



## ORIGINAL ARTICLE

# Treatment of Melasma with the Photoacoustic Twin Pulse Mode of Low-Fluence 1,064 nm Q-Switched Nd:YAG Laser

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**Background:** Low-fluence 1,064 nm Q-switched Nd:YAG laser has been widely used for the treatment of melasma. Although new Q-switched Nd:YAG lasers with photoacoustic twin pulse (PTP) mode have been recently developed for high-efficiency, there is limited information available for the new technique. **Objective:** This study was designed to investigate the efficacy and adverse effects after few sessions of repeated low fluence 1,064 nm Q-switched Nd:YAG laser treatment with PTP mode in Asian women with melasma. **Methods:** Twenty-two Korean women were treated with a total of five sessions of low-fluence PTP mode Nd:YAG laser treatment (Pastelle<sup>®</sup>) at 2 weeks interval. Responses to treatments were evaluated by using Melasma Area and Severity Index (MASI) scoring, colorimeter measurement, and the investigators' and patients' overall assessments. Adverse events were recorded at each visit. **Results:** Investigators' and patients' overall assessment showed that 'significantly improved' was assessed by 13 (59.1%) and 19 of 22 patients (86.4%), respectively. MASI scores were significantly reduced by 20.4%. The lightness, measured by using a colorimeter, was significantly increased by 1.3 point. Notable adverse events were not observed.

**Conclusion:** After 5 sessions of laser therapy alone, about 60% of the subjects showed significant improvement. Few sessions of repeated laser toning treatment using the PTP mode is a safe and effective way to treat facial melasma. (*Ann Dermatol* 28(3) 290~296, 2016)

**-Keywords-**

Laser toning, Melasma, Nd:YAG laser, Photoacoustic twin pulse

## INTRODUCTION

Various methods are used to treat facial melasma, ranging from avoidance of exposure to the sun to topical bleaching agents to ablative resurfacing, but these methods can be ineffective especially in dark skinned Asian women. In addition, the efficacy is unsatisfactory when considering the occurrence of adverse effects, such as skin irritation, pain, persistent erythema, and rebound hyperpigmentation<sup>1</sup>. Melasma can be easily exacerbated by inadvertent ultraviolet light exposure or mild irritation. Consequently, the most recent practical treatment approach would be a non-invasive, risk-free procedure with no recovery time that would efficiently induce remission<sup>2</sup>.

In these circumstances, low-fluence 1,064 nm Q-switched Nd:YAG laser therapy (so called 'laser toning') has emerged since mid-2000s<sup>3</sup>. Previous studies demonstrated that facial melasma lesions could be improved by multiple sessions of 1,064 nm Q-switched Nd:YAG laser treatment at lower sub-thermolytic fluence<sup>4-11</sup>. The main advantage of this laser therapy is that it requires minimal downtime and causes lower incidence of complications.

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Recently, new Q-switched Nd:YAG lasers which are capable of utilizing the photoacoustic twin pulse (PTP) mode, such as RevLite<sup>®</sup> (HOYA ConBio, Fremont, CA, USA) and Pastelle<sup>®</sup> (Won Technology Co., Ltd, Daejeon, Korea), have been developed for high-efficiency laser toning. PTP is the latest technology in which successive two beams are emitted at very short intervals (100~130  $\mu$ sec) and then synergistically produce higher peak power than those produced by a single beam from the current Nd:YAG lasers. Although there were some previous reports regarding low-fluence Nd:YAG laser therapy for melasma, little information exists about the efficacy and safety of laser toning with PTP mode. In this study, we performed an open-label controlled clinical experiment to evaluate the degree of improvement and side effects of PTP mode 1,064 nm Q-switched Nd:YAG laser toning in Asian women with moderate-to-severe melasma. Using the results from previous studies as historical controls, this study was aimed to investigate the efficacy and safety of laser toning with PTP mode.

## MATERIALS AND METHODS

### Study subjects

Twenty-two Korean women with melasma who had a Melasma Area and Severity Index (MASI) score of 3 or more on their face were enrolled. Patients who were pregnant, lactating, or on any hormonal therapy were excluded. Patients who had used bleaching agents such as hydroquinone cream, or who had received laser treatment within 2 months prior to the study were also excluded. Subjects were instructed not to use any other forms of treatment or functional cosmetics during the 12-week study period. This clinical study was approved by the Institutional Review Board of Dankook University Hospital (Cheonan, Korea) (IRB No. 201204-014) and written informed consent was obtained from the subjects in accordance with the Helsinki declaration.

### Treatment methods

All subjects were treated with a total of five sessions low-fluence 1,064 nm Q-switched Nd:YAG laser treatment (Pastelle<sup>®</sup>) at 2 weeks interval. Two dermatologists performed laser treatment using a PTP toning mode with a collimated, 1,064 nm wavelength, 7 mm spot size, fluence of 2.5 J/cm<sup>2</sup> and 5~7 passes per treatment. Each patient was treated by a single dermatologist throughout the study period. Laser therapy was stopped when mild erythema appeared without petechiae around the melasma lesion. The mean count of laser shots was 2,914.02  $\pm$  696.24 per session. No anesthesia was necessary prior to the

treatment. Subjects were advised to avoid direct sun exposure and to apply broad-spectrum sunscreen during and after the treatment.

### Efficacy assessment

Clinical and photographic evaluations for improvement (a decrease in the appearance of melasma) were conducted at baseline and at the last follow-up visit (2 weeks after the last treatment). High-quality digital photographs were taken from the front and sides under the same lighting conditions using a digital camera (D400; Nikon, Tokyo, Japan). Responses to treatments were evaluated at the last follow-up visit by using MASI scoring, colorimeter measurement, and the investigators' and patients' overall assessments. The MASI values were determined to quantify changes in pigmentation, as previously described<sup>12,13</sup>. In addition, objective measurement of skin color was conducted at the darkest spot with a colorimeter (CR-400; Minolta, Tokyo, Japan). Measurement of brightness (L\* value) were obtained three times, and the average value was calculated. Two blinded investigators independently assessed the percent improvement between the pre- and post-treatment using digital images. The mean improvement percent was further graded as: worse (<0%), unchanged (0% improvement), slightly improved (>0%, <25.0%), moderately improved ( $\geq$ 25.0%, <50.0%), much improved ( $\geq$ 50.0%, <75.0%), and very much improved ( $\geq$ 75.0%,  $\leq$ 100%). All subjects were also requested to self-evaluate the post-treatment improvement after 5 treatment sessions as worse (<0%), unchanged (0% improvement), slightly improved (>0%, <25.0%), moderately improved ( $\geq$ 25.0%, <50.0%), much improved ( $\geq$ 50.0%, <75.0%), and very much improved ( $\geq$ 75.0%,  $\leq$ 100%).

### Safety assessment

At each visit, adverse events of low-fluence Q-switched Nd:YAG laser therapy were evaluated. Patients were asked to notify the side effects such as procedural pain, erythema, swelling, post-inflammatory hyper- or hypo-pigmentation, facial dryness, itching and other side effects during and after the treatment. The intensity of both pain and erythema following the procedure was also evaluated. The pain scale ranged from 0 (none) to 6 (severe), and the degree of erythema was divided into 5 grades: none, minimal, mild, moderate, and severe.

### Statistical analysis

Measured values were expressed as the means  $\pm$  standard deviations (SD). Statistical analyses were performed using SPSS software (version 12.0; SPSS Inc., Chicago, IL, USA). MASI scores and colorimeter measurements (L\* values)

were analyzed using the nonparametric Wilcoxon sign-rank test and Student's paired t-test, respectively.  $p < 0.05$  was accepted as significant.

## RESULTS

### Patient characteristics

All 22 subjects were of skin type III or IV without any medical problem; the mean age ( $\pm$ SD) was 41 ( $\pm$ 6.51) years; and the range of age was 32~59 years. All patients completed the study.

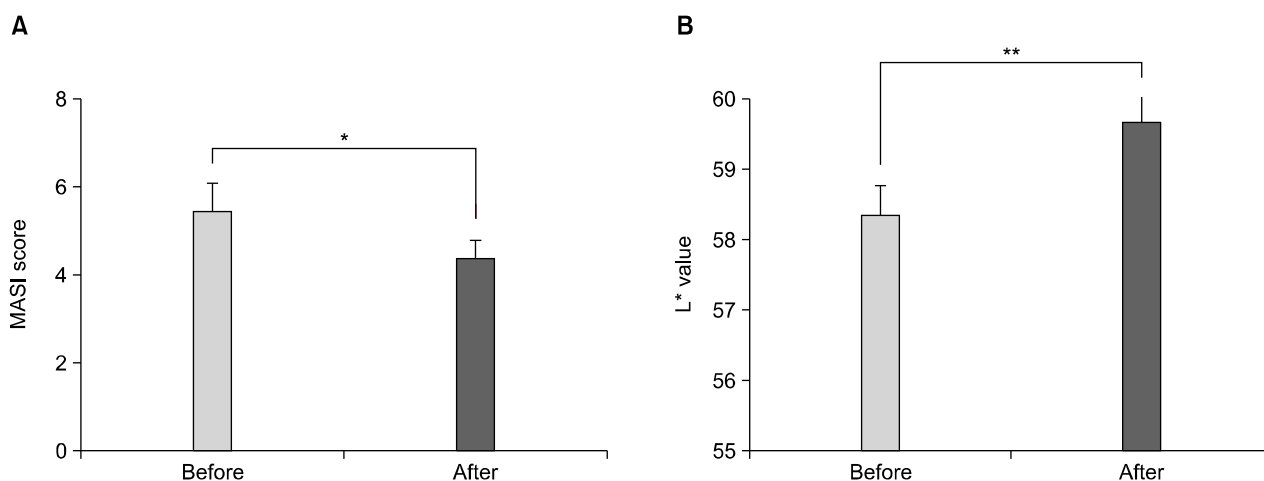
### Efficacy

#### 1) MASI score

MASI scores significantly reduced from  $5.46 \pm 2.9$  to  $4.35 \pm 1.99$  following 5 sessions of PTP toning laser treatments ( $p = 0.025$ ) (Fig. 1A, Fig. 2). The mean percentage of improvement was 20.3%. Only 4 of 22 patients demonstrated an increase in MASI scores.

#### 2) Colorimeter measurement

A higher  $L^*$  value reflects brighter skin tone. After 5 treatments, the  $L^*$  value significantly increased by 1.3 point



**Fig. 1.** Changes of (A) Melasma Area and Severity Index (MASI) score and (B) skin brightness with 5 sessions of photoacoustic twin pulse mode laser toning.  $L^*$  values were measured by colorimeter. \* $p < 0.05$ , \*\* $p < 0.01$ .



**Fig. 2.** A 40-year-old female with phototype III skin. (A) Before treatment (MASI=10.1), (B) two weeks after completion of five treatments showing about 60% improvement of melasma (MASI=4.4). Note the improvement of left cheek after treatment. MASI: Melasma Area and Severity Index.

(from  $58.34 \pm 2.66$  to  $59.64 \pm 2.46$ ,  $p < 0.0001$ ) (Fig. 1B).

### 3) Assessment by investigators and patients

More than 25.0% of improvement including ‘moderately improved’, ‘much improved’, and ‘very much improved’ were considered as ‘significantly improved’. The investigators’ assessment showed that 13 of 22 patients (59.1%) were evaluated as “significantly improved” (Fig. 3A). The most prevalent grade was ‘moderately improved’, which accounted for 50.0%. The mean improvement percentage assessed by the investigators was 31.9% ( $\pm 13.48$ ), which corresponded to ‘moderately improved’.

The patients’ global assessment demonstrated that 19 of

22 patients (86.4%) indicated that they were ‘significantly improved’ (Fig. 3B). The average percent of improvement was 52.8% ( $\pm 18.41$ ), which corresponded to ‘much improved’. Interestingly, statistically significant difference was found between the average improvement percentage of the two assessment groups ( $p < 0.001$ ).

### Adverse effects

Although few patients experienced adverse events including erythema, dryness, pain, and itching, the adverse events were generally mild and resolved within 24 hours without specific treatment (Fig. 4A, B). Three people had recognizable pain during the procedure, but only one re-

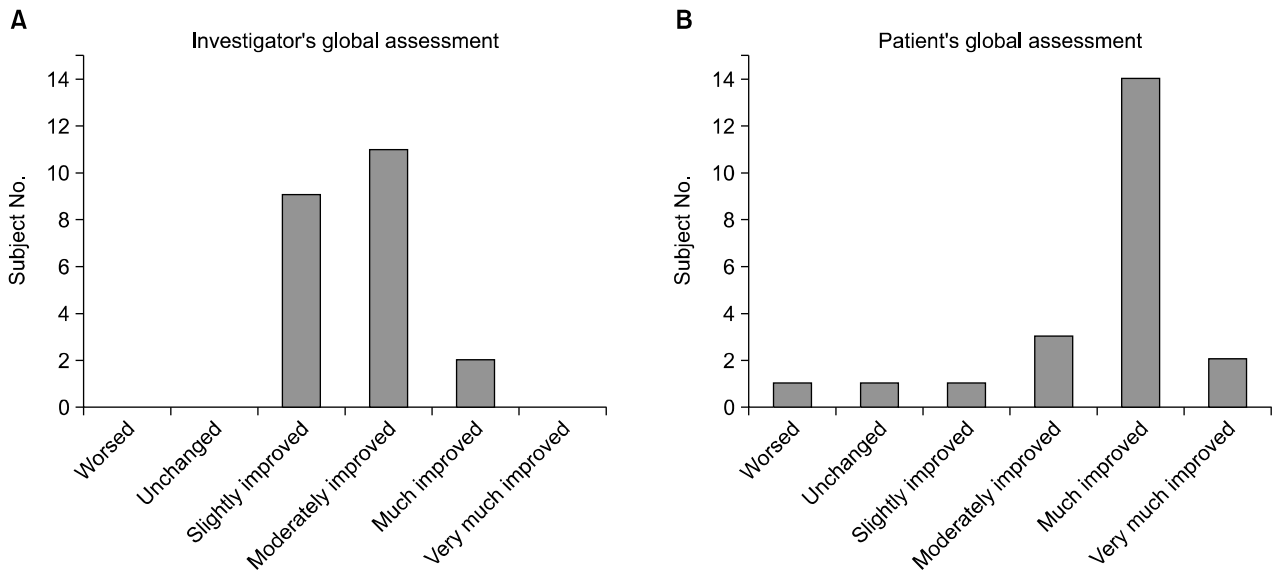


Fig. 3. Global assessments evaluated by (A) investigators and (B) patients.

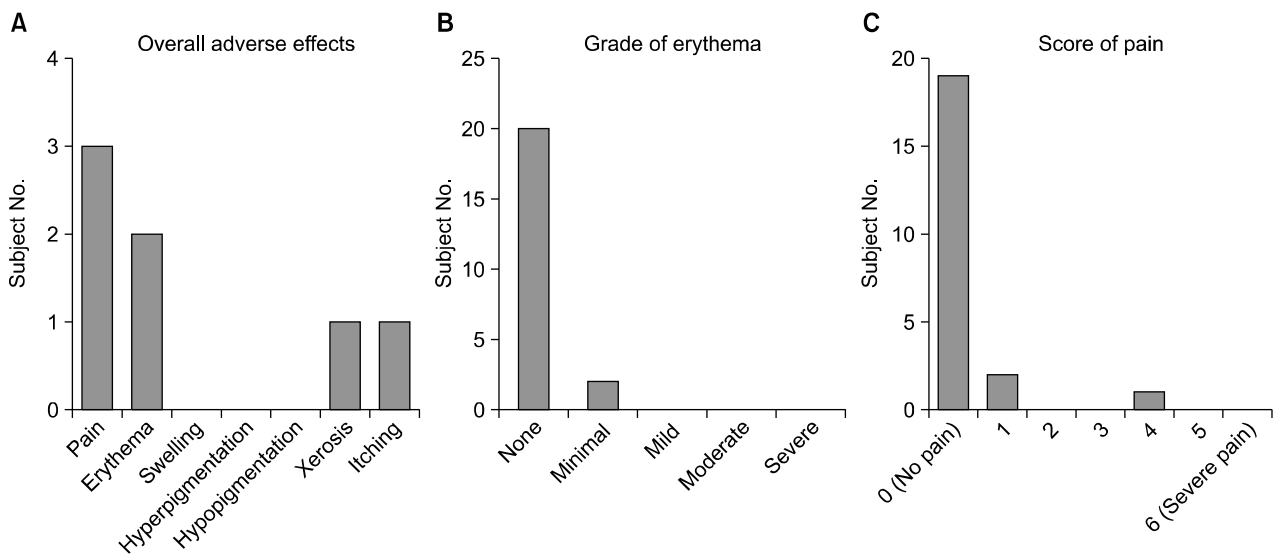


Fig. 4. Adverse effects of photoacoustic twin pulse mode laser toning treatments. (A) Overall, (B) erythema grade, (C) pain score.

ported moderate pain (4 on the scale) (Fig. 4C). There was immediate fine facial hair whitening in some subjects during the laser treatment, but none complained about this phenomenon. Serious adverse events such as post-inflammatory hypo- or hyper-pigmentation were not observed in any of the patients and no patient dropped out of the study due to such events.

## DISCUSSION

Q-switched Nd:YAG lasers emit a beam at the level of nanoseconds pulse width to selectively destroy melanosomes without affecting surrounding tissue. Especially, the collimated 1,064 nm Q-switched Nd:YAG laser which delivers laser beam evenly throughout the dermis is able to treat a pigmented lesion located deep within the dermis.

For achieving stable treatment results in melasma, it is important to minimize the unwanted side effects such as inflammation or skin irritation. Laser toning with 1,064 nm Q-switched Nd:YAG laser was devised as a way to reduce rebound aggravation of melasma or post-inflammatory hyperpigmentation due to such secondary stimulations which can be caused by other existing treatment modalities. The mechanism of laser toning has been proposed to be due to the fragmentation of subcellular-specific organelle melanin granules in the dendrites and subsequent dispersion into the cytoplasm without cellular destruction by repetitive doses of laser energy with a sub-photothermolytic fluence ( $<5 \text{ J/cm}^2$ ) over a large spot size, the so called "subcellular selective photothermolysis"<sup>14,15</sup>.

PTP is a unique laser emitting mode in which double pulses are delivered within one Q-switching cycle. Each pulse has relatively weak energy compared to the standard single Q-switched beam, but they can transfer higher peak energy (up to 60% more) to the target melanosome than a single beam because double beams are successively irradiated at very short intervals (100~130  $\mu\text{sec}$ ) and their energy can be accumulated. As a result, the high peak energy instantly increases the temperature of the chromophore, leading to pressure changes and vibration, which then effectively destroys the chromophore through the form of a shock wave (photoacoustic effect).

Q-switching engineering in this study produces a pulse width of 20 ns on single Q-switching. The pulse width between the first and the second Q-switching in the double Q-switching PTP mode is about 100  $\mu\text{s}$ . The instant peak energy of the singly Q-switched beam is 1.3 J, whereas the energy of doubly Q-switched beams (each beam energy is about 0.8 J) in the PTP mode is 1.6 J, and as a result, the instant peak energy is increased up to 123% (<http://www.wtlaser.com/kr/products/pastelle.asp>). PTP can

also offer safer treatment owing to the minimization of the thermal damage, by using a collimate beam mode, which involves a unique dispersion of high peak energy, and low fluence<sup>4</sup>.

However, there are some weak points in this laser toning therapy. It delivers a sub-threshold dose of laser at a time and therefore, this treatment modality definitely requires many treatment sessions and a treatment period of several months to obtain satisfactory clinical improvement<sup>5,11</sup>.

When compared with the results of other studies using low fluence Q-switched Nd:YAG treatments, even after considering methodological variability, about 60% of the subjects in our study had 'significantly improved', whereas previous publications showed an improvement range of 50%~90%<sup>2,4,5,10,16</sup>. Therefore, the degree of improvement of global assessment in our study was not likely to be superior. However, it should be considered that five sessions of laser toning monotherapy were conducted in this study and it is a fewer treatment session than those of other previous studies, which conducted 5 to 15 times of mono- or combined-laser therapies. Moreover, the objective colorimeter L\* value increased by 1.3 point in our study, and this showed better improvement as compared to an increase of 1.1 point after laser toning therapy of 10 times weekly in the same ethnic group<sup>17</sup>.

Similar to this study, a prospective single arm clinical study was recently conducted in which 50 Korean women with melasma were treated with 15 weeks of weekly treatments, using another PTP mode Q-switched Nd:YAG laser at 1,064 nm with a fluence of 2.8  $\text{J/cm}^2$ , and an 8-mm spot size<sup>4</sup>. They reported that both patients and investigators rated the treatment outcome as "good improvement" on average with improvement rate of  $\geq 50\%$  and  $< 75\%$  without any serious side effects. Considering the fewer treatment sessions, the more increased level of skin brightness value by using objective colorimeter after laser monotherapy, the efficacy of PTP laser toning in our study is thought to be of a significant level. It can be presumed that further increasing the number of treatment sessions may show a better effect.

Interestingly, the overall global assessment of patients revealed more improvement than that of the investigators, and this can be assumed to be due to the low incidence of discomfort or side effects and the feeling that the skin is generally clearer after the treatment. In fact, a large number of subjects were pleased with the results and noted their facial hue became brighter through the treatments (data not shown). When assessing the MASI score at the final visit, the improvement of dark color was more prominent than the degree of regression of melasma area (data not shown). As the treatment progressed, eventually, the

dark hue of the melasma gradually got brighter.

Reported complications from laser toning include pain during the procedure, rebound of melasma, hyperpigmentation, guttate leukoderma, physical urticaria, acneiform eruption, minute petechiae, whitening of fine facial hair, and herpes simplex reactivation<sup>2,4,16,18</sup>. Confetti-like hypopigmentation or punctate leukoderma, the most distressing complication of repeated low fluence laser therapy, can develop after several sessions (2 to 7 weekly based treatment sessions)<sup>18,19</sup>. In this study, only a few patients experienced transient and tolerable adverse events including erythema, dryness, pain, and itching. Although 4 out of 22 patients showed mild increase in MASI score at the last follow-up visit, there was no significant adverse event such as punctate leukoderma in spite of the delivery of approximately 3,000 laser shots and a fluence of 2.5 J/cm<sup>2</sup>. Therefore, the laser used in this study can be considered safe and tolerable.

Melasma can commonly reappear in some degrees after a certain period despite of proper treatments<sup>10</sup>. However, we did not evaluate the recurrence or long term result of efficacy in our melasma patients. In addition, this study was not designed as the comparison study such as a trial using split-face or having control group. These are major limitations of our study. Nevertheless, we have put a meaning on achieving significant improvement of melasma by using relatively few treatment sessions in relatively short duration without any burden to the patients.

In summary, a total of 22 Korean women with facial melasma were treated using low fluence 1,064 nm Q-switched PTP mode Nd:YAG laser therapy. After 5 sessions of laser therapy alone, about 60% of the subjects showed significant improvement, and no notable adverse events were observed. This study demonstrated that few sessions of repeated laser toning treatment using the PTP mode could be a safe and effective way to treat facial melasma.

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