Clinical Applications of a Non-ablative Fractional Dual Laser (1550/1927 nm)

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The non-ablative fractional dual laser is equipped with two types of lasers, 1550 nm and 1927 nm in one device, and was approved by the United States Food and Drug Administration in 2013. The advantages of the non-ablative fractional laser (NAFL) include fewer side effects such as erythema, edema, post-laser pigmentation, and scab formation. Thus, the NAFL is preferred by both practitioners and consumers because it is convenient and safe for use. The 1550 nm erbium glass and 1927 nm thulium lasers are representative NAFLs that have been developed separately and are often used as a single-wavelength laser with proven clinical efficacy in various indications. The 1550 nm wavelength laser penetrates the dermis layer and the 1927 nm wavelength laser is effective for epidermal lesions. Therefore, targeting the skin layer can be easily achieved with both the 1550 and 1927 nm lasers, respectively, or in combination. Clinically, the 1550 nm laser is effective in the treatment of mild to moderate sagging and wrinkles, scars, and resurfacing. The 1927 nm laser improves skin texture and treats skin pigmentation and wounds. It can also be used for drug delivery. The selection and utilization rate of NAFL has been increasing in recent times, due to changes in lifestyle patterns and the need for beauty treatments with fewer side effects and short downtime. In this study, we present a plan for safe and effective laser therapy through a review of literature. Clinical applications of the multifunctional NAFL are also described.

Key words

Nonablative laser Treatment; Rejuvenation; Acne; Melasma

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INTRODUCTION

Since the concept of 'fractional thermolysis' was first introduced by Huzaira et al. in 2003 and the first fractional thermolysis device was made in 2004, various models of fractional laser have been steadily developed in the clinical field of skin rejuvenation.¹ The Fraxel® laser (Solta Medical, Hayward, CA, USA) has evolved into one of the most well-known fractional lasers in the masses along with various models of several wavelengths, of which the Fraxel Dual® laser is the latest model. The Fraxel Dual® laser (Solta Medical) is a nonablative fractional laser (NAFL) developed by mounting lasers of two wavelengths, 1550 nm and 1927 nm in a single device, and had received the United States Food and Drug Administration (FDA) approval in 2013 (Table 1).²

Compared to ablative fractional laser (AFL), NAFL creates a microthermal treatment zone (MTZ) without removing the epidermis and provides a therapeutic effect in a non-peeling manner. The advantages of the NAFL include the rare formation of the scabs, few incidences of erythema and edema, short duration, low post-laser pigmentation, and rare permanent side effects. So, it is preferred both for practitioners and consumers because of its convenience and safety.³⁻⁵ The 1550 nm erbium glass (Er:glass) and 1927 nm thulium laser are representative NAFLs that have been developed separately and are often used as single-wavelength laser and have been proven to have clinical efficacy in various indications. While the 1550 nm wavelength can penetrate the dermis layer, the 1927 nm wavelength is suitable for the epidermal lesion. So, targeted skin layer can be easily achieved with both 1550 nm and 1927 nm respectively, or in combination.² The dual laser, which incorporates these two wavelengths in one device, can be seen as a device that maximizes the advantages of the nonablative fractional treatment method. Clinically, the 1550 nm laser can be applied to the treatment of various skin problems such as mild to moderate sagging, scars, rejuvenation of aging skin, and

acne vulgaris. The 1927 nm laser improves skin texture and treats skin pigmentation, drug delivery, and superficial wounds.²

However, it is a well-established theory that AFL is superior to NAFL in terms of clinical efficacy. It is undeniable that repeated NAFL treatments are necessary to attain the effects of a single treatment of AFL.⁶ Nevertheless, the frequency of difficult complications such as post-inflammatory pigmentation (PIH) and permanent scars which are especially common in oriental and female skin, is extremely low after NAFL treatment rather than AFL. The selection and utilization rate of NAFL is higher in modern society, considering the lifestyle patterns and treatment needs of beauty treatment patients who prefer fewer side effects. This tendency is expected to further expand in the field of skin laser treatment.⁷⁻⁹ Therefore, the consideration of the clinical application of NAFL would be meaningful.

CLINICAL APPLICATION

Skin rejuvenation

Like all the organs in our body, the skin also ages based on age favorites. As an internal factor of skin aging, the main cause is the shortening of telomeres at gene terminals and changes in hormones, and ultraviolet (UV) rays are the most important cause as an external factor. Smoking, stress, malnutrition, and pollutants have been also demonstrated to external factors in skin aging. Under such condition, reactive oxygen species (ROS) are generated, thereby promoting cell aging.^{10,11} Skin aging induces changes in the pre-structured layers of the face.¹² Aged (or photoaged) skin shows macroscopic wrinkles, pigmentation, skin atrophy, and loss of organized epidermal and dermal architecture, flattening of rete ridge, cutaneous thinning with reducing collagen fiber in histologically. With aging, collagen content in the dermis decreases by 1% every year, and it has been reported that the decrease is particularly clear with about 20% in photoaged areas until the age of 80 years. In addition to the reduction in collagen produced by senescent fibroblasts, glycosaminoglycan is also reduced, and senile fibroblasts also exhibit a late response to growth factors. Interestingly, when measuring the procollagen gene expression in aged skin, collagen loss is most pronounced in the upper third of the dermis, which is probably associated with UV skin penetration.¹¹

Both ablative and nonablative fractional laser are effective for dermis remodeling and show similar histological findings and changes in the molecular mediator.³ Ablative laser resurfacing has been known as the most effective

Table 1. FDA-approved area of Fraxel Dual® laser (<http://fda.gov>)

Wavelength	FDA approved Clinical Indication (2013)
1550 nm laser	Skin resurfacing, soft tissue coagulation procedure, treatment of dyschromia and cutaneous diseases (such as lentigos, actinic keratosis, and melasma) treatment of periorbital wrinkles, acne scars and surgical scars
1927 nm laser	Soft tissue coagulation, actinic keratosis, treatment of pigmented lesions (such as lentigos, freckle)

FDA, the United States Food and Drug Administration.

method for treating wrinkles, and atrophic scars, but it sometimes has long recovery periods after treatment with side effects such as erythema, pigmentation, and high frequency of herpes infections.¹³ With the development of fractional photothermolysis methods that can reduce the downtime and side effects, there have been attempts to replace the fractional technology as alternative and the use of NAFL is increasing. One of the representative NAFL is the 1550 nm Er:glass laser.¹⁴ Although ablative laser resurfacing is gold standard treatment in severe photoaged skin,^{8,9} the NAFL showed the similar clinical results in mild to moderate cases. Moreover, it showed an increase in the success rate of treatment when used in combination with treatments such as botulinum toxin and filler.^{14,15}

A single one-time NAFL treatment has little impressive improvement effect, but it does not interfere with daily life. As the treatment has only a few inconveniences and side effects, it is easy to repeat the treatment and can be used in combination with other devices. This usefulness

of the therapy opens up the possibility of clinical use of NAFL for the treatment of mild and moderate skin aging. In addition, in patients with Fitzpatrick skin types IV to VI, the 1550 nm Er:glass laser reduced the frequency of side effects.¹⁶ This report is thought to help in laser treatment of oriental people who are fragile to side effects such as post-inflammatory hyperpigmentation (PIH) associated with laser. In our cases, patients with Fitzpatrick type III-IV can experience fewer side effects and recurrences during nonablative fractional dual laser treatment (Fig. 1). Side effects after laser are usually slight and temporary. According to the literature investigated by Fraxel Dual® Laser, about 5% of treated patients showed side effects; 1.8% of prolonged erythema, PIH (1.1%), erythema exacerbation (0.9%), herpes recurrence (0.6%), and acne recurrence (0.2%). But long-term severe adverse reactions were not reported.^{17,18}

We recommend considering two treatment strategic models at the time of designing treatment methods and setting parameters according to the purpose of treat-

Fig. 1. Skin rejuvenation cases treated with nonablative fractional dual laser. (A) Preclinical photograph. (B) Clinical photograph after treatment. Improvement in the wrinkles on the entire face can be seen. (C) Preclinical photograph. (D) Clinical photograph after treatment. Improvement in the wrinkles on the forehead can be seen.

ment. One strategy is inducing heat energy to wrinkles directly with high energy. And the other one is indirect heating transmission with medium to low energy overlapping and channeling which can be effectively performed to increase the penetration of the drug and active ingredient (Fig. 2). In the 1550 nm Er:glass laser, the primary chromophore is water in the tissue, the absorption into hemoglobin becomes much higher compared to the lasers with a shorter wavelength band of 1320 nm and 1440 nm. So, the light and heat effect can be well-transmitted into the dermis in a relatively short time. After four treatments at 6-week intervals, dermis thickness has been reported to increase by approximately 17%, and the collagen synthesis were not shown difference significantly despite of the energy level (15 mJ vs. 70 mJ). Therefore, lower microbeam energy and high microbeam density are important to achieve optimal treatment.¹³

However, post-laser pigmentation studies suggest a slightly different effect, which affects beam density more than energy. The report showed that increasing the number of treatments with low density improved clinical efficacy and reduced PIH (from 18.2 to 6%).^{15,16} In other words, we propose that a strategy of increasing microbeam density to increase collagen synthesis, whereas increasing the number of treatments with low density nesting is effective in pigmentation treatments.

The 1927 nm thulium laser demonstrated effective results in terms of improvement in pigmented lesions and resurfacing of photoaged skin even in the relatively low energy of 5-10 mJ.¹⁸ Nonfractional ablative dual laser for skin rejuvenation is a new single or combination therapy that reduces side effects, discomfort, duration of illness, and provides safe and effective therapeutic effects in a

way that enables the continuation of daily life without any problems.

Acne scar

Acne is a chronic inflammatory skin disease that 80% of adolescents and young adults experience, with repeated inflammation and secondary complications such as pigmentation, scarring, and erythema, along with cosmetic problems and the development of low self-esteem. It has been reported that there exists a possibility of social and psychological effects such as emotional difficulty, social isolation, anger, and depression.¹⁹ Acne is caused by multiple factors: 1) sebum produced by sebaceous gland, 2) formation of sebum colony pocket of *Cutibacterium acnes*, 3) change in keratinization process, and 4) inflammatory-mediated secretion.²⁰ The first-line treatments for acne are conventionally topical and oral medications, but the side effects and contraindications of the medications, which often do not provide complete improvement, can be significant, and the frequent recurrence of acne is clinically proven. In such cases, the alternative treatment should be needed.²⁰

The Er:glass laser reacts with water-containing epidermal keratinocytes, collagen, blood vessels, and other skin tissues, and partially damages the sebum. In general, the wavelength band that exhibits the optimal photothermal effect of the sebaceous glands is 1210-1760 nm, and the 1550 nm and 1540 nm Er:glass lasers are absorbed by the sebaceous gland and surrounding dermal matrix.^{15,21} The depth of the sebaceous gland is 200-1000 μm , and to treat acne, it is necessary to penetrate to a depth of about 400 μm , which can cause heat damage to the sebaceous gland and follicular infundibulum. The principle of treating acne using the Er:glass laser can be divided into two parts. One method is that the heat causes directly injury to the sebaceous gland and infundibulum directly, and the other one is drug delivery with photosensitivity agent.^{22,23,25}

Looking at the studies on short-term and medium- to long-term effects for the treatment of acne using the 1540 nm or 1550 nm Er:glass laser. Bogle et al. treated patients with moderate to severe inflammatory facial acne four times at two-week intervals. Six months after treatment (10 J/cm², 4-6 pulses), 68% of patients and 78% of physicians reported improvement.²² In another study, 1550 nm laser was followed up every 3 months for 1 year after 4 treatments (30-40 mJ) at 2-week intervals, thereby resulting in a significant reduction in the number of acne lesions and the size of sebaceous gland.²³ According to the medium- to long-term study, follow-up results of 1550 nm laser after 4 treatments (169 spot density and

Fig. 2. Schematic diagram of two treatment strategies for nonablative fractional dual laser. PDT, photodynamic therapy.

15-30 mJ/cm²) at 4-week intervals, showed improvement of 72% in 6 months and 79% in 1 year. The side effects were temporary erythema and edema, and some patients showed recurrence of acne and increased skin sensitization, but all the patients had reduced sebum-induced skin slippage.²¹ In another long-term study using a 1540 nm laser for facial acne, 71% improvement was reported after 6 months after 4 treatments (20% nest, 40 J/cm²) at 4-week intervals and 79% per year. The subjects responded well to various acne lesions such as nodules, comedones, papules, and pustules with reduced sebum-induced skin slippage.²⁴ In summary, it was observed that the therapeutic effect of Er:glass laser is excellent, and the effect maintained for a relatively long period of time without remarkable side effects. Considering the burden of long-term oral peels prescription, the NAFL is good option as alternative treatment for active acne vulgaris and depressed acne scar together.

In the following method, the energy absorption is increased when a photosensitive agent is applied during the operation of Er:glass laser. Studies have shown that applying 7.5% aminolevulinic acid (ALA) after 1550 nm laser treatment increased the absorption of photosensitive agents depending on the laser energy and operation time.²⁵ By taking advantage of this point, it is possible to treat acne scars and sebaceous gland at the same time to reduce the onset of acne as well as to improve the wound. So, two treatment objectives can be achieved, thereby leading to the patient's satisfaction. We believe that it is possible to improve the degree and therapeutic effect in a short period of time and propose the method as an effective strategy.

The optimal standard for scar treatment is known as the ablative laser. However, due to the long recovery time, discomfort, and several side effects that occur during large-scale laser peeling, fractional type of ablative laser using CO₂ and Er:YAG are often used.^{1,8} Even with AFL, however, at least a week time is required for the scab to fall off spontaneously, which can interfere with daily life. Considering the side effects such as deposition and erythema, NAFL can be an alternative method. A comparative study of the facial acne scars shows that the AFL has a better improvement effect than the NAFL (AFL 26-83% vs. NAFL 26-50%). However, the duration of erythema (AFL 3-14 days vs. NAFL 1 day), the incidence of PIH (AFL 92.3% vs. NAFL 13%), the pain score (AFL 5.9-8.1 vs. NAFL 3.9-5.6) provide a good idea about the benefits of NAFL treatment.¹ If so, when is the optimal timing to manage scars with the NAFL treatment? Concerning thyroid surgery with a 1550 nm laser, a study revealed that

treating the wound 3 weeks after surgery was significantly better than the group that started the treatment 3 months and 6 months after surgery.²⁶ In the future, it is thought that numerous attempts will be made to start relatively early scar treatment using the NAFL after surgery. Based on this theory, satisfactory results were obtained that the acne scar was treated with a nonablative fractional dual laser (Fig. 3).

Melasma

How can the 1550 nm or 1927 nm laser, of which chromophore is water, help treat pigmented diseases and melasma? The mechanism of treatment for pigmented diseases by NAFL can be summarized as follows. 1) Emission of melanin by the 'melanin shuttle' mechanism, 2) Increased selective penetration of whitening agents, 3) Recovery of the dermis environment by an increase in fibroblasts and inhibition of physiological melanin action. All the effects can be observed simultaneously.^{18,27}

The process of the melanin shuttle is as follows. The microscopic thermal zones (MTZ) generated by fractionated photothermolysis also affect keratinocytes and collagen fibers, thereby forming cylindrical necrosis of

Fig. 3. Acne scar cases treated with nonablative fractional dual laser. (A) Preclinical photograph. (B) Clinical photograph after treatment. Acute acne can be resolved after treatment. (C) Preclinical photograph. (D) Clinical photograph after treatment. Improvement of the chronic acne scars can be seen.

Fig. 4. Melasma case treated with nonablative fractional dual laser. (A) Preclinical photograph. (B) Clinical photograph after treatment. Improvement in the melasma around the left eye can be seen. (C) Preclinical photograph (polarized). (D) Clinical photograph after treatment (polarized). Improvement in the melasma around the left eye can be seen.

intraepidermal keratinocytes called microscopic epidermal necrotic debris (MENDs). Keratinocytes and dermal tissue move towards the stratum corneum and are removed. The mechanism by which NAFL removes melanin from the dermis and epidermis is called 'Melanin Shuttles'.²⁸ Also, as with the AFL, application of drugs and active ingredients after NAFL treatment increases delivery, and application of a whitening agent after selective laser treatment of pigmented lesions increases the whitening effect on the target area.²⁹ Nowadays, a focus of melasma and pigmented diseases has been changed to the surrounding skin environment from a melanocyte-centric perspective. Melanocytes are affected by cell-to-cell interaction with keratinocytes or dermal fibroblasts, and studies have been established that involve genes, paracrine factors, and receptors, but they are still unclear. The process of melanogenesis and migration is affected by various external stimuli and the nervous and hormonal systems. The melanocytes at the cellular level are affected by the reaction of cytokines and receptors secreted by keratinocytes and fibroblasts (paracrine factors). They are affected by a dual inhibitory effect with regulatory proteins of gene expression.³⁰ In the Wnt receptor of melanocytes, the intracellular reaction related to melanin synthesis is

suppressed by Wnt inhibitory factor (WIF), and when WIF is suppressed or blocked (double suppression), melanin synthesis is conversely increased.³¹ Looking at the effects of pigments on factors derived from fibroblasts in the dermis, the action is like a double-edged sword. For example, Dickkopf 1 (DKK1) and neuregulin-1 are reported to be associated with physiologic pigmentation, and stem cell factor (SCF), hepatocyte growth factor (HGF), and basic fibroblast growth (bFGF) are reported as arguments associated with pathologic pigmentation. Especially, the SCF secreted from fibroblasts is known as a typical aggravating factor for melasma. DKK1 secreted from fibroblasts in the dermis has been reported to suppress the Wnt signal pathway. Compared to the torso, palm and sole showed hypopigmented state. Some researchers explained its phenomenon due to the Wnt inhibitory effect of DKK1.³² Also, the WIF-1 is a typical tumor suppressor that has various effects on the body, and it suppresses cancer and skin pigments.³³ In melasma lesions, the WIF-1 which a suppressor of canonical and noncanonical Wnt signaling, appears to be down-regulated. Decreased WIF-1 from fibroblasts and even from keratinocytes are known to significantly stimulate the production of melanin and the transmission of some melanocytes to form melasma. In one of WIF studies, regulation of Wnt and DKK signaling pathways is usually observed in pigmented disorders, they suggested that the regulation of Wnt inhibitory factors and DDK pathways in the dermis and epidermis would be effective to treat melasma.^{31,34} From this point of view, it is interesting to note how the 1550 nm laser treatment affects fibroblasts. It is believed that laser induced-activated fibroblasts could affect surrounding fibroblasts by signal transmission. This concept can be used to treat pigmented diseases, and if research on the exact conditions comes out, it will be of great help in the treatment.

From a clinical point of view, various attempts and studies have been continued to treat pigmented diseases and melasma in Asian skin. Unlike white people, they have potential complications such as post-laser induced PIH or hypopigmentation, and recurrence. To overcome these limitations, various studies have been attempted to treat melasma with low energy and density of NAFL treatment. In studies used to treat melasma with the 1550 nm laser alone, the results showed temporary improvement and then the possibility of recurrence exacerbation emerged. For example, in a study conducted with 1550 nm laser alone (6-10 mJ, 2000-2500 MTZ / cm², 4 treatments at 2-week intervals) in patients with Fitzpatrick Scale III / IV, melanocyte count and peripheral keratinocytes reported a decrease in melanin content and patients with

Fitzpatrick Scale III / IV stains Treatment) after 1550 nm laser treatment (6-12 mJ, 1-2 week intervals, 4-6 times).²⁷ However in another report, at 12-week follow-up, patient ratings were 75-100% and physician ratings were 50-60% improvement, while the initial 1-2 treatment results were better than the result of medium- to long-term follow up.³⁵ In another study, a division comparing the 1064 nm Q-switched Nd:YAG (1064 QSNY) single treatment and the merged treatment (1064 QSNY laser plus 1550 nm laser) at Fitzpatrick skin type III / IV melasma patients, this study results revealed a significant improvement in each group, but no significant difference between the two groups could be demonstrated at 4 and 12 weeks after the last treatment.³⁶

The 1927 nm laser, which attracted attention in the treatment of pigmented diseases, also showed good effects at the early stages, but recurrence and rebound phenomenon were observed. Treatment of melasma with 1927 nm laser improved the Melasma Area and Severity Index (MASI) score by 28-45%, but the effect diminished 2 months after treatment and a recurrence was reported at 3 months.³⁷ The effects of the single NAFL treatment of melasma showed various and temporary outcomes in either the 1550 nm or 1927 nm lasers. Thus, increasing the number of treatments with low-density and low-energy is a key of reducing the side effects to treat pigmented diseases. Long-term planned research is demanded to increase the efficacy of NAFL in field of melasma treatment.³⁷

Meanwhile, the laser merge therapy has been proposed to overcome the above-mentioned problem. A recent combination therapy study reported treatment of patients with Fitzpatrick skin types II-IV with a combination of 595 pulse dye laser and 1927 nm laser. Its result showed that 54% of patients improved their melasma and the efficacy was prolonged until 3 months without complications.³⁸ Also another merge therapy with topical tranexamic acid delivery, a repeat every 3 months treatment was safe and effective in long-term follow up.³⁹

Summarizing the melasma treatments using NAFL, it is helpful to treat melasma, but further studies are considered necessary which improve the medium- to long-term effects as well as combination therapy, especially according to the skin characteristics of Asians.

CONCLUSION

In the present study, the literature and actual clinical cases of the features and clinical applications of the nonablative fractional dual laser, which is a multi-laser

were examined. The fact that it is possible to return to a quick daily life and that there are relatively few sequelae are advantages for busy modern people. There are certainly limits to monotherapy, but there is no doubt that it is a good laser that can provide great satisfaction to patients when used accurately and effectively in case of a variety of lesions. We hope that this article will be useful for safe and effective laser treatment.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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