

Transcutaneous laser treatment of leg veins

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Received: 17 September 2013 / Accepted: 24 October 2013 / Published online: 13 November 2013
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Abstract Leg telangiectasias and reticular veins are a common complaint affecting more than 80 % of the population to some extent. To date, the gold standard remains sclerotherapy for most patients. However, there may be some specific situations, where sclerotherapy is contraindicated such as needle phobia, allergy to certain sclerosing agents, and the presence of vessels smaller than the diameter of a 30-gauge needle (including telangiectatic matting). In these cases, transcutaneous laser therapy is a valuable alternative. Currently, different laser modalities have been proposed for the management of leg veins. The aim of this article is to present an overview of the basic principles of transcutaneous laser therapy of leg veins and to review the existing literature on this subject, including the most recent developments. The 532-nm potassium titanyl phosphate (KTP) laser, the 585–600-nm pulsed dye laser, the 755-nm alexandrite laser, various 800–983-nm diode lasers, and the 1,064-nm neodymium yttrium–aluminum–garnet (Nd:YAG) laser and various intense pulsed light sources

have been investigated for this indication. The KTP and pulsed dye laser are an effective treatment option for small vessels (<1 mm). The side effect profile is usually favorable to that of longer wavelength modalities. For larger veins, the use of a longer wavelength is required. According to the scarce evidence available, the Nd:YAG laser produces better clinical results than the alexandrite and diode laser. Penetration depth is high, whereas absorption by melanin is low, making the Nd:YAG laser suitable for the treatment of larger and deeply located veins and for the treatment of patients with dark skin types. Clinical outcome of Nd:YAG laser therapy approximates that of sclerotherapy, although the latter is associated with less pain. New developments include (1) the use of a nonuniform pulse sequence or a dual-wavelength modality, inducing methemoglobin formation and enhancing the optical absorption properties of the target structure, (2) pulse stacking and multiple pass laser treatment, (3) combination of laser therapy with sclerotherapy or radiofrequency, and (4) indocyanin green enhanced laser therapy. Future studies will have to confirm the role of these developments in the treatment of leg veins. The literature still lacks double-blind controlled clinical trials comparing the different laser modalities with each other and with sclerotherapy. Such trials should be the focus of future research.

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Keywords Laser · Leg vein · Leg vessel · Vascular lesions ·
Telangiectasia · Lower extremity

Introduction

Leg telangiectasias and reticular veins are a common cosmetic complaint, affecting more than 80 % of the population to some extent [1–3]. Clinical and experimental evidence suggests that valvular incompetence leading to a rise in venous pressure and peripheral vein wall weakness in the superficial venous system is responsible for the development of varicose veins,

reticular veins, and telangiectasias, although these may not be the only mechanisms [4]. The lesions are generally believed to be caused by multiple factors, including genetic predisposition, hormonal factors, gravity, occupation, pregnancy, and trauma, becoming increasingly apparent with age [1, 5].

Therapeutic options include sclerotherapy, surgical procedures, and treatment with different laser systems [6, 7]. Leg telangiectasias are as a rule more difficult to treat than facial telangiectasias [8]. Sclerotherapy is typically considered the first line of treatment for leg veins smaller than 4 mm in diameter. Frequent side effects are pain and hyperpigmentation, caused by hemosiderin deposition through extravasated erythrocytes or by postinflammatory hypermelanosis. Rarely, systemic allergic reactions, skin necrosis, and thrombophlebitis may occur [6, 7, 9]. Moreover, patients with needle phobia may have aversions to this invasive procedure [10, 11]. Lasers have been used to treat dilated leg veins since the 1970s [12, 13]. Lasers have some theoretical advantages compared with sclerotherapy for treating leg telangiectasias. For example, the risk of hemosiderin deposition would be expected to be lower, as blood vessels are effectively coagulated, preventing inflammation and extravasation of erythrocytes. Early treatments used a variety of wavelengths and radiant exposures resulting in lack of vascular selectivity and thermal confinement leading to unacceptable results, hyperpigmentation, and scarring in many cases [14]. In the early laser era, especially argon laser modalities were frequently used in the treatment of leg telangiectasias [12, 13, 15].

In the 1980s, Anderson and Parrish introduced the theory of selective photothermolysis. With this technique, blood vessels are selectively obliterated while sparing the surrounding tissue based on three essential requirements: (1) a wavelength that penetrates deeply enough and is preferentially absorbed by hemoglobin, (2) an exposure duration (pulse width; pulse duration) less than or equal to the thermal relaxation time of the target structure, and (3) sufficient radiant exposure to cause irreversible damage to the target structure [16]. Nowadays, all vascular laser modalities are based on this principle.

In this article, we review the literature on transcutaneous laser treatment options of pathologically dilated veins originating from the cutaneous microcirculation of the lower extremity. We discuss the efficacy of various laser modalities and settings as compared to other therapies such as sclerotherapy. Furthermore, we present a number of general recommendations that should aid the clinician in his choice for the appropriate therapy for this disorder.

Anatomy and pathology of the lower extremity cutaneous microcirculation

A basic understanding of the anatomy of the cutaneous microcirculation and its pathological mechanisms is mandatory

for clinicians treating abnormalities of the small vasculature of the lower extremities, as diameter and localization of the affected vessel largely determine the treatment of choice.

Essentially, the cutaneous microcirculation consists of two horizontal plexuses. The superficial plexus is formed by arterioles, venules, and capillaries located in the papillary dermis 1–1.5 mm under the skin surface, whereas the deep plexus is found at the dermal subcutaneous interface and is directly interconnected to the superficial plexus by vertically oriented vessels. The deep plexus is connected to perforating vessels from the underlying muscle. Hence, the veins of the deep plexus drain on the veins of the macrocirculation of both the superficial compartment, including the great and small saphenous vein, and the deep compartment [17, 18].

Pathological dilation of lower extremity veins can be explained by abnormalities in the organization and ultrastructure of the cutaneous microvasculature rather than by neovascularization [19]. Histological examination demonstrates dilated blood vessels in a normal dermal stroma with a single endothelial cell lining, limited muscularis, and adventitia [20].

Pathologically dilated vessels of the venous microcirculation can be subdivided in telangiectasias (≤ 0.3 mm, < 1 mm according to some authors [4]), venulectasias (0.4–2 mm), and reticular veins (> 2 mm). A distinct pathological feature is telangiectatic matting, which is defined as a fine network of dilated telangiectatic veins and is often the result of an earlier treatment, such as sclerotherapy [21]. Telangiectasias may be red or blue depending on the dominance of an arteriolar or venous component respectively [22]. Telangiectasias and venulectasias originate from the superficial plexus. Reticular veins, however, are situated in the deep dermis and subcutis and have a blue appearance [4, 21]. Reticular veins often have an insufficient connection with the venous system [23]. Dilated leg veins often originate from a so called feeder vein, a dilated draining vein that causes an increase in hydrostatic pressure in all of its tributaries [24]. Treatment of the feeder vein is crucial in the prevention of recurrences. When considering laser treatment, these characteristics are of pivotal importance in the choice of the laser modality and settings.

Parameters and settings

The first consideration in the selection of a laser is to determine the spectral absorption peaks of the target chromophore and the penetration depth of the chosen wavelength. Once the appropriate laser is selected, it is important to choose the correct settings. These include the pulse duration, radiant exposure, spot size, and cooling parameters.

Choosing the appropriate settings is complex. Direct skin responses that result from the laser tissue interaction offer the opportunity to adjust the laser settings according to a set of wanted clinical endpoints. Either the occurrence of

an intravascular darkening resulting from coagulation or immediate disappearance of the vein should be visible. However, complete immediate disappearance of the vein can also be based on a temporary laser-induced vasospasm, while the vein remains patent. Larger telangiectasias and reticular veins do not vanish immediately but slowly over several months after treatment. Nevertheless, directly after the laser treatment, a cessation of refilling of the treated vessel should be observed. If refilling is still present, laser settings are presumably not sufficiently aggressive or multiple passes are required. On the other hand, if persistent purpura is seen, there is a considerable risk of hemosiderin deposition and subsequent hyperpigmentation. These observations implicate that the reaction of the treated skin should be carefully observed immediately after deliverance of a test pulse, before treating the entire lesion [21]. A grayish appearance observed immediately after laser treatment implicates epidermal necrosis and should therefore be avoided.

Wavelength

Selective photothermolysis begins with local absorption of light energy in target chromophores such as hemoglobin in vascular lesions or melanin in pigmented lesions. Oxyhemoglobin is usually the target chromophore when treating vascular lesions, and has major absorption peaks at 410, 540, and 577 nm with smaller peaks at 920–940 nm in its absorption spectrum (Fig. 1) [25–28]. The lasers used to treat vascular lesions have wavelengths that are well absorbed by hemoglobin. However, one should be aware of concurrent absorption by melanin, which is maximal at short wavelengths [25]. This may result in unwanted clinical effects such as hypopigmentation, especially when treating persons with dark skin types. As melanin in the normally pigmented skin is situated in the epidermis, overheating of the melanosomes may even induce epidermal necrosis, eliciting clinical blistering or at the long term even scarring.

In addition, penetration depth is also mainly determined by wavelength (Fig. 2). As a rule, longer wavelengths have less scattering and a larger penetration depth [25, 27]. Theoretically, longer wavelengths may therefore be preferred for deeper and larger vascular lesions such as reticular veins, whereas shorter wavelengths may be suited for superficial vascular lesions such as telangiectasias.

Pulse duration

Another important parameter is pulse duration. Ideally, pulse duration is equal to or only slightly larger than the thermal relaxation time of the targeted structure. Essentially, the thermal relaxation time is defined as the time required for the heated tissue to lose about half of its heat. It is proportional to the square of the target's diameter. When pulses longer than

the thermal relaxation time are used, energy transfer to surrounding nonvascular structures will occur, causing nonspecific thermal damage. Contrarily, when very short pulses are used, energy is delivered to the target faster than it can diffuse away, ultimately leading to formation of an explosive vapor bubble, rupture of vascular structures, and extravasation of erythrocytes [29]. For noncapillary vessels, selective photothermolysis requires millisecond domain pulses [30, 31]. With exposure durations in the millisecond domain, damage to smaller vessels (capillaries) is reduced or avoided, as they cool faster than the large veins. As the diameter of leg veins may vary considerable in a single patient, appropriate changes to the pulse duration are often required during the treatment.

Radiant exposure

The lasers should be capable of delivering enough radiant exposure (often, but incorrectly, referred to as fluence, as the fluence is the total amount of light energy per cross sectional area *inside* the tissue [32]) that is defined as the incident laser energy per unit area. A higher radiant exposure will be required for deeply located target vessels and for weakly absorbed wavelengths. The use of higher radiant exposures, however, will inevitably lead to more collateral thermal damage [33].

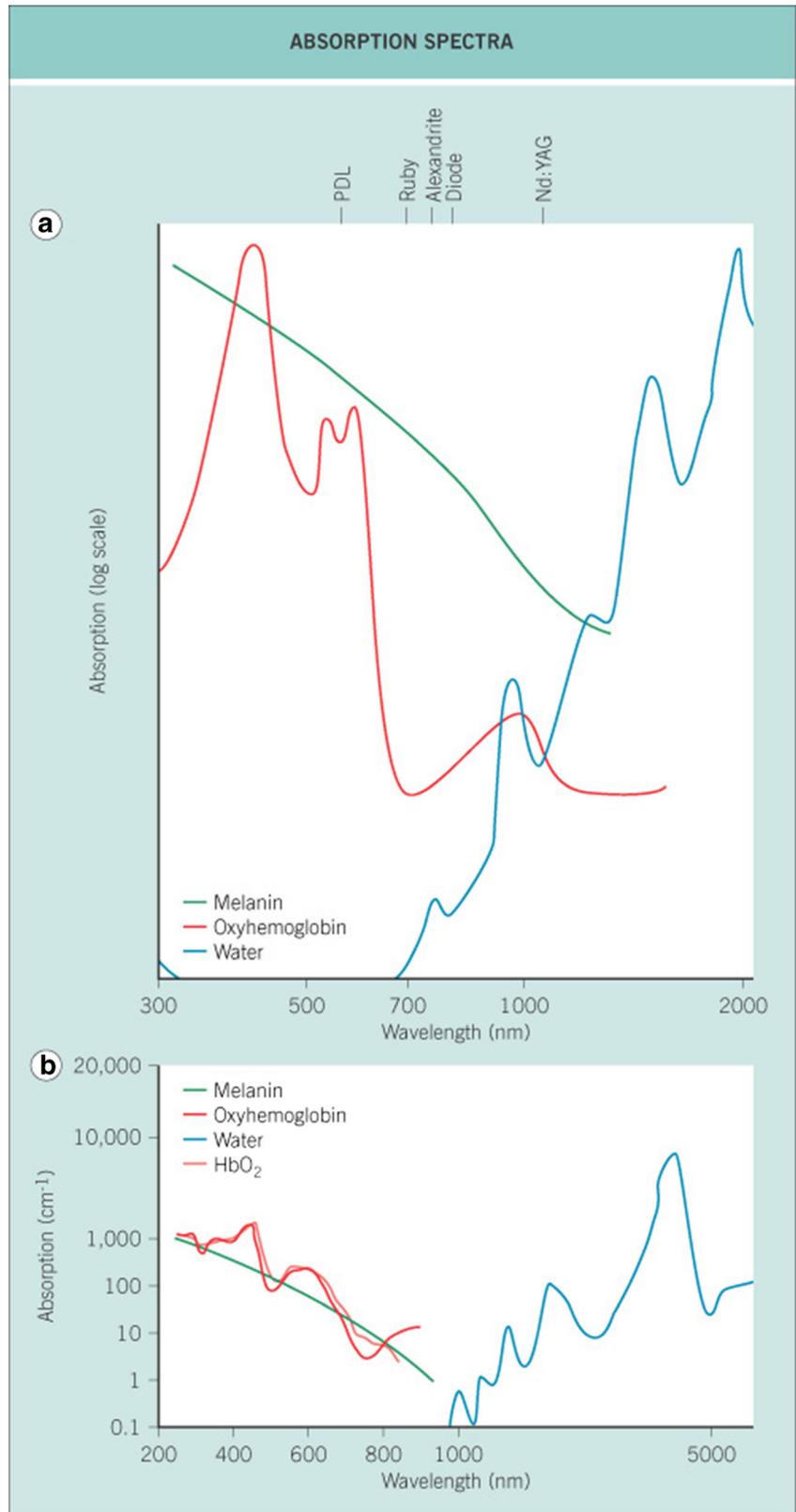
Spot size

Spot size should be adjusted to the diameter and the depth of the target vessel to minimize surrounding damage. Larger spot sizes tend to have deeper dermal penetration at equal radiant exposure values without increasing epidermal damage.

Cooling

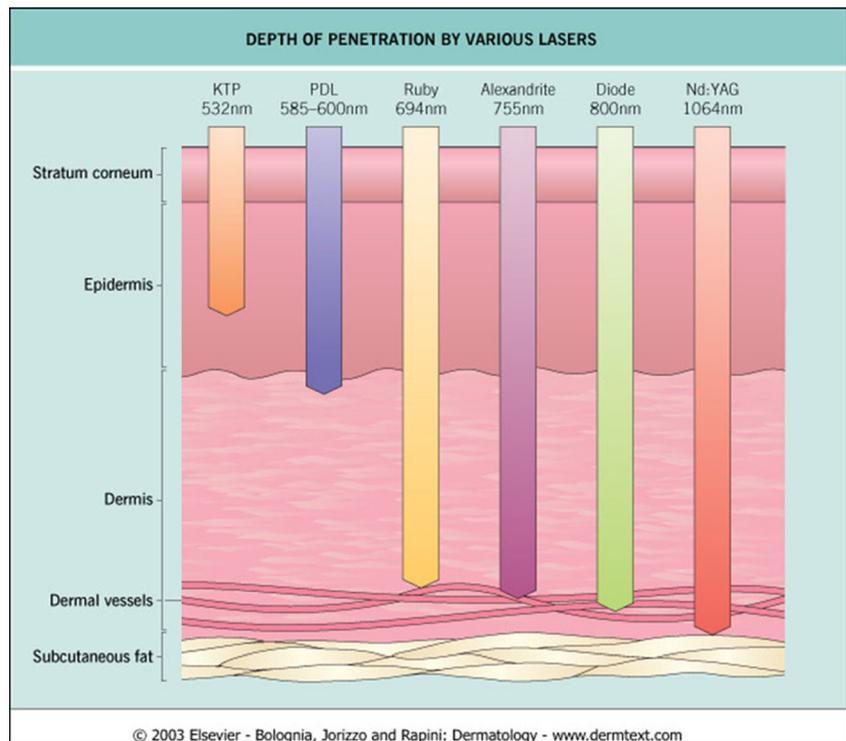
In the treatment of all vascular lesions, cooling of the skin surface is crucial to minimize epidermal damage and allow high radiant exposure. Since epidermal melanin and hemoglobin are competing chromophores for laser absorption, epidermal thermal damage may occur, depending on the epidermal melanin content. Treatment at high radiant exposure in patients with a dark skin type or excessive suntan can induce side effects varying from hypopigmentation to epidermal necrosis [34, 35]. On the other hand, sustained cooling using ice cubes, chilled water, or cold air devices will also reduce the core temperature of the target structure, compromising treatment efficacy. Moreover, undercooling of the epidermis may occur. Air cooling has the advantage that the device can be used for different procedures and for large areas of skin. However, caution is mandatory especially in patients with darker skin types as postinflammatory hyperpigmentation due to air cooling has been reported [36].

Fig. 1 Absorption spectra of various chromophores. (This figure was published in *Dermatology*, Bologna JL, Jorizzo JL, Rapini RP, p. 2146, Copyright Mosby Elsevier, 2003)



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Fig. 2 Depth of penetration by various lasers. (This figure was published in *Dermatology*, Bologna JL, Jorizzo JL, Rapini RP, p. 2148, Copyright Mosby Elsevier, 2003)



Because of the limitations of sustained cooling methods, various dynamic cooling systems have been developed. Cryogen cooling with a nitrogen or tetrafluoroethane spurt is widely used. When a cryogen spurt is applied to the skin surface for an appropriately short period of time (on the order of tens of milliseconds), the cooling remains localized in the epidermis [34, 37, 38]. A significant reduction in pain score can be achieved when adequate dynamic cooling is used [39, 40].

Another frequently used cooling system is contact cooling [41], consisting of a cooled transparent sapphire contact plate that is placed on the skin during laser treatment. One should be cautious not to compress the vascular abnormality too much, removing nearly all target chromophore from the treated skin.

Technique

The practical implementation of the laser treatment varies upon the chosen laser modality. Laser manuals supplied by manufacturers often contain some recommendations regarding the technical approach, but laser strategy is highly dependent on wavelength, laser settings, and patient characteristics. Generally, when using short wavelength modalities (<600 nm), a considerable overlap of 10–30 % between subsequent pulses is acceptable because radiant exposure is usually relatively low. Due to the Gaussian profile of the laser beam, the absolute energy in the periphery of the spot is lower than in the center, leading to a dotted

appearance on the skin and possibly incomplete clearing of the leg vein, if the spots are too far apart. At longer wavelengths, higher radiant exposure is required. In this situation, overlap between pulses should be avoided, due to the risk of bulk tissue heating and necrosis.

Recent studies on the effect of irradiated vessel length demonstrate that the spatial extent of photocoagulation has considerable influence on the long-term removal of coagulated blood vessels. When only a short segment of a blood vessel was photocoagulated, reperfusion of the blood vessel was consistently observed; when the length of the coagulated segment was increased, the probability of long-term removal increased substantially [42].

Preoperative evaluation

A medical history and physical examination are important initial steps in the preoperative evaluation. Factors such as suntan must be evaluated before laser treatment. To reduce pigment-related problems, patients should be counseled that they should prevent tanning by means of adequate sun protection, e.g., sun protective factor, before and until several weeks after laser therapy, as laser treatment of the tanned skin may increase the risk of laser-induced pigment alterations. Some medication may increase the risk of scarring (e.g., isotretinoin) or purpura (e.g., nonsteroidal anti-inflammatory drugs and anticoagulants).

During the physical examination, the physician should evaluate the type and size of the leg veins. The patient should be examined in an upright position to better identify patterns of telangiectasias, reticular veins, and varicose veins.

In addition, Duplex ultrasound of both the superficial and deep venous system might be desirable, as 26 % of patients with telangiectasias have some form of trunk varicose veins (vs. 14 % of patients without telangiectasias) [3]. In these cases, appropriate treatment of the trunk varicose veins may be considered, such as endovenous thermal ablation (laser or radiofrequency based), (foam) sclerotherapy, and (rarely) surgery. For theoretical reasons, it is generally assumed that telangiectasias and reticular veins tend to recur if the causative mechanism of increased venous pressure in the larger veins is left untreated, although to our knowledge, this has never been confirmed in clinical studies. It has been shown that incompetence of the third generation tributaries of the great saphenous vein are associated with reflux in the microvenous network of the skin, especially in the presence of incompetence of the great saphenous vein itself.[43] An important group, however, is formed by the patients with essential telangiectasias, where no causative mechanism is identified. These telangiectasias are usually more progressive and show a higher tendency to recur. In conclusion, knowledge about the causative mechanisms of dilated leg veins may give important prognostic information. Finally, as previously discussed, identification of the feeder vein is a crucial part of the preoperative assessment [24].

Types of vascular lasers and light sources

There are currently many laser devices available, and different wavelengths have been employed to treat leg veins: the 532-nm potassium titanyl phosphate (KTP) laser, the 585–600-nm pulsed dye laser, the 755-nm alexandrite laser, various 800–983-nm diode lasers, and the 1,064-nm neodymium yttrium–aluminum–garnet (Nd:YAG) laser. In addition, intense pulsed light has been studied in the treatment of leg veins. Recently, lasers and light sources have emerged that combine two different lasers or light/energy sources. Below, the various lasers and light sources are discussed separately in detail. All laser modalities discussed in this article are long pulsed (i.e., have millisecond range pulses) and should not be confused with very short pulsed quality-switched (Q-switched) lasers with the same wavelength.

532-nm KTP laser

The KTP laser uses an Nd:YAG crystal to produce light that is passed through a KTP crystal that frequency doubles the initial wavelength of 1,064 to 532-nm.

At 532 nm, absorption is very high not only for oxyhemoglobin but also for melanin (Fig. 1), whereas penetration is <1 mm (Fig. 2). High absorption by melanin limits the use of this laser modality in dark skinned people, as there is a substantial risk of hypopigmentation [44].

According to the literature, KTP laser therapy is mainly effective in the treatment of leg veins smaller than 1 mm in diameter [44–48]. Only few studies investigated the efficacy of the KTP laser in the treatment of larger veins. Massey and Katz report good results in veins of 1–2 mm in diameter after two treatment sessions [49]. Other authors, however, report no improvement at all after three sessions [50, 51]. In the existing studies, laser settings show a wide heterogeneity. Pulse durations range from 10 to 100 ms, spot sizes range from 0.75 to 5 mm, and radiant exposure ranges from 12 to 38 J/cm². Moreover, in some studies, multiple passes or stacked pulses were applied [44, 45].

In the treatment of veins smaller than 1 mm in diameter, KTP laser therapy is slightly less effective than Nd:YAG laser therapy, but as a result of the more favorable side effect profile, the KTP laser is often preferred by patients [50]. The KTP laser is also considered slightly less effective than the 595 nm pulsed dye laser, but treatment with the pulsed dye laser is more painful and is more frequently associated with the development of purpura [45, 46].

585–600-nm pulsed dye laser

Pulsed dye lasers use a rhodamine dye that is dissolved in a solvent and pumped by a flashlamp. Pulsed dye lasers have been proven safe and effective in the treatment of a variety of vascular lesions, including port wine stains [52]. Various modalities are available with slight variations in wavelengths. Absorption by oxyhemoglobin is significantly lower than at 532 nm (Fig. 1). Absorption by melanin is also lower than for the KTP laser, but still much higher than for example for the Nd:YAG laser. In the literature, transient hypopigmentation is reported in a minority of cases [53–55]. Penetration depth is approximately 1.25 mm (Fig. 2). In modern pulsed dye laser devices, various differently shaped tips are available. Beside the classic tip producing a round beam profile, ovally shaped tips have been specifically developed for the treatment of long and narrow blood vessels.

As the KTP laser, the pulsed dye laser is most effective in veins smaller than 1 mm in diameter. There is limited evidence that efficacy drops when veins larger than 1 mm in diameter are treated [56]. There is no consensus among authors regarding laser settings. Most authors used a relatively short pulse duration (1.5 ms), but other authors proclaim that pulse duration should be dependent on target vessel size and use pulse durations up to 20 ms for larger veins. One study showed no significant difference in clinical outcome between a 1.5- and 4-ms pulse duration [57]. With

regard to side effects, longer pulse durations are favorable, as they result in less purpura, postinflammatory hyperpigmentation, and hemosiderin deposition. Radiant exposure varies from 15 to 24 J/cm² [40, 53–56].

In the few comparative studies conducted so far, the pulsed dye laser proved to be slightly superior to the KTP laser in the removal of leg veins. A minor side effect that is occasionally seen after pulsed dye laser but not after KTP laser treatment is the formation of persistent purpura [45, 46]. In order to decrease the frequency of these purpura, longer pulse durations or lower radiant exposure may be used.

755-nm alexandrite laser

The 755-nm laser uses an alexandrite crystal and has a relatively high absorption coefficient for deoxyhemoglobin, but absolute absorption by both oxyhemoglobin and deoxyhemoglobin is only a small fraction of the absorption of the wavelengths produced by KTP and pulsed dye lasers (Fig. 1). Absorption by melanin is higher than absorption by hemoglobin, limiting the use of this laser in dark skin types. It is primarily used for laser hair removal. Its main advantage is its large penetration depth, which can reach up to 2.5–3 mm (Fig. 2). These characteristics make this laser useful for various deeper and more resistant vascular lesions, containing a large proportion of deoxygenated hemoglobin. Due to the relatively low absorption by oxyhemoglobin and the selective absorption by deoxyhemoglobin, arteries are unlikely to be targeted by this laser, which might be an advantage above other laser modalities with a high penetration depth, such as the Nd:YAG laser [58].

Because of the relatively low absorption coefficient, alexandrite lasers are primarily suitable for the treatment of veins larger than about 0.5 mm [59, 60]. Treatment of smaller vessels requires a radiant exposure that will inevitably lead to epidermal damage, as a result of absorption by melanin [60]. Usually, pulse durations of more than 3 ms are used, as shorter pulse durations are also associated with epidermal damage, especially in patients with skin type III or higher. Mean optimal radiant exposure is approximately 90 J/cm² in light skin types, depending on the characteristics of the vessel, while larger spot sizes, e.g., 6 mm, generate more response [60].

800–983-nm diode laser

Multiple diode lasers are now available, and different systems can emit infrared light at a variety of wavelengths, including 800, 810, 940, and 983 nm. These wavelengths are situated on both sides of the third peak in the oxyhemoglobin absorption curve (Fig. 1). Above 900 nm, absorption by melanin is lower

than absorption by oxyhemoglobin. This makes diode lasers a safer treatment option for patients with darker skin types than the alexandrite laser. With increasing wavelength, penetration depth increases.

As the alexandrite laser, the various diode lasers are generally used for the treatment of larger vessels, which contain more target chromophore (hemoglobin) and are located deeper in the dermis [61, 62]. In a study by Trelles and colleagues [61], veins with a diameter of 3–4 mm showed the most response. Laser settings are dependent on the chosen wavelength. No uniform recommendations can be given because of the large variety of available laser systems, operating at different wavelengths. Pulse duration is normally chosen in the order of tens to hundreds of milliseconds. Most studies report radiant exposures of several hundreds of Joules per square centimeter.

Compared to the 1,064-nm Nd:YAG and alexandrite laser, the 810-nm diode laser produces less predictable results and less clearance of leg veins up to 3 mm in diameter in a comparative study by Eremia and colleagues [63]. However, it proved to be a safer treatment option in patients with skin types up to IV compared to the alexandrite laser. It should be mentioned though that, in this study, relatively short pulse durations for the alexandrite laser were used, which may have increased the risk of side effects [63].

1,064-nm Nd:YAG laser

This laser uses an Nd:YAG crystal in order to produce light at a wavelength of 1,064 nm and operates at a peak of oxyhemoglobin absorption. Absorption by melanin at this wavelength is lower than for any other laser type used for vascular procedures (Fig. 1). Nd:YAG laser treatment is therefore supposed to be especially effective and safe in darker skin types. At 1,064 nm, penetration depth is at its peak at more than 4 mm (Fig. 2). This makes the Nd:YAG laser a suitable treatment modality for deeply located veins.

Of all vascular lasers used for the treatment of leg veins, the 1,064-nm Nd:YAG laser has been most extensively studied. Results (patient and physician reported) are believed to be better in larger veins (>2 mm), but good results in smaller veins have also been reported [50, 64, 65]. However, these larger veins can normally also be treated by sclerotherapy, which is regarded the gold standard. Various studies with an inpatient design have been conducted comparing Nd:YAG laser treatment to sclerotherapy. Clinical improvement up to 3 months after either treatment modality is comparable or slightly in favor of Nd:YAG laser therapy, but the existing studies are consequent in their conclusion that laser therapy is more painful and is associated with less favorable patients' satisfaction scores. One study showed better clearance following sclerotherapy [11]. Side effects such as hyperpigmentation or telangiectatic matting may be seen after both treatments [66–68].

There are only few studies comparing the efficacy of the Nd:YAG laser with other laser modalities. As expected on a theoretical basis, the Nd:YAG laser gives superior clinical improvement in larger veins (>1 mm) compared to the KTP laser, but also smaller vessels have shown to respond better to the former laser. On the other hand, Nd:YAG laser treatment is associated with higher pain scores and a higher risk of postinflammatory hyperpigmentation [50]. In a study comparing the clinical efficacy of Nd:YAG, alexandrite, and diode laser, results were clearly in favor of the Nd:YAG laser. However, these data should be interpreted with caution, as the results are not corrected for target vessel diameter. The Nd:YAG laser was considered safer than the alexandrite laser regarding the risk of telangiectatic matting [63]. In the only study comparing Nd:YAG laser and IPL, both patient and physician reported clinical outcomes were in favor of the Nd:YAG laser [69].

It should be mentioned though that, in all comparative studies, laser parameters such as radiant exposure, pulse duration, and spot size were never the same for the compared laser modalities. Instead, the authors usually chose the laser parameters that they supposed to be optimal based on their clinical experience and the immediate reaction of the skin. This design interferes with the assessment of the purely technical capability of different laser modalities, although it may give a more realistic reflection of routine clinical practice.

When treating leg veins with the Nd:YAG laser, the use of a relatively long pulse duration (≥ 40 ms) is generally recommended, as shorter pulse lengths are associated with the occurrence of extravasation of erythrocytes and hence hemosiderin deposition [70]. As for all laser modalities, laser settings should always depend on target vessel size, color, and skin type. In 2003, Sadick [71] proposed a number of recommendations on laser settings, using spot sizes varying from 1.5 to 3 mm, radiant exposures varying from 250 to 600 J/cm² and pulse widths varying from 30 to 60 ms. Larger spot sizes may be even more effective for some indications, but will cause the procedure to be more painful.

Recurrence of dilated leg veins after treatment with the Nd:YAG laser is infrequent. After 1 year, <10 % of leg veins tend to recur, according to the available literature [72, 73]. In other patients, histological evidence of thrombus recanalization was found 6 months after laser treatment, without clinical signs of recurrence [73].

Intense pulsed light

Intense pulsed light systems use a flashlamp that emits high intensity noncoherent and polychromatic broad-spectrum light (from 500 to 1,200 nm). The light is emitted in pulses with various pulse durations and intervals in a large rectangular spot of up to 1 × 4 cm. Various cutoff filters can be used to

exclude certain wavelengths. IPL devices are commonly used with the 550 and 570 nm filters to deliver primarily yellow and red light, with a minor component of near-infrared light. The use of multiple wavelengths implies a significant risk of damaging nonvascular structures. However, IPL sources are widely used in clinical practice, and specialized clinics have a wide experience with this treatment. Clinical evidence for IPL in the treatment of leg veins is scarce but especially small vessels are believed to respond well to IPL treatment. In a multicenter trial of 159 patients, Goldman and Eckhouse [74] reported 90 % clearance rate with vessels smaller than 0.2 mm and 80 % clearance rate with vessels 0.2–1 mm in diameter. Schroeter et al. reported immediate clearing in 73.6 % of patients and in 84.3 % of patients after 4 weeks [75].

Additional considerations and recent developments

In 2003, a theory was proposed by Mordon et al., suggesting induction of methemoglobin (Met-Hb) formation in the target vein after irradiation with a laser. In the near infrared, the optical absorption of Met-Hb is three to four times higher than the other chemical constituents of blood. Consequently, as the first laser pulse alters the optical characteristics of the heme molecule in the blood vessel, more efficient absorption is induced for the subsequent the near-infrared pulses [76]. In a study evaluating the clinical efficacy for leg veins of using a nonuniform pulse sequence of three consecutive 1,064-nm pulses, results are similar or superior to those reported in the literature on 1,064 nm Nd:YAG lasers alone [76]. Based on this principle, a dual wavelength laser was also developed with sequential wavelength delivery: 595 nm from a pulsed dye laser (PDL) followed by 1,064 nm from a Nd:YAG laser. Due to an alteration of the blood's absorption characteristics by PDL, lower treatment fluences of the Nd:YAG laser can be used. These dual wavelength laser modalities (e.g., 585 and 1,064 nm) have been reported to be effective in the treatment of leg veins, although veins smaller than 1 mm are thought to be more refractory to this treatment [77]. However, the additional value over single wavelength treatment has never been established.

Another new approach is the application of multiple stacked pulses to increase efficacy of a laser treatment: while using a low radiant exposure per pulse, as a series of stacked low-energy pulses may achieve the energy required for vessel obliteration without excessive heat propagation to the surrounding tissue. Hereby, pain and collateral thermal damage to the surrounding tissue are supposed to be minimized. When using a low radiant exposure per pulse, up to eight stacked pulses can be applied. Good results using the pulse stacking technique have been achieved in both small and large vessels with the KTP, the Nd:YAG, and the 800-nm

diode laser [44, 61, 76]. A similar approach is the treatment in multiple low radiant exposure passes, where an area of skin is treated multiple times during one treatment session [47, 48, 78–80]. Caution should be given when considering pulse stacking or multiple passes as the treated area may be at risk of bulk heating. Cooling during delivery of the multiple pulses or passes significantly reduces this risk.

In addition to these techniques based on the application of multiple pulses, several combination therapies have been investigated. The combination of sclerotherapy followed by Nd:YAG laser treatment has been investigated but results are contradictory [67, 81]. When using the combination of these therapies, a low radiant exposure is thought to be sufficient [81]. Contrarily, combination of pulsed dye laser and sclerotherapy is of no additional value, but still does give all the complications associated with sclerotherapy [82]. Furthermore, a number of devices have been developed enabling combined treatment with diode laser and radiofrequency. Some good results have been reported, but studies comparing this combination with laser therapy alone are lacking [83–85].

More recently, a new paradigm was introduced in the treatment of leg veins, as Shafirstein and colleagues simulated enhanced efficacy of the alexandrite and diode laser after intravenous injection of indocyanine green in a mathematical model. When dissolved in plasma, the absorption spectrum of indocyanine green exhibits a strong absorption band from 700 to 801 nm. Thus, systemic administration of indocyanin green shortly before laser treatment at the appropriate wavelength improves selective absorption and hence coagulation of the blood vessel. According to this model, the additional rise in intravascular temperature is not accompanied by a rise in epidermal temperature [86]. In the past 3 years, several clinical studies have confirmed this hypothesis, making indocyanine green augmented laser therapy a promising treatment option for leg veins. In a study by Klein et al. [87], indocyanine green augmented 810-nm diode laser therapy showed to be more effective than pulsed dye laser therapy and diode laser therapy alone. This superiority over pulsed dye laser therapy can however be partially attributed to the efficacy of indocyanine augmented diode laser therapy in vessels larger than 1 mm, where pulsed dye laser therapy is already known to be less effective. Side effect profiles of both pulsed dye and indocyanine green augmented diode laser therapy were rather similar [87]. In a recent study by the same study group comparing Nd:YAG laser therapy and indocyanine augmented diode laser therapy, clearance rates were significantly in favor of the latter, although associated with higher pain scores. In this study, it was also advocated that higher doses of indocyanine green may enhance treatment efficacy in smaller veins [88].

A recent preclinical study by Rubin et al. [58] shows that laser light at 694 nm, a wavelength produced by the existing ruby laser, exhibits an even stronger selectivity for deoxyhemoglobin versus oxyhemoglobin than the alexandrite

laser. This laser may be theoretically capable of selectively coagulating dilated veins, leaving arterial structures intact. Future studies have to confirm this.

Summary and recommendations

Various laser modalities have been used in the treatment of dilated leg veins in the past decades, with variable results. However, studies comparing these interventions with sclerotherapy, which is regarded the gold standard, are scarce. Only the Nd:YAG laser has shown to be similarly effective as sclerotherapy in comparative studies [66–68]. These studies lack a follow-up of longer than 3 months, so that a comparison of recurrence rate cannot be made. According to the Cochrane systematic review on sclerotherapy for leg telangiectasias, no reliable data on recurrence rates after sclerotherapy exist, making any statement on long-term superiority of either laser treatment or sclerotherapy impossible [89]. Side effects such as hyperpigmentation and telangiectatic matting may occur after both Nd:YAG laser therapy and sclerotherapy. Maybe, the side effect profile of shorter wavelength lasers such as the pulsed dye laser is more favorable. Nd:YAG laser therapy proved to be more painful than sclerotherapy and is associated with less favorable patient satisfaction scores [21, 66–68]. Sometimes, multiple laser sessions are needed. Sclerotherapy is safe, by far less expensive, and easier than laser therapy. In arborizing telangiectasias, injection of a sclerosing agent in the supplying vein is often sufficient, whereas in laser therapy, the affected area of skin usually must be treated vein by vein, increasing pain and the risk of side effects. Moreover, different leg veins in the same patient require constant adjustment of laser settings or even require the use of different laser modalities. For these reasons, to date, sclerotherapy remains the gold standard in most cases.

There may be, however, some specific indications where sclerotherapy is not possible or desirable. In these cases, laser therapy might be a solution. Patient with needle phobia, allergy to certain sclerosing agents, and vessels smaller than the diameter of a 30-gauge needle (including telangiectatic matting) may benefit from laser treatment [21]. Patients with veins located primarily on the ankle, where sclerotherapy is believed to be contraindicated, may also be treated by laser therapy. An advantage of laser therapy is that posttreatment compression therapy is not needed.

The choice of the appropriate laser should be primarily guided by target vessel size. Shorter wavelength (<600 nm) laser modalities are safest and most effective in the treatment of small veins (<1 mm). The pulsed dye laser gives slightly better results than the KTP laser [45, 46]. For larger veins the use of a laser modality operating at a longer wavelength is recommended. Judging purely from vessel clearance rate, the Nd:YAG laser is the modality of choice for medium to large

sized veins, but high pain scores and a relatively high risk of hyperpigmentation might limit its use [50]. The Nd:YAG laser is the safest option for patients with dark skin types due to low absorption by melanin of the 1,064 nm wavelength. Alternative options are diode or alexandrite lasers [63]. A unique feature of the alexandrite laser wavelength is its relatively high absorption by deoxyhemoglobin, so that arteries are unlikely to be targeted. This selectivity for venous blood is even stronger for the 694-nm ruby laser, although this laser type has not yet been investigated in the treatment of leg veins [58].

Beside laser therapy, treatment with multiple wavelength IPL sources can be considered [74], but controlled clinical trials are lacking and the use of multiple wavelengths implies a significant risk of damaging nonvascular structures and a low reproducibility of clinical outcome. IPL is therefore not regarded as first line treatment.

An emergent technology is indocyanine green augmented laser therapy. Results are promising, but overall evidence is still too low to justify this technique as standard therapy [87, 88].

In conclusion, sclerotherapy remains the gold standard for the treatment of small (<4 mm) leg veins. Laser therapy might offer a helpful alternative when sclerotherapy is contraindicated. Further controlled clinical trials comparing various laser modalities to the gold standard are mandatory. Laser settings should be further optimized in dose response studies and future research should determine the role of indocyanine green augmented laser therapy in the treatment of leg telangiectasias and reticular veins.

Funding sources None declared

Conflicts of interest None declared

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