Thermal Damage of the Inner Vein Wall During Endovenous Laser Treatment: Key Role of Energy Absorption by Intravascular Blood

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BACKGROUND. Despite the clinical efficacy of endovenous laser treatment (EVLT), its mode of action is incompletely understood.

OBJECTIVE. To evaluate the role of intravascular blood for the effective transfer of thermal damage to the vein wall through absorption of laser energy.

METHODS. Laser energy (15 J/pulse, 940 nm) was endovenously administered to explanted greater saphenous vein (GSV) segments filled with blood ($n = 5$) or normal saline ($n = 5$) in addition to GSVs under in vivo conditions immediately prior to stripping. Histopathology was performed on serial sections to examine specific patterns of damage. Furthermore, in vitro generation of steam bubbles by different diode lasers (810, 940, and 980 nm) was examined in saline, plasma, and hemolytic blood.

RESULTS. In saline-filled veins, EVLT-induced vessel wall injury was confined to the site of direct laser impact. In contrast, blood-filled veins exhibited thermal damage in more remote areas including the vein wall opposite to the laser impact. Steam bubbles were generated in hemolytic blood by all three lasers, while no bubbles could be produced in normal saline or plasma.

CONCLUSION. Intravascular blood plays a key role for homogeneously distributed thermal damage of the inner vein wall during EVLT.

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RECENTLY, MINIMALLY invasive techniques have been clinically introduced for the effective treatment of varicose veins. In particular, VNUS closure[1,2] and endovenous laser treatment (EVLT)[3–5] have been shown to abolish reflux in the incompetent greater saphenous vein (GSV). Short-term efficacy has been reported as greater than 90%[1,2] and 95%,[3–5] respectively, comparing well with the results of classic surgery including high ligation and stripping of the GSV.[2] However, while the mode of action of VNUS closure has been studied in detail, the mechanisms of EVLT action are still not completely understood. It has been shown that EVLT, unlike VNUS, does not lead to occlusion of the vein by significant shrinkage of the vessel wall,[6] but instead causes a thrombotic occlusion of the laser-treated vein.[5]

Histopathologic examination of laser-treated veins revealed perforation of the vein wall at the site of direct laser impact and thermal damage of adjacent vein wall areas.[5,6] For the latter effect, laser-induced steam bubble formation has been postulated as the responsible mechanism,[5] implicating a putative role for intravascular blood serving as a chromophore absorbing the laser energy. In order, to further clarify the role of intravascular blood during EVLT, we performed comparative in vitro and in vivo experiments in the presence or absence of intravascular blood.

Patients and Methods

Administration of Laser Energy to GSV Samples

EVLT was applied as previously described in detail.[5] In brief, a 600 μm bare fiber with an outer diameter of 1.00 mm was connected to a 940 nm diode laser. Under in vivo conditions (see Patients), the fiber was inserted below the knee into the surgically exposed GSV. The fiber was advanced proximally to the point of high ligation of the GSV and subsequently withdrawn in steps of about 3–5 mm while

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laser energy was applied.[5] Identical laser parameters were chosen for the in vitro experiments with GSVs (see below).

In Vitro Experiments With GSVs

After classic varicose vein surgery of the GSV under tumescent local anesthesia,[7,8] the stripped vein segment was transferred to a saline bath at room temperature. The veins were cut into pieces 10 cm in length, and each piece was ligated at the proximal end before the laser fiber was inserted from the distal end. The vein was then filled either with heparinized blood (500 IU heparin/20 ml of blood) or with normal saline. After the distal end was ligated tightly around the laser fiber, single laser pulses of 15 J (15 W, 1 second) were delivered every 3–5 mm during stepwise withdrawal of the fiber tip. During the entire procedure the vein was bathed completely in normal saline solution. A total of 10 specimens, 5 filled with blood and 5 filled with normal saline during treatment, were subsequently fixed in formaldehyde, embedded in 1 mm rings in paraffin blocks, and studied histologically in routine hematoxylin and eosin stains on serial 5 μm sections. Each section was evaluated with respect to signs of thermal damage at the site of direct laser impact, at the adjacent area, and at more distant sites. Particular attention was given to the vein wall opposing the site of direct laser impact.

Patients

Two patients scheduled for classic varicose vein surgery under tumescent local anesthesia[7] consented to undergo experimental EVLT in the interval between high ligation and stripping of the GSV. One patient received EVLT with a blood-filled GSV. In the second patient, conditions were identical, apart from the fact that blood was washed out of the GSV and replaced by normal saline prior to EVLT. Complete replacement of blood by saline solution was confirmed visually by a flexible vascular fiberscope. The time interval between EVLT and invaginated stripping was 15 minutes. The vein was then cut into 2 cm sections, fixed in formaldehyde, and embedded in paraffin blocks for later histologic examination.

Laser-Generated Steam Bubbles in Normal Saline, Plasma, or Hemolytic Blood

An in vitro setup to measure laser-generated steam bubble sizes was used as previously described.[5] Diode lasers with 810 nm, 940 nm, and 980 nm were used with appropriate 600 μm fibers as provided by the manufacturers. Before starting the comparative experiments, the energy output of each device was calibrated at the fiber tip with a power meter. Before each experiment, the fiber tips were freshly cut to avoid secondary carbonization effects. Each laser wavelength was tested in tubes filled with normal saline, human plasma, and hemolytic blood by administration of pulses between 3 and 16 J. Plasma was obtained by centrifugation of heparinized blood for 20 minutes at 2000 g. Hemolytic blood was produced by replacing the removed plasma with equal volumes of distilled water.

Results

EVLT was performed under in vitro conditions on GSV segments either filled with blood ($n = 5$) or filled with normal saline ($n = 5$). In addition, EVLT was performed in vivo after high ligation but before stripping of the GSV, in a vessel filled with either blood or normal saline. The generation of steam bubbles in normal saline, plasma, and hemolytic blood was examined for laser wavelengths of 810, 940, and 980 nm under in vitro conditions.

Pathologic Examination of GSV Segments Receiving In Vitro EVLT

A minimum of 20 hematoxylin and eosin-stained serial sections of each vein segment were examined microscopically. Detectable changes of the vein wall, attributable to endovenous laser action, were highly reproducible. Figure 1 displays representative cross sections of laser-treated GSV segments. In saline-filled veins, vein wall damage was exclusively confined to the site of direct laser impact (Figure 1B), while adjacent regions (Figure 1A) and, in particular, the opposite side of the vein wall (Figure 1C) show virtually no signs of tissue damage. In contrast, pronounced thermal damage was detectable along the entire vein wall in blood-filled veins (Figure 1D,E), even at the vein wall opposite the laser impact (Figure 1F).

Pathologic Examination of EVLT Effects on Surgically Removed Veins

The histopathologic examination of veins stripped after EVLT under in vivo conditions showed a similar pattern of thermal damage as the veins treated under in vitro conditions described above. Figure 2 displays representative sections of laser-generated complete perforations of the vein wall produced from the saline-filled (Figure 2A,B) or blood-filled (Figure 2D,E) vein. Again, the immediate site of laser impact exhibited a comparable extent of coagulative necrosis, regardless of whether the vein contained saline (Figure 2A) or blood (Figure 2D). However, even the immediately adjacent inner vein wall showed distinct differences in the extent of thermal damage (Figure 2A,B,D,E), with severe injury in the blood-filled vein and a virtually normal situation in the saline-filled vein. Also, the vein wall located at the opposite site of the laser impact showed heat damage in the blood-filled vein (Figure

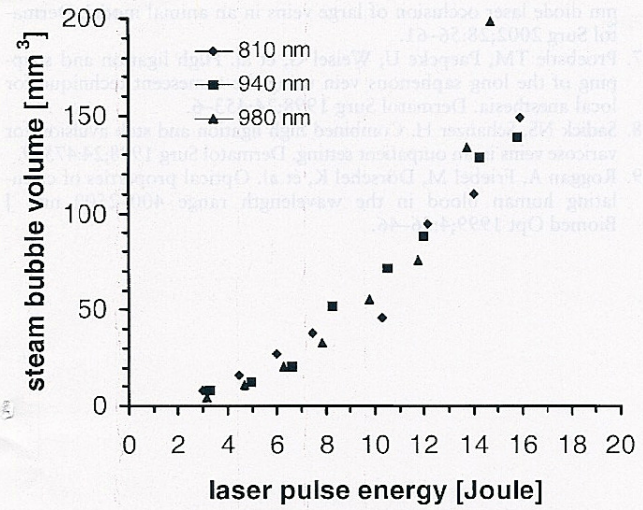

Figure 3. Laser-induced steam bubble volume in hemolytic blood plotted against delivered pulse energy for wavelengths of 810 nm (rhomboid), 940 nm (square), and 980 nm (triangle). No steam bubbles were produced with any of the experimental conditions in normal saline or plasma (data not displayed).

occlusion and EVLT have completely different modes of action. EVLT almost completely lacks the shrinkage effect of the vessels caused by prolonged exposure to moderate heat (85°C) in radiofrequency occlusion. Instead, EVLT causes perforation of the vein wall at the site of direct laser impact,[5,6] as a morphologic correlate for the consecutively observed perivenular ecchymoses.

In a previous report,[5] we proposed that laser-generated steam bubbles transfer a substantial amount of thermal damage to the vein wall during EVLT. These steam bubbles are created because of the high absorption of 940 nm laser energy in blood, with a technical penetration of only 0.3 mm. In water, this penetration depth is as much as 45 mm,[9] which is more than 100-fold deeper than in blood. Conversely, this implies that the absorption of 940 nm laser energy in water is less than 1% when compared to blood. Since under the particular topographic conditions of an endovascular laser fiber, a laser beam hits the vein wall within a markedly shorter distance than 45 mm, it can be concluded that heat generation by laser absorption cannot play a major role within a saline-filled vein. In this case, a laser beam of less than 1 mm diameter, with a fluence of more than 1500 J/cm^2, directly hits the vein wall, leading to complete perforating ablation of tissue (Figures 1A,B and 2A,B).

Our experimental setup tested this hypothesis under in vitro and in vivo conditions, providing histopathologic evidence: In a saline-filled vein almost the entire amount of focused laser energy is transferred to a small area at the vein wall, while in a blood-filled vein the thermal damage extends over a much wider topographic range of the inner vein wall, including the perilesional area and even areas opposite the immediate laser impact. This concordance between the in vitro and in vivo results suggests a sufficient correlation and validity of our in vitro model for the in vivo situation, despite the fact that under in vivo conditions the vein is much more compressed from outside by the presence of tumescent local anesthesia. However, one could speculate if a reduced, but still blood-filled, lumen of the vein could even facilitate laser-induced damage: relatively lower energies would suffice, because steam bubbles do not need to be generated in sizes that would be necessary to transfer homogenous damage to larger veins.

Evidence that blood plays not only a key role in absorption of 940 nm laser energy but also in absorption of 810 nm and 980 nm laser energy was provided by in vitro examination of steam bubble generation. While neither normal saline nor plasma were able to absorb laser energy substantially enough to generate steam bubbles, all three tested lasers produced comparable steam bubbles when exposed to hemolytic blood. Such steam bubbles, in all three laser systems, indicate that blood temperature passes the point of boiling at the site of the laser tip, thus transferring heat energy homogeneously to the inner vessel wall. The formation of these steam bubbles during EVLT could easily be monitored real time by duplex scanning, even allowing a continuous pullback of the laser fiber with the laser in continuous wave mode. One may speculate if with such a continuous pullback technique, perforations of the vein wall during EVLT could be avoided. However, a too-slow pullback velocity would certainly lead to a completely perforating longitudinal cut in the vein wall. Further experiments are needed on this topic. Therefore we hope that this improved knowledge about the exact mode of action of laser-induced vein damage may contribute to an improvement of endovenous laser treatment.

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