

Fractional Thulium Laser Combined with a Topical Growth Factor Serum Increases Hair Density and Thickness in Male and Female Androgenic Alopecia: A Pilot Study

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Disclosure: Dr. Taub has equity in SkinQRI. Complimentary growth factor serum was supplied to the researchers.

ABSTRACT

Introduction: A new treatment consisting of 1927nm fractional laser followed by application of a sterile growth factor solution has potential to treat androgenic alopecia (AGA). We set out to assess the efficacy of 1927nm laser as a topical assisted delivery system with a proprietary growth factor serum to improve androgenic alopecia, as well as to determine the number of treatments needed.

Methods: Ten subjects with mild to moderate AGA had a fiducial point tattooed on the temporal or parietal scalp. The subjects were split into three groups based on the number of treatments. A 1927nm laser was applied to the scalp followed by topical application of the sterile hair growth solution. Clinical and quantified trichoscopic photography were performed at baseline and then at 6, 12, and 24 weeks after the final treatment session.

Results: All 10 subjects reported no side effects and were subjectively satisfied with their result. Hair parameters showed increased hair density and diameter, both achieving statistical significance over the six-month period. There was no difference between the groups of varying numbers of treatments.

Conclusion: Combining fractional 1927nm laser treatments with a growth factor topical solution is safe and effective in the treatment of AGA. Three treatments at 4-weekly intervals is the best choice for treatment protocol.

Keywords: androgenetic alopecia, fractional laser, hair density, hair diameter, laser assisted topical delivery system

INTRODUCTION

Androgenic alopecia (AGA) commonly occurs in both males and females and is also known as male and female pattern hair loss.¹ In males, AGA is usually seen when they reach their 30s or 40s, but it can occur in the teens and twenties with around 50% of the male population being affected. In females, approximately 25% of AGA is associated with menopause, but 40% are affected by hair loss by age 50.² In male pattern AGA, the most common pattern is with the hairline receding to give the characteristic “M” pattern concomitantly with thinning at the parietal area (in hair transplant literature this is referred to as the mid-scalp), with the potential for the two areas to coalesce.¹ In females, thinning tends to start more at the parietal area and midline, with loss at the hairline being seen more towards the later stages.¹

One of the major causative factors of AGA is the effect of male hormone on the hair follicle. Conversion of testosterone to dihydrotestosterone (DHT)³ reduces the functioning of the dermal papilla in the hair bulb, thereby interfering with the anagen growth phase of the hair growth cycle. This shift of the hair follicles from anagen into catagen and telogen leads to shorter anagen growth phases, increased senescence of the dermal papilla, and production of hairs with ever-decreasing individual diameters. Not only are the number of hairs diminished, resulting in clinical evidence of hair loss, but the hair that does exist is finer and more fragile.

Adults suffering from AGA are increasingly seeking treatment from dermatologists in addition to the growing number of specialist hair loss clinics. Treatments have been mostly associated with the application of minoxidil solution as well as oral anti-androgens for men and women, although finasteride/dutasteride are contraindicated in premenopausal females with spironolactone having some efficacy as monotherapy.² The antiandrogens slow down the conversion of

testosterone to DHT by blocking the action of the compound 5-alpha reductase.² Another recent addition to the hair loss armamentarium that has gained popularity is platelet-rich plasma injections (PRP).⁴ PRP contains growth factors that are used for wound healing, including some that also stimulate certain portions of the hair life cycle. Although many patients have improvement with these treatments, the variables or incomplete response leads them to seek alternative or additional therapies. A new topical product that is suitable for both males and females contains growth factors and peptides influencing each stage of the life cycle. This formula is specific to hair growth needs. However, the formulation is not a drug and is not intended to be injected (for more information, see patent: <https://uspto.report/patent/grant/10,894,074>).

Several approaches have been reported to overcome the skin barrier to assist the intradermal delivery of active ingredients, including photobiomodulation (low level light therapy, or LLLT),⁵ microneedling with or without radiofrequency,^{6,7} and lasers.^{8,9} One laser wavelength that has recently attracted favorable attention to deliver actives to the dermis is 1927nm delivered by the thulium fiber laser, as reported by Cho and colleagues.¹⁰ The present study used the latest version of the system applied in the Cho study (LaseMD ULTRA, Lutronic Corp, Goyang, South Korea), a thulium fiber laser delivering a fractionated beam at the 1927nm wavelength, combined with topical application of a different patented growth factor serum.

SUBJECTS AND METHODS

Ten Korean subjects (7 males and 3 females, ages ranging from 29 to 50 years old) with mild to moderate AGA (Norwood Ia-IIb) were recruited into the study. Each subject's scalp was divided into the left and right sides, and fiducial markers were tattooed onto the scalp just into the

The treatment period for all 10 subjects was 12 weeks. Treatment sessions for all subjects were carried out with the fractional thulium laser over the entire scalp using a plastic tip to part the hairs that allows the 1927 to emit at a power output of 1W, pulse energy of 1mj in dynamic mode, for 4 passes total (approximately 4-5% density overall). The interaction between the 1927nm energy and tissue at these parameters was minimally invasive and subablative with virtually no downtime, as discussed below.

FIGURE 2. The 12-week and 6-month protocols for both clinic (Tx) and at home (open circle) treatments for Groups A, B, and C.

		Treatment weeks												Follow-up weeks				
		0	1	2	3	4	5	6	7	8	9	10	11	12	1 ~ 6	~ 12	~ 24	
Group A	B/L	Tx	Tx	Tx	Tx	Tx	Tx	Tx	Tx	Tx	Tx	Tx	Tx		A1	A2	A3	
	○	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	
Group B	B/L		Tx		Tx		Tx		Tx		Tx		Tx		A1	A2	A3	
	○	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	
Group C	B/L				Tx				Tx				Tx		A1	A2	A3	
	○	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	

B/L = Baseline assessment; A1, A2, A3 = Follow-up assessments; Tx = Treatment sessions

○ → → → → ○ Daily home regimen with serum and shampoo

hairline at the bilateral area of frontal hair loss (7 subjects) or just into the hairline on the left side of the parietal hair loss area and the right-side area of the frontal hair loss area (3 subjects) (Figure 1). The fiducial markers were used to ensure that the same areas were assessed for density and individual hair diameter with a dedi-

Having had the elements of the trial fully explained to them, including possible results and adverse side effects, all subjects gave written informed consent for their participation in the pilot study and for the use of their clinical photography. The study was carried out adhering to the precepts of the World Medical Association Declaration of Helsinki (2013).

All 10 subjects completed the full trial protocol, including the follow-up assessments and the home-care regimen. Subjects reported very little or no discomfort during or after treatment with transient and very mild erythema lasting 1-2 hours as the only side effect, and all subjects were satisfied with the results.

4). These findings were echoed in the objective trichoscopic data, with the greatest improvement generally seen at the 3-month assessment point. High statistical significance (p .0004-.0001) was seen between baseline findings and all assessment points, including the 6-month point.

The trial protocol called for the subjects to be allocated to three groups with different frequency of laser treatment protocols during the 12-week treatment period. Group A had 12 sessions at weekly intervals, Group B had 6 sessions at 2-week intervals, and Group C had 3 sessions at 4-week intervals. Figure 7 compares changes in density and diameter among the three groups with no group showing higher

FIGURE 5. Line graphs illustrating the course of improvement for each individual subject in hair density as hair counts per 0.24cm² sample area (a) and individual hair diameter expressed in μm (b) as assessed by the trichoscopic diagnostic system.

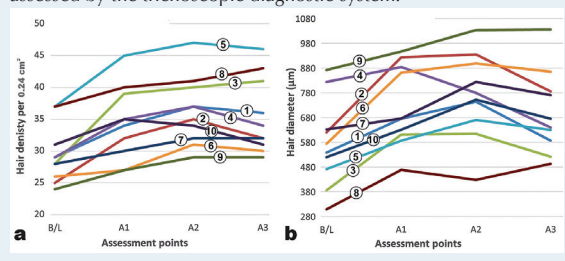
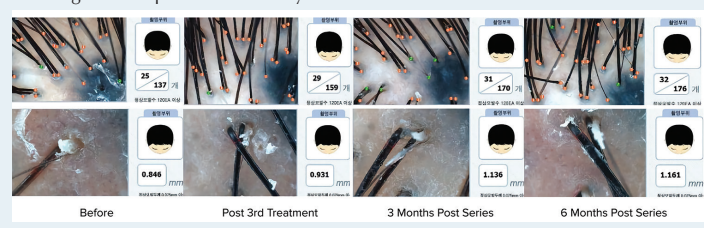
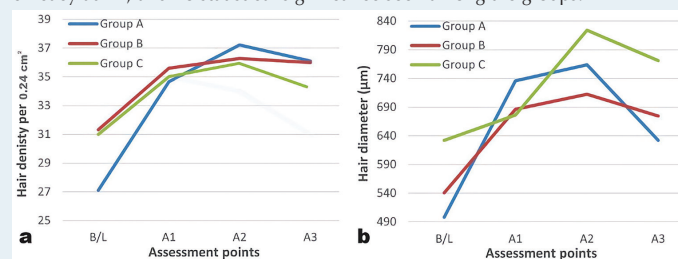


FIGURE 6. Imaging from the hair & scalp trichoscopic diagnostic system for Case 1, showing in the top row hair density and in the bottom row hair thickness.



statistical significance in improvement. Because of the low number of subjects in each group, the statistical power is also very low, but a trend towards a similar level of efficacy is clearly seen among all three groups.

FIGURE 7. Line graphs illustrating the course of improvement in Groups A, B, and C in hair density (a) and hair diameter (b) from baseline through assessment points A1, A2, and A3. The pattern is the same among the three groups with greatest efficacy at A2, and no statistical significance seen among the groups.



DISCUSSION

As mentioned, DHT is recognized as one of the major causative factors in the induction of pattern baldness. The driving force behind anagen, the growth phase in the hair cycle, is the influence of the dermal papilla on the active differentiation of stem cells within the hair bulb.¹¹ These stem cells are “pushed” by the dermal papilla to differentiate to produce keratinocytes and keratin, which forms the cortex, the bulk of the growing hair shaft, and the protective cuticle.¹² DHT interferes with the signaling processes that support differentiation and induces breakdown of the anagen phase thereby forcing the hair into catagen (transformational phase) and prolonged telogen (resting phase). Subsequent anagen phases become shorter and hairs become progressively thinner and weaker. The growth factor solution in this study contains a specific patented blend of synthetic oligo- and polypeptides designed to augment the protein signaling processes and boost the driving power of the dermal papilla during the anagen phase of hair growth, thereby counteracting the deleterious effects of DHT, thus prolonging the anagen phase.

Most DHT blockers are oral prescription medications. There

has been a grassroots movement to highlight adverse effects such as impotence, erectile dysfunction, and depression for men who take them, leading to reluctance and/or poor compliance by patients.¹³ Females can only safely take them if they are post-menopausal, and they seem to have less response to them than males.¹⁴ Females are also given oral spironolactone, which seems to work much better as an acne therapy than as a hair loss therapy (personal observation by author).

Topical minoxidil is the oldest therapy that has scientific evidence of efficacy. The mechanism of action is believed to be dilation and expansion of the capillary bed in the scalp to increase nutrition to the papillae, counteracting the miniaturization process. Although this is widely utilized with some success, it often isn’t successful at all or only partially, or has some other characteristics, such as stickiness of formulation or initial shedding of hair, that lead many to abandon it.¹⁵

The problem with topical products of any kind is that they need to reach the dermis to be effective. The hair follicle bulb, where the dermal papilla does its critical work, is deep in the scalp subcutis. The epidermis, in particular the stratum corneum, the waterproof outer layer of the epidermis, plays a very important role as part of the skin barrier function, preventing toxic substances, microbials, and allergens from entering the dermis and causing harm to dermal cells and extracellular matrix. Unfortunately, the skin barrier function equally prevents beneficial substances from reaching the dermis, and the role of the laser is to temporarily defeat, but not permanently destroy, the power of the skin barrier function, especially the stratum corneum. Although each polypeptide in the treatment preparations is wrapped individually in liposomes and have been proven to penetrate hair follicles to the bulge where most of the growth factor receptors are present, laser assisted topical delivery was hypothesized to greatly increase the potential concentration of actives reaching the dermis, as has been shown with other topical therapies.¹⁶

The 1927nm laser wavelength was chosen because it has a better absorption in water than the 1540nm wavelength typical of nonablative Er:glass lasers, but less than the fully ablative wavelengths of the Er:YAG (2940 nm) and CO₂ (10600 nm) lasers (Figure 8). Figure 9 illustrates the histology of the 1927nm fractional laser’s impact on skin at the parameters used in the present study. The stratum corneum has been temporarily disrupted, the tight cell-cell adhesion of the stratum spinosum has been transiently degraded, and very mild and controlled coagulation has occurred in the very superficial dermis with minimal disruption to the dermoepidermal junction. This combination of events should allow topically applied solution to make its way more easily through the epidermis and into the dermis, especially when the ingredients are encapsulated in nano-liposomes. Additional benefits arise from the

FIGURE 8. The water absorption curve in the near and mid-infrared waveband showing the absorption coefficients for the nonablative Er:glass and ablative Er:YAG and CO₂ lasers compared with the subablative LaseMD ULTRA.

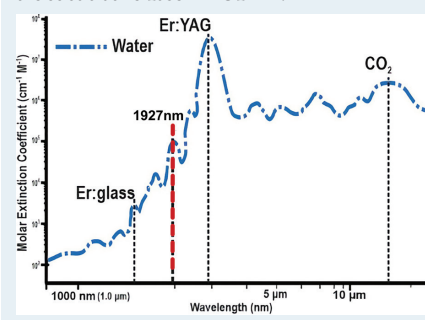
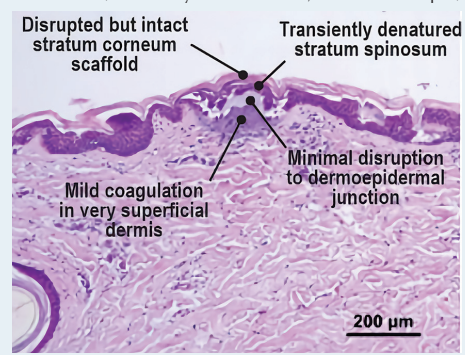


FIGURE 9. Histological specimen showing a typical ULTRA impact in human skin at low parameters: see text for details. (Hematoxylin-eosin stain, scale bar 200 μ m)



mechanism. Because the resulting reaction is gentle and subablative, downtime for the patient is extremely short and discomfort is virtually nonexistent (occasional mild sunburn sensation that resolves within a few to 48 hours).

There was little difference in the efficacy for both increased hair density and thicker hair diameter among the groups in the study (Figure 7). Being able to demonstrate a statistically significant increase in both hair density and hair diameter was the most important finding of the study. Most patients are concerned with the appearance of the coverage of their scalp or the ability to visualize the scalp beneath the hair. The hair diameter finding gives the added benefit of making the hairs appear thicker as well as more numerous.

One might have assumed that a higher number of treatment sessions with shorter intervals between treatments would have produced better results than a lower number of sessions with longer intervals, but no such advantage was seen in the present study. It could well be, given the large interindividual differences seen among the subjects (Figure 5), that a study with a larger patient population for the three groups would show an advantage for more laser treatment sessions and shorter intervals. It is also possible that the papillae or bulbs have limits to the degree or time in which they can produce more or better hairs. However, it is not always possible either from the viewpoint of finance or time constraints for patients to attend more frequently, so the preliminary results from this pilot study should give hope that this will be a more practical therapeutic option. The 24-week time point is a strength of the study, with hair density and diameter remaining statistically significantly improved versus baseline. Given the fact that many did see the hair counts start to fall could indicate that a treatment every 3 months may be optimal. A weighting of products to determine usage of home therapy was not undertaken.

The major limitations of this study are its size and the lack of a control group. It may be possible that either the 1927nm fractional laser treatments or the treatment solution alone caused the results. The main aim of this pilot study was to assess the efficacy of the fractional 1927nm thulium laser as laser assisted topical delivery for the growth factor solution, and this efficacy was clearly illustrated for both hair density and individual hair diameter. A previously performed similar study using the 1927 laser, a 12 $\times$ 1 week time point, and a different proprietary solution showed good results with respect to hair counts and diameter as well.¹⁰ In the prior study, more aggressive param-

eters were used for the 1927nm laser, and there was a slightly better result on the portion of scalp receiving solution that was not statistically significant. One cannot discount the fact that through absorption, the growth factors could have also stimulated the opposite side of the scalp because all patients had one portion of their scalp with solution applied immediately after treatment as well as use of take-home product.

CONCLUSION

This pilot study has demonstrated that a fractional 1927nm laser acts as an efficient topical delivery system for a proprietary growth factor solution, producing statistically significant results for both hair density and hair diameter, and clinically apparent hair growth with patient satisfaction that lasted until the six-month follow-up. Further studies with larger populations are encouraged and needed to confirm the optimistic results of this small population study.

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