

Long-term outcomes of laser treatment for congenital melanocytic nevi



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Background: Although various laser treatments have been tried for congenital melanocytic nevi (CMNs), only small retrospective studies with short-term follow-up had been done to assess outcomes.

Objective: We analyzed the long-term outcomes of laser treatment for CMN and compared these outcomes with those of a combination treatment including partial excision and lasers.

Methods: Patients with CMN treated with lasers were retrospectively reviewed, and patients with >3 years of follow-up were grouped as the long-term follow-up group.

Results: A total of 67 cases of CMN were reviewed. Among 20 patients (20/52, 38.5%) with near total clearance during laser-only treatment, 11 patients were in the long-term follow-up group, and 5 of 11 showed repigmentation. In total, 15 patients showed repigmentation regardless of clearance, and the mean period until repigmentation was 3.93 years from the initial treatment. Patients with partial excision and laser combination treatment showed higher Investigator's Global Assessment scores, fewer laser treatments, and shorter treatment periods compared with patients with laser-only treatment.

Limitations: This is a retrospective study, and various laser devices were used.

Conclusion: More than 4 years of follow-up is required to evaluate the efficacy of lasers in CMN, and partial excision and laser combination treatment might be an effective treatment option. (J Am Acad Dermatol 2019;80:523-31.)

Key words: congenital melanocytic nevi; laser treatment; partial excision; repigmentation.

Congenital melanocytic nevi (CMNs) are nevi that present at birth or develop within the first few weeks of life; they occur in 1%-2% of the population. CMNs are known to have no pathologic complications other than an increased risk for melanoma, which is mainly associated with giant CMNs of diameters ≥ 20 cm or with multiple small CMNs.¹ However, CMNs might have a greater impact on quality of life due to their effect on cosmetic appearance; patients often want their removal. For

Abbreviations used:

CMN:	Congenital melanocytic nevus
IGA:	Investigator's Global Assessment
YAG:	yttrium aluminum garnet
Er:YAG:	erbium-doped yttrium aluminum garnet

complete removal, staged excision is the current treatment of choice. However, surgical removal is not always possible; in some cases, their removal might

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Funding sources: Basic Science Research Program, National Research Foundation of Korea, supported by the Ministry of Science, ICT and Future Planning (2017R1C1B2005574).

Conflicts of interest: None disclosed.

Accepted for publication August 3, 2018.

Reprints not available from the authors.

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Published online September 15, 2018.

0190-9622/\$36.00

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<https://doi.org/10.1016/j.jaad.2018.08.046>

leave evident scarring due to location and size. For patients with these CMNs, various treatment options have been tried, such as chemical peels, dermabrasion and lasers.² Laser treatment is divided into 2 groups (ablative laser and pigment-specific laser), and the combination of these 2 is the ideal treatment option for CMN.³⁻⁵ Even though laser treatment for CMN removal has been widely used, there is no well-planned prospective study on this treatment—only small retrospective studies with short-term follow-up periods.^{6,7} In theory, repigmentation is possible because excessive melanocytes can remain after the laser treatment and several cases of repigmentation had been reported.^{8,9} This retrospective study with long-term follow-up was designed to determine the recurrence rate and period until repigmentation after laser treatment of CMNs. For some patients, combination treatment of partial excision followed by laser treatment was performed. We also analyzed the general outcomes of this combination method compared with laser-only treatment.

METHOD

Patient selection

We enrolled 67 patients with CMNs treated by laser in 2 different hospitals (Severance Hospital, Seoul, Korea, and Gangnam Severance Hospital, Seoul, Korea) by 2 dermatologists (Drs Chung and Roh) during 2000-2017 who had ≥ 1 year of follow-up. Fifty-two patients were treated by laser only, and 15 patients were treated by a combination of partial excisions followed by laser. Retrospective review of medical records and digital photographs was done for all patients. Patients with >1 year of follow-up were classified as the midterm follow-up group and those with >3 years of follow-up as the long-term follow-up group.

Laser treatment

Before treatment, informed consent was obtained from the patient after sufficient consultation had occurred about the risks and benefits of the treatment. Pigmentation laser treatment with or without ablative laser treatments was done as combination therapy. The use of single or combination therapy was decided on by the dermatologist on the day of treatment, depending on the gross visible

pigmentation depth or the patient's preference regarding managing exudative fluids after treatment. When combination laser treatment was chosen, ablative laser treatment was performed, followed by pigment-specific laser treatment on the same day. A 1064-nm Q-switched neodymium-doped yttrium aluminum garnet (YAG) laser (Spectra VRM,

Lutronic, Korea, 3–5-mm spot size, 5–10-Hz frequency, 5–8-J power) was used for pigment-specific laser treatment. A fractional CO₂ laser (eCO₂, Lutronic, Korea, 120- μ m beam size, peak power of 30 W, 50–120-mJ pulse energy, 200 spots/cm² spot density) and erbium-doped YAG (Er:YAG) laser (SP Dynamics, Fotona, Slovenia, R11, SP mode, 3-mm spot size, 10-15 J/cm², 1-2 pass for ablation depth of 50-

100 μ m) were used for ablative laser treatment during the first step of the combination treatment. The fractional CO₂ laser was used to treat patients with minimal residual pigmentation combined with texture irregularity, and the Er:YAG laser was used to treat patients with more residual pigmentation and nevi requiring deeper ablation. Attempts were made to perform treatments monthly, but many treatments were delayed due to patient availability; the average treatment interval was 3 months apart. The same laser devices and laser treatment methods were applied for patients who underwent the combination treatment of partial excisions followed by laser treatments.

Clinical evaluation and outcome measurement

The electronic medical records were used to review information on initial nevus size, color, location, number of treatments, and follow-up period. Clinical photographs were taken with a digital camera before each treatment. The photographs taken before the first treatment and after the final treatment were reviewed by 3 different reviewers (1 dermatologist, 1 dermatologic trainee, and 1 nondermatologist medical doctor) without any patient information. Clinical outcomes were measured by using the Investigator's Global Assessment (IGA) score on a 7-point scale of improvement as follows: 1 for worsened, 2 for no change, 3 for minor (1%-25%), 4 for moderate (26%-50%), 5 for marked (51%-90%), 6 for near total (91%-99%), and 7 for total improvement (100%)

CAPSULE SUMMARY

- Various lasers have been applied for removal of surgically challenging congenital melanocytic nevi (CMNs).
- We evaluated the efficacy of lasers on CMN with a long-term follow-up period.
- Repigmentation of CMN after laser treatment occurs quite frequently and gradually; therefore, >4 years of follow-up is recommended to evaluate the efficacy of lasers.

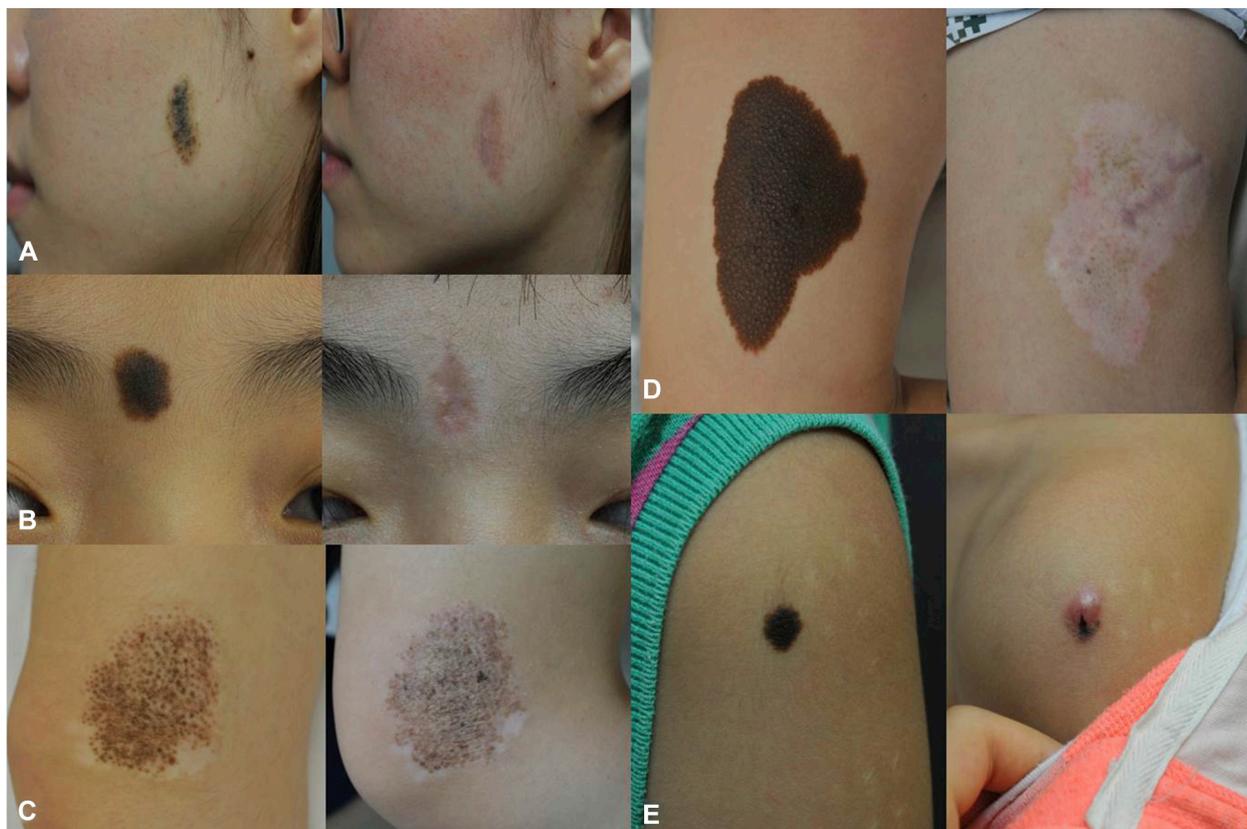


Fig 1. Side effects of laser treatment: erythema (A), depression (B), texture irregularity (C), hypopigmentation (D), and hypertrophic scar (E).

(Supplemental Table I; available at <http://www.jaad.org>). The average IGA score of the 3 reviewers for each patient was used for outcome analysis. The side effects of laser treatment were classified as erythema, hypopigmentation, depression, hypertrophic scar, and texture irregularity (Fig 1), and the existence of each side effect was evaluated in the final clinical photographs. Repigmentation was evaluated by reviewing all the photographs of a patient and was identified when pigment could be seen again at the site where it had been cleared (Fig 2).

Statistical analysis

Data were analyzed with dedicated software (GraphPad Prism version 7.00 for Windows [GraphPad, La Jolla, CA] and SPSS version 18.0 for Windows [IBM Co, Armonk, NY]). Unpaired 2-sample *t* test with Welch correction was used to evaluate differences in outcomes for different CMNs sizes, colors, and treatment methods.

RESULTS

Of the 67 included patients, 52 received laser treatment only and 15 received the combination treatment of partial excision followed by laser

(Fig 3). The mean patient age was 13.42 years, and female (45/67, 67.16%) patients were more predominant than male patients (22/67, 32.84%). CMNs were more frequently located on the face (44/67, 65.67%) than the extremities (18/67, 26.87%) or trunk (5/67, 7.46%), and the mean size of the CMNs was 36.57 cm². The mean follow-up period was 3.40 years.

Of the 52 patients treated by laser only, 23 patients were classified in the long-term follow-up group. Of the 15 patients with combination treatment, 10 patients were classified into the long-term follow-up group. The demographics of the midterm and long-term follow-up groups are shown in Table I. In the long-term follow-up group with laser-only treatment, female (78.3%) patients were more predominant than male (21.7%) patients. In this group, the mean age at first treatment was 13.09 years, and CMNs were mostly located on the face (69.9%) followed by the extremities (21.7%) and trunk (8.7%). Mean size of the CMNs in the laser-only treatment group was 48.49 cm², larger than the mean size of the CMNs (28.23 cm²) treated by combination therapy.

The IGA scores rated by 3 reviewers showed interrater reliability (intraclass correlation coefficient 0.872). In the laser-only treatment group, 20 patients



Fig 2. **A**, Patient at baseline with congenital melanocytic nevus. **B**, Partial clearance observed after 10 sessions of laser treatment. **C**, Repigmentation observed 1 year after clearance.

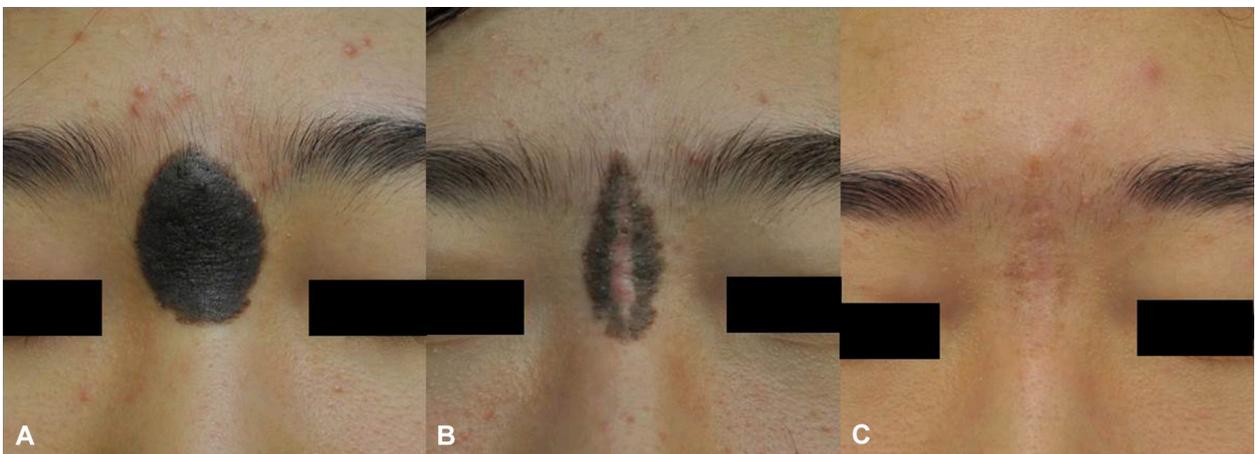


Fig 3. A patient treated by combination of partial excision and laser treatments. Minimal partial excisions were performed and the remaining nevus was treated with laser. Patient at baseline (**A**), after partial excision (**B**), and after 6 sessions of laser treatments (20 months after the excision) (**C**).

(20/52, 38.5%) showed nearly total clearance of pigmentation (IGA score >5) during or after the laser treatment, 11 of which were in the long-term follow-up group. Of the patients in the long-term follow-up group, 5 (5/11, 45.5%) showed repigmentation during follow-up and 6 (6/11, 54.5%) showed a nearly total response or absence of pigment at the final visit. Photographs of these 11 patients with near total to total clearance of pigmentation are shown in [Supplemental Fig 1-11](#) (available at <http://www.jaad.org>).

Regardless of pigment clearance, 15 patients (52/15, 28.8%) showed repigmentation after laser-only treatment, 11 of which were in the long-term follow-up group. The mean period until repigmentation, irrespective of number of treatments, was 3.93 ± 2.58 years from the initial treatment session and 1.59 ± 1.63 years from pigment clearance. The time period to repigmentation is shown in [Fig 4](#). Patient age at first treatment was significantly greater

among patients who showed repigmentation than those who did not show repigmentation (16.45 ± 61.686 vs 10.00 ± 2.128 , $P = .0274$, [Fig 5](#)).

When analyzed according to CMN size, the IGA score recorded at the last visit was significantly lower among larger CMNs than smaller CMNs ([Fig 6, A](#)). Generally, brown CMNs showed less favorable outcomes than black CMNs. However, the difference was not statistically significant ([Fig 6, B](#)). In the laser-only treatment group, treatment period was negatively correlated with final IGA score ($P = .0362$, [Fig 6, C](#)).

When comparing laser-only and combination treatments, the mean final IGA scores for the laser-only treatment group and combination treatment group was 4.47 and 5.51, respectively. In the long-term follow-up group, the final IGA scores were 4.73 and 5.53 for the laser-only and combination treatment groups, respectively. The difference in the final IGA score between laser-only and combination

Table I. Baseline patient demographics and outcomes

Category	Laser-only treatment group		Excision and laser combination group	
	Midterm,* N = 52	Long-term,† N = 23	Midterm,* N = 15	Long-term,† N = 10
Patient age, y, mean (range)	13.29 (1-49)	13.09 (3-29)	12.47 (3-28)	11.1 (3-28)
Patient sex				
Male	15 (28.8)	5 (21.7)	7 (46.7)	5 (0.5)
Female	37 (71.2)	18 (78.3)	8 (53.3)	5 (0.5)
Nevus location				
Face	35 (67.3)	16 (69.6)	9 (60.0)	8 (80.0)
Trunk	4 (7.7)	2 (8.7)	1 (6.7)	1 (10.0)
Extremity	13 (25.0)	5 (21.7)	5 (33.3)	1 (10.0)
Nevus size, cm ² , mean (range)	41.51 (0.09-600)	48.49 (0.16-600)	19.42 (2-150)	28.23 (2-150)
Nevus color				
Brown component	32 (61.5)	14 (60.9)	7 (46.7)	6 (60.0)
Black component	28 (53.8)	14 (60.9)	13 (86.7)	8 (80.0)
Gray component	6 (11.5)	3 (13.0)	2 (13.3)	1 (10.0)
No. laser treatments, mean (range)	14.20 (2-45)	23.19 (8-45)	6.00 (1-17)	5.27 (1-17)
Total follow-up period, y, mean (SD)	3.45 (2.54)	5.63 (2.38)	3.20 (1.21)	3.65 (1.25)
Outcomes				
Laser treatment side effect, n (%)				
None	18 (34.6)	6 (26.1)	13 (86.7)	9 (90.0)
Erythema	23 (44.2)	10 (43.5)	2 (13.3)	1 (10.0)
Hypopigmentation	11 (21.2)	8 (34.8)		
Depression	6 (11.5)	3 (13.0)	1 (6.7)	1 (10.0)
Hypertrophic scar	4 (7.7)	1 (4.3)		
Irregular texture	9 (17.3)	4 (17.4)		
IGA score, mean (SD)	4.47 (1.17)	4.73 (1.07)	5.51 (0.78)	5.53 (0.85)
Patient score, n (%)				
≤4	16 (30.8)	5 (21.7)	1 (6.7)	1 (10.0)
4 < score ≤ 5	21 (40.4)	10 (43.5)	4 (26.7)	2 (20.0)
5 < score ≤ 7	15 (28.8)	8 (34.8)	8 (66.7)	7 (70.0)
Patients with repigmentation, n (%)	15 (28.8)	11 (47.8)	4 (26.7)	3 (30.0)
Time to repigmentation, y, mean (range)	3.93 (1-10)	4.77 (2-10)	1.50 (0.5-3)	1.83 (0.5-3)

IGA, Investigator's Global Assessment; SD, standard deviation.

*Patients with >1 year of follow-up were classified into the midterm follow-up group.

†Patients with >3 years of follow-up were classified into the long-term follow-up group.

treatment groups was significant (4.732 ± 0.2227 vs 5.534 ± 0.2680 , $P = .0315$). The percentage of patients who showed nearly total clearance of pigmentation on the last visit (final IGA score >5) was much higher in the combination treatment group than the laser-only treatment group (8/15 [66.7%] vs 15/52 [28.8%], [Table I](#)). The number of laser treatments (6.600 ± 1.529 vs 23.10 ± 2.039 , $P < .0001$) and treatment period (3.650 ± 0.3948 years vs 5.630 ± 0.5081 years, $P = .0044$) were significantly decreased in patients with combination treatment compared with patients with laser-only treatment ([Fig 7](#)).

The most common side effect of laser treatment was erythema (43.6%), followed by hypopigmentation (34.8%) and texture irregularity (17.4%) ([Table I](#); [Fig 8, A](#)). Texture irregularities were more commonly observed in patients with higher numbers of laser

treatments ([Fig 8, B](#)); however, this finding was not statistically significant.

DISCUSSION

In this study, we retrospectively reviewed the outcomes of laser treatment after a long-term follow-up period to evaluate the efficacy of lasers in the treatment of CMNs. In a total of 67 patients, 52 patients received laser-only treatment, and 15 patients received a combination of partial excision followed by laser treatment. Among these patients, 23 patients who were treated with laser only were followed up for ≥ 3 years. In this group, 11 patients (52.2%) showed nearly total clearance of pigmentation (IGA score >5) during or after the laser treatment. However, 5 patients (5/11, 45.5%) showed repigmentation. A total of 11 patients among 23 patients in long-term followed-up group showed

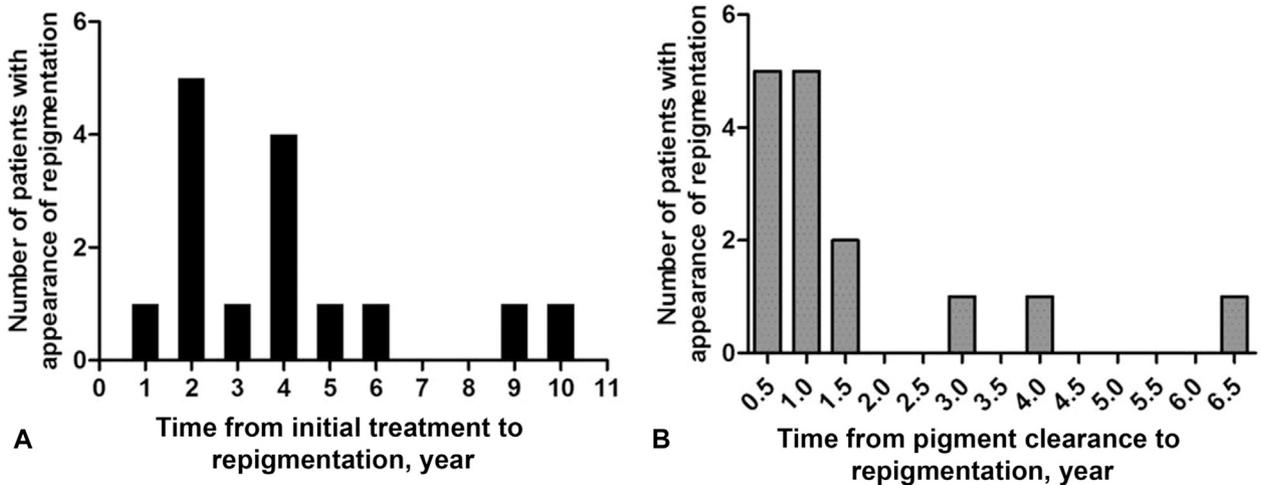


Fig 4. Time to repigmentation of 15 patients. **A**, Time to repigmentation from initial treatment. The mean time from initial treatment to repigmentation was 3.93 ± 2.58 years. **B**, Time to repigmentation from pigment clearance. The mean time from pigment clearance to repigmentation was 1.59 ± 1.63 years.

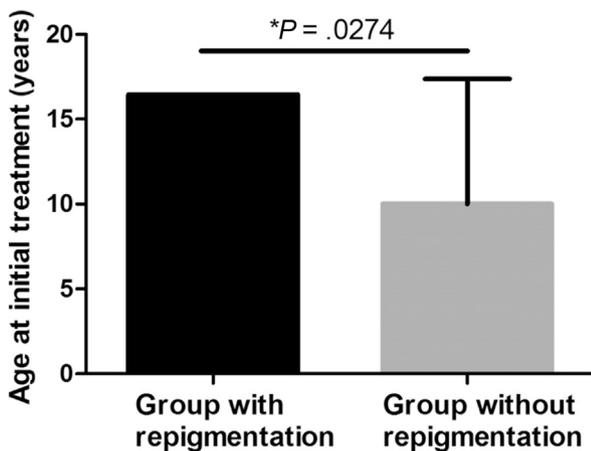


Fig 5. Comparison of age at initial laser treatment. Error bars indicate standard deviation. Patients with repigmentation were significantly older at initial treatment than those without repigmentation ($P = .0274$). *Statistically significant.

repigmentation regardless of pigment clearance. The mean period until repigmentation, irrespective of number of treatments, was 3.93 years from the initial session and 1.59 years from pigment clearance. When compared with the 10 patients with combination treatment of partial excision followed by laser treatment in the long-term follow-up group, patients with combination treatment showed higher IGA scores, fewer laser treatments, and shorter treatment periods compared with patients with laser-only treatment.

Surgical excision is known to be the treatment of choice for removing CMNs. However, laser treatments have been used for CMNs located on

cosmetically sensitive areas, such as nasal tips, periorbital areas, glabella, and cheeks, with great physical tension. Our results also showed that the face (69.6%) was the most common location of nevi for the laser-only treatment group. The most common laser modalities used for nevus removal are ablative lasers and pigment-specific lasers. Pigment-specific lasers are known to remove melanin pigments and superficial melanocytes, and ablative lasers work by delivering an intense wavelength of light to the skin, which removes superficial melanocytes. Therefore, melanocytes located in the deep dermis remain even after laser treatments. Repigmentation is a well-known result of laser treatment in CMN, and in previous studies, the rate of repigmentation after combination ablative and pigment-specific laser treatment varied 10%–82%.^{3,4,10–12} In a review by Eggen et al regarding laser treatments on CMN, repigmentation appeared in 13% of patients after combination treatment of ablative and Q-switched lasers.⁶ The repigmentation rate was lower with combination laser treatment (13%) than Q-switched laser-only treatment (51%), and the follow-up period varied from 3 months to 3 years in the study by Eggen et al.⁶ In our study, repigmentation appeared in 47.8% of patients, even when using a combination of ablative and Q-switched lasers on long-term follow-up. We assume that the higher rate of repigmentation seen in our study is due to the longer follow-up period. Considering the mean period until repigmentation in our study, we suggest that ≥ 4 years of treatment and follow-up is needed to clear recurred pigmentation and evaluate the efficacy of laser treatment on

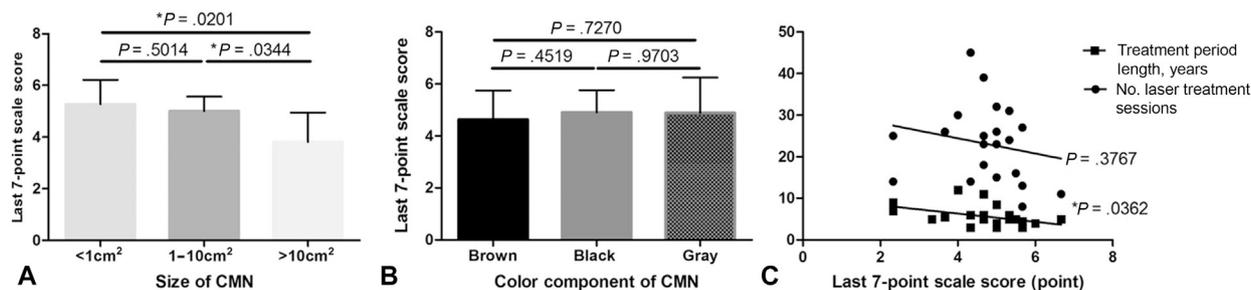


Fig 6. Comparison of final Investigator's Global Assessment (IGA) score according to size (A) and color (B) of CMN, treatment period, and number of laser treatments (C) in long-term follow-up group with laser-only treatment. A, Final IGA score was significantly lower in larger CMNs (1-way analysis of variance with Bonferroni correction, $P = .0127$). Error bars indicate standard deviation. B, Final IGA score was not significantly different among CMNs of different colors. Error bars indicate standard deviation. C, Length of treatment period negatively correlated with final IGA score among patients treated by laser only. CMN, Congenital melanocytic nevus. *Statistically significant.

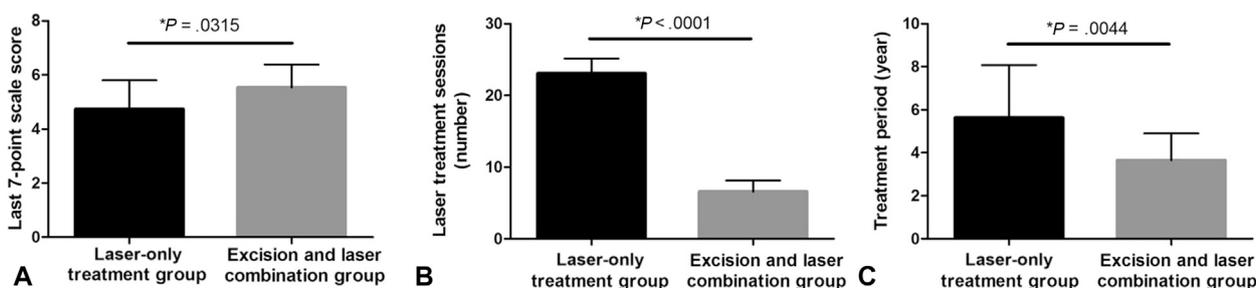


Fig 7. Comparison of outcomes between laser-only treatment and excision and laser combination treatment groups. Error bars indicate standard deviation. A, Comparison of final Investigator's Global Assessment scores. B, Comparison of number of laser treatments. C, Comparison of treatment periods between laser-only treatment group and combination treatment group. *Statistically significant.

CMN. Also, in our study, the incidence of repigmentation was significantly higher in relation to the age of initial treatment. This finding suggests that dermatologists might need to warn patients about the possibility of repigmentation after laser treatment, especially for those who start treatment at a relatively older age.

In this study, the outcome of laser treatments negatively correlated with treatment period. This finding can be explained by the efficacy of laser treatments, ie, patients with good responses to pigment-specific or ablative lasers can easily achieve their goal and stop the treatment, but patients with poorer responses get repeated treatments. This finding also implies that patients might not achieve favorable results, despite repeated laser treatments after their CMNs show poor early responses.

Common side effects and complications of laser treatments are persistent erythema, dyspigmentation, textural changes, hypertrophic scarring, and depressed scarring.^{4,5,8,13} In our study, frequent side

effects after laser treatments were erythema (43.5%), hypopigmentation (34.8%), and texture irregularity (17.4%) of the lesion, which was consistent with previous reports. However, the overall rate of side effects after laser treatment was much higher than that reported for the use of combination ablative and pigment-specific lasers on acquired melanocytic nevus (<20%).⁴ The reason for the higher rate of side effects could be due to the deeper and wider distribution of melanocytes in CMNs than acquired melanocytic nevi. When compared according to the number of treatments, the differences in the occurrence of each side effect was not statistically significant. Considering that erythema is generally accepted as an acute side effect of laser treatment, the higher rate of erythema (43.5%) shown in this study implies that erythema might persistently remain after repeated laser treatments in many more patients than was previously considered. Hypopigmentation and texture irregularity of the treated area, known to appear after repeated laser

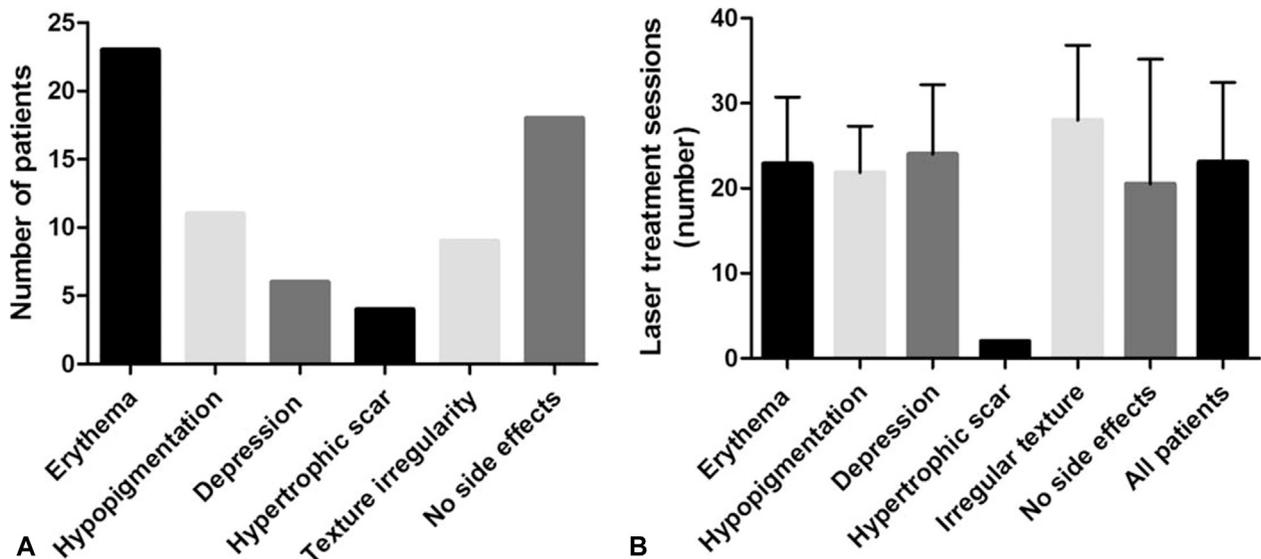


Fig 8. **A**, Number of patients with each side effect. **B**, Number of laser treatments and side effects. Error bars indicate standard deviation.

ablations, also appeared in 34.8% and 17.4% of patients, respectively, in the long-term follow-up group. Although patients might find these side effects more favorable than the cosmetic appearance of the CMN lesion before treatment, the possibility of persistent erythema, dyspigmentation, and texture irregularity should be explained to the patient, so they can make an educated choice before starting laser treatments.

As seen in our results, laser-only treatment did not show satisfactory results. The mean final IGA score was 4.73 in the long-term follow-up group. Only 1 patient in the long-term follow-up group with laser-only treatment received a score of 7 from 2 raters. Most patients with laser-only treatment had pigment remaining, cosmetically visible marks left as depigmentation, depressive scars or persistent erythema, or repigmentation.

Lim et al showed that treating with a combination of surgical excision and Er:YAG laser ablation in a single session can achieve good-to-excellent results in 83% (11/13) of patients.¹⁴ We also used a modified form of this combination treatment; partial excision followed by laser treatments in patients with CMNs on cosmetically sensitive areas. As a result, the final outcome of this combination treatment was more favorable than laser-only treatment. Moreover, the number of treatment sessions were fewer and treatment periods shorter than the laser-only treatment group. Therefore, combination treatment might be an effective treatment option for CMN.

This study has several limitations. First, it was a retrospective study with inherent limitations. Second, various laser devices were used rather than

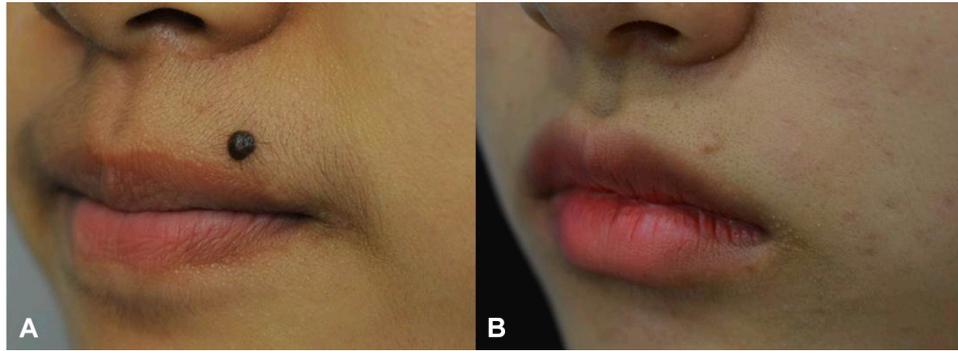
a single device or certain parameter. Although various laser devices had been used, variations between dermatologists were relatively controlled for by including patients treated by only 2 dermatologists. Third, the number of patients was relatively small and might not effectively power statistical analysis for significance. Nevertheless, the strength of this study is that it provides information regarding the clinical outcomes of laser treatment on CMNs. However, further prospective studies with well controlled designs are needed for better validation.

In conclusion, a treatment and follow-up period of >4 years is required to clear pigmentation and evaluate the efficacy of laser treatments in CMN patients. For surgically challenging CMNs, combination treatment with partial excision followed by laser treatment might be an effective option.

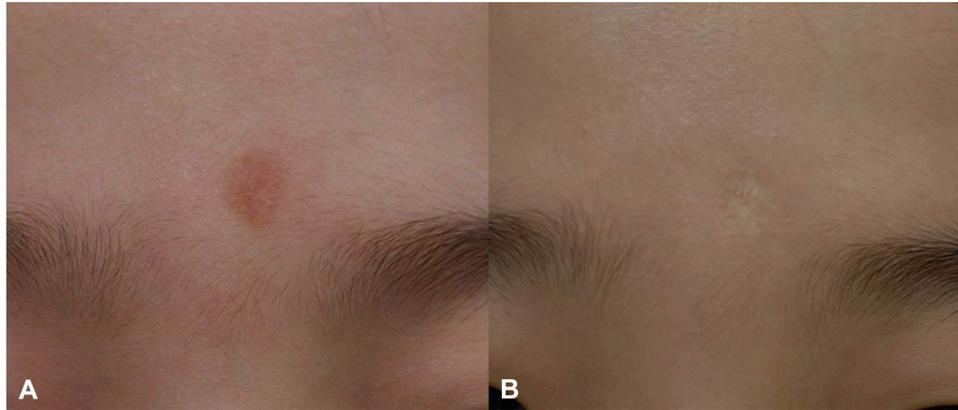
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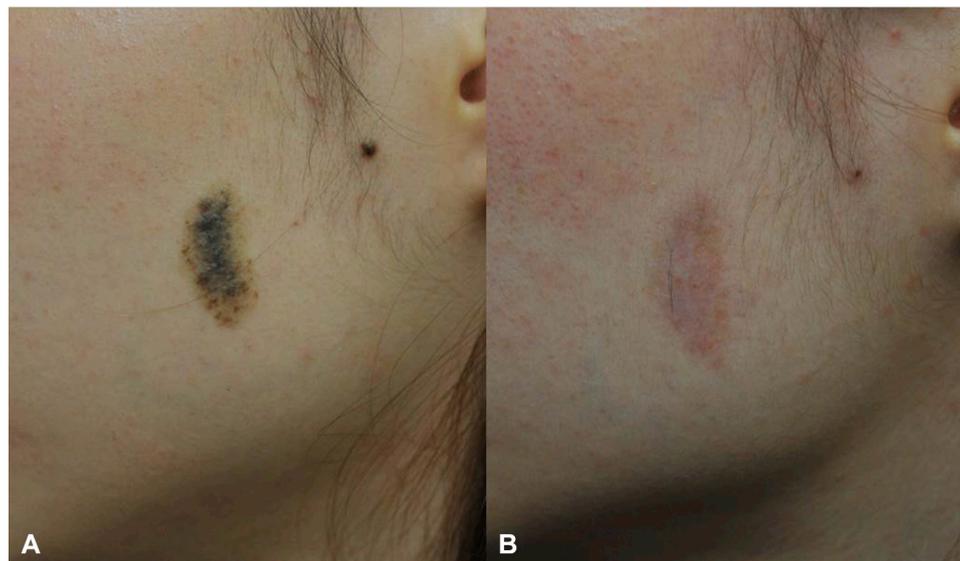
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Supplemental Fig 1. Patient 1 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed no repigmentation. Patient before treatment (**A**) and at last visit (**B**). Final IGA score from each rater: 7, 6, 7. Averaged final IGA score: 6.67.



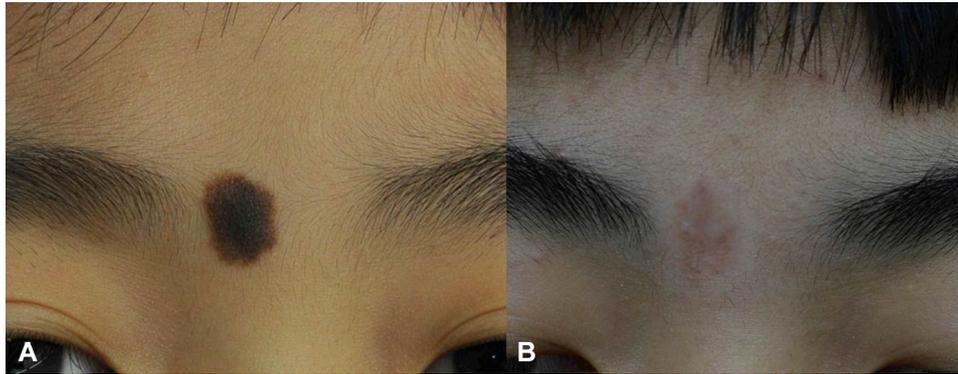
Supplemental Fig 2. Patient 2 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed no repigmentation. Patient before treatment (**A**) and at last visit (**B**). Final IGA score from each rater: 6, 6, 6. Average final IGA score: 6.00.



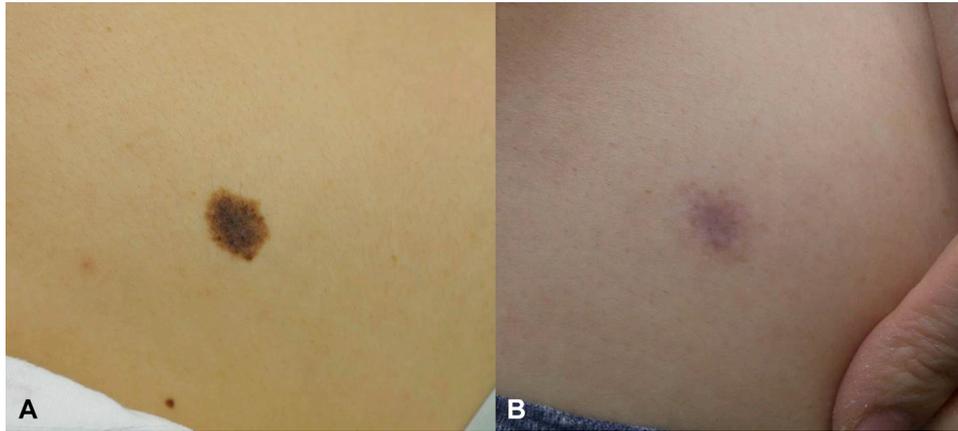
Supplemental Fig 3. Patient 3 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed no repigmentation. Patient before treatment (**A**) and at last visit (**B**). Final IGA score from each rater: 6, 4, 6. Average final IGA score: 5.33.



Supplemental Fig 4. Patient 4 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed no repigmentation. Patient before treatment (**A**) and at last visit (**B**). Final IGA score from each rater: 6, 5, 6. Average final IGA score: 5.67.



Supplemental Fig 5. Patient 5 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed no repigmentation. Patient before treatment (**A**) and at last visit (**B**). Final IGA score from each rater: 6, 5, 5. Average final IGA score: 5.33.



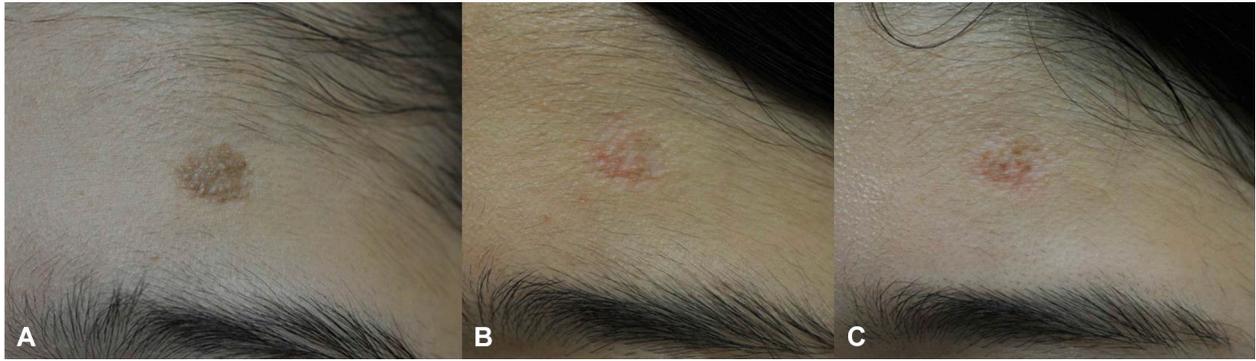
Supplemental Fig 6. Patient 6 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed no repigmentation. Patient before treatment (**A**) and at last visit (**B**). (final IGA score from each rater: 6, 4, 6. Average final IGA score: 5.33.



Supplemental Fig 7. Patient 7 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed repigmentation. Patient before treatment (**A**), after laser treatments with maximum pigment clearance (**B**), and after repigmentation (**C**). Near total clearance of pigmentation before repigmentation. Final IGA score on last visit of 5.67.



Supplemental Fig 8. Patient 8 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed repigmentation. Patient before treatment (**A**), after laser treatments with maximum pigment clearance (**B**), and after repigmentation (**C**). Near total clearance of pigmentation before repigmentation. Final IGA score on last visit of 5.00.



Supplemental Fig 9. Patient 9 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed repigmentation. Patient before treatment (**A**), after laser treatments with maximum pigment clearance (**B**), and after repigmentation (**C**). Near total clearance of pigmentation before repigmentation. Final IGA score on last visit of 5.50.



Supplemental Fig 10. Patient 10 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed repigmentation. Patient before treatment (**A**), after laser treatments with maximum pigment clearance (**B**), and after repigmentation (**C**). Near total clearance of pigmentation before repigmentation. Final IGA score on last visit of 4.67.



Supplemental Fig 11. Patient 11 with near total clearance of pigmentation (Investigator's Global Assessment [IGA] score >5) in long-term followed-up group. Patient displayed repigmentation. Patient before treatment (**A**), after laser treatments with maximum pigment clearance (**B**), and after repigmentation (**C**). Near total clearance of pigmentation before repigmentation. Final IGA score on last visit of 3.67.

Supplemental Table I. Descriptions of IGA (7-point scale) scoring system

IGA score	General improvement	Scoring in description
1	Worsened	Severe scarring
2	0%	Pigment clearance of <30%
3	1%-25%	Pigment clearance of 30%-50%
4	26%-50%	Pigment clearance of 50%-70% or pigment clearance of 70%-90% with prominent side effects*
5	51%-90%	Pigment clearance of 70%-90% with or without mild side effects or pigment clearance of 90%-99% with side effects
6	91%-99%	Pigment clearance of 90%-99% without side effects or pigment clearance of 100% with mild side effects
7	100%	Total pigment clearance without side effects (cosmetically cleared)

IGA, Investigator's Global Assessment.

*Side effect includes persistent erythema, hypopigmentation, depression and texture irregularity caused by laser treatments.