Low-level light therapy (LLLT) for cosmetics and dermatology

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Low-level light therapy (LLLT) for cosmetics and dermatology

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Abstract

Over the last few years, low-level laser (light) therapy (LLLT) has been demonstrated to be beneficial to the field of aesthetic medicine, specifically aesthetic dermatology. LLLT encompasses a broad spectrum of procedures, primarily cosmetic, which provide treatment options for a myriad of dermatological conditions. Dermatological disorders involving inflammation, acne, scars, aging and pigmentation have been investigated with the assistance of animal models and clinical trials. The most commercially successful use of LLLT is for managing alopecia (hair loss) in both men and women. LLLT also seems to play an influential role in procedures such as lipoplasty and liposuction, allowing for noninvasive and non-thermal methods of subcutaneous fat reduction. LLLT offers a means to address such conditions with improved efficacy versatility and no known side-effects; however comprehensive literature reports covering the utility of LLLT are scarce and thus the need for coverage arises.

1. LLLT in Dermatology

Low-level laser (or light) therapy (LLLT), phototherapy or photobiomodulation refers to the use of photons to alter biological activity. Non-thermal, coherent light sources (lasers) or non-coherent light sources consisting of filtered lamps or light-emitting diodes (LED) are used in this type of therapy for reducing pain and inflammation, augmenting tissue repair and regeneration, deeper tissues and nerves, and preventing tissue damage [1, 2]. In the last few decades non-ablative laser therapies have been used increasingly for the aesthetic treatment of fine wrinkles, photoaged skin and scars, a process known as photorejuvenation. More recently they have also been used for inflammatory acne [3]. Their potential use for other dermatological conditions and cosmetics such as vitiligo, psoriasis, photoprotection, hair regrowth and fat reduction have been shown by several studies. In this chapter, we will briefly mention about these cosmetic and dermatological applications of LLLT, starting with its current and potential use in cosmetic dermatology and various skin conditions, hair loss treatment and lastly in fat reduction procedures and cellulite treatment.

1.1. LLLT for Skin Rejuvenation:

Skin aging and photoaging is a process that may present with a relatively early onset, sometimes as early as during the late 20s or early 30s of an individual's life. Common signs and symptoms of skin aging include skin wrinkling, dyspigmentation, telangiectasia, and reduced elasticity. At the histological and molecular level, common noticeable features include; reduced collagen content, collagen fiber fragmentation, elastotic degeneration of elastic fibers, presence of dilated and tortuous dermal vessels, disorientation and atrophy of the epidermis along with an up-regulation of matrix metalloproteinases (MMPs), especially MMP-1 and MMP-2. Skin aging is considered to be a process affected by both chronological and environmental elements but the single most influential factor responsible for accelerated skin aging seems to be photodamage induced primarily through ultraviolet (UV) radiation exposure.

Low-level light therapy (LLLT) is a novel treatment option available for non-thermal and non-ablative skin rejuvenation which has been shown to be effective for improving skin conditions such as wrinkles and skin laxity

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(Figure 1) [4]. It is a treatment modality that has been shown to provide increased rates of skin rejuvenation and wound healing with great efficacy, while also reducing post-operative pain, edema and several types of inflammation making it highly desirable tool. Early studies by Abergel et al. [5] and Yu et al. [6] reported an increase in production of pro-collagen, collagen, basic fibroblast growth factors (bFGF) and proliferation of fibroblasts after exposure to low-energy laser irradiation *in vitro* and *in vivo* animal models. Implementation of LLLT sources with wavelengths of 633 nm/830 nm is most common in cases of clinical application involving wound healing and skin rejuvenation. LLLT is now used for the healing of even non healing wounds through restoration of collagenesis/collagenase imbalances and allows for rapid and enhanced wound healing in general. Lee et al. conducted a study to investigate the histological and ultrastructural alterations that followed a series of phototherapies utilizing combinations of light emitting diodes (LEDs) of 830 nm, 55 mW/cm^2, 66 J/ cm^2 and 633 nm, 105 mW/ cm^2, 126 J/ cm^2. They observed alteration in the status of MMPs and tissue inhibitors of metalloproteinases (TIMPs) [7]The study also showed increased mRNA levels of interleukin-1 beta (IL-1ß), tumor necrosis factor alpha (TNF-α), intercellular adhesion molecule 1 (ICAM-1), and connexin 43 (Cx43) following LED phototherapy whereas IL-6 levels were decreased [7]. Subsequently the study also demonstrated a well-marked increase in the amount of collagen in the post-treatment specimens [7]. It is thought that the deliberate development of photothermally-mediated wounds is responsible for the recruitment of pro-inflammatory cytokines IL-1ß and TNF-α in order cause wound repair. The generation of such a wound healing cascade thus contributes to new collagen synthesis [7]. LLLT may induce this wound healing process through athermal and atraumatic induction of a subclinical 'quasi-wound', even without any actual wounding created by thermal damage which can possibly cause complications as in some other laser treatments [7]. MMP activities are known to be inhibited by TIMPs, suggesting the possibility of other mechanisms for increased collagen synthesis through induction of TIMPs. Collectively viewing these findings, they are suggestive of the idea that an increased production of IL-1ß and TNF-α might be responsible for induction of MMP activity as an early response to light treatment, which might possibly contribute to the removal of photodamaged collagen fragments in order to facilitate collagen biosynthesis of new fragments. Furthermore, as a consequence of the therapy there may be increased concentrations of TIMPs that most likely play a role in the protection of the newly synthesized collagen, from proteolytic degradation by MMPs [7]. Subsequently, heightened expression of Cx43 may possibly enhance cell-cell communication between dermal components, especially between fibroblasts, allowing for greater synchrony between cellular responses, following the effects of photobiostimulation from LLLT in order to promote synthesis of new collagen in a greater area including even the regions that did not receive light irradiation [7]. A clinical study conducted by Weiss et al. demonstrated the benefits of LLLT over traditional thermal-based rejuvenation modalities. A group of 300 patients were administered LLLT (590 nm, 0.10 J/cm^2) alone, and another group of 600 patients received a combination of LLLT with a thermal-based photorejuvenation procedure. Of the patients who received just the light treatment, 90% reported an observed softening of skin textures as well as a reduction in skin coarseness and fine lines that ranged from small alterations to significant changes [8].It was observed that patients who received a form of LLLT (n = 152) reported a noticeable reduction in post-treatment erythema and an overall impression of increased efficacy versus patients that received treatment through a thermal photorejuvenation laser or light source lacking any sort of LLLT photomodulation [8, 9]. Reduction in post-treatment erythema can most likely be attributed to the anti-inflammatory effects of LLLT. [10]. Utilizing different pulsing sequence parameters, a multicenter clinical trial was conducted, wherein 90 patients received 8 LLLT treatments over 4 weeks [11-14]. The study presented desirable results with more than 90% of patients improving by at least one Fitzpatrick photoaging category and 65% of the patients displaying global improvement in facial texture, fine lines, background erythema and pigmentation with results peaking at 4 to 6 months following completion of the 8 treatments. Noticeable increases in papillary dermal collagen and reductions in MMP-1 were generally observed. A study conducted by Barolet et al. also proved to be consistent with the aforementioned studies. The study used a 3-D model of tissue-engineered Human Reconstructed Skin (HRS) to investigate the potential of LLLT (660 nm, 50 mW/cm, 4 J/cm^2) in collagen and MMP-1 modulation. The results showed up-regulation of collagen and down-regulation MMP-1 *in vitro* [10]. A split-face, single-blinded clinical study was then carried out to assess the results of this light treatment on skin texture and appearance of individuals

with aged/photoaged skin [10]. Profilometry quantification demonstrated that more than 90% of individuals had a reduction in rhytid depth and surface roughness, and, 87% of the individuals reported that they have experienced a reduction in the Fitzpatrick wrinkling severity score following 12 LLLT treatments [10].

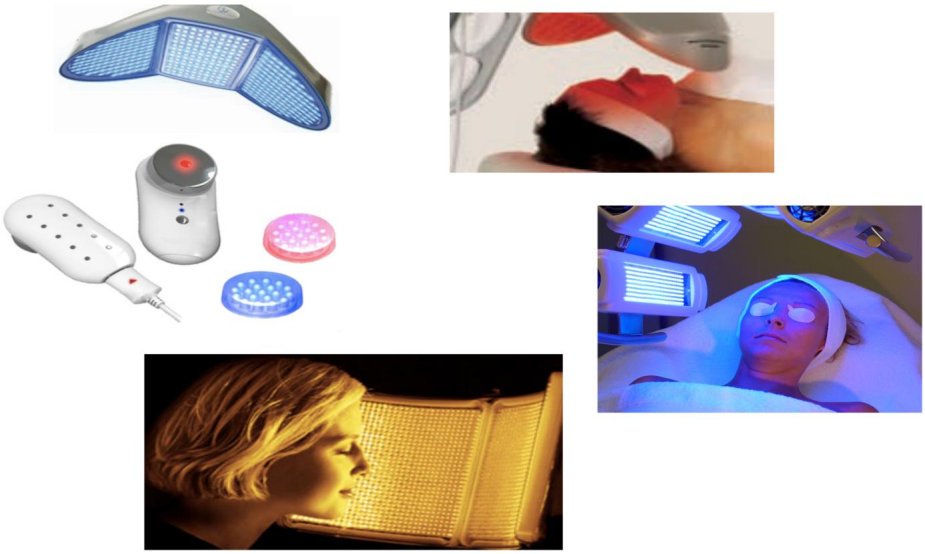

Figure 1: Examples of LLLT devices used for skin rejuvenation.

2. LLLT for Treatment of Hair Loss:

2.1 Hair and Types of Hair Loss:

Hair is amongst the fastest growing tissues of the body, undergoing repetitive and regenerative cyclical change, where each cycle consists of telogen (resting), anagen (active) and catagen (physiological involution) stages **(Figure 2)** [15]. During the transition from telogen to anagen there is stringent regulation of the activation of epithelial bulge stem cells and the transient amplifying (TA) progeny cells arise from the secondary hair germ cells [16]. Along the duration of the anagen phase, the TA cells display resilient proliferation within the epithelial matrix of the hair follicle. As a result, the end product of the hair cycle i.e. the bulk of the hair filament is formed through terminal differentiation of the proliferating trichocytes. The prime regulatory element of progenitor cell activation, hair matrix cell proliferation and terminal differentiation of trichocytes is believed to be the dermal papilla of the hair follicle [17].

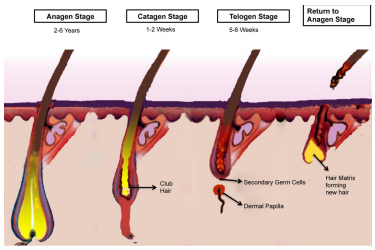

Figure 2: Stages of hair cycle

The anagen stage represents the growth stage of the hair cycle and may last 2 to 6 years. The cagaten stage, which generally lasts 1 to 2 weeks, is when transitioning of club hair is observed as it progresses towards the skin pore and the dermal papilla begins to separate from the hair follicle. The telogen stage which lasts from 5 to 6 weeks, exhibits complete dermal papillary separation from the hair follicle. Lastly, the cycle progresses again towards the anagen stage as the dermal papilla joins up with the hair follicle and the hair matrix starts synthesizing new hair.

Androgenetic alopecia (AGA) is the most common form of hair loss in men affecting almost 50% of the male population [18]. As the name suggests, AGA refers to hair loss induced in genetically susceptible individuals due to the effects of androgens such as testosterone – a lipophilic hormone that diffuses across the cell membrane to carry out its function, and its derivative dihydrotestosterone (DHT), which is a more active form of testosterone. The enzyme responsible for the conversion of testosterone to DHT is 5-α reductase. Two types of 5-α reductase enzymes exist; Type 1 which is prevalent in keratinocytes, fibroblasts, sweat glands, and sebocytes, and Type 2 found in skin and the inner root sheath of hair follicles [19]. DHT acts by binding to its nuclear androgen receptor (AR) which is responsible for regulation of gene expression [19]. Abnormal androgen signaling is responsible for disruption of epithelial progenitor cell activation and transient amplifying cell proliferation which forms the essential pathophysiological basis for AGA[20]. The exact genes associated with the process of hair loss are not entirely known however, a few of the genes proposed for hair growth include desmoglein, activin, epidermal growth factor (EGF), fibroblast growth factor (FGF), lymphoid-enhancer factor-1 (LEF-1), and sonic hedgehog [19]. Presently, amongst the treatment options available, the most common include use of minoxidil, finasteride or surgical hair transplantation [18]. Recently, the United States Food and Drug Administration (FDA) has approved the use of LLLT as a novel treatment modality for hair loss **(Figure 3)** [21].

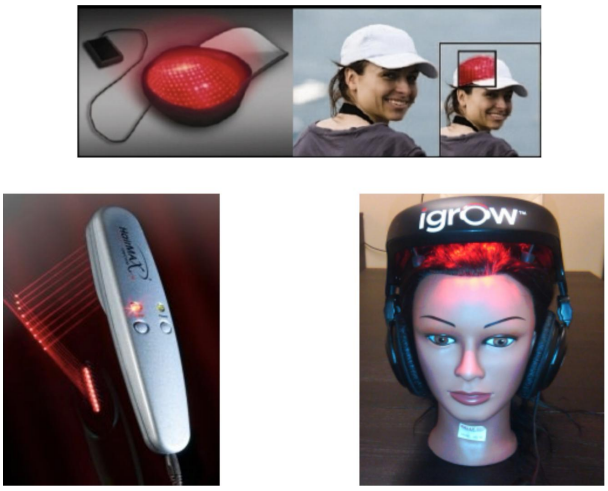

Figure 3: Examples of LLLT devices for treatment of hair loss.

2.2 LLLT for Treatment of Hair Loss:

In 2007, the FDA approved LLLT as a possible treatment modality for hair loss **(Figure 4)** [21]. It is believed that LLLT can stimulate reentry of anagen hair follicles into telgoen stage, bring about greater rates of proliferation in active anagen follicles, prevent development of premature catagen stage and extend the duration of the anagen phase [21, 22]. Although the exact underlying mechanism as to how LLLT brings about hair growth is not known, there have been several proposals. There is evidence suggestive of the action of LLLT on mitochondria leading to increased adenosine triphosphate (ATP) production, modulation of reactive oxygen species (ROS) and stimulation

of transcription factors [1]. These transcription factors in turn are responsible for synthesis of proteins that cause certain down-stream responses leading to enhanced proliferation and migration of cells, modulation of cytokine levels, growth factors and mediators of inflammation and increased tissue oxygenation [1].

In one study conducted by Yamazaki and colleagues, irradiated the backs of Sprague Dawley rats using a linearly polarized IR, where an up-regulation of hepatocyte growth factor (HGF) and HGF activator expression was discovered [23]. Another study reported increases in temperature of the skin and improved blood flow around the stellate ganglion area, following treatment with LLLT [24]. The exact mechanism for the action of minoxidil in treating hair loss is not entirely understood, but it is known that minoxidil does contain nitric oxide (NO) which is an important cellular signaling molecule and vasodilator [25] that is influential to a variety of physiological and pathological processes [26]. Furthermore, NO is a regulator of the opening of ATP-dependent potassium (K^+) channels and is thus responsible for the hyperpolarization of cell membranes [27]. Also, It has been suggested that ATP sensitive K^+ channels of the mitochondria and elevated levels of NO might be involved in the mechanism of action of LLLT [28-30] in areas of the brain and heart [30-32]. Thus given the dependency of both minoxidil and LLLT on the aforementioned factors there is possibly some mechanistic overlap between the two modalities. A study conducted by Weiss et al. demonstrated that LLLT is able to modulate 5-α reductase, the enzyme responsible for the conversion of testosterone to DTH, as well as alter the genetic expression of vascular endothelial growth factor (VEGF), which plays an influential role in hair follicle growth and thus LLLT is able to stimulate hair growth [33-35]. Furthermore, it has been demonstrated that LLLT may stimulate hair growth through modulation of inflammatory processes and immunological responses [36]. A study conducted by Wikramanayake et al. on C3H/HeJ AA mouse models supported this assumption, wherein the mice were given exposure to a laser comb and it was observed that the treatment led to an increase in the quantity of hair follicles where the majority of the follicles in anagen phase were seen to have decreased inflammatory infiltrates [21]. Taking into account the disruptive effect that inflammatory infiltrates have on hair follicles along with the notion that several cytokines such as interferon gamma (IFN-γ), IL-1α and β, TNF- α, MHC and Fas-antigen and macrophage migration inhibitory factor are all involved in cyclic hair growth as well as the pathogenesis of AA, LLLT may be able to play significant role in the treatment of AA due to its modulating effects on inflammation [21].

2.2.1 LLLT for Alopecia Areata:

A clinical study was carried out to investigate the effect of LLLT on treatment of AA consisting of a sample size of 15 patients (6 men, 9 women) utilizing Super Lizer TM, a medical instrument operating on polarized linear light with a high output (1.8 W) of IR radiation (600-1600 nm) possessing sufficient penetration depth to reach deep subcutaneous tissue [37]. The patients received a 3 minute laser treatment on the scalp either once a week or once every 2 weeks and were administered additional carpronium chloride 5% twice daily to all lesions [37]. Supplemental oral antihistamines, cepharanthin and glycyrrhizin (extracts of Chinese medicine herbs) were prescribed as well [37]. The results of the study showed that 47% of the patients experienced hair growth 1.6 months earlier on areas irradiated with laser when compared to the areas that were not irradiated[37]. In another study conducted by Wikramanayake et al. the hair growth stimulating effects of LLLT, on C3H/HeJ mouse model of AA, were exhibited using a HairMax Laser Comb® (The comb emits 9 beams of light, while utilizing the attached combs for parting of hair and allowing for better delivery of laser to scalp at a wavelength of 655 nm), where the mice were irradiated 20 seconds daily three times a week for a cumulative 6 weeks **(Figure 4)** [21]. As the treatment was concluded, increased hair regrowth was observed in the mice that were treated, but the sham treatment group showed no difference in hair growth [21]. Histological examination of mice tissue showed that there was an increased content of anagen phase follicles in the light treated mice, whereas the sham treatment group exhibited more telogen follicles [21].

2.2.2 LLLT for Androgenetic Alopecia:

Shukla et a. investigated the effect of helium-neon (He-Ne) laser (632 nm), at doses of 1 and 5 J/cm^2 at 24 hour intervals for 5 days, on the cyclical hair follicle growth of Swiss albino mice skin, both with and without administration of testosterone [38]. The results showed that the mice that received He-Ne laser at a dose of 1 J/ cm^2 showed greater proportions of hair follicles in the anagen phase when compared those of the control group, which received no testosterone or He-Ne laser treatment. Furthermore, exposure of the mice to a dosage of 5 J/cm^2 showed a decrease in the proportion of hair follicles in the anagen phase when compared to the control group, which can possibly be attributed to the biphasic effect of LLLT [1, 38]. It was also noted that treatment with testosterone displayed an inhibition of hair growth with respect to the control group, which was indicated by a significant reduction in the proportion of catagen hair follicles [38]. Despite this finding, mice that were administered He-Ne laser at 1 J/cm^2 with testosterone still showed an increased percentage of anagen stage follicles when compared to testosterone alone. However when testosterone treated mice were exposed to He-Ne laser dose of 5 J/cm^2 a two-fold increase in the telogen stage hair follicles was observed [38]. The results showed that hair promoting ability of LLLT (He-Ne laser 1 J/cm^2) was higher in combination with testosterone, thus it can be proposed that cells possessing slow rates of growth or being subjected to stressful conditions respond better to the stimulatory effects of LLLT. Another noteworthy finding of the study was that; in the skin irradiated by the He-Ne laser (1 J/cm^2), some of the anagen follicles possessed a different orientation and appeared from a greater depth [38]. These follicles are characteristic of late anagen phase of the hair growth cycle and thus it is suggested that LLLT may act by prolonging the anagen phase of the hair follicles [39, 40]. Also, in the He-Ne (1 J/cm^2) irradiated skin that received testosterone treatment it was observed that the hair follicles originated from the middle of the dermis and such type of follicles are generally seen during early anagen phase [38].Thus when considering the above mentioned observations, it can be concluded that LLLT is able to stimulate re-entry of telogen and catagen follicles into anagen phase.

24 male androgenetic alopecia (AGA) patients were evaluated via global photography and phototrichogram using 655 nm red light and 780 nm IR light once a day for a period of 10 minutes [41]. Following 14 weeks of treatment significant increases in hair density and anagen/telogen ratio were observed at both the vertex and occiput, with 83% patients reporting that the treatment resulted in satisfactory results [41].

Satino et al. conducted a study to investigate the efficacy of LLLT on hair growth and tensile strength involving 28 male and 7 female AGA patients [42]. Each patient was given a 655 nm HairMax LaserComb® to use at home for a period of 6 months, applying it for five to ten minutes per day on alternate days [42]. Regarding the tensile strength of the hair, the results showed improvements in hair growth in all treated areas for both male and female sexes, however in the case of males the greatest improvements were observed in the vertex area whereas for females, the best improvements were seen in the temporal area [42]. With regards to hair count, again all treated areas of both sexes showed improvement, but the vertex area showed the greatest improvement for the male patients [42]. Leavitt et al. conducted a double-blind, sham device-controlled, multi-center, randomized 26 week trial where they tested the same device on 110 male AGA patients [22]. The patients were made to use the device three times a week for fifteen minutes for a total period of 26 weeks [22]. Noticeable increases in mean terminal density of hair had been reported in the treatment group when compared to the sham treatment group [22]. Also, subjective assessments of the patients over the 26 week period reported prominent improvements in overall hair regrowth, decreased rate of hair loss, thicker feeling hair, scalp health and hair shine [22].

2.2.3 LLLT for Chemotherapy Induced Alopecia

Around 65% of the patients receiving chemotherapy for cancer develop alopecia which can have detrimental effects on psychological health of the patient [43]. It has been proposed that LLLT could serve as treatment modality to stimulate and promote hair growth in cases of chemotherapy induced alopecia. In one study, a rat model was given varying regimens of chemotherapy is conjunction with LLLT administered with a device possessing components (laser unit and switch, lacking comb or handle) of the Hair Max LaserComb [44]. In all rats that were given laser

treatment, hair regrowth occurred at a faster rate when compared to the sham treatment group. Additionally, LLLT did not hinder the efficacy of the chemotherapeutic procedures [44].

3. LLLT for Fat Reduction

3.1 Lipoplasty and Liposuction:

Charles Dujarrier, a French surgeon, first introduced the concept of lipoplasty (also known as liposuction) in the 1920s. Dujarrier attempted to perform body sculpting on the knees of one of his patients, a ballerina, but ultimately the patient ended up developing gangrene, leading to amputation of her affected limb and thus the notion of lipoplasty faced a major setback [45]. In 1974, Dr. Giorgio Fischer and his son reintroduced liposuction, and they innovatively utilized oscillating blades within a cannula to chisel away subcutaneous fat [46]. In 1983, YG Illouz reported his 5-year experience with a new liposuction technique that could utilize relatively large cannulas along with suction tubing to securely remove fat from several regions of the body [47]. This ushered in the era of modern lipoplasty. Over the following decades, the concept of tumescent liposuction allowed for better results and decreased morbidity associated with liposuction.

3.2 LLLT for Fat Reduction:

In 2000 Niera et al. demonstrated the use of low level laser as new means for liposuction, and successfully utilized it with doses that did not produce any detectable increases in tissue temperature or cause any noticeable macroscopic alterations in the tissue structure [48, 49]. Prior investigations concerned with the effects of LLLT on wound healing, pain relief and edema prevention paved the way for this therapeutic application [50, 51]. The development of LLLT as a therapeutic modality to augment liposuction while avoiding macroscopic tissue alterations were based on determination of optimal parameters such as wavelength and power output for use [52]. Evidence suggests that wavelengths suitable for biomodulation range between 630 and 640 nm [53-58]. Niera et al. made several intriguing observations regarding the effects of LLLT on adipocytes. They utilized low level diode laser (635 nm) and a maximal power of 10mW with energy values ranging from 1.2 to 3.6 J/cm^2 [48]. Using scanning electron microscopy (SEM) and transmission electron microscopy (TEM) it was demonstrated that adipocyte plasma membranes exhibited transitory pore formation as result of irradiation. It was formulated that this enabled the release of intracellular lipids from the adipocytes and thus supplemented the liposuction as it was expected to reduce the time taken for the procedure, allowed for extraction of greater volumes of fat and overall, reduced the energy expenditure of the surgeon.

Although the findings associated with LLLT enjoyed much praise and enthusiasm, an extensively study conducted put these findings surrounding LLLT into question [59]. In their study, cultured human preadipocytes did not show any differences when compared to non-irradiated cells after 60 minutes of irradiation using an LLLT source (635 nm and fluence 1 J/cm^2) [59]. Furthermore, histological examination of lipoaspirates, in a porcine model exposed to LLLT for 30 minutes and human lipoaspirates, failed to demonstrate transitory pores when analyzed using SEM [59]. Additional data, raised questions regarding the ability of red light (635 nm) to effectively penetrate below the skin, into the sub-dermal tissues [60]. Peter Foddor supportively stated: “One could postulate that the presence of the black dots on scanning electron microscopy images on the surface of fat cells reported by Neira et al. could represent an artifact.” [59]. Since the data reported by Brown et al. from 2004, there have been several publications reporting the efficacy of LLLT.

3.2.1 Mechanism of Action of LLLT on Fat Reduction:

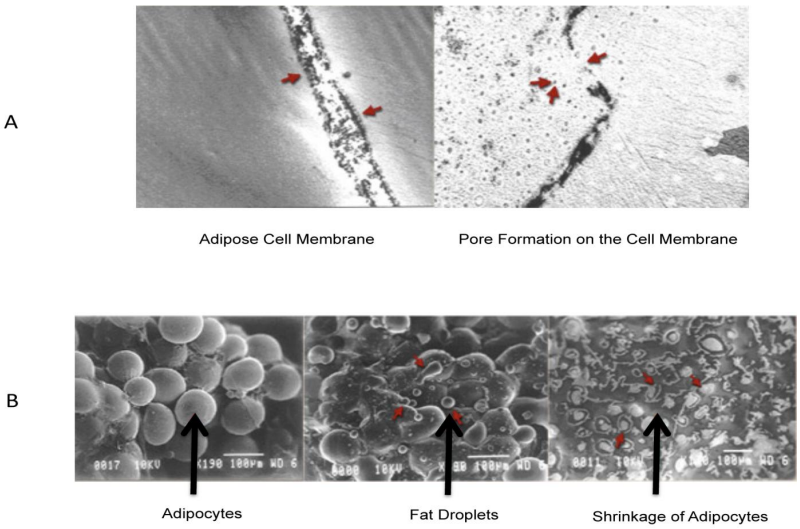

Figure 4: Formation of transitory micropores and shrinkage of adipocytes following LLLT. **A.** Formation of a transitory pore forming in the bi-lipid membrane of an adipose cell causing fatty contents of the cell to evacuate [48]. **B.** Secretion of triglycerides and fatty acids and shrinkage of adipocytes [48].

In the original paper published by Neira et al. the fat liberating effects of LLLT on adipocytes were attributed to its ability to induce transitioning micropores which were visualized with the help of SEM (**Figure 4)** [48].Furthermore, it was postulated that this stimulated the release of intracellular lipids from the adipocytes. Based on this, it was formulated that up to 99% of the fat stored within the adipocytes could be released and subsequently removed with the help of LLLT (635 nm, 10W intensity, 6 minutes irradiation time) [48]. Re-cultured adipocytes exhibited a tendency to attain their native cellular conformation which was further confirmed by Caruso-Davis et al. utilizing a live-dead assay to assess the viability of these adipocytes following irradiation [61]. Increase in ROS following LLLT has been proposed to bring about lipid peroxidation within the cell membrane which may cause damage and may present as the transitory pores. This may cause temporary damage that presents as transitory micropores. [30, 62-64]. However, when Brown et al. attempted to replicate Neira et al's findings [48], they failed to visualize any transitory micropores via SEM [59]. No further SEM studies have documented these pores, but many publications have reported findings that indirectly support the transitory micropore formation theory. Another proposed mechanism that explains the release of intracellular lipids form adipocytes, suggests the activation of the compliment cascade which is responsible for induction of adipocyte apoptosis and subsequent release of intracellular lipid components [61]. To test the feasibility of this theory Caruso-Davis et al. exposed differentiated human adipocytes to plasma and exposed one group of cells to laser, while the control group received no laser intervention [61]. Other evidence is suggestive of LLLT's ability to stimulate an increase in cAMP levels [65, 66]. cAMP is accountable for activation of certain protein kinases which further activate certain enzymes and these enzymes are responsible for the breakdown of triglycerides into fatty acids and glycerol both of which can penetrate the adipocyte membrane [67, 68]. However, findings from Caruso-Davis et al's studies on *in vitro* cell cultures of human adipocytes treated with LLLT (635-680 nm for 10 min) did not exhibit any increase in glycerol and fatty acid levels suggesting that fat liberation from adipocytes in response to LLLT is not due to lypolytic stimulation of the adipose tissue. Interestingly enough, as the cellular components were being examined, the presence of triglycerides in the supernatant seemed to support the theory involving transient pore formation in adipocytes [61]. Although these mechanisms have been worked out independently, the mechanism by which triglycerides would traverse the adipocyte lipid membrane remains the most enigmatic.

Following the initial results that Neira et al. obtained [48], they extracted samples of adipose tissue from lipectomy

samples obtained from patients through the tumescent method and exposed them to a 10-mW diode laser (635 nm) with total fluence values ranging from 1.2 - 3.6 J/cm^2 for a period of 0 to 6 minutes. They discovered that the tumescent method facilitated laser penetration and intensity, thus allowing for enhanced fat liquefaction [48]. A similar set up to test the effect of LLLT on the lipectomy, where 12 female patients undergoing lipectomy received extraction of both deep and superficial fat, infra-umbilically, using the tumescent method, followed by LLLT **(Figure 6)** [48]. Results again showed the synergistic ability of LLLT to effectively work with the tumescent technique for effective fat removal [48]. It was observed that without laser irradiation the fat tissue remained intact and the fat cells maintained their original spherical shape. The supplementary effect of the tumescent method on LLLT is thought to due to stimulation of epinephrine induced cAMP production by adenyl cyclase and/or enhanced penetrative ability and intensity facilitated by the tumescent solution [48].

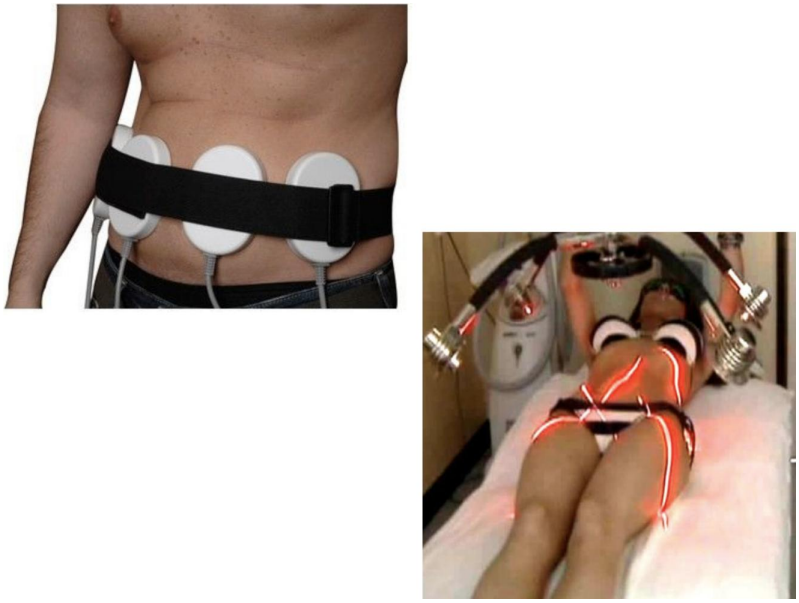

Figure 5: Examples of external LLLT devices for use in fat reduction and cellulite treatment.

4. Conclusion:

LLLT has been investigated as a novel therapeutic modality for treatment and management of several dermatological conditions. Majority of the applicable effects of LLLT are applicable for some form of skin rejuvenation (reversal of photodamage for the most part). Thus, several studies have demonstrated the use of LLLT for photorejuvination, treatment of acne, vitiligo, photoprotection, etc. and more recent studies demonstrate the potential LLLT possesses for treatment of alopecia, fat and cellulite. Moreover, LLLT serves as a modality that is more patient-friendly through its noninvasive actions with very mild side-effects, if any. LLLT shows promise for future applications being a novel treatment modality that works with great efficacy in combination with certain existing options. With growing acceptance and extensive research in the field of photomedicine it can be proposed that LLLT among other phototherapeutic modalities will continue to grow and emerge as a versatile tool in the field of dermatology.

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