A Treatment of Medium-to-Giant Congenital Melanocytic Nevi with Combined Er:YAG Laser and Long-Pulsed Alexandrite Laser

Kyung Tae Hong1
Jung Min Lim2
Sang Eun Lee2

1Yonsei Modern Skin Clinic, Seoul, Korea
2Department of Dermatology, Gangnam Severance Hospital, Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul, Korea

Background and Objectives
Lasers are alternative methods of treatment for congenital melanocytic nevi (CMN) located on cosmetically sensitive or surgically challenging areas. Long-pulsed pigment lasers can show greater efficacy than Q-switched lasers in destroying nevomelanocytic nests, and partial epidermal ablation by Er:YAG lasers allow pigment lasers to penetrate deeper into the skin. In this study, we evaluated the efficacy of combined Er:YAG and long-pulsed alexandrite (LP-Alex) laser treatment for medium to giant CMN.

Materials and Methods
Six patients were enrolled. All nevi were treated with combined Er:YAG and LP-Alex lasers at an interval of 9-12 weeks. Persistent erythema was further treated using long-pulsed dye lasers (LPDL).

Results
All medium CMN showed good-to-excellent pigment removal after 1.83 sessions of combined laser treatment. Giant CMN showed good pigment removal after a single treatment. No severe textural changes, hypertrophic scars, or depigmentation were observed. Moderate hypertrophic scarring was revealed in one patient; mottled hypopigmentation was observed in one patient; and persistent erythema was noted in two patients, which decreased with further LPDL treatment. Repigmentation or malignant transformation was not observed during the follow-up period of 2-9 months.

Conclusion
Combined Er:YAG and LP-Alex laser treatment appears to be effective for removing medium-to-giant CMN with minimal adverse effects.

Key words
Congenital melanocytic nevi; Er:YAG Laser; Long-pulsed Alexandrite Laser
INTRODUCTION

Congenital melanocytic nevi (CMN) occur in approximately 1-3% of newborns. Treatment is often required to achieve better cosmetic appearances or to reduce the potential risk of malignant transformation, and surgical excision is currently recommended as a treatment of choice. However, some CMN are located on the cosmetically sensitive areas and raise the concerns about postoperative scars or deformities. Also, large CMN are difficult to remove in total, as nevomelanocytes may be located in deeper structures.

Lasers have been used to treat CMN as a partial thickness removal strategy, which may reduce the risk of malignant transformation without surgery-related complications. Q-switched (QS) mode pigment-specific lasers, including ruby (694 nm), alexandrite (755 nm), and Nd:YAG (1,064 nm), and ablative lasers, such as CO2 and Er:YAG, have been used to treat CMN, alone or in combination with each other. Clinical results have been variable, partly due to the deep dermal involvement of nevomelanocytes. Histological analyses have demonstrated the persistence of nevus cells in the dermis after various laser treatments, leaving the possibility of recurrence. In order to solve this problem, many studies have utilized ruby lasers in various combinations of different modes, including normal mode, QS mode, and long-pulsed mode. Some of these studies reported good results, although multiple treatment sessions were required.

Partial epidermal ablation prior to pigment-specific laser treatment may increase the efficacy of dermal pigment removal by eliminating epidermal melanin and the upper epidermis itself, which act as competitive chromophores. We have previously applied this concept of combined laser treatment with Er:YAG laser and long-pulsed alexandrite (LP-Alex) laser to the treatment of acquired and small CMN. The aim of this study was to investigate the efficacy and safety of this combined laser treatment with Er:YAG laser and LP-Alex laser for medium to giant CMN.

MATERIALS AND METHODS

Six Korean patients with medium to giant CMN were enrolled, and a total of seven lesions were selected for the treatment (Table 1). All patients underwent sequential treatment combining Er:YAG and LP-Alex lasers at 9-12 week intervals. Informed consent was obtained from each participant or their parents, if they were 18 years or less. This study was approved by the Institutional Review Board of Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea.

To establish the optimal LP-Alex laser parameters, we first compared the efficacy and safety of combined laser treatment using multiple different LP-Alex pulse widths as a pilot study. A single session test treatment was performed using pulse widths of 500 μs, 3 ms, 5 ms, and 10 ms on each quadrant of a designated portion of the lesion in patient 1. Other parameters including fluence and spot size of LP-Alex laser were not changed.

Combined laser treatment was performed according to the following protocol. First, Er:YAG laser was applied (Action II; Lutronic, Goyang, South Korea) to partially ablate the epidermis (spot size 4 mm, pulse width 250 μs, energy density 5 J/cm², 1 or 2 passes). Then, LP-Alex laser was applied (Clarity; Lutronic) to eliminate the remaining nevomelanocytic nests (spot size 5 mm, energy density 30-50 J/cm², single or multiple passes). Cooling was done by the intelligent cooling device (ICD), set to 20 ms post-pulse and no pre- or inter-pulse cooling. For the giant CMN in patient 1, a test treatment was performed

Table 1. Clinical data and results of combined laser treatment

| No. | Sex/Age | Size (cm) | Location | Number of treatments | Further treatments | Results (score on 5-point scale) | Complications |
|-----|---------|-----------|----------|----------------------|-------------------|-------------------------------|---------------|
| 1   | M/21    | 32 × 28   | Rt. Lower leg | 1                     | None              | 3                             | None          |
| 2   | M/22    | 2 × 1.5   | Rt. Arm    | 1                     | None              | 5                             | Mild erythema |
| 3   | F/12    | 4 × 2     | Lt. Upper arm | 1                     | LPDL*, 3 sessions  | 4                             | Moderate erythema |
|     |         |           |           |                      |                   |                               | Mild textural change |
| 4   | F/17    | 4 × 3     | Neck      | 5                     | None              | 4                             | Moderate hypertrophic scarring |
| 5   | F/21    | 9 × 8     | Rt. Calf  | 2                     | LPDL*, 5 sessions | 5                             | Moderate erythema |
|     |         |           |           |                      |                   |                               | Mottled hypopigmentation |
| 6   | F/1     | 2 × 1.5   | Rt. Temple | 1                     | None              | 2                             | None          |
|     |         | 1.5 × 1   | Rt. Cheek | 1                     | None              | 2                             | None          |

*LPDL, Long-pulsed dye laser.
first, and the results were assessed at 6-8 weeks before confirming the parameters used to treat the whole lesion. No post-treatment cooling was done. The area was covered with a hydrocolloid dressing (DuoDerm Extra Thin; ConvaTec, Uxbridge, UK), and the patient received frequent dressing changes during the first week after treatment. Topical anesthesia was applied in small lesions and tumescent local anesthesia was performed in large or giant CMN.

If undue erythema persisted in the treated area for 8-12 weeks after treatment, a long-pulsed dye laser (LPDL) (V-Beam; Candela, Wayland, MA, USA) was used (spot size 3 mm, energy density 8 J/cm², pre- and inter-DCD cooling) at 6-week intervals.

Standardized photographs with a digital camera were taken at the initial visit, before each laser session, and 2-9 months after the final treatment. Clinical response was scored using a 5-point scale: grade 1 (lightening of 0-25%) = poor (no change), grade 2 (lightening of 26-50%) = fair (slight improvement), grade 3 (lightening of 51-75%) = good (improvement, enabling differentiation from the surrounding healthy skin), grade 4 (lightening of 76-95%) = excellent (difficulty in differentiating the lesion from the surrounding healthy skin), grade 5 (lightening more than 95%) = clear (near-complete disappearance of the lesion).

RESULTS

The clinical features and results of treatment are summarized in Table 1. Combined Er:YAG/LP-Alex laser treatment of medium sized CMN resulted in an average improvement score of 3.67 (good to excellent). An average of 1.83 sessions was required to make the lesions similar in color to surrounding skin. In most patients, re-epithelialization was completed by the end of the second week after treatment. Severe abnormalities in skin texture or hypertrophic scars were not seen, but moderate scarring was noted after elimination of pigment in one patient. Dyspigmentation was also absent except one patient, who showed focal and mild hypopigmentation in the treated area. Repigmentation was not observed during the 2-9 months of follow up. Persistent moderate erythema was observed in two patients, but improved after 3-5 sessions of LPDL treatment.

Patient 1

Patient 1 was a 21-year-old male with a giant CMN involving most of his lower right leg (Fig. 1, 2). First, we first compared the efficacy and safety of combined Er:YAG/LP-Alex laser treatment using multiple different LP-Alex pulse widths of 500 μs, 3 ms, 5 ms, and 10 ms, on each quadrant of a designated portion of the lesion (Fig. 1). A single session of treatment was performed, while keeping the other parameters of LP-Alex laser unchanged (spot size 5 mm, fluence 40 J/cm²). 15 days after treatment, the areas treated with 500 μs and 3 ms were completely re-epithelialized, while the areas treated with 5 ms and 10 ms were not (Fig. 1C). 8 weeks after treatment, the area treated with 3 ms showed excellent removal of pigmentation compared to the area treated with 10 ms, and the area treated with 5ms showed incomplete re-epithelialization with possible scarring (Fig. 1D). This result suggests that the optimal pulse width of LP-Alex is 3 ms, which shows effective pigment removal and minimal downtime.

Next, we performed a test treatment on a 3 x 3 cm area located at the lower medial part of the lesion. Hair was shaved before treatment to prevent potential burns (Fig. 2E). After a single session of Er:YAG/LP-Alex laser treatment (spot size 5 mm, pulse width 3 ms, fluence 40 J/cm² for LP-Alex), immediate and near complete removal...
of pigmentation was observed (Fig. 2F). 8 weeks later, the treated area remained clear with no textural abnormalities or repigmentation (Fig. 2G). Then, a larger area was treated using the same parameters (Fig. 2H). 15 weeks after a single session, pigmentation was significantly reduced, showing good lightening (51-75%) of the treated area. Areas relatively lighter in color before treatment achieved an appearance similar to the surrounding skin (Fig. 2I).

Patient 2

Patient 2 was a 22-year-old male with two small (0.5 × 0.5 cm) and one medium-sized (2.0 × 1.5 cm) CMN on his right arm (Fig. 3A). The two small lesions were treated with LP-Alex only, and the medium-sized lesion was treated with combined Er:YAG/LP-Alex laser treatment (spot size 5 mm, pulse width 3 ms, fluence 45 J/cm² for LP-Alex). Near complete clearance of pigmentation was observed after a single session of treatment. No repigmentation or textural changes occurred, but mild erythema persisted 7 months after treatment (Fig. 3B).

Patient 3

Patient 3 was a 12-year-old girl with a medium-sized (4 × 2 cm) CMN on her upper left arm. She previously received 2 laser treatments elsewhere (laser type unknown).
but the lesion had recurred (Fig. 4A). Pigmentation was significantly cleared after a single session of Er:YAG/LP-Alex laser treatment (spot size 5 mm, pulse width 3 ms, fluence 40 J/cm² for LP-Alex), but a moderate degree of erythema and mild textural change remained 4 weeks after treatment (Fig. 4B). To eliminate the remaining erythema, 3 sessions of LPDL treatment were performed at 6-week intervals. The erythema faded 3 weeks after the final LPDL treatment without repigmentation (Fig. 4C).

**Patient 4**

Patient 4 was a 17-year-old girl with a medium-sized
Patient 4 was a 17-year-old girl with a medium CMN on her anterior neck, which was previously treated with CO2 laser leaving remnant pigment and scarring (A). Excellent pigment removal was seen after 5 sessions of treatment, despite revealing moderate hypertrophic scarring (B).

Patient 5 was a 21-year-old female with medium-sized (9 × 8 cm) CMN on her right calf (Fig. 6A). She had received more than 10 sessions of Er:YAG laser treatment elsewhere, which was not effective. Near complete clearance of pigmentation was observed after two sessions of combined Er:YAG/LP-Alex laser treatment (spot size 5 mm, pulse width 3 ms, fluence 50 J/cm² for LP-Alex). Persistent erythema remained, but responded well to 5 sessions of LPDL treatment at 6-week intervals. No obvious repigmentation or textural changes were seen 9 months after the final treatment, but mottled hypopigmentation was observed (Fig. 6B).

Patient 6 was a 1-year-old girl with a giant CMN involving most of her lower right leg. Previous treatments with staged excisions were unsuccessful with scarring, so we deferred treatment of that lesion. She also had two medium-sized CMN on her right temple and cheek (Fig. 7A, 7C). One session of Er:YAG/LP-Alex laser treatment
[spot size 5 mm, pulse width 3 ms, fluence 30 J/cm² for LP-Alex] was performed for each lesion. 2 months after treatment, pigment removal was incomplete, but central clearance of pigmentation was observed (Fig. 7B, 7D).

**DISCUSSION**

To date, no gold standard exists for the treatment of CMN, particularly in medium sized to giant lesions. Lasers can be used as an alternative partial-thickness approach to CMN treatment. Numerous pigment-specific and ablative laser systems have been studied, and recent articles suggest that pigment-specific lasers are more efficient. The consensus from the current literature is that long-pulsed pigment-specific lasers with wavelengths of 755 nm and 1,064 nm can offer more efficient destruction of nevi than pigment-specific QS lasers, as longer pulse duration can better target nests of cells rather than individual pigmented cells.5,18

Regarding pigment-specific lasers, a balance between melanin absorption and penetration depth is needed in order to reach deep dermal targets. High melanin absorption limits penetration depth, as with the KTP (532 nm), long-pulsed dye (590 nm), and ruby (694 nm) lasers. Increasing the energy level or number of treatment sessions has the potential of delivering unacceptable epidermal and even dermal damage, causing adverse effects. The QS or normal mode ruby laser may bring clinical improvement, but fails to completely remove nevomelanocytes histologically.5,7 The 1,064 nm Nd:YAG laser offers some absorption in melanin, but water starts to become a chromophore at that wavelength, therefore a wavelength which is better absorbed in melanin than 1064 nm is required to treat CMN, at a long pulse width.

Recently, the LP-Alex (755 nm) laser has shown efficacy in the treatment of superficial pigmented lesions.19,20 However, the major setback of the interaction between the 755 nm wavelength and Asian skin is the preponderance of epidermal melanin in the skin, which acts as a competing chromophore. It therefore is necessary to partially eliminate the epidermis, particularly the highly reflective and refractive stratum corneum and the pigmented stratum granulosum beneath it, prior to LP-Alex treatment, in order to increase the efficacy for destroying dermal components of CMN.

The Er:YAG laser is well-recognized as having the high-

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**Fig. 7.** Patient 6 was a 1-year-old female infant with two medium CMN on the right temporal (A) and zygomatic regions (C). Good removal of pigment is maintained 8 months after a single treatment (B, D).
'est absorption coefficient in water, showing clean ablation of the epidermis by 2-5 μm, leaving minimal residual thermal damage to the dermis. We therefore decided to combine Er:YAG laser with LP-Alex laser for CMN treatment and developed Er:YAG laser parameters to ablate the epidermis partially, thereby creating the area of partial detachment of the epidermis through which LP-Alex laser irradiation can be effectively delivered to the dermal targets. The long pulsed modes of LP-Alex laser can offer effective thermal damage to large nevomelanocytic nests and deep-seated nevus cells. Also, we demonstrated that the optimal pulse width of LP-Alex laser for CMN treatment is 3 ms, in terms of efficacy and short downtime.

The advantages of this concept of combination therapy are as follows: Er:YAG laser would remove most of the epidermal melanin, thereby removing the competing chromophores for the 755 nm energy. The lack of melanin in the epidermis would minimize the possibility of causing photothermal damage, which could lead to postinflammatory hyperpigmentation. Partial epidermal ablation using Er:YAG laser would prevent energy loss, which occurs by reflection from the stratum corneum and refraction by the stratum corneum and underlying epidermal layers. This can maximize the amount and quality of the 755 nm laser energy reaching the dermal target, and thus a lower fluence of LP-Alex is enough to eliminate pigment. The subsequent application of LP-Alex laser through the partially ablated epidermis created above the target can optimize tissue reaction and selectively destroy nevomelanocytic nests and amelanotic dermal melanocytes, by selective photothermolysis and an extended but controlled wave of secondary heat.

Combination laser techniques using nonselective ablative lasers and pigment selective lasers have been used in CMN treatment with varying results. Chong et al. used CO2 and Q-switched Alexandrite (QS-Alex) laser for small to medium CMN and reported good results with little or no scarring or postinflammatory hyperpigmentation. Kim et al. also treated small to medium CMN with CO2 and QS-Alex lasers which showed good reduction in pigmentation, but 67% showed textural changes and about 30% showed dyspigmentation after treatment. Al-Hadithy et al. treated CMN with both ultrapulse CO2 and frequency doubled QS Nd:YAG lasers and reported a good response in 87% of patients and treatment failure in 10%, but hypertrophic scarring and recurrence was observed in 10%. In this study, our laser protocol has shown excellent efficacy for medium-sized CMN treatment, showing more than 75% lightening in all cases after an average of 2.3 sessions. Moderate hypertrophic scarring was seen in one patient. Persistent erythema was observed occasionally but was well controlled with LPDL. No obvious repigmentation was observed during the 2-9 months of follow-up.

Treatment of giant CMN is more challenging than medium-sized lesion and remains problematic because of the very large area covered, the irregular nature of nevomelanocyte distribution and the varying depth of pigment involvement. Previously, treatment of giant CMN has been attempted with QS ruby lasers alone or combination with pulsed dye lasers. QS ruby lasers have shown effectiveness in several studies, but multiple treatment sessions were required. A previous case report of early serial QS ruby laser treatment for an infant with a giant CMN showed excellent results with 11 sessions of treatment. Funayama et al. reported significant pigment removal of giant CMN in six patients using combined pulsed dye laser and QS ruby laser treatment with minimal scarring, but the average number of treatments necessary was 7.7 sessions. Our patient with giant CMN achieved good (51-75%) reduction of pigment after only one session of combined Er:YAG/LP-Alex laser treatment, and no signs of malignant transformation in the treated area were seen in follow-up. Near complete clearance of pigment was achieved in areas relatively lighter in color, but pigmented nevomelanocytic nests might persist in the deeper dermal layers in darker areas, which would require further treatment sessions.

The limitations of this study include the small number of patients, the retrospective study design, and the limited duration of follow-up. Therefore, more clinical data and longer follow-up periods are required to validate the efficacy and safety of this treatment modality.

In conclusion, the sequential combination of Er:YAG laser and LP-Alex laser can produce good to excellent pigment removal in medium-sized and giant CMN with minimal risk of scarring and repigmentation. Giant CMN must be treated in sections rather than trying to treat the entire area with our protocol. Although combined Er:YAG/LP-Alex laser treatment cannot assure complete destruction of nevomelanocytic nests histologically, it may be a novel approach for treating CMN which cannot be surgically excised.

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Combined Er:YAG & LP-Alex for Medium to Giant CMN
Kyung Tae Hong, et al.

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