

# Chapter 20

## Light-Emitting Diode Phototherapy

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### **Abstract**

- Phototherapy is the process of using light as a therapeutic modality. In contrast to photosurgery, phototherapy induces its effect without producing significant heat damage to the target tissue.
- The light-emitting diode (LED) is a solid state semiconductor chip which emits light when an electric current is applied to it, and LED-based systems represent one type of phototherapy source that has a variety of clinical applications.
- Laser energy entered the arena in 1960 with Maiman's ruby laser, and attenuated laser beams were used for phototherapeutic purposes as low level laser therapy (LLLT) in the late 1960s, pioneered by the late Endre Mester and colleagues.

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- Light-emitting diodes (LEDs) were then tried as a phototherapeutic source, but were mostly inefficient due to their wide divergence, limited and unstable output powers and a wide waveband which limited target specificity.
- The advent of the “NASA LED” in 1998 changed this, when Whelan and colleagues developed an LED that was many orders of magnitude more powerful than existing LEDs with a stable output power, and, most importantly, a quasimonochromatic beam. They thus offered an excellent new phototherapy source with biological target-specific wavelengths. The acronym ‘LLLT’ is thus still used, but with the readily available clinically useful LEDs being widely reported in a large variety of indications, LLLT now stands for low level LIGHT therapy so that LED phototherapy is part of the LLLT family.
- A large body of low level laser therapy literature exists where the systems were either laser diode (LD)-based systems at specific wavelengths or the 633 nm helium:neon (He:Ne) laser. Taking these previously reported data into consideration, phototherapeutic LED-based systems were built based on the same effective wavelengths, but incorporating the inherent advantages of LEDs: namely a very efficient light source; able to be mounted in large planar arrays to treat large areas of the body in a hands-free manner; and comparatively inexpensive compared even with LDs thereby helping to minimize cost to the clinician and patient.
- LED phototherapy has now been well-reported in many clinical fields where it is used to:
  - accelerate and enhance wound healing in acute and chronic wounds of all etiologies
  - control inflammation and erythema
  - speed up the healing of bone damage, even for slow union fractures
  - attenuate and control acute and chronic pain of all types
  - improve results of any aspect of aesthetic and cosmetic surgery

- rejuvenate photodamaged skin
  - provide prophylaxis against hypertrophic scar formation
  - attenuate hyperactive melanocytes in acquired-type pigmentary disorders
  - treat circulatory disorders such as Raynaud’s disease, vasculogenic ulcers and diabetic foot
- This chapter will focus on the photobiological basics behind LED phototherapy and examine the mechanisms which have currently been elucidated, as well as providing some basic studies underlying the success of LED phototherapy in many fields. The potential user, however, should carefully ascertain the specific qualities of any LED system in regard to the true wavelength, active irradiated area and certified irradiance or power density. Furthermore, the user must match the wavelength with the desired target to ensure efficient absorption, because, as the first law of photobiology points out, without absorption there can be no reaction.
  - In conclusion, LED phototherapy at appropriate wavelengths is safe and effective, easy to apply, pain- and side effect-free and well tolerated by patients of all ages.

**Keywords** Quasimonochromaticity • Photobioactivation • Mitochondria • Cytochrome-c oxidase • Systemic effect • Wound healing

## Introduction

“*Nihil novi sub sole*” (‘there is nothing new under the sun’) can be found in the fourth century Vulgate Bible, and it certainly applies to the use of light energy to achieve a measurable clinical effect of some kind in living tissue in a non-invasive manner, but without heating tissue or causing any significant skin damage. The idea of using light as therapy is not a new idea. In fact, the first use of phototherapy can be dated back to ancient Egypt, where the sun

was used a therapeutic source of light [1]. Heliotherapy, phototherapy with the sun, persisted through the Greek and Roman civilizations and can actually still occasionally be seen today as a suggested cure for certain skin diseases such as psoriasis [2]. However, the sun can be a fickle light source, and is not available at night. It was Nobel Laureate Nils Finsen who developed the first electrically-powered phototherapy light source at the turn of the twentieth Century, and his arc lamp was used in the cure of a number of skin conditions including lupus erythematosus [3]. The laser first appeared in 1960, Maiman's ruby laser, with therapeutic as distinct to surgical indications reported in 1968, and the first truly clinically useful LED was developed in 1998.

### *What Is Phototherapy*

Phototherapy is the application of some form of light energy to achieve a clinical effect in an athermal and atraumatic manner. It has also been called low level laser therapy (LLLT) [4], or more recently, low level light therapy with the same acronym of LLLT. The reader should note that in LLLT, the 'level' referred to has nothing at all to do with the light source, so when people talk about using a 'low level laser' (or low level light), they're mistaken! In LLLT, the 'level' is the level of reaction induced in the tissue by the light source. The level is 'low', i.e., below the damage threshold of the cell, and is used for a therapeutic rather than a surgical effect, hence 'low level light therapy'. A 20 W CO<sub>2</sub> laser defocused to a 10 cm diameter spot has an irradiance of just over 250 mW/cm<sup>2</sup>: this is an LLLT power density, and will produce no heat or damage in the target tissue. If the level of photon stimulation exceeds the damage threshold of the cell, then the treatment is classified under photosurgery, or high level light therapy (HLLT), with sufficient energy eventually resulting in cell death. This is illustrated in Fig. 20.1

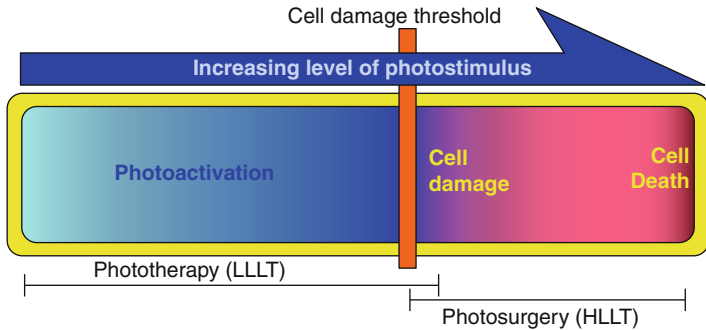


FIGURE 20.1 Schematic depicting a cell showing the cell damage threshold. As the light stimulus increases in magnitude, the cell becomes photoactivated with no energy lost through heat or damage. The maximum point of photoactivation is just before the damage threshold is reached. Once the damage threshold is passed, the degree of damage to the cell increases concomitantly with the incident light energy through a photothermal reaction until finally the cell survival threshold is passed and cell death occurs. Note there is a little grey area between the phototherapy and photosurgery components just beyond the damage threshold. In this zone, although slightly damaged, the cell is still alive and capable of some activity: this would correspond to the early stages of protein denaturation

### *Why Use LEDs?*

#### Power and Quasimonochromaticity

If the authors had been asked this question 15 years or so ago, they would now be chuckling quietly, because LEDs were simply a very bright, cheap and cheerful light source, creating colorful christmas lights and highly visible traffic signals but with little or no therapeutic benefit. This did not stop some manufacturers from putting together so-called ‘cluster probes’ with a number of old-generation LEDs which more often than not surrounded, or were interspersed with, laser diodes (LDs). The reported efficacy of these probes was most probably

down to the presence of the LDs, which were delivering coherent light energy with photon intensities many times those of the LEDs.

The work at the NASA-associated Space Medicine Laboratory by Harry Whelan and colleagues signaled a new generation of LEDs in 1998, the 'NASA LED' [5], which was very swiftly shown by the same group to have beneficial clinical effects in wound healing [6]. The NASA LED was several orders of magnitude more powerful than the previous generation of LEDs, had stable output powers, and delivered the vast majority of its photons at a rated wavelength rather than a waveband, in other words, it was quasimonochromatic. Finally it was possible to source a 633 nm LED rather than simply a 'red' LED. Many cellular and subcellular targets are very wavelength specific: quasimonochromaticity was therefore a powerful advantage of the new-generation LED.

## Efficiency

LEDs require a very little electrical energy to produce a great deal of light, and are therefore a very economical and efficient electricity-to-light converter, offering rates around and over 85 %, whereas the most efficient lasers are around 10 %. There is no filament, and no discharge tube, so there is virtually no energy lost as heat from the LED itself.

## Clinical Practicality

A number of LEDs can be mounted on multiple articulated panels to treat a large area of the human body in one single session, and in a hands-free manner. This makes LED-based systems clinic-friendly and therapist-non intensive. The articulation of the panels allows them to be adjusted to treat both flat and contoured areas of the body, ensuring uniform distance from the LEDs to the target tissue.

## Light-Tissue Interaction

### *Importance of Wavelength*

As already stated above, the first law of photobiology demands that absorption must take place before any reaction can be expected. The one single factor which determines absorption in a biological target is the **wavelength** of the incident photons. Not only that, the wavelength also decrees the depth to which the light energy will intrinsically penetrate into tissue. Following reports from Karu and others [7], it has been shown that there is a ‘window’ waveband within which light energy will penetrate well into tissue. This extends from around 610 nm to around 1,700 nm, after which water absorption gradually limits penetration. The shorter visible light wavelengths are preferentially absorbed in the competing chromophores of epidermal melanin and dermal blood, so that limits their penetration capacity. Figure 20.2 illustrates schematically the penetration of light into tissue based on data from Smith’s illustration of the penetration of ‘white’ light through a human hand in vivo [8]. The deepest penetrating wavelength is from 820 to 840 nm, because this is at the bottom of the water absorption curve. 1,064 nm, the wavelength of the Nd:YAG, is often erroneously stated to be the best penetrating wavelength, but even at 1,064 nm water absorption is a limiting factor.

### *Waveband and Primary Response*

The basic reaction at a cellular level in LED phototherapy is photoreception, followed by signal transduction and amplification and finally the photoresponse [7]. The waveband within which the light energy falls, namely visible and near-infrared (near-IR), determines the target’s primary response to photon absorption.

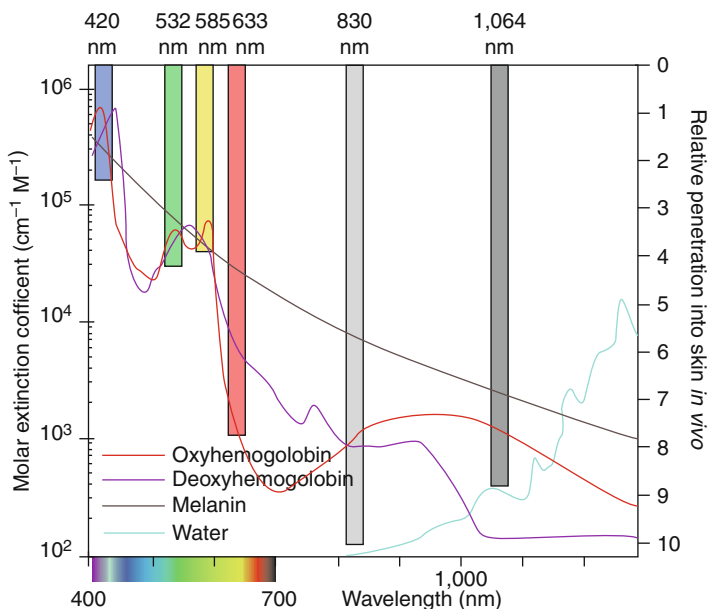


FIGURE 20.2 Relative depth of penetration into living tissue of a variety of visible light and near IR wavelengths (right-hand axis) overlying the absorption spectra of the biological chromophores: blood, melanin and water. These can explain why the shorter visible light wavelengths from blue to yellow cannot penetrate very deeply into tissue. Using LEDs at these wavelengths will therefore limit penetration to the epidermis and very superficial dermis. At only 48 nm more than 585 nm, penetration at 633 nm is increased by about 3.5 orders of magnitude allowing visible red light at that wavelength to penetrate well into the skin, reaching and passing through the subdermal fatty layer. Deepest penetration is at the bottom of the water absorption curve (820–840 nm), as seen by the 830 nm example. 830 nm is capable of penetrating some centimeters into tissue with appropriate photon intensity. At 1,064 nm, the wavelength of the Nd:YAG laser, the water absorption curve starts to rise so water becomes an important chromophore and penetration of 1,064 nm light energy into tissue (over 75 % water content) is slightly limited by water absorption



## Visible Light

- Visible light penetrates through the cell membrane
- Preferential absorption occurs in organelles within the cell.
- For the red wavelengths, especially 633 nm, the primary photoacceptor, or chromophore, is cytochrome-c oxidase (COX) which is the terminal enzyme of the mitochondrial respiratory chain [9], mitochondria being the adenosine triphosphate (ATP) factories of the cell.
- ATP is the basic fuel for the human metabolism.
- The light energy is transferred to the COX and initiates a primary photochemical cascade which results in the production of ATP, and also the powerful signaling components, calcium ions ( $Ca^{++}$ ) and protons ( $H^+$ ) [10].
- Increased intracellular levels of ATP,  $Ca^{++}$  and  $H^+$  kick-start the membrane transport mechanisms such as the sodium-potassium ( $Na^+/K^+$ -ATPase) pump.
- Excellulation of these components occurs. This raises their extracellular levels, and they can then activate nearby unirradiated cells. This is known as the bystander theory [11], and can account for the systemic effect of LLLT whereby unirradiated areas of the body receive indirect benefit from the irradiated area.

## Near-Infrared Light

- On the other hand, cell membranes are not transparent to near IR light.
- Near IR light is primarily absorbed in the cell membrane where the primary response is photophysical, not photochemical, due to changes in the rotational and vibrational state of the membrane molecules.
- $Na^+/K^+$ -ATPase membrane transport mechanism is immediately initiated.
- Mitochondria are called upon to produce more ATP to meet the increased energy requirement of the cell.
- The same ATP production cascade as for visible light is thus induced, but as a secondary response to the primary photophysical reaction in the cell membrane.

Despite the difference in primary response between visible and near-IR light, the end result is the same, namely a photoactivated cell. When cells are in a photoactivated state one or more of three things can happen:

- If the cell is damaged or compromised, it will repair itself, or be repaired.
- If the cell has a function, e.g., collagen and elastin synthesis by fibroblasts, it will perform that function more efficiently.
- If proliferation is required, the cell will proliferate.

## Validation Through Basic and Clinical Research

### *LLLT and Skin Cells*

Including the laser phototherapy-related literature, a very large number of papers has been published which validate the photoactivation of cells by a variety of wavelengths, both in vitro and in vivo. Since most laser diode (LD)-based experiments involved a defocused beam to encompass the target vessel containing the cells in an appropriate medium, the incident irradiance can be arguably equated to LED energy at appropriate irradiances and distances, although the photon intensity of even a defocused LD is still greater than that of an LED-based system. This can be compensated for by an increased dose ( $J/cm^2$ ) through longer irradiation times.

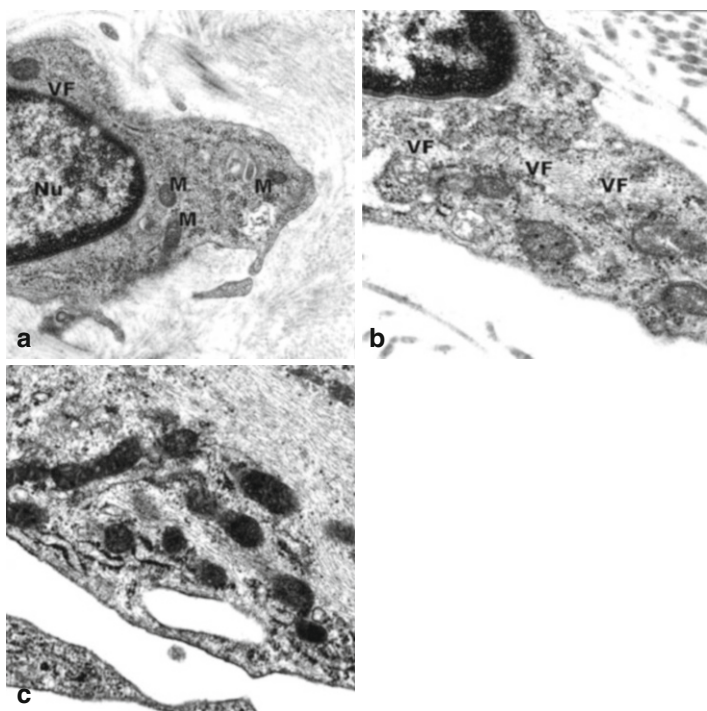
From the data of over 30 years of LLLT, two wavelengths have been highlighted as having the greatest effect on the action mechanism of skin cells, including epidermal keratinocytes, and fibroblasts, mast cells, macrophages and neutrophils in the dermis: 633 nm in the visible red, and 830 nm in the near-IR [12]. With the current ability to source LEDs at almost any specific wavelength in the visible red and near-IR wavebands, other wavelengths are emerging as potential candidates for LED phototherapy, but 633 and 830 nm remain those most reported on.

## Fibroblasts and Collagen

Omi and colleagues examined the effect of 633 nm LED phototherapy on human skin *in vivo* [13]. Subjects ( $n=8$ ) had punch biopsies taken from an arm on day zero before treatment, and the same arm of the subjects was treated three times at  $126 \text{ J/cm}^2/\text{session}$  on day zero, 2 and 4, with subsequent biopsies taken from the treated arm on day 2 before treatment, and then again on days 4 before treatment and finally on 6 (48 h after the final treatment). Specimens were routinely processed for electron microscopy in ultrathin slices stained with uranyl acetate/lead citrate and double stained with oolong tea extract for vimentin [14], vimentin being one of the building blocks of collagen through copolymerization in the Golgi complex with desmin. Figure 20.3a shows a transmission electron photomicrograph of a fibroblast in unirradiated tissue at baseline, with normal morphology. Mitochondria were noted, with small pockets of vimentin fibrils, and many vimentin granules seen as small black dots. Note that vimentin fibrils are required for copolymerization, rather than the granular vimentin. At 48 h after the first treatment (Fig. 20.3b), there were more mitochondria seen in every field, more vimentin fibrils and fewer vimentin granules. Furthermore, chromatin was seen to have accumulated at the nuclear membrane, suggestive of preparation for ribosomal mRNA signaling. In Fig. 20.3c, 48 h after the final irradiation, a dramatic change was seen in fibroblast morphology and activity.

There were significantly many more mitochondria which were electron dense showing high ATP activity, including so-called giant mitochondria, with very few vimentin granules and a mass of vimentin fibrils. These findings suggested that the fibroblast was photoactivated, and was entering a highly fibroplastic state with imminent enhanced collagen production. Lee and colleagues, in a split-face, controlled and double-blinded study with 127 subjects [15], examined the effects of LED phototherapy on skin rejuvenation using 633 nm alone, 830 nm alone and 830 nm followed by 633 nm compared with sham-irradiated control. Punch biopsies were

taken from the irradiated and unirradiated sides of the face at 2 weeks after the final session (8 sessions over 4 weeks) and examined with light and transmission electron microscopy. Figure 20.4 shows enhanced collagenesis in an 830 nm-irradiated specimen compared with the contralateral unirradiated side in the same patient, and Fig. 20.5 shows the same for elastin, both sets of specimens being taken from 830 nm-irradiated subjects. In addition to the light microscopic findings, transmission electron microscopy at 2 weeks after the final session showed plump, active fibroblasts in 830 nm irradiated tissue, surrounded by well-organized collagen fiber bundles, compared with rather anemic-looking fibroblasts in the contralateral unirradiated tissue with poorly organized collagen. As for the degree of collagenesis



and elastinogenesis, the 830 nm group was superior to the combination group, statistically so for skin elasticity, and the combination group was in turn superior to the 633 nm group. All three groups were statistically significantly superior to both the unirradiated side of the face and the sham-irradiated control group.

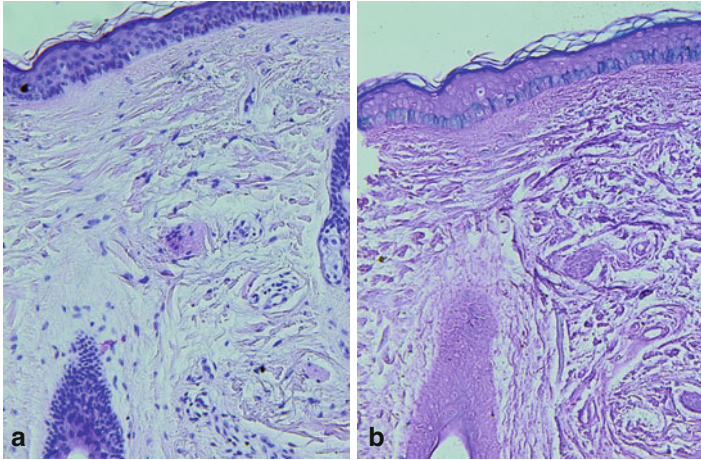
## Mast Cells

Calderhead and colleagues explored the role of 830 nm LED phototherapy in the activation of mast cell degranulation in the skin of normal healthy individuals (eight subjects), *in vivo* [16]. A single session of 830 nm LED phototherapy was given

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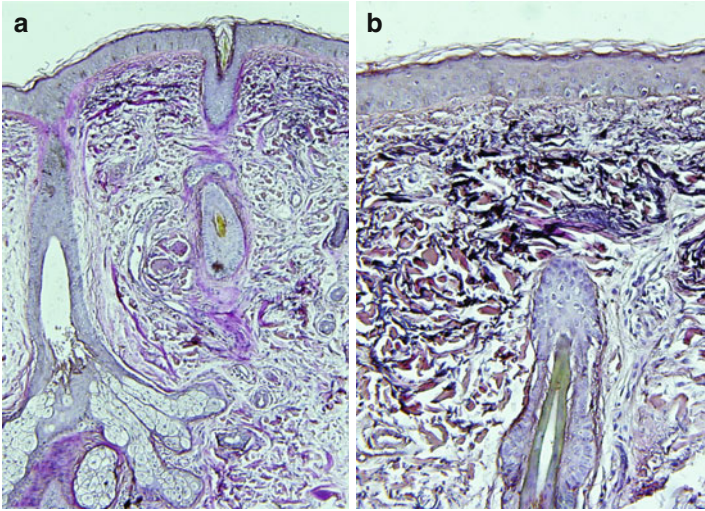
FIGURE 20.3 Effect of 633 nm LED phototherapy on fibroblasts *in vivo* (see text for experimental details) as shown by transmission electron microscopy (TEM). **(a)** Photomicrograph of normal tissue at baseline, preirradiation. Part of a fibroblast displaying normal architecture is seen with the nucleus (*Nu*) containing chromatin to the left of the image. Mitochondria (*M*) can be seen in the cytosol to the right. A small pocket of vimentin fibrils (*VF*) is seen just above the nucleus. Multiple small black dots exist in the cytosol: these are vimentin granules stained by the oolong tea extract (TEM, magnification  $\times 12,000$ ). **(b)** Specimen at a higher magnification taken from an irradiated arm 48 h after a single irradiation (633 nm, 126 J/cm<sup>2</sup>). The number of mitochondria has increased considerably, and there are large amounts of vimentin fibrils (*VF*) in the cytosol, converted from vimentin granules, the number of which has dropped. The chromatin has apparently located next to the nuclear membrane (*top left*) suggesting the cell is preparing for ribosomal mRNA signaling (TEM, magnification  $\times 30,000$ ). **(c)** At 48 h after three irradiation sessions, a dramatic change has occurred in the fibroblast architecture. Hardly any vimentin granules can be seen, and the cytosol is full of vimentin fibers. Mitochondria have significantly increased in number, including a so-called giant mitochondrion, and are electron dense showing high ATP synthesis activity. The cell is now highly fibroplastic (TEM, magnification  $\times 30,000$ ). All photomicrographs courtesy of T Omi MD PhD)



**FIGURE 20.4** Effect of 830 nm LED-LLLT on collagen synthesis. **(a)** Specimen from the unirradiated side of a patient's face in the 830 nm-treated group. Dermal collagen is poorly organized with many interstitial spaces. **(b)** At 2 weeks after the final LED phototherapy session in this specimen from the 830 nm LED-irradiated side of the same patient, a much younger-looking dermal matrix is seen. Collagen fibers and bundles have increased and better organized down into the mid-reticular dermis, with much smaller interstitial spaces. The Grenz layer at the dermoepidermal junction is linearly organized and thicker, with a more cellularly active-looking epidermis (Skin, hematoxylin and eosin, original magnification  $\times 200$ . Microphotography courtesy of SY Celine Lee, MD)

on one forearm, the other serving as an unirradiated control. Punch biopsies were taken from the irradiated arm at baseline and 48 h post-irradiation, and from the unirradiated arm at the 48 h point, and examined with transmission electron microscopy. In addition, an independent count of mast cells, macrophages and neutrophils per field was conducted in eight fields per subject.

No morphological change was seen in the unirradiated arm at 48 h post irradiation compared with baseline, with no increase in cell count. In the irradiated arm, mast cell degranulation was induced, with at least 50 % of the granules being



**FIGURE 20.5** Effect of 830 nm LED-LLLT on elastin synthesis. **(a)** Specimen from the unirradiated side of a patient's face in the 830 nm-treated group. Elastic fibers are haphazardly organized and sparse, especially in the deeper dermis and in the Grenz layer. **(b)** At 2 weeks after the final LED phototherapy session in this specimen from the 830 nm LED-irradiated side of the same patient, the elastic fibers have increased in number and density, and are better organized, even in the deeper dermis. A profusion of fine, linearly organized elastic fibers is seen in the Grenz layer. Note also the thicker epidermis (Skin, Verhoeff-van Giessen stain, original magnification  $\times 200$ . Microphotography courtesy of SY Celine Lee, MD)

excellulated into the matrix. As a result, a mild inflammatory response was noted as if the tissue had been wounded, but the morphology was otherwise normal. The cell counts of all cells of interest, the major wound healing cells, were significantly higher in the irradiated arm.

The authors proposed that this creation of a 'quasi-wound' was the first stage of photoinducing the wound healing cycle, resulting in the neocollagenesis and elastinogenesis necessary for good skin rejuvenation and additionally suggesting an important role of the mast cell in 830 nm LED phototherapy for wound healing.

## Macrophages and Neutrophils

The literature also contains good evidence that phototherapy at certain wavelengths activates macrophages and increases their ability to synthesize mediators of wound repair. Low incident doses of visible red and near-IR coherent and non-coherent light energy increased the phagocytic activity of macrophages through enhanced chemotaxis and internalization [17, 18], but at the same time significantly increased the production of fibroblast growth factor (FGF). As for neutrophils, *in vitro* irradiation with 830 nm [19, 20] and other wavelengths including 633 nm [20] significantly increased their ability to identify, move to and engulf targets, and then destroy them more effectively through enhanced respiratory burst activity. Furthermore, release of trophic factors was also enhanced following irradiation with low incident doses of light energy.

### *The Systemic Effect of LED Phototherapy*

The earliest proof that phototherapy of one area would induce effects in a distant unirradiated area came from the pivotal study in the early 1970s by the late Endre Mester on torpid crural ulcers with a treatment-resistant history of at least 6 months, whereby treatment with a HeNe laser brought about healing of the irradiated ulcers in the vast majority of the 1,000-plus patients in 3–4 weeks [21].

Subsequently, the ulcers on the contralateral limb also started to heal even though they had not been treated directly with the 633 nm LLLT. More recently, a very convincing controlled study with 830 nm LED phototherapy in an animal model showed significantly more rapid healing of standardized wounds on the dorsum of the LED-irradiated animals compared with the wounds on the backs of the unirradiated controls [22], with the LED energy being restricted to the abdomen of the irradiated animals. In other words, an indirect, systemic effect of LED phototherapy was clearly demonstrated.



## Dosimetry

Because of the wide range of wavelengths used in LED phototherapy, and given the fact that the photons in each wavelength have both a different inherent level of energy with longer wavelengths having a lower electron volts (eV) value than shorter ones and different principal targets, any thoughts on dosimetry must be rather general. One can, of course, look to the literature where a rather bewildering range of doses is given, but very often all parameters are incomplete. Knowing the dose in  $\text{J}/\text{cm}^2$  is important, but as that parameter is composed of both the intensity in  $\text{W}/\text{cm}^2$  (or  $\text{mW}/\text{cm}^2$ ) and the exposure time in seconds, a dose of  $30 \text{ J}/\text{cm}^2$  could be  $300 \text{ mW}/\text{cm}^2$  for 100 s,  $30 \text{ W}/\text{cm}^2$  for 1 s or  $300 \text{ W}/\text{cm}^2$  for 0.1 s. These sets of parameters would produce, respectively, very little heat if any, quite a bit of heat and a great deal of heat in the target tissue with only the first set approximating an LLLT-like effect, but all three having the same dose. Another three variables to be considered are the size of the LED active area, (treatment head), the angle of divergence of the LEDs and the distance between the head and the target tissue. The clinician has to look at the recommendations of the manufacturer, and trust that the manufacturer has performed due diligence with dose-ranging studies and hopefully had some corroborative literature published on the clinical application of their system.

Here are some examples from the literature in which all the parameters were given and can therefore be used as a basis for thinking about the ideal dose. In the study mentioned above by Lee et al. which compared 633 and 830 nm LED-LLLT for skin rejuvenation, and showed efficacy of these wavelengths at a histological and ultrastructural level [15], the dose for the 633 nm component was  $96 \text{ J}/\text{cm}^2$  with an intensity of  $80 \text{ mW}/\text{cm}^2$  over 20 min. For the 830 nm component, the dose was  $60 \text{ J}/\text{cm}^2$  comprising an intensity of  $50 \text{ mW}/\text{cm}^2$  over 20 min. The same dose of  $96 \text{ J}/\text{cm}^2$  for 633 nm energy was also advocated by Lee and colleagues in their article already cited above on the combination of 415 nm visible blue and 633 nm

for the successful light-only treatment of active acne [11], with a dose of  $48 \text{ J/cm}^2$  for the 415 nm component ( $40 \text{ mW/cm}^2$  for 20 min). The article cited above showing the systemic effect of 830 nm LED-LLLT on wound healing also used  $60 \text{ J/cm}^2$  ( $100 \text{ mW/cm}^2$  for 10 min). The literature would suggest for 830 nm LED-LLLT that the effective range lies between 40 and  $80 \text{ J/cm}^2$ , with a fair body of evidence pointing to  $60 \text{ J/cm}^2$ .

Phototherapy systems from different manufacturers are, however, different, and in the absence of strong and validated recommendations from the manufacturer regarding the correct parameters, the clinician or therapist will very often have to conduct their own dose-ranging studies to arrive empirically at the ideal dose for that particular system.

## Conclusions

- It is impossible in this short article to summarize the entire body of literature on phototherapy with LEDs and defocused laser diode sources, but the authors believe that we have adequately demonstrated that LLLT using LEDs is a fast-emerging and truly viable alternative to the proven efficacy with laser diode-based LLLT, employing the wavelengths already proven and tested with the latter.
- LED phototherapy can be applied by a trained therapist or nurse, freeing up the clinician for other duties, is easy to apply, pain- and side-effect free and is tolerated well by patients of all ages. The current article has not even mentioned the effect of LED-LLLT on blood flow, but that is more appropriate for the section elsewhere in this book on lasers and light in wound healing, so please refer to that section for information on this important aspect of LED phototherapy.
- A recent review article by Kim and Calderhead made a convincing argument that LED-LLLT was indeed effective [23], and as more and more of the many ongoing controlled and clinical studies come to an end and the data are collated, the authors are sure that LED phototherapy will take its rightful place in a large variety of indications.

- Although the stand-alone indications of LED phototherapy are interesting, perhaps even more exciting is the enormous potential of LED phototherapy as an adjunct to any kind of surgical procedure or post-trauma to obtain faster relief from pain, edema and erythema, and enhanced, more rapid wound healing. However, and there is always a 'however' with LLLT, a great deal depends on the quality of the LEDs in the following order of importance: the wavelength must be correct for the target, with the LEDs emitting a very narrow band around the rated wavelength e.g., within  $\pm 5$  nm or so; the irradiance must be adequate; and the dose sufficient. Provided these conditions are met, LED phototherapy WILL work, and work well.

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