Evaluation of Endovenous Laser Ablation for Varicose Veins Using a Computer Simulation Model

(Secondary publication)

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Background and aims: Endovenous laser ablation (EVLA) has been well-reported as a minimally invasive method to deal with varices of the lower extremities. The lasers used fall into two categories: pigment, i.e., hemoglobin-specific lasers in the visible and near-infrared (near-IR) wavebands and longer wavelength mid-infrared lasers where the chromophore is water. The fiber used to deliver the laser energy is also important, and not enough attention has been paid to this element of EVLA. The present study was therefore designed to compare EVLA delivered through two specific fiber types coupled with a near-IR laser wavelength where water was the major chromophore.

Materials and methods: A laser diode system at the wavelength of 1470 nm was used as the laser energy source near a peak in the water absorption spectrum. Laser energy was delivered with two specific types of optical fiber, a RadialTM fiber and a Radial 2ringTM fiber (CeramOptec, Germany), and EVLA was evaluated using a computer simulation model taking light transport into account based on the Monte Carlo method and temperature distribution with the heat conduction equation.

Results and conclusions: It was confirmed from both the simulation model and a previously published *ex vivo* experiment that carbonization and sticking during EVLA caused by excess temperature rise can be minimized by using the Radial 2ring fiber compared with the Radial fiber, coupled with the 1470 nm wavelength. In the future, lasers with different wavelengths or optical fibers with differing irradiation modes may appear as candidate systems for EVLA. It is important to evaluate safety and efficacy carefully using the methods in the present study before moving to *in vivo* indications in human subjects.

Keywords: varicose veins • endovenous laser ablation • computer simulation • Monte Carlo method • heat conduction equation

Introduction

Endovenous laser ablation (EVLA) is a highly effective and minimally invasive treatment for varices of the lower extremities caused by incompetent saphenous veins, where post-operative occlusion rates of the treated veins as high as 95% have been reported in the literature ¹⁾. In the clinical setting, near-infrared (near-IR) lasers at wavelengths of 810 nm, 940 nm, 980 nm, 1064 nm, 1320 nm, 1470 nm and 2 μ m have been used in

combination with bare fibers with laser emission from simple flat cleaved end faces. The chromophores of the lasers differ according to the wavelength but can be grossly be grouped into two. Laser energy at wavelengths between 810 nm–1064 nm is absorbed mainly by hemoglobin where coagulation deep into the soft tissue can be achieved without the influence of water. Conversely lasers at wavelengths of 1320 nm, 1470 nm and 2 μ m are absorbed strongly by water contained in the blood and venous walls. This allows for vasoconstriction at lower energy levels and since the laser energy cannot penetrate deep into soft tissue, a safer

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and more effective treatment can be anticipated. Complications associated with EVLA such as pain of the thighs, bruising, thrombophlebitis, deep vein thrombosis, pulmonary thromboembolism, neural disorders and arterio-venous fistula have previously been reported²⁾ and the usage of lasers with high absorption in water is anticipated to lessen post-operative complications such as pain and bruising. Recent reports state that not only the selection of the wavelength but also the irradiation method affects the treatment outcome and decreases the incidence of post-operative complications such as pain and bruising³⁻⁷⁾. It is probable that developments and progress of new devices with differing irradiation methods and wavelengths will appear, but in order for such novel devices to be used clinically, they must first obtain regulatory approval through various time consuming and costly non-clinical and clinical trials.

Since clinical outcomes are highly dependent on the experience and technique of the attending surgeon, an objective method for the evaluation of the efficacy and safety of any novel device is warranted. In general, the investigation of the optimal treatment parameters such as wavelengths and irradiation methods is time consuming and costly, but if such investigation can be achieved through computer simulations, it would be highly effective in expediting the process of obtaining the appropriate regulatory approval. In the present study, therefore, the authors analyzed the results of light-heat propagation computer simulation, a combination of calculations of light transport and heat conduction concerning the venous wall temperature changes during an EVLA procedure, based on the premise of

using a 1470 nm laser diode in combination with an ELVeS RadialTM fiber and an ELVeS Radial 2ringTM fiber (CeramOptec GmbH, Germany) which can irradiate light laterally. The results of the analysis were compared to that of an *ex-vivo* experiment using resected veins.

Materials and methods

In this simulation, calculations were made on the premise that the laser device being used was a regulatory-approved system for EVLA in Japan, a 1470 nm wavelength laser diode with a maximum output power of 15 W (LEONARDO[®] 1470 (ELVeS laser 1470 in Japan), CeramOptec). The fibers being used were the ELVeS RadialTM fiber (not approved in Japan) and the ELVeS Radial 2ringTM fiber (approved in Japan) both which emit laser energy laterally. **Figure 1** shows the positioning of venous tissue, blood and the optical fiber used in the simulation. The assumption was that a blood-filled vein with a lumen diameter of 3.85 mm was being treated with EVLA using a fiber placed along the vein's central axis. The fiber is retracted at rate of 1 mm/s while laser energy is emitted laterally throughout⁸⁾. The principle behind the simulation of this light-heat propagation throughout the blood and venous tissue is described below, based on the calculation of light transport by the Monte Carlo model and the calculation of heat transport using the heat conduction equation.

Calculation of light transport

In order to calculate the light transport through blood and venous tissue three approaches were used: simula-

Fig. 1: Schematic of the simulated conditions for EVLA using (a) Radial fiber and (b) Radial 2ring fiber.

tion codes based on the Monte Carlo method developed by Wang et al.; the Monte Carlo modeling of light transport in multi-layered tissues (MCML); and the convolution for responses to a finite diameter photon beam incident on multi-layered tissues (CONV)⁹⁻¹¹⁾. MCML allows the calculation of light transport within multi-layered structures and in this simulation the layers were set as the blood layer 1 mm thick from the surface of the optical fiber to the inner surface of the vein, and the venous tissue layer set at a thickness of 2 mm. It was postulated that the blood and venous tissue layers were flat and uniform in structure and light transport was calculated for the diameter or depths ranging to 3 mm. The absorption coefficients and scattering coefficients of blood and venous tissue at the wavelength of 1470 nm, were determined through actual measurements of porcine blood and human venous tissue, as listed in **Table 1**^{6, 7)}. The refractive index 1.38¹²⁾ and anisotropy factor 0.9 were taken from the literature¹³⁾. For the refractive index of the optical fiber, 1.45 was used, being the refractive index of fused silica at the wavelength of 1500 nm¹⁴⁾. In this simulation, it was assumed that the intensity of the laser energy followed a Gaussian distribution and was incident on blood perpendicularly from the optical

fiber. The energy densities of each coordinate of the circular cylindrical coordinate system were calculated, where the laser beam was set as the central axis. **Figure 2** shows the laser power distribution of the Radial fiber and Radial 2ring fiber along the central axis measured using a power meter (S122C, Thorlabs) covered by a pinhole with a diameter of 1 mm^{6, 7)}. From the results, the beam diameters where the incident laser light intensity is $1/e^2$ (~13.5%) of maximum intensity were 1.40 mm for the Radial fiber and 1.375 mm and 1.50 mm for the Radial 2ring fiber as shown as cone 1 and cone 2 in **Figure 1b**. In this simulation, it was assumed for the Radial fiber that all incident power was delivered laterally in a single cone, whereas for the Radial 2ring fiber the power was delivered from cones 1 and 2. In the case of the Radial fiber, laser power incident on blood was determined from a ratio between the surface area of a cylinder with a diameter d of 1.85 mm (the external diameter of the Radial fiber) and a width w of 1.40 mm and the area of a circle with a diameter same as w of 1.40 mm. On the other hand, in the case of the Radial 2ring fiber, the ratio of the laser power between cones 1 and 2 was assumed to be 16:9 according to the ratio of the respective geometrical cross sectional areas of the

Table 1: Optical properties at the wavelength of 1470 nm and thermal properties of blood and venous wall used in the simulation model taking account of light-heat propagation.

	Absorption coefficient μ_a [cm ⁻¹]	Scattering coefficient μ_s [cm ⁻¹]	Refractive index	Anisotropy factor	Density ρ [kg/m ³]	Specific heat C_p [J/(kg · K)]	Thermal conductivity λ [W/(m · K)]
Blood	18.3	176	1.38	0.9	1048	3598	0.552
Venous wall	18.2	151	1.38	0.9	1020	3450	0.501

Fig. 2: Laser power distribution at the surface of the (a) Radial fiber and (b) Radial 2ring fiber along the central axis measured using a power sensor covered by a pinhole with a diameter of 1 mm.

Fig. 3: Schematic of the calculation of the laser power used as the input for the computer simulation and the model used in the Monte Carlo simulation.

cones. Since the external diameter of the Radial 2ring fiber is 1.85 mm, laser power incident on blood for the cone 1 or cone 2 was determined from a ratio between the surface area of a cylinder with a diameter d of 1.85 mm and a width w of 1.375 or 1.50 mm and the area of a circle with a diameter same as w of 1.375 or 1.50 mm, respectively. Although in actual use both the Radial and Radial 2ring fibers emit laser energy forwards^{4, 6, 7)}, in this simulation this was disregarded in order to simplify the simulation. The number of Monte-Carlo simulation trials (number of incident photons) was set at 10^6 and the grid size for the calculation was set at 50 μ m for both depth and radius.

Heat transport calculation

From the intra-tissue energy density distribution attained by the Monte-Carlo simulation, temperature rises and their temporal changes due to heat conduction were calculated through numerical analysis. Whereas a cylindrical coordinate system with an axis along the center of the laser beam was used for the energy density distribution calculated with the light transport simulation, the 2-dimensional heat conduction equation shown below was used for the calculations of heat transport in order to simplify the calculations. The energy density attained from the Monte-Carlo simulation was substituted for the energy density of the heat source S (W/m^3) of the heat conduction equation and the thermodynamic temperature T (K) was calculated for any given time t when the heat source moved in the same manner as the retraction of the fiber shown in **Figure 4**.

$$\rho C_p \frac{\partial T}{\partial t} = \lambda \left(\frac{\partial^2 T}{\partial x^2} + \frac{\partial^2 T}{\partial y^2} \right) + S$$

The density ρ , specific heat C_p and thermal conductivity λ used in this calculation are listed in **Table 1** and are those cited in the literature for blood¹⁵⁻¹⁷⁾ and for the venous wall¹⁸⁾. The above equation was dis-

cretized using a finite difference method, i.e., the Crank-Nicolson method by employing the central difference along the time axis. The obtained solution was converged using the successive over-relaxation method. The temporal profiles of the temperatures of each coordinate were calculated at a time step of 0.1 s. The initial temperature of the blood, vein and fiber was set at 37°C, and the boundary condition for the bilateral and lower boundaries was fixed at 37°C. Additionally, the temperature of blood in contact with the optical fiber ($y = 0$ mm in **Figure 4**) was used as

Fig. 4: Schematic of the computer simulation model to estimate the temperature distribution by solving the heat transfer equation.

the fiber temperature at 0.1 s later. In this simulation, in order to compare the Radial fiber and Radial 2ring fiber in the simplest of settings, complex phenomena such as bubble formation, morphological changes in venous tissue, and histologic changes accompanying coagulation were not taken into consideration.

Results and discussion

The results of the simulation, temporal profiles of the temperature at the vicinity of the surface of the venous wall, i.e., at the position $x = 0$ mm, $y = 1.05$ mm in **Figure 4** at laser powers of 5.8, 8.9, and 11.8 W and a fiber retraction speed of 1 mm/s are shown in **Figure 5**. It is clear that the maximum temperature of the vein wall is lower when the Radial 2ring fiber was used at all laser power settings. The purpose of EVLA is to constrict and obstruct the vein through coagulative denaturation. In order to prevent unnecessary carbonization and vaporization, it is thought that a temperature less than 100°C should be maintained for a certain period of time. From the results shown in **Figure 5**, the temperature grossly exceeded 100°C when the Radial fiber was used at laser powers of 8.9 and 11.8 W which means that excessive heating for the purpose of EVLA has occurred. On the other hand, when the Radial 2ring fiber was used, the maximum temperature at the laser power of 11.8 W was 85°C lower than that of the Radial fiber, hence there was less risk of carbonization and vaporization compared to the Radial fiber at the same laser power.

Fig. 5: Temporal profiles of the temperature at the vicinity of the surface of the venous wall, i.e., at the position $x = 0$ mm, $y = 1.05$ mm in Fig.4.

In a study in which *ex vivo* experiments were actually performed under the same conditions as the present simulation, namely a wavelength of 1470 nm and a fiber retraction speed of 1 mm/s using porcine blood and human venous tissue, stated that when a Radial fiber was used, successful vein constriction with no carbonization or perforation of tissue was achieved at a laser power of 5.8 W, however at laser powers of 8.9 and 11.8 W sticking of the fiber was seen in 40 and 60% of the attempts, respectively ⁷⁾. In this same study successful vein constriction without carbonization, perforation of tissue and sticking of the fiber was achieved at all laser powers when the Radial 2ring fiber was used.

The present study has some limitations. In the present simulation, the aspect of forward laser emission from the fibers was ignored and the model was based on the assumption that blood and the venous wall would present a smooth plane. Also complex phenomena such as bubble formation, venous tissue distortion and histological changes accompanying coagulation were not taken into consideration. Due to the omission of such considerations, the absolute values of the calculated temperatures contain inherent errors which could be large. The induction of latent heat accompanying the phase change of blood from liquid to vapor was not taken into consideration, and this may have led to an overestimation of temperature in the simulation, but the tendency seen in the simulation sufficed to explain the results of the previously reported *ex vivo* experiment carried out under the same conditions as the present simulation, and with the same types of optical fiber. Improving the precision of the simulation according to necessity may further help when designing new laser fibers and laser light sources, and planning EVLA treatments in the a clinical setting.

The reduction of costs and time involved in the regulatory approval of new medical devices to be used in the clinical setting is very important. Simulations can effectively search for optimum laser irradiation parameters through exhaustive trials and evaluations which is very difficult to do in a clinical trial, and also produce highly reproducible, quantitative evaluations under even the most extreme of conditions in a short period of time. Even further, simulations can be used for the theoretical elucidation of clinically occurring phenomena such as in this EVLA simulation, and lead to furthering the safe and effective clinical applications of EVLA.

Conclusions

The present study as an established theoretical simulation confirmed that the combination of a 1470 nm laser diode with a Radial 2ring fiber used for endovenous laser ablation resulted in less excessive heating of venous tissue and avoided carbonization and sticking compared to that produced by the same laser used with a Radial fiber. This confirmation is made through both our computer simulations, and the results of an *ex vivo* study performed under exactly the same conditions as the simulation. In the future, lasers with different wavelengths or optical fibers with differing beam delivery modes may appear. In order to evaluate the novel devices for clinical application, the light-heat propagation simulation using the Monte-Carlo simula-

tion of light transport combined with solving of the heat conduction equation, as used in the present study, proved extremely effective. Utilizing computer simulations may not only enhance the efficiency of novel equipment designs but also may help in structuring theoretical interpretations of results gained through clinical or non-clinical trials. Highly reproducible and quantitative evaluation of laser irradiation parameters can be performed in short periods and therefore computer simulations may become extremely valuable for promoting clinical application of many novel medical devices, and not just limited to those used for endovenous laser ablation.

Disclosure of conflicts of interests

No conflicts of interests exist

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