cellular activity would have been reached (C–D in Fig. 1) and activity would now be dropping off (D–E in Fig. 1). (B) Reactions associated with mid level laser treatment (MLLT) (reversible damage) and high-level light therapy (irreversible damage and cell death).

therefore, also impossible to focus LEDs. These factors of beam divergence and lack of photon phase inherently make LEDs intrinsically much safer light sources than lasers or laser diodes. Nevertheless, eye protection when using therapeutic LED systems is always a sound idea.

- They can be mounted in large area planar arrays, thus allowing hands-free operation in a clinician non-intensive manner.
- They are comparatively inexpensive, with one single laser diode from a laser pointer costing the equivalent of upwards of 200 LEDs.

WHY SHOULD LIGHT-EMITTING DIODES BE USED IN PHOTOTHERAPY SYSTEMS?

LEDs have 5 main inherent advantages.

- They need only a little electricity in to produce a great deal of light.
- They are solid state, requiring neither filaments nor flashlamps for activation.
- They are quasimonochromatic (narrow bandwidth of a few nanometers), allowing precise target specificity.

Additionally, LED phototherapy has its own good points: LED-LLLT can be applied by a trained nurse or therapist, freeing up the clinician for other patients; it is pain free and side effect free; and LED-LLLT is well tolerated by patients of all ages, from infants to centenarians.

IMPORTANCE OF PARAMETERS

LED-LLLT is based on very low incident photon intensities. Misunderstandings regarding parameters, such as wavelength, power density, and

Table 1
The level of tissue reaction does not depend on the output power of the laser

Laser Type	Output Power (Units as Shown)	Spot Size at Tissue (Units as Shown)	Power Density	Level of Tissue Reaction
CO ₂	60 W	15 cm	0.8 W/cm ²	Therapeutic (LLLT)
Diode	60 mW	50 μm	3000 W/cm ²	Destructive (HLLT)

Abbreviations: CO₂, carbon dioxide; HLLT, high-level light therapy.

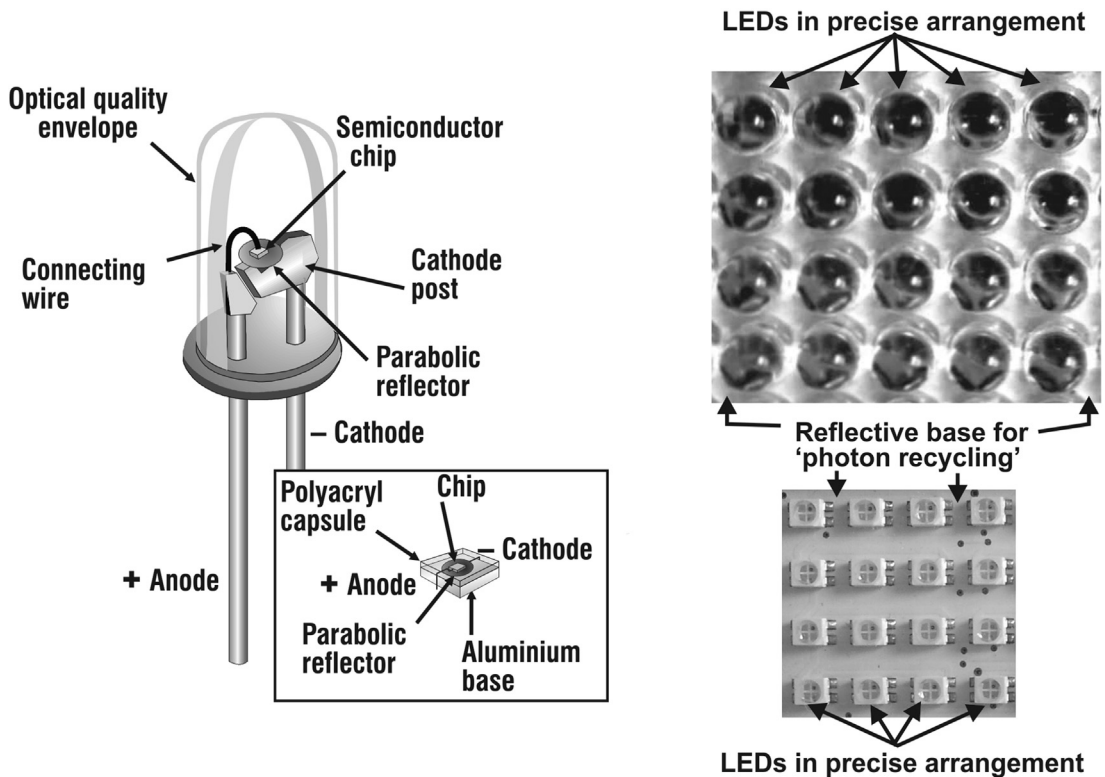


Fig. 3. Dome-type (upper left and right) and on board chip (OBC)-type (left inset, lower right) LEDs. Both types share the same basic construction, with a reflector helping to channel light in a forward direction. The newer OBC type of LED is much neater than the older dome-type, as can be seen in the photographs on the right.

dose (energy density), can lead to positive results in one study and negative results in another. There is one parameter above all others that accounts not only for what the target will be, otherwise known as the chromophore, but also how deep the light energy will intrinsically penetrate into the tissue. One might be excused for thinking it is the output power of a system, but they would be mistaken: it is the wavelength.

IMPORTANCE OF WAVELENGTH

All tissue targets have an optimum wavelength at which they absorb light, as illustrated in **Fig. 4** showing the absorption curves of the biological targets, namely, the pigments (melanin, oxyhemoglobin, and deoxyhemoglobin) and tissue water on the x-axis. The y-axis denotes the coefficient of absorption expressed as $\text{cm}^{-1}\text{M}^{-1}$ in logarithmic units, for example, a log value of 6 is 5 greater than a log value of 1 but represents a difference of 100,000-fold, that is, 5 orders of magnitude.

The preeminent Russian photobiologist Tiina Karu⁹ has identified the photo-biomodulation band at around 620 nm visible red to around

1000 nm in the near infrared; based on the data seen in **Fig. 4**, the reader will understand why: minimal absorption in competing chromophores will allow deeper penetration with absorption in non-pigmented chromophores, such as cytochrome c oxidase (CCO) for visible light and elements on the cell membrane for infrared light.¹⁰

Absorption Versus Penetration

The higher the absorption of a specific wavelength, the poorer the penetration of that wavelength into the tissue beyond its absorbing chromophore: on the other hand, the poorer the absorption of light in a chromophore, the better the penetration of that wavelength into tissue. Consider **Fig. 5**, based on photo-spectrographic data of the penetration of light at wavelengths from 500 nm in the blue-green band to 1010 nm in the near infrared¹¹ shown on the x-axis and the logarithmic optical density of the target tissue units on the y-axis. Penetration is shown graphically on the z-axis. It can be clearly seen that green and yellow light has very poor penetration into living tissue, because of the competing

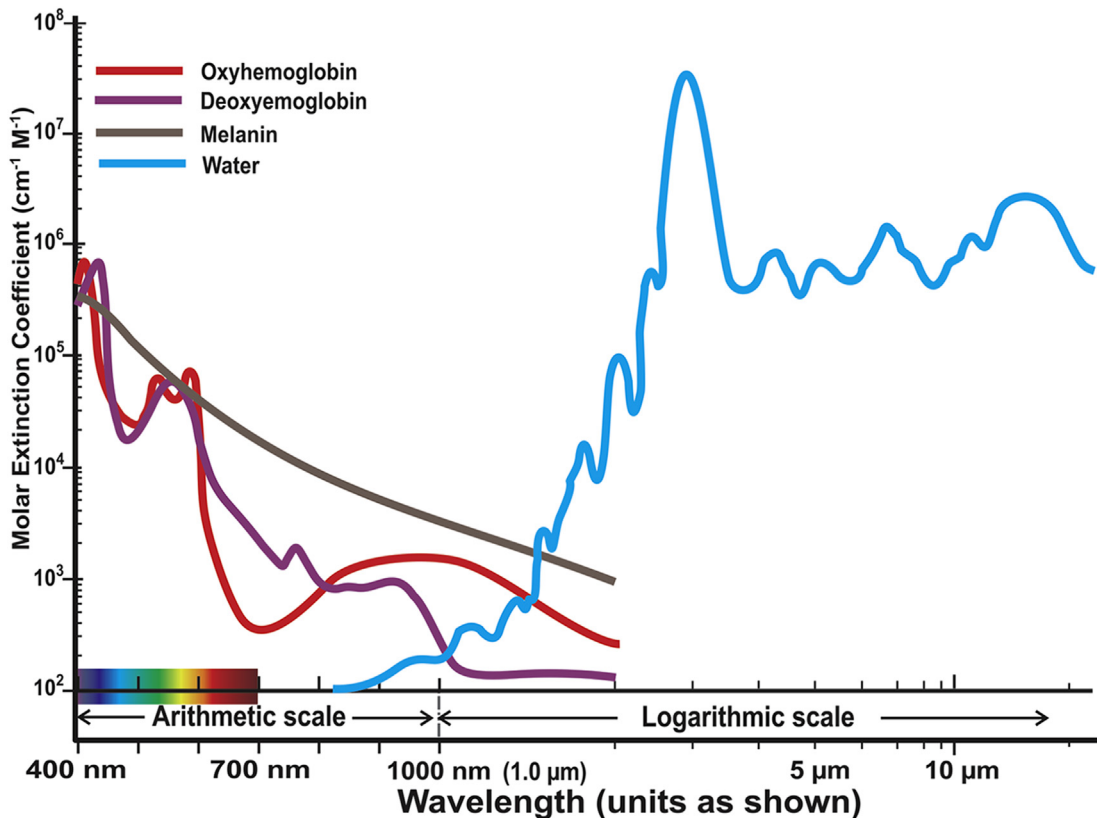


Fig. 4. Absorption spectra for the biological chromophores of blood (oxyhemoglobin and deoxyhemoglobin) melanin and water shown from the visible through the near- to the midinfrared wavebands.

chromophores of blood and melanin. Therefore, if one wants to reach targets deeper in the dermis, these wavelengths are not at all suitable. A shift of only 43 nm from the 590 nm yellow to the 633 nm red wavelength induces a gain in

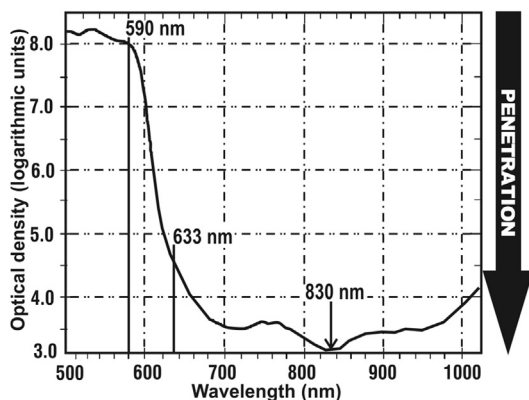


Fig. 5. Penetration of broad waveband light through a human hand in vivo. Note that the optical density units are logarithmic. (Adapted from Smith KC. Laser (and LED) therapy is phototherapy. Photomed Laser Surg 2005;23:78–80.)

penetration of well more than 3 orders of magnitude; at 830 nm, the gain is near 5 orders of magnitude. This wavelength is well within Karu's photo-biomodulation band.

Penetration plays a major role in LED-LLLT, when considering target depth. There are some cellular targets in the epidermis, such as the basal layer mother keratinocytes, Merkel cells, and the dendritic cells, namely, melanocytes and Langerhans cells. These cells are extremely important as far as keeping the epidermis healthy and happy is concerned. After all, when patients look in the mirror after a rejuvenation regimen, they do not care about beautiful blood vessels and artfully entwined collagen fibers; they see their epidermis, and woe to the practitioner who has forgotten this. For these cells, there is an arguable role for the green and particularly the yellow LED systems. On the other hand, the major cells of interest for wound healing and rejuvenation are located in the dermal extracellular matrix, namely, the fibroblasts, mast cells, neutrophils, and macrophages. For them, neither the green nor the yellow wavelengths will penetrate deeply enough. The 830 nm is the wavelength of choice to

photoactivate all of these cells in vivo and to increase their action potential in an athermal and atraumatic manner.¹²

LIGHT-EMITTING DIODE–LOW LEVEL LIGHT THERAPY MECHANISM OF ACTION

The exact complex mechanisms have been more or less elucidated but are beyond the scope of this article, but suffice it to say that visible light targets mitochondrial CCO, whereas near-infrared energy targets the cell membrane.

CCO, or complex IV, is the end-terminal enzyme in the respiratory chain in the mitochondrion, the energy factory of the cell. To put it simply, via a complex series of interactions, CCO is responsible for synthesizing adenosine triphosphate (ATP), the fuel of the cell and indeed the entire organism. Visible light is absorbed in CCO and induces a photochemical cascade, the end result of which is ATP and some powerful cell-cell signaling compounds, namely, calcium ions (Ca^{++}) and protons (H^+). The transport mechanisms in the cell membrane, such as the sodium-potassium pump (Na^+/K^+ -ATPase), are prodded into action; intracellular and extracellular exchange occurs between the cell and the extracellular matrix.

In the case of near-infrared light, cell membranes are more or less opaque at this waveband and so the incoming energy is fully absorbed in the cellular membrane where, via a photo-physical response involving rotational and vibrational exchanges, the absorbed energy alters the electron status of the molecules making up the membrane. The cellular transport mechanisms are instantly activated, and the mitochondria are prodded into action to produce more ATP to fuel this sudden cellular activity. This process induces the same cascade as with visible light, but it is an indirect photo-physical response rather than a direct photochemical one. However, the end result is the same, namely, an athermally and atraumatically photoactivated cell. These different processes are summed up in **Fig. 6**.¹⁰

POWER DENSITY AND ENERGY DENSITY

Power Density

Lasers, laser diodes, and LEDs deliver a rated output power, lasers usually in watts and laser diodes and LEDs in milliwatts. The output power of a system is by itself meaningless until the laser energy strikes a target and absorption occurs. The size or area of the incident beam of light gives the unit area of the tissue being targeted, and when we take the incident power of the beam (in watts) and divide it by the area of the target (in

square centimeters), we arrive at the power density, also referred to as the irradiance usually expressed in milliwatts per square centimeter for LLLT systems. **Table 1** shows the importance of power density compared with output power.

Energy Density

When we take the time for which the beam is incident on tissue, often called the exposure time, expressed in seconds, and multiply this by the power density in watts per square centimeter, we end up with the energy density in joules per square centimeter, which is also referred to as the dose.

Table 2 shows that the dose is, however, less important than the power density. A pulse width of 5 ns delivers an energy density of 0.5 J/cm^2 , but the tissue reaction would be explosive with a very high power density. An LED system with a very low power density can also give an energy density of around 0.5 J/cm^2 ; this will definitely induce an athermal phototherapeutic reaction. In the third example, a system delivering 1 W/cm^2 , still well within the LLLT power density range, will produce an apparently high dose of 360 J/cm^2 ; but the reaction will still be athermal and atraumatic, as demonstrated by Calderhead and Inomata.¹³

In short, the magnitude of the dose may not be related to the ultimate tissue effect. It is the power density that determines above everything else the biological effect. If the power density is likened to the medicine, then the energy density is the dose. As any pharmacist will tell you, if the medicine is not right, playing around with the dose is not going to make much of a difference.

CLINICAL APPLICATIONS OF LIGHT-EMITTING DIODE–LOW LEVEL LIGHT THERAPY FOR THE PLASTIC SURGEON

Aging is a complex phenomenon combining biological or intrinsic aging with the influence of extrinsic environmental factors, the most important of which is probably the effect of solar UV. The end result is degradation of the extracellular matrix with poorly arranged collagen fibers, elastic fibers that have lost their elasticity, and a ground substance that is less lubricating than it was. The epidermis tends to thin out, with less active cellularity, a disorganized stratum corneum, and flattened rete ridges.

Although the dermis could be said to support the skin, it is the epidermis that patients see in the mirror, so unless the epidermis can somehow be refreshed, patients will end up looking at the same old epidermis and will not be happy no matter how much improvement can be seen

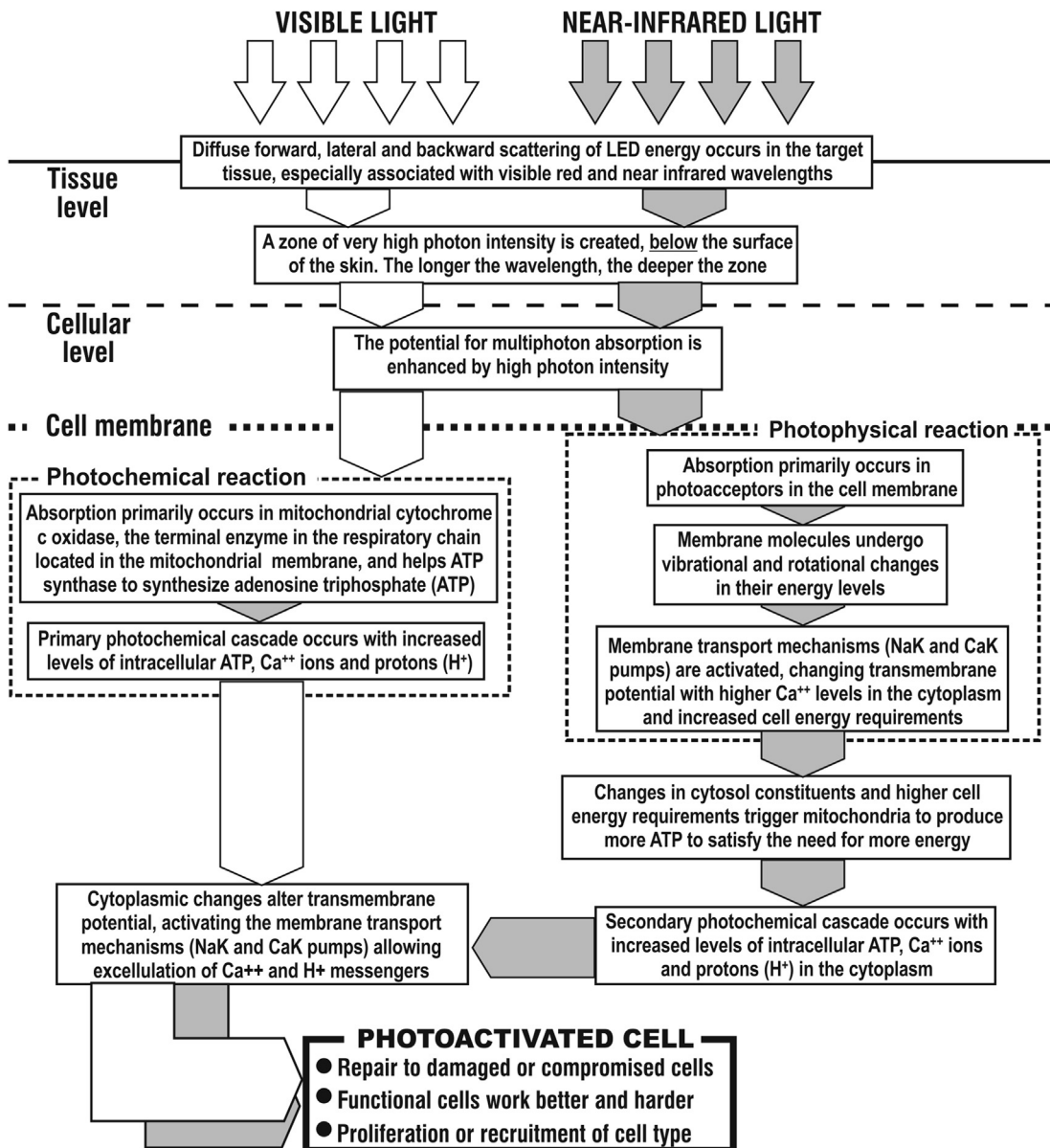


Fig. 6. Comparison of the basic LLLT reactions: the photochemical reaction induced by visible light and the photophysical reaction produced by near infrared light. (From Kim WS, Calderhead RG. Is light-emitting diode low level light therapy (LED-LLLT) really effective? *Laser Ther* 2011;20:205–15; and Courtesy of JMLL Ltd, Tokyo, Japan; with permission.)

Table 2
Importance of power density illustrated over that of energy density

Power Density	Exposure Time	Energy Density	Biological Effect
100,000 W/cm ²	5 ns	0.5 J/cm ²	Photodestructive
60 mW/cm ²	8.5 s	0.5 J/cm ²	Phototherapeutic
1 W/cm ²	1 h	360.0 J/cm ²	Phototherapeutic

histologically to the dermal structures and overall condition. LED energy has to pass through the epidermis on its way down to the dermis, and certain wavelengths are known to beneficially affect epidermal basal layer cells, namely, 590 nm yellow, 633 nm red, and 830 nm near-infrared. As previously discussed, the epidermis is the main target for 590 nm, whereas both 633 nm and 830 nm will not only target epidermal cells but will also affect dermal components. All of these wavelengths will, therefore, athermally and atraumatically photoactivate the epidermal basal layer cells, namely, mother keratinocytes and melanocytes, but will also have some interesting effects on Merkel cells and other dendritic cells, such as Langerhans cells. Increased extracellular levels of ATP are noted, as well as powerful signaling components, including Ca^{++} and H^+ . However, if the targets are cells in the extracellular matrix to achieve dermal restructuring, then because of its poor penetration the 590 nm is practically of no use (see Fig. 5); but both 633 nm and 830 nm wavelengths will penetrate deeply enough. Of these two, the literature has consistently suggested that 830 nm targets a larger number of the necessary cell types and has a better effect on the overall skin-rejuvenation process.^{10,14}

Light-Emitting Diode–Low Level Light Therapy as a Stand-alone Modality for the Aging Face

The ideal combination for stand-alone LED-LLLT in skin rejuvenation would, therefore, be 590 nm applied first to target specifically the epidermis, followed by 830 nm, which will not only boost epidermal cellular activity but will also photoactivate mast cells, macrophages, neutrophils (if present), and of course fibroblasts. It has to be noted that the effect is not instantly visible; but on the other hand, increasing efficacy is seen over a 12-week follow-up. This requires good patient education.

Fig. 7 shows patient satisfaction with stand-alone LED-LLLT in 3 split-face groups, comparing LED-LLLT with 830 nm and 633 nm on their own and the sequential combination of these two wavelengths from an excellent facial rejuvenation study by Lee and colleagues.¹⁴ Only the excellent results are shown. In all 3 groups, there is some level of satisfaction at the end of the 4-week treatment regimen; but as the 12-week follow-up progresses, levels of satisfaction increase steadily for all 3 groups without any other treatment allowed or given, except washing the face in hypoallergenic soap. Note also that the 830-nm group

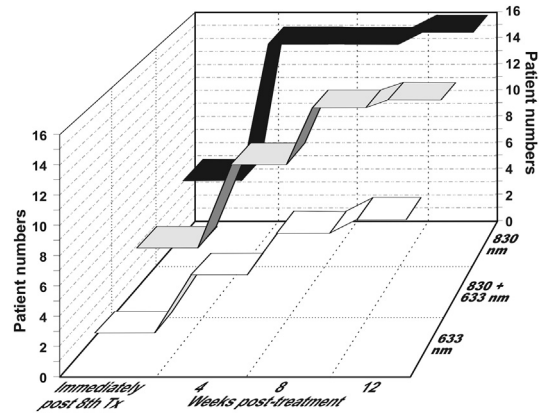


Fig. 7. Subjective patient satisfaction scores, excellent only, shown at the end of the 4-week treatment period, then at 4, 8, and 12 weeks after the eighth and final treatment, compared among the 633-nm-only, 830- and 633-nm combination, and 830-nm-only groups. Tx, treatment. (Data from Lee SY, Park KH, Choi JW, et al. A prospective, randomized, placebo-controlled, double-blinded, and split-face clinical study on LED phototherapy for skin rejuvenation: clinical, profilometric, histologic, ultrastructural, and biochemical evaluations and comparison of three different treatment settings. *J Photochem Photobiol B* 2007;88:51–67.)

achieved the greatest level of satisfaction the quickest.

This gradual improvement is the result of the remodeling process; even atraumatic and athermal LED-LLLT can, therefore, induce neocollagenesis and neoelastinogenesis and furthermore enhance remodeling. Fig. 8 shows significant collagenesis and elastinogenesis from patients in the same study as discussed earlier 2 weeks after the final treatment session, comparing the treated side of the face with the untreated side of the face. The 83-nm group also showed significantly improved skin elasticity than the others as measured with a cutometer. This improved skin elasticity was not only a nice new epidermis, as distinct to a same old epidermis, but also a substantially remodeled dermal matrix for which the aging clock had been turned back. Stand-alone LED-LLLT, therefore, has a role to play in rejuvenation of the aging face; but it does take time, and results are not instantly visible.

830-nm Light-Emitting Diode–Low Level Light Therapy as an Adjunctive Modality

Even more exciting than the stand-alone options for 830-nm LED-LLLT is its ability to be used in conjunction with any other procedure or approach which alters patients' tissue architecture in any

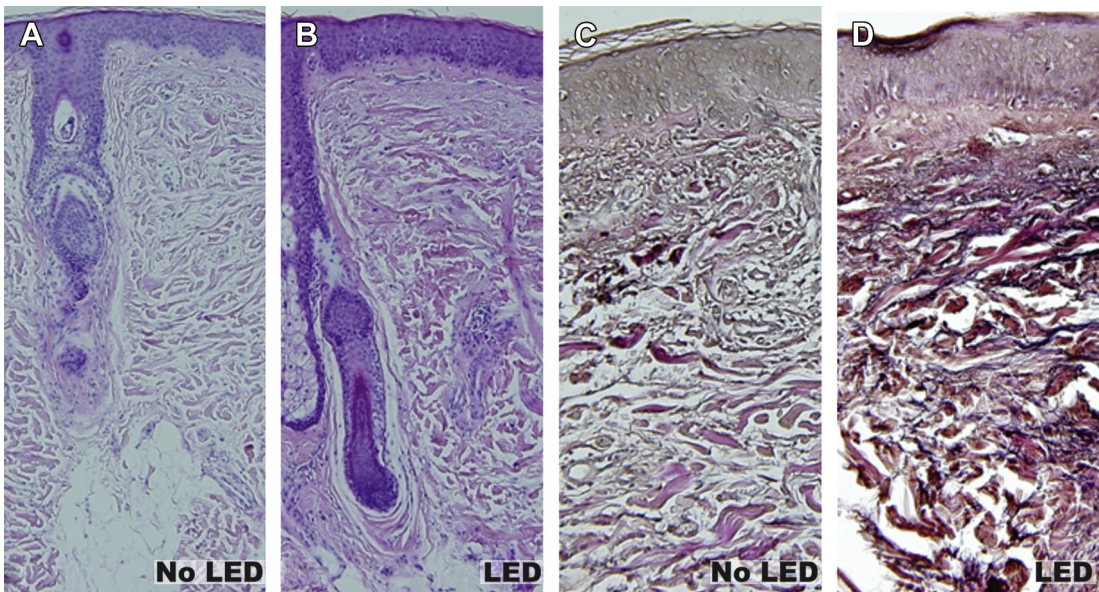


Fig. 8. Biopsy specimens compared between the side of the face not treated with 830-nm LED (A, C) and the treated side (B, D) at 2 weeks after the final LED session. The treated sides both show significantly higher collagen (A, B) and elastin (C, D) fiber density with good alignment, particularly at the Grenz zone, a thicker and more cellular epidermis, and a better organized stratum corneum. ([A, B]: hematoxylin and eosin, original magnification $\times 100$; [C, D]: elastica van Giessen, original magnification $\times 200$). (Courtesy of Celine SY Lee, MD, UCLA, CA.)

way.¹⁵ It has been shown to speed up wound healing (by better than 50%), minimize side effects, and decrease downtime (Fig. 9)¹⁶; the ability of LED-LLLT to help prevent hypertrophic scarring after surgery has also been shown in a controlled

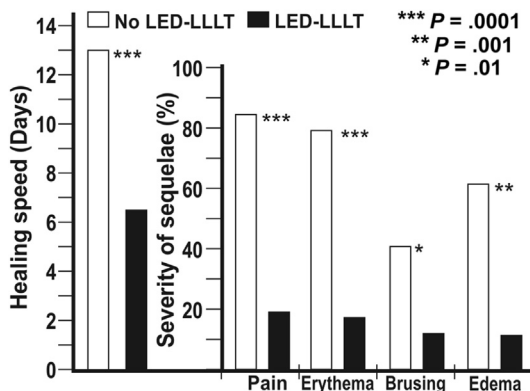


Fig. 9. Results compared in a 60-patient study on full face ablative resurfacing with (30 patients) and without (30 patients) LED-LLLT. The LED-treated group had significantly faster wound healing and significantly milder sequelae compared with the untreated group. (Data from Trelles MA, Allones I, Mayo E. Combined visible light and infrared light-emitting diode (LED) therapy enhances wound healing after laser ablative resurfacing of photodamaged facial skin. *Med Laser Appl* 2006;28:165–75.)

study on thyroidectomy scars.¹⁷ The usual regimen is to apply the LED-LLLT as soon as possible after trauma, accidental or iatrogenic, immediately postoperatively in the latter if possible; then treat 24 hours and again 72 hours after surgery or whatever procedure has been performed. The recommend optimal dose is around 60 J/cm². For severe trauma or an extensive surgical procedure, a further 6 sessions can be given twice weekly over 3 weeks, separating the sessions by at least 2 days.

In the case of postsurgical adjunctive 830-nm LED-LLLT, it really does not matter which procedure is performed: a mild microdermabrasion all the way up to rhytidectomy and anything in between, including medical intervention with creams and sera. Applying the 830-nm energy is pain free (and will even alleviate pain), side effect free (it controls side effects), and is well tolerated by patients of all ages. Many patients fall asleep during their 830-nm LED session, as this wavelength has been shown to enhance the parasympathetic rest and relax response, so as a destressor it is also a valuable tool. LED-LLLT after fractional ablative or nonablative laser, after fractional radio-frequency, and after microneedling with or without any application of cosmeceuticals has cut the minimal downtime even further by swiftly reducing erythema and edema and has improved results. As for cosmeceutical delivery, especially stem

cell-related compounds, a very recent study has shown that 830-nm LED-LLLT increases the activity of human adipose-derived stem cells *in vitro* and potentiates activity *in vivo* in an animal model.¹⁸

SUMMARY

LED-LLLT is emerging from the mists of black magic as a solid medico-scientific modality, with a substantial buildup of corroborative bodies of evidence for both its efficacy and some elucidation of the modes of action. Reports are appearing from many different specialties; however, of particular interest to the plastic surgeon treating the aging face is the proven action of LED-LLLT on skin cells in both the epidermis and dermis as well as enhanced blood flow. Thus, LED-LLLT is a safe and effective stand-alone therapy for patients who are prepared to wait until the final effect is perceived or, much more excitingly, represents a new tool in the rejuvenation armamentarium for the surgeon to enhance existing results.

In brief, LED-LLLT is safe and effective, easy to apply, pain free, side effect free, and, in the opinion of the authors, will undoubtedly become a major adjunctive modality for the plastic surgeon dealing with the aging face.

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