Treatment of Acquired and Small Congenital Melanocytic Nevi With Combined Er:YAG Laser and Long-Pulsed Alexandrite Laser in Asian Skin

Sang Eun Lee, MD, PhD,* Ji Young Choi, MD,† Kyung Tai Hong, MD,† and Kyung Real Lee, MD‡

BACKGROUND There is no gold standard for the treatment of benign melanocytic nevi for cosmetic purposes.

OBJECTIVE To investigate the efficacy and safety of combined treatment with the short-pulsed erbium:yttrium–aluminum–garnet (Er:YAG) and long-pulsed alexandrite laser for acquired melanocytic nevi (AMN) and small congenital melanocytic nevi (CMN).

METHODS Fifty-eight AMN and 7 small CMN in 24 Korean patients were treated with Er:YAG laser followed by long-pulsed alexandrite laser at 1-month intervals.

RESULTS At 8 weeks after the final treatment, all treated nevi showed complete removal of pigmentation, and the mean overall improvement score assessed by physicians, with a quartile grading scale, was 3.6 ± 0.7. The mean number of treatment sessions required to treat CMN (1.5 ± 0.3) was significantly greater than that for junctional (1.1 ± 0.2) or compound (1.2 ± 0.5) AMN. Postinflammatory hyperpigmentation (4.6%), erythema (9.2%), hypertrophic scars (1.5%), and mild atrophic scars (10.8%) were observed, but all resolved within 6 months, except for hypertrophic scars and 1 atrophic scar. Recurrence of pigmentation was observed in 1 CMN (1.5%) during 6 months of follow-up.

CONCLUSION Combined treatment with Er:YAG laser and long-pulsed alexandrite laser is effective for the removal of small benign melanocytic nevi with minimal adverse effects and low recurrence rates.

The authors have indicated no significant interest with commercial supporters.

Acquired melanocytic nevi (AMN) are common cosmetic concerns in Asians. Excisional biopsy with histological confirmation of any suspicious pigmented lesions with atypical features is the gold standard treatment, especially in white populations. However, the majority of common AMN in nonacral skin of Asians are not premalignant lesions. Small (<1.5 cm) congenital melanocytic nevi (CMN) are also considered benign lesions with low malignant potential. Surgical excision is a well-established conventional option; however, lasers are increasingly used for the treatment of small CMN located in cosmetically sensitive areas.

Until recently, removal of melanocytic nevi has been performed with ablative lasers such as carbon dioxide (CO₂) and erbium:yttrium–aluminum–garnet (Er:YAG) lasers or pigment-specific Q-switched (QS) lasers. CO₂ laser ablation can easily treat AMN but is associated with a high risk for scarring, dyspigmentation, or persistent erythema, especially in patients with dark skin.

Pigment-specific QS lasers including the QS ruby (694 nm), alexandrite (755 nm), and neodymium-doped yttrium aluminum garnet (Nd:YAG) lasers also have been used to treat AMN and CMN but are less effective.
not consistently satisfactory. By selective photothermolysis, QS lasers with a nanosecond pulse width can selectively disrupt individual pigment-containing cells. However, histologically, melanocytic nevi are comprised both isolated and nests of nevomelanocytes.10–12 Thus, QS mode lasers alone are insufficient to completely remove melanocytic nevi. In addition, QS lasers frequently cause post-therapy pigmen
tary changes because of perilesional photomechanical damages and direct melanin stimulation in darkskinned individuals.13

In contrast to the QS lasers, pigment lasers with longpulse durations (microsecond to millisecond) allow less spatially selective but more gentle heating of target chromophores. Therefore, they can treat superficial pigmented lesions including lentigines, seborrheic keratoses, and Becker nevus with fewer unwanted pigmen
tary changes.14–16 Theoretically, long-pulsed pigment lasers may be more effective than QS mode lasers for the treatment of melanocytic nevi because they target individual cells and the clusters of nevus cells. However, previous reports of long-pulsed alexandrite,17,18 ruby,12 and 532-nm Nd:YAG19 lasers have shown limited efficacy in certain small and flat AMN. Despite long-pulsed laser treatments of AMN with high fluence and multiple pulse stacking, remaining nevus cells have been seen in the deep dermis after histological analysis.12,17 These observations suggest that the achievement of an adequate penetration depth to target the chromophore is also an important factor in melanocytic nevi removal using lasers.

Recent case reports show successful treatment of medium-sized and large-sized CMN with a combination of CO2 lasers and various pigment-specific QS lasers.11 The exposure of deep-seated nevomelanocytes to the pigment-specific laser forms the basis of these combination treatments, along with the additional removal of superficial nevus cells by CO2 laser ablation. However, CO2 laser–associated adverse effects such as scarring also have been reported.11 Because of a greater absorption coefficient for water, Er:YAG laser has a better safety profile than CO2 lasers; however, to the best

of the authors’ knowledge, no reports have cited the use of Er:YAG laser in combination with a long-pulsed pigment laser for benign melanocytic nevi removal.

The aim of this study was to evaluate the effectiveness and safety of combined treatment with Er:YAG laser ablation and long-pulsed alexandrite laser for AMN and small CMN.

Methods

This prospective study was approved by the Institutional Review Board of Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea. Twenty-four Korean patients with a total of 65 clinically benign-appearing melanocytic nevi were enrolled in this study. Before enrollment, all nevi were examined by 2 dermatologists. Using naked eye examination, the authors excluded atypical nevi with a diameter of 6 mm or larger plus one or more atypical features including asymmetry, border irregularity, and color variability. Melanocytic nevi with recent changes were also excluded. All lesions were examined with a dermoscope (Dermlite II Pro HR; 3Gen, San Juan Capistrano, CA), and pigmented nevi showing abnormal dermoscopic findings using a 3-point checklist were excluded.

Fifty-eight melanocytic nevi were chosen and categorized based on the gross morphologic features into junctional (flat or just palpable pigmented lesions) or compound (dome-shaped pigmented lesions) types. Seven CMN did not exceed 1.5 cm in diameter and were categorized as small CMN. Patients with a personal or family history of melanoma, hypertrophic scarring, or keloid formation were excluded. Patients who underwent removal of nevi by various laser therapies within the previous 3 months were also excluded.

All melanocytic nevi were treated with multiple sessions of a combined laser treatment modality, short-pulsed Er:YAG laser and long-pulsed 755-nm alexandrite laser treatment, at 1-month intervals. Topical anesthetics (EMLA cream 5%; AstraZeneca AB, Sodertalje, Sweden) were used 1 hour before laser therapy. All nevi were first treated with Er:YAG laser
(Contour; Sciton Laser Corp., Palo Alto, CA) with a 100-microsecond short-pulse duration, a spot size of 2 mm, and a 25-mm ablation depth without coagulation. At each session, Er:YAG laser was delivered with 1 or 2 passes for flat-pigmented lesions and multiple passes for mammilated or dome-shaped pigmented lesions until even surfaces were formed with wiping the skin between the passes. After Er:YAG ablation, patients were treated with the 755-nm alexandrite laser (Clarity; Lutronic, Goyang, Korea) using pulse durations of 3 milliseconds with a fluence of 30 to 35 J/cm² and a spot size of 5 mm. Preirradiation cooling was not performed to lower the required fluence for effective treatment. The authors performed a 20 milliseconds of postirradiation cooling with a dynamic cooling device to cool the epidermis. Junctional AMN were treated with 1 or 2 stacked pulses, whereas compound AMN and small CMN were treated with 3 to 5 stacked pulses of the alexandrite laser or until the appearance of off-bubbles on the irradiated lesions. The number of treatment sessions was adjusted to the clinical response of each nevus. Treatment was terminated when complete pigment clearance was determined by the investigator. The post-therapy wounds were covered with a hydrocolloid dressing (DuoDerm Extra Thin; ConvaTec, Uxbridge, United Kingdom), which was changed regularly by the patients until complete reepithelialization occurred.

Standardized photographs with a digital camera (Nikon D90, Tokyo, Japan) were taken at the initial visit, before each laser session, and 8 weeks and 6 months after the final treatment. The photographs taken at baseline and 8 weeks after the final treatment were evaluated by independent physicians blinded to the study design. They objectively evaluated clinical responses in terms of pigment clearance, skin texture, and overall appearance. Clinical response was scored using a quartile grading scale as follows: Grade 1 (0%–25%) = minimal to no improvement, Grade 2 (26%–50%) = moderate improvement, Grade 3 (51%–75%) = marked improvement, and Grade 4 (more than 75%) = near total improvement. To evaluate and compare post-therapy healing time in terms of reepithelialization and erythema according to the type of nevus, all patients were examined by physicians at 1, 2, 3, 4, and 8 weeks and 6 months after the final treatment. The occurrence of reepithelialization and the occurrence and duration of adverse effects such as dyspigmentation, persistent erythema, hypertrophic scar, or atrophic scar were recorded at each post-therapy visit.

The mean number of treatment sessions and the overall improvement scores of junctional acquired, compound acquired, and congenital subtypes of melanocytic nevi were compared using Fisher exact test. All analyses were performed using commercial software (version 12.0; SPSS Inc., Chicago, IL). p < .05 were considered statistically significant.

Results

Twenty-four patients (14 women and 10 men; mean age: 32.4 ± 8.9 years; range: 8–63 years; Fitzpatrick skin Types III and IV) with benign melanocytic nevi completed this study.

The authors treated 65 melanocytic nevi, including 58 acquired nevi and 7 CMN. Of 58 AMN, 46 nevi (79.3%) were flat or just palpable pigmented lesions and were categorized as junctional nevi. Twelve nevi (20.7%) were dome-shaped pigmented lesions and were categorized as compound type. All 7 CMN were smaller than 1.5 cm in diameter, thus categorized as small CMN. All melanocytic nevi were relocated on the face and nape. Sixty-five melanocytic nevi underwent a mean of 1.26 ± 0.3 treatment sessions of the combined treatment with Er:YAG and long-pulsed alexandrite laser.

All treated nevi showed clinically complete clearance of pigmentation. The mean improvement score in skin texture and overall appearance by the physician’s global assessment was 3.3 ± 0.6 and 3.6 ± 0.7, respectively, according to a quartile grading scale at 8 weeks after therapy (Table 1; Figures 1–3).

The types of melanocytic nevi did not have any statistically significant effects on the objective
improvement score ($p > .05$; Fisher exact test) (Table 1). The 2 types of AMN did not differ in the number of treatments needed (1.1 $\pm$ 0.2 in the junctional type vs 1.2 $\pm$ 0.5 in the compound/intradermal type). However, the mean number of treatments to clearance was significantly greater in the CMN group (1.5 $\pm$ 0.3) compared with the junctional ($p < .05$; Fisher exact test) or compound AMN ($p < .05$; Fisher exact test) groups (Table 1).

The authors also evaluated the time to reepithelialization and the duration of post-treatment erythema. All patients showed transient crusting and erythema immediately after the treatment. Reepithelialization occurred within 1 week of the treatment in all treated sites. Post-treatment erythema lasted 2 to 3 weeks in 84.6% of the treated melanocytic nevi. In most of the AMN (91.3% of the junctional type and 75% of the compound type), erythema faded within 3 weeks, whereas erythema lasted 3 to 4 weeks in 42.9% of CMN.

The combined laser treatment in this study was well tolerated in all patients and caused no serious adverse effects at the 6-month follow-up (Table 2). At the 8-week follow-up, 3 of the treated nevi (4.6%) (2 junctional and 1 compound AMN) presented post-treatment hyperpigmentation and persistent erythema was reported in 6 of the treated nevi (9.2%) (3 junctional and 2 compound AMN and 1 CMN). At the 6-month follow-up, both post-treatment hyperpigmentation and erythema resolved without any further interventions. One CMN on the nape showed a hypertrophic scar. Mild atrophic

**TABLE 1. Treatment Responses of 65 Benign Melanocytic Nevi After Combined Treatment With Er:YAG Laser and Long-Pulsed Alexandrite Laser According to the Type of Nevus**

<table>
<thead>
<tr>
<th>Type of Nevus</th>
<th>Mean No. Treatment</th>
<th>Pigment Clearance</th>
<th>Skin Texture</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Junctional (n = 46)</td>
<td>1.1 $\pm$ 0.2</td>
<td>4</td>
<td>3.5 $\pm$ 0.6</td>
<td>3.7 $\pm$ 0.4</td>
</tr>
<tr>
<td>Compound (n = 12)</td>
<td>1.2 $\pm$ 0.5</td>
<td>4</td>
<td>3.3 $\pm$ 0.5</td>
<td>3.5 $\pm$ 0.8</td>
</tr>
<tr>
<td>Small congenital (n = 7)</td>
<td>1.5 $\pm$ 0.3</td>
<td>4</td>
<td>3.2 $\pm$ 0.7</td>
<td>3.4 $\pm$ 0.5</td>
</tr>
<tr>
<td>Total (n = 65)</td>
<td>1.2 $\pm$ 0.3</td>
<td>4</td>
<td>3.3 $\pm$ 0.6</td>
<td>3.6 $\pm$ 0.7</td>
</tr>
</tbody>
</table>

Quartile grading scale: Grade 1 = 0% to 25% improvement, Grade 2 = 26% to 50% improvement, Grade 3 = 51% to 75% improvement, and Grade 4 = more than 75% improvement.

Figure 1. Multiple acquired junctional melanocytic nevi in a 52-year-old man (A) and 45-year-old man (C) before treatment and (B and D) 2 months after 1 session of the combined Er:YAG laser and long-pulsed alexandrite laser treatment.
change in skin texture was reported in 7 of the treated nevi (10.8%) (4 junctional and 2 compound AMN and 1 CMN). The hypertrophic scar and 1 atrophic scar that occurred in CMN persisted for the 6-month follow-up period, but the atrophic changes that occurred in 6 AMN were mild and resolved gradually within the 6-month follow-up. None of the treated AMN recurred during follow-up, but 1 CMN was repigmented 6 months after the final treatment.

Discussion

The authors have shown that the combined treatment of Er:YAG laser ablation followed by long-pulsed 755-nm alexandrite laser can effectively remove common AMN and small CMN. More importantly, this study showed that benign melanocytic nevus removal by this combination therapy can be performed safely with minimal post-treatment pigmentary changes, persistent erythema, and other adverse effects such as scarring in Asian patients with Fitzpatrick skin Types III and VI. In addition, the authors observed a low risk for recurrent pigmentation during 6 months of follow-up.

Subgroup analysis indicated that there was no significant difference in the clinical responses assessed by physicians between the types of melanocytic nevi. However, CMN required a significantly higher number of combined treatments than junctional or compound AMN (1.5 ± 0.3 vs 1.1 ± 0.2, p < .05 and 1.5 ± 0.3 vs 1.2 ± 0.5, p < .05; Fisher exact test). This suggests that the type of nevus based on the depth of nevus cells is an important determinant of the number of treatments required for complete removal.

Figure 2. Acquired compound melanocytic nevus on the lower eyelid in a 19-year-old man (A) and on the lateral sidewall of nose in a 38-year-old woman (C) before treatment and (B and D) 2 months after 1 session of the combined Er:YAG laser and long-pulsed alexandrite laser treatment.
There is no gold standard for the treatment of small benign melanocytic nevi for cosmetic purposes. To reduce the side effects from ablative lasers and to overcome the limited efficacy of pigment-specific QS lasers, long-pulsed pigment-specific lasers have been tried to treat acquired nevi and CMN with varying results.\textsuperscript{12,17–19} Reda and colleagues\textsuperscript{17} used the long-pulsed alexandrite laser to treat small melanocytic nevi and achieved moderate to significant lightening of color in 76.92% of treated AMNs; however, there was histologically incomplete removal of nevus cells in the deeper dermal layers. Wang and colleagues\textsuperscript{18} evaluated 100-microsecond pulsed alexandrite laser for AMN, achieving clearance in 92.5% of the treated nevi; however, this study found a recurrence rate of 3.7% and atrophic scarring and hyperpigmentation in 28.3% and 20.8% of treated sites, respectively. Duke and colleagues\textsuperscript{12} reported the efficacy of long-pulsed and QS ruby laser to treat AMN and CMN and found pigment lightening in 32% and 100% of nevi treated with long-pulsed laser alone and both lasers, respectively. Alshami\textsuperscript{19} evaluated the long-pulsed 532-nm Nd:YAG laser for AMN in 350 patients with Fitzpatrick skin Type IV and reported that all nevi were completely removed with a single session. However, 7.1% of patients showed recurrence within 2 to 6 months and 20% and 10% of patients showed hyperpigmentation and scars, respectively.

**Figure 3.** Small congenital melanocytic nevus on the neck in a 16-year-old woman (A) and 11-year-old woman (C) before treatment and (B and D) 2 months after 1 session of the combined Er:YAG laser and long-pulsed alexandrite laser treatment.

**TABLE 2.** Complications and Recurrence Rates of 65 Benign Melanocytic Nevi After Combined Treatment With Er:YAG Laser and Long-Pulsed Alexandrite Laser According to the Type of Nevus

<table>
<thead>
<tr>
<th>Type of Nevus</th>
<th>Hyperpigmentation (%)</th>
<th>Persistent Erythema (%)</th>
<th>Hypertrophic Scar (%)</th>
<th>Atrophic Scar (%)</th>
<th>Recurrence, No. Nevi (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Junctional (n = 46)</td>
<td>2 (4.3)</td>
<td>3 (6.5)</td>
<td>0</td>
<td>4 (8.7)</td>
<td>0</td>
</tr>
<tr>
<td>Compound (n = 12)</td>
<td>1 (8.3)</td>
<td>2 (16.7)</td>
<td>0</td>
<td>2 (16.7)</td>
<td>0</td>
</tr>
<tr>
<td>Small congenital (n = 7)</td>
<td>0</td>
<td>1 (14.3)</td>
<td>1 (14.3)</td>
<td>1 (14.3)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>Total (n = 65)</td>
<td>3 (4.6)</td>
<td>6 (9.2)</td>
<td>1 (1.5)</td>
<td>7 (10.8)</td>
<td>1 (1.5)</td>
</tr>
</tbody>
</table>

100-microsecond pulsed alexandrite laser for AMN, achieving clearance in 92.5% of the treated nevi; 6 months and 20% and 10% of patients showed hyperpigmentation and scars, respectively.
To the best of the authors’ knowledge, this is the first published study reporting the use of Er:YAG laser followed by long-pulsed alexandrite laser for the treatment of acquired nevi and CMN. The authors found clinically complete removal of pigment in all the 65 treated nevi, with all nevi having greater than 50% improvement in skin texture and overall appearance assessed by physicians. The authors observed a low recurrence rate of 1.5% over 6 months of follow-up.

Previous works suggest that long-pulsed pigment-specific laser monotherapy may be insufficient for complete removal of melanocytic nevi, clinically and histologically.\(^{12,17}\) The results suggest that the partial ablation of the epidermis by Er:YAG laser before treatment with long-pulsed alexandrite laser has a beneficial effect leading to complete clearance and low recurrence of melanocytic nevi. The clinical improvement achieved in this study may be explained as follows. First, the epidermal ablation by Er:YAG laser may shorten the distance between target chromophores and the light source and reduce the scattering of the laser beam by decreasing the surface reflectance. This enables deeper penetration of the long-pulsed alexandrite laser than would be possible with alexandrite laser alone. Second, the removal of competing epidermal melanin by Er:YAG laser ablation may also promote the penetration of alexandrite laser radiation, resulting in more efficient delivery of photons to the deep dermal components of the nevi.\(^{20}\) The greater penetration depth could result in the destruction of nevomelanocytes located in the deeper dermis.

In addition, it is important to note that this combined laser treatment was associated with a low occurrence of adverse effects such as hyperpigmentation and scarring in patients with Fitzpatrick skin Type III to IV. In theory, epidermal ablation before long-pulsed alexandrite laser enhances photon delivery; therefore, this combined treatment may require lower fluence of the long-pulsed alexandrite laser as compared to the use of laser alone. The lower fluence may reduce the risk for nonselective damage surrounding the target, minimizing adverse effects. Previous studies examining the efficacy of the long-pulsed alexandrite laser for treating superficial pigmented lesions and melanocytic nevi have applied fluences above 35 J/cm\(^2\) (range, 35–50 J/cm\(^2\)) at a 3-millisecond pulse width.\(^{14,16,17}\) Whereas, with the Er:YAG laser pretreatment, the authors observed complete removal of melanocytic nevi by long-pulsed alexandrite laser at fluences below 35 J/cm\(^2\) (range, 30–35 J/cm\(^2\)) with the same pulse width of 3 milliseconds. These findings support the lower risk for posttherapy complications in this study.

The use of combined CO\(_2\) and QS pigment-specific lasers has been proven to be effective in the treatment of CMN.\(^{11}\) However, CO\(_2\) laser may cause scarring, hyperpigmentation, or persistent erythema. Therefore, the authors used Er:YAG laser with a 100-microsecond-pulse-width/forepidermalablationinourn combination treatment. Erbium:yttrium–aluminum–garnet laser can ablate tissue with a small penetration, predictable depth, and minimal thermal damage, enabling fine and controlled superficial ablation with minimal scarring. In addition, the lack of thermal damage to subjacent structures may provide a short downtime. In this study, all treated nevi showed a short healing time with reepithelialization within 1 week and a relatively short duration of post-treatment erythema (84.6%) that lasted 2 to 3 weeks. This is favorable when compared with previous studies reporting that the average duration of post-laser erythema was 4.5 weeks after single-pass CO\(_2\) laser treatment and 3.6 weeks after long-pulsed Er:YAG laser treatment.\(^{21}\) From these findings, the authors suggest that short-pulsed Er:YAG laser and long-pulsed pigment-specific laser are an ideal combination for benign melanocytic nevi removal. This combined laser treatment is effective than pigment lasers alone and have less downtime and a lower risk for complications than the combined CO\(_2\) and pigment-specific laser treatment.

Although the development of laser technology provides diverse approaches for the treatment of melanocytic nevi, the use of lasers for the treatment of congenital and AMN is still a controversial issue. The main concern is that the effect of laser irradiation on nevomelanocytes may cause malignant transformation because the long-term effects of laser-induced thermal damage on melanocytes are still unclear. However,
various studies suggested a different hypothesis that removing the bulk of nevomelanocytes by laser may reduce the risk for malignant transformation of nevi. Therefore, laser treatment of melanocytic nevi should only be considered for benign lesions, and cautious follow-up is necessary.

Limitation of this study is the lack of histopathologic examination of the melanocytic nevi before and after the laser treatment to confirm the hypothesis that the combined treatment of both short-pulsed Er:YAG laser and long-pulsed pigment-specific laser might lead to enhanced destruction of deeper nevus cells. Another limitation is a short follow-up up to 9 months after laser therapy. Further studies with extended follow-up are needed to determine the long-term efficacy of this combined laser treatment on removal of melanocytic nevi.

In summary, this is the first prospective study showing that the combined treatment with Er:YAG laser and long-pulsed alexandrite laser is effective and safe in removing benign melanocytic nevi in patients with darker skin types. Long-pulsed pigment-specific lasers enable the effective destruction of nevus cells and their clusters, with the minimal disadvantage of QS mode-associated photomechanical damages. With Er:YAG laser, an adequate penetration of pigment-specific laser beam to the depth of the target nevus cells can be achieved by enhanced photodelivery without complications related to CO₂ laser ablation. The authors therefore propose that this combination laser treatment can be considered as an effective and safe therapeutic method for the removal of AMN and small CMN.

References


Address correspondence and reprint requests to: Kyung

© 2015 by the American Society for Dermatologic Surgery, Inc. Published by Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.
Real Lee, MD, Human Dermatology Clinic, Korea
Dermatology Research Institute, Bundang-Gu, Seongnam-si,
Gyeonggi-do 463–828, Korea, or e-mail:
teamdoctor78@naver.com