LED Therapy in Treating Androgenetic Alopecia

AN INDUSTRY WHITE PAPER

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Executive Summary

There are many FDA-cleared medical devices for treatment of alopecia, falling under one of two broad categories depending upon the light source, either lasers or light-emitting diodes (LEDs).

The evidence presented herein demonstrates LEDs are a superior choice for hair therapeutic devices:

- Separate randomized, placebo-controlled, double-blind, multicenter studies of four different FDA-approved treatments for AGA demonstrated the greatest increase in hair growth from an at-home LED device, followed by an at-home laser device, and then two pharmacological treatments.
- The wider spectral bands of peak wavelength light transmitted by LEDs create greater absorbance of photons by cellular chromophores and photoreceptors, resulting in more biological effects.
- Light generated by LEDs penetrates human facial skin 16% more effectively than that of lasers.
- There is no evidence that the unique physical properties of laser light, such as coherence or collimation, produce better, or different degrees of photobiomodulation than LED light does. In fact, the light dispersal pattern of lasers limits the coverage of the skin, yielding less effective dosing.
- These key findings demonstrate that there are specific clinical advantages of LED light-based devices including uniformity of scalp coverage, better absorption, and greater activation of target tissue.

While it is understood lasers have enjoyed a longer track record which has allowed for greater acceptance in the field, contemporary research, as outlined above, shows LEDs are, in fact, a better choice for hair therapeutic devices.

Background

For patients with androgenetic alopecia (AGA) there are multiple treatment options, including light therapy to induce cell proliferation[1,2,3]. Such phototherapy is now commonly used either as part of a treatment regime or as a standalone treatment to arrest hair loss or stimulate hair growth. The purpose of this paper is to assist hair-loss treatment professionals in choosing the best light therapy option for their patients.

FDA-cleared devices using light to treat AGA fall under two broad categories: those utilizing LEDs as the light source and those utilizing lasers. The application of light to human cells to directly induce cellular activity is known as photobiomodulation (PBM)[2]. The light sources used in PBM are of low intensity, hence the treatment is termed low-level light therapy (LLLT)[3,4].

As laser-based devices were first to be used for PBM, and specifically for treatment of hair loss, there is broad evidence for the efficacy of lasers[7]. However, in contemporary research, there is a rapidly growing and substantial body of evidence for the effectiveness of LED-based devices[3].

That research, as well as underlying scientific theory, indicates that LEDs are at least as effective as lasers. In fact, there are several distinct, science-based clinical advantages to choosing an LED device over a laser device for treatment of hair loss.

This paper will:

- Highlight the current clinical evidence comparing the effectiveness of the two light sources.
- Outline the scientific points for why LEDs are just as effective for producing photobiomodulation.
- Describe the clinical advantages which highlight LEDs as a better choice than laser-based therapy for treatment of hair loss.

Clinical Evidence Comparing Lasers to LEDs for Light Therapy of Alopecia

LED phototherapy has been reported to be effective in a variety of clinical conditions, including wound healing, skin rejuvenation, pain reduction, viral diseases, and allergy-related conditions[3].

To date (April 2024), there are no published head-to-head studies directly comparing the use of lasers versus LEDs to treat AGA. However, from the published study data of the various FDA-approved treatments for AGA, we can extract results showing the effectiveness of an LED device compared to a laser device and two pharmacological treatments; these results are seen in Table 1.

TABLE 1:
NET CHANGE IN HAIR COUNT FOR VARIOUS FDA-APPROVED TREATMENTS FOR ANDROGENETIC ALOPECIA, EVIDENCE FROM RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, MULTICENTER STUDIES

TREATMENT	NET CHANGE IN HAIR COUNT
REVIAN RED® LED CAP	+26.3 HAIRS/CM2 AT 16 WEEKS[11]
HAIRMAX® LASERCOMB	+19.1 HAIRS/CM2 AT 16 WEEKS[12]
MINOXIDIL (ROGAINE®)	+16.2 HAIRS/CM2 AT 16 WEEKS[13]
FINASTERIDE (PROPECIA®)	+11.6 HAIRS/CM2 AT 26 WEEKS[14]

The net change in hair count for each treatment was calculated using the following formula:

$$\text{NET CHANGE IN HAIR COUNT} = \left(\text{MEAN \# OF } \frac{\text{hairs}}{\text{cm}^2}\right) - \left(\text{MEAN \# OF } \frac{\text{hairs}}{\text{cm}^2}\right) \text{PLACEBO}$$

For the two medical devices, the placebo patients were those who used a similar device with only sham illumination. Specifically, the sham LED cap emitted no light and the sham laser comb emitted white light. As seen in the table, all four treatments resulted in a positive net change in hair count, but the increase was significantly greater with the LED device. Notably, both medical devices performed better than the two systemic pharmaceutical compounds. In addition, the medical devices were used on both male and female patients, while the Minoxidil and finasteride trials only included male patients. The age range of study patients in the Revian LED cap trial was broader than that of the Hairmax laser comb trial, 19–69 years old vs. 25-61 years old, respectively.

Preclinical and animal studies have directly compared the two light treatment modalities for various medical conditions. A literature search for a clinical comparison found two papers from the same research group; neither of those studies evaluated the treatment of hair loss. The two studies are summarized in Table 2.

TABLE 2:
STUDIES DIRECTLY COMPARING LASER AND LED LIGHT THERAPY FOR OTHER CLINICAL CONDITIONS, AS OF FEBRUARY 2024

STUDY TITLE, AUTHORS, PUBLICATION DATE	PARAMETERS	FINDINGS
Photobiomodulation (Laser and LED) on sternotomy healing in hyperglycemic and normoglycemic patients who underwent coronary bypass surgery with internal mammary artery grafts: a randomized, double-blind study with follow-up[5]. Lima et al, 2017.	120 patients who underwent coronary artery bypass graft (CABG) surgery, randomly allocated into 4 groups of 30 patients each: control, placebo, laser, and LED. On the 8th postoperative day, their incision healing was evaluated by three blinded researchers for degree of hyperemia and wound closure. Sternotomy dehiscence was evaluated up to 1 month postop.	Patients who received LED and laser therapy had better improvements in hyperemia and wound closure compared to control and placebo groups ($p \le 0.05$) at 8 days postop. The improvements between the LED and laser therapy group were no different, to an even more significant p-value, $p \le 0.005$. At one month postop, no sternotomy dehiscence occurred in either the LED or laser groups but did occur in 1 patient in the placebo group and 2 in the control group.
Low-level laser and light-emitting diode therapy for pain control in hyperglycemic and normoglycemic patients who underwent coronary bypass surgery with internal mammary artery grafts: a randomized, double-blind study with follow-up[6]. Lima et al, 2016.	120 patients who had CABG surgery; randomly divided into 4 groups of 30 patients each: control, placebo, laser, and LED. On 6th and 8th postop days, pain levels evaluated by visual analog scale (VAS) and McGill Pain Questionnaire.	Laser and LED groups both showed greater decreases in pain than the placebo and control groups. No significant differences in pain reduction between laser and LED groups ($p \le 0.05$).

Both studies demonstrated that LEDs were as effective as lasers for treating sternotomy wound healing and providing pain relief after coronary artery bypass surgery.

In summary, direct, head-to-head clinical trials comparing LEDs and lasers concluded that LEDs were at least as effective as lasers for locally administered medical interventions. With regard to the treatment of androgenetic alopecia, there are multiple, scientifically backed clinical reasons why an LED device is more effective than a laser device in increasing hair growth; those reasons are outlined in the clinical advantages section, below.

There is No Sound Scientific Basis for Purported Greater Efficacy of Lasers over LEDs

PBM is initiated through absorption of light by cellular photoreceptors. This triggers the activation of multiple secondary cellular pathways, leading to significant shifts in cellular metabolism, cell signaling, cytokine secretion, and even gene expression[7]. Laser light has certain unique physical properties such as coherence and collimation; proponents of laser therapy claim these as the basis for the superiority of lasers to LEDs in the treatment of hair loss. However, the research supporting such reasoning is comprised of outdated and lower-quality literature. For example, the 2014 book titled Laser phototherapy-clinical practice and scientific background presented an argument favoring lasers over LEDs using supporting references published from 1973 – 2000. The majority of the cited publications are not indexed by the pre-eminent scientific publishing database PubMed[7], which complicates critical analysis of these nearly 25-year-old works within the context of advancements made in state-of-the-art LED treatment. Comparisons done during that period were flawed because clinically useful LEDs did not become available until after 1998, when a team at NASA developed LEDs with less light divergence, much higher and more stable output power, and other desirable optical properties[3]. The first clinical study using those advanced LEDs for phototherapy was published in 2001[17].

More recent research, conducted within the last 20 years, leads to the conclusion that photobiomodulation is not dependent on the collimation or coherence of lasers. In fact, physiological effects are produced by uncollimated, noncoherent LED devices[7].

Clinical Advantages of LEDs Over Lasers for Treatment of Hair Loss

As stated earlier, there are several science-backed clinical advantages to using LEDs rather than lasers for treatment of hair loss. Those include:

1. Greater area and uniformity of scalp coverage
2. Wider spectral peaks (wider emission spectrum)
3. Better penetration/transmittance

These advantages are discussed in greater detail, as follows:

1. Greater area and uniformity of scalp coverage

LEDs emit light in a Lambertian pattern that is broader than the limited pattern created by a laser diode. Specifically, multimode/transverse mode/broad-area lasers emit light in an oval-like pattern typically found in laser-based medical devices. This pattern leaves treatment "dead spots" where no light is being applied to the target tissue. To illustrate this, we compared the light emission patterns of two caps currently approved for treating hair loss: the laser-based Capillus PRO S1® and the LED-based Revian Red.

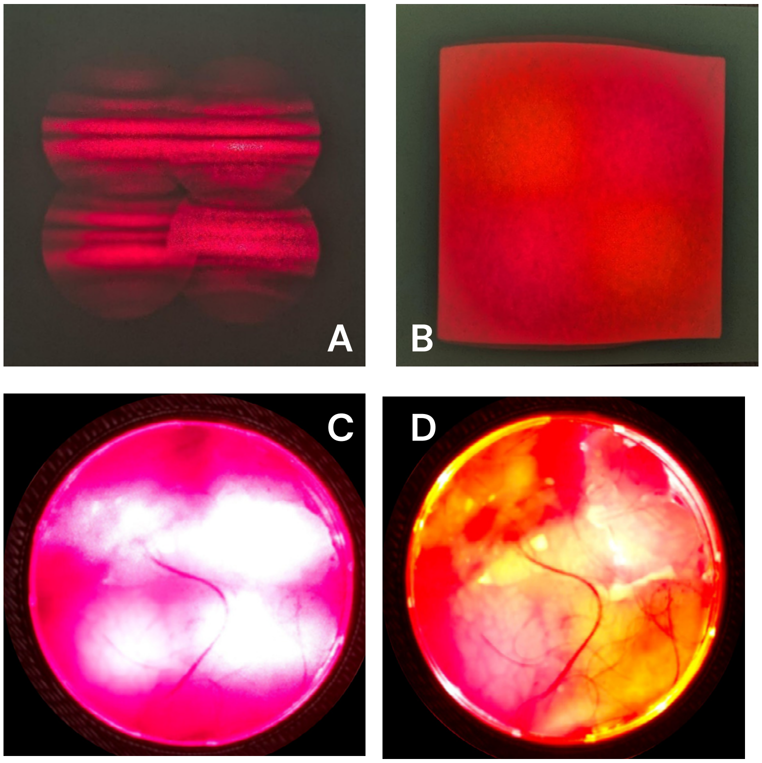

FIGURE 1:
COMPARISON OF LIGHT EMISSION PATTERNS OF LASER DIODES VS. LEDS [10]

Image A shows the emission pattern of 4 laser diodes taken from the Capillus PRO S1® laser cap, while Image B shows the emission pattern of 4 LEDs taken from the Revian Red LED cap, both through paper. Image C shows the emission pattern of the same laser diodes through a human skin sample and Image D shows the emission pattern of the same LEDs through that same skin sample.

PHOTOS BY REVIAN, INC.

As seen in Figure 1, Image A, the laser diodes produce oval or near-oval emission patterns, whereas the LEDs produce a continuous plane of light, as seen in Image B. Comparing images C and D, the emission patterns of laser and LED, respectively, through human skin, we observed that there is more uniform distribution of light throughout the entire field with the LED illumination than with the laser. This is evidenced by the greater clarity and greater number of blood vessels seen in the same skin sample when illuminated by the LEDs.

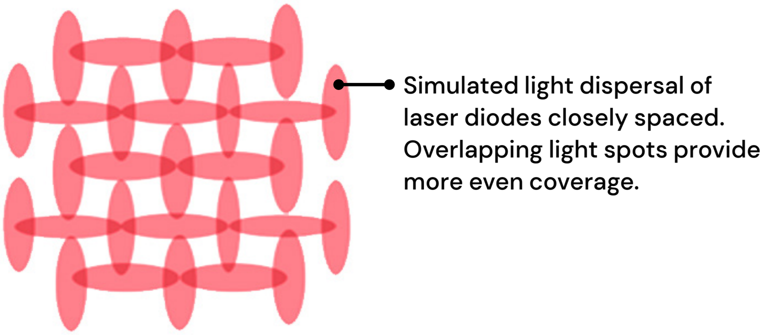

FIGURE 2:
SIMULATED LIGHT DISPERSAL PATTERN OF LASER DIODES SPACED CLOSELY TOGETHER
Image taken from a white paper by Capillus, LLC[8]. The manufacturer's caption points out the benefit of overlapping light spots, but it is also clear there are multiple gaps between the light spots themselves.

Even though the laser diodes in the Capillus cap are broad-area laser diodes with broad-beam diffraction and are spaced closely together, the oval-shaped light dispersion zones produce a crosshatch pattern that does not adequately cover a target surface area, as seen in Figure 2.

While LED treatment ensures broad, continuous coverage of the scalp, laser treatments, due to the physical limitation of the lasers themselves, have holes or gaps in their coverage that inherently lead to inconsistent coverage of the scalp and, ultimately, less effective treatment.

2. Wider spectral peaks (wider emission spectrum)

As seen in Figure 3, LEDs have much wider emission peaks in their emission spectra than do lasers. This means they will provide some photons with longer and shorter wavelengths than that of the primary emission wavelength. When multiple wavelengths near that of the primary one are transmitted, there is greater spectral overlap and therefore greater likelihood that the target tissue is effectively treated.

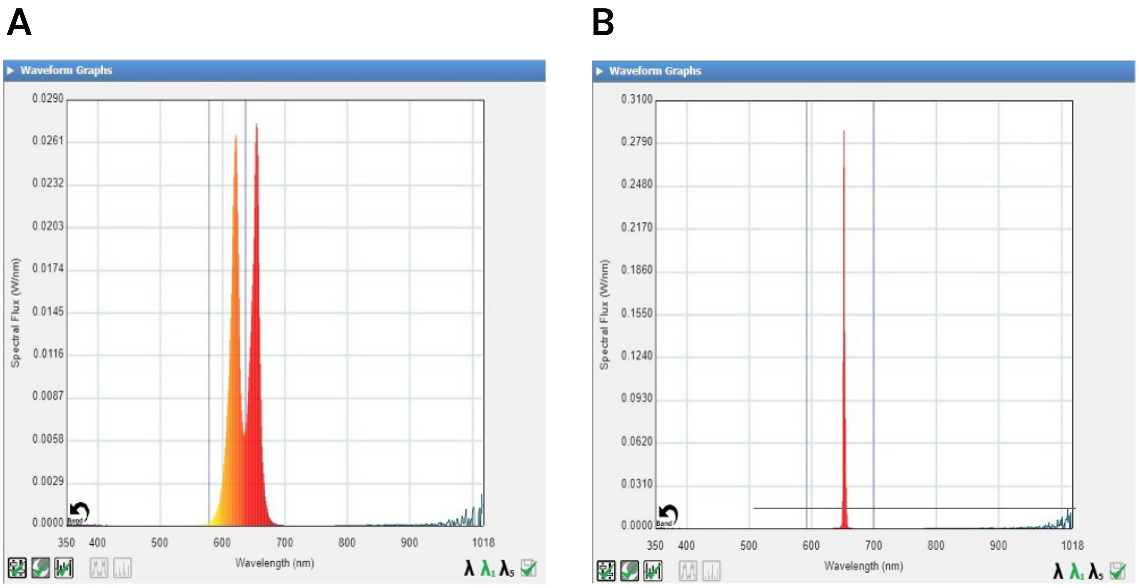

FIGURE 3:
LIGHT EMISSION SPECTRUM OF LED VERSUS LASER LIGHT SOURCE[10]

Graph A: Light emission spectrum from the Revian Red cap LEDs. Graph B: Light emission spectrum from the Capillus PRO S1 cap lasers. As can be seen from these graphs, the total width of the emission spectra for the LED is greater than that of the laser. Not only does the LED emit in dual peaks (at 621.7 and 655.4 nm, respectively) but the full-width measurements at half-max peak are 14.2 nm for the lower peak and 13.5 nm for the higher peak. Taken together, they give a spectral width of 27.7 nm. In contrast, the laser emits in a single peak at 652.4 nm and that emission has a full-width measurement at half-max peak of only 2.5 nm.

The wavelengths of light used to treat AGA are in the red-to-near infrared range, which spans from 630 – 830 nm in the electromagnetic spectrum. In human skin, cytochrome c oxidase (CCO) is the photoacceptor, the molecule directly activated by that specific light. CCO is a key enzyme in cellular respiration, the process that generates energy for all mammalian cells, and in other important cellular pathways, including DNA synthesis. CCO has not one, but four light-accepting molecular centers, chromophores, that stimulate DNA synthesis. Each of those chromophores absorbs light of a different peak wavelength within the red-to-near-infrared spectrum. Those four peak wavelengths are 620, 680, 760, and 820 nm, respectively, and there is considerable spectral overlap between them, creating a wide band of light absorption[15]. It logically follows that the wider the beam of light being transmitted to the skin, the greater the number of photons of each of those four different wavelengths will be absorbed. As more photons are absorbed, more of the corresponding chromophores will be activated. In addition, as we will discuss in the next section, the wider the beam of light incident (falling) upon the skin, the greater the depth of penetration of that light.

3. Better penetration/transmission

Any light therapy used to promote hair growth must penetrate the skin deeply enough to stimulate a biological response. For treatment of AGA and hair loss, both LED devices and laser devices utilize red-to-near-infrared light. It is already established that light of those wavelengths penetrates most deeply into human skin, as seen in Figure 4.

LIGHT PENETRATION INTO SKIN

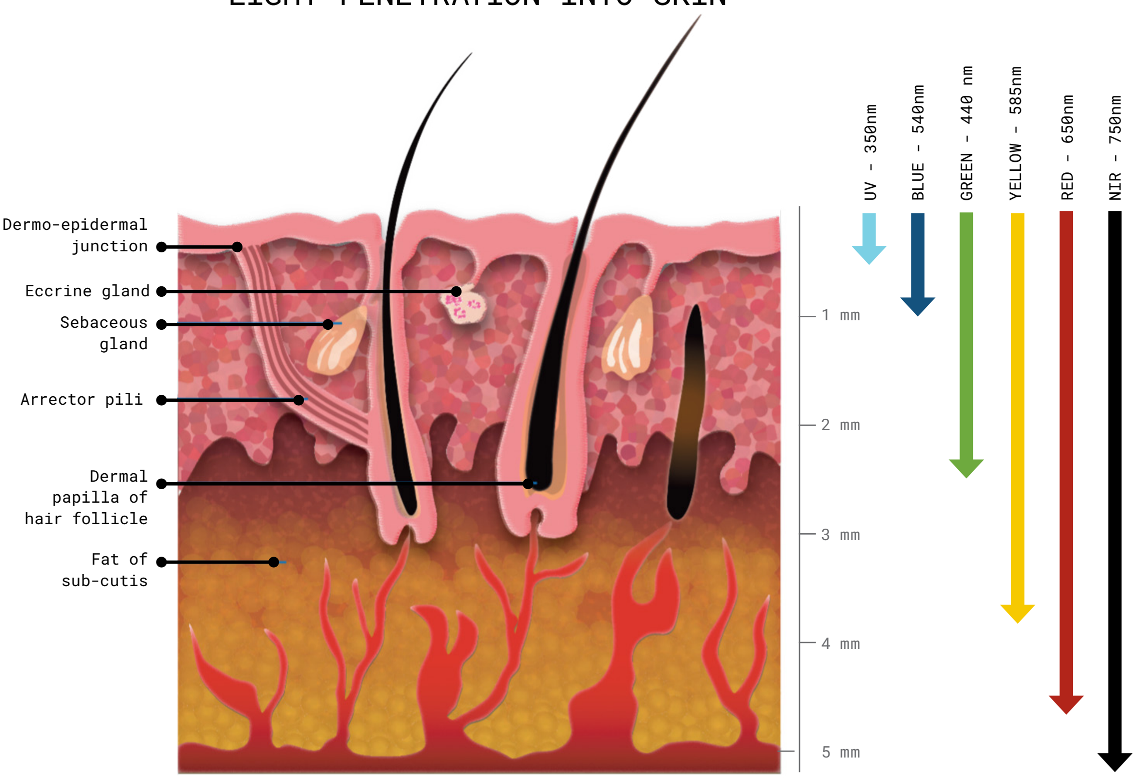

FIGURE 4:
DEPTHS OF SKIN PENETRATION BY DIFFERENT WAVELENGTHS OF LIGHT
With respect to hair growth, it can be seen that the dermal papillae of hair follicles lie approximately 2 to 3 mm below the skin surface. Red light penetrates even beyond those, to a depth of 4 – 5 mm, while blue light barely reaches 1 mm into the tissue and ultraviolet light hardly penetrates it at all [16].

One of the most debated topics regarding the difference between LEDs and lasers is around the ability to penetrate tissue. The most current research effectively answers this question; LEDs yield a 16% greater transmittance through skin than lasers. This study[10] shows light emitted by LEDs used in the Revian RED cap penetrate 4-5 mm thick human skin samples at a transmission range of 17.1 – 18.4%, while the laser diodes of a market-leading laser therapy cap penetrated the same skin only at a range of 15.0 – 15.8%.

Computer simulations have corroborated the empirical evidence of greater percent transmission by LED light. Using such simulations, it has been established that the wider the incident beam of light upon the skin, the deeper the penetration. Specifically, the wider the treatment area, or "spot size", the less lateral scattering of the light energy, resulting in greater penetration depth[16]. As a result, lower energy densities are needed with LEDs to achieve the same depth of penetration as lasers for treatment.

Summary and Conclusion

In summary, clinical data extracted from four separate, high-quality studies of four different, FDA-approved treatments for AGA showed the greatest increase in hair growth from the at-home, red light LED device, followed by the at-home, red light laser device and then the two drug treatments. There are sound scientific reasons for the superiority of LED treatment of hair loss, including greater and more uniform coverage of the scalp, up to 16% greater penetration of human skin, and activation of greater numbers of light acceptors in target tissue. Several of these reasons have been validated by laboratory experiments.

In conclusion, data from clinical studies as well as laboratory experiments based on the scientific principles underlying both laser and LED light all demonstrate that red light LED therapy is the best choice for at-home treatment of androgenetic alopecia.

Bibliography

1. Torres AE, Lim HW. Photobiomodulation for the management of hair loss. Photodermatol Photoimmunol Photomed. 2021; 37:91–98
2. Dompe C, Moncrieff L, Matys J, Grzech-Leniak K, Kocherova I, Bryja A, Bruska M, Dominiak M, Mozdziak P, Skiba THI, Shibli JA, Angelova Volponi A, Kempisty B, Dyszkiewicz-Konwiska M. Photobiomodulation-Underlying Mechanism and Clinical Applications. J Clin Med. 2020 Jun 3;9(6):1724. doi: 10.3390/jcm9061724. PMID: 32503238; PMCID: PMC7356229.
3. Kim WS, Calderhead RG. Is light-emitting diode phototherapy (LED-LLLT) really effective? Laser Ther. 2011; 20(3):205-15. doi: 10.5978/islsm.20.205. PMID: 24155530; PMCID: PMC3799034.
4. Ohshiro, T. NEW CLASSIFICATION FOR SINGLE-SYSTEM LIGHT TREATMENT. Laser, 20, 11-15.
5. Lima AC, Fernandes GA, de Barros AR, Gonzaga IC, de Oliveira RA, Nicolau RA. Photobiomodulation (Laser and LED) on sternotomy healing in hyperglycemic and normoglycemic patients who underwent coronary bypass surgery with internal mammary artery grafts: a randomized, double-blind study with follow-up. Photomed Laser Surg. 2017; 35(1): 24-31.
6. Lima AC, Fernandes GA, Gonzaga IC, de Barros AR, de Oliveira RA, Nicolau RA. Low-level laser and light-emitting diode therapy for pain control in hyperglycemic and normoglycemic patients who underwent coronary bypass surgery with internal mammary artery grafts: a randomized, double-blind study with follow-up. Photomed Laser Surg. 2016; 34(6): 244-251.
7. Heiskanen V, Hamblin MR. Photobiomodulation: lasers vs. light emitting diodes? Photochem Photobiol Sci. 2018; 17(8): 1003-1017.
8. The treatment of androgenetic alopecia with LLL devices. A discussion of industry knowledge. Patricia Schnoor. Updated October 16, 2017. © Capillus, LLC; All rights reserved.
9. Sinclair R, Murrell D, Spelman L, et al. Clinical safety and efficacy of an at-home, dual wavelength red light hair growth system in subjects with androgenetic alopecia. https://revian.com/downloads/Clinical-Efficacy-At-Home-Dual-Wavelength-Red-Light-Hair-Growth-System-Subjects-With-Androgenetic-Alopecia.pdf. Accessed September 23, 2020.
10. Internal research at Revian, Inc.
11. REV-01 Clinical Study Report. A Prospective, Randomized, Controlled, Double-Blind Study that Evaluates the Safety and Efficacy of Three Active REVIAN Caps versus a Non-Active REVIAN Cap (SHAM) in Participants with Pattern Hair Loss (Androgenic Alopecia). ClinicalTrials.gov number NCT4019795. Report date: 31 July 2023. Sponsor: Revian Inc.
12. Jimenez, J. J., Wikramanayake, T. C., Bergfeld, W., Hordinsky, M., Hickman, J. G., Hamblin, M. R., & Schachner, L. A. (2014). Efficacy and safety of a low-level laser device in the treatment of male and female pattern hair loss: a multicenter, randomized, sham device-controlled, double-blind study. American journal of clinical dermatology, 15, 115-127.
13. Olsen, E. A., Whiting, D., Bergfeld, W., Miller, J., Hordinsky, M., Wanser, R., ... & Kohut, B. (2007). A multicenter, randomized, placebo-controlled, double-blind clinical trial of a novel formulation of 5% minoxidil topical foam versus placebo in the treatment of androgenetic alopecia in men. Journal of the American Academy of Dermatology, 57(5), 767-774.
14. Leyden, J., Dunlap, F., Miller, B., Winters, P., Lebwohl, M., Hecker, D., ... & Waldstreicher, J. (1999). Finasteride in the treatment of men with frontal male pattern hair loss. Journal of the American Academy of Dermatology, 40(6), 930-937.
15. Karu, T. I. (2010). Multiple roles of cytochrome c oxidase in mammalian cells under action of red and IRA radiation. IUBMB life, 62(8), 607-610.
16. Ash, C., Dubec, M., Donne, K., & Bashford, T. (2017). Effect of wavelength and beam width on penetration in light-tissue interaction using computational methods. Lasers Med Sci, 32, 1909-1918.
17. Whelan, H. T., Smits Jr, R. L., Buchman, E. V., Whelan, N. T., Turner, S. G., Margolis, D. A., ... & Caviness, J. (2001). Effect of NASA light-emitting diode irradiation on wound healing. Journal of clinical laser medicine & surgery, 19(6), 305-314.

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