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Low Level Laser Therapy (LLLT) (Photobiomodulation=PBM) and the Effectiveness of current Devices for Treating Hair loss

Photobiomodulation (PBM), also called low level laser therapy (LLLT), is a treatment used to stimulate hair follicles to grow. It is often used in conjunction with other hair loss therapies. While some patients have seen a benefit, others have not. There are many types of devices with varying energy output. Some devices may be purchased directly by consumers, and others are only to be used in the physician's office. Despite a burgeoning array of such devices on the market today, important questions about dosing and efficacy remain unanswered.

Consumers should be aware of these unanswered questions in order to make an informed decision. Dr Buckley recommends seeking the advice of a hair loss specialist who is knowledgeable about various types of hair loss and the full array of options to appropriately and effectively treat them.

Frequently Asked Questions

Would I be a good candidate for Photobiomodulation Therapy

The answer is, there is much we don't know about the optimal wavelengths and dosing for Photobiomodulation therapy to treat hair loss. Despite the studies that have been performed, important questions remain unanswered. For patients, it is advisable that prior to making the decision to purchase an OTC device to treat their hair loss all therapies and options should be reviewed with a hair loss specialist.

How does Photobiomodulation work for stimulating hair growth?

Researchers are not certain how PBM works to stimulate hair growth but believe it has to do with stimulating hair to enter the growth phase (anagen re-entry), prolongation of the growth cycle (prolongation of anagen), proliferation of hair in the active growth cycle (anagen), and prevention of premature catagen (the rest phase of hair growth).

It has even been postulated to have an effect on modulating 5 alpha reductase activity—the enzyme that converts testosterone into dihydrotestosterone (DHT)—with the latter considered to be a cause of hair loss in androgenetic alopecia (AGA). (5) Studies are ongoing to further identify cellular targets and the mechanisms of action for hair growth stimulation, as this will assist researchers to identify the optimal wavelengths and dosing.

Is there an optimal wavelength for stimulating hair growth?

The short answer is, probably, but it may not yet be available in current devices. Some researchers believe the chromophore responsible for PBM response in hair growth stimulation is Cytochrome C oxidase, found inside of mitochondria. Tissue culture experiments have shown peak DNA production in 4 wavelength ranges, felt to be a reflection of Cytochrome C oxidase activity : 614-624nm; 668-684n, 751-772nm and 813-846nm. (ref

1, 6) More recent research specific to hair growth evaluated the response of various wavelengths on the shaven backs of Sprague-Dawley rats using diodes of 632, 670, 785 and 830nm. The higher wavelengths of 830 nm and 785 nm resulted in a significant effect on hair growth stimulation, with 830 nm being most effective (ref Lasers Med Sci). The original study by Mester used a ruby laser with wavelength 694 nm to achieve the first hair growth resulting from PBM therapy.

Interestingly, none of the currently marketed devices use a wavelength of 694 nm, 785 nm or 830nm. To date most of the FDA cleared devices in the US use lower wavelengths varying from 635nm, 650nm, and 655nm with one at 678 nm. The reasons for this have little to do with the previously mentioned scientific studies, and everything to do with the cost of FDA pre market approval (PMA) vs the 510K clearance process for low risk medical devices. The impact of the regulatory process on device development will be further discussed below. Importantly, human study results from some of these available devices suggest a hair growth benefit for some patients. However, closer scrutiny raises questions about methodology and whether study conclusions can apply in real use settings, as well as whether any benefits identified would be greater if optical parameters were optimized.

What are the optimal dosing regimens for Photobiomodulation devices?

Important optical parameters for PBM include wavelength, as well as irradiance or power density (mW/cm2)—how bright the light is, distance of the target from the light source, and frequency and duration with which light is applied to the head/scalp (ex 3 times weekly for 20 minutes); as well as the duration or course of therapy (6 months, 12 months etc). Determining optimal dosing seems especially important given the characteristic of LLLT known as the biphasic dose response , a phenomenon believed to occur in both animals and humans—where too little energy results in no response, and too much energy could actually have a detrimental effect on target tissue.

Researchers investigating optimal dosing regimens for hair growth performed a review of 90 published studies and observed a confusingly wide array of dosing schedules and irradiance or power densities which varied by as much as two orders of magnitude—making it impossible to identify ” optimal” parameters. (ref) Furthermore, none of the OTC devices published any justification for their recommended dosing, nor did they

address why there were no dosing adjustments based on Fitzpatrick skin typing. The latter classification was developed to aid in dosing for skin phototherapy based on the presence of the chromophore, melanin, in skin and hair which absorbs laser light.

The FDA apparently recognized this factor, however, and has only approved the OTC devices for Fitzpatrick Skin types 1-4 which does not include patients with darker skin and hair where melanin would be expected to absorb a considerable amount of the light before it could reach other cellular targets.

What is FDA 510K clearance and how does this impact LLLT or PBM device development?

For low risk medical devices, the US- FDA allows companies to go through a markedly faster and cheaper process to bring their products to the marketplace. This process is called 510K clearance, and is not the equivalent of “FDA approval.” For this clearance process, a company is required to establish their device as equivalent in safety to a previously approved device with similar characteristics (the predicate device). In contrast, the Pre-market “Approval “(PMA) process requires safety and efficacy studies, takes more time time, and usually costs millions of dollars.

Several of the PBM devices being marketed today with 510K clearance have no studies to prove efficacy. For companies that went through the PMA process to produce the first predicate device, there is little incentive to produce another novel device that may be used by another company as a predicate at a much lower development cost.

Because of this, the 510K clearance process encourages “copy cat” wavelengths and device styles, rather than novel and possibly more effective wavelengths or devices. For example, the first PBM device to achieve 510K clearance listed as predicates, a variety of FDA approved and unapproved laser based devices including non hair growth devices intended for hair removal and pain relief. Since then this first device has been listed on subsequently 510 K cleared PBM devices on the market to treat hair loss.

Another limitation of direct to consumer sales of PBM devices is the necessity to adhere to laser safety precautions for Class 3a or 3R lasers. The latter limits the device power to 5 mW(.005 W) to avoid eye hazards, regardless of whether a higher power device could be more effective. The incentive for companies to market direct to consumers for higher sales volume and profits is clear.

However, this may obviate the development of devices with higher and possibly more effective power levels because it would place them in a laser class that could not be sold directly to consumers. Currently there are many studies documenting PBM efficacy for various tissues and therapies, with devices exceeding 5 mW.

Are there any reliable studies on the effectiveness of the LLLT (PBM) devices?

There have been studies evaluating the effectiveness of a variety of PBM devices to treat hair loss, including 655 nm laser combs, and helmets which combined 650 nm, or 655 nm laser diodes with LED lights. However, questions have been raised about possible flaws in the methodology of these studies. First of all, while it is generally accepted the gold standard for evidence based medical studies is the randomized, controlled trial, where patients with the same medical condition are randomly selected to be treated with the real medical therapy vs a placebo (not real, but looks alike) —the data required to prove effectiveness of a hair growth promoter is very specific.

Patient self report is deemed too subjective and found to be unreliable and is often positive in placebo groups. Even global photographs can have a degree of subjective bias if performed improperly. Strict adherence to standardized photo position, lighting, hair color and hair style do offer some measure of credible evidence. Nevertheless, while most studies do include the use of global photographs the gold standard for establishing hair growth is phototrichogram evidence. The latter are areas of treated scalp trimmed to approximately 1 mm so hairs do not overlap, but are not so short as to be unseen, and tattooed so the precise area is measured for hair counts at intervals to determine if an increase or decrease has occurred. New hairs generally take about 3 months to grow out from a follicle, so growth promoter assessment is often done at monthly intervals assessing the emergence of new hairs, as well as the possibility of improvements in hair fiber caliber.

Did these studies present photo-trichograms to prove effective increased hair growth?

Out of a sample size of 269 patients the laser comb study did present one very credible phototrichogram to document improved caliber and growth. However, skeptics point out there should have been more than one credible phototrichogram out of this sample to document efficacy. Other studies did not publish credible and easily assessed phototrichograms. Notably there were several patients in the placebo groups of all studies with equivalent and small hair count increases to many patients in the treated group. For example, there were reports of 100% increased hair counts among placebo patients in the helmet studies, suggesting some type of counting error. The helmet studies also suffered from small sample sizes.

Did the studies have sufficiently large sample size and study duration to provide adequate medical evidence to recommend them?

All sample sizes for each of the dfferent devices studied were <100 patients. (several different laser combs were used in the largest study) None of the studies were longer than 26 weeks (~6 months), with no published evidence to date to determine if any hair growth benefits from PBM devices would be enduring with long term use.

Were there any other concerns about the photobiomodulation studies?

There was no documented scientific justification behind the dosing schedules. Energy doses were highly variable. No adjustments were made for hair and skin color (Fitzpatrick skin type), and none of the devices were cleared for use on darker skin patients (Fitzpatrick Type 5-6). Furthermore, since areas of hair growth assessment had to be shaved for hair counts, and light was beamed directly on these areas, it necessarily provided added opportunity for a PBM effect that would not necessarily be expected on areas of the scalp covered by hair.

Computer models have calculated that hair coverage can impede light transmission by > 30%, especially with dark hair. This raises questions about whether patients who did respond to the PBM device under study conditions, would actually experience the same response without shaving the hair.

Defining Low level laser therapy light or PBM

Laser light is collimated, that is, it is not diffuse and light waves are focused in a beam or column until they hit a target that either reflects, transmits, scatters or absorbs it. A chromophore is a tissue target that absorbs a particular wavelength of light. Various tissue chromophores include water, hemoglobin, melanin or other cellular components such as mitochondria. The wavelength for various PBM therapies includes the visible light spectrum from 500nm-1100nm; the other defining characteristic is low power from 1mW-500mW and power density from 1mW-500mW/cm2.

This low power does not heat tissue. Two factors are most important for achieving an effect from photobiomodulation. First of all, in order for the PBM to cause bio-stimulation , light of a particular wavelength must reach and be absorbed by a particular tissue target or chromophore. Secondly, the wavelength must be carried by energy or power through the skin, to reach the target, such as a hair follicle. The range of low power which can biostimulate without tissue heating, as previously noted, is 1 mW-500 mW. However, all over the counter PBM devices are limited by laser safety regulations to just 5mW of power—in order to protect consumer's eyes, not based on efficacy to achieve a tissue response.

A device with 100 times the power of over the counter (OTC) devices would still be considered a 'cool' laser– and would not burn or destroy tissue, but could not be sold direct to consumers in most countries because it exceeds regulated power limits for ocular safety. This limitation must be kept in mind as we review currently available OTC devices for treating hair loss.

References

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Evaluation of wavelength-dependent hair growth effects on low-level laser therapy: an experimental animal study.
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doi: 10.7860/JCDR/2015/15561.6955 PMCID: PMC4717791

TABLE 1. Summary of Low-Level Laser Light Therapy Devices approved by the United States Food and Drug Administration

DEVICE CHARACTERISTICS	CAPILLUS 82 (ULTRA)	CAPILLUS 202 (PLUS)	CAPILLUS 272 (PRO)	HAIRMAX LASERCOMB 7	HAIRMAX LASERCOMB 9		HAIRMAX LASERCOMB 12	HAIRMAX LASERBAND 41
Shape	Sports cap	Sports cap	Sports cap	Comb	Comb		Comb	Headband
Laser diode quantity/ wavelength	82/650	202/650	272/650	7/655	9/655		12/655	41/655
Light emitting diode quantity/wavelength	N/A	N/A	N/A	N/A	N/A		N/A	N/A
Power/diode	≤5mW	≤5mW	≤5mW	≤5mW	≤5mW		≤5mW	≤5mW
Total power output	≤410mW	≤1010mW	≤1360mW	≤35mW	≤45mW		≤60mW	≤205mW
Treatment regimen	30 mins	30 mins	30 mins	15 mins	11 mins		8 mins	3 mins
Frequency	3–4 times/week	3–4 times/week	3–4 times/week	3 times/week	3 times/week		3 times/week	3 times/week
Price (US$)	999	1999	2999	295	395		495	595
Sample size	N/A	N/A	44 F	7F 28 M	110 M	21 F 11 M	141 F 128 M	N/A
Duration of study	N/A	N/A	17 weeks	Cohort 6 mo	26 weeks	Cohort 2 yr	26 weeks	N/A
Outcome	N/A	N/A	51% increase in terminal hair counts as compared with sham-treated control patients	Total hair counts increased by 93.5% and total hair tensile strength increased by 78.9%	Mean terminal hair density increased by 19.8 hairs/cm^2	8 with significant improvement, 20 with moderate improvement, 4 with no improvement	Overall, terminal hair density increased by 15.27 hairs/cm^2	N/A

N/A: not applicable

TABLE 1 (continued). Summary of Low-Level Laser Light Therapy Devices approved by the United States Food and Drug Administration

DEVICE CHARACTERISTICS	HAIRMAX LASERBAND 82	REGROW 272 BY HAIRMAX	IGROW			IRESTORE ESSENTIAL	IRESTORE PROFESSIONAL	LASERCAP LCPRO
Shape	Headband	Sports cap	Helmet			Helmet	Helmet	Sports cap
Laser diode quantity/ wavelength	82/655	272/655	21/655			21/650	82/650	224/650
Light emitting diode quantity/wavelength	N/A	N/A	30/655			30/660	200/650	N/A
Power/diode	≤5mW	≤5mW	≤5mW			≤5mW	≤5mW	≤5mW
Total power output	≤410mW	≤1360mW	≤255mW			≤255mW	≤1410mW	≤1120mW
Treatment regimen	90 secs	30 mins	25 mins			25 mins	25 mins	36 mins
Frequency	3 times/week	3 times/week	Every other day			Every other day	Every other day	Every other day
Price (US$)	795	999	695			695	1195	2995
Sample size	N/A	N/A	44 M	47 F	45 F	N/A	N/A	N/A
Duration of study	N/A	N/A	16 weeks	16 weeks	16 weeks	N/A	N/A	N/A
Outcome	N/A	N/A	35% increase in terminal hair count	37% increase in terminal hair count	Average hair density of 207±12.97/cm^2	N/A	N/A	N/A

N/A: not applicable

TABLE 1 (continued). Summary of Low-Level Laser Light Therapy Devices approved by the United States Food and Drug Administration

ATTRIBUTES	NUTRASTIM LASER HAIR COMB	THERADOME LH 40 EVO	THERADOME LH 80 PRO	LASERCAP SD	LASERCAP HD	LASERCAP HD+	ILLUMIFLOW 148	ILLUMIFLOW 272	IHELMET 200
Shape	Comb	Helmet	Helmet	Sports cap	Sports cap	Sports cap	Sports cap	Sports cap	Helmet
Laser diode quantity/ wavelength	12/655	40/678	80/678	80/650	224/650	304/650	148/650	272/650	200/650
Light emitting diode quantity/ wavelength	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Power/diode	≤5mW	≤5mW	≤5mW	≤5mW	≤5mW	≤5mW	≤5mW	≤ 5mW	≤5mW
Total power output	≤60mW	≤200mW	≤400mW	≤400mW	≤1120mW	≤1520mW	≤740mW	≤1360mW	≤1000mW
Treatment regimen	8 mins	20 mins	20 mins	30 mins	30 mins	30 mins	30 mins	30 mins	30 mins
Frequency	3 times/week	4 times/week	2 times/week	Every other day	Evert other day	Every other day	Every other day	Every other day	Every other day
Price (US$)	279	595	895	N/A	N/A	N/A	549	799	1199
Sample size	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Duration of study	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Outcome	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

N/A: not applicable

TABLE 1 (continued). Summary of Low-Level Laser Light Therapy Devices approved by the United States Food and Drug Administration

ATTRIBUTES	GRIVAMAX 148	GRIVAMAX 272	REVIAN RED	DERMASCALP 148	DERMASCALP 272	BOSLEY REVITALIZER 164	BOSLEY REVITALIZER 272	KIIEER 148	KIIEER 272
Shape	Sports cap	Sports cap	Sports cap	Sports cap	Sports cap	Sports cap	Sports cap	Sports cap	Sports cap
Laser diode quantity/ wavelength	148/650	272/650	–	148/650	272/650	164/650	272/650	148/650	272/650
Light emitting diode quantity/ wavelength	–	–	119/620–660	–	–	–	–	–	–
Power/diode	≤5mW	≤ mW	≤5mW	≤5mW	≤5mW	≤5mW	≤5mW	≤5mW	≤5mW
Total power output	≤740mW	≤1360mW	≤595mW	≤740mW	≤1360mW	≤820mW	≤1360mW	≤740mW	≤1360mW
Treatment regimen	30 mins	30 mins	10	30 mins	30 mins	30 mins	30 mins	30 mins	30 mins
Frequency	Every other day	Every other day	Everyday	3 times/week	3 times/week	Evert other day	Every other day	Every other day	Every other day
Price (US$)	549	849	995	N/A	N/A	1599	2599	549	845
Sample size	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Duration of study	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Outcome	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

N/A: not applicable

Table 1 refference:

Lueangarun S,et alA Systematic Review and Meta-analysis of Randomized Controlled Trials of United States Food and Drug Administration-Approved, Home-use, Low-Level Light/Laser Therapy Devices for Pattern Hair Loss: Device Design and Technology.*J Clin Aesthet Dermatol.* 2021;14(11):E64–E75.Suparuj Lueangarun,et al

Examples of US suppliers (not necessarily endorsed by Dr Buckley):

The Capillus Pro S1 features 304 medical-grade laser diodes delivering 0.87 J/cm² dose of light energy to the hair follicles (**US discount price $2,124.15**) The regular size caps fit most heads, with a head circumference of up to 23". If your head circumference is greater than 23" inches please contact customer service for ordering a larger size. https://www.capillus.com/products/capillus-pro-s1

LaserCap HD+. FDA-cleared laser therapy for male and female pattern hair loss. The LaserCap HD+ contains 304 laser diodes, delivering 3.93 J/cm² dose of light energy to the hair follicles. (**US price $2,995)** **https://lasercap.com/product/lasercap-hd-plus/**

LASER 272 POWERFLEX CAP (EU) €2.080,95 272 Medical-Grade diode Lasers. 7 minutes of treatment time, 3 days a week. https://hairmax.co.uk/collections/laser-devices/products/laser-272-powerflex-cap-eu

LASERBAND 82 ComfortFlex (EU) €1.042,95 Unique ComfortFlex Band design with 82 Medical-Grade diode Lasers. https://hairmax.co.uk/collections/laser-devices/products/laserband-82-comfortflex-eu

This article is based on information from **The International Society of Hair Restoration Surgery (ISHRS)**: www.ishrs.org

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