Received: 8 November 2021 | Revised: 30 January 2022 | Accepted: 20 February 2022

DOI: 10.1111/dth.15406

ORIGINAL ARTICLE

DERMATOLOGIC THERAPY WILEY

An exploration of optimal time and safety of 595-nm pulsed dye laser for the treatment of early superficial infantile hemangioma

Hui-Yi He | Wei-Kang Shi | Ji-Cong Jiang | Yu Gao | Xi-Mao Xue

Department of Dermatology, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China

Correspondence
Xi-Mao Xue and Yu Gao, Department of Dermatology, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou 325027, Zhejiang Province, China.
Email: xueximao2021@163.com and gaoyu0570@sina.com

Funding information
National Nature Science Foundation of China, Grant/Award Number: 81801862

Abstract

Infantile hemangioma (IH) is the most common benign vascular tumor that occurs in infants and young children. Studies have shown laser therapy to reduce the proliferation of superficial IH and promote its regression, but the optimal timing for treatment has not been determined. Our study explores the timing and safety of 595-nm pulsed dye laser (PDL) treatment for early superficial IH. We retrospectively analyzed 180 cases of superficial IH treated with 595-nm PDL. Data was organized according to patient age at the first visit. Six months after the initial treatment, patients were evaluated using a grade IV classification method, and the clinical curative effect of each group was calculated. The number of laser treatments and the occurrence of adverse reactions were recorded simultaneously. The overall effective and cure rates were 98.3% and 84.4%, respectively, with no significant difference in rates between groups ($p > 0.05$). There was a statistically significant difference in the number of laser treatments among the age groups ($p < 0.05$). The average laser frequency: "0–2 months group" < "2–4 months group" < "4–6 months group." The overall incidence of adverse reactions was 11.1%, and 12 (6.7%) cases had short-term adverse reactions, with no statistically significant differences between groups ($p > 0.05$). Eight cases had long-term adverse reactions. This difference between groups was statistically significant ($p < 0.05$). Younger children (≤2 months of age) receiving 595-nm PDL treatment for IH require relatively fewer treatment times than other children (>2 months of age), have a shorter course of disease, experience better curative effect, and have fewer sequelae reactions.

KEYWORDS
595-nm pulse dye laser, early treatment, infantile hemangioma, laser therapy

1 | INTRODUCTION

Infantile hemangioma (IH) is the most common benign vascular tumor that occurs in infants and young children, with an incidence of 4%–

Hui-Yi He and Wei-Kang Shi contributed equally to this work.

5%. IH can be divided into superficial, deep, and mixed types. The superficial type is most commonly seen in clinical practice, with an incidence of 50%–60%.[1] Superficial hemangiomas are located in the upper dermis, with red papules, nodules, or plaques as the main manifestations. IH has a unique natural history that includes a rapid proliferation period, a regression period, and a complete regression period.[2] The vast majority of IH cases begin to proliferate around 1 week after birth, and the growth rate reaches its maximum between 5 and 8 weeks of age. About 80% of the absolute growth of IH is completed by 5 months of age. The growth rate then slows, gradually stabilizes by 12 months, and thereafter begins to subside spontaneously. Approximately 85%–90% of children with IH experience complete regression by the age of 4 years.[3] Because IH can resolve spontaneously, early scholars believed that, except for cases with severe complications requiring treatment, most cases of IH can be treated with a "wait-and-watch" strategy. However, studies have shown that IH in the eyelids, parotid glands, and nose tip may persist or only partially subside. Moreover, approximately 69% of children with IH will have sequelae of varying degrees, such as cellulite accumulation, scars, pigmentation, telangiectasia, and skin redundancy after IH naturally subsides.[4]

In order to deal with the serious psychological and economic burdens that are faced by children and their families as a result of the untimely or improper treatment of IH, early intervention of IH is needed and appropriate treatment methods must be selected. There are many treatment options, including laser treatment, topical drug therapy, oral drug therapy, local injection therapy, and surgical resection. Among them, laser therapy has become an increasingly important treatment method for patients with IH. Existing studies have shown that laser therapy can reduce the proliferation of superficial IH and promote its regression. However, the optimal timing for laser treatment of IH remains inconclusive. Our research explores this optimal timing for and safety of laser treatment of superficial IH in its early stages.

2 | PATIENTS AND METHODS

2.1 | Participants

This study was conducted in accordance with the Declaration of Helsinki and approved by the independent ethics committee of The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University. Written informed consent was obtained from the patients' guardians. This study was a retrospective study including 180 children with superficial IH who were treated with 595 nm pulsed dye laser (PDL) in a dermatology clinic from August 2019 to August 2021. Among them, 68 were males and 112 were females. The male to female ratio was 1:1.65, and the age range was 0.07–6 months, with an average age of 3.08 ± 1.73 months. The locations of hemangioma were as follows: 59 cases presented with IH on the head, face, and neck; 57 cases presented with IH on the limbs; and 64 cases presented with IH on the trunk. Participants were divided into 6 groups according to their age at the first visit. Thirty cases were included in each of the following groups: "0–1 month group," "1–2 months group", "2–3 months group," "3–4 months group," "4–5 months group," and "5–6 months group." There were no significant differences in sex and location of IH among the groups ($p < 0.05$). Participant characteristics are shown in Table 1. Before starting this study, our hospital explained the purpose and methods of the study to the families of the children. The families of the children agreed to participate in the clinical study and signed an informed consent form for their participation in it.

2.2 | Inclusion criteria

(1) Finally diagnosed as a child with superficial IH according to the International Vascular Diseases (ISSVA) diagnostic criteria, clinical manifestations and color Doppler ultrasound results; (2) Age 0–6 months; (3) Only 1 skin lesion; (4) IH at low to moderate risk; (5) Major complications of IH, such as ulcers, bleeding, infection, and hence forth, are not accompanied and expected not to occur; (6) No treatment for hemangioma has been performed before the treatment; (7) IH is not serious enough Oral propranolol is required; (8) Parents have a strong willingness to treat; (9) Can receive at least 6 months follow-up after treatment; (10) Exclude bronchial asthma or family history of asthma, as well as bradycardia, sinus block and Severe heart diseases such as cardiac malformations; (11) Exclude other severe organic diseases.

2.3 | Treatment

2.3.1 | Use of instruments

The Vbeam PDL produced by Candela (USA), was used for treatment with the following settings: a wavelength of 595-nm, a pulse interval of 0.45 ~ 40 ms, an energy density of 6.0 ~ 7.5 J/cm^2, and a spot diameter of 5 ~ 10 mm.

A dynamic cooling device (DCD) with a jet of 30 ~ 40 ms and an operating interval of 20 ~ 30 ms was also used.

2.3.2 | Before treatment protocols

Before treatment, the treatment area of the child was cleaned and specific information about the child's skin hemangioma, including the area and color of the hemangioma, was checked and recorded. To establish a treatment file for each patient, the child's body temperature and skin condition were recorded, and a digital camera was used to take pictures of the skin. 5% lidocaine cream was applied to the skin lesion area for 40–60 min. A small-dose spot test was also performed to observe the response of the child's hemangioma and determine the best treatment dose.

TABLE 1 Baseline Characteristics at Time of Inclusion [n(%)]

Characteristic	Sex, n(%)		Location, n(%)			Average age at first visit (months) ($\bar{x} \pm 1.96s$)
	Male	Female	Head and face	Trunk	Limbs	
0–1 month group	9 (30)	21 (70)	11 (36.7)	10 (33.3)	9 (30)	0.73±0.26
1–2 month group	16 (53.3)	14 (46.7)	11 (36.7)	10 (33.3)	9 (30)	1.58±0.29
2–3 month group	9 (30)	21 (70)	10 (33.3)	10 (33.3)	10 (33.3)	2.48±0.32
3–4 month group	13 (43.3)	17 (56.7)	14 (46.7)	8 (26.7)	8 (26.7)	3.52±0.28
4–5 month group	9 (30)	21 (70)	9 (30)	9 (30)	12 (40)	4.51±0.27
5–6 month group	12 (40)	18 (60)	10 (33.3)	11 (36.7)	9 (30)	5.70±0.31
Total	68 (37.8)	112 (62.2)	59 (32.8)	64 (35.6)	57 (31.7)	3.09±1.73

2.3.3 | During treatment protocols

In the course of clinical treatment, the treatment parameters were set according to the specific condition of the child's skin hemangioma. The treatment end-point was determined to be the point at which the skin lesion turned dark brown.

2.3.4 | After treatment protocols

After each treatment, ice packs were applied to the tumor site for 30 min, and the family members of the child were asked to keep the tumor site clean and protected from light for 1 week. Re-examination was preformed after 4 weeks. Parameters of the second treatment were adjusted appropriately, according to the effect of the first treatment to achieve the best treatment effect.

2.4 | Follow-up and adverse reaction records

The treatment cycle was repeated once every 4 weeks. After treatment, follow-up was performed every week to 6 months after the treatment ended. The occurrence of adverse reactions, including purpura, edema, and erythema immediately after treatment, and the presence of erosions, ulcers, hyperpigmentation after treatment, hypopigmentation, and scars were recorded.

2.5 | Efficacy Criteria

The area of hemangioma regression was calculated based on the photographs taken before treatment and the skin's condition 6 months after the patient's initial treatment. The color change of the hemangioma was observed using the photographs, and the treatment efficacy was evaluated by combining these observations. The results were evaluated by doctors who have received unified training of hemangioma. The clinical efficacy evaluation adopts the internationally accepted grade IV classification, Grade I: tumor regression ≤25%, Grade II: tumor regression 26% ~ 50%, Grade III: tumor regression 51% ~ 75%, Grade IV: tumor regression 76% ~ 100%. Grade I is assessed as invalid, Grade II is assessed as effective, Grade III is assessed as markedly effective, and Grade IV is assessed as cured. Effective rate = (effective + markedly effective + cured) number of cases / total number of cases. Grades I, II, and III are rated as uncured, and Grade IV is rated as cured. Cure rate = number of cured cases/ total number of cases. For children with clinical curative effect of Grade IV and above, count the number of laser treatments performed to achieve the curative effect.

2.6 | Statistical methods

Statistical analyses were performed using the SPSS 26.0. The efficacy evaluation and treatment frequency comparison among different groups were performed using the Kruskal-Wallis H test. The comparison of adverse reactions was performed using the Chi-square test. Statistical significance was set at $p < 0.05$.

3 | RESULTS

The overall effective rate of treatment in 180 children with superficial IH who underwent 595-nm PDL was 98.3%, and the cure rate was 84.4%. (Figure 1).

3.1 | Comparison of curative effect in children of different ages

The effective rates for each group were as follows: 100% for the "0–1 month group," 100% for the "1–2 months group", 96.7% for the "2–3 months group", 96.7% for the "3–4 months group", 96.7% for the "4–5 months group", and 100% for the "5–6 months group". There was no significant difference in the effective rate of treatment among the groups ($p > 0.05$).

The cure rates of each group were 93.3% in the "0–1 month group", 90% in the "1–2 months group", 80% in the "2–3 months group", 83.3% in the "3–4 months group", 66.7% in the "4–5 months group", and 83.3% in the "5–6 months group". There was no significant difference in cure rates among the groups ($p > 0.05$) (Table 2).

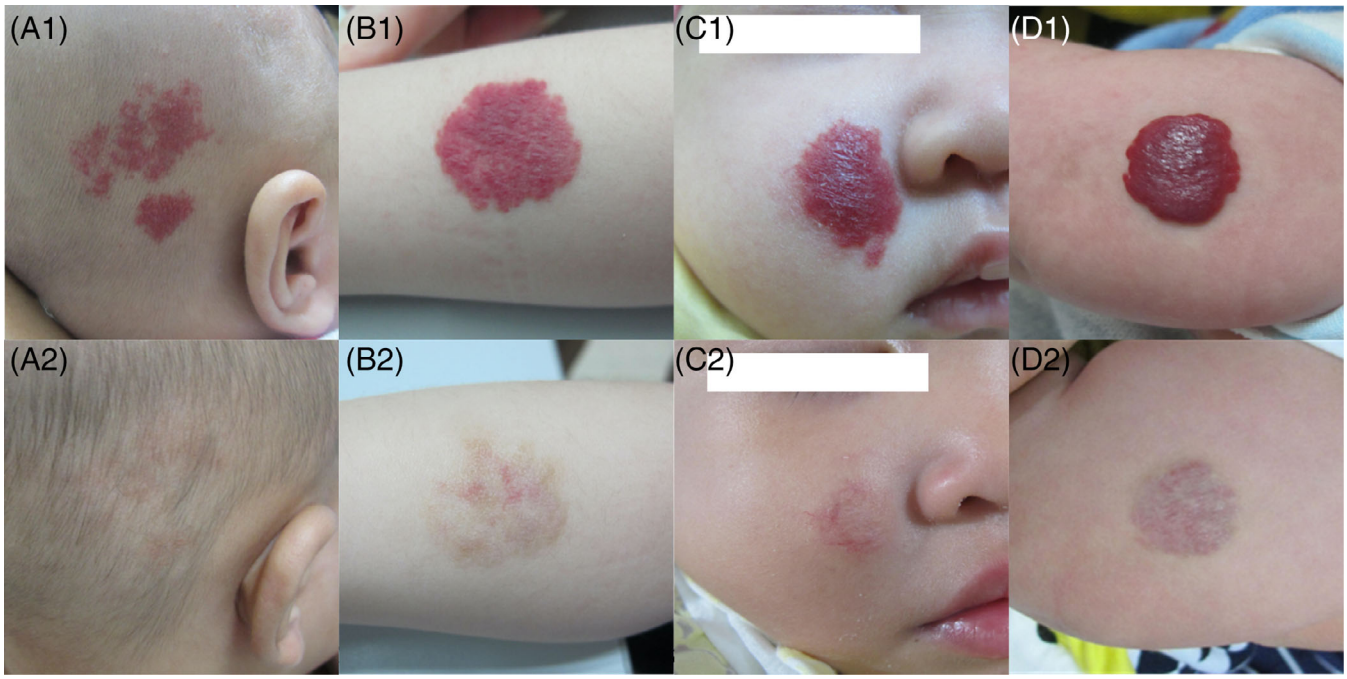

FIGURE 1 Comparison of patients before and after treatment

TABLE 2 Comparison of efficacy for six groups[n (%)]

	Efficacy rank					
Classify	I	II	III	IV	Efficacy rate (%)	Cure rate (%)
0–1 month group	—	—	2 (6.7)	28 (93.3)	100	93.3
1–2 month group	—	—	3 (10)	27 (90)	100	90
2–3 month group	1 (3.3)	—	2 (6.7)	27 (90)	96.7	90
3–4 month group	1 (3.3)	1 (3.3)	3 (10)	25 (83.3)	96.7	83.3
4–5 month group	1 (3.3)	2 (6.7)	7 (23.3)	20 (66.7)	96.7	66.7
5–6 month group	—	2 (6.7)	3 (10)	25 (83.3)	100	83.3
Total	3 (1.6)	5 (2.7)	20 (11.1)	152 (84.4)	98.3	84.4
Z value	—				6.82	6.63
p value	—				0.24	0.25

3.2 | Comparison of the number of treatments for children of different ages

The average number of laser treatments for children in each group meeting the IV level evaluation criteria were: "0–1 month group", 2.32 ± 0.296 times; "1–2 month group", 2.52 ± 0.269 times; "2–3 months group", 3.44 ± 0.326 times; "3–4 months group", 3.36 ± 0.251 times; "4–5 month group", 4.15 ± 0.293 times; and "5–6 months group", 3.60 ± 0.306 time (Table 3). Cross-group analysis of the average laser treatment times were as follows: "0–1 month group" < "1–2 months group" < "2–3 months group" < "3–4 months group" < "5–6 months group" < "4–5 months group". There was a statistically significant difference in the number of treatments among the six groups ($p < 0.05$) (Figure 2).

Further pairwise comparison results showed the following: "0-1 month group" and "1–2 months group"; "1–2 months group" and "2–3 months group"; "2–3 months group" and "3–4 months group"; "3–4 months group" and "4–5 months group"; and "4–5 months group" and "5–6 months group" have no significant difference ($p > 0.05$), when evaluated as the average number of lasers used between two adjacent groups. The average laser frequency of treatment in the "0–1 month group" was less than that in the "2–3 months group", the "3–4 months group", the "4–5 months group", and the "5–6 months group". For the "1–2 months group", the average laser frequency was less than that for the "3–4 months group", the "4–5 months group", and the "5–6 months group". Similarly, the average laser frequency for the "2–3 months group" was less than that for the "4–5 months group" and the "5–6 months group". Finally, the average laser frequency for the "3–4 months group" was less than that for the "5–6 months group". This difference between the groups was statistically significant ($p < 0.05$).

TABLE 3 Comparison of the average number of laser treatments for six group

Group	Number of people at Grade IV [n (%)]	Average number of laser treatments (times) ($\bar{x} \pm 1.96s$)
0–1 month group	28 (93.3)	2.32±0.296
1–2 month group	27 (90)	2.52±0.269
2–3 month group	27 (90)	3.44± 0.326
3–4 month group	25 (83.3)	3.36±0.251
4–5 month group	20 (66.7)	4.15±0.293
5–6 month group	25 (83.3)	3.60±0.306
Z value	4.028	
p value	0.00	

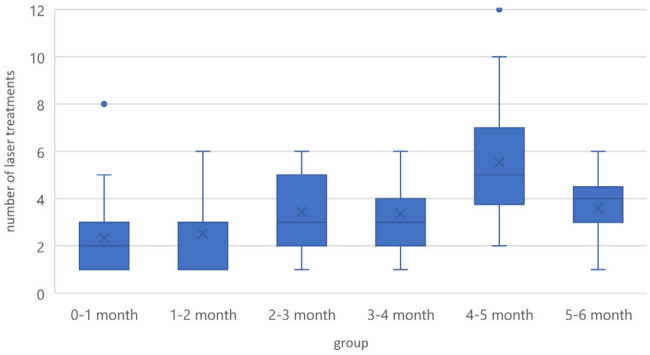

FIGURE 2 Comparison of the number of laser treatments for six group

Combining the six groups of children into three groups based on their ages, the average number of laser treatments was obtained and reported as follows: "0–2 months group" < "2–4 months group" < "4–6 months group". There was a statistically significant difference between the groups ($p < 0.05$) (Table 4).

3.3 | Comparison of curative effects of different treatment sites

Among the 180 children with IH, 59 (32.8%) were located in the head and neck, 64 (35.6%) in the trunk, and 57 (31.7%) in the limbs. Among them, the effective rate of head and neck was 98.3%, the cure rate was 88.1%, there were 0 cases of grade I, 1 case of grade II (1.7%), 6 cases of grade III (10.2%), and 52 cases of grade IV (88.1%).), the average number of laser treatments was 3.78 ± 0.29. The effective rate of the trunk was 98.4%, and the cure rate was 95.3%, including 0 cases in grade I, 1 (1.6%) in grade II, 2 (3.1%) in grade III, and 61 (95.3%) in grade IV. The average number of laser treatments 3.84 ± 0.28. The effective rate of the limbs was 94.8%, and the cure rate was 86.0%. There were 2 (3.5%) cases in grade I, 1 (1.8%) in grade II, 5 (8.8%) in grade III, and 49 (86.0%) in grade IV. The number of laser treatments was 4.14 ± 0.40. There was no significant difference in the effective rate and the average number of laser treatments among the three groups, and the Kruskal-Wallis H test indicated that $p > 0.05$

TABLE 4 Comparison of the average number of laser treatments for three group

Group	Number of people at Grade IV [n (%)]	Average number of laser treatments (times) ($\bar{x} \pm 1.96s$)
0–2 month group	55 (91.7)	2.42±0.20
2–4 month group	52 (86.7)	3.40±0.21
4–5 month group	45 (75)	3.84± 0.22
Z value	3.57	
p value	0.01	

3.4 | Comparison of adverse reactions

A total of 20 children had complications, and the overall incidence of adverse events was 11.1%.

Among those with complications, there were 12 cases of short-term adverse reactions, such as purpura, edema, erythema, blisters, and scabs. Five adverse reaction cases (16.7%) occurred in the "0–1 month group", 2 cases (6.7%) occurred in the "1–2 month group", 1 case (3.3%) occurred in the "2–3 months group", 2 cases (6.7%) occurred in the "3–4 months group", 1 case (3.3%) occurred in the "4–5 months group", and 1 case (3.3%) occurred in the "5–6 months group". All such cases resolved spontaneously within 1 week, and there was no statistically significant difference in occurrence of adverse reactions between the groups ($p > 0.05$).

There were eight cases of long-term adverse reactions such as ulcers, local dry skin desquamation and itching, pigmentation, remaining fibrofatty scars, and skin sagging. No long-term adverse reactions occurred in the "0–1 months", "1–2 months", "2–3 months", or "3–4 months" groups. One case (3.3%) occurred in the "4–5 months group", and 7 long-term adverse reaction cases (23.3%) occurred in the "5–6 months group". The difference between groups was statistically significant ($p < 0.05$) (Table 5).

4 | DISCUSSION

IH is the most common benign tumor in children and is caused by the abnormal proliferation of vascular endothelial cells. Its pathogenesis and exact etiology are not yet fully understood. Premature birth, low-birth weight, vaginal bleeding in early pregnancy, the use of progesterone, preeclampsia, and placenta previa are all risk factors for IH.[5] For superficial IH, the current recommended treatment involves a wait-and-see approach. However, research reports indicate that up to approximately 69% of untreated or inadequately treated IH cannot be completely resolved. This may lead to residual sequelae after resolution, including telangiectasia, skin atrophy, excess skin, scars, or fibrous fatty tissue, which may

TABLE 5 Comparison of adverse reactions for six groups [n (%)]

Adverse reactions	Short-term adverse reactions*	Long-term adverse reactions*
0–1 month group	5 (16.7)	0
1–2 month group	2 (6.7)	0
2–3 month group	1 (3.3)	0
3–4 month group	2 (6.7)	0
4–5 month group	1 (3.3)	1 (3.3)
5–6 month group	1 (3.3)	7 (23.3)
Total	12 (6.7)	8 (4.4)
F value	0.5	4.5
p value	0.779	0.034

Note: *Short-term adverse reactions include cyanosis, erythema, edema, blisters, and so forth. *Long-term adverse reactions include ulcers, pigmentation, leftover fibrous fatty scars and loose skin, and so forth.

seriously affect the mental health and quality of life of children and their families.[6]

The current methods for treating IH include oral propranolol, topical timolol, oral glucocorticoids, laser treatment, surgical treatment, injection treatment, and freezing. In systemic treatment, propranolol is the first-line drug for the treatment of complex infant hemangioma. It has relatively high-safety results, but there are risks to this treatment that include bradycardia, blood pressure decline, atrioventricular block, and blood sugar decline. Such outcomes are due to the drug's high lipophilicity. Moreover, the ability of propranolol to penetrate the blood–brain barrier has a theoretical risk of affecting neurodevelopment or cognition and is not suitable for low-risk superficial hemangiomas.[7] Topical timolol solution for treatment of IH is considered to be highly effective and safe, but there is a risk of systemic absorption, and the current topical dosage form and therapeutic dose are not standardized. Patients and parents also have poor compliance with this treatment method.[8]

Laser therapy has a long history as a standardized treatment for IH, and 595-nm PDL is currently the most commonly used method for the treatment of superficial IH. The mechanism is based on the selective photothermal action of oxygenated hemoglobin as the target, which causes oxygenated red blood cells to burst and block the blood vessels.[9] This results in the degeneration and necrosis of vascular endothelial cells, thereby destroying the capillaries in the hemangioma, and finally causes the hemangioma to shrink.[10] Studies have shown that laser treatment also inhibits the growth of hemangioma endothelial cells by affecting the cytokine signaling pathway, whereby the degree of impact is affected by energy and time within a certain range.[11]

The 595-nm PDL equipped with a DCD system can not only reduce the skin surface temperature and avoid laser heat damage to the skin, but it can also cool the skin and anesthetize the skin to relieve pain.[12] It is considered a treatment for ulcerative hemangiomas and capillaries.[13] The 595-nm PDL is the laser of choice for vascular malformations and residual capillary dilation. Due to the thermally induced lysis of collagen, it can promote the deposition of adipose tissue and correct anatomical aberrations, promote tissue remodeling, and is associated with the reduction of transforming growth factor-B1 (TGF-B1).[6] Complications after PDL treatment can manifest as immediate purpura, erythema, edema, and blisters. Most of these complications will subside spontaneously after 1 week. A large number of studies[14–16]have confirmed that 595-nm PDL treatment is highly efficient, safe, and has few adverse reactions in the treatment of IHs.

The studies of Chang et al.[17] and Tollefson et al.[18] showed that massive growth of hemangiomas and the resulting skin changes occur in the early stages of the disease. Effective treatments to prevent skin changes during the rapid growth phase may help prevent irreparable skin changes. Many studies[16,19] have pointed out that the use of 595-nm PDL to treat early IH can reduce the tumor's proliferation phase, prevent its further expansion, and accelerate its degeneration. The treatment has been shown to be fast and effective, with low-adverse reactions. However, there is no literature that discusses the best time for early treatment.

Our research found that the use of 595-nm PDL to treat early superficial IH has a high-effective rate and cure rate. The overall effective rate of 180 children reached 98.3%, and the cure rate reached 84.4%. Cross-group analysis showed that the younger the patient age at the time of initial treatment, the shorter the course of the disease, the lower the average number of laser treatments required to reach the cure standard, the better the treatment effect, the shorter the regression time, and the fewer the after-effects.

We speculate that the size and thickness of the hemangioma during the initial treatment are the key factors that determine the subsequent treatment effect and time. The smaller the area, the thinner the hemangioma, and the better the treatment effect. The first few weeks to several months of life are critical for the growth of hemangiomas. IH usually appears before 4 weeks of age, and its fastest growing stage is before 8 weeks of age, particularly between 5.5–7.5 weeks. At 5 months of age, most of the growth is completed.[20] Thus, with age, the size and thickness of hemangiomas and the distribution of blood vessel walls increase. Laser treatment of the hemangioma during the rapid proliferation period can significantly reduce the volume and proliferation of the hemangioma, as well as promote its degeneration stage earlier.

The results of the study suggest that the average number of laser treatments in the "5–6 months group" is less than that of the "4–5 months group," which may be related to the proliferation cycle of hemangioma. Most hemangiomas grow to an average of 80% of their final size when patients are 5 months old. The growth rate after 5 months of age is significantly lower than the growth rate in the first few months after birth. 595-nm PDL laser can accelerate the regression speed of hemangiomas. In further comparison, we found that there was no significant difference in the average number of laser treatments between two adjacent groups, such as the "0-1 month group" and the "1–2 months group". This may be related to the study's smaller sample size and shorter follow-up time.

In terms of adverse reactions, the overall incidence of adverse reactions was 11.1%, most of which were short-term adverse reactions and resolved spontaneously about 1 week after the end of treatment. The number of short-term adverse reactions in the "0–1 month

group" was significantly higher than that in the remaining five groups. We speculate that this may be related to the younger age of the newborn, thereby having thinner skin and poorer tolerance. Therefore, more attention should be given to the adjustment of laser energy during treatment. In terms of long-term sequelae, the "5–6 months group" had more cases of skin sagging and left fibrofatty scars than the other groups. This may be related to the late treatment time and the overgrowth of tumors that caused irreparable skin damage.

Overall, 595-nm PDL had a good effect on early (0–6 months old) superficial IH. Therefore, early diagnosis of hemangiomas in infants and young children should be performed. 595-nm PDL can significantly reduce the size of the lesion, reduce its proliferation, shorten the course of the disease, and cause fewer adverse reactions and safety concerns. Compared with the traditional "wait-and-see" treatment approach, early intervention for IH with 595-nm PDL is a more appropriate treatment method.

ACKNOWLEDGMENTS

This study is supported by the National Natural Science Foundation of China (81801862).

CONFLICTS OF INTEREST

The authors report no conflicts of interest for this work.

AUTHOR CONTRIBUTION

Hui-Yi He: Data curation, Writing - Original Draft. Wei-Kang Shi: data curation, Formal analysis, Software. Ji-Cong Jiang: Methodology, Supervision, Validation. Yu Gao: Conceptualization, Resources. Xi-Mao Xue: writing-reviewing and editing.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Hui-Yi He https://orcid.org/0000-0003-3667-6662

REFERENCES

1. Rodríguez Bandera A, Sebaratnam D, Wargon O, Wong L. Infantile hemangioma. Part 1: epidemiology, pathogenesis, clinical presentation and assessment. *J Am Acad Dermatol*. 2021;85(6):1379-1392.
2. Darrow D, Greene A, Mancini A, Nopper A. Diagnosis and Management of Infantile Hemangioma: executive summary. *Pediatrics*. 2015; 136(4):786-791.
3. Olsen G, Nackers A, Drolet B. Infantile and congenital hemangiomas. *Semin Pediatr Surg*. 2020;29(5):150969.
4. Reinisch J. Discussion: untreated hemangiomas: growth pattern and residual lesions. *Plast Reconstr Surg*. 2011;127(4):1649.
5. Materna-Kiryluk A, Wiśniewska K, Więckowska B, et al. *Genetic and Environmental Risk Factors for Isolated Hemangiomas in Infants*. Vol 7; Children (Basel); 2020:10.
6. Muñoz-Garza F, Ríos M, Roé-Crespo E, et al. Efficacy and safety of topical Timolol for the treatment of infantile hemangioma in the early proliferative stage: a randomized clinical trial. *JAMA Dermatol*. 2021; 157(5):583-587.
7. Anderson R, Parrish J. Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation. *Science (New York, NY)*. 1983;220(4596):524-527.
8. Borderud SP, Li Y, Burkhalter JE, Sheffer CE, Ostroff JS. Electronic cigarette use among patients with cancer: characteristics of electronic cigarette users and their smoking cessation outcomes. *Cancer*. 2015; 121(5):800.
9. Husain Z, Alster T. The role of lasers and intense pulsed light technology in dermatology. *Clinic Cosmetic Invest Dermatol*. 2016;9:29-40.
10. Chen W, Liu S, Yang C, Yang S. Clinical efficacy of the 595 nm pulsed dye laser in the treatment of childhood superficial hemangioma - analysis of 10-year application in Chinese patients. *J Dermatolog Treat*. 2015;26(1):54-58.
11. Zhu Y, Wan X, Abliz P. Effects of laser irradiation on growth factors and cell apoptosis of in vitro cultured infant hemangioma endothelial cells. *Life Sci*. 2019;233:116685.
12. Loh T, Cotton C, Vasic J, Goldberg G. Current practices in pediatric dermatology laser therapy: an international survey. *Lasers Surg Med*. 2020;53(7):946–952.
13. Chelleri C, Monzani N, Gelmetti C, et al. Residual lesions after pharmacological and dye-laser treatment of infantile hemangiomas: critical review of 432 cases. *Lasers Surg Med*. 2020;52(7):597-603.
14. Lin M, Lin C, Hu S, et al. The application of 595-nm pulsed dye laser for vascular anomalies in a Chinese population: a 10-year experience. *J Cosmetic Laser Therapy Off Pub Eur Soc Laser Dermatol*. 2019;21(3): 171-178.
15. Chen Q, Chang L, Qiu Y, et al. Comparison of the efficacy between topical timolol and pulsed dye laser in the treatment of ulcerated infantile haemangiomas: a randomized controlled study. *J Eur Acad Dermatol Venereol JEADV*. 2021;35(4):e303-e305.
16. Rizzo C, Brightman L, Chapas A, et al. Outcomes of childhood hemangiomas treated with the pulsed-dye laser with dynamic cooling: a retrospective chart analysis. *Dermatol Surg Off Pub Am Soc Dermatol Surg*. 2009;35(12):1947-1954.
17. Chang L, Haggstrom A, Drolet B, et al. Growth characteristics of infantile hemangiomas: implications for management. *Pediatrics*. 2008;122(2):360-367.
18. Tollefson M, Frieden I. Early growth of infantile hemangiomas: what parents' photographs tell us. *Pediatrics*. 2012;130(2):e314-e320.
19. Hohenleutner S, Badur-Ganter E, Landthaler M, Hohenleutner U. Long-term results in the treatment of childhood hemangioma with the flashlamp-pumped pulsed dye laser: an evaluation of 617 cases. *Lasers Surg Med*. 2001;28(3):273-277.
20. McNab M, García C, Tabak D, Aranibar L, Castro A, Wortsman X. Subclinical ultrasound characteristics of infantile hemangiomas that may potentially affect involution. *J Ultrasound Med*. 2021;40(6):1125-1130.

How to cite this article: He H-Y, Shi W-K, Jiang J-C, Gao Y, Xue X-M. An exploration of optimal time and safety of 595-nm pulsed dye laser for the treatment of early superficial infantile hemangioma. *Dermatologic Therapy*. 2022;35(5): e15406. doi:10.1111/dth.15406