Treatment of periorbital wrinkles with 1,550 and 1,565 nm Er:Glass fractional photothermolysis lasers: A simultaneous split-face trial

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Treatment of periorbital wrinkles with 1,550 and 1,565 nm Er:Glass fractional photothermolysis lasers: A simultaneous split-face trial

Directed by Professor Kee Yang Chung

The Master's Thesis
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

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June 2008

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June 2008

ACKNOWLEDGEMENTS

First of all, I give warm thanks to my thesis supervisor, professor Kee Yang Chung, for his supervision and encouragement to successfully complete this thesis.

I also give my appreciation to professors Kwan Chul Tark and Kwang Hoon Lee who gave me experienced advices and warm supports. I also thank Dr. Hye-Jin Chung for great support, technical assistance and encouragement in carrying out this study.

I would like to express my gratitude to my parents and family members for their continuous caring and love throughout my life.

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ABSTRACT

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Fractional photothermolysis using a 1,550 nm Er:Glass laser is effective in treating periorbital wrinkles and, in order to achieve deeper penetration, a treatment method using a 1,565 nm Er:Glass laser has been recently developed. This study was conducted to evaluate and compare the clinical effects of the 1,550 and 1,565 nm Er:Glass lasers in the treatment of periorbital wrinkles. We documented changes of collagen and elastic fibers in dermis in a split face trial. In this study, we evaluated the treatment of 20 participants who had their right periorbital area exposed to a 1,550 nm Er:Glass laser and their left periorbital area exposed to a 1,565 nm Er:Glass laser. All participants received five treatments at 3-week intervals. Clinical improvement was evaluated by the patients themselves and also by two physicians who compared pre- and post-treatment photographs using a 4-point score system (0 =< 25%, 1 = 25%–50%, 2 = 51%–75%, 3 => 75% improvement) at 1 and 3 month time points after the final treatment. Skin biopsies were done in five volunteers before treatment and 3 months after the final treatment. The mean improvement score at the 1 month time point for the 1,550 nm Er:Glass laser was 1.53±0.71, while it was 1.63±0.66 after the treatment with 1,565 nm Er:Glass laser. The mean improvement scores 3 months after the treatment with the 1,550 nm and 1,565 nm Er:Glass lasers were 1.25±0.62 and 1.28±0.59, respectively. There was no statistically significant differences between the two lasers at the 1 month and 3 month time points after treatment. Histologic examination revealed increased epidermal thickening and decreased solar elastosis 3 months after the final laser treatment. The change of collagen deposition, however, was not definite. In conclusion, both the 1,550 nm and 1,565 nm Er:Glass lasers are safe and effective modalities in the treatment of periorbital wrinkles without significant difference between the two lasers.

Key words: periorbital wrinkle, 1,550 nm Er:Glass laser, 1,565 nm Er:Glass laser, photothermolysis

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I. INTRODUCTION

There is an increasing demand for an effective and safe laser treatment that can repair photoaged skin. Two treatment modalities, ablative and nonablative lasers, have been developed to address this demand[1]. Ablative lasers provide the greatest improvement, but significant adverse effects limit their use. Nonablative lasers have reduced adverse effects but have limited efficacy[2-5]. Fractional photothermolysis (FP) is a new skin resurfacing laser technology for treating wrinkles, melanocytic pigmentation, scars, and photodamaged skin. FP produces arrays of microscopic thermal wounds called microscopic treatment zones (MTZs) at specific depths in the skin without injuring the surrounding tissue. Since each MTZ is surrounded by uninjured tissue, the dermis rapidly heals around these columns of thermal damage, which in turn stimulates progressive collagen remodeling[1,6].

FP has many advantages over other methods. Wounding is not apparent because the stratum corneum remains intact during treatment and acts as a natural bandage. Downtime is minimal and erythema is mild, permitting patients to put on make-up immediately after treatment. As with other nonablative laser modalities, multiple treatments are required. FP represents an alternative for the treatment of dermatologic conditions without the adverse effects of ablative laser devices and can be used on all parts of the body[1,6].

Intrinsically aged skin shows atrophic epidermis and dermis. Decreases in dermal elastic fibers, vascularity, fibroblast number, and biosynthetic capacity all contribute to overall skin fragility and impaired function. In photodamaged skin, collagen is degraded and large amounts of abnormal elastin accumulate, both of which contribute to the loss of elasticity[7]. In addition, there is also disorganization of the elastic network in photodamaged skin[8]. Collagen remodeling and formation after non-ablative and ablative resurfacing is thought to be a primary component in the reduction of wrinkles and the improvement of skin texture. The increase and reorganization of elastic fibers is an important contributor to the results of the studies on dermatoheliosis in sun-damaged skin[9].

FP using a 1,550 nm Er:Glass laser is effective in treating periorbital wrinkles[10]. Recently, a method using a 1,565 nm Er:Glass laser has been developed in order to achieve deeper penetration and greater clinical improvement.

The objective of this study was to evaluate and compare the effects of 1,550 nm and 1,565 nm Er:Glass lasers in the treatment of periorbital wrinkles. Furthermore, in a split face trial, we also evaluated the changes in the epidermis, formation of new collagen, and changes in the elastic fiber in the dermis after laser treatment.

II. PATIENTS AND METHODS

A. Patients

Twenty healthy participants with periorbital wrinkles were recruited. The institutional review board approved the protocol and informed consent was obtained from each participant before they participated in the study. All participants were female. Patients who had concomitant treatments to the involved skin areas, a history of keloid scarring, isotretinoin use, or nonablative laser procedures within 1 year of study initiation, ablative resurfacing procedures within 3 years of the study initiation, pregnancy, or who were taking immunosuppressive drugs, were excluded in this study. The range of ages was 37~65 years old, with an average age of 52 years.

B. Treatment

In all subjects, the right periorbital area was exposed to the 1,550 nm Er:Glass laser and the left periorbital area was exposed to the 1,565 nm Er:Glass laser. In five volunteers, skin biopsies were completed before treatments had started and 3 months after the final treatments. All subjects received five treatments at 3-week intervals with pulse energies of 15~18 mJ using a 6 x 6 mm handpiece tip in a dynamic mode. Each laser treatment covered approximately 15~20 cm^2 of each periorbital area. One treatment created a microscopic treatment zone with a density of approximately 500 spots per cm^2. The treatment was conducted using the following steps:

(1) The volunteers were told to wash their face and photographs were taken using a digital camera before the treatment.

(2) Before treatment, the involved skin was prepared with alcohol and the margin of involved skin was marked with water-soluble ink.

(3) Volunteers were anesthetized using topical 9.6% lidocaine cream without occlusion for 20 minutes.

(4) The right periorbital area was exposed to the 1,550 nm Er:Glass laser and the left periorbital area was exposed 1,565 nm Er:Glass laser in all subjects.

(5) During the treatment, the areas were frequently cooled down with ice packs.

(6) After the treatment, the areas were cooled down with ice packs for 20 minutes and antibiotic ointment was applied.

C. Assessment of clinical effect

Photographic documentation using identical camera settings, lighting, and patient position were obtained before treatment and at 1 and 3 month time points after the final treatment. Clinical improvement was evaluated by patients themselves and also two blinded physicians by observing the comparative photographs and rating the results using a 4-point score system (0 = < 25%, 1 = 25%-50%, 2 = 51%-75%, 3 = > 75% improvement) at 1 and 3 month time points after the last treatment. Complications were recorded at each treatment and at follow-up visits. In addition, the areas containing the wrinkles were measured using magnified images. After zooming each picture to match the pupil size, both lower eyelids were divided into three parts. The middle section, which corresponded to the width and length of pupil, was selected and the area of the folds in the section was measured using an image analysis program (Simple PCIp®, Compix Inc., C-Imaging Systems, PA, USA). Each measurement was compared to the corresponding pre-treatment measurement. The average percentage change with respect to the pre-treatment measurement was recorded. At the 1 and 3 month time points after the last treatment, patients completed an anonymous satisfaction questionnaire, in which they rated their perceived improvement and satisfaction on five categories (worse, no improvement, mild improvement, moderate improvement, excellent improvement).

D. Assessment of histologic change

Skin biopsies were done in five volunteers before treatment and again 3 months after the final treatments using a 3 mm biopsy punch. Before treatment, the biopsy was performed on crow's feet at a 1cm distance from the lateral margin of the eye. The biopsy after treatment was performed right next to the previous biopsy site. The excised skin was fixed in formalin and embedded in paraffin. Samples were stained by hematoxylin-eosin and epidermal architecture, thickness, amount, and the quality of dermal collagen formation were all evaluated. Verhoeff-van Gieson staining was performed to evaluate the change of elastic fibers. Masson's trichrome staining was performed to better demonstrate changes in dermal collagen. Histologic findings from the Verhoeff-van Gieson and Masson's trichrome stains were observed by blind inspection of the samples, but were not quantified. Slides were read and measured by two blinded dermatologists.

E. Statistical analysis

Statistical analysis was performed using the Wilcoxon signed rank test. A P-value of less than 0.05 was considered significant.

III. RESULTS

A. Degree of clinical improvement

Maximal clinical improvement was evident 1 month after treatment (Figure 1). The mean improvement score at the 1 month time point with the 1,550 nm Er:Glass laser was 1.53±0.71 and the mean improvement score with 1,565 nm Er:Glass laser was 1.63±0.66. The mean improvement scores at the 3 month time point was 1.25±0.62 and 1.28±0.59 for 1,550 nm and 1,565 nm Er:Glass lasers, respectively. Statistically significant differences were not observed between the two lasers at the 1 month and 3 month time points after treatment. Photographs of a representative subject who showed an excellent response are shown in Figure 2. The clinical improvement score evaluated by the patients paralleled the clinical improvement score evaluated by physicians (Figure 3).

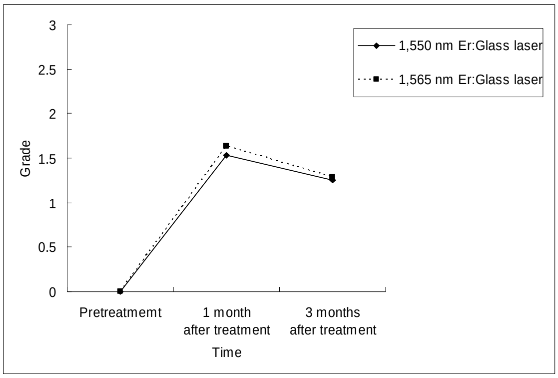

Figure 1. Mean clinical improvement scores assessed by physicians (Grading score: 0 =< 25%, 1 = 25%–50%, 2 = 51%–75%, 3 => 75% improvement).

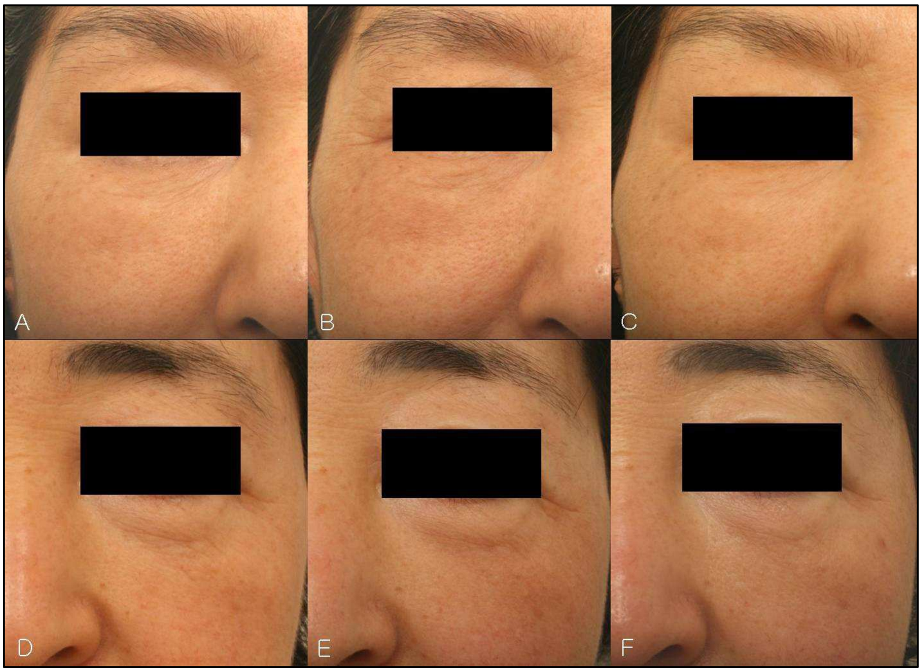

Figure 2. Comparison of clinical improvement of periorbital wrinkles before and after treatment using 1,550 and 1,565 nm Er:Glass lasers. Before treatment (A), 1 month after treatment (B) and 3 months after treatment (C) using a 1,550 nm Er:Glass laser. Before treatment (D), 1 month after treatment (E) and 3 months after treatment (F) using a 1,565 nm Er:Glass laser.

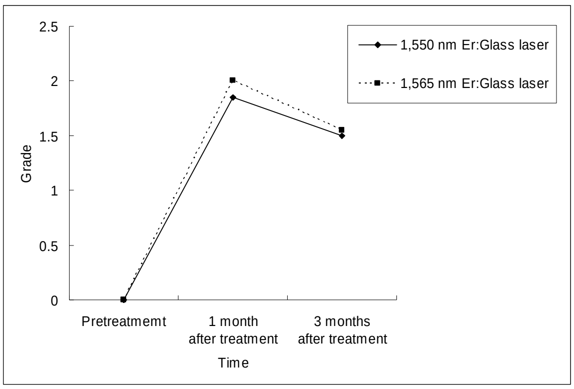

Figure 3. Mean clinical improvement scores assessed by patients (Grading score: 0 = < 25%, 1 = 25%–50%, 2 = 51%–75%, 3 = > 75% improvement).

B. Mean percentage change of areas with wrinkles

Maximal percentage change was also observed 1 month after treatment (Figure 4). At this time point, we found a 10.9 % reduction in the wrinkle area in the patients treated with the 1,550 nm Er:Glass laser and 11.8 % reduction in the patients treated with the 1,565 nm Er:Glass laser ($P<0.05$). The reduction in the areas with wrinkles at 3 months after the treatment was 8.2 % and 8.6 % for the areas treated with the 1,550 nm and 1,565 nm Er:Glass lasers, respectively ($P<0.05$). Statistically significant differences were not observed between the two laser types at the 1 month ($P=0.295$) and 3 month time points ($P=0.404$) after treatment.

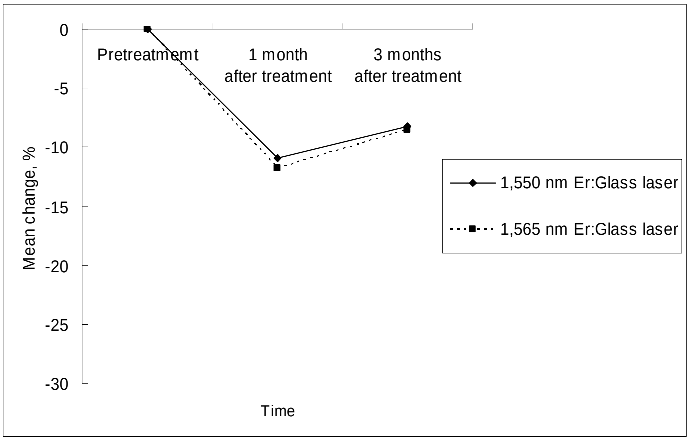

Figure 4. Mean percentage change of areas with wrinkles

C. Patient satisfaction

At least moderate improvement in periorbital wrinkles 1 month after treatment was observed in 70% and 75% of the 1,550 nm and 1,565 nm Er:Glass laser treatments groups, respectively. Three months after treatment, the improvements declined to 40% and 45% in the 1,550 nm and 1,565 nm Er:Glass laser treatment groups, respectively (Figure 5).

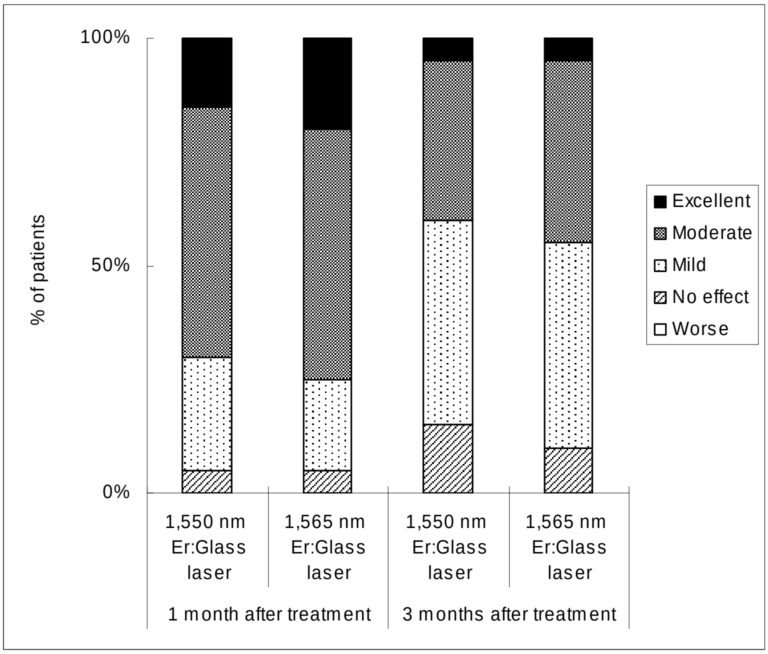

Figure 5. Patient satisfaction at 1 month and 3 months after final treatment

D. Histologic changes

Histologic tissue examination revealed flattened rete ridges and clumped elastin in the pretreatment specimens. In contrast, increases in epidermal thickness and undulating rete ridge patterns were seen in all biopsy specimens 3 months after the final laser treatment (Figure 6 and Table 1).

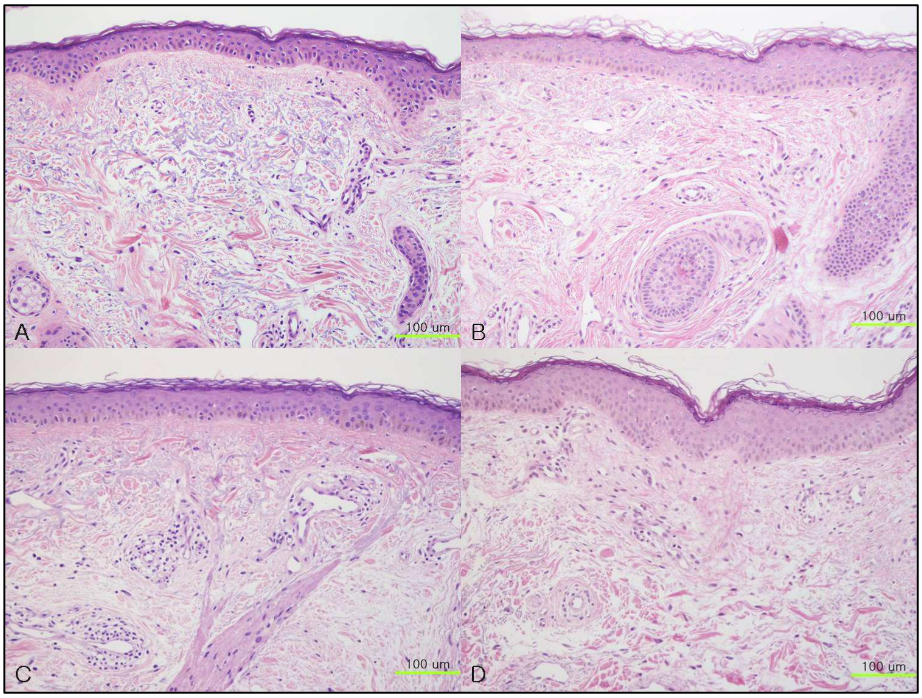

Figure 6. Histologic findings of periorbital skin before and after treatment using the 1,550 and 1,565 nm Er:Glass lasers, Hematoxylin and eosin stain (x 200). (Before treatment (A) and 3 months after treatment (B) using the 1,550 nm Er:Glass laser; before treatment (C) and 3 months after treatment (D) using the 1,565 nm Er:Glass laser).

	Epidermal thickness (μm)			
	1,550 nm Er:Glass laser		1,565 nm Er:Glass laser	
Patients	Before treatment	3 months after treatment	Before treatment	3 months after treatment
1	62.50	86.50	73.70	76.75
2	85.50	89.05	75.75	89.60
3	84.00	103.50	70.65	102.10
4	54.25	80.70	56.30	78.35
5	83.45	95.90	82.95	94.00
Average	73.94	91.13	71.87	88.16

Table 1. Measurement of epidermal thickness before treatment and 3 months after treatment using the 1,550 and 1,565 nm Er:Glass lasers.

Decreased solar elastosis and restoration of the fine candelabra-like network of elastic fibers in the upper dermis were seen in all biopsy specimens obtained 3 months after the last treatment (Figure 7).

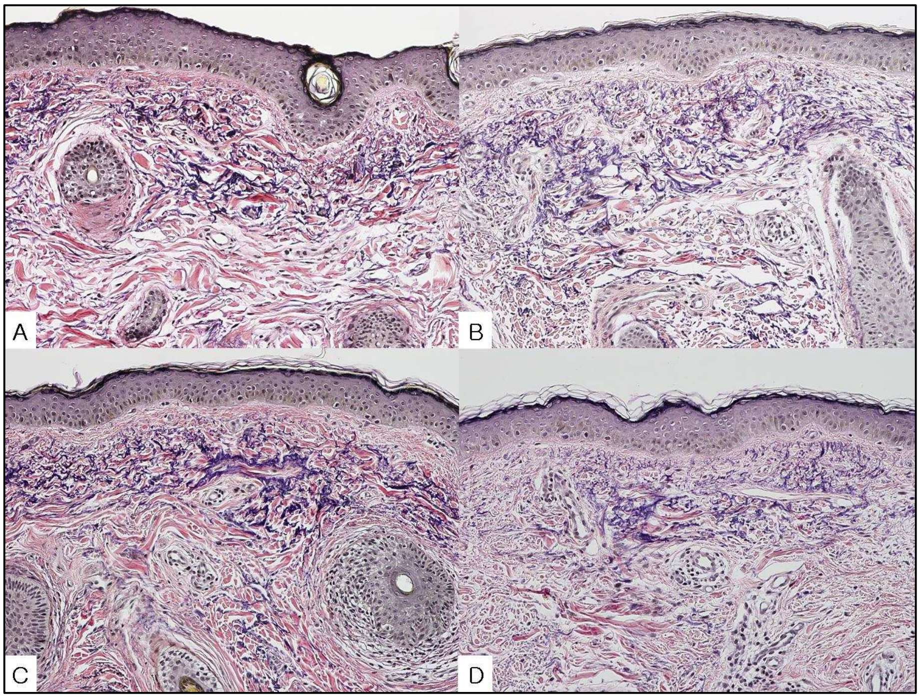

Figure 7. Histologic findings of periorbital skin before and after treatment using the 1,550 and 1,565 nm Er:Glass lasers, Verhoeff-van Gieson stain (x200). (Before treatment (A) and 3 months after treatment (B) using the 1,550 nm Er:Glass laser; before treatment (C) and 3 months after treatment (D) using the 1,565 nm Er:Glass laser).

The change in collagen deposition was not definite. We observed either an increase or no change in the collagen content (Table 2 and Figure 8). Three patients, each treated with the 1,550 nm and 1,565 nm Er:Glass lasers, showed an increase in collagen deposition. Table 2 shows that the change of collagen deposition is correlated with clinical improvement. When the clinical improvement score of the wrinkle was more than 1 (on a score of 0–3), an increase of collagen content was observed.

	1,550 nm Er:Glass laser		1,565 nm Er:Glass laser	
Patients	Collagen change	Degree of Improvement	Collagen change	Degree of Improvement
1	+	1	No change	0.5
2	+	2	+	2
3	No change	0.5	+	1
4	No change	0.5	+	1.5
5	+	1	No change	0.5

Table 2. Correlation of collagen change and clinical improvement 3 months after treatment using the 1,550 and 1,565 nm Er:Glass lasers (+: increase in collagen content). The degree of improvement was evaluated by two blinded physicians using a 4-point score (0 =< 25%, 1 = 25%–50%, 2 = 51%–75%, 3 => 75% improvement) at the 3 month time point after the last treatment.

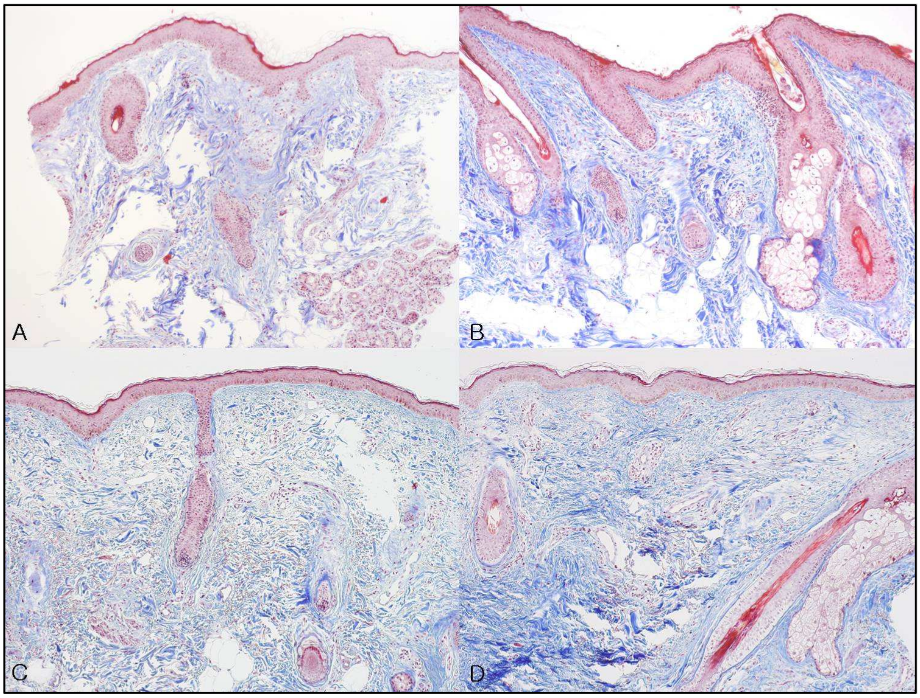

Figure 8. Histologic findings of periorbital skin before and after treatment using the 1,550 and 1,565 nm Er:Glass lasers, Masson’s trichrome stain (x100). (Before treatment (A) and 3 months after treatment (B) using the 1,550 nm Er:Glass laser; before treatment (C) and 3 months fter treatment (D) using the 1,565 nm Er:Glass laser).

E. Complications

The treatments were well tolerated and complications were limited and transient. Posttreatment erythema and localized edema were observed in all patients and generally resolved within 2~3 days after treatment. Bronzing of the skin occurred in 6 out of 20 patients (30%). Three out of twenty patients (15%) noted a darkening of their pre-existing pigmentary lesions (lentigines, melasma-like lesions). One patient developed postinflammatory hyperpigmentation due to contact dermatitis induced by the topical anesthetic cream. These pigmentary alterations were resolved in all patients within 2 months.

IV. DISCUSSION

Ablative and nonablative lasers have been used successfully over the past decade to improve many of the signs of photodamaged skin[3]. Ablative lasers (CO_2 or Er:YAG lasers) remove the entire epidermis of the treatment area. Treatments using these lasers have become increasingly unpopular due to the significant risks of prolonged recovery time, possible permanent hypopigmentation and scarring. Nonablative lasers (1,320 nm Nd:YAG and 1,450 nm diode laser) have become the treatment of choice for photorejuvenation. These lasers can create controlled dermal wounds without epidermal disruption. Nonablative lasers stimulate collagen fiber synthesis to reduce wrinkles. Although minimal morbidity is encountered, the final effect is clearly more subtle than the effects seen with the ablative laser technique[2-5]. To overcome the disadvantages of conventional ablative and nonablative laser therapies, researchers have studied the clinical effects of FP[1]. Ablative and nonablative laser technologies produce layers of thermal heating whereas FP produces columns of thermal heating. Photothermolysis refers to the destruction of tissue by radiation-induced thermal damage. In FP, tissue damage occurs in microscopic columns that extend into the dermis and is not restricted to a specific target tissue. Since each MTZ is surrounded by uninjured tissue, keratinocytes have a shorter migration path and healing is much quicker[5].

Our study investigated and compared the efficacy of 1,550 nm and 1,565 nm Er:Glass lasers for treatment of periorbital wrinkles. The results showed that both lasers were effective in the treatment of periorbital wrinkles and a difference in treatment effect was not observed. A study by Manstein et al [1] evaluated the efficacy of FP for the treatment of lateral periorbital wrinkles in 30 subjects with Fitzpatrick skin type II to III. In this study, patients were treated four times (2,500 MTZ/cm^2 at 6–12 mJ) at 2~3 week intervals. In the study by Manstein et al, mild to moderate improvement in wrinkles was reported by the subjects and investigators 1 month and 3 months after treatment. One month after treatment, the mean clinical improvement in the wrinkle was 2.5±1.2 (on a scale of 1–6) as assessed by independent investigators. Three months after treatment, this effect decreased to 1.6±1.3. In a different study, Wanner et al[11] investigated the efficacy of FP for facial photodamage, rhytides and dyspigmentation in 30 patients with Fitzpatrick skin types I to III. The patients in their study were treated with three times (2,000 MTZ/cm^2 at 8 mJ) over a 3 to 4-week period. The investigators reported a mean improvement of 2.23, 2.10, and 1.96 at the 3, 6, and 9 month time points after treatment, respectively. In our study, the mean score of clinical improvement at the 1 month time point after treatment with the 1,550 nm Er:Glass laser was 1.53±0.71 and the mean score of clinical improvement for 1,565 nm Er:Glass laser was 1.63±0.66. Furthermore, the mean scores of improvement at the 3 month time point was 1.25±0.62 and 1.28±0.59 for the patients treated with the 1,550 nm and 1,565 nm Er:Glass lasers, respectively. The results of our study are consistent with previous reports[1,11] that used FP for the treatment of periorbital wrinkles. Geronemus[5] reported on the use of FP for the treatment of fine and moderate rhytides but noted less impressive results in deeper rhytides. This finding was consistent with the results of our study, as we also found that deep rhytides were less responsive to treatment than shallow rhytides.

We also tried to objectively evaluate the clinical effect after treatment. Although we measured a part of the wrinkled area on the lower eyelid, the mean percentage change of the area with wrinkles paralleled the clinical improvement score evaluated by the physicians.

In the previous studies, there were several dark skinned subjects who demonstrated little or no significant pigmentation abnormalities after FP at low or medium MTZ densities per treatment[1]. However, our study showed a darkening of pigmentary lesions after treatment. Further study will be needed to accurately assess the pigmentary effect of FP in dark-skinned people.

We also evaluated the changes in the epidermis, formation of new collagen, and the change in the elastic fiber in the dermis after FP. The histologic manifestations of photodamaged skin include thin epidermis, flattened rete ridges, loss of collagen, and abnormal clumping of elastic fibers in the superficial dermis. In our study, histologic examination showed increased epidermal thickness and decreased solar elastosis 3 months after the final treatment. However, the change in collagen deposition was variable.

Previous studies have shown that the continuity of the epidermal basal cell layer is restored 24 hours after FP and that complete epidermal regeneration is obtained 7 days after the treatment[9]. In our study, the thickness of the epidermis and granular layers increased 3 months after treatment with either laser type.

Young skin is tight but with aging the skin becomes progressively lax. This can be ascribed to degenerative changes in the elastic fibers and their organization. The common feature of wrinkles is the deterioration of the elastic tissue network. The fine candelabra-like network of elastic fibers inserted into the basal lamina of young protected skin is replaced by clumped masses of amorphous material beneath the dermo-epidermal junction[12,13]. In our study, decreased solar elastosis and restoration of fine candelabra-like network of elastic fibers in the upper dermis were seen in all biopsy specimens taken 3 months after the last treatment.

Collagen remodeling and formation after non-ablative and ablative resurfacing is thought to be a primary component in the reduction of rhytides and the improvement of skin texture. Three months after exposure, there is no evidence of decreased collagen III staining throughout the dermis, which shows that thermally damaged collagen inside the MTZ is completely replaced with new collagen after 3 months. There is no evidence of residual fibrosis but theses findings may be related to a single FP treatment[9]. The changes in collagen deposition were not consistent in our study, as we observed either an increase or no change in collagen content after multiple FP treatments. However, when the clinical improvement of wrinkles was more than 1 (on a score of 0–3), an increase of collagen content was observed. When the clinical improvement score was higher, the increase in collagen deposition was more obvious. Therefore, an increase in collagen deposition may be related to the degree of clinical improvement.

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V. CONCLUSION

Maximal clinical improvement of periorbital wrinkles was evident 1 month after the last treatment and the effect decreased somewhat 3 months after the last treatment. Statistically significant differences were not observed between the treatment results produced with the 1,550 nm and 1,565 nm Er:Glass lasers. Histologic examination showed increased epidermal thickening and decreased solar elastosis at the 3 month time point after the final treatment. However, the degree of collagen deposition was not definite.

Our study shows that fractional photothermolysis using both 1,550 nm and 1,565 nm Er:Glass lasers is a safe and effective treatment to reduce periorbital wrinkles without significant difference between the two lasers.

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국 문 요 약

눈가 주름에 대한 1,550 nm 및 1,565 nm Er:Glass 레이저의 치료 효과 비교 연구

<지도교수 정기양>

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1,550 nm Er:Glass 레이저를 이용한 fractional photothermolysis는 눈가주변의 주름 치료에 효과적이며, 최근에 1,565 nm Er:Glass 레이저가 새롭게 개발되었다. 본 연구에서는 두 레이저의 치료효과를 조사하고 비교하고자 하였으며, 치료 후 조직 검사를 통해 표피변화, 진피 내 교원질과 탄력소의 변화를 알아보고자 하였다. 눈가 주름으로 세브란스 병원 피부과에 내원한 20명의 여자환자를 대상으로 하였다. 오른쪽 눈가주름은 1,550 nm Er:Glass 레이저로 치료하였으며 왼쪽 눈가주름은 1,565 nm Er:Glass 레이저로 치료하였다. 모든 환자들은 3주 간격으로 총 5회 치료하였다. 환자와 두 명의 피부과 의사가 치료종료 1달 후와 3달 후에 4-point score (0 = < 25%, 1 = 25%–50%, 2 = 51%–75%, 3 = > 75% improvement)을 이용하여 임상적 평가를 시행하였다. 또한 5명의 환자는 연구시작전과 치료종료 3달 후에 눈가주름에서 조직 검사를 시행하였다. 치료종료 1달 후에 1,550 nm Er:Glass 레이저로 치료한 부위는 1.53±0.71의 호전, 1,565 nm Er:Glass 레이저로 치료한 부위는 1.63±0.66의 호전을 보였다. 치료종료 3달 후에 1,550 nm Er:Glass

레이저로 치료한 부위는 1.25±0.62의 호전, 1,565 nm Er:Glass 레이저로 치료한 부위는 1.28±0.59의 호전을 보였다. 두 레이저간의 치료효과는 통계적으로 유의한 차이를 보이지 않았다. 치료 후 조직학적 검사상 표피의 두께증가, 일광탄력 섬유증의 감소가 관찰되었지만 교원질의 변화는 일정하지 않았다. 이상의 결과로 1,550 nm 과 1,565 nm Er:Glass 레이저는 눈가주름의 치료에 효과적이며, 두 레이저의 치료효과는 차이를 보이지 않음을 알 수 있었다.

핵심되는 말: 눈가주름, 1,550 nm Er:Glass 레이저, 1,565 nm Er:Glass 레이저, photothermolysis