Received: 24 February 2020 | Accepted: 25 March 2020
DOI: 10.1111/dth.13341

ORIGINAL ARTICLE

DERMATOLOGIC THERAPY WILEY

New technology for coagulation of dilated vessels using the combined effects of several modes of generation and wavelengths in one laser pulse for the treatment of pediatric hemangiomas: Open prospective study

Tatyana V. Trapeznikova[1] | Tatyana P. Pisklakova[2] | Vladimir V. Khomchenko[2] | Natalia G. Kalashnikova[3] | Torello Lotti[4] | Mohammad Jafferany[5]

[1]Department of Dermatology, FSBOU VPO "Southern Ural State Medical University", Chelyabinsk, Russia
[2]Scientific Department, Linline Medical System, Minsk, Republic of Belarus
[3]Department of Dermatology, Linline Clinic Chain, Dermatology, Moscow, Russia
[4]Department of Dermatology, University G. Marconi of Rome, Dermatology and Venereology, Rome, Italy
[5]College of Medicine, Central Michigan University, Saginaw, Michigan

Correspondence
Mohammad Jafferany, College of Medicine, Central Michigan University, East Campus, Saginaw, MI.
Email: mjafferany@yahoo.com

Abstract

An open, prospective, nonrandomized study of 122 children with infantile hemangiomas aged 1 to 24 months was conducted to evaluate the effectiveness and safety of treatment with multiline laser equipment using the Nd:YAP Q-Sw/KTP emitters with the combined use of two wavelengths of 1079/540 nm. The average age of the children was (6.3 ± 0.3) months, 22 of them were boys (18.0%) and 100 were girls (82.0%). An erythometry and ultrasound examination were performed to determine the depth of the neoplasm, to assess its blood flow, and the presence and diameter of the supply vessels. Studies of these indicators were conducted for patients before and after the treatment. Laser treatment was performed on 109 patients with 119 hemangiomas. A total of 81 superficial hemangiomas underwent a short course of laser therapy (2-5 procedures) and remaining patients with 38 combined hemangiomas received a long course of laser treatment, consisting of 6 to 10 procedures. Restoration of normal color, skin relief, and the absence of scars were noted in post-treatment sample on evaluation. After the course of treatment, erythometry readings corresponded to the values of normal skin and decreased to 110 to 80 cu. Ultrasound examination showed vascular formation and feed vessels were not visualized.

KEYWORDS
childhood hemangioma, infantile hemangioma, KTP laser, Nd:YAP, skin hemangiomas, vascular

1 | INTRODUCTION

Infantile hemangiomas are the most common vascular skin pathology in children, which is seen in 2% to 5.5% of infants in the first year of life. In girls, this type of vascular neoplasm is detected 2 to 5 times more often than in boys.[1]

Some researchers believe that the wait and watch approach is justified, and infantile hemangiomas do not require treatment, since spontaneous regression of most vascular neoplasms takes place over 5 to 8 years; therefore, regular dynamic monitoring of the neoplasm during this period is enough.[2] Untimely treatment may cause complications and tumor growth continues. Therein, the underlying tissues are destroyed, jeopardizing the functions of closely located organs and significant cosmetic damage.[3-5] This happens typically in hemangiomas located on the mucous membranes of the oral cavity, in the immediate vicinity of the auricle, in the periorbital and anogenital regions, and on the hands and feet.[6] The unpredictability of "behavior" is the main characteristic of hemangiomas. For example, hemangioma of the cheek (in the form of a dot) can turn into a deep and large tumor over the course of 2 to 3 weeks.[7] Due to this unpredictability, the emphasis should be given in making decisions related to the choice of patient management (to observe or to treat?); to determine the indications for starting therapy; and the choice of the treatment method.

All hemangioma treatment methods can be classified as conservative, surgical, and combined. The surgical method is the first method that was used to treat hemangiomas. Surgical treatment of vascular tumors today can be witnessed in cases of obstruction, ulceration, large hemangiomas, as well as tumors that are not amenable to therapy by other methods. The result of this treatment method is scar formation. In some cases, sclerosing therapy is applied. When administrating the sclerosing substances, complications may occur such as ulceration with subsequent scar formation. Liquid nitrogen treatment is currently less commonly used. Cryotherapy in cosmetically functional significant areas (eg, in the area of the hands) can lead to complications such as postoperative scars, deformations of the border areas, and pigmentation disorders. Upon prescribing systemic corticosteroids in the treatment of hemangiomas in children, Keller and Patel (2015) noted temporary side effects of facial cushingozid (71%), dyspeptic symptoms (21%), fungal infections (6%), and stunted growth in children (35%).[8] Hemangiomas of complex anatomical localizations, where it is impossible to use other treatment methods, for example, the orbit or retrobulbar space, are subject to radiation treatment. In recent years, nonselective beta-blockers have begun to be used in the treatment of hemangiomas of early childhood. The most common serious side effects of systemic use of propranolol have been noted as bradycardia, hypotension, and hypoglycemia.[6] Selective photothermolysis is the method which selectively affect the vessels of the tumor without damaging the epidermis. The physical basis of this technique is the absorption of a light wave of a given length by the target structure (in the case of hemangiomas—oxyhemoglobin), followed by the conversion of light energy into heat (photothermolysis).[9] But not all laser systems meet these requirements. The laser wavelength reflects the penetration depth of the tissue.

The first laser device for the treatment of vascular skin pathology was argon. Attempts to use an argon laser to coagulate larger vessels, such as vessels of hemangiomas or telangiectasias, have shown the inefficiency of this laser at a high risk of scarring. Then, for the purpose of coagulation of dilated blood vessels, frequency-doubling neodymium lasers (532 nm), metal vapor and dye lasers (575-595 nm), diode (810-980 nm), and neodymium (1064 μm) lasers were used. Moreover, the use of radiation in the yellow-green part of the spectrum is recommended for hemangioma vessels, and infrared for larger ones. The rationale for this choice is that longer wavelength radiation is able to penetrate deeper into the skin, which allows for the coagulation of deeper and larger vessels. In other words, the radiation that is worse absorbed by the blood is chosen, which should not contribute to the selectivity of exposure. In addition, the durations of the pulses used also differ significantly from the thermal relaxation time (TRT) of the coagulated vessels. For example, The Candela "V Beam" device; wavelength 595 nm; pulse duration from 0.45 to 40 ms. The Candela "Gentle Pro Series" device; wavelength 1.064 μm; pulse duration from 0.25 to 100 ms. The Lumenis "Light Sheer INFINITY" device; wavelengths 805/1060 nm; pulse duration from 5 to 400 ms. At the same time, dilated vessels have completely different ranges of TRT, from hundreds of microseconds for angio-dysplasia to a few milliseconds for dilated veins of telangiectasia, which means that the conditions of thermal selectivity are not met. Optical selectivity is also a big question, since in this entire spectral range, melanin absorbs radiation more efficiently than hemoglobin.[5]

All laser methods are thermal, but all laser devices can cause selective heating of only dilated vessels, heating of surrounding tissues and natural vessels will also inevitably occur, which can cause necrosis, and as a result, a scar. In addition, parasitic chromophores that absorb the action of the laser are not taken into account, and in this case, the risk of destruction of surrounding tissues is large. Therapy of infantile hemangiomas is a serious problem, none of the above methods are selective and safe.[10] Given the mechanisms occurring in biological tissues irradiated with a laser, a method has been developed that significantly exceeds the classical ones in terms of selectivity: Nd:YAP Q-Sw/KTP using two wavelengths of 1079/540 nm. (Khomchenko V.V., The method of laser coagulation of blood vessels. Eurasian Patent No. 004277).

2 | MATERIALS AND METHODS

A comprehensive prospective study of patients with infantile hemangiomas was carried out in Linline Laser Cosmetology Clinic and the Department of Plastic Surgery and Cosmetology of the Institute of Additional Education of the South Ural State Medical University, Chelyabinsk, Russia. The study was approved by the ethics committee of the South Ural State Medical University No. 11 dated November 9, 2013. The study included 122 children aged 1 to 24 months: 22 of them were boys (18%), 100 were girls (82%), the gender ratio was 1:4.5. The average age of the children at the time of the examination was 5.1 ± 1.2 months: girls—5.35 ± 1.3 months, boys—4.1 ± 1.2 months.

All patients were diagnosed with infantile hemangioma. The criteria for inclusion of patients in the study were the following: (a) the presence of verified infantile hemangioma in children of the first 2 years of life; and (b) informed parental consent to participate in research and laser treatment. Photo documentation was maintained throughout the treatment process.

The exclusion criteria were: (a) active bacterial, viral, or fungal infection in the area of intended treatment; (b) acute or chronic disease in the acute stage; (c) severe infectious disease (hepatitis, HIV, syphilis); and (d) previous laser and surgical treatments of hemangiomas, and treatment with corticosteroids and beta-blockers. The study included clinical evaluation of hemangiomas, tumor localization, determination of hemangioma area, and an ultrasound. During the clinical examination of the child, the number of vascular neoplasms, color, borders, tumor surface, area, and elevation above the surface of healthy skin, pulsation during palpation, and anatomical localization were evaluated. The main criterion for evaluating the tumor was determining the size of the vascular neoplasm; calculating the area of the infantile hemangioma.

At the first treatment and in the progress after treatment, hemangiomas were photographed with a Samsung EX1 10.0 Mega Pixels digital camera under the same lighting and angle. To calculate the rate of tumor proliferation, the hemangioma area, and the ratio of its growth relative to the patient's body area in progress were determined. In addition, an erythema of the hemangiomas and symmetric healthy skin area was carried out in arbitrary units; ultrasound examination of hemangiomas to determine the depth of the neoplasm, assess its blood flow, the presence and diameter of the supply vessels. Studies of these indicators were conducted for patients before treatment and after completion of the course of therapy.

The factors affecting the choice of management and the need to start treatment are the rate of hemangioma proliferation, anatomical localization of the tumor, and the depth of tumor localization (superficial, combined, deep).[1,7]

To determine the growth of hemangiomas, the tumor area over the time course was determined. For this, a transparent film-pallet was used, drawn into squares with a side of 1 cm and 0.5 cm. The calculation of the tumor area during the initial examination was carried out by applying a film to the hemangioma and counting the sum of the squares and half of the squares covering the hemangioma, obtaining the value of S_1 (area measurement in cm^2). After 4 weeks, the area measurement was repeated and an S_2 value was obtained upon re-examination. Next, the surface area of the patient's body was determined by the formula.

$$S_{body} = \sqrt{\frac{\text{body weight} \times \text{growth}}{3600}} \times 10\,000\ (\text{Mosteller's formula, 1987}).$$

This method allows for the objectification of the growth of the tumor relative to the patient's body area.

$$\left(\frac{S_2 - S_1}{S_1} - \frac{S_{body2} - S_{body1}}{S_{body2}}\right) \times 10.$$

If the value calculated by the formula exceeds 10, then this objectively confirms the growth of the hemangioma and the need for treatment of the neoplasm.[4]

Dangerous anatomical zones of vascular tumors include the oral mucosa, auricle, periorbital region, lower back, perineum, hands, and feet. The face can be divided into two divisions: peripheral and central, the latter includes such vital areas as periorbital, nasal, and perioral (Figure 1).

Localization of the tumor in the periorbital region can cause visual impairment: lack of binocular vision, astigmatism, corneal deformities, strabismus, eyelid ptosis, amblyopia, blindness.[1] Hemangiomas in the nasal area can lead to respiratory failure and aesthetic derangements. Hemangioma in the perioral region can lead to deformation of the mouth gap, and the inability to eat (Figures 2-4).

An ultrasound examination of the hemangiomas was carried out on a digital multifunction scanner Mindray DC-3 and Toshiba Nemio XG using B-mode, color Doppler mapping (color doppler flow imaging), and energy Doppler mapping, including directional (Power, DirPower). A multifrequency linear sensor with a frequency of 5 to 10 MHz and a convex sensor with a frequency of 2 to 5 MHz were used. Based on the study, the location of the tumor, the number of supply vessels and the diameter of the vessels, and the type of vascularization were determined.

Estimating the depth of the tumor, according to the classification proposed by Mulliken and Glowacki (1982): simple (superficial), cavernous (deep), mixed (combined) isolated the clinical form for the

FIGURE 2 Deep hemangioma in the central region of the face

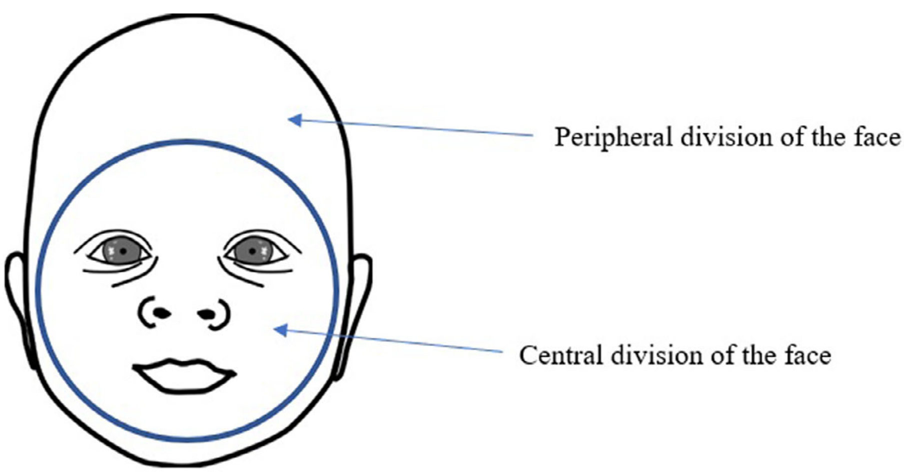

FIGURE 1 Divisions of the face

FIGURE 3 Superficial hemangioma of the central part of the face (periorbital region)

FIGURE 4 Combined hemangioma in the central part of the face (lower lip area)

TABLE 1 Localization of infantile hemangiomas

Body parts	Localization	n (%)	P
Head; N = 51 (38.6%)	Hairy part (1)	19 (37.3%)	
	Peripheral part of the face (2)	26 (51%)	$.0001_{2\text{-}3}$
	Central part of the face (3)	6 (11.7%)	$.0001_{1\text{-}3}$
Neck		0	
Torso; N = 55 (41.7%)	Front surface (4)	28 (50.9%)	$.0001_{4\text{-}6}$
	Back surface/lumbar region (5)	19/2 (34.6%/3.6%)	$.0001_{5\text{-}6}$
	Anogenital region (6)	6 (10.9%)	
Limbs; N = 26 (19.7%)	Top	14 (53.8%)	$.0001_{4\text{-}6}$
	Bottom	12 (46.2%)	$.0001_{5\text{-}6}$

TABLE 2 Clinical types of hemangiomas in the general group

No.	Clinical varieties of hemangiomas	Amount of hemangiomas	%	P
1	Superficial (I)	84	63.6	$.0001_{1\text{-}2}$
2	Combined (II)	38	28.8	$.007_{1\text{-}3}$
3	Deep (III)	10	7.6	$.005_{3\text{-}2}$
Total		132	100	

subsequent choice of treatment tactics.[11] Visual manifestations usually fit into the following clinical picture. Superficial hemangiomas had a bright red color, and exophytic growth, towering above the surface of the skin. Combined clinically look like foci in the form of blue masses with fuzzy borders, on the surface of which are red colored telangiectasia. Clinically deep vascular tumors were a bluish knot, and elastic upon palpation. During the ultrasound, mixed tumors were in the dermis and on the border with subcutaneous fat, while deep tumors were located in the subcutaneous fat, growing in the underlying tissue (Table 1).

In our study, 85 patients (64.4%) recorded rapid proliferation of a vascular tumor.

According to an ultrasound scan, out of 132 hemangiomas, 84 (63.6%) superficial hemangiomas (tumor depth less than 0.5 cm), combined tumors (tumor depth greater than 0.5 cm, but less than 1.0 cm) were revealed in 38 patients (28.8%), and deep (tumor depth greater than 1.0 cm) in 10 children (7.57%; Table 2).

The indicators obtained during the study were entered into an electronic database. Statistical data processing were carried out using the software package Statistica version 7.0. Comparison of qualitative parameters was performed using the Fisher's exact test.

3 | LASER EQUIPMENT AND TECHNOLOGY

The purpose of this technology is the creation of an artificial chromophore inside a vessel with subsequent selective coagulation of only pathological vessels, without damage to normal unexpanded vessels, and without violating the integrity of the skin. The practical implementation of laser treatment of hemangiomas was carried out on the basis of the Multiline device (Linline Medical System) using an Nd:YAP/KTP emitter. This technology is based on the following: during one pulse of the pump lamp, three trains of laser pulses are generated. The first part is a train of pulses with a radiation wavelength of 1.079 μm, which is poorly absorbed by water, hemoglobin, and melanin. Pulses have little energy and are located close to each other, which makes the result of their exposure similar to the effect of a long pulse. The result of the absorption of the radiation from this train is thermal tumescence, which squeezes blood from natural capillaries. After 100 to 150 microseconds, following the first train; the radiation of the next train of Q-Sw pulses with already significantly greater power and a wavelength of 0.54 μm, which is well absorbed by both oxyhemoglobin and deoxyhemoglobin, is supplied to the same area. The result of this absorption is the formation of a new chromophore inside the coagulated vessels. The third train, which follows immediately after the second, is a long sequence of Q-Sw pulses with a wavelength of 1.079 μm, well absorbed by the new chromophore, but poorly by water, hemoglobin, and melanin (Figure 5).

The use of Q-Sw pulses in this train allows one to further increase the absorption coefficient of the new chromophore. Due to this, the energy of the third train can be reduced, which allows for the coagulation of the vessel and the minimization of thermal damage to tissues that fall into the area of laser exposure. Unlike the classical methods of transcutaneous laser coagulation of dilated blood vessels, this method does not require additional cooling (I.I. Pikerknya and V.V. Khomchenko, "High-intensity laser in the field of medicine"). This method has such important properties, such as the absence of bleeding, sufficient painlessness, and the ability to targetedly impact a clearly defined area of integumentary tissues, the absence of significant interaction on healthy tissues.[10]

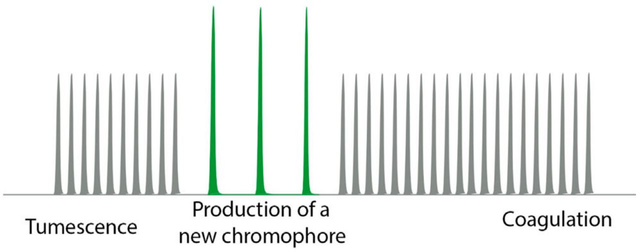

FIGURE 5 Laser pulse for selective coagulation of blood vessels

4 | PROCEDURE

During the laser procedure, topical anesthesia was not used. The procedure is painless, during which a hot tingling sensation is felt. The skin before the procedure should be clean and dry. Parameters when using a 3 mm nozzle: mode 7.07 to 38.9 J/cm^2, frequency 1 to 3 Hz; processing in scanning mode without overlapping light spots, until the tumor turns darker. Different

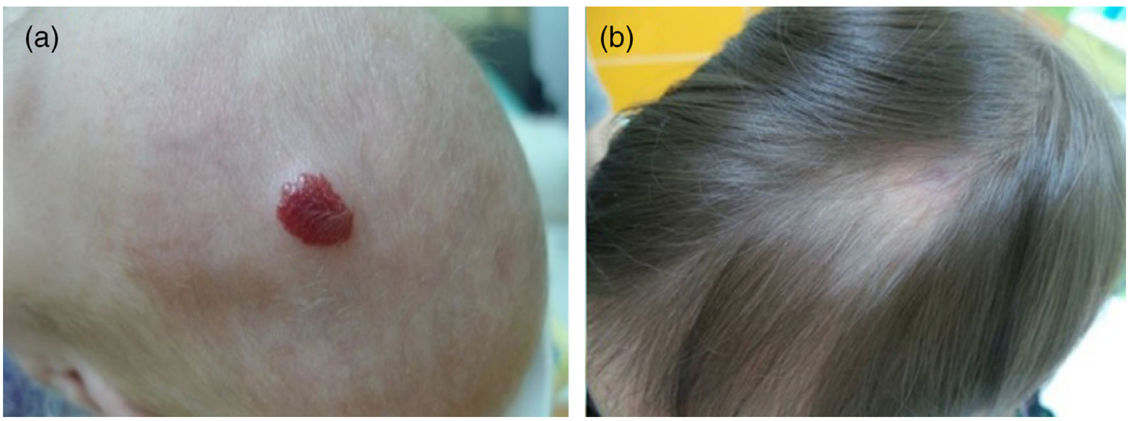

FIGURE 6 Patient D, age: 2 months. Diagnosis: combined hemangioma of the scalp. (a), Before laser treatment and, (b), after seven sessions of laser treatment

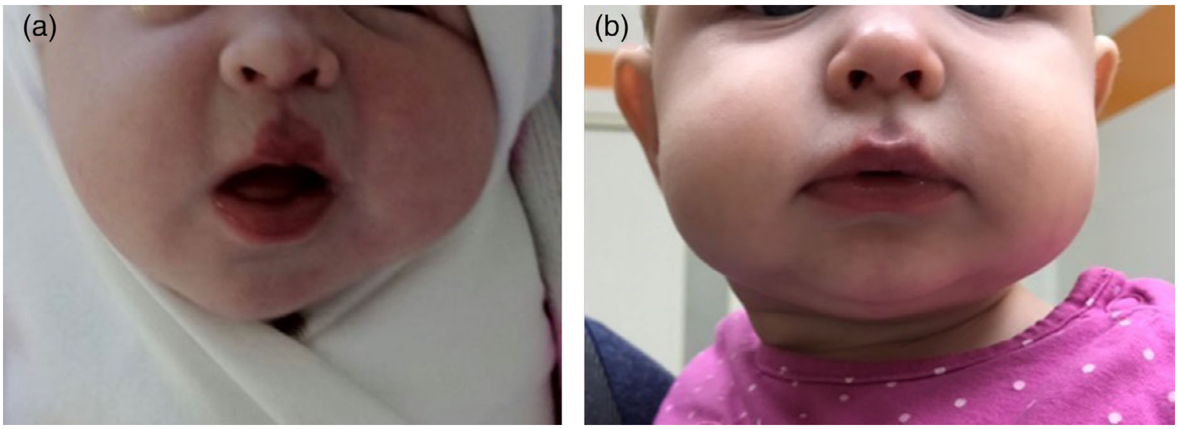

FIGURE 7 Patient U, age: 1 month. Diagnosis: superficial hemangioma of the, (a), perioral region to, (b), after four sessions of laser treatment

localization of infantile hemangiomas required the use of different energy values from minimum to maximum. The smallest values were used to treat tumors localized in the central zone of the face, anogenital region, and on the skin of the palms and soles, which is associated with the thickness of the dermis and the features of blood supply. The treatment was repeated at intervals of 2 to 8 weeks. In the progressive stage of a vascular tumor, the interval to the next laser treatment session was 2 weeks, which minimized the possibility of a relapse of the neoplasm. If the tumor was in the stabilization stage, the treatment was carried out with a longer interval, which ranged from 4 to 6 weeks. After the procedure, patients were advised to limit the use of a hot bath during the day. After the procedure, the darkening of the tumor was observed up to 5 days. There was no rehabilitation period. Special post-treatment care was not performed. With superficial hemangiomas, a short course of laser treatment was a mode of 7.07 to 14.10 J/cm^2, with a frequency of 1 to 2 Hz (1-5 procedures), with combined ones; a long course with laser energy of 14.10 to 21.20 J/cm^2, with a frequency of 2 to 3 Hz, which amounted to 6 to 10 procedures.

Side effects such as edema, hyperemia, changes in pigmentation, scars, during the course of therapy were not observed.

5 | RESULTS

A group of children selected for laser treatment, in the amount of 109 people with a total of 119 hemangiomas, underwent a laser treatment with an Nd:YAP/KTP Q-switched device with wavelengths of 1079/540 nm. In 30 (22.7%) cases, superficial hemangiomas were laser treated to accelerate involution.

We used the following criteria for the effectiveness of laser treatment of infantile hemangiomas:

- clinical (examination and palpation, area measurement);
- instrumental (erythometry, ultrasound diagnostics);

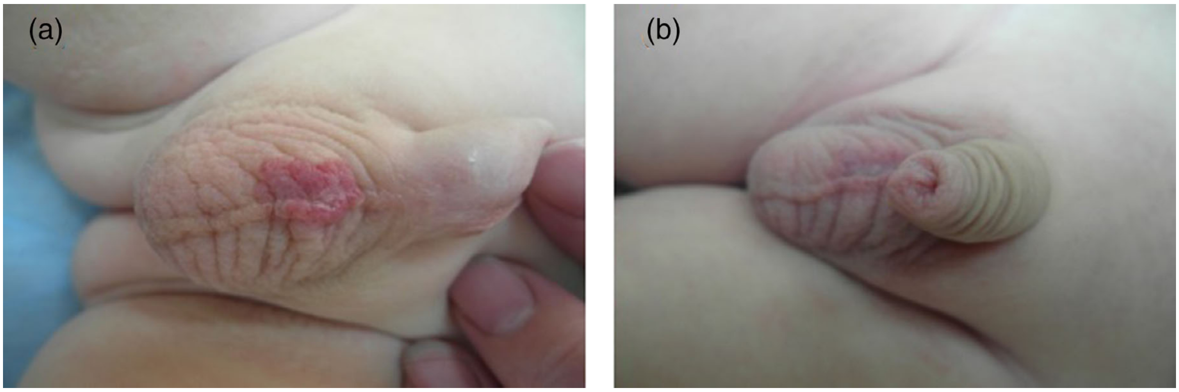

FIGURE 8 Patient K, age: 2 months. Diagnosis: combined hemangioma of early childhood scrotum area. (a), Before and, (b), after seven sessions of laser treatment

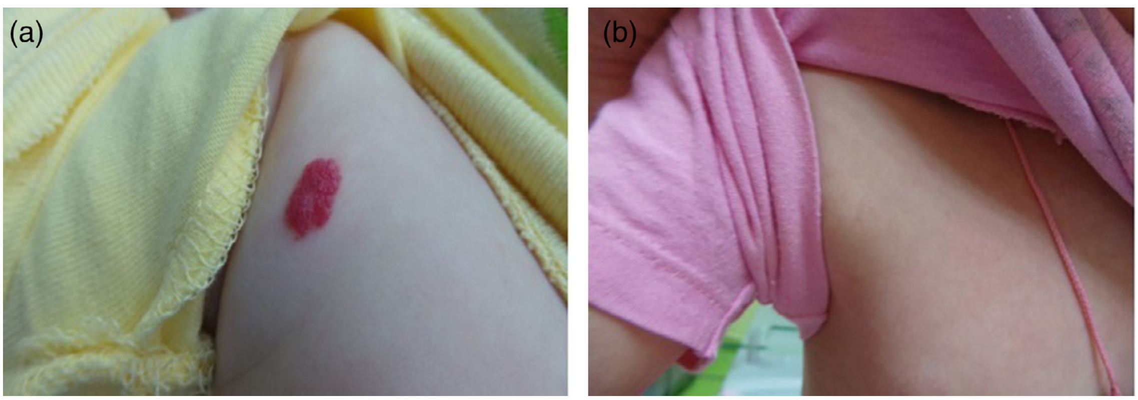

FIGURE 9 Patient M, age: 3 months. Diagnosis: superficial hemangioma of the chest area. (a), Before and, (b), after five sessions of laser treatment

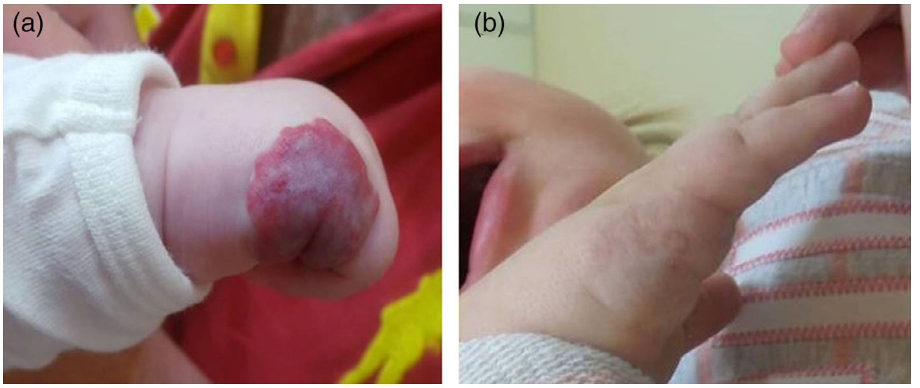

FIGURE 10 Patient E, age: 5 months. Diagnosis: combined hemangioma of the right hand. (a), Before and, (b), after 10 sessions of laser treatment

- aesthetic—a Subject Satisfaction Questionnaire for patient (parent) satisfaction (very good, good, partly good, no changes) and a categorical International Aesthetic Improvement Scale (GAIS).

Clinical evaluation showed restoration of normal color and skin relief, the absence of scars in 100% with superficial hemangiomas and in 92.1% with combined tumors. Erythometry values did not differ after treatment with a control area of the healthy skin. Ultrasound examination after completion of therapy showed the absence of blood flow, structural pathology of the dermis and hypodermis at the sites of hemangioma localization. With an objective assessment of the aesthetic, all respondents (parents) noted that their expectations from treatment were met: 97.2% of parents rated the therapeutic effect as "very good result", 2.8%—as "good result" after a course of laser treatment. None of the respondents gave a negative assessment. The average score for a medical evaluation of the result on the GAIS scale was 2.98 with a maximum of 3.0. The aesthetic assessment of treatment outcomes by parents completely coincided with the medical assessment. The results are illustrated in Figures 5 to 8.

6 | DISCUSSION

Although here are varieties of methods for the treatment of hemangioma available, there are currently no objective criteria for selecting patients for a specific treatment method, in particular for laser therapy of infantile hemangiomas with the Nd:YAP/KTP apparatus, or for evaluating the results of treatment of infantile hemangiomas. The optimal treatment regimens for infantile hemangiomas with a laser device have not been developed, taking into consideration objective clinical and instrumental characteristics of the tumor. There are no quantitative estimates of treatment outcomes for infantile hemangiomas (Figures 9 and 10).

The choice of medical treatment including dynamic observation or treatment; the possibility of complications due to expectant treatment and with inadequate therapy; and the choice of method in the treatment of children of the first year of life is still a big question. After our study, we received 97.2% of cases with a very good result. It appears that treatment of infantile hemangiomas with the Nd:YAP/KTP method is highly effective. But no result is absolute. It is worth comparing the effectiveness of treatment with other laser methods, which will serve as a separate topic for future research.

7 | CONCLUSION

We used a new method with a combined result of two long waves 1079/540 nm on multiline laser equipment using Nd:YAR Q-Sw/KTP emitters for the treatment of infantile hemangiomas. We conducted an open, prospective, nonrandomized study of 122 children with infantile hemangiomas aged 1 to 24 months. This method of laser coagulation of blood vessels has proved the selectivity of exposure to pathological dilated vessels. In a clinical evaluation after a course of treatment, restoration of normal color, skin relief, and the absence of scars were noted. After the course of treatment, erythometry readings corresponded to the values of normal skin and decreased to 110 to 80 cu. According to the ultrasound, vascular formation and feed vessels were not visualized; no changes were detected in the structures of the dermis and the hypodermis. With an objective assessment of the aesthetic result, 97.2% of parents rated the therapeutic effect as "a very good result." Assessment of treatment results on a GAIS scale was 2.98 points with a maximum of 3.0. The aesthetic assessment of treatment outcomes by parents completely coincided with the medical assessment. Side effects with laser treatment by Nd:YAP/KTP were not detected.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

ORCID

Torello Lotti https://orcid.org/0000-0003-0840-1936
Mohammad Jafferany https://orcid.org/0000-0001-6358-9068

REFERENCES

1. Spence-Shishido AA, Good WV, Baselga E. Hemangiomas and the eye. *Clin Dermatol*. 2015;33(2):170-182.
2. Durack A, Gass JK. Assessing skin disease in children. *Paediatr Child Health*. 2015;25(2):49-53.

3. Imai H, Hidaka N, Murakami T, et al. In utero sonographic findings of giant hepatic hemangioma and associated perinatal complications: a report of two cases. *J Med Ultrasound*. 2015;23(1):46-51.
4. Krema H. Primary surgical excision for pediatric orbital capillary hemangioma. *Semin Ophthalmol*. 2015;30(3):214-217.
5. Shen L, Zhou G, Zhao J. Pulsed dye laser therapy for infantile hemangiomas: a systemic review and meta-analysis. *QJM*. 2015;108(6):473-480.
6. Jadhav V, Tolat S. Dramatic response of propranolol inhemangioma: report of two cases. *Ind J Dermatol Venereol Lepr*. 2010;76(6):691-694.
7. Gey A, Ezzidine K, Diallo A, et al. Stay in NICU and infantile haemangioma development. *EADV*. 2015;29:566-573.
8. Keller RG, Patel KG. Evidence-based medicine in the treatment of infantile hemangiomas. *Facial Plast Surg Clin North Am*. 2015;23(3):373-392.
9. Ravenscroft J. Management of infantile haemangioma. *Paediatr Child Health*. 2015;25(2):60-65.
10. Pikerenya II, Khomchenko VV. Highly intensive lasers in the field of medicine [in Russian]. *Monografiya Minsk: BelMAPO*. 2017; 130-144.
11. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: A classification based on endothelial characteristics. *Plast Reconstr Surg*. 1982; 69:412-422.

How to cite this article: Trapeznikova TV, Pisklakova TP, Khomchenko VV, Kalashnikova NG, Lotti T, Jafferany M. New technology for coagulation of dilated vessels using the combined effects of several modes of generation and wavelengths in one laser pulse for the treatment of pediatric hemangiomas: Open prospective study. *Dermatologic Therapy*. 2020;e13341. https://doi.org/10.1111/dth.13341