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Angeli E. Torres
Henry Ford Health, atorres5@hfhs.org

Henry W. Lim
Henry Ford Health, hlim1@hfhs.org

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REVIEW ARTICLE

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Photobiomodulation for the management of hair loss

Angeli Eloise Torres | Henry W. Lim

Photomedicine and Photobiology Unit, Department of Dermatology, Henry Ford Health System, Detroit, MI, USA

Correspondence
Henry W. Lim, MD, Department of Dermatology, Henry Ford Medical Center, 3031 West Grand Boulevard, Suite 800, Detroit, Michigan 48202, USA.
Email: hlim1@hfhs.org

Abstract

Photobiomodulation, otherwise known as low-level laser (or light) therapy, is an emerging modality for the management of hair loss. Several randomized trials have demonstrated that it is safe and potentially effective on its own or in combination with standard therapies. These devices come in many forms including wearable caps or helmets that afford hands-free and discreet use. Models with light-emitting diodes (LEDs) are less expensive compared to laser-based devices and do not require laser safety considerations, thus facilitating ease of home use. Limitations include cost of the unit, risk of information bias, and lack of standardized protocols. Finally, as with any hair loss treatment, patients' expectations with regards to therapeutic outcomes must be managed.

KEYWORDS

alopecia, hair growth, low-level laser, low-level light therapy, photobiomodulation

1 | INTRODUCTION

It is estimated that about 50% of men and women will experience some form of hair loss over the course of a lifetime.[1] Although hair loss in itself does not directly result in any functional impairment, its impact on an individual's outward appearance can cause significant psychological issues including anxiety, depression, social phobia, post-traumatic stress disorder, and suicidality.[1] Regardless of the type of alopecia, the prospect of a long-term and even permanent hair loss is especially distressing to patients, prompting them to seek treatment aggressively. Many options, both prescription and over-the-counter, are available and have been used to treat different types of hair loss albeit with varying success.

An emerging treatment for hair loss is photobiomodulation (PBM), which is also known as low-level laser (or light) therapy (LLLT). The terms PBM and LLLT will be used interchangeably throughout this article. PBM was first introduced during the 1960s and has been used for a variety of indications including wound healing, nerve regeneration, pain reduction, body contouring, and even tinnitus.[2,3] Its potential for hair restoration was first discovered in 1967 by Endre Mester after inadvertently inducing hair regrowth in experimental mice using a ruby laser.[4] In 2007, the HairMax LaserComb (Lexington International) became the first LLLT device to be granted clearance by the United States Food and Drug Administration (US FDA) for the treatment of pattern hair loss in men and was expanded to include women in 2011. As of September 2020, there are 66 LLLT devices registered with the US FDA.[5]

Low-level laser (or light) therapy devices are generally categorized into: (a) stationary hoods, (b) hand-held combs or brushes, (c) headbands, and (d) caps or helmets.[6] Stationary hood designs are common in office-based LLLT devices like the Capillus272 Office Pro (Curallux)[7] and the Sunetics Clinical Laser (Sunetics International Marketing Group).[8] Combs and brushes are capable of parting the hairs on the scalp thus facilitating better penetration of light to the hair follicle; however, they require manual movement by the patient especially for those with extensive scalp involvement. In contrast, hat-based systems such as caps or helmets have the advantage of being "hands-free".[9] Caps in particular offer the added benefit of discreet use. An example is the Capillus Laser Therapy Cap (Curallux), which received FDA clearance in 2015.[5] Following its commercial success, the potential role of LLLT in the management of other types of hair loss such as alopecia areata (AA) and scarring alopecias have

been explored, although no device has been approved by the US FDA for these indications. This review focuses on clinical studies involving home LLLT devices that employ a hat-based system and their efficacy on different types of alopecia.

2 | BASIC CONCEPTS IN PHOTOBIOMODULATION

Photobiomodulation involves the use of light within the visible red (600-700 nm) or near infrared (NIR) (700 nm-1400 m) range[10] that is produced from a laser or light-emitting diode (LED) source. These wavelengths coincide with the "optical window" of mammalian skin, that is, the wavelength at which there is maximal absorption of light.[11] Unlike regular lasers which produce tissue heating or ablation, absorption of light by a chromophore in PBM produces a photochemical effect that is analogous to photosynthesis in plants.[11] Cytochrome C oxidase, a member of the mitochondrial electron transport chain, acts as the chromophore that leads to production of adenosine triphosphate (ATP), generation of reactive oxygen species, and induction of cell signaling. This results in cell proliferation, down-regulation of inflammation, increased tissue oxygenation, wound healing, nerve regeneration, and pain reduction.[12] Recently, PBM has been found to enhance the expression of signaling molecules of the Wnt/B-catenin pathway, which is involved in the initiation of growth and development of hair follicles.[13]

A key concept in PBM is the precise modulation of the dose delivered whereby too low of a dose would be inadequate to produce a response, while too high would cause an inhibitory effect.[11] This concept has been demonstrated in several dose-response studies.[14,15] It is also thought to be responsible for the paradoxical hair growth that is sometimes seen in laser hair removal, as well as the failure of LLLT to produce hair growth in some trials.[11] For purposes of hair growth, a dose of 4 J/cm^2 at wavelengths between 630 and 660 nm, irradiance of 5 mW/cm^2 and treatment duration of 10-20 minutes is typically employed.[6] The total dose delivered to the scalp and the time required to deliver the desired dose are determined by the number of laser diode or LED units built into the device, such that a greater number of units will have higher power density or irradiance, and therefore require less time to deliver a desired dose.[6]

As mentioned, the light generated in LLLT may either come from a laser or LED source. Until the early 2000s, LLLT devices reported in literature consisted of purely lasers, either from a helium-neon (He-Ne) lamp or laser diode. It was believed that the beneficial effects of PBM were due to the laser's innate properties, namely coherence, monochromaticity, or collimation. However, one review argued that since PBM is meant to elicit a photochemical rather than a thermal or ablative effect, it is not necessary for the light source to be coherent.[16] Several in vitro, animal, and human studies comparing photobiomodulation using laser versus LED (an incoherent light source) revealed that the two are equally effective in terms of wound healing, reducing inflammation, and relieving pain.[17-20] Furthermore, LEDs are less expensive and do not require the cautionary measures that must be observed with lasers, which facilitates ease of home use.[16] The key differences between laser and LED are summarized in Table 1. Currently, many commercially available PBM devices have light sources that consist of LED only (Revian Red, PhotonMD Inc.),[21] or a combination of laser and LED (Tables 2 and 3).

TABLE 1 Differences between laser and light-emitting diode (LED)

Laser	LED
Coherent	Incoherent
Collimated	Divergent
Very narrow bandwidth (<1 nm)	Wider bandwidth (1-2 nm)
Higher cost per mW	Lower cost per mW

3 | PHOTOBIOMODULATION AS HAIR LOSS TREATMENT

3.1 | Androgenetic alopecia

Androgenetic alopecia (AGA) is the most common type of hair loss in both men and women. It affects 80% of Caucasian men and up to 42% of Caucasian women by the age of 70,[22] hence, it has been regarded by some as a normal part of the aging process. The characteristic pathology is a progressive miniaturization of the hair follicle that leads to formation of thin, short (vellus) hair. Currently, the only treatments approved by the United States Food and Drug Administration (US FDA) for AGA are topical minoxidil solution and oral finasteride,[23] while oral dutasteride is approved in South Korea and Japan.[24] Other options include oral bicalutamide,[25] oral spironolactone, intralesional injections with platelet rich plasma (PRP), and hair transplant.[23]

Several randomized controlled studies have demonstrated that PBM for AGA is safe and effective either alone or in combination with prevailing therapies. One of the earliest studies investigated the hair growth promoting capability of a 655 nm laser handheld LLLT device with a comb attachment (HairMax LaserComb; Lexington International) in men with AGA. Results showed that patients who used the HairMax LaserComb for 15 minutes thrice weekly for 26 weeks had increased terminal hair density from baseline, while those who received a sham device noted a decrease in terminal hair density. No serious adverse effects were reported.[26] It was this study that eventually paved the way for FDA clearance of the HairMax LaserComb.[27]

The 650 nm Capillus Laser Therapy Cap (Curallux), then known as the Handi-Dome Laser device, was debuted in a trial by Friedman et al In this study, 44 women with AGA were randomized to undergo home treatment with either the laser cap or a

TABLE 2 Summary of PBM/LLLT devices evaluated for the treatment of androgenetic alopecia in human trials

Device	Specifications	Irradiance[a] (mW/cm^2)	Study design	Subjects	Treatment parameters	Results	Reference
HairMax LaserComb[b]	655 nm laser (9 units)	Not specified	Double-blind, sham device-controlled, multicenter RCT	110 males	15 min, 3×/wk for 26 wks	Significant increase in mean terminal hair density by 19.8 hairs/cm^2 in device-treated group versus decrease by 7.6 hairs/cm^2 in sham-treated group.	26
			Retrospective observational study	42 (21 females, 11 males)	8-15 min, 3×/wk, variable duration (2-24 mo)	Significant improvement in 25% (8/32), moderate improvement in 63% (20/32), and no improvement in 12% (4/32) based on global photographic assessment.	34
Capillus Laser Therapy Cap (CapillusPro)[c]	650 nm laser diode (272 units)	5	Double-blind, sham device-controlled, multicenter RCT	44 females	30 min, every other day for 17 wks	Significant increase in terminal hair counts by 51% compared to sham-treated patients.	28
RAMACAP helmet[d]	660 ± 10 nm laser diode (224 units)	3.5 (max: 5), Dose: 4 J/cm^2	Double-blind, sham device-controlled, single center RCT	40 (20 females, 20 males)	20 min, 3×/wk for 24 wks	Device-treated group showed significant increase in mean hair density by 10.21 hairs/cm^2 versus 3.95 hairs/cm^2 in sham-treated group) and mean hair diameter by 6.11 μm (versus 3.76 μm in sham-treated group).	9
Oaze helmet[e]	630 nm LED (24 units), 660 nm LEDs (18 units), 650 nm laser diode (27 units)	3.5 (630 nm), 2.5 (660 nm), 4 (650 nm)	Double-blind, sham device-controlled, multicenter RCT	40 (14 females, 26 males)	18 min, daily for 24 wks	Device-treated group showed significant increase in mean hair density by 17.2 hairs/cm^2 (versus decrease by 2.1 hairs/cm^2 in sham-treated group) and mean hair thickness by 12.6 μm (versus 3.9 μm in sham-treated group).	29
iRestore ID-520 helmet[f]	660 ± 5 nm LED (27 units), 650 ± 10 nm laser diode (27 units)	≤22 (LED), ≤4.6 (laser)	Double-blind, half-head, sham device-controlled, single center RCT	100 (17 females, 83 males)	30 min, 3×/wk for 24 wks	Significant increase in hair coverage (14.2%) on LLLT-treated side versus sham-treated side (11.8%) based on gross photographic assessment; Device-treated side showed significant increase in hair count, hair thickness and investigator's global assessment versus sham-treated side	30
Revian Red cap[g]	620 nm and 660 nm LED (119 units)	Not specified	Double-blind, sham device-controlled, multicenter RCT	81 (21 females, 60 males)	10 min daily for 26 wks	Average increase in target area hair count by 26.3 per cm^2 as early as 16 wks among device-treated group versus sham-treated group.	32

(Continues)

TABLE 2 (Continued)

Device	Specifications	Irradiance[a] (mW/cm^2)	Study design	Subjects	Treatment parameters	Results	Reference
iGrow helmet[h]	655 nm laser diode (21 units), 650-670 nm LED (30 units)	<5	Single-blind, single center, three-arm RCT	45 females	25 min, 3×/wk for 4 mo	Downgrading of Ludwig classification in all patients, but greatest in LLLT + minoxidil; LLLT monotherapy patients showed significant increase in hair density from baseline, but no significant difference when compared to LLLT + minoxidil and minoxidil alone.	33

Abbreviations: F, female; LLLT, low-level light (or laser) therapy; M, male; PBM, photobiomodulation; RCT, randomized controlled trial.

[a]Per unit of laser or LED.

[b]Lexington International, Boca Raton, Florida.

[c]Curallux, Miami, Florida.

[d]Ramathibodi Hospital Division of Dermatology and National Innovation Agency, Thailand.

[e]Won Technology, Daejeon, Korea.

[f]WELLMIKE Technology Corporation, New Taipei City, Taiwan.

[g]PhotonMD Inc., Morrisville, North Carolina.

[h]Apira Science, Boca Raton, Florida.

TABLE 3 Summary of PBM/LLLT devices evaluated for the treatment of other types of hair loss in human trials

Device	Specifications	Irradiance[a] (mW/cm^2)	Study design	Subjects	Treatment parameters	Results	Reference
Alopecia areata							
Super Lizer[b]	600-1600 nm polarized linear light with probe (in-office procedure)	1.8	Single-arm study	15 (9 females, 6 males)	4-s pulses every 1 s for 3 min, every 1 or 2 wks, variable duration (average: 1.8 mo)	Hair regrowth in more than 50% of involved areas in 7 out 15 patients	40
Lichen planopilaris							
Capillus Laser Therapy Cap (CapillusPro)[c]	650 nm laser diode (272 units)	5	Case series	42-year-old, female	6 min daily for 18 mo	Reduction peripilar casts on dermoscopy and improvement of symptoms (itching)	42
Capillus Laser Therapy Cap (Capellux 19)[c]	660 nm laser diode (204 units)	25.5	Case series	28-year-old, female	7 min daily for 12 mo	Reduction peripilar casts on dermoscopy and improvement of symptoms (itching)	42
Tricoglam helmet[d]	650 nm LED (105 units)	5	Case series	2 females (60- and 65-year-old)	5 min/d or 20 min, 2×/wk for 6 mo	Reduction peripilar casts on dermoscopy and improvement of symptoms (itching)	42

Abbreviations: F, female; LLLT, low-level light (or laser) therapy; M, male; PBM, photobiomodulation; RCT, randomized controlled trial.

[a]Per unit of laser or LED.

[b]Tokyo Iken, Tokyo, Japan.

[c]Curallux, Miami, Florida.

[d]Jeffrey Paul's Hair & Scalp Specialists, Fairview Park, Ohio.

sham device for 30 minutes every other day for 17 weeks. Results showed that participants who received the active device had 51% more terminal hair count from baseline compared to controls and no adverse reactions or side effects were reported.[28] Similarly, a study done in Thailand revealed that men and women who used a 660 nm helmet-type laser device for 24 weeks exhibited greater mean hair density and diameter by almost 3-fold, and 2-fold, respectively, compared to placebo. Two laser-treated participants reported pruritus that resolved spontaneously and did not warrant discontinuation of therapy.[9]

A helmet-type device (Oaze; Won Technology) consisting of 630 nm LEDs, 660 nm LEDs, and 650 nm laser diodes was utilized in a study by Kim et al In this trial, participants who underwent LLLT for 18 minutes daily for 24 weeks exhibited greater hair density and hair thickness from baseline compared to placebo (sham device).[29] In addition, a 24-week half-head comparison of a laser-LED helmet device (650 nm laser diode with 660 nm LED) versus placebo revealed significantly greater increases in hair coverage, hair count, and hair thickness from baseline on the treated side as compared to the non-treated side which showed a decrease in these parameters. Eczema, pruritus, and acneiform eruption were the reported side effects.[30]

In 2018, an all-LED, dual wavelength (620 nm and 660 nm) LLLT cap device known as the Revian Red (PhotonMD Inc.) received FDA clearance for the treatment of AGA in men and women.[31] Its efficacy and safety were evaluated in a prospective, randomized controlled, double-blind study involving 81 subjects who were asked to use the device for 10 minutes daily. Results showed that after 16 weeks, patients who were treated with Revian Red had an average increase in target area hair count by 26.3 per cm^2 The most common treatment-related adverse effects were pruritus, dandruff, and rash.[32]

Photobiomodulation has been found to work synergistically with approved therapies for AGA. One study involving 45 women compared LLLT with a laser-LED helmet device (iGrow, Apira Science) versus minoxidil 5% solution versus a combination of the two. After 4 months, all treatment groups exhibited downgrading of Ludwig classification for female pattern hair loss, with greatest improvement seen among those who utilized combination therapy.[33] Similarly, a study conducted by Munck et al[34] compared the combination of HairMax LaserComb with topical minoxidil or oral finasteride versus HairMax LaserComb alone and found that LLLT on its own is potentially effective but works better when co-administered with medical therapy.

The exact mechanism as to how PBM induces hair growth in AGA is still poorly understood but is postulated to be due to increased proliferation of matrix cells in the hair follicle as a result of the activation of the cellular respiratory chain.[26,35] Additionally, the irradiation causes an increase in blood circulation at the dermal papilla, which provides a boost of metabolic activity to the proliferating cells.[10,26] PBM has also been hypothesized to drive telogen follicles into anagen phase and prolong its duration, resulting in production of longer and thicker (terminal) hair.[23]

3.2 | Alopecia areata

Alopecia areata (AA) is an autoimmune, inflammatory, non-scarring hair loss disorder with a lifetime incidence of 1.7%-2.1%. It can occur at any age, but is most prevalent among children and young adults.[36] The characteristic histologic finding is a peribulbar infiltration of T-lymphocytes resembling a "swarm of bees."[37] A variety of therapeutic agents including topical, intralesional, and systemic treatments have been used in AA, but none have been proven to sustain remission.[38]

Unlike AGA, there is limited data regarding PBM for AA. A 2012 animal study revealed that the HairMax LaserComb successfully elicited hair growth in a C3H/HeJ mouse model for AA with histologic evidence of increased anagen hair follicles. This was in contrast to sham-treated mice which demonstrated no response and showed telogen follicles with absent hair shafts on histology.[39] Meanwhile, one study which utilized an infrared light instrument (Super Lizer; Tokyo Iken) successfully elicited hair regrowth in 7 out of 15 patients in an average of 1.8 months of 1-2× weekly use. There were no adverse reactions except for a sensation of heat reported by one patient.[40]

The mechanism through which PBM induces hair growth in AA is thought to be anti-inflammatory. Activation of the electron transport chain shifts the macrophage activated in AA from a pro-inflammatory M1 to an anti-inflammatory M2 phenotype, thereby reducing the inflammation that otherwise attacks the hair follicle and causes hair loss.[6]

3.3 | Lichen planopilaris

Lichen planopilaris (LPP) is a scarring type of hair loss that tends to be more frequent among adult females.[41] In general, scarring alopecias differ from non-scarring alopecias in that inflammation results in destruction of the hair follicle that leads to permanent loss of hair growing capability. As such, the goal of therapy is to retard the progression of hair loss by reducing inflammation.[42]

In a case series of four females aged 28-65 with lichen planopilaris, the use of a 650 nm laser cap device for 5-7 minutes daily as an adjuvant to medical therapy resulted in decreased clinical and dermoscopic signs of active disease, namely scalp erythema, pruritus, hair shedding, and peripilar casts at 3 months. There was also evident regrowth of hair and no adverse reactions were reported. Of note, no comparison with medical therapy alone was presented. Reduction of inflammation is the likely mechanism of PBM in these cases.[42]

4 | LIMITATIONS OF PHOTOBIOMODULATION

Photobiomodulation has several limitations. Among them, the most evident is the cost of the unit. The price of the PBM devices

mentioned in this review range from US $200 (HairMax LaserComb) to US $3000 (Capillus Laser Therapy Cap).[43-45] LEDs cost significantly lower than lasers. One review noted that the cost per mW of LEDs is about 100× lower than lasers.[16] Hence, their addition in some models may be an effort to lower costs.

While majority of the LLLT devices available in the market are designed for home use, given the upfront cost of these units, office-based treatment may be suitable for patients who wish to have a trial of PBM prior to purchasing their own device.[46] However, in-office PBM can be inconvenient for patients who have poor access to a medical facility, or who have limited availability in their schedule to commit to regular clinic visits. To date, there are no studies comparing home-based versus office-based PBM.

Another limitation is the lack of a standardized protocol.[42] Despite positive results in numerous trials, the efficacy data of PBM were specific to the device tested, and therefore are difficult to extrapolate. Besides a risk for bias due to most studies being sponsored by the manufacturer, there is variability in the devices and treatment parameters used in these trials (see Tables 2 and 3). In addition, there is not enough data to determine the ideal patient candidate.[47] A vast majority of these devices have been tested on patients with Fitzpatrick skin phototype I-IV only, which is likely due to anticipated difficulties with visualizing the hair in patients with darker skin thus precluding proper evaluation (ie, hair counting). As such, whether skin phototype, hair texture, or hair follicle shape affects the efficacy of PBM remains to be determined.[48]

5 | CONCLUSION

Photobiomodulation or LLLT is a safe and potentially effective modality for the management of hair loss. It can be conveniently administered from home, and certain models offer hands-free, discreet use.

Among the devices reviewed above, the Capillus Laser Therapy Cap stands out in terms of design (sports cap style), treatment time (6-7 minute sessions daily), and available data (tested on different types of hair loss). However, further large-scale studies on the different LLLT devices are needed in order to corroborate efficacy data, establish an optimal treatment protocol, and determine the ideal patient candidate. Based on currently available data, PBM may be recommended as an alternative for failed standard therapy or as an adjunct to prevailing treatments. The cost of PBM devices is a limitation, although combined laser-LED devices are less expensive options. Lastly, management of patients' expectations is an essential part of patient education.

CONFLICT OF INTEREST

AET has no relevant disclosures. HWL is an investigator for Incyte, Beiersdorf, L'Oréal, Pfizer, PCORI, has served as consultant for Pierre Fabre, ISDIN, Ferndale, and Galderma, and has participated as a speaker in general educational session for Pierre Fabre, Eli Lilly, Johnson & Johnson, and Ra Medical System.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

ORCID

Angeli Eloise Torres https://orcid.org/0000-0002-9551-2118
Henry W. Lim https://orcid.org/0000-0002-1576-1115

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