Light-based therapies in the treatment of alopecia

Christina S Oh* BA, Maria Karim* MD, Elizabeth J Klein MD, Lu Yin MD, Daniel Gutierrez MD, Jerry Shapiro MD, Kristen Lo Sicco MD

*Authors contributed equally

Affiliations: The Ronald O Perelman Department of Dermatology, New York University Grossman School of Medicine, New York, New York

Corresponding Author: Kristen Lo Sicco MD, The Ronald O Perelman Department of Dermatology, New York University Grossman School of Medicine, 222 East 41st Street, 16th Floor, New York, NY 10016, Email: kristen.losicco@nyulangone.org

Abstract

All types of alopecia, including androgenetic alopecia, alopecia areata, and lichen planopilaris/frontal fibrosing alopecia, affect over half of men and women. Though a common dermatological experience, many patients with visible hair loss report significant psychological and social distress and, consequently seek treatment. Current existing therapeutic regimens have proven to be efficacious, though may result in various adverse effects and require lifelong use. Laser and light-based therapies have been emerging in the current literature as a safe and alternative treatment, but their utilization for treating alopecia is poorly understood. This review evaluates the existing evidence regarding the use of lasers in the treatment of various forms of alopecia. Overall, there has been promising evidence for potential alopecia treatment efficacy: low-level light therapy for androgenetic alopecia, fractional laser for androgenetic alopecia, and excimer laser for alopecia areata.

Keywords: alopecia, excimer, fractional, laser, light therapy

Introduction

Lasers and other light-based therapies have been used in treating a variety of conditions in dermatology. Although their utility in the treatment of hirsutism and conditions of excess hair growth is increasingly recognized, their utilization for treating alopecia is poorly understood. Lasers have been proposed as a treatment for various types of alopecia including androgenetic alopecia (AGA), alopecia areata (AA), and lichen planopilaris (LPP)/frontal fibrosing alopecia (FFA). This review evaluates the existing evidence regarding the use of lasers in the treatment of various kinds of alopecia (**Table 1**).

The PubMed database was searched using a combination of the terms "laser" and "frontal fibrosing alopecia," "lichen planopilaris," "androgenic alopecia," "androgenetic alopecia," "male pattern hair loss," "female pattern hair loss," and "alopecia areata." Conference abstracts and articles not published in English were excluded from analysis. A total of 72 unique articles focusing on outcomes of laser devices for the treatment of alopecia on human patients were evaluated.

Discussion

Low level laser therapy

Low-level laser therapy (LLLT) utilizes wavelengths in the red or infrared light range. Low-level laser therapy may be anti-inflammatory and is used to treat a variety of conditions including rheumatoid arthritis, osteoarthritis, and cutaneous wounds [1]. Multiple mechanisms may potentiate its role in promoting hair growth, including stimulating cytochrome c oxidase to release nitric oxide, increasing production of crucial transcription factors including redox factor-1 dependent activator protein-1, nuclear factor kappa B, and p53, and activating transcription factor/cAMP response element binding protein and, hypoxia-inducible

factor-1 [2–4]. As a result one may see reversion of telogen hairs to anagen phase [5], and induction of follicular stem cell proliferation via increased heat shock proteins. These have been noted to be present only in hair follicles in the catagen and anagen phases of hair growth and absent from hair follicles in the telogen phase [6–9], contributing to the growth of newer, thicker, and more pigmented hairs. The advantages of LLLT are outlined by its ease of use, well-tolerated side effect profile, lack of systemic side effects, and overall efficacy. Disadvantages associated with LLLT use include the variety in parameter selection (e.g., wavelength, fluence, time of pulse) which may result in negative outcomes owing to incorrect parameter usage rather than the inherent ineffectiveness of LLLT [4].

There are multiple FDA-cleared commercial LLLT products, though frequency and duration of treatments vary. An FDA-cleared product, the HairMax LaserComb® (Lexington International, Boca Raton, Florida), recommends usage three times a week with treatment time varying from 8-11 minutes depending on the device. Other FDA-cleared devices like the Theradome EVO LH40® or Theradome PRO LH80® recommend usage 2-4 times a week for 20 minutes.

Androgenetic alopecia

Several randomized-controlled trials (RCT) evaluating the treatment of AGA with LLLT have demonstrated efficacy. Leavitt et al. performed a study sponsored by Lexington International, manufacturers of HairMax 655nm devices [10]. The double-blinded multicenter RCT included 123 patients, though 24 patients were excluded from final analyses because of non-compliance, loss to follow-up, and deviations from baseline entry criteria [10]. Of note, 10 patients from the treatment group and only one from the control group were prematurely terminated from the study for unspecified reasons. Hair density was measured via standardized macro photograph analysis of software-aided count of terminal hairs. Compared to controls, patients treated with the HairMax LaserComb® had increased hair density (P<0.0001) and better patient satisfaction (P=0.01), though the physicians' scores of overall assessment of hair growth between groups did not differ significantly (P=0.45).

Jimenez et al. later conducted a sponsored multicenter double-blinded RCT using 7-, 9-, and 12-beam HairMax LaserCombs® [11]. Terminal hair density was measured at baseline and at 16- and 26-week follow-ups via macro photographs taken with the Canfield Epilume System and analyzed by an independent evaluator with TrichoScience software (Tricholog, Moscow, Russia) assistance. Similar to Leavitt et al., a significant increase in hair density in all treatment groups compared to the control group was observed (P<0.002). Laser treatment patients generally had higher patient satisfaction, though the difference was not consistently significant.

Pooling populations from these studies yielded a total population of 348 individuals (**Table 2**). Notably, the majority of the patients were Fitzpatrick skin type III White men. The mean baseline hair densities were similar between the two groups (150.5 hairs/cm^2 in the treatment group versus 156.2 hairs/cm^2 in the control group) and the change in hair counts after 26 weeks was greater in the treatment group (19.76 hairs/cm^2 versus -0.02 hairs/cm^2), (**Table 3**). Both Leavitt et al. and Jiminez et al.'s baseline patient populations were healthy 25-

Table 2. *Demographic characteristics of 348 patients treated for androgenetic alopecia with HairMax LaserComb in two randomized control trials [10,11].*

Age	**Total study population**	
Average	47.8 years	
Range	25-61 years	
Race		
White	324 (93.1%)	
Black	1 (0.3%)	
Asian	2 (0.6%)	
Other	4 (1.1%)	
Ethnicity		
Hispanic	22 (6.3%)	
Fitzpatrick skin type		
Type I	14 (4.0%)	
Type II	88 (25.3%)	
Type III	160 (46%)	
Type IV	86 (24.7%)	
Sex	Treatment (N=231)	Control (N=117)
Male	149 (64.5%)	77 (65.8%)
Female	82 (35.5%)	40 (34.2%)

Table 3. *Hair counts before and after treatment of androgenetic alopecia with HairMax LaserComb in two randomized control trials [10,11].*

	Treatment (N=220)	Control (N=115)
Baseline	150.5	156.2
Change from baseline	19.76	-0.02

60-year-olds, all AGA subjects who had not taken hair-altering medications within six months of the study.

Use of the 655nm iGrow® helmet (Apira Science, Boca Raton, Florida) has been studied in two sponsored RCTs [1213]. Both studies found significant increases in hair counts in the treatment group after 16 weeks. The methodologies for the two studies were identical and combining the study populations yielded a total population of 91 patients of Fitzpatrick I-IV skin types (47 women, 44 men). When combined, the baseline hair density, measured over an area of 2.85cm^2 by a blinded investigator, is similar between the control group (65.5 hairs/cm^2) and the treatment group (62.2 hairs/cm^2). After treatment, the control group had 72 hairs/cm^2 and the treatment group 95.1 hairs/cm^2 (P=0.001). The paradoxical increase in hair density in the control group was hypothesized to reflect a true placebo effect or seasonal variation.

The iGrow® helmet was also evaluated in conjunction with topical 5% minoxidil twice daily in women and compared to topical 5% minoxidil solution in conjunction with 25 minutes of LLLT monotherapy every other day over four months [14]. The investigators found significantly increased hair density with all three treatments and combination therapy resulted in the highest patient satisfaction [15]. Treatment with two to three 20 minute sessions per week of LLLT (785nm LDU 8024PN/8024BN laser, Germany) in conjunction with topical 5% minoxidil twice daily for 26 weeks resulted in increased hair density, hair diameter, and better patient satisfaction compared to treatment with topical 5% minoxidil alone [15]. Similarly, use of the iHelmet® device (650nm) for 30 minutes every other day when used in combination with topical 5% minoxidil twice daily for six months increased hair density and hair diameter greater than topical 5% minoxidil alone [16].

A real-world study analyzing 1383 patients using the iHelmet® device found that in patients with mild AGA, the device was moderately effective (scoring 1-3 on a 6-item questionnaire) for 51.9% of users compared to 57.4% for patients with moderate-to-severe AGA [17]. The device was significantly effective (scoring 4-6 on a 6-item questionnaire) for 27.7% of users with mild AGA and 20.0% for those with moderate-to-severe AGA. The study's efficacy questionnaire assessed six items: 1) scalp oil secretion reduced, 2) scalp dandruff reduced, 3) scalp rash reduced, 4) daily hair loss reduced, 5) new hair regrowth or hair density increased, and 6) hair became thicker. Scalp dandruff condition (P=0.04), scalp rash (P=0.01) and itchy scalp symptoms (P=0.003) were positively associated with efficacy assessments [17]. It is important to note that the efficacy grading system included other symptoms besides hair growth and has no direct measurement of hair density changes. The efficacy assessment may be helpful however for evaluating multiple symptoms commonly associated with AGA.

Interestingly, treatment with the 590nm GentleWaves® device pulsed once daily for 70 seconds has been shown to increase the effectiveness of 2% topical minoxidil lotion twice daily for 5 consecutive days per week for a duration of six months, boosting its efficacy to a level comparable to that of 5% topical minoxidil. Hair density was measured by the Tiff counting method, analyzing a one cm^2 area of a phototrichogram [18].

A sponsored randomized split-head study by WELLMIKE Technology Corporation showed treatment with 660nm iRestore ID-520 (WELLMIKE Technology Corp., New Taipei City, Taiwan) for 30 minutes three times per week for 24 weeks exhibited a significantly greater hair coverage of 14.2% than the sham-treated group at 11.8% (P<0.001), despite the sham-treatment group beginning at a higher baseline than the treatment group. Interestingly, no differences in assessments of subjects' treatment satisfaction were seen [19]. Comparably, another sponsored multicenter randomized double-blind sham-device controlled trial assessed the efficacy of

the Oaze helmet (Won Technology, Daejeon, Korea) 18 minutes once daily for 24 weeks with varying wavelengths at 630nm, 640nm, and 650nm. The study showed a significant increase in mean hair density change of 17.2±12.1 hairs/cm^2 (P=0.003) in the LLLT-treated group compared to the -2.1±18.3 hairs/cm^2 (P=0.01), [1]. However, similar to results seen with the iRestore helmet, there were no significant differences in subjects' assessments between the treatment and control groups [119].

Twice-weekly treatment sessions with the Hair Growth System (TOPHAT655) 655nm device for 16 weeks also resulted in significantly improved hair counts in patients with female pattern hair loss, with a baseline mean of 222.3±33.5 to 255.3±30.4 (P=0.007) total hair count/high power field after the completion of the treatment regimen [20]. A sponsored multicenter randomized control trial using the Capillus272 Pro (Capillus, LLC, Miami, Florida) 650nm device every other day 30 minutes/treatment for 17 weeks increased terminal hair counts by 51% compared to sham-treatment (P<0.001), [8]. In contrast, the Capellux®, an LED cap-shaped photobiomodulation device, when applied for 12 minutes twice daily used in conjunction with topical minoxidil 5% solution applied twice daily for six months did not show significantly different results between the sham and the treatment group. This may be attributed to a few factors including use of the half-head model study design, which inherently carries limitations such as potential crossover of the light, use of an LED device rather than a laser, and the use of different irradiation frequency. Nevertheless, this study suggests the importance of using laser devices for photobiomodulation, rather than a more diffuse administration of LED-dosed therapy [21].

A multicenter randomized placebo-controlled study using the Cold X5 Hairlaser (Spencer Forrest, Los Angeles, California), which delivered 650nm pulses via direct scalp contact for 15 minutes three times a week, demonstrated an increase in mean hair counts, calculated with the imaging vendor Canfield, over 26 weeks of treatment (P<0.0001). No control group was used in their study [20]. Treatment of AGA with the 660nm RAMACAP (Ramathibodi Hospital and National Innovation Agency, Bangkok, Thailand), [22] and a dual 655nm and 808nm laser scanner (Zeinab Khodamrdi), [23] showed increased hair density and hair diameter with both products.

There are many products providing LLLT for AGA. In general, the findings have suggested that lasers may increase hair density and possibly hair shaft diameter. However, although objective quantitative measures may show statistically significant improvement with LLLT, there are questions remaining regarding its efficacy in improving patient satisfaction (clinically relevant efficacy) measured via subjective scores. Furthermore, standard dosages and treatment frequencies for LLLT to treat AGA are lacking. There is also a paucity of studies assessing the benefit of long-term maintenance and lack of emphasis on comparing patient characteristics that may be prognostic for treatment response.

Alopecia areata

Studies supporting use of LLLT for AA treatment are scarce, and limited to case series, including one trialing low-pulsed diode laser (wavelength 904nm, pulse duration 25ms), the results of which suggested LLLT may increase hair growth in AA [24].

Lichen planopilaris/frontal fibrosing alopecia

Low-level laser therapy has shown to increase PPARγ expression in mouse models, which presents a possible mechanism of action for therapeutic effect [25]. PPARγ is an anti-inflammatory receptor and its dysfunction may be implicated in the pathogenesis of certain cicatricial alopecias [26]. Multiple case series have reported the therapeutic effects of PPARγ agonists such as pioglitazone for LPP [26,27].

Treatment of LPP with red light at 630nm for 15 minutes daily for 6 months with Ledsmedical (Skymedic, Barcelona, Spain) reduced pruritus, pain, erythema, and perifollicular erythema, which ultimately decreased Lichen Planopilaris Activity Index (LPPAI) scores [25]. Terminal hair shaft thickness was initially increased with subsequent narrowing after further LLLT treatment, possibly related to treatment tachyphylaxis or potential untreated concomitant AGA [25]. The most important indicator of inflammatory activity in patients with LPP (perifollicular scaling) was not

reduced in this study. However, although symptoms are part of the LPPAI scoring system only a minority of LPP patients have associated symptoms.

Excimer laser

The excimer laser utilizes both a noble and reactive gas, such as xenon and chloride, respectively, to create a pseudo-molecule called an excimer or "excited dimer." Once these dimers dissociate, the result is the production of a wavelength of 308nm in the ultraviolet range, which is able to penetrate epidermal cells and fibroblasts [28]. The excimer laser is combined with the use of a fiber optic cable to direct the laser to targeted application sites and to preserve adjacent molecules. Once the light reaches its target, nuclear DNA absorbs ultraviolet B radiation and p53 is upregulated, resulting in destruction of DNA and the induction of cell apoptosis. This in turn, stimulates wound-induced healing for hair regrowth. Studies have also investigated the use of an excimer lamp, which also emits light with a wavelength of 308nm, but differs from the laser in terms of light coherence and radiation, to treat AA [29,30].

Advantages associated with excimer laser include targeted treatment and relatively few adverse reactions. In addition, the use of this device decreases the required number of treatment sessions and accumulation of ultraviolet B exposure when compared to other types of phototherapy, especially in the treatment of conditions such as psoriasis and vitiligo [28]. Disadvantages associated with excimer laser use include its high associated cost and potential for erythema, blistering, and hyperpigmentation.

Alopecia areata

Several studies have investigated the efficacy of the excimer laser for AA. Al-Mutairi's controlled open study demonstrated that the 308nm excimer laser may be effective in treating scalp AA in children with recalcitrant patches, though it was not effective in improving the alopecic patches on the arms and legs of patients with alopecia totalis [31]. However, like most AA therapies, alopecia recurred after therapy discontinuation and atopic diathesis, particularly bronchial asthma, was identified as a worse prognostic factor of treatment response. Positive responses have been found for scalp AA in adults treated with the excimer laser [32–35], though in one study the results were potentially confounded by intralesional corticosteroid injections into alopecic scalp patches not receiving laser treatment [34]. In addition to benefits on the scalp, utility of excimer treatment in beards has also been shown [35]. Two studies investigated the treatment of AA with VTRAC excimer lamp (PhotoMedex, Montgomeryville, Pennsylvania) and both found improvements in alopecic patches, though patients with a single AA lesion seemed to respond better to treatment than patients with multiple lesions [29,30]. Despite the prevalence of data indicating excimer laser may be used to treat AA, treatment protocols and duration of therapies for continued use are limited. More studies are necessary to establish longitudinal AA treatment protocols and to identify candidates most likely to benefit from excimer laser, as some studies have indicated lower efficacy in patients with diffuse and extensive disease. It is important to consider the excimer laser as a potential painless therapy option for the adolescent population, which may outweigh the high cost and the logistical burden required to receive treatment multiple times per week.

Lichen planopilaris/frontal fibrosing alopecia

There is a paucity of literature describing excimer laser for the treatment of LPP/FFA. One study of 11 patients with biopsy-proven LPP and its variants found improvement in redness and fewer inflammatory and hyperkeratotic lesions after a total mean dose of 4300mJ/cm^2 for 11 sessions (on average) of excimer laser treatment [36]. Clinical examination, disease severity patient reports, and photographic documentation taken at baseline and after each treatment was analyzed. Scalp pain and pruritus were significantly reduced in those who experienced symptoms [36]. Three patients experienced increased hair growth and two were in stable remission [36]. In another small survey of three patients with FFA, all patients treated with excimer laser responded to therapy. However, excimer treatment protocols were not detailed [37]. Although no reports of Koebnerization from excimer laser UV treatment burn have been reported, clinicians should be cautious with the rate of

treatment dose escalation to mitigate risk of potential disease exacerbation.

Fractional laser

Fractional lasers produce small columns of thermal injury known as microthermal zones and can be classified as fully or partially ablative. Fractional lasers may stimulate hair growth through improved absorption of topical therapies or from the remodeling process following minor wounding. It is suggested that Wnt ligand overexpression and wounding leads epidermal cells in wounds to assume the phenotype of hair follicle stem cells in animal studies, with increased expression of alkaline phosphatase, Wnt10b, Shh, and keratin 17, among other molecules [38,39]. The Wnt/βcatenin signaling pathway is critical in driving the process of stem cell proliferation, including hair follicles [40]. High levels of Wnt ligand in the epidermis have been implicated in increased hair follicle regeneration, promoting hair growth and differentiation to terminal hairs [38,40]. A 1550nm fractional erbium glass laser has been shown to induce hair regrowth in an alopecia mouse model at varying irradiation energies and densities. Subsequently, the same fractional laser was investigated in human patients as a split-head study over a 10-week period, consisting of 5 treatment sessions (energy 5mJ, density 300 spots/cm^2) given at two-week intervals, resulting in increased hair density and hair regrowth rates [39].

However, one study did not find Wnt10A and IGF1 mRNA upregulation despite increased hair count, hair shaft diameter, and anagen to telogen ratio after fractional laser treatment [40]. Disadvantages associated with fractional lasers include discomfort, itching, and mild postprocedural erythema [40].

Androgenetic alopecia

There are several studies investigating fractional lasers, both alone and in conjunction with topical treatments, to treat AGA. Multiple studies using the 1550nm mosaic laser (Lutronic, Seoul, Korea) found beneficial effects of the fractional laser in increasing hair density and hair growth in patients with AGA [39–41], though one paper noted a return to baseline hair density levels four months after conclusion of laser treatment [39]. Therefore, continued maintenance treatment is likely needed, though the dosing and frequency of treatment has yet to be determined. Similarly, the 1540nm fractional erbium-glass laser was found to increase hair density and diameter after 5 months of 2-week interval treatment [42].

Studies have also evaluated fractional laser treatment of AGA in conjunction with topical growth factors [43], topical 5% minoxidil [44], and topical 0.05% finasteride and growth factors [45]. The 1060nm Pixel CO_2 (Alma Lasers Ltd., Esthetic Mode, Israel) was used with topical growth factors solution (AQ Skin Solutions®, USA) for six sessions at 2-week intervals and subjects had increased hair density and telogen to anagen transition measured with a scanning electron microscope (Hitachi TM3000, Hitachi, Tokyo, Japan), [43]. The combination treatment of 1550nm fractional Er:glass laser (Finescan, TNC Meditron, Bangkok, Thailand) with topical 5% minoxidil solution for 24 weeks in 2-week intervals increased hair density and hair diameter. It resulted in better dermatologist and participant global photographic assessment evaluations compared to treatment with minoxidil alone [44]. Non-ablative 1550nm Fraxel laser (Solta Medical, Hayward, California) treatment followed by topical 0.05% finasteride 2ml solution compounded with distilled water and growth factors (vascular endothelial growth factor, basic fibroblast growth factor, insulin-like growth factor, and cooper peptide 1.2%) in four patients resulted in photographic improvement showing increased hair density [45]. Er:YAG laser (SP Dynamis, Fotona, Slovenia) with SMOOTH™ mode used as a monotherapy resulted in a decreased in AGA grade (Ludwig scale for female/Norwood-Hamilton scale for male), improvement in hair quality by blinded clinical evaluation, and increased patient satisfaction scoring [17].

Su et al. evaluated the efficacy of ablative 2940nm Er: YAG fractional laser (MCL31 Dermablate, Asclepion Laser Technologies, Jena, Germany, N25 mode, pulse energy 20–25J, pulse time 300μs), performed every two weeks over a 12-week treatment course (6 treatments total), in conjunction with oral finasteride and topical minoxidil 5% solution for two years, and noted significant regrowth as measured by a

decrease in Hamilton–Norwood classification and subjective improvement based on scalp photography [46]. A 1550nm fractional CO_2 laser was also investigated in conjunction with topical platelet-rich plasma (PRP) in 8 patients with AGA with low energy (pulse energy of 12mJ and density of 800 spots/cm^2) and high energy (pulse energy of 22mJ and density of 400 spots/cm^2), [47]. A combination of the fractional laser and 20-minute application of topical PRP in two-week intervals for 32 weeks resulted in a significant increase in total and terminal hair densities, noted at 6 weeks in the high energy group (179.14±45.64, P<0.05) and at 16 weeks in the low energy group (203.57±53.03, P<0.05). Greater changes in total hair density were noted weekly with high pulse energy treatment (1.42 hair/cm^2) compared to low pulse energy treatment (1.04 hair/cm^2, P=0.023), [47]. Fractional CO_2 laser (DEKA Smartxide^2 DOT/RF c60, Italy) used for six sessions with 2-week intervals in conjunction with topical 5% minoxidil solution twice daily for 12 weeks for has also been shown to result in a more significant increase in hair density compared to topical minoxidil application alone or laser therapy alone [48].

Overall, there is evidence supporting the use of fractional laser therapy as a potentially effective treatment for AGA, both alone and in conjunction with topical treatments. However, studies are needed to elucidate optimal treatment dosages, regimens, and maintenance therapy. Additionally, cost is a deterrent for treatments not covered by insurance.

Alopecia areata

There are several studies using fractional laser devices for patients with AA. A cohort study of eight AA patients with no treatment three months prior to the study was treated with fractional laser (1550nm non-ablative fractional erbium-glass laser, GSD, Shenzhen, China) every two weeks for 10 sessions in conjunction with topical 5% minoxidil tincture twice daily. New hair regrowth of 30%-50% was observed after three months of treatment in patients with patchy AA. There was complete regrowth in one alopecia totalis patient, one alopecia universalis patient with scalp lesions, and one patient with multiple lesions. One patient discontinued treatment owing to lack of improvement in hair growth after three sessions, and another patient with one lesion observed no change in hair regrowth [49]. Similarly, a case-controlled, single-blinded, comparative study treated 30 patients with patchy AA with a non-ablative fractional 1540nm erbium-glass laser (Quanta System S.P.A DNA laser technology, Milan, Italy) in weekly intervals with topical 2% minoxidil solution (for women) or Rogaine® 5% minoxidil (for men) twice daily for six weeks. The percentage of regrowth increased significantly (60%) in the treatment group compared to the control group (16%, P=0.002), [50].

A randomized split-side comparative prospective controlled trial treated 30 patients with patchy AA using a fractional CO_2 laser (Punto, Deka) followed by topical triamcinolone acetonide (10mg/ml) monthly for 6 sessions and compared the outcomes to another treatment group, microneedling (1.5mm), followed by topical corticosteroid. Response to treatment was assessed with the SALT score and both groups showed a statistically significant reduction in SALT score (P<0.001) exhibiting substantial hair regrowth. The microneedling group showed more improvement when compared to the laser treatment group (P=0.013), [51]. In contrast, a similar randomized controlled trial compared the efficacy of topical application of triamcinolone acetonide (10mg/ml) after a 1,060nm fractional CO_2 laser (DEKA Smartxide) versus microneedling via a Dermapen® (1.5mm, DermapenWorld, Australia) every three weeks for four sessions. No statistical difference was seen between the groups [52]. Another randomized controlled trial evaluated by SALT score the efficacy of monthly PRP intradermal injection alone, 1060nm fractional CO_2 laser (HiScan DOT tip of SmartXide DOT®, DEKA, Italy) followed by PRP topically, and microneedling via Dermaroller® (1.5mm needles, Dermaroller GmbH, Germany) followed by PRP topically for three months. All treatment groups showed improvement, though no significant difference between the groups by the physicians' clinical assessment (P=0.268) was noted [53]. Overall, more research is needed to determine which modality, laser or microneedling, serves as a

better transepidermal drug delivery system for AA patients.

There have been multiple case reports and series for recalcitrant AA as well, treated with fractional laser therapy (Mosaic, Lutronic, Seoul, Korea) and 10600nm fractional CO_2 laser (eCO_2 fractional CO_2 laser from Lutronics, Korea) and topical triamcinolone solution (10mg/ml) demonstrating efficacy ranging from complete regrowth in all lesions to 75% regrowth [54,55]. The utility of the 2940nm fractional Er: YAG laser (Fotona; Dualis SP, Ljubljana, Slovenia) was investigated in 25 patients with previously unresponsive alopecia areata [56]. After three sessions administered at 4-6-week intervals, the mean percent change in SALT score was 17.4±3.5%. Notably, 5 patients who were treated for alopecic patches in the beard area were found to have a 39±34.2 % regrowth rate [56]. Regrowth has been seen in both treatment resistant patchy AA, alopecia totalis, and alopecia universalis [49,52,55].

El-Husseiny et al. compared the efficacy and safety of fractional CO_2 laser ($FRCO_2$) to intralesional corticosteroid injections in 20 patients with at least two patches of AA [57]. One patch was treated with intralesional triamcinolone acetonide (ILTAC) 2.6mg/ml (maximum three ml injected per session, 0.1ml/point injections at 0.5cm to 1.0cm intervals) monthly for a maximum of three sessions while another patch was treated with $FRCO_2$ laser (Fire-Xel Bison laser; Korea (pulse width: 1026-1346μs, repeat delay: single, overlap: two times, density: 0.8 and energy 30.7-40.3mJ) every two weeks for a total of 3-6 sessions [57]. Three months after the last session, a greater improvement ($P<0.001$) was seen with $FRCO_2$ laser compared to ILTAC regarding hair density assessed with folliscopic examination ($FRCO_2$ median hair density 39.5 hairs/cm^2, ILTAC median hair density 11.50 hairs/cm^2, $P<0.001$) and patient satisfaction [57]. Notably, the study had a short follow up duration of only three months. Therefore, the long-term benefit of treatment without additional therapy is unknown.

Halim et al. evaluated the efficacy of fractional carbon dioxide laser compared to fractional carbon dioxide laser in conjunction with topical betamethasone valerate cream and topical betamethasone valerate cream alone in 30 patients with patchy AA [58]. The $FRCO_2$ laser group received treatment every two weeks for a total of 8 sessions (DEKA SmartXide Fractional CO_2 laser, power: 16, Dwell time: 600, Spacing: 600, Stack: two Fluence: 2.13 J/cm^2). Patients in the combination therapy group applied betamethasone valerate cream immediately after the laser session and twice daily in between laser sessions. Patients treated with betamethasone valerate monotherapy applied the cream twice daily. At the conclusion of the treatment period, patients treated with $FRCO_2$ laser alone or $FRCO_2$ laser and betamethasone valerate together had a statistically significant greater reduction in SALT score compared to patients treated with betamethasone valerate cream alone ($P=0.002$, $P=0.003$), though there was no statistically significant difference between patients who received betamethasone in conjunction with laser and those who received laser treatment alone ($P=1.00$). Side effects reported amongst patients who received $FRCO_2$ laser treatment were limited to transient erythema and scaling [58].

Similarly, a comparative study of two treatment modalities, topical clobetasol propionate (0.05%) cream once daily for three months versus fractional laser (2940nm, fractional Erbium:YAG laser) followed by clobetasol propionate (0.05%) cream once every two weeks was studied. Both treatment modalities showed significant reduction in SALT score, with the score being more evident in the laser-corticosteroid group ($P<0.035$), [59]. One possible mechanism of therapeutic effect may be improved transepidermal drug delivery. Fractional laser may also induce T cell apoptosis, scatter perifollicular lymphocytes around the microthermal zones created in the dermis by the laser [54], and cause minor wound healing, ultimately stimulating hair growth [38,54,60].

Lichen planopilaris/frontal fibrosing alopecia

There is little evidence regarding the use of fractional lasers to treat LPP/FFA, limited to case reports and series demonstrating partial hair regrowth and thickening after ablative 10600nm fractional laser treatment (eCO_2, Lutronics, Seoul, Korea) and reduced morbidity with the 1064nm Nd:YAG 1064nm non-ablative laser [61,62].

Other lasers

Alopecia areata

Titanium:sapphire laser's (TSL) exact mechanism in causing hair growth has not yet been fully elucidated but immune system modulation is proposed to play a central role. Similarly to the excimer laser, TSL is proposed to cause reduction in IL17 levels, increase levels of regulatory T cells and apoptosis of autoreactive T cells, and propagate the Wnt/βcatenin signaling pathway [63]. Hae et al. investigated the 311nm TSL for treating 19 patients with AA (3 with alopecia totalis, 16 with patchy AA) at weekly or twice weekly intervals at an initial treatment dose of 300mJ/cm^2, increasing by 50mJ/cm^2 at each subsequent treatment session until post treatment erythema appeared [63]. A median maximum dose of 700mJ/cm^2 after a median of 14 treatments resulted in excellent (75-99%) to complete hair regrowth in 14 patients, including one patient with alopecia totalis. Of the remaining 5 patients, three reported good (50-74%) or moderate (25-49%) hair regrowth and two patients with alopecia totalis had no hair regrowth. Reported side effects were limited to persistent erythema lasting over 48 hours with spontaneous improvement after several days [63]. Advantages associated with TSL include its non-invasive nature, minimally associated pain, and favorable side effect profile. Disadvantages of TSL for hair growth include persistent erythema, potential for blistering, and hyperpigmentation, as demonstrated in a randomized controlled trial investigating the efficacy of TSL compared to excimer laser for the treatment of vitiligo [64].

Conclusion

Lasers offer possible adjunctive treatment to existing systemic and topical therapies for various types of alopecia and may improve treatment compliance by patients who find it cumbersome to regularly apply topical treatments or for those who are averse to repeated intralesional therapy. Studies demonstrate potential benefits from lasers but, treatment details, including optimal treatment schedules, dosages, and maintenance therapy have not yet been established. Additionally, despite a medical diagnosis of alopecia, unfortunately most laser therapy is not covered by insurance and may be cost prohibitive for patients.

Overall, the lasers with the most promising evidence for potential alopecia treatment efficacy are LLLT for AGA, fractional laser for AGA, and excimer laser for AA. Several studies have evaluated the use of LLLT therapy to treat AGA. There are also several recent studies suggesting fractional laser, both as monotherapy and in conjunction with topical therapy, is a potential AGA treatment. However, it is important to consider the limitations of these studies; most studied patients were White male patients. To account for variations in patient populations and better understand patient outcomes, patient demographics should be included in all subsequent studies. Furthermore, a standardized method to analyze hair growth improvement is needed, as many studies use subjective measures to analyze efficacy of different LLLT therapies. Several small studies indicate excimer laser may treat AA. In comparison to the published literature regarding laser therapy for other forms of alopecia, the treatment of LPP/FFA with lasers is less robust and consists primarily of smaller case series and reports.

Furthermore, although quantitative hair measurements may improve with laser treatment, the patients' subjective evaluations of their conditions may not [1,19]. Additional controlled studies comparing treatment regimens with regards to dosing, frequency, maintenance therapy, and prognostic predictors of response to laser therapy, are necessary for lasers to become a more commonly utilized alopecia therapy. Although non-UV light laser therapies may be cost prohibitive, more studies are necessary to determine long-term cost effectiveness compared to more expensive therapeutics (such as Janus kinase inhibitors for the treatment of more severe AA).

Potential conflicts of interest

The authors declare no conflicts of interest.

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Table 1. *Lasers included in review.*

	Type of light, wavelength	Mechanism of stimulating hair growth	Type of alopecia investigated for treating	Adverse effects	Measures of efficacy	Average cost	Study results of laser therapy**		
								Hair change	
							Study name	Control	Laser
Low-level light therapy	Red and near infrared light 600-1070nm	Increased transcription of growth factors, reversion of telogen hairs to anagen phase, and induction of follicular stem cell proliferation	AGA AA LPP/FFA	Dry skin Pruritus Scalp tenderness Irritation Warm sensation Temporary hair shedding	Hair density (hairs/cm^2), symptom questionnaires, hair shaft diameter, LPPAI scores, % regrowth, global photography	$50-$150 per session	Leavitt [10] Jimenez [11] Fan [19] Amer [20] Suchonwanit [22]	4µm -8h/cm^2 12% -- 4h/cm^2	13µm 20h/cm^2 14% 16% 10h/cm^2
							Waiz [24]***	0%	94%
Fractional laser	Invisible infrared light 10,600nm	Production of microthermal zones, improved absorption of topical therapies, minor wounding stimulating growth	AGA AA LPP/FFA	Mild pain Erythema Edema Pruritus Hyperpigmentation	Hair density (hairs/cm^2), symptom questionnaires, hair shaft diameter, global photography, Hamilton-Norwood scale, % regrowth, SALT scores	Ablative $2,500 Non-ablative $1,445 per session	Meephansan [40] Lee [41] Alhattab [42] Huang [43]	70h/cm^2 100h/cm^2 73h/cm^2 114h/cm^2	94h/cm^2 157h/cm^2 83h/cm^2 143h/cm^2
							Tanakol [56]*** El-Husseiny [57]	-- 12h/cm^{2*}	62.5% 40h/cm^2
Excimer laser	Ultraviolet light 308nm	Induction of T cell apoptosis	AA LPP/FFA	Erythema Hyperpigmentation Burns	% regrowth	Often covered by insurance, $200-$21,000 per year	Ohtsuki [30] Al-Mutairi [31] Byun [34] Al-Mutairi [35]***	0% 0% -- --	50% 60% 50% 42%
311nm titanium: sapphire laser	Ultraviolet light 311nm	Photobiological effects of immune system Immunomodulation	AA	Erythema	% regrowth	Often covered by insurance	Lee [63]****	--	74%

AA, alopecia areata; AGA, androgenetic alopecia; FFA, frontal fibrosing alopecia; h/cm2, hairs/cm^2; hrct, hair count; LPP, lichen planopilaris.
*Median hair density of intralesional corticosteroid injections (control) vs. fractional laser (test).
**All studies had a washout period of previous treatment for hair loss or had never had previous treatment before.
***Patches tested were recalcitrant.
****Some patients did not have a washout period of prior medical treatments.
Yellow color = laser for AGA treatment.
Blue color = laser for AA treatment, unit is in terms of percent regrowth.