

Report

Long pulsed 1064 nm Nd:YAG laser treatment for wrinkle reduction and skin laxity: evaluation of new parametersJong Soo Hong¹, MD, Song Youn Park¹, MD, Kyle K. Seo¹, MD, PhD, Boncheol L. Goo², MD, Eun Jung Hwang¹, MD, Gyeong Yul Park¹, MD, and Hee Chul Eun¹, MD, PhD¹Department of Dermatology, Seoul National University College of Medicine, Seoul, and ²Clinique L Dermatology, Goyang, Korea**Correspondence**Hee Chul Eun, MD, PhD,
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Conflicts of interest: None.

doi: 10.1111/ijd.12626

Abstract**Introduction** Among non-ablative devices for wrinkle reduction and skin laxity, long pulsed 1064 nm Nd:YAG laser (LPND) has considerable effectiveness. It can penetrate to deep dermis due to its longer wavelength. This study assesses the efficacy and safety of LPND applying new parameters for skin rejuvenation in Korean subjects.**Methods** A prospective randomized split-faced study was done ($n = 20$). Half of the face was treated with three passes of LPND at a spot size of 12 mm, 20–24 J/cm² fluence, 12 ms width, and frequency of 2 Hz, for three sessions, every four weeks. Outcomes were measured by wrinkle evaluation of blinded investigators, subjects' self-assessment, objective measurements of elasticity, and skin biopsy.**Results** Four weeks after the final treatment sessions, the average wrinkle grades of the treated side were reduced by 45.1%. Skin elasticity was significantly increased. The increment of collagen and elastic fiber in papillary dermis was confirmed histologically. No adverse reaction was reported. Pain on the treated side was mild without needing anesthesia.**Discussion** The authors studied new parameters for LPND for improvement of wrinkles and skin laxity with fewer treatment sessions without serious complications. Histologic findings corresponded to clinical improvement.**Conclusion** New parameters of LPND can achieve wrinkle improvement with few side effects.**Introduction**

Skin aging is characterized by cutaneous signs such as wrinkles and increased skin laxity.¹ As the face is prone to wrinkling and cosmetically is an important area, patients are more concerned with wrinkles on the face than those of any other area.²

Diverse treatment modalities have been used to improve skin wrinkling and laxity, including chemical peeling, soft tissue filler, laser ablation, and facelift surgery. Recently, laser ablation has been highlighted because it is relatively effective and has a shorter recovery time compared to other methods.³ Laser ablation is classified into ablative laser and non-ablative laser. Generally, ablative lasers are considered more effective than non-ablative ones in treating rhytides,⁴ but they have a prolonged recovery time and more chance of complications, such as postinflammatory hyperpigmentation due to excessive thermal energy transferred to adjacent tissue.^{5,6} As people of Asian background are prone to

postinflammatory hyperpigmentation, non-ablative lasers are preferred albeit non-ablative lasers have less impressive results in short time.⁷

Among many kinds of non-ablative laser, long pulsed 1064 nm Nd:YAG laser (LPND) can deliver energy to deep dermis where heat-induced damage results in collagen and elastin regeneration. Patients with Fitzpatrick skin type III or more can be treated using LPND with less risk because the wavelengths of the infrared area are weakly attracted to melanin. Many studies evaluating the applicability of LPND have been done recently. Early studies mainly used a longer pulse duration (PD).⁸ As Nd:YAG lasers with various PD were being developed, studies with shorter PD were also performed.⁹ However, to our knowledge, there are no studies using PD between the two poles, and studies of East Asians of Fitzpatrick skin type III or IV are lacking. Thus, we aimed to study the efficacy and safety of LPND with intermediate PD in treating facial wrinkles and improving skin laxity using objective evaluation.

Materials and methods

Study subjects

The design of this trial is a prospective, split-face, randomized, evaluator blinded study. It was carried out according to the principle of the Helsinki Declaration, approved by the Institutional Review Board of Seoul National University Hospital. The investigator in charge received informed consent from the study participants after thorough explanation of this clinical trial.

Twenty-two Korean female subjects with Fitzpatrick skin types III or IV were enrolled in this study. Participants with a history of treatment for wrinkles within one month or participants using an oral retinoid within six months, acute illness, underlying diabetes or hypertension, breastfeeding, or pregnancy, were excluded. Subjects were graded for wrinkle severity score (WSS) at baseline (0–5 grading scales, minimum 0; Table 1) and were judged eligible for study with grades of 2 or greater.¹⁰

Laser device and parameters

A laser device of LPND (Clarity LPY™; Lutronic Coporation, Ilsan, Korea) was used. After randomly designating a treatment side on the left or right, LPND with fluences of 20–24 J/cm², 12 mm spot size, 12 ms PD, and 2 Hz frequency were applied without overlapping, with three passes on that side. Three sessions with a 4-week interval were done. Subjects did not use any anesthesia or cooling device during treatment but were allowed to apply an icepack after treatment for 10–15 minutes. All the participants were instructed to use their own cosmetics as usual and sunscreen regularly.

Subjective evaluations

Participants visited the clinic every four weeks for evaluation. The last visit was done on week 12, four weeks after the third treatment. The participants subjectively evaluated the degree of satisfaction (from a minimum 0 to a maximum 10), compared to the control side, and were asked for complications such as pain or erythema after last treatment. Photographs were taken every visit using standardized light and position. Using the photographs, three blinded dermatologists independently

evaluated the effect of treatment with the wrinkle grading system mentioned above.¹⁰

Objective evaluations

To evaluate the effect of LPND measured using a Cutometer®, MPA 580 (Courage+Khazaka Electronic GmbH, Cologne, Germany), which is a non-invasive biomedical elasticity gauge device. It measures the vertical deformation of the skin when it is pulled by controlled vacuum into the circular aperture, evaluating skin laxity. Among the measurement values, R2 reflects the overall elasticity and R5 represents the net elasticity.¹¹ For the purpose of accuracy, subjects were not allowed any makeup or cleansing of their faces for two hours before measurement and stayed for 30 minutes in a room that had a steady temperature and humidity (20 °C, 40%).

Histologic evaluation

At the last visit after 12 weeks, fresh tissue was obtained from both cheeks with a 2 mm punch from volunteered subjects. Hematoxylin and eosin, Masson's trichrome stain, and immunohistochemistry for tropoelastin were done. To evaluate stained color objectively, the proportion of collagen and elastic fiber (blue and red each) was measured on images by IMAGEJ analysis (National Institute of Health, Bethesda, MD, USA, downloaded from <http://rsb.info.nih.gov/ij/download.html>). The color deconvolution algorithm, which calculates the contribution of red, green, and blue based on stain-specific RGB absorption, was used for analysis.¹²

Statistical analysis

SPSS 12.0 (SPSS Inc., Chicago, IL, USA) was used for analysis. Objective wrinkle severity, subjective assessment, R2, R5, and histological change from baseline to each visit were compared using the Friedman test. The difference of parameters compared to control was analyzed with the Wilcoxon matched pairs signed ranks test. $P = 0.05$ was considered statistically significant.

Results

Demographics

Among 22 female eligible participants, 20 completed the 12-week trial. The other two left the study due to personal reasons and not treatment complications. The mean age of participants was 46.3 (32–57) years old.

Clinical evaluation by investigator

The serial change of WSS compared to control is shown in Figure 1. At baseline, there was no significant difference between the two groups (2.93 ± 0.69 for treatment, 3.02 ± 0.72 for each control side). The WSS of the treated side improved from the second visit to 2.57 ± 0.61 ($P < 0.001$) and improved 45% at the last visit, com-

Table 1 Wrinkle grading scale

Grade	Criteria
0	No evidence of line or wrinkles
1	A few short barely perceptible lines/wrinkles
2	A few shallow lines/wrinkles that are discreetly visible, no deep lines/wrinkles
3	Shallow easily visible lines/wrinkles
4	Moderate number of fine lines/wrinkles
5	Many deep lines

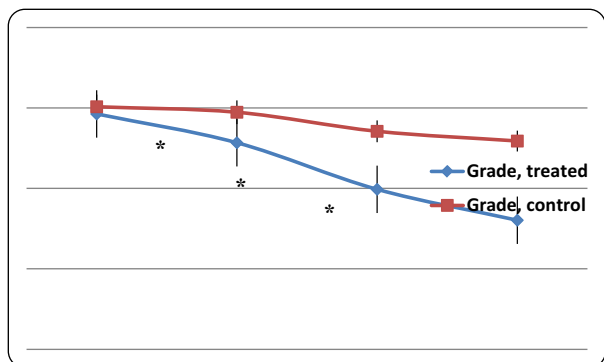


Figure 1 Change of wrinkle grades evaluated by blinded investigators. * $P < 0.05$ between treated side and control side

Table 2 Change of evaluation parameters

	Baseline	2nd visit	3rd visit	4th visit
Wrinkle severity score				
Treatment	2.93 ± 0.69	2.57 ± 0.61	1.98 ± 0.63	1.61 ± 0.61
Control	3.02 ± 0.72	2.95 ± 0.73	2.71 ± 0.58	2.59 ± 0.61
P value	0.003	<0.001	<0.001	<0.001
Degree of satisfaction				
Overall	0	1.79 ± 2.12	4.05 ± 3.31	5.79 ± 2.23
P value	<0.001			
R2				
Treatment	0.76 ± 0.09	0.81 ± 0.09	0.83 ± 0.18	0.91 ± 0.06
Control	0.76 ± 0.08	0.77 ± 0.06	0.78 ± 0.07	0.75 ± 0.07
P value	0.872	0.117	0.024	<0.001
R5				
Treatment	0.58 ± 0.17	0.58 ± 0.10	0.61 ± 0.12	0.77 ± 0.08
Control	0.56 ± 0.11	0.53 ± 0.10	0.52 ± 0.08	0.55 ± 0.12
P value	0.717	0.044	0.001	< 0.001

pared to the baseline as 1.61 ± 0.61 ($P < 0.001$). The control side did not show a significant difference at each visit from baseline. The WSS of the treated compared to the control side at each visit differed significantly from the second visit showing definite improvement of the treat-

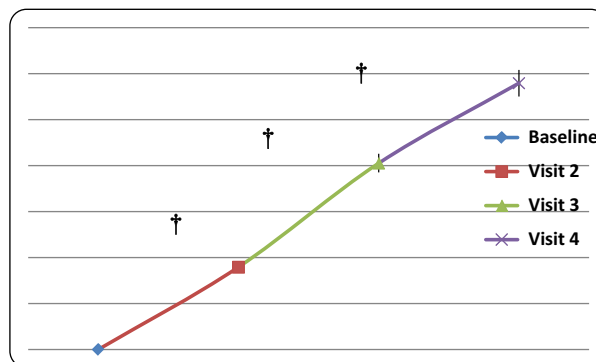


Figure 3 Patient assessment of improvement in the depth of their wrinkles and skin laxity (ranging from 0 to 10, in which 0 was same as control side and 10 meant currently with no wrinkle). † $P < 0.05$ between each visit and baseline

ted side (Table 2). Figure 2 demonstrates photographs of both sides after treatment.

Clinical evaluation by subjects

The mean of subjectively evaluated degree of satisfaction compared to control side are presented in Figure 3. After the first treatment (second visit), the satisfaction score improved from 0 at baseline to 1.79 ± 2.12 . The score increased to 4.05 ± 3.31 and 5.79 ± 2.23 at the third and fourth visit, respectively, each showing more improvement as the treatment was repeated. At all three visits, the score differed significantly from baseline ($P < 0.001$) (Table 2).

Objective evaluation of skin elasticity

The change in elasticity was measured by the Cutometer®. R2 increased gradually on the treated side with 0.76 ± 0.09 , 0.81 ± 0.09 , 0.83 ± 0.18 , 0.91 ± 0.06 for baseline, and second, third, and fourth visit each ($P < 0.001$). The R2 of the control side was 0.76 ± 0.08 , 0.77 ± 0.06 , 0.78 ± 0.07 , and 0.75 ± 0.07 showing no tendency. When the treated side was compared to the control at each visit, R2 revealed a significant difference

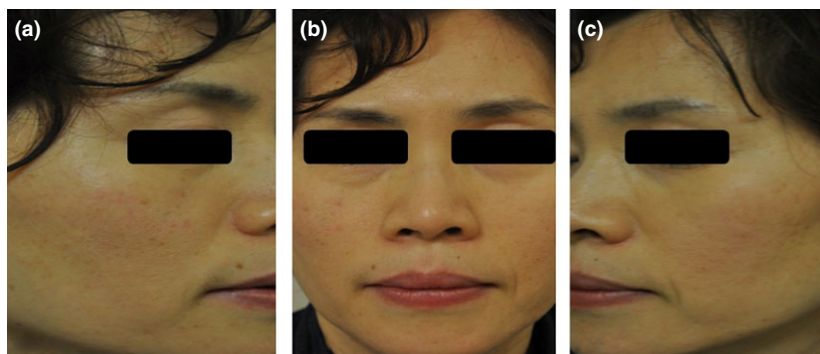


Figure 2 Improvement in a 54-year-old woman with many fine and coarse wrinkles. The right half face is treated (a) and the other half is untreated (c)

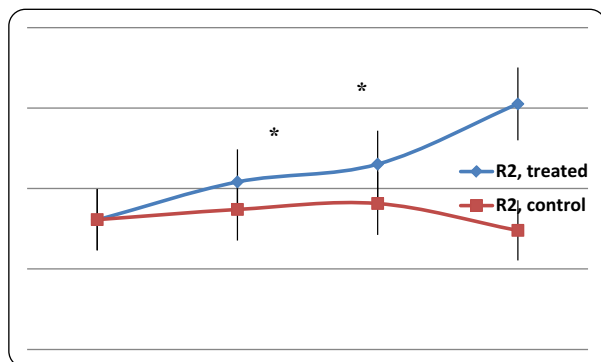


Figure 4 Improvement of the R2 value. * $P < 0.05$ between treated side and control side

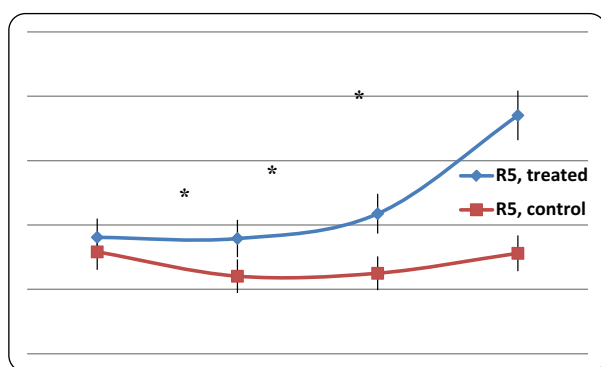


Figure 5 Improvement of the R5 value. * $P < 0.05$ between treated side and control side

from the third visit after two treatment sessions ($P = 0.024$). The difference was maintained until the last visit ($P < 0.001$) (Fig. 4). R5 increased from 0.58 ± 0.17 at baseline to 0.77 ± 0.08 at the last visit ($P < 0.001$). The R5 of the control did not show a significant increase in value at each visit (0.56 ± 0.11 , 0.55 ± 0.12 , baseline, and the last visit each). When the treated side was compared to the control at each visit, R5 differed significantly from the second visit ($P = 0.044$) until the last visit ($P < 0.001$) (Table 2; Fig. 5).

Histologic evaluation

Four subjects volunteered for the biopsy. Using Masson's trichrome stain, the proportion of collagen fiber on the treated side was 45.4% and that of control was 25.9% with definite significance ($P = 0.028$). The IHC of tropoelastin revealed an elastin proportion of 25.4 and 21.5% for the treated and control side each ($P = 0.028$) (Table 3).

Complication and safety issue

There was no serious complication reported. Some participants complained about mild pain during treatment but not severe enough to interfere with it. The visual

Table 3 Proportion of Masson's trichrome and immunohistochemical stained fibers for collagen and tropoelastin for each. They are increased on treated side

Proportion (%)	Treated side	Control side	P value
Collagen fiber	45.4	25.9	0.028
Tropoelastin	25.4	21.5	0.028

analogue scale of the pain was distributed between 2 and 3. Mild erythema was observed right after treatment, completely improving within 30 minutes.

Discussion

Recently, studies have been conducted with various lasers and parameters for skin rejuvenation.¹³⁻¹⁵ Non-ablative lasers have a shorter recovery time and lower rate of complication such as post-inflammatory hyperpigmentation than ablative ones.¹⁶ Among non-invasive treatment devices with rapid recovery, LPND has been known to be equivalent or more superior than other treatment modalities.^{17,18} These non-ablative lasers are thought to work through thermal energy transferred to small vessels and tissues in upper dermis, which stimulate dermal fibroblasts to induce collagen and elastin regeneration.^{16,19} Regarding the hypothesis above, LPND has the advantage of reaching deeply located blood vessels and transferring energy to collagen adjacent to vessels while bypassing the epidermis.²⁰

The first time LPND was used for improvement in skin quality, a long PD was used. Dayan *et al.* studied LPND with 50 ms PD and 22 J pulse energy. After seven sessions, they reported 20% improvement of wrinkles and skin laxity.⁸ Long PD of 50 ms was based on the theory PD longer than thermal relaxation time of melanin (3-10 ms) can deliver energy to dermis around the melanin. Taylor and Prokopenko studied LPND with 50 ms PD, 50 J/cm², and three passes a time. After a session, they observed 30% improvement of wrinkles, reporting only one session could result in a better outcome than previous studies. They applied local anesthesia before applying high energy and mentioned the possibility of erythema or vesicles after treatment.¹⁷ Key reported 47.5% improvement of wrinkles after one session treated with 50 ms, 50 J/cm², and two passes.¹⁸ Some studies use a very short PD. Schmults *et al.* tried LPND with 0.3 ms PD, 7-9 J/cm² fluence, and three sessions at 2-week intervals. New collagen fiber formation was observed in histology, suggesting short PD and low energy laser are effective in treating wrinkles.⁹ Trelles *et al.* used the same parameters as Schmults *et al.*, reporting continuing satisfaction by participants after six months follow-up.²¹ A study by Chiba *et al.* used the laser at 0.3 ms PD and

13 J/cm². After two to seven treatments, 10 of 19 participants showed good or superior improvement without side effects.²²

The present study fixed PD to 12 ms with a fluence of 20–24 J/cm² to reduce the pain sufficiently to tolerate treatment without anesthesia and to get the equivalent effectiveness of high energy. At the last follow-up, evaluation by experts revealed 45.1% improvement and 57.9% improvement by subjects. Measurement with a cutometer also demonstrated the increase of R2 and R5, compared to baseline coinciding with clinical assessment. In comparison with Dayan *et al.*, the present study shortened PD with similar energy, achieving an effective result with fewer treatment sessions. Although we had more treatment sessions than the studies with higher energy, the pain was much reduced in our study than the ones with higher energy. The significance of the parameter for this study is that one can get satisfactory improvement of wrinkle and skin laxity after relatively fewer sessions with tolerable pain or long recovery time. No significant complications such as scar or hypopigmentation were reported, probably because shorter PD and lower fluence than treatment of other conditions, such as port wine stain, were used. Collagen and elastic fibers are responsible for skin stretch and relax.²³ The authors observed new collagen formation, increment of collagen fiber, and tropoelastin on the treated side histologically. These cellular changes are correlated to clinical improvement.

Small sample size and relatively short follow-up period could be limitations in our study. A larger sample size and subjects from other races or age groups can clarify the value of LPND in the treatment of wrinkles. As LPNDs shorter downtime allows easy application for treatment, further studies of combination treatment with other methods will have significance in the future.

Recently, non-ablative lasers are popular for improving skin quality. Among these non-ablative lasers, we have proved that LPND can be an effective device that improves skin laxity by adjusting treatment parameters. However, doctors need to pay attention to complications such as scars because it penetrates deep into dermis with its long wavelength. More studies are needed to find safe and effective parameters for LPND.

Acknowledgments

All of the authors have no information to declare, and all of the authors have no conflicts of interest to disclose.

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