

Objective assessment of skin rejuvenation using near-infrared 1064-nm neodymium: YAG laser in Asians

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Background: We reported previously that near-infrared (NIR) irradiation provides long-lasting stimulation of elastin, and is efficient for skin rejuvenation. Many studies have indicated the efficacy of various types of laser, but did not include sufficiently objective evaluation. Therefore, we evaluated the efficacy of NIR laser treatment not only subjectively but also objectively.

Methods: Fifty Japanese patients were treated with a NIR 1064-nm neodymium: YAG laser. Objective computer assessments were performed by Canfield VISIA Complexion Analysis for improvement of dilated pores, skin texture, and wrinkles. The volunteers then provided subjective assessments. Histological evaluations of elastin were performed by Victoria blue staining up to 90 days post-treatment in four Japanese volunteers.

Results: Mean pretreatment percentiles of dilated pores, skin texture, and wrinkles were 51.08 ± 24.82 , 54.7 ± 26.33 , and 58.02 ± 28.61 , respectively. Mean post-treatment percentiles of dilated pores, skin texture, and wrinkles were 53.58 ± 23.89 , 58.58 ± 24.44 , and 62.2 ± 25.39 , respectively. All objective computer assessments evaluated by percentiles in dilated pores, skin texture, and wrinkles showed significant improvement after NIR laser treatment. Ninety-six percent, 100%, and 98% of volunteers reported satisfaction with the improvement of dilated pores, skin texture, and wrinkles, respectively. NIR laser treatment appeared to increase the amount of elastin at day 30, which then decreased slightly but was still elevated at day 90 compared with nonirradiated controls on day 0. Thickening of the epidermis was detected on day 30, and epidermal smoothness persisted for up to 90 days. No treatment-related adverse events were observed.

Conclusions: NIR irradiation increased elastin in the dermis, and achieved skin rejuvenation. The results indicated that NIR irradiation provides safe and effective long-term stimulation of elastin, which is beneficial for improving dilated pores, skin texture, and wrinkles.

Keywords: near-infrared laser, elastin, skin rejuvenation, objective assessment

Introduction

We reported previously that near-infrared (NIR) irradiation provides long-lasting stimulation of elastin, and is efficient for skin rejuvenation.¹ NIR devices are effective for skin rejuvenation.²⁻⁷ Recently, nonablative lasers and radiofrequency devices have been widely used for skin rejuvenation, and they are thought to stimulate dermal collagen remodeling. Nonablative lasers alter dermal collagen structure by thermal induction of collagen neosynthesis and remodeling, as evidenced by increased levels of collagen, elastin, and collagenase.^{8,9}

NIR irradiation increases the amounts of collagen in human dermal fibroblasts, and can clinically improve skin texture.¹⁰ NIR can penetrate deep into human tissue,

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where it can cause photochemical changes,¹¹ and induce various responses in the skin and subcutaneous tissues.^{1,12–18}

NIR releases free radicals,¹⁹ and inflammatory chemical mediators that stimulate the collagen healing process, resulting in induction of new dermal collagen production by fibroblasts.²⁰

Many studies have suggested the efficacy of various types of laser, but these studies did not include sufficiently objective evaluation. Further, numerous studies revealed collagen stimulation, whereas stimulation of elastin was not assessed in detail.

We hypothesized that NIR irradiation provides safe and effective long-term stimulation of elastin, which is beneficial for improving dilated pores, skin texture, and wrinkles. To test this hypothesis, we evaluated the efficacy of NIR laser treatment not only subjectively but also objectively, and examined changes in the amount of elastin histologically.

Materials and methods

Japanese volunteers

Fifty Japanese volunteers (48 females and 2 males) aged 21–73 years (mean age, 42.8 ± 11.73 years) with Fitzpatrick skin type III to V were enrolled in this study.

Serial skin biopsies were taken from cheeks of another four Japanese volunteers (three females and one male) with Fitzpatrick skin type III ($n = 2$) and IV ($n = 2$), ranging in age from 33 to 41 years (mean age, 37.25 ± 4.35 years).

All of four volunteers had visited the Clinica Tanaka Anti-Aging Center seeking to remove some pigmented nevus and achieve skin rejuvenation on their cheeks. When each pigmented nevus was removed in the spindle shape, the excess skin on either side of the pigmented nevus was submitted for biopsies. None of the subjects had a history of any type of skin disease or any cosmetic procedures affecting the treatment areas within the last 3 years. Control biopsies received neither treatment nor irradiation. All biopsies were taken at least 1 cm from previous biopsies to ensure wound healing would not affect adjacent biopsy sites.

No topical pretreatment was used, and the post-treatment skin care regimen consisted of a gentle cleanser and sunblock. All volunteers gave their written informed consent for participation in the study, and for the taking of their photographs and biopsies, after reading the experimental protocol and being advised about the risks of the treatment.

NIR irradiation

A NIR 1064-nm neodymium: YAG laser (Laser Genesis; Cutera, Inc, Brisbane, CA), with a wavelength of 1064-nm, spot size of 5 mm, energy fluence of 14 J/cm^2 , pulse duration

of 0.3 or 1.0 ms, and a repetition rate of 7 Hz was used to evaluate the effects of NIR.

Fifty Japanese volunteers were treated on both cheeks. Three rounds of treatment with a 4-week interval between treatments were performed. Another four volunteers for histological evaluation were treated with one round of NIR irradiation on only one cheek.

The treated area received 1000 pulses with a pulse duration of 0.3 ms, and 3000 pulses with a pulse duration of 1.0 ms per cheek. In accordance with the manufacturer's instructions, the treatment head was held approximately 2 cm from the skin. The treatment was administered by manually scanning the rapidly pulsed laser in an even painting motion throughout the entire treatment area. If the volunteer reported a strong sensation of heat, scanning was performed slightly faster and/or the treatment head was moved slightly farther (0.5–1 cm) from the skin to avoid the strong sensation of heat. No topical anesthetics or oral analgesics were administered before, during, or after the treatment, and no skin cooling was required.

Objective computer assessments

Digital photographs and facial surface analysis were conducted as objective computer assessments by Canfield VISIA Complexion Analysis (Fairfield, NJ). This system consists of a standardized lighting booth and operating software running on Windows. Eight surface analyses were performed immediately after capturing images with color, UV, and cross-polarized photographs. Captured images and analysis results were stored on a PC. Improvements in dilated pores, skin texture, and wrinkles were evaluated by percentiles which were calculated comparing with sex-, age-, and ethnicity-matched data. Percentiles measure position from the bottom, and are used for determining the relative standing of an individual in a population.

Subjective volunteer assessments

Subjective volunteer assessments were performed using questionnaires, in which the volunteers were asked to give their degree of satisfaction in terms of dilated pores, skin texture, and wrinkles based on a 5-point scale from 0 to 4 (0 = worse; 1 = little satisfaction or not satisfied; 2 = fairly satisfied; 3 = satisfied; and 4 = very satisfied). Questionnaires were given 1 month after the final treatment.

Histological evaluation

Human skin specimens (3–5 from each patient) were obtained from the cheeks for microscopic investigation. Biopsies were

taken prior to irradiation as a control and at 30 and 90 days after irradiation. The specimens were fixed in 20% neutral buffered formalin, processed for paraffin embedding, and serially sectioned in the sagittal plane (3–4 μm thick). Elastin densities stained by Victoria blue staining in the dermis were calculated for all time points in an area approximately 0.48 mm high \times 0.64 mm wide in the dermis, which is a field of $\times 200$ magnification. Images were scanned and quantified in five representative fields per section, and subsequently averaged to obtain a final score. The sections were photographed under an Olympus BX50 microscope (Olympus, Tokyo, Japan). The digital photographs were processed using Adobe Photoshop (Adobe, San Jose, CA).

Statistical analyses

The differences between pre- and post-treatment values were examined for statistical significance using Wilcoxon's signed-rank test. $P < 0.05$ was set as a cutoff for statistical significance. Data are presented as means \pm standard deviation.

Results

The mean pretreatment percentiles of dilated pores, skin texture, and wrinkles were 51.08 ± 24.82 , 54.7 ± 26.33 , and 58.02 ± 28.61 , respectively. The mean post-treatment percentiles of dilated pores, skin texture, and wrinkles were 53.58 ± 23.89 , 58.58 ± 24.44 , and 62.2 ± 25.39 , respectively. All objective computer assessments evaluated by percentiles in dilated pores, skin texture, and wrinkles showed significant improvement after NIR laser treatments ($P < 0.05$) (Figures 1–3).

All volunteers answered the questionnaire. Ninety-six percent, 100%, and 98% of volunteers were satisfied with the results for improvements in dilated pores, skin texture, and wrinkles, respectively (Figure 3).

The mean degrees of satisfaction in terms of dilated pores, skin texture, and wrinkles based on a 5-point scale from 0 to 4 were 2.64 ± 0.898 , 2.92 ± 0.634 , and 2.56 ± 0.705 , respectively.

The NIR laser appeared to increase the amount of elastin on day 30, which then decreased slightly, but was still elevated on day 90 compared with nonirradiated controls on day 0 in Fitzpatrick skin type III and IV biopsies (Figure 4).

There were no apparent differences in elastin between type III and IV biopsies at any time point. Thickening of the epidermis was detected on day 30, and epidermal smoothness persisted up to 90 days. There were no treatment-related adverse events.

Discussion

NIR irradiation increased elastin in the dermis, and could achieve a skin rejuvenation effect.

All objective computer assessments of dilated pores, skin texture, and wrinkles showed significant improvements, and most volunteers were satisfied with the results after NIR laser treatments. Further, NIR laser treatment appeared to induce long-term stimulation of elastin. The results indicated that NIR irradiation provides safe and effective long-term stimulation of elastin, which is beneficial for skin rejuvenation by improving dilated pores, skin texture, and wrinkles.

VISIA Complexion Analysis is an effective visual communication tool for skin rejuvenation. Standardized lighting and object positioning are essential for appropriate evaluation. Photographs are taken with the subject's face set into the booth using the chin cup and head-rest. The software displays the initial captured image on the PC screen, while the live preview function allows the operator to instruct the subject to adjust their face position. These standardized conditions are crucial for comparison of treatment effects. The system is an efficient way to evaluate improvements in dilated pores, skin texture, and wrinkles associated with treatment.

Most NIR lasers use cryogen or contact cooling to deliver NIR while sparing the epidermis. In contrast, the NIR 1064-nm laser used in this study produces gradual dermal heating through cumulative absorption by oxyhemoglobin within the dermal microvasculature, and no epidermal cooling is needed as treatment-associated discomfort is minimal.⁹ This wavelength is mildly absorbed by water, but shows a preference for proteinaceous targets, such as blood vessels and collagen. Due to the scattering effect on this wavelength, the area of greatest photon density – the target area – is 1–2 mm below the surface, which is the region for nonablative skin rejuvenation.²¹ NIR irradiation simulating solar NIR at specific wavelengths with pre- and parallel-irradiational contact cooling nonthermally induces long-term stimulation of collagen and elastin, which provides resiliency and elasticity of the skin, resulting in improvement of wrinkles.¹

Elastin produced by fibroblasts is one of the major proteins of connective tissue, and it plays an important role in providing skin elasticity. The loss of normal elastic fiber functions is a common age-associated feature of both photoaging and intrinsic aging processes.²² Actinically damaged skin is characterized by accumulation of elastotic material, while in sun-protected areas the number of elastic

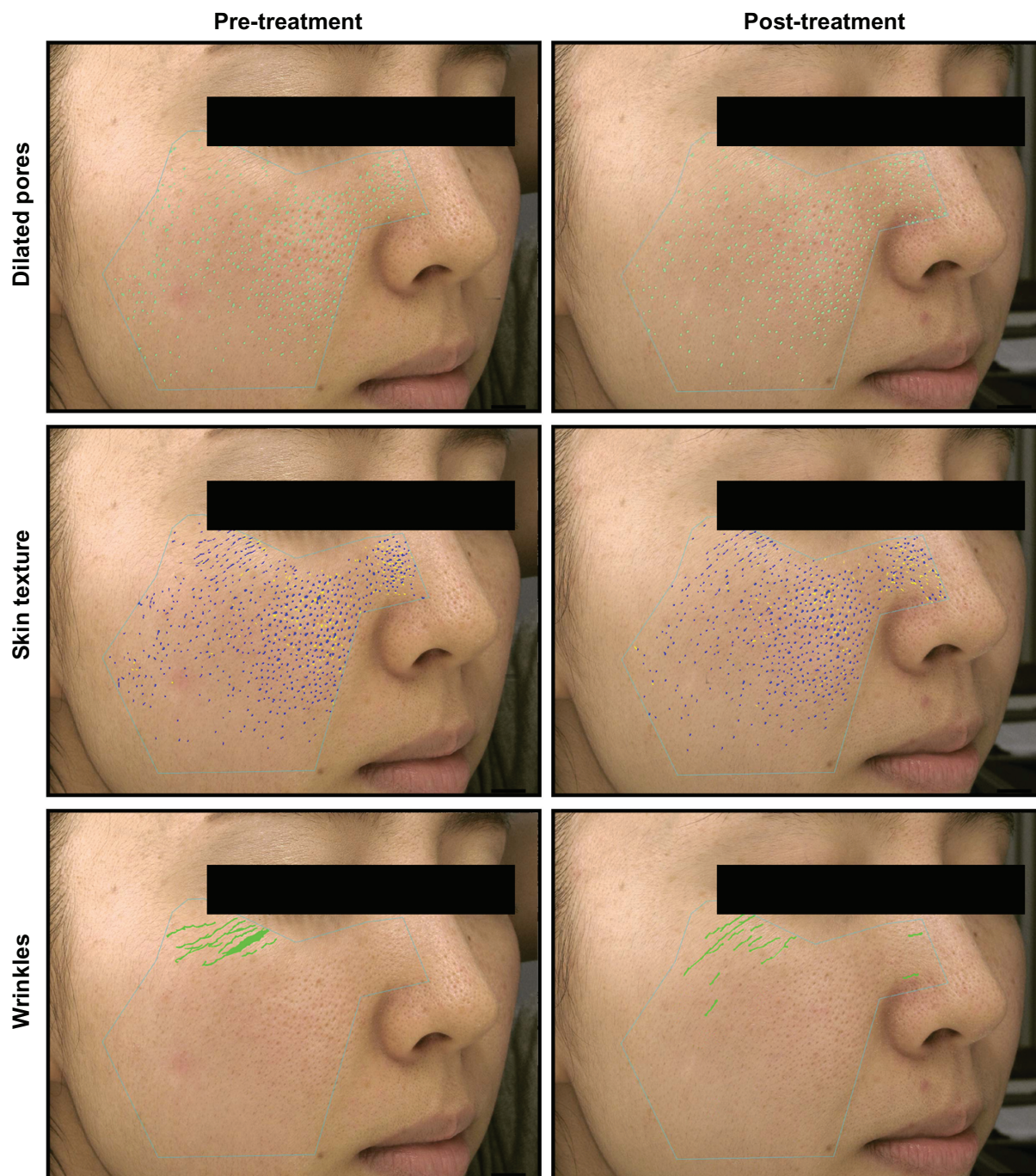


Figure 1 Representative photographs of rejuvenation effects treated with a near-infrared (NIR) 1064-nm neodymium: YAG laser. Pretreatment (left column), a 30-year-old Japanese woman exhibited dilated pores (first row), coarse skin texture (second row), and wrinkles (third row). Post-treatment (right column), significant improvements were noted in dilated pores, skin texture, and wrinkles. The objective computer assessment was performed using Canfield VISIA Complexion Analysis, in which dilated pores (light blue), skin texture (blue), and wrinkles (green) were evaluated.

fibers is decreased.²³ Accelerated aging and sagging of the skin are seen in several hereditary disorders involving collagen or elastin deficiency.^{23–25} Both collagen and elastin are turned over slowly in tissues, and are therefore susceptible to age-related changes.²⁶ Increases in relatively thin elastic fibers without irregular elastic fibers, such as

solar elastosis, were seen in this and our previous studies, suggesting that this NIR irradiation treatment can achieve skin rejuvenation.

The levels of tropoelastin and fibrillin 1, which are major components of elastic fibers, were still increasing 28 days after laser treatment, and tropoelastin mRNA levels

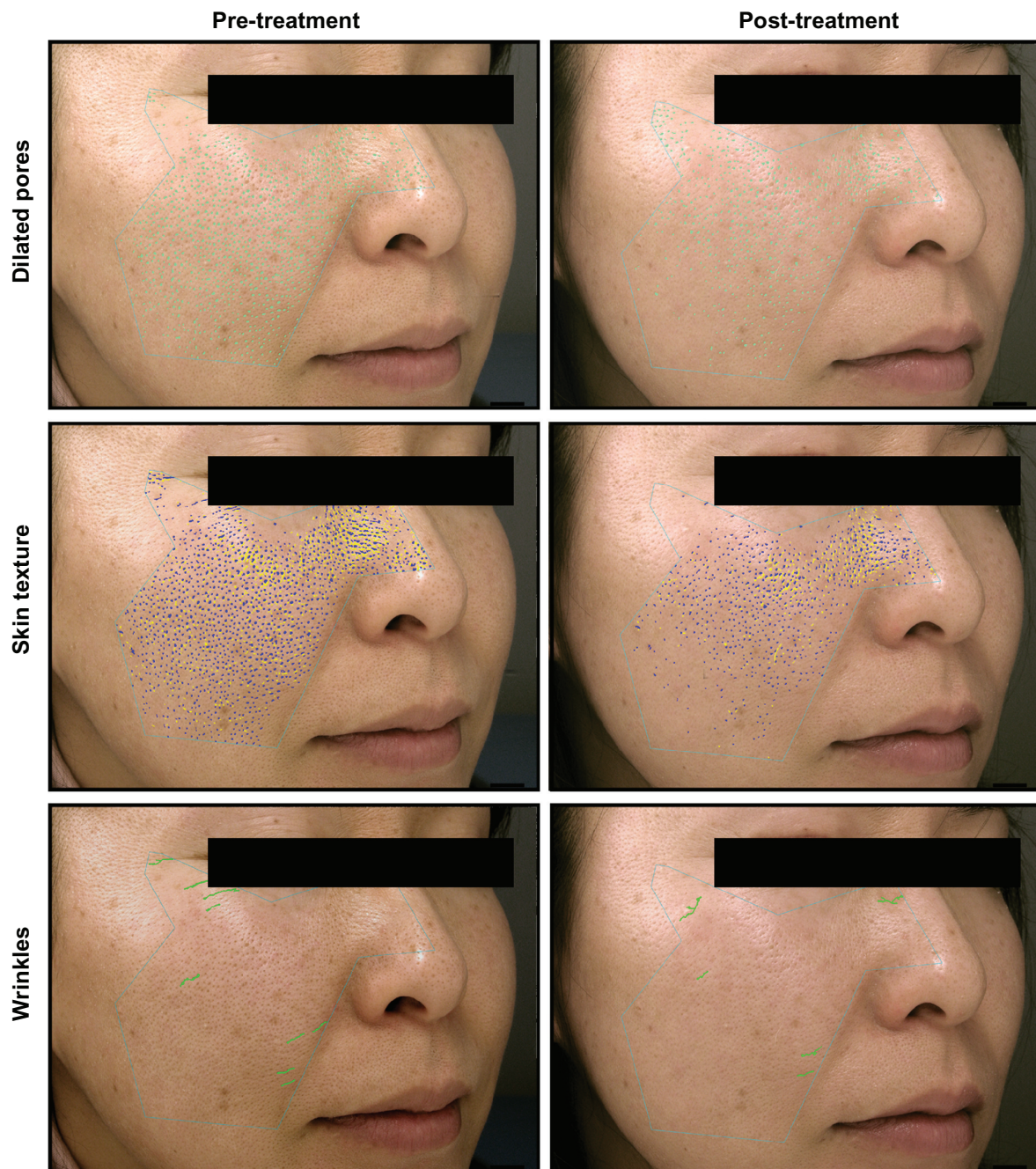


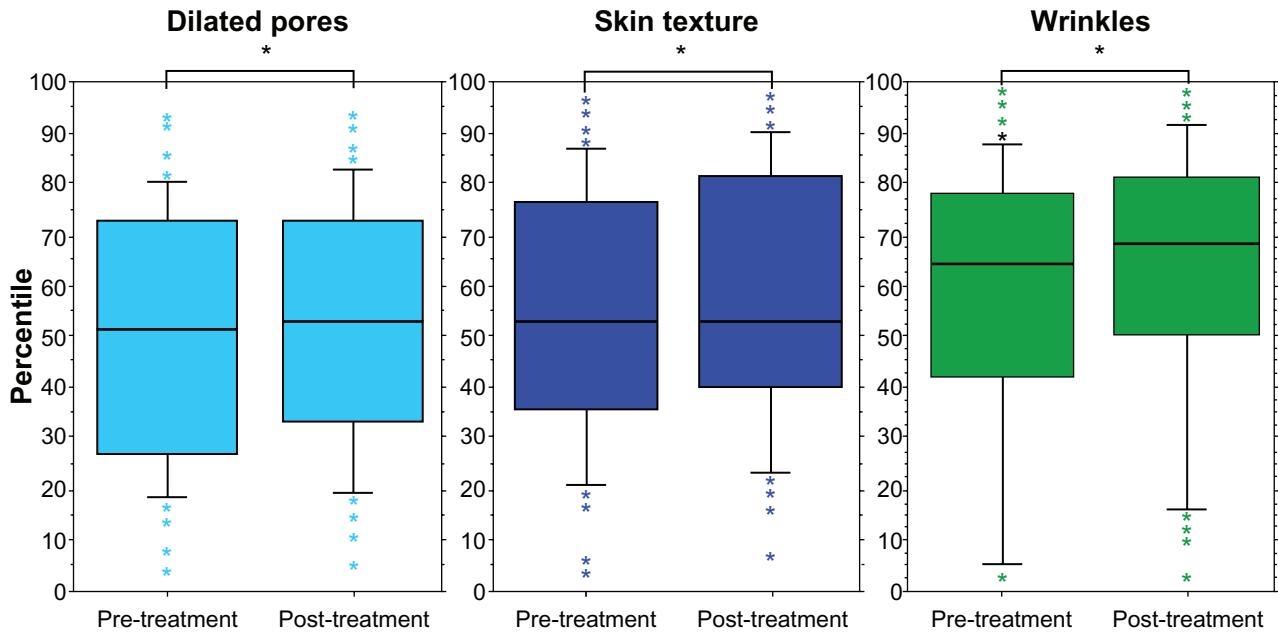
Figure 2 Representative photographs of rejuvenation effects treated with the NIR laser. Pretreatment (left column), a 30-year-old Japanese woman exhibited dilated pores (first row), coarse skin texture (second row), and wrinkles (third row). Post-treatment (right column), significant improvements were noted in dilated pores (light blue), skin texture (blue), and wrinkles (green).

remained elevated after 6 months.²⁷ The effects of NIR irradiation on elastin persisted for 3 months, which was much longer than the effects on collagen.¹ Due to long-term stimulation of elastin, resiliency and elasticity of the skin after NIR treatment would persist for a long time. NIR increases the amount of water retained in the dermis by inducing vasodilation and the expression of collagen and

elastin. Smoothing and thickening of the epidermis may be induced by accumulation of collagen and elastin to protect the subcutaneous tissues against NIR, which should be investigated further in future studies.

It should be noted that this was a preliminary study based on a fairly small number of skin biopsies. The number of biopsies was small because of practical limitations in the

Objective computer assessments



Subjective volunteer assessments

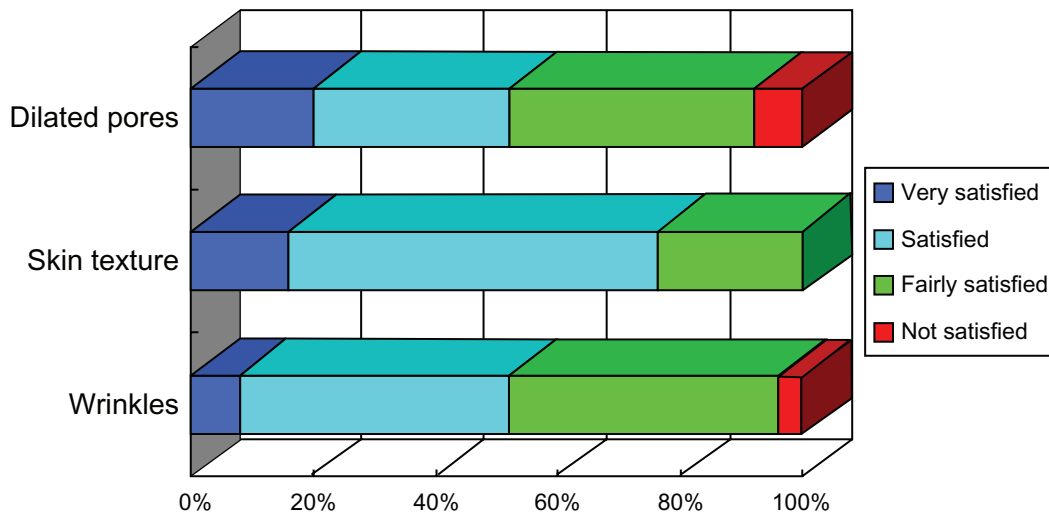


Figure 3 All objective computer assessments of dilated pores (light blue), skin texture (blue), and wrinkles (green) showed significant improvement after NIR laser treatments (above).

Notes: Data represent the means \pm SD. Significant differences are indicated (* $P < 0.05$). Subjective volunteer assessments were performed using questionnaires (lower). The volunteers were asked to give their degree of satisfaction in terms of dilated pores, skin texture, and wrinkles. Subjective volunteer assessments are shown as follows: very satisfied (blue), satisfied (light blue), fairly satisfied (green), and not satisfied (red). Questionnaires were given 1 month after the final treatment. Ninety-six percent, 100%, and 98% of volunteers were satisfied with the improvements in dilated pores, skin texture, and wrinkles, respectively.

number of serial biopsy specimens that could be obtained from the face. While there may be a subtle influence of taking serial biopsies near previous biopsy sites, there is no evidence that a distance of 1 cm from previous biopsies would be insufficient to ensure that wound healing would not affect adjacent biopsy sites. However, we cannot

exclude the possibility that UV and NIR exposure in everyday life may affect the changes demonstrated in this study. Further studies in this area are warranted in larger numbers of patients and with longer post-treatment periods, to evaluate variations in treatment parameters and correlations with UV exposure.

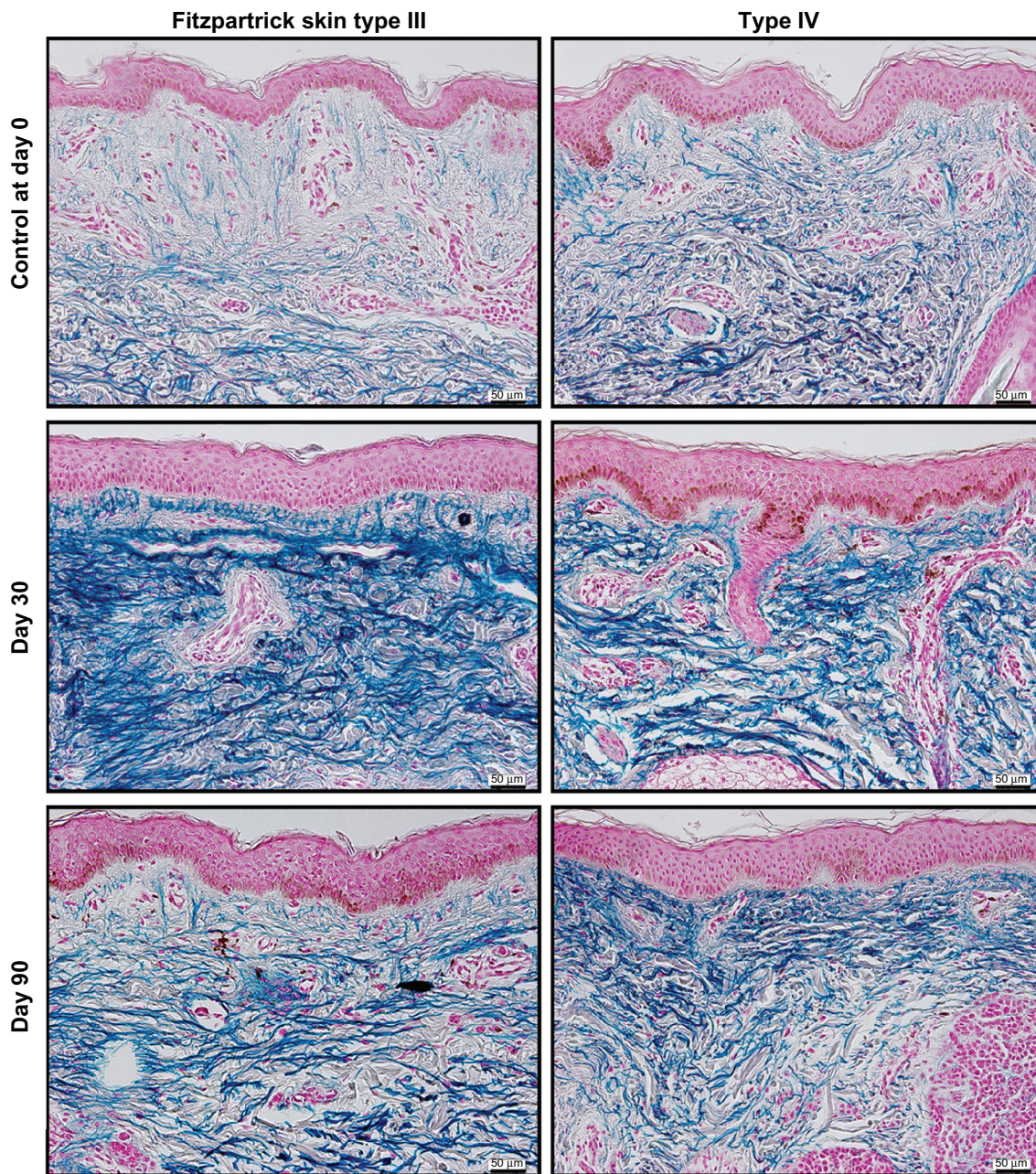


Figure 4 Representative histology of Japanese volunteers' cheek skin with Fitzpatrick skin type III (left column, a 41-year-old Japanese female) and Fitzpatrick skin type IV (right column, a 41-year-old Japanese female) evaluated by Victoria blue staining. Control on day 0 (first row). At 30 days (day 30) after NIR laser treatment (second row). Day 90 (third row).

Notes: Elastic fibers are stained blue. Scale bars = 50 μ m.

NIR increased elastin in the dermis, and achieved skin rejuvenation. The results indicate that NIR irradiation provides safe and effective long-term stimulation of elastin, which is beneficial for improving dilated pores, skin texture, and wrinkles.

Acknowledgments

We thank Ikuo Matsuyama for histological staining, and the members of Cutera Inc for helpful comments.

Disclosure

The authors report no conflicts of interest in this work.

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