

Response of spider leg veins to pulsed diode laser (810 nm): a clinical, histological and remission spectroscopy study

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BACKGROUND: Spider leg veins are common. Their treatment with laser or intensified light therapy shows generally variable success rates and often adverse side effects such as hyper- or hypopigmentation. This study was performed to investigate whether pulsed diode laser (810 nm) treatment is effective and safe.

METHODS: Thirty-five female patients with spider leg veins were included in this prospective trial. They were treated twice with a pulsed diode laser (810 nm; spot size 12 mm, frequency 2–4 Hz, pulse width 60 msec, fluence 80–100 J cm⁻²). Laser therapy was performed on day 0 and day 14. Clinical assessments were before and after the first laser therapy, after 2 weeks, 8 weeks, and one year. Skin biopsies were taken before and immediately after the first laser treatment, and after 10 weeks. Contact-free remittance spectroscopy was performed before laser treatment, immediately after the first treatment, after 2 weeks and 8 weeks.

RESULTS: After the first treatment 15 patients showed a complete disappearance (CR); in the remaining 20 patients a remarkable improvement

(RI) was noted (n=35). After six months of follow-up CR was seen in 6 patients, RI in 6, a stable situation in 9, and scar formation in 1 patient (n=21). The effect was almost completely stable during one year of follow-up. The examination of histological specimens before and after laser treatment showed no cellular inflammatory reaction. The mean vascular area was significantly reduced after the first (p<0.05) and after the second (p<0.05) laser treatment. Spectral analysis showed a marked decrease of peaks for oxygenized haemoglobin immediately after laser treatment and during the follow-up. Safety profile was excellent without purpuric reaction or pigmentary changes. Mild scarring was observed in two patients at the end of follow-up.

CONCLUSIONS: Pulsed diode laser therapy (810 nm) is an effective and safe treatment option for spider leg veins. The effects can be seen immediately. Objective monitoring by non-invasive remission spectroscopy and histology of biopsy specimens demonstrates selectivity of the laser action. *J Cosmetic & Laser Ther* 2003; 5: 1–6

Introduction

Spider leg veins are common findings on the lower limbs. About 40–50% of adults develop these acquired leg

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telangiectases. The most important risk factor is age. Chronic venous insufficiency and pregnancy are other known risk factors.^{1,2}

Spider leg veins are composed of a feeder vessel and ectatic venous sprouts localized in the reticular dermis at a depth between 180 μm to 1 mm. The blue telangiectases consist of permanently dilated, small blood venules with normal or moderately thickened vessel walls without inflammatory changes; the red ones represent the arterial loops of capillaries with higher oxygenation.^{3,4} The spider leg veins represent an important aesthetic problem. They are more difficult to treat than facial telangiectases.^{5,6}

Sclerotherapy has been used for larger vessels and laser or intensified light therapy was applied in particular for smaller vessels with variable efficacy and side effects.⁷⁻¹⁰ Injection treatment may cause ulcerations in 0.2 to 1.2% of patients,¹¹ dependent on the sclerosant and the experience of the doctor.¹²

The long-pulsed dye laser (595 nm) is useful for larger calibre and deep dermal vessels with an optimum of about three treatments. Adverse effects such as purpura and pigmentary changes are frequent.¹³⁻¹⁸ Long-pulsed neodym (Nd)-YAG lasers (532 nm) were used with success for vessels with a diameter <1 mm with fewer side effects.¹⁹⁻²¹ Usually several treatments are necessary to obtain clinically satisfactory results. The long-pulsed Nd-YAG (1064 nm) laser permits a deep penetration into the skin. Initial data with spider leg veins seem to be promising.²²⁻²⁶ Recently, preliminary studies have shown satisfactory results and minimal adverse effects with the 810 nm diode laser.²⁷

The present study was conducted to provide clinical data on the efficacy and safety of a high-power diode laser (810 nm) for spider leg veins and to investigate the morphological and functional effects for dermal microvasculature. Therefore punch biopsies were performed and quantitative histological examinations were carried out on haematoxylin-eosin stained section. Contact-free remission spectroscopy was used to investigate tissue qualities including oxygenized haemoglobin levels *in vivo*.

Material and methods

Patients

The study received approval from the Ethical Committee. Inclusion criteria were the presence of spider leg veins on untanned skin without other signs of venous or arterial disease. Exclusion criteria included age of less than 18 years, pregnancy or lactation, bleeding disorders, active acute or chronic infections and autoimmune disease, immunosuppression or phototherapy, photosensitivity, leg ulcers (current or historic) and peripheral neuropathy, scarring in the treatment area, non-compliance, tanning or regular use of sunbed. The patients were advised not to use sauna or steam bath for four weeks after laser treatment.

All patients were collected from the Department of Dermatology, Jena. A total of 35 female Caucasians were recruited and entered the study after informed consent. The age ranged from 20 to 60 years with 60% of patients

between 41 and 60 years. Their skin type according to Fitzpatrick was I ($n=2$), II ($n=29$) or III ($n=4$). The localization of the spider leg veins and their maximum diameter were determined. Spider veins were classified according to Weiss and Weiss (1993):²⁸ type 1 (red colour, diameter 0.1 to 1.0 mm; 'telangiectasia'), type 1a (colour light red, diameter <0.2 mm; 'matting'), type 2 (bluish, diameter 1 to 2 mm; 'venectasia'), type 3 (bluish, diameter 2 to 4 mm; 'reticular veins').

Clinical outcome was graded as complete response, when the treated vessels completely disappeared without scarring, as 'marked improvement' in cases with at least 80% improvement, as 'improvement' in case of at least 50% improvement, and as 'stable' in any case of less than 50% improvement. Scarring was graded as 'worsening'. Follow-up was performed at different time points: two weeks after the first treatment, after eight weeks and one year. Clinical investigations were not blinded.

Laser treatment

Topical EMLA® cream (AstraZeneca, Wedel, Germany) was applied one hour before laser treatment under occlusion. The laser treatment was realized with an 810 nm pulsed high-power diode laser with a cooled handpiece (MedioStar, Asclepion-Meditec, Jena). The spot size was 12 mm, the frequency 2-4 Hz, the pulse width 60 msec, and the fluence 80-100 Jcm^{-2} . In very pain-sensitive patients the fluence was reduced to 60 Jcm^{-2} . Two laser courses were applied, at day 0 and day 14.

Histology

Skin biopsies were taken after local anaesthesia with mepivacain 1% (Scandicain 1%®, AstraZeneca) using a biopsy punch (Stiefel Laboratorium, Offenbach, Germany). The specimens were routinely processed, paraffin embedded and stained with haematoxylin-eosin. Sections of 5 μm were used for blinded morphologic investigations and quantitative analysis by planimetry²⁹ using SigmaScanPro® software (SPSS Inc., Chicago).

Optical-thermal simulation of a blood vessel under the influence of NIR laser radiation

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A computer model of blood vessel heating under the action of laser radiation incident on the upper skin layer (epidermis) is adopted, as described recently. The vessel with a radius R is situated in one of the skin layers (dermis).³⁰ In this case laser radiation is absorbed by the skin layers (epidermis and dermis) and blood haemoglobin, resulting in temperature increase inside the blood vessel. Before attaining the blood vessel, laser radiation is absorbed and scattered in the epidermis and dermis. The temperature distribution inside the epidermis and dermis is calculated by the equation of heat conduction and corresponding boundary and initial conditions. The heat source function inside the skin layers is given by the incident intensity of laser radiation, the effective extinction

coefficients of the epidermis and dermis and reduced scattering coefficients, respectively. The optical properties of μ_a and μ_s of various skin layers are taken from Jan S. Dam et al. (2001).³¹ The solving of formulated system of equations is allowed to have the temperature T along the laser radiation propagation direction. Details of the physical and simulation background will be published elsewhere.

Remission spectroscopy

Contact-free remission spectroscopy was performed under constant ambient light conditions with a visible light (VIS)/near infrared (NIR) diode-array spectrometer system SKINREM (Zeiss Jena and J & M Analytische Mess- und Analysentechnik Aachen, Germany) with contact-free measuring head.^{32,33} Measurements were taken in the VIS/NIR-range (400 to 1600 nm) at the same time and without any contact with the skin surface. The radiation of a 20 W halogen lamp was transmitted by quartz fibres to the contact-free measuring head resulting in a radiated area

of 4 mm diameter. The remitted light from the skin was detected using two quartz fibres within the centre of the illuminated area. By the special construction of the fibre optic device the measuring head detected exclusively the remitted radiation. The distance of the measuring head to the skin surface was adjusted to 1 mm.^{32,33}

The reproducibility of the arrangement of the order of 0.03% was evaluated with subsequent remittances of a Spectralon® standard, and calculating the mean difference within the whole spectral range. The reproducibility of the spectral method was investigated by 20 repetitive readings of the same area of skin. The relative standard deviations were less than 2% in the spectral range 600 to 1300 nm, and about 4% in the range of the haemoglobin double peak.

Remission spectra of patients before and after laser treatment were assigned to the clinical and histological findings. We used 5 measuring points in each patient (Figure 1). The mean values, standard deviations and their first deviations were calculated and tested on significance (significance level 0.05).

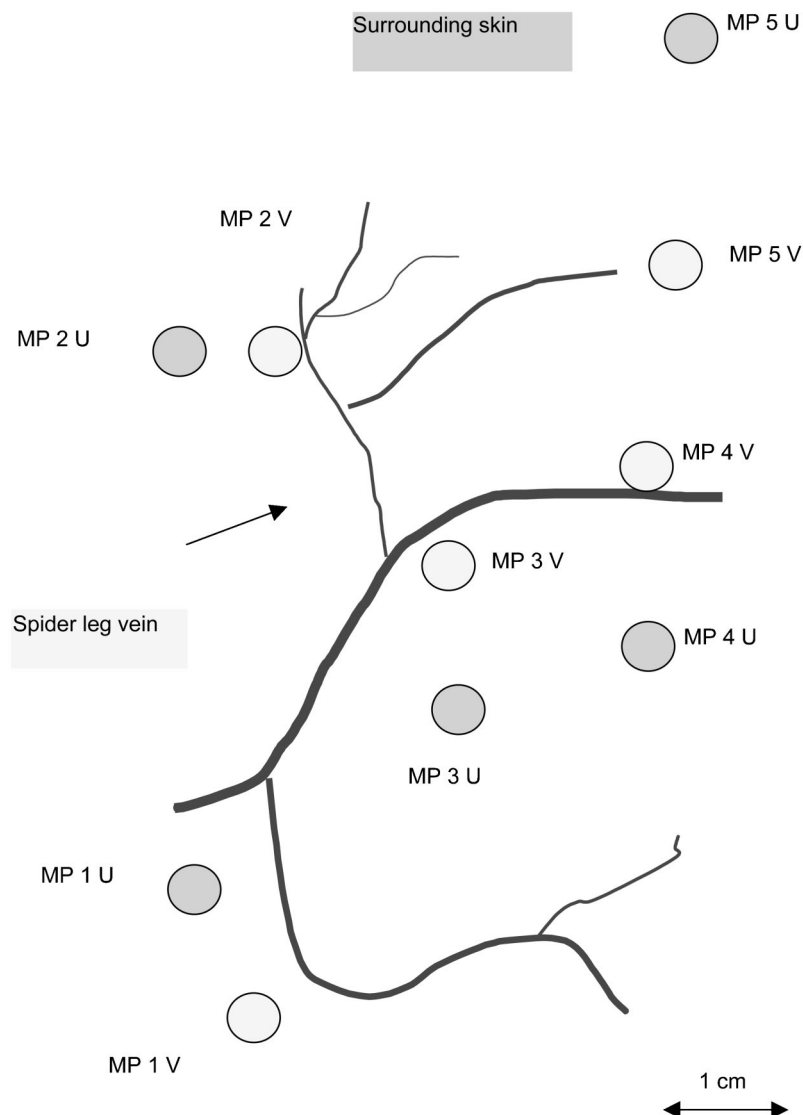


Figure 1
Schematic presentation of measuring points (MP) for spectroscopic reading of spider leg veins (V) and surrounding skin (U).

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Results

③ Clinical evaluation

The clinical effects of laser treatment were easily appreciated since small calibre leg veins showed an immediate contraction with disappearance of the vessel margins during first application. In 15 patients there was a complete disappearance, in the remaining 20 patients a remarkable improvement. There was a drop-out of two patients between day 0 and day 14 because of non-medical reasons. After two weeks a complete response was still obvious in 3 patients (of 33), and an improvement was obvious in 30 patients. Six months after the second laser treatment 12 patients had dropped out. A complete response was seen in 6 patients, an improvement in 6, a stable situation in 9, and some degree of worsening in 1 patient (scar formation). Of the patients that were lost during follow-up, 9 showed an improvement, 3 had an unchanged clinical presentation, 1 had some scarring three days after the second laser treatment. After one year of follow-up 7 patients were available. Four had a complete response, three an improvement (Figure 2a and b).

Histological findings

Histological specimens were available from 33 patients. The examination of specimens before and after laser treatment showed no cellular inflammatory reaction. Ectatic venules obvious in the pre-treatment specimens were remarkably diminished in post-treatment sections (Figure 3a and b).

The mean vascular area was 398 pixels in untreated sections, 54.6 pixels after the first ($p<0.05$) and 93.1 ($p<0.05$) and after the second laser treatment. The difference between the first and second laser treatment was statistically not significant.

Optical-thermal simulation of a blood vessel under the influence of NIR laser radiation

The used simulation wavelength was 810 nm. The vessel diameters were varied in the range 50 to 700 μm . As recent investigations have shown,³⁰ the maximum values of energy density inside the cylindrical blood vessels can considerably exceed the incident radiation (by a factor of 2.5–3) in dependence on the vessel size. It should be noted that the

Patient	Age (years)	Fitzpatrick skin type	1. laser treatment	2 weeks	2. laser treatment	6 months	1 year
1	38	II	CR	PR	CR	CR	
2	48	II	CR	PR	PD	PR	
3	53	II	CR	PR	PR	CR	CR
4	59	II	drop out				
5	62	II	CR	PR	PR	PR	PR
6	47	II	PR	PR	PR	PR	PR
7	34	II	CR	PR		relapse	
8	25	II	CR	PR	PR	PR	PR
9	27	I-II	CR	PR	relapse		
10	56	II	CR	PR	PR	CR	CR
11	48	II	CR	PR	PR	PR	CR
12	50	II-III	CR	PR	PR		
13	32	II-III	CR	CR	PR		
14	38	II	CR	PR	PR	relapse	
15	43	I-II	CR	PR	relapse		
16	25	II-III	CR	PR	PR	PR	
17	54	II	PR	PR	PR	relapse	
18	57	II-III	PR	PR	CR	CR	
19	28	II	PR	PR	PR		
20	58	II	PR	PR	PR	relapse	
21	60	II-III	PR	CR	PR		
22	47	II-III	PR	CR	PR	PR	
23	50	II	PR	PR	PR	PR	
24	53	II	PR	PR	PR	PR	
25	32	II	PR	PR	PR	CR	CR
26	46	I	PR	PR	PR	relapse	
27	49	II	PR	PR	relapse	relapse	
28	23	I	PR	PR	PR		
29	37	II	PR				relapse
30	47	II	PR	PR	CR	CR	
31	52	II	PR	PR	PR	relapse	
32	42	II-III	PR	PR	PR	CR	
33	60	II	PR	PR	PR		PR
34	20	I-II	PR	PR	PR		
35	27	II-III	PR	PR			PR

CR=complete remission; PR=partial remission.

Table 1

Patients and outcome.

⑧



Figure 2
Clinical response of leg spider veins to diode laser: (a) before and (b) six months after treatment.

source function within the blood vessel is substantially unhomogeneous. The maximum value area of heat sources is situated on the illuminated vessel surface. In moving from the illuminated part of the cylinder to the shadow the energy density is reduced (by a factor of 3–3.5) to the minimal value which is on the shaded vessel surface. With increased blood vessel radius, from 50 to 500 μm , the maximum of the source function is increased by a factor of 1.7.

When considering the investigative results of blood vessel heating under the action of laser radiation, the temperature field characteristics do not in practice correlate with the source function distributions within the vessels. Maximum temperature area is not on the surface, but inside the vessel near to its centre. The temperature increases when moving from the illuminated surface to the vessel centre, falls in its shaded part and reaches a minimum near the shaded surface. The maximum heating temperature inside the vessel depends on the fluence; with increase of the incident fluence from 60 J/cm^2 to 100 J/cm^2 at a pulse duration 60 ms the maximum temperature within the vessel increases from 335 K to 355 K. When the depth of the localization of the veins increases, maximum temperature inside the vessels substantially decreases. Increase of the vessel sizes leads initially to an increase

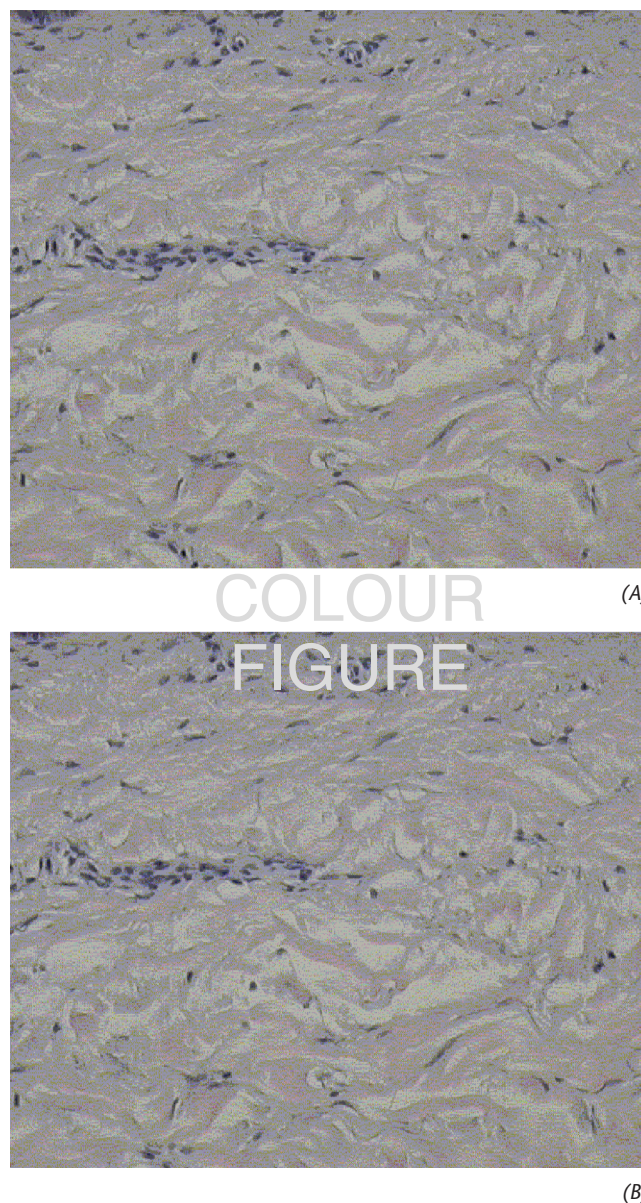


Figure 3
Histological examination of laser effects. Dermal vessels before treatment (a) with ectasia (b). After a single treatment complete disappearance of ectatic veins without inflammation.

of the maximum temperature inside them; but, from a certain radius of the veins ($\sim 0.3\text{--}0.35\text{ mm}$), T_{max} becomes stable and does not change (Figure 4). Therefore, it can theoretically be deduced that at near-infrared wavelengths the efficacy of laser radiation on vessel therapy will be reduced at low vessel diameters. In accordance with our experimental results, discussed later, the NIR laser therapy of spider veins seems to be more effective at higher vessel diameters.

Remission spectroscopy

Spectral analysis showed intra- and inter-individual variations not related to physical factors, but to functional status. The relative standard deviation for spider leg veins varied from 20% to 25%, but for the surrounding skin the

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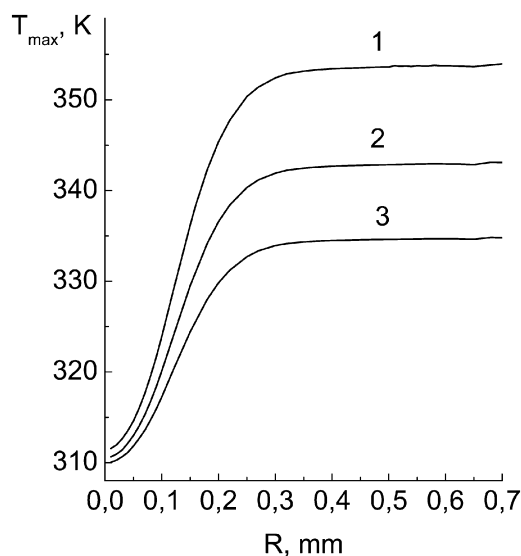


Figure 4
Maximum temperature inside the vessel vs vessel radius at different values of localization depth: 1- $d=1$ mm; 2- $d=2$ mm; 3- $d=3$ mm. The incident fluence is 100 J/cm^2 .

standard variation was only 11% to 13%. A characteristic spider leg vein response is shown in Figure 5 for patient 5 (Fitzpatrick skin type II).

When focusing on remission peaks for oxygenized haemoglobin, responders showed a marked decrease immediately following laser treatment and during the follow-up, whereas in non-responders there was no difference.

Adverse effects

During laser therapy there was a mild burning sensation in almost all patients. There was no purpuric reaction. Scarring was observed in two patients at the end of follow-up (patients 7 and 29). We observed no pigmentary changes in the other patients.

Discussion

Laser therapy of spider leg veins has become of increasing interest. In the past yellow pulsed dye lasers have been used with an improved selectivity to blue argon laser reducing the non-specific absorption by melanin.^{5,34} The coagulating effect of yellow lasers, however, is limited to a thickness of less than $100\ \mu\text{m}$. In the case of vessels with a diameter greater than $0.1\ \text{mm}$ yellow lasers are less effective since coagulation remains incomplete.^{35,36}

Near-infrared (NIR) laser offers advantages compared to yellow dye or argon laser. The epidermal melanin absorption decreases with longer wave length. This diminishes the spread of light and allows the treatment of deeper-lying vessels. Haemoglobin remains the major target chromophore with a moderate absorption. Spectral computer simulations for superficial small sized vessels (diameter $50\ \mu\text{m}$; depth $300\ \mu\text{m}$) develop a temperature peak when treated with light between 500 and 600 nm.

Larger and deeper-lying vessels (diameter 1 mm, depth 1 mm) reach the temperature peak with light of 900 nm wavelength.³⁰ Since most spider leg veins are of diameters 0.3 to 2 mm, with reticular veins up to 3 mm, the use of a NIR laser would at least theoretically allow more successful therapy, as it was calculated for 810 nm laser light in the present paper.

In a recent study, 50 patients with spider leg veins were treated with the a long pulse frequency-doubled Neodymium (Nd):YAG laser (532 nm) with a cooling device. Seventy-three percent of patients had greater than 50% improvement after one treatment. Eighty-three percent were graded better than 50% after a second treatment. The results have been supported by other studies using the same laser type in patients with spider leg veins. After two sessions with a cooled handpiece an improvement was observed in 64% to 85% of patients.^{20,23,37-39} Unwanted side effects include pain, temporary but sometimes more persistent hyperpigmentation, scarring, and blistering.^{21,26}

In a recent study with 20 patients, one treatment with the Nd:YAG laser (1024 nm) achieved a clearance of more than 75% in two-thirds of small vessels measuring 1 to 3 mm in diameter. The fluence was $100\ \text{Jcm}^{-2}$ with 50 ms pulse duration.²⁶

After a single treatment with a 1064 nm Nd:YAG laser (multiple synchronized pulsing, spot size 6 mm; pulse duration 14 ms; fluence $13\ \text{Jcm}^{-2}$) of blue spider vein ectasias a skin biopsy was taken for analysis.²⁴ Treated areas revealed perivascular haemorrhage, thrombi, fragmentation and homogenization of elastic fibres, and eosinophilia of vessel walls. Expression of heat shock protein hsp 70 and transforming growth factor beta was increased in treated vessels.

Histological investigations after a single pulsed dye laser treatment of spider leg veins (585 nm; fluence 6.5 to $8\ \text{Jcm}^{-2}$; pulse width 0.45 ms) after 3, 7 and 14 days demonstrated a sequelae of changes: on day 3 suprabasal vesiculation and vascular thrombosis were observed. Vessel walls showed disruption leading to erythrocyte extravasation. After two weeks almost 50% of vessels were re-canalised. Hyperpigmentation was due to dermal haemosiderin deposits.⁴⁰

Based on early experiences with spider leg veins with an 810 nm diode laser (fluence 12.7 to $17.8\ \text{Jcm}^{-2}$, pulse width 0.1s; spot size 5 mm) ($n=10$) neither scarring nor pigmentary or purpuric side effects were noted.²⁷ In a comparative study on spider leg veins, angiomas and facial telangiectases, using a diode laser of 532 nm and a NIR diode laser (940 nm), the latter was found to be superior.⁴¹

We observed no histological evidence of inflammation in the present study. A short duration inflammatory response during the first 14 days following laser treatment cannot be ruled out. The effect on improvement of spider leg veins was evident as shown by quantitative histopathology which demonstrated a decrease of vascularity in the upper dermis. Despite limited comparative trials a complete systematic evaluation of different laser types for spider leg veins and other acquired telangiectases is not yet available.^{5,14,26,42}

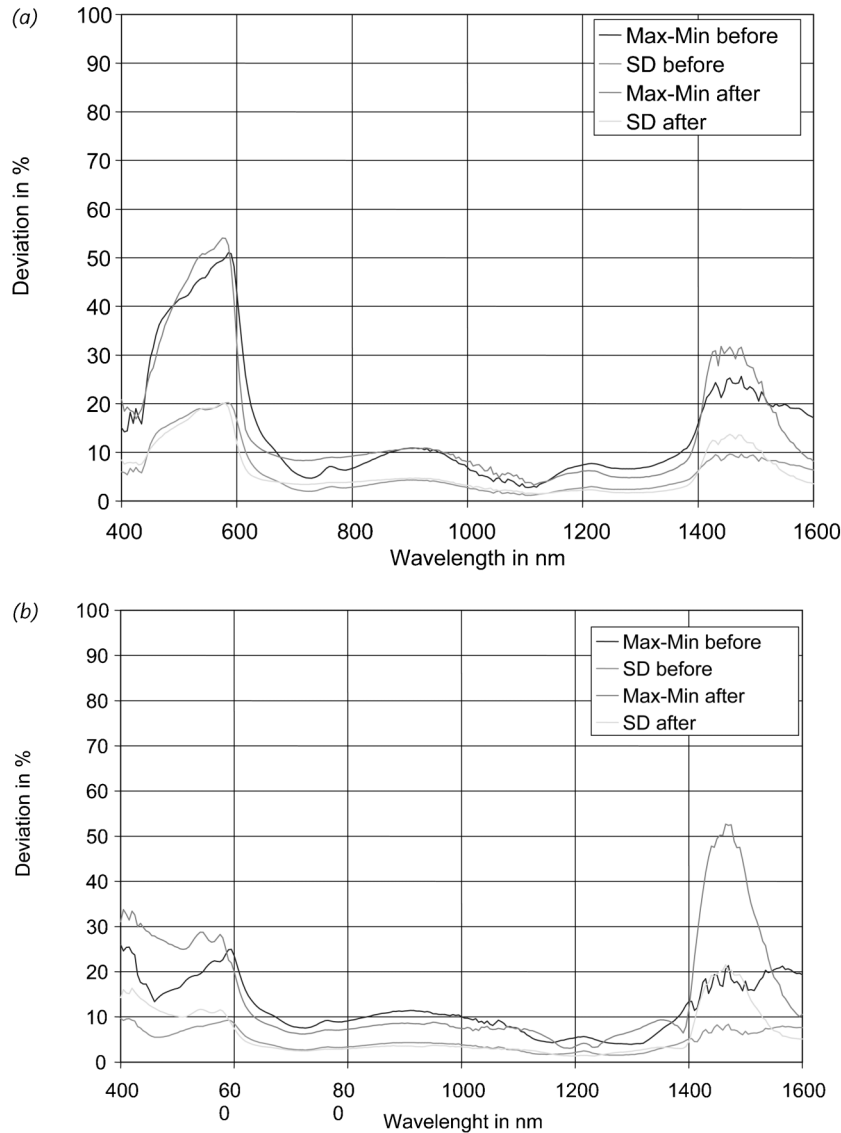


Figure 5

Differences between maximum and minimal spectral value (Max-Min) and standard deviations (SD) of five measuring points before and after a single laser treatment (patient 5). (a) spider leg veins; (b) surrounding skin.

We also used remission spectroscopy to evaluate the laser effect. Optical qualities of blood have been investigated *in vitro*.⁴³ For red laser light of 633 nm and a temperature of 20°C the absorption coefficient μ_a is almost linear dependent between a haematocrit of 10% and 50%. With an increasing shear rate and haemolysis the absorption coefficient decreases.⁴³ Using a laser wavelength of 586 nm it was calculated that heat diffusion is of minor importance for coagulation. At 2.9 Jcm⁻² radiant exposure (pulse length 0.5 ms) the reflectance was increased independent of total radiant exposure of the pulse. This was caused by blood coagulation. A second increase in reflection and in transmission occurred near 6.3 Jcm⁻² and was due to blood vaporization.⁴⁴

Irreversible laser coagulation needs an intravascular temperature between 45°C and 100°C. *In vitro* studies suggest a three-phase model: (1) heating phase, (2) primary coagulation and (3) secondary coagulation. Spreading is markedly increased in phase 1 at 532 nm. Denaturation of

haemoglobin and cytoplasm and production of small size Mie-particles is thought to be responsible.⁴⁵ In phase 2 a microscopic coagulum develops. Remission increases due to blood clotting.^{44,46}

The present data give the first evidence of a decrease of remission after laser treatment of spider leg veins. This cannot be explained by intravascular coagulation, but by disappearance of dermal vessels. The theoretical calculation for laser-vessel interactions suggested a better effect in dermal vessels of larger diameter. The calculation, however, does not completely fit with the clinical observations. This might be explained by the use of a cooling handpiece during laser treatment which could have been influenced the vascular diameter.

In conclusion, the present study provides evidence both on the clinical viewpoint and on histological and remission spectroscopic investigations on the therapeutic efficacy of diode laser treatment of spider leg veins. The treatment protocol in this study was limited to two laser applications.

In clinical practice better overall results seem possible when in selected cases the frequency of laser treatment is increased. Despite this, the study clearly demonstrates

that diode laser therapy of spider leg veins shows a low frequency of unwanted side effects, and most of these are only temporary and mild.

References

1. Bernstein EF. Clinical characteristics of 500 consecutive patients presenting for laser removal of lower extremity spider veins. *Dermatol Surg* 2001; **27**: 31–3.
2. Thibault P, Bray A, Wlodarczyk J, Lewis W. Cosmetic leg veins: evaluation using duplex venous imaging. *Dermatol Surg Oncol* 1990; **16**: 612–18.
3. Sommer A, Van Mierlo PL, Neumann HA, Kessels AG. Red and blue telangiectases. Differences in oxygenation? *Dermatol Surg* 1997; **23**: 55–9.
4. Requena L, Sanguenza OP. Cutaneous vascular anomalies. Part I. Hamartomas, malformations, and dilation of pre-existing vessels. *J Am Acad Dermatol* 1997; **37**: 523–49.
5. Hercogova J, Brazzini B, Hautmann G, et al. Laser treatment of cutaneous vascular lesions: face and leg telangiectases. *J Eur Acad Dermatol Venereol* 2002; **16**: 12–18.
6. Major, 2002.....
7. Dee R. A logical approach to the injection treatment of varicose and spider veins. *Conn Med* 1999; **63**: 391–8.
8. Green D. Sclerotherapy for varicose and telangiectatic veins. *Am Fam Physician* 1992; **46**: 827–37.
9. Loo WJ, Lanigan SW. Recent advances in laser therapy for the treatment of cutaneous vascular disorders. *Lasers Med Sci* 2002; **17**: 9–12.
10. Goldman MP. Treatment of leg veins with lasers and intense pulsed light. Preliminary considerations and a review of present technology. *Dermatol Clin* 2001; **19**: 467–73.
11. Bihari I, Magyar E. Reasons for ulceration after injection treatment of telangiectasia. *Dermatol Surg* 2001; **27**: 133–6.
12. Conrad P, Malouf GM, Stacey MC. The Australian polidcanol (aethoxysklerol) study. Results at 2 years. *Dermatol Surg* 1995; **21**: 334–6.
13. Hsai J, Lowery JA, Zelickson B. Treatment of leg telangiectases using a long pulsed dye laser at 595 nm. *Laser Surg Med* 1997; **20**: 1–5.
14. West TB, Alster TS. Comparison of the long-pulse dye (590–595 nm) and KTP (532 nm) lasers in the treatment of facial and leg telangiectases. *Dermatol Surg* 2000; **24**: 221–6.
15. McDaniel DH, Ash K, Lord J, et al. Laser therapy of spider leg veins: clinical evaluation of a new long pulsed alexandrite laser. *Dermatol Surg* 1999; **25**: 52–8.
16. Reichert D. Evaluation of the long-pulse dye laser for the treatment of leg telangiectases. *Dermatol Surg* 2000; **24**: 737–40.
17. Busher et al. 2000.....
18. Goldman MP, Sadick NS, Weiss RA. Treatment of spider veins with the 595 nm pulsed-dye laser. *J Am Acad Dermatol* 2000; **42**: 849–50.
19. Adrian RM. Treatment of leg telangiectases using a long-pulse frequency doubled neodymium:YAG laser at 532 nm. *Dermatol Surg* 2000; **24**: 19–23.
20. Bernstein EF, Kornbluth S, Brown DB, Black J. Treatment of spider veins using a 10 millisecond pulse-duration frequency-doubled neodymium YAG laser. *Dermatol Surg* 1999; **25**: 316–20.
21. McMeekin TO. Treatment of spider veins of the leg using a long-pulsed Nd:YAG laser (Versapulse) at 532 nm. *J Cutan Laser Ther* 1999; **1**: 179–80.
22. Weiss RA, Weiss MA. Early clinical results with a multiple synchronized pulse 1064 nm laser for leg telangiectases and reticular veins. *Dermatol Surg* 1999; **25**: 399–402.
23. Sadick NS. Long-term results with a multiple synchronized-pulse 1064 nm Nd:YAG laser for the treatment of leg venulectases and reticular veins. *Dermatol Surg* 2001; **27**: 365–9.
24. Sadick NS, Prieto G, Shea CR, et al. Clinical and pathophysiological correlates of 1064 nm Nd:Yag laser treatment of reticular veins and venulectasias. *Arch Dermatol* 2001; **137**: 613–17.
25. Major A, Brazzini B, Campolmi P, et al. Nd:YAG 1064 nm laser in the treatment of facial and leg telangiectases. *J Eur Acad Dermatol Venereol* 2001; **15**: 559–65.
26. Omura NE, Dover JS, Arndt KA, Kauvar ANB. Treatment of reticular leg veins with a 1064 nm long-pulsed Nd:YAG laser. *J Am Acad Dermatol* 2003; **48**: 76–81.
27. Varma S, Lanigan SW. Laser therapy of telangiectatic leg veins: clinical evaluation of the 810 nm diode laser. *Clin Exp Dermatol* 2000; **25**: 419–22.
28. Weiss and Weiss, 1993.....
29. Baak JPA, Oort J. A Manual of Morphometry in Diagnostic Pathology Berlin: Springer, 1983.
30. Astafyeva LG, Zheltov GI, Rubanov AS. Modelling of blood vessel heating by laser radiation. *Optics and Spectroscopy* 2001; **90**: 244–9.
31. Dam JS, Pedersen CB, Dalgaard T, et al. Fibre-optic probe for non-invasive real-time determination of tissue optical properties at multiple wavelengths. *Appl Optics* 2001; **40**: 1155–64.
32. Schmidt W-D, Fassler D, Zimmermann G, et al. Non-contacting diffuse VIS-NIR spectroscopy of human skin for evaluation of skin type and time-dependent micro-circulation. *Proc SPIE* 2000; **4160**: 91–102.
33. Schmidt W-D, Liebold K, Fassler W-D, Wollina U. Contact-free spectroscopy of leg ulcers: principle, technique, and calculation of spectroscopic wound scores. *J Invest Dermatol* 2001; **114**: 531–5.
34. Weiss RA, Dover JS. Laser surgery of leg veins. *Dermatol Clin* 2002; **20**: 19–36.
35. McCoy S, Hanna M, Anderson P, et al. An evaluation of the copper-bromide laser for treating telangiectasia. *Dermatol Surg* 1996; **22**: 551–7.
36. McCoy SE. Copper bromide laser treatment of facial telangiectasia: results of patients treated over five years. *Laser Surg Med* 1997; **21**: 329–40.
37. Rogachefsky AS, Silapunt S, Goldberg DJ. Nd:YAG laser (1064 nm) irradiation for lower extremity telangiectases and small reticular veins: efficacy as measured by vessel colour and size. *Dermatol Surg* 2002; **28**: 220–23.
38. Massay RA, Katz BE. Successful treatment of spider leg veins with a high-energy, long-pulse, frequency-doubled neodymium:YAG laser (HELP-G). *Dermatol Surg* 1999; **25**: 677–80.
39. Eremia S, Do CYL. Treatment of leg and face veins with a cryogen spray variable pulse width 1064-nm Nd:YAG laser – a prospective study of 47 patients. *J Cosmetic Laser Ther* 2001; **3**: 147–53.

40. Wiek K, Vanscheidt W, Ishkhanian S, et al. Selektive Photothermolyse von Besenreiservarizen und Telangiectasien der unteren Extremität. *Hautarzt* 1996; **47**: 258–63.
41. Barton JK, Frangineas G, Pummer H, Black JF. Cooperative phenomena in two-pulse, two-colour laser photocoagulation of cutaneous blood vessels. *Photochem Photobiol* 2001; **73**: 642–50.
42. Apfelberg DB, Smith T, Maser MR, et al. Study of three laser systems for treatment of superficial varicosities of the lower extremity. *Lasers Surg Med* 1987; **7**: 219–23.
43. Roggan A, Friebel M, Dörschel K, et al. Optical properties of circulating human blood in the wavelength range 400–2500 nm. *J Biomed Optics* 1999; **4**: 36–46.
44. Verkruyse W, Nilsson AMK, Milner TE, et al. Optical absorption of blood depends on temperature during a 0.5 ms laser pulse at 586 nm. *Photochem Photobiol* 2000; **67**: 276–81.
45. Barton JK, Rollins A, Yazdanfar S, et al. Photothermal coagulation of blood vessels: a comparison of high-speed optical coherence tomography and numerical modelling. *Phys Med Biol* 2001; **46**: 1665–78.
46. Tan OT. Ultrastructural changes in red blood cells following pulsed irradiation in vitro. *J Invest Dermatol* 1989; **92**: 100–104.

Authors Queries

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Query Reference	Query	Remarks
1	“Optical thermal simulation section” I found sentence 5 (para 1) confusing, and have adjusted it. Do you agree?	
2	“Optical thermal simulation section” penultimate sentence I found confusing. Can it be reworded?	
3	There is reference to Fig 2. but as this refers to photographs of legs before and after, should this not be identified in a more discrete manner?	
4	References: I have converted to Vancouver style.	
5	Reference No 6. Major, 2000 is missing. Can author insert, please?	
6	Reference No. 17. Busher et al. is missing. Can author insert, please?	
7	Reference No 28. Weiss and Weiss, 1993 is missing. Can author insert, please?	
8	Table 1 : has no reference in the text, but I suspect author would wish to name it in “Results – Clinical evaluation” section. Please insert in appropriate place.	