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# Reduced recanalization rates of the great saphenous vein after endovenous laser treatment with increased energy dosing: Definition of a threshold for the endovenous fluence equivalent

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*Background:* Recent reports indicated a correlation between the amount of energy released during endovenous laser treatment (ELT) of the great saphenous vein (GSV) and the success and durability of the procedure. Our objective was to analyze the influence of increased energy dosing on immediate occlusion and recanalization rates after ELT of the GSV. *Methods:* GSVs were treated with either 15 or 30 W of laser power by using a 940-nm diode laser with continuous fiber pullback and tumescent local anesthesia. Patients were followed up prospectively with duplex ultrasonography at day 1 and at 1, 3, 6, and 12 months.

*Results:* A total of 114 GSVs were treated with 15 W, and 149 GSVs were treated with 30 W. The average endovenous fluence equivalents were  $12.8 \pm 5.1 \text{ J/cm}^2$  and  $35.1 \pm 15.6 \text{ J/cm}^2$ , respectively. GSV occlusion rates according to the method of Kaplan and Meier for the 15- and 30-W groups were 95.6% and 100%, respectively, at day 1, 90.4% and 100% at 3 months, and 82.7% and 97.0% at 12 months after ELT (log-rank; P = .001). An endovenous fluence equivalent exceeding 20 J/cm<sup>2</sup> was associated with durable GSV occlusion after 12 months' follow-up, thus suggesting a schedule for dosing of laser energy with respect to the vein diameter.

*Conclusions*: Higher dosing of laser energy shows a 100% immediate success rate and a significantly reduced recanalization rate during 12 months' follow-up. (J Vasc Surg 2006;44:834-9.)

During recent years, endoluminal treatment modalities have evolved for the thermal ablation of the incompetent great saphenous vein (GSV). Soon after the introduction of a bipolar endovenous radiofrequency closure technique,<sup>1</sup> endovenous laser treatment (ELT) of the GSV was presented, initially using diode lasers with 810- and 940-nm wavelengths.<sup>2</sup> From the very beginning, besides the discussion of whether major tributaries at the saphenofemoral junction can be left untreated, the immediate success rate of endovenous occlusion of the GSV and its durability were in the focus. Soon it became apparent that, particularly after ELT, recanalization of initially occluded GSVs is a relevant process that starts immediately thereafter.<sup>3,4</sup> Multiple regression analysis of a prospectively obtained set of clinical data finally suggested that as soon as 3 months after laser treatment, there might be a dose-response relationship between laser energy and a persistent occlusion of the GSV.<sup>5</sup> As a consequence of these findings, we changed our

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endovenous laser standard protocol from a 15-W continuous pullback to a to a 30-W continuous pullback treatment schedule. Reducing the pullback speed at the same time, we were able to administer approximately a threefold amount of laser energy per centimeter of vein length.

In this study, we prospectively followed up the recanalization events of the above-mentioned 15- and 30-W treatment cohorts for 12 months after ELT to test the hypothesis that an increase of the dose of laser energy would result in improved immediate success and recanalization rates.

## PATIENTS AND METHODS

Patients. Patients with chronic venous insufficiency of all clinical stages presented for routine evaluation in our phlebology clinic. If the clinical stage was C2 or higher and functional testing by duplex scanning showed an incompetent GSV with reflux of more than 500 milliseconds after the Valsalva maneuver or manual augmentation, patients were selected for ELT in an outpatient setting. The first patient cohort was treated with a 940-nm diode laser at 15 W of laser power. After we detected a dose-response relationship between administered laser energy and treatment success,<sup>5</sup> our standard treatment was changed to 30 W of laser power for consecutive patients. There were no specific exclusion criteria, apart from concomitant acute disease preventing any surgical or interventional treatment of varicose veins. Patients had to give written informed consent in accordance with the Helsinki declaration. The

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	Group				
Variable	940 nm, 15 W	940 nm, 30 W			
No. patients	N = 85	N = 118			
Female sex	n = 61 (73%)	n = 77 (65%)			
Age, y, median (range)	61 (27-93)	55 (16-78)			
BMI, kg/m <sup>2</sup> , median	· · · ·	. ,			
(range)	25.3 (16.8-48.8)	25.4 (17.4-47.3)			
GSV diameter, mm,		,			
median (range)*	6.1 (2.0-17.3)	6.7 (2.8-16.1)			
Treated vein length, cm,	· · · · · ·	· · · · ·			
median (range)	60 (18-90)	55 (15-90)			
TLA (mL) per centimeter	· · · ·	· /			
vein length,					
$(\text{mean} \pm \text{SD})$	$9.5 \pm 2.9$	$11.1 \pm 3.8$			
No. treated legs	114 (100%)	149 (100%)			
C <sub>2</sub>	114 (100%)	149 (100%)			
$\tilde{C_3}$	60 (53%)	78 (52%)			
$C_4$	63 (55%)	38 (26%)			
C <sub>5</sub>	2 (2%)	4 (3%)			
C <sub>6</sub>	19 (17%)	6 (4%)			
E <sub>P</sub>	109 (96%)	146 (98%)			
Es	5 (4%)	3 (2%)			
As	114 (100%)	149 (100%)			
$A_{\rm P}$	69 (61%)	51 (34%)			
A <sub>D</sub>	5 (4%)	3 (2%)			
P <sub>R</sub>	114 (100%)	149 (100%)			
Po	0 (0%)	0 (0%)			

 Table I. Patient characteristics and CEAP classification of treated legs

*BMI*, body mass index; *TLA*, tumescent local anesthesia; *GSV*, great saphenous vein.

Data are n (%) unless otherwise noted.

\*Measured in the supine position.

treated patients were representative of the patient population referred to a university clinic (Table I).

Administration of laser energy. At the time of this study, ELT was the only treatment. Additional treatment measures such as sclerotherapy or miniphlebectomy were scheduled 3 months after ELT, if necessary. In the first cohort of patients (group A), 15 W of laser power of a 940-nm diode laser (Dornier MedTech Europe, Wessling, Germany) was administered continuously while the laser fiber was pulled back manually with a constant velocity of approximately 5 mm/s. In the second cohort (group B), laser treatment was administered with the same laser system but with 30 W of laser power and a constant pullback velocity of approximately 3 to 4 mm/s. The maximum vein diameter at the saphenofemoral junction before treatment, the length of the treated vein, and the total laser treatment time were measured.

Otherwise, ELT was performed as previously described.<sup>4</sup> In brief, the GSV was punctured with duplex guidance at the distal point of reflux with an 18-gauge needle. With the help of a coated J-tip guidewire (0.035 inches), a 5F angiocatheter was placed with duplex guidance close to the saphenofemoral junction. The guidewire then was replaced by a 600- $\mu$ m laser fiber connected to a 940-nm diode laser. The desired position of the laser fiber tip was again ascertained by duplex scanning. After posi-

tioning of the fiber tip, tumescent local anesthesia was infiltrated with duplex guidance and a motor pump into the perivenous intrafascial space. One liter of tumescent local anesthesia was prepared from 1 L of physiological saline (0.9%), prilocaine 700 mg, epinephrine 1 mg, and 10 mL of bicarbonate 8.4%, as described previously.<sup>6</sup> Without further delay after infiltration, laser energy was administered as described previously.

After complete removal of the fiber, an eccentric compression bandage was applied over the course of the treated vein for 24 hours. Additionally, the patient had to wear graduated compression stockings (30 mm Hg) continuously day and night for 8 days. For the same period, patients had to administer low-molecular-weight heparin (2500 IU dalteparin subcutaneously) once daily. No sedation was applied, and the patients had to walk immediately after the procedure. Diclofenac was prescribed (75 mg twice daily), and patients were advised to use it for pain control as necessary.

Calculation of energy deposits. After each treatment, the total amount of delivered laser energy was displayed in joules by the laser device. The quotient of total laser energy in joules and the treated vein length in centimeters was then used to calculate the average linear endovenous energy density (LEED). To take into account different diameters of the GSV with respect to the administered laser energy, a cylindrical approximation of the inner vein surface was used to calculate a fluencelike parameter.<sup>5</sup> The diameter of the vein was measured with patients in the supine position before the start of ELT on the basis of the assumption that even after administration of tumescent anesthesia, the inner vein surface is still there, even if it is folded; therefore, the vein in its entirety appears with a smaller diameter in ultrasound B-scan. The quotient of released laser energy in joules and the approximated inner vein surface we call the endovenous fluence equivalent (EFE). To call it equivalent seems necessary because EFE does not exactly resemble the definition of a fluence: unlike in transcutaneous laser treatment, in which the laser beam hits the targeted surface perpendicularly and in a homogenous fashion, in ELT the laser beam geometry is inhomogeneous with respect to the targeted inner vein surface.

Follow-up examinations. Patients were re-examined with duplex B-scan at day 1 after the procedure and 1, 3, 6, and 12 months thereafter. The GSV was tested for recanalization by use of color duplex and compression sonography elicited by the ultrasound probe. The distance from the saphenofemoral junction to the beginning of the occluded vein segment was measured, and if this distance exceeded 5 cm or if any part of the treated GSV showed flow signals on augmentation or Valsalva maneuver, then the GSV was judged recanalized. If recanalization did not affect the entire length of the treated GSV, then the recanalization was termed incomplete, either proximally or distally. At the same time, duplex scanning was used to detect new pathologic refluxes, particularly within the tributaries originating from the saphenofemoral junction or perforating veins in the course of the treated GSV.

Variable	Day 1	1 mo	3 mo	6 mo	12 mo
15 W					
Lost to follow-up	0	0	0	2	10
Limbs at risk	114	109	105	101	88
Occluded GSVs	108	105	103	98	83
Proximally recanalized	1*	1	0	0	1
Distally recanalized	0	0	0	1	1
Completely recanalized	5	3	2	2	3
Total recanalization events	6*	4	2	3	5
Kaplan-Meier estimate	95.6%	92.1%	90.4%	87.7%	82.7%
30 Ŵ					
Lost to follow-up	0	0	0	19	30
Limbs at risk	149	149	149	130	100
Occluded GSVs	149	149	149	130	97
Proximally recanalized	0	0	0	0	1
Distally recanalized	0	0	0	0	2
Completely recanalized	0	0	0	0	0
Total recanalization events	0	0	0	0	3
Kaplan-Meier estimate	100%	100%	100%	100%	97%

Table II. Duplex follow-up of GSVs after ELT: limbs at risk and recanalization events

GSV, Great saphenous vein; ELT, endovenous laser treatment.

\*One initially unoccluded GSV closed completely within the first week after ELT in both treatment groups.

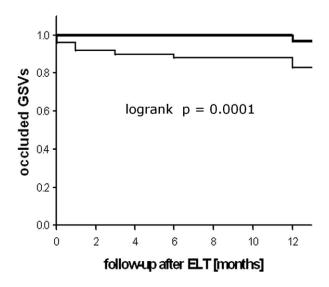
**Statistical evaluation.** Statistical analysis was performed by using the StatXact 3.0 software package (Cytel Software Corporation, Cambridge, Mass). LEEDs and EFEs were compared by using the Wilcoxon/Mann-Whitney test. The log-rank test was used to compare the 15- and 30-W cohorts in Kaplan-Meier analysis. All tests were two sided.

# RESULTS

In group A, with continuous use of a 940-nm laser at 15 W, ELT of the GSV was performed on 85 patients (114 limbs). In group B, 118 patients (149 limbs) were treated with 30 W (Table I). The median treated vein length was 60 cm (range, 18-90 cm) in group A and 55 cm (range, 15 –90 cm) in group B. The maximum diameters of the GSV, age of patients, body mass index, and distribution of sex were similar in the two groups (Table I). Clinical stages before treatment according to the CEAP classification were slightly asymmetric (Table I): legs of patients receiving 15-W treatment showed a higher rate of skin alterations (C4) and venous ulcer disease (C5 and C6). The amount of tumescent local anesthesia infiltrated along the GSV did not differ significantly between the treatment groups (Table I).

Immediate success rates. At day 1 after ELT in the 30-W cohort, all GSVs were completely closed by duplex ultrasound examination, thus resulting in an immediate occlusion rate of 100% (Table II). In the 15-W cohort, 6 (5.2%) of 114 treated vessels remained open at day 1 after treatment. However, 1 week after ELT, one of these initially open GSVs showed a complete occlusion, thus resulting in a total immediate closure rate of 95.6%. The difference in immediate occlusion rates between the two groups was statistically significant (P = .029).

**Recanalization of GSVs during follow-up.** At 1, 3, and 6 months after ELT in the 30-W group, no recanalized GSV was observed. After 12 months, one complete recanalization and two incomplete recanalizations were observed



**Fig 1.** Kaplan-Meier plot of recanalization events observed during 12 months' follow-up in great saphenous veins *(GSVs)* treated with either 15 or 30 W of laser power according to data displayed in Table II. The standard error of Kaplan-Meier estimates was less than 0.05 at all times. *ELT*, Endovenous laser treatment.

(Table II). With 100 limbs at risk at that time, this represents an occlusion rate of 97% at 12 months. In the 15-W group, partial and complete recanalizations occurred more frequently during the follow-up period (recanalization at 3 months, 9.6%; occlusion rate at 12 months, 82.7%; Table II). It is interesting to note that besides recanalization events originating from the saphenofemoral junction, recanalization originating from more distal parts of the GSV was also observed. The number of occluded and recanalized limbs of any recanalization patterns were analyzed together according to the method of Kaplan and

Variable	Recanalized until 3 mo after ELT	Occluded 3 mo after ELT	P value	Recanalized until 12 mo after ELT	Occluded 12 mo after ELT*	P value
15 W						
No. events	11	103		7	84	
LEED $(J/cm)$	18.4 (13.1-28.2)	24.2 (11.8-35.5)	.0014	22.5 (11.8-30.0)	24.3 (13.9-35.5)	.32
$EFE (J/cm^2)$	7.4 (5.0-11.0)	12.8 (2.8-37.3)	< .0001	11.2 (4.2-16.8)	13.0 (2.8-37.3)	.20
30 W	· · · · ·					
No. events	0	149		3†	97	
LEED $(J/cm)$	_	68.4 (33.0-156.0)		60.0 (47.4-100.0)	64.2 (33.0-104.1)	.99
$EFE (J/cm^2)$	—	32.2 (13.1–93.7)	—	18.6 (15.9-67.8)	32.3 (13.1-89.6)	.43

Table III. Linear endovenous energy densities (LEED) and endovenous fluence equivalents (EFE) for occluded and recanalized GSVs

GSV, Great saphenous vein; ELT, endovenous laser treatment.

P values are results of Wilcoxon/Mann-Whitney tests, recanalized vs occluded GSVs at 3 and at 12 mo.

<sup>†</sup>GSV recanalizations with 30 W:

One complete recanalization; total treated vein length was only 15 cm (100 J/cm).

One distal recanalization with pathologic reflux transferred by the V. acc. anterior; the proximal 20 cm of the GSV was still occluded (47.4 J/cm).

One distal recanalization originating from a medial thigh perforator (60 J/cm).

\*Only patients with completed 12-mo follow-up were included.

Meier, taking into account censored data of limbs that were lost to follow-up (Fig 1). Log-rank testing of these data revealed a significantly reduced recanalization frequency for the 30-W treatment group (P = .0001).

Linear endovenous energy density. With ELT at 15 W, an average LEED of 23.6  $\pm$  4.9 J/cm of vein length  $(\text{mean} \pm \text{SD})$  was delivered. The maximum LEED values that were administered in recanalized GSVs were 28.2 and 30.0 J/cm for 6 and 12 months' follow-up, respectively (Table III). With ELT at 30 W and a reduced pullback velocity, an average LEED of  $69.9 \pm 18.7$  J/cm of vein was administered. Recanalization events were seen only at 12 months' follow-up when this energy level was delivered, whereas earlier recanalizations were not observed in this cohort. Additionally, the maximum LEED administered to one subsequently recanalized GSV was 100 J/cm, an outlier that could be related to a treated vein length of only 15 cm. The other two events were incomplete recanalizations, with LEEDs of 47 and 60 J/cm of vein length.

As displayed in Table III, LEED values of GSVs that recanalized within the first 3 months after ELT (median, 18.4 J/cm) differed significant from LEED values of GSVs that were still occluded after this time (median, 24.2 J/cm). Remarkably, LEED values of GSVs that recanalized at 6 or 12 months after ELT did not show such a difference when compared with values of GSVs that were still occluded after 12 months.

Endovenous fluence equivalent. Calculating the EFE resulted in an average value of  $12.8 \pm 5.1 \text{ J/cm}^2$  (mean  $\pm$  SD) for the 15-W cohort and an average of  $35.1 \pm 15.6 \text{ J/cm}^2$  for the 30-W group. Again, recanalizations that happened within the first 3 months after ELT among GSVs treated with 15 W were significantly linked to lower levels of administered EFE (median, 7.4 J/cm<sup>2</sup>) compared with EFE values of GSVs that were still closed after 3 months (median, 12.8 J/cm<sup>2</sup>; Table III). In contrast, EFE values of

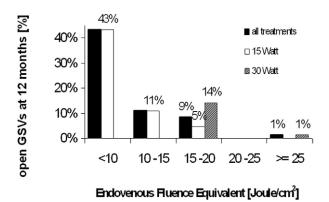


Fig 2. Recanalization rates observed during 12 months of follow-up drawn against clustered endovenous fluence equivalents. *Open bars* represent great saphenous veins *(GSVs)* treated with 15 W of laser power, *hatched bars* represent GSVs treated with 30 W of laser power, and *solid bars* represent the cumulative results of both groups.

GSVs that recanalized between 3 and 12 months after the intervention did not differ significantly from EFE values of GSVs that were still occluded at 12 months, and this was true for the 15- and 30-W treatment groups (Table III). However, the amount of EFE administered during ELT was inversely related to the subsequently observed recanalization rates during 12 months' follow-up (Fig 2). Additionally, examining only those limbs with complete 12-month follow-up demonstrated a clear inverse relationship between EFE and recanalization rates (Table IV). Taking together both groups over the period of 12 months—apart from the single outlier at 67.8 J/cm<sup>2</sup> with an extraordinarily short treated vein length of only 15 cm—the maximum EFE associated with recanalization during that period was 18.6 J/cm<sup>2</sup>.

Table IV. GSV recanalization rates during 12 months' follow-up after endovenous laser treatment with respect to the
administered endovenous fluence equivalent (EFE): only limbs with complete 12-mo follow-up were included

$EFE (J/cm^2)$						
Treatment group	x < 10	$10 \le x < 15$	$15 \le x < 20$	$20 \le x < 25$	$25 \le x$	Total
15-W group recanalization rate 30-W group recanalization rate Both groups; cumulative						19 of 102 (18.6%) 3 of 100 (3.0%)
recanalization rate	13 of 30 (43.3%)	5 of 45 (11.1%)	3 of 35 (8.6%)	$0 { m of } 20 { m (0\%)}$	1 of 71 (1.4%)	22 of 201 (10.9%)

	Table V.	Side effects after	15- or 30-W	laser treatment
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Variable	15 W: all treatments	30 W: all treatments	30 W: EFE <25 J/cm <sup>2</sup>	30 W: EFE $\geq$ 25 J/cm <sup>2</sup>
No. treated legs	107	145	39	106
Longitudinal endovenous energy densit	V,			
J/cm; median (range)	23.5 (11.8-35.5)	68.4 (33-156)	53.1 (33-106)	72.2 (40.8-156)
EFE, J/cm <sup>2</sup> , median (range)	12.2 (2.8-37.4)	32.1 (13.1-93.7)	20.6 (13.1-24.9)	37.4 (25.0-93.7)
Side effects, % affected limbs; median (n	naximum) duration (wk)			
No side effects	7%	3%	3%	3%
Ecchymosis	78%; 2 (8)	80%; 2 (12)	82%; 2 (4)	79%; 2 (12)
Pain	72%; 1 (4)	79%; 1.3 (12)	82%; 1.2 (3)	78%; 1.3 (12)
Analgesics	55%; 1 (4)	64%; 0.3 (4)	59%; 1 (3)	65%; 0.3 (4)
Induration along vein	62%; 4 (16)	63%; 4(52+)	56%; 4 (24)	65%; 4(52+)
Phlebitic reaction	11%; 1.5 (4)	12%; 1(2)	5%; 1.3 (1.5)	14%; 1 (2)
Paresthesia	5%; 2 (4)	12%; 4(52+)	13%; 2 (4)	11%; 4(52+)
Hyperpigmentation	1%; 26 (26)	3%; 39 (52+)	3%; 26 (26)	3%; 39 (52+)

EFE, Endovenous fluence equivalents.

Side effects. Side effects were recorded from 107 limbs in the 15-W group and from 145 limbs in the 30-W group (Table V). In the latter group, 39 had been treated with an EFE less than 25 J/cm<sup>2</sup> and 106 with an EFE of 25 J/cm<sup>2</sup> or greater. This discrimination was made at 25  $J/cm^2$  to examine whether side effects would be less below this limit, thus allowing the physician to treat the patients' GSVs in a window between 20 and 25 J/cm<sup>2</sup> and achieve both reliable occlusion results and a favorable side-effect profile. However, when the frequencies of the listed side effects between each column in Table V were analyzed by using the Fisher exact test, no statistically significant difference could be detected. The same was true when the Wilcoxon/Mann-Whitney test was used to detect differences among duration intervals of various side effects, eg, durations of paresthesia or posttreatment induration.

The most frequent side effects (in the order of 80%) were ecchymoses and pain at the treatment site. Use of analgesics and subcutaneous indurations were noted in approximately 60% of treated limbs. Other side effects were far less frequent; however, the duration of some side effects reached 1 year in some patients. Among these long-duration side effects were induration, paresthesia, and hyperpigmentation. Hyperpigmentation, which was observed in 1% to 3% of treated limbs, also showed the longest median duration (6-9 months). No severe side effects such as skin burns, infections, deep vein thrombosis, or pulmonary embolism have been observed.

## DISCUSSION

When ELT was introduced for ablation of saphenous veins, little was known about the mechanisms of action and frequency of recanalization events after such interventions. Articles on a potential dose-response relationship between energy dosing during ELT and the subsequent durability of the vein occlusion were not published before 2004.<sup>5,7</sup> We performed a multiple regression analysis on procedural and clinical parameters of ELT and determined EFE to be the parameter that was the most significant predictor of subsequent recanalization events.<sup>5</sup> Similarly, another study with a total recanalization rate of approximately 20% during the first 6 months after ELT did not observe such recanalizations if more than 80 J of laser energy had been administered on each centimeter of treated GSV.7 Subsequently, Timperman<sup>8</sup> treated 100 patients with the intention to exceed this level of 80 J/cm. However, in contrast to what could have been expected, this subsequent study showed five (5%) recanalization events during the first 6 months of follow-up, even though at least 80 J/cm were administered in all of these cases. Four additional cases were initial treatment failures, thus leading to an unexpectedly low total occlusion rate of 91% after 6 months.

In this study, we were able to demonstrate a striking improvement in recanalization events during the first 12 months of follow-up when the energy dose was increased with a laser power of 30 W. Whereas in the 15-W group,

with lower energy dosing, an overall recanalization rate of approximately 18% was observed during 12 months of follow-up, this rate decreased to 3% in the 30-W group. Furthermore, the three cases of recanalization in the latter group were either incomplete (n = 2) or a total recanalization of a short GSV segment of only 15 cm of treatment length. Finally, our rate of initial failures of GSV occlusion decreased from 5 (4.4%) of 114 cases in the 15-W group to 0 in the 30-W group. Additionally, apart from one outlier at 67.8 J/cm<sup>2</sup>, an EFE of more than 18.6 J/cm<sup>2</sup> was not associated with any recanalization events during 12 months of follow-up. Thus, it seems reasonable to suggest a threshold of 20 J/cm<sup>2</sup> for daily use in ELT of the GSV. This simply transfers to an LEED of 6.3 J/cm for each millimeter of vein diameter (eg, the threshold LEED for a 6-mmdiameter vein would be six times 6.3 J/cm, resulting in approximately 38 J/cm, whereas a 10-mm diameter vein should be treated with 63 J/cm).

Although it seems clear that sufficient dosing of laser energy is the key for durable vein occlusions, the role of the 30-W laser power we used in this study is less defined. Whether the same results could have been achieved by delivering the same amounts of laser energy with a laser power of 15 W cannot be answered by this study. Additionally, the reason for the differences between Timperman's results<sup>8</sup> and the results of our present study is unknown. It must be a matter of speculation why he still observed failures of initial vein occlusion and additionally had a 5% recanalization rate during the first 6 months after the intervention despite using an EFE of 80 J/cm.

If we take a closer look at the technical differences between Timperman's and our treatment protocol, the following points can be discussed. In both studies, a continuous pullback technique was engaged; however, because Timperman used only 14 W of continuous laser power, he had to use a much slower pullback velocity of approximately 6 cm of vein per second to exceed an energy dose of 80 J/cm. This slow velocity, together with a potentially vein-perforating laser wavelength of 810 nm,<sup>9</sup> could result in axial cuts through the vein wall and lead to a paravasal delivery of laser energy. We suggest that our 30-W protocol with continuous fiber pullback might have at least two advantages even if the laser wavelength of 940 nm also could perforate the vein wall. First, 30 W of ELT generates more vigorous steam bubble movements that can be easily monitored by ultrasound B-scan moving along the vein axis over several centimeters. This behavior also enhances convective heat transfer by enhancing the movements of laserheated intravenous blood. Second, a faster pullback speed of approximately 3 cm/s might account for fewer axial vein perforations. However, to prove these hypotheses and answer these questions, comparative studies need to be conducted prospectively. It is interesting to note that in this study, the side effects (Table V) did not differ significantly between laser schedules with different laser power and different energy doses delivered during ELT.

This study proves a threshold value for energy dosing but cannot answer the question about the definitive role of 30 W of laser power. Another interesting hint concerning the mechanisms of recanalization appears in Table III. The significant dose-response relationship seems most pronounced in conjunction with early recanalizations during the first 3 months after ELT. When looking at LEED and EFE values in conjunction with recanalization events at 6 or 12 months' follow-up, it becomes apparent that these LEED and EFE values are not significantly different for recanalized and occluded GSVs. It could be speculated that in these patients whose GSVs were found recanalized at 6 and 12 months, a neovascularization process was biologically more active than in patients with still-occluded GSVs. An interesting mechanism of how inflammation of perivenous tissue and arteriovenous fistulation could contribute to such recanalization events was proposed recently.<sup>10</sup>

In conclusion, there is a pronounced dose-response relationship between the administered EFE and durable success of ELT of the GSV. A threshold value of  $20 \text{ J/cm}^2$  was proposed for the EFE, and this translates to a LEED of 6.3 J/cm for each millimeter diameter of the treated vein.

### AUTHOR CONTRIBUTIONS

Conception and design: TMP Analysis and interpretation: TMP Data collection: TMP, TM, SH Writing the article: TMP, TM, SH Critical revision of the article: TMP, TM, SH Final approval of the article: TMP, TM, SH Statistical analysis: TMP Obtained funding: TMP Overall responsibility: TMP

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