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# A Retrospective Analysis of the Treatment of Melasma Using a Fractional Long-Pulsed Alexandrite Laser in Korean Patients

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BACKGROUND Long-pulsed, 755-nm, alexandrite lasers have been shown to be effective and safe in the treatment of pigmentary lesions.

OBJECTIVE Clinical outcomes and side effects in the treatment of melasma using a fractional, long-pulsed, alexandrite laser were assessed.

MATERIALS AND METHODS Forty-eight patients with melasma received 2 to 4 treatment sessions of fractional, long-pulsed, alexandrite laser at 2 to 3 weeks intervals. The parameter of treatment was 60 to 80 J/cm$^2$ without dynamic cooling device using 15-mm spot size of fractional hand piece, with a 0.5- to 1-millisecond pulse width.

RESULTS The mean modified melasma area and severity index score decreased significantly 2 months after the final treatment compared with baseline (16.5 ± 8.2 vs 11.5 ± 7.0; $p = .002$). The patients with epidermal type melasma were more effective compared to dermal type ($p < .001$).

CONCLUSION Long-pulsed alexandrite lasers using a fractional hand piece are moderately effective in the treatment of melasma with low risk of adverse effects, and it is suggested that fractional, long-pulsed, alexandrite laser with combination of other modalities can be an additional therapeutic option in patients with melasma.

*The authors have indicated no significant interest with commercial supporters.*

Melasma is an acquired pigmentary disorder that presents as irregular brown macules and patches on the face, and it is a frequent cosmetic concern, particularly in women. The actual pathogenesis of melasma remains controversial, although various etiologies, such as ultraviolet light exposure, genetic factors, pregnancy, and phototoxic drugs, are considered to be causative or aggravating factors.[1–3] Based on the pattern of melanin deposition in the skin, as noted on histologic examinations, melasma can be divided into 3 types: epidermal, dermal, and mixed.[4]

Although this condition commonly occurs, its treatment is challenging. Topical agents, including broad-spectrum sunscreens, hydroquinone, retinoic acid, corticosteroid, and azelaic acid are considered to be the first-line and long-term maintenance treatment options for melasma; however, the efficacy of topical agents is limited, and additional treatments are often required.[5] In recent years, various physical therapies have been used to treat melasma, including Q-switched neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser, intense pulsed light (IPL), and chemical peeling; however, these treatments are also not completely satisfactory, and subsequent complications such as postinflammatory hyperpigmentation are frequently reported.[6–9]

In the present study, it is aimed to evaluate the efficacy and safety of using a fractional, 755-nm, long-pulsed, alexandrite laser in Korean patients with

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melasma who primarily have a Fitzpatrick skin type of III or IV.

## Materials and Methods

### Study Patients

Female Korean patients who underwent treatment with a 755-nm, long-pulsed, alexandrite laser (Noblex; FineMEC, Seoul, South Korea) for the management of melasma between 2014 and 2015 were retrospectively analyzed. The medical records were carefully reviewed, and the findings of detailed history taking and physical examination were analyzed. The results of Wood's lamp examination, which was performed to determine the types of melasma, were also collected. All patients who received long-pulsed alexandrite laser treatment for melasma were reviewed, and those who used bleaching cream containing hydroquinone or those who received laser treatment on their face at least 6 months before this treatment were excluded.

### Laser Treatment

The patients were treated with a 755-nm, long-pulsed, alexandrite laser without topical anesthesia. The lesions were treated with settings of 60 to 80 J/cm$^2$ without a dynamic cooling device using a 15-mm spot size of fractional hand piece and with a 0.5- to 1-millisecond pulse width. A fractional hand piece has 130 small dots that are each 400 μm in size. At the setting of 60 J/cm$^2$ with a 15-mm fractional tip, approximately 9.5 J of energy is emitted. Fluences were determined based on the patient's Fitzpatrick skin type, pigmentation of lesions, and background skin color. The clinical end points were defined as perilesional erythema and/or an ashy gray colored microcrust formation. Patients were advised to avoid direct sunlight and to use broad-spectrum sunscreen regularly. Each patient underwent 2 to 4 treatments at 2 to 3 weeks of intervals, depending on their clinical response.

### Evaluations

Clinical evaluations for improvement in pigmentation were performed by 2 dermatologists, who compared the photographs obtained at baseline, before each treatment session, and 2 months after the final treatment. Standard digital photographs were obtained under the same conditions using the A-one Lite imaging system (Bomtec, Seoul, South Korea). This system allows for consistent positioning of the patient's head and obtains images with a resolution of 10 megapixels.

The clinicians objectively evaluated the overall improvement in melasma using a quartile grading scale: Grade 1, <25% (minimal to no improvement); Grade 2, 26% to 50% (moderate improvement); Grade 3, 51% to 75% (marked improvement); and Grade 4, >75% (near total improvement).

The modified melasma area and severity index (mMASI) score was also evaluated by the 2 investigators using digital photographs obtained before the first treatment and 2 months after the final treatment session.[10] The mMASI score was calculated based on the percentage of the involved area (0, 0%; 1, <10%; 2, 10%–29%; 3, 30%–49%; 4, 50%–69%; 5, 70%–89%; and 6, 90%–100%); darkness of the pigmentation (0, absent or normal skin color without evidence of hyperpigmentation; 1, slight visible hyperpigmentation; 2, mild visible hyperpigmentation; 3, marked hyperpigmentation; 4, severe hyperpigmentation); and homogeneity or density of hyperpigmentation (0, minimal; 1, slight; 2, mild; 3, marked; 4, severe).

mMASI score = (darkness of pigmentation + homogeneity) × area.

All patients self-assessed the improvement in their melasma at the 8-week follow-up point: >75% clearance (excellent), 51% to 75% clearance (good), 26% to 50% clearance (fair), ≤25% clearance (poor), and worsening.

Any complications and side effects recorded at each visit (erythema, edema, burning, petechiae, bulla, and postinflammatory hyperpigmentation or hypopigmentation) were also reviewed.

### Statistical Analysis

Statistical analyses were performed using SPSS software (version 21.0; SPSS, Inc., Chicago, IL).

Continuous variables (e.g., age, duration, mMASI score) are expressed as mean ± standard deviation. The mMASI score was evaluated using the *t*-test. A *p* value of <.05 was considered statistically significant.

## Results

### *Demographic Data of the Patients*

A total of 65 patients received long-pulsed alexandrite laser treatment for melasma. Of these, 17 patients who received other treatment concomitantly, such as bleaching cream or oral tranexamic acid, or who received laser treatment within the 6 months before the long-pulsed alexandrite laser were excluded. A total of 48 patients (all women) with melasma were finally included in the analysis (Fitzpatrick skin Type III, $n = 27$; Fitzpatrick skin Type IV, $n = 21$). The mean age of the patients was 44.1 ± 9.6 years, and the mean duration of melasma was 10.5 ± 8.7 years. The demographic data of the study are shown in Table 1.

**TABLE 1. Demographics of the Patients**

| *Variables* | *Results* |
|---|---|
| Age, yr | |
| Mean ± standard deviation | 44.1 ± 9.6 |
| Range | 27–66 |
| Sex, n (%) | |
| Female | 48 (100) |
| Male | 0 (0) |
| Duration of melasma, yr | |
| Mean ± standard deviation | 10.5 ± 8.7 |
| Range | 2–20 |
| Skin type, n (%) | |
| Type III | 27 (56.3) |
| Type IV | 21 (43.7) |
| Occupation, n (%) | |
| Working | 28 (58.3) |
| Not working | 20 (41.7) |
| Marital status, n (%) | |
| Married | 42 (87.5) |
| Unmarried | 6 (12.5) |
| Family history, n (%) | |
| Positive | 6 (12.5) |
| Negative | 42 (87.5) |
| Subtype of melasma by Wood light, n (%) | |
| Epidermal | 11 (22.9) |
| Dermal | 8 (16.7) |
| Mixed | 29 (60.4) |

### *Modified Melasma Area and Severity Index Assessment*

The mean mMASI score decreased significantly at 2 months after the final treatment, compared with the baseline value (16.5 ± 8.2 vs 11.5 ± 7.0; $p = .002$), indicating a 30.5% reduction in the mMASI score. The patients with epidermal type of melasma showed significant improvement in the mMASI score, as compared to the patients with the dermal type of melasma ($p < .001$); however, no significant difference in the mMASI improvement rate was observed between the patients with the epidermal and mixed type of melasma ($p = .148$) (Table 2).

Assessments according to the quartile grading scale indicated that 41.7% of the patients showed 51% to 75% (Grade 3) improvement, whereas 31.3% of the patients showed 26% to 50% (Grade 2) improvement (Table 3).

The clinical efficacy of the laser treatments has been demonstrated in Figures 1–3, which indicate the changes in melasma before and after the treatment.

Moreover, the patients received additional advantages, including brighter skin tone and homogenous pigmentation.

### *Patient Self-Assessment*

At the end of the study period, 5 patients (10.4%) rated their improvement as excellent, whereas most of the patients rated their improvement as either good or fair (34, 70.8%). None of the patients reported worsening of the melasma (Table 4).

### *Safety Assessment*

The minor side effects experienced by patients included mild erythema and a heating sensation, which developed within 1 day. Most of the patients developed microcrust over the treatment lesions, which spontaneously peeled off within 1 week without any dyspigmentation or scars. Moreover, 1 patient

**TABLE 2. Mean of Improvement Percentage of mMASI Score According to the Type of Melasma Determined by Wood Light**

| *Type of Melasma by Wood Light* | *Change in mMASI From Baseline to 8 wk Follow-up After Last Treatment* | *Mean Improvement Percentage (%)* | *p* |
|---|---|---|---|
| Epidermal | −8.1 ± 8.1 | 42.7 ± 16.4 | |
| Dermal | −3.6 ± 1.2 | 16.5 ± 5.3 | <.001* |
| Mixed | −4.7 ± 3.5 | 32.5 ± 17.0 | .148 |

All values are mean ± standard deviation.
*$p$ values < .05 considered statistically significant.
mMASI, modified melasma area and severity index.

reported postinflammatory hyperpigmentation, but this had improved by the 2-month follow-up.

## Discussion

Melasma is a cutaneous pigmentary disorder that is commonly diagnosed in middle-aged women. It is a relatively common cosmetic concern among Asians and has a negative impact on a patient's quality of life. Treatments of melasma are costly, time consuming, and challenging because of the recurrent and refractory nature of the disease. Although various treatment options for melasma have been introduced, no specific satisfactory treatment modality has been established. However, IPL and Q-switched Nd:YAG are the 2 most frequently used treatment options for melasma. Indeed, IPL emits a broad-spectrum of light, ranging from 500 nm to 1,200 nm, with a long pulse width (in milliseconds). Because IPL emits a broad spectrum of wavelengths, the light can be absorbed by more than one chromophore, including melanin, oxyhemoglobin, and water; hence, it was expected to show efficacy to the different kinds of dermatologic fields. However, its efficacy is limited to epidermal pigmentary or vascular lesions, and it frequently shows unsatisfactory treatment results for melasma.[11] The 1,064-nm, Q-switched, Nd:YAG laser has been recently adapted for the treatment of melasma, with a short pulse width (in nanoseconds). The use of this laser at a low dose (under the threshold), with a short pulse width (in nanoseconds), yields substantial and long-term effects for melasma treatment.[12,13] However, as a low fluence level of laser treatment with a high number of repetitions is required to achieve a satisfactory outcome; the patients need to visit the clinic regularly for long periods, which may be a burden for some patients. Moreover, undesirable dyspigmentation, such as confetti-like hypopigmentation, can also occur.[14,15]

**TABLE 3. Percent Improvement Rate at the End of Laser Treatment**

| *Quartile Grading Scale* | *n (%)* |
|---|---|
| 76%–100% (Grade 4) | 2 (4.1) |
| 51%–75% (Grade 3) | 20 (41.7) |
| 26%–50% (Grade 2) | 15 (31.3) |
| 0%–25% or darker (Grade 1) | 11 (22.9) |

Pigment-specific, long-pulsed lasers, with pulse widths of microseconds to milliseconds, have been recently found to be effective for treating epidermal pigmentary lesions. A long-pulsed alexandrite laser, with a setting of 35 to 50 J/cm$^2$, spot size of 7 mm, and a pulse width of 5 milliseconds, was effective for the treatment of solar lentigines in patients with Fitzpatrick skin Types II to IV.[16] A prospective split-face study that compared the efficacy and adverse effects between Q-switched alexandrite laser with a 50-nanosecond pulse width and a long-pulsed alexandrite laser with a 100-μs pulse width indicated that the long-pulsed alexandrite laser achieved effective clinical results, equivalent to the Q-switched alexandrite laser, for the treatment of freckles and lentigines, and it is associated with a lower risk for adverse effects in patients with darker skin types.[17]

The Q-switched laser, which delivers high energy with a short pulse width, causes not only photothermal effect but also photomechanical effect.[18] Photomechanical effects can be transmitted to the


**Figure 1.** Standard and ultraviolet light photography of a 44-year-old woman (quartile grading scale grade, 4). (A and B) Image at baseline showing mottled, "confetti-like" hypopigmented macules with surrounding melasma, with an mMASI score of 20, after multiple low-fluence 1,064-nm Nd:YAG laser treatments at a private clinic. (C and D) Image at 2 months after the final treatment with 1 session with a long-pulsed alexandrite laser showing a decrease in hypopigmented macules and surrounding hyperpigmentation, along with improved homogeneity, with a mMASI score of 6 and improvement rate of 70.0%.

oxyhemoglobin and melanin of the normal skin around the lesion, which leads to vessel inflammation and the activation of normal melanocytes, resulting in an increased risk of postinflammtoary hyperpigmentation. On the other hand, long-pulsed laser seems to have a more gentle heating effect than Q-switched laser, resulting in an overall whitening effect. Although there is a possibility of scarring in the surrounding tissue, the energy transmitted within the long pulse duration primarily acts on melanosome-containing keratinocytes on the epidermis and has an effect on the epidermal pigmentation.[19] Therefore, by decreasing the exposure energy to a level that would not cause epidermal injury, the long-pulsed laser is effective for epidermal pigmentation through a purely photothermal effect.

The current findings indicated that the mean mMASI score decreased significantly at 2 months after the final treatment, from 16.5 ± 8.2 to 11.5 ± 7, indicating a 30.5% reduction; this rate is not lower than that reported in 23 Korean patients with melasma (19 with


**Figure 2.** Standard and ultraviolet light photography of a 48-year-old woman (quartile grading scale grade, 3). (A and B) Patient at baseline, with an mMASI score of 9. (C and D) Patient at 2 months after the final treatment, with an mMASI score of 4 and improvement rate of 55.6% (arrows); improvement in skin texture is also noticed.

mixed and 4 with epidermal type of melasma) who underwent 10 treatments with Q-switched Nd:YAG.[20]

The authors attribute the effectiveness of the long-pulsed alexandrite laser for treating melasma to the fractional hand piece that is used in the present study. A 755-nm, long-pulsed, alexandrite laser, which is capable of deep penetration, has a strong absorbency in melanin and hence an effect on melanin-containing cells. However, due to the risk of scarring, the use of high energy is limited. To overcome this limit, a fractional hand piece that transfers energy through a dot method was introduced. A lens array is applied in the fractional tip to obtain 130 dots, 400-μm size in a 15-mm spot and to reduce the area to which energy is transferred to 10% of the entire spot. Relatively high energy with a long pulse duration can be used with the application of this fractional hand piece, and this application can be conducted safely even under energy level higher than what is traditionally used.

It is also believed that the rejuvenation effect of the laser may contribute to the positive results. The heat energy delivered with the long pulse duration can stimulate collagen and activate fibroblasts in the dermal layer, thus resulting in collagen regeneration and remodeling.[21] A histologic analysis of 56 Korean


**Figure 3.** Standard and ultraviolet light photography of a 45-year-old woman (quartile grading scale grade, 2). (A and B) Patient at baseline, with an mMASI score of 12. (C and D) Patient at 2 months after the final treatment, with an mMASI score of 6 and improvement rate of 50.0% (arrows); improvement in skin texture is also observed.

patients with melasma indicated that increased vascularity, collagen degeneration, solar elastosis, and basal hyperpigmentation are common characteristics observed in melasma patients.[22] Given these histologic changes, it seems that the additional rejuvenation effect of long-pulsed alexandrite laser can contribute to melasma treatment. It is noted that most patients—even those who did not show mMASI improvement in the present study—experienced favorable changes in skin texture and color of the laser site. As the dermal temperature increases, the rejuvenation effect increases. As the fluence is higher and spot size is larger, the dermal temperature is able to reach a higher level. The smaller spot size of the fractional hand piece may cause more scattering of the laser beam, and consequently, a decreased penetration depth, limiting the actual depth that beam reaches. However, the fractional hand piece enables a further increase in the dermal temperature by allowing the use of a comparatively high fluence. In addition, a dynamic cooling device was not used, enabling further increase in dermal temperature. These additional effects are expected to

**TABLE 4. Patient Self-Assessment of Melasma Improvement**

| *Improvement of Melasma* | *n (%)* |
|---|---|
| Excellent | 5 (10.4) |
| Good | 17 (35.4) |
| Fair | 17 (35.4) |
| Poor | 9 (18.8) |
| Worse | 0 |

be able to elevate temperature to a level that exhibits rejuvenation effect.

In the present study, it is noticed that the dermal type of melasma was more likely to show lower mMASI improvement rates as compared to other types of melasma, thus indicating that the melasma subtype had an effect on the clinical response to treatment when long-pulsed alexandrite lasers are used. This inconsistency in efficacy may be because the long-pulsed alexandrite laser is more likely to target epidermal pigments rather than dermal components. As mentioned above, a decreased penetration depth due to the use of fractional hand piece results in less energy reaching the dermis than with the traditional long-pulsed alexandrite laser, which could result in a decreased treatment effect on dermal type, compared to epidermal melasma.

The discomfort induced by laser treatment should also be considered. During and immediately after the procedure, most patients experienced slight erythema and a mild heating sensation, although these symptoms resolved within 1 day without any dyspigmentation or scar. The lack of downtime of treatment can reduce discomfort and the treatment burden in patients.

In conclusion, a fractional, long-pulsed, 755-nm alexandrite laser was adapted for the treatment of melasma in patients with a Fitzpatrick skin Type III or IV. It is believed that long-pulsed alexandrite laser is effective and has few side effects in the treatment of melasma. However, as the outcome of monotherapy with the long-pulsed alexandrite laser was not completely satisfactory for patients, and because the melasma subtype affected the efficacy of long-pulsed alexandrite laser, a combination with other modalities, such as topical agents and chemical peels, may be needed to optimize the management in unsatisfactory cases. Furthermore, when choosing the long-pulsed alexandrite laser for the treatment of melasma, the melasma subtype should be carefully considered. It is believed that the fractional long-pulsed alexandrite laser can be an additional therapeutic option in the treatment of melasma, and a prospective, split-face, randomized study and long-term safety analysis of this treatment is required to verify our findings.

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