

Effect of Pullback Speed and the Distance between the Skin and Vein on the Performance of Endovenous Laser Treatment by Numerical Simulation

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ABSTRACT

Introduction: Endovenous laser treatment (ELT) is a new treatment method for the reflux of the great saphenous vein. A successful ELT is dependent on the selection of optimum parameters required to achieve optimal vein damage while avoiding side effects including skin burns. The mathematical modeling of ELT can be used to understand the process of ELT. This study was conducted to examine the effect of laser pullback speed and the distance between the vein and skin on the performance of ELT.

Material and Methods: The finite element method was used to develop optical-thermal damage models and simulate the process of ELT process. Firstly, light distribution was modeled using the diffusion approximation of the transport theory. On the second step, temperature rise was determined by solving the bioheat equation. Considering the temperature field, the extension of laser-induced tissue damage was estimated using Arrhenius model.

Results: Regarding the results, pullback speed and the distance between the vein and the skin distance can affect the process of ELT. Moreover, the pullback speed of 1 mm/s, 2 mm/s, and 4mm/s were suitable for the treatment of varicose veins located in a depth of 15 mm, 10 mm, and 5 mm, respectively.

Conclusion: In the ELT method, the pullback speed should be determined considering the geometry of the varicose vein segments, especially the distance between the skin and vein.

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Introduction

According to the literature, varicose veins affect more than 25% of women and 15% of men throughout their life, and almost half of the people older than 50 years old suffer from varicose veins-related issues [1]. Varicose veins become enlarged, look twisted, and lead to heavy legs syndrome and worsened pain after sitting or standing for a long time. In addition, varicose veins can contribute in the development of blood clot that is one of the causes of pulmonary embolism [2].

Typically, the muscle pump in the calves works against the gravity and returns venous blood to the heart. Moreover, the veins have pairs of leaflet valves to prevent venous reflux. The malfunction of these leaflets is the primary cause of varicose veins [3]. Non-surgical treatments for varicose veins include sclerotherapy, compression stockings, elevating the legs, and exercise. The traditional surgical option in the cases of disease progression are vein stripping and the removal of the inflicted veins [4].

Ligation method is defined as tying or ligating of the veins through an incision in the skin, which has several adverse effects entailing scar, varicose veins

recurrence, hemorrhage, and infection. Furthermore, surgery may worsen blood flow in the veins in the case of damaged deep vein system [5]. Recently, less invasive treatment modalities such as ultrasound-guided foam sclerotherapy, radiofrequency ablation (RFA), and endovenous laser treatment (ELT) have been proposed as alternatives to surgical treatment [4, 6].

RFA and ELT are minimally invasive ultrasound-guided techniques for treating varicose veins. In RFA, thermal energy is delivered to vein through a radiofrequency catheter to destroy the refluxing vein segment. However, in ELT method, thermal energy is released to both the blood and vein wall leading to localized tissue damage [7]. In this method, an optical fiber is inserted into the diseased vein by interventional radiologist or vascular surgeon. Then, the laser is turned on and pulled back simultaneously to shine the interior part of the vein. The emitted laser light is scattered and directly absorbed by the vein wall, blood, and surrounding tissues which increases the temperature that triggers occlusion mechanisms. Eventually, it leads to the contraction and obliteration

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of the vein [8, 9]. The associated adverse effects of ELT is less than 10%, which is lower than the side effects of RFA method [7].

Moreover, in ELT method, the occlusion rate which is dependent on the amount of energy administered over a specified area is higher than the RFA technique [7, 10]. Numerous studies demonstrated that ELT is safe and efficient, and the success of this method is reported to be more than 90% [4, 11, 12]. However, no international consensus is available on a best treatment protocol so far. The most important adverse effects of ELT include skin burns, pulmonary embolism, deep venous thrombosis, and nerve injury [13-15].

Generally, skin burns are classified as first-, second-, third-, and fourth-degree. First-degree burn occurs when the temperature of the skin reaches to 44 °C. First-degree burns appear red without blisters and pain and typically lasts around three days. A fourth-degree burn is needed for the complete contraction of the vein during ELT. For this purpose, the temperature of the vein wall should reach to 57 °C. Considering the variability of the distance between the vein and the skin in different patients, the temperature of the vein wall and the skin might not be constant for different patients after ELT [4, 16].

Different groups used mathematical modeling for better understanding of the role of various parameters on the efficiency of ELT [8, 13, 17]. Initial works focused on the pulsed mode of ELT which may be performed using different wavelengths (e.g., 810 nm, 940 nm, and 980 nm) [13]. In the pulsed mode of ELT, the total amount of administered energy relies on the distance between pulses, pulse duration, and power of laser [14].

Several studies suggested that the continuous mode of ELT can be substituted for the pulsed mode [8, 14, 15]. In the continuous mode of ELT, the amount of energy depends on the power of laser and the duration of treatment. The duration of ELT is determined by laser pullback speed [11]. It is believed that the pulsed mode of ELT is associated with higher risk of adverse effects such as vein rupture compared to the continuous mode of ELT [14].

Mordon et al. used a two-dimensional model consisting of the blood vessel and surrounding tissue. The effect of vein wall thickness, pullback speed, power of laser, and wavelength on the permanent damage to the blood vessel was examined for both pulsed and continuous modes of ELT. They found that although the amount of required energy for continuous mode of ELT was higher than the pulsed mode, the continuous mode was more preferred by clinicians due to easy process of standardization and short treatment duration. Furthermore, the influence of different wavelengths on the efficiency of ELT was negligible. Nevertheless, they did not consider the possibility of skin burns in their model and assumed a

constant distance between the skin and the vein for all models [8].

Marqa et al. evaluated the combined effect of the distance between the skin and vein and surface cooling system on the skin temperature and vein wall temperature during the administration of pulsed mode of ELT. They assumed constant laser pullback speed for all models and suggested to use surface cooling system for the veins located in a depth of 5 mm to avoid skin burns. However, the effect of the depth from the skin to the vein on the efficiency of the continuous mode of ELT was unclear.

In our previous study, the laser was considered to be fixed inside the lumen of the varicose vein. We showed that the distance between the skin and vein significantly affect the temperature distribution of the vein wall and the skin [18]. In the present study, the movement of laser during ELT was considered and added to our previous model. Numerical simulation was used to investigate the combined effect of different depths of the vein from the skin and laser pullback speeds on the performance of the continuous mode of ELT.

In this study, a three-dimensional computational modeling was used to optimize laser pullback speed for different geometries in the continuous mode of ELT. To reach this goal, heat transfer between the laser and the vein wall and the extension of tissue damage were modeled in different cases. In addition, the laser pullback speed in different geometries was optimized regarding complete endovenous ablation and skin burn prevention.

Materials and Methods

Model Geometry

A three-dimensional model was built to describe the underlying physics of the thermal laser-tissue interactions. We used the geometry of the saphenous vein that was firstly defined by Marqa et al. based on ultrasound imaging [13]. Our geometry was consisted of a cube of 40×40×40 mm³ containing the vein, blood, perivenous tissues, and skin (Figure 1). The saphenous veins with the diameter of 5 mm were parallel to the skin surface at the depths of 5 mm, 10 mm, and 15 mm to examine the effect of the depth of the vein from the skin on the ELT process.

Additionally, the perivenous tissue was considered to be homogenous. The laser with the power of 15 W started to radiate when it was located in the lumen of the vein and at 10 mm to the lateral surface of the domain. Laser moved linearly through the vein with a constant pullback speed and continuous radiation until it reached to the distance of 10 mm to the opposite surface. Three different speeds (e.g., 1 mm/s, 2 mm/s, and 4 mm/s) were used to find out the effect of pullback speed on the efficiency of ELT process.

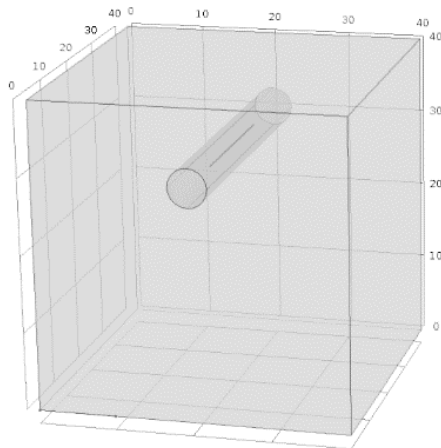


Figure 1. The geometry of the venous, perivenous tissues, skin, and the laser probe.

The duration of irradiation was considered as the ratio of the length passed by laser (20mm) to the laser pullback speed. Heat energy irradiated by the laser was transferred via conduction and convection and absorbed by the blood and other tissues.

Governing equation and boundary condition

It was hypothesized that only the temperature distribution within the model is required for accurate prediction of thermal-induced tissue damage [13]. Solution was implemented in three main steps as followed:

- 1- The photon absorption in different tissues was determined using the theory of transport.
- 2- Bioheat equation was solved to estimate temperature distribution in the numerical domain.
- 3- The extension of tissue damage was calculated using Arrhenius model.

Photon absorption

The light diffusion approximation of equation used in our simulation can be observed below [19]:

$$D \cdot \nabla \phi(r) + \mu_a \cdot \phi(r) = Q(r) \quad (1)$$

Where ϕ is the light fluence rate (W/mm^2), Q is the source term (W/mm^3) and represents the power injected per unit volume. The parameter μ_a is the absorption coefficient (mm^{-1}) and D is the diffusion coefficient (mm) defined by the following equation:

$$D = \frac{1}{3(\mu_a + \mu'_s)} \quad (2)$$

In the above formula, μ'_s is the reduced scattering coefficient of the tissue [20]. Heat absorption due to laser exposure was considered as a direct function of light fluence rate and the absorption coefficient (μ_a) and was calculated using the following equation [20]:

$$Q_{abs(r,t)} = \mu_a \cdot \phi(r) \quad (3)$$

Bioheat equation

The absorbed heat in tissues causes a local elevation in temperature [21]. Pennes equation (the well-known bioheat transfer equation) was used as a governing

equation to describe the heat transfer within different tissues and it is defined as below:

$$C_p \cdot \frac{\partial T(r,t)}{\partial t} - \nabla \cdot (k \cdot \nabla T(r,t)) = w_b \cdot C_p \cdot [T_b - T(r,t)] + Q_{abs(r,t)} + Q_{met} \quad (4)$$

T , C_p , ρ , k , w_b , r , Q_{met} , and Q_{abs} , represent temperature (K), thermal capacity ($J/mm^3.K$), tissue density (g/mm^3), thermal conductivity of tissue ($W/mm.K$), blood flow rate ($ml/g.min$), radial distance from the source (mm), metabolic source of heat (W/mm), and laser heat source (W/mm), which was defined by equation 3, respectively. The initial temperature of the blood and tissues was set as $37^\circ C$. Moreover, the boundary conditions for the bioheat equation were specified as below:

$$T = T_b \text{ for the cylindrical wall}$$

$$\vec{n} \cdot k \cdot \nabla T = 0 \text{ For all other surfaces}$$

It is worth mentioning that, \vec{n} is considered as the direction of the heat flux [13, 22].

Thermal damage

Thermal-induced tissue damage can be mathematically described by a first-order thermochemical equation, in which temperature history determines the damage [13, 22]. The extension of damage is quantified using a dimensionless positive parameter ($\Omega_{(r,t)}$), which expresses the probability of tissue damage. It depends on the temperature and the duration of exposure and can be computed using Arrhenius model as below [23]:

$$\Omega_{(r,t)} = \ln \left(\frac{C_{(r,0)}}{C_{(r,\tau)}} \right) = A_f \int_0^t \exp \left(\frac{-E_a}{R \cdot T(r,t)} \right) dt \quad (5)$$

In the above equation, $C_{(r,0)}$ and $C_{(r,\tau)}$ represent the concentrations of the intact tissue at the beginning and at the time τ , respectively. The temperature dependent parameters such as A_f and E_a that are called frequency factor and activation energy, respectively, can be determined by experiments. Additionally, the parameters R and T stand for the ideal gas constant and temperature, respectively.

The thermal threshold for tissue damage was selected to be $\Omega=1$, which results in irreversible cell damage [13, 22]. We used the optical and thermal parameters that were reported in the previous studies (Table 1) [13, 24]. By assuming the spheroid shape for the extension of thermal damage, its optimal ranges were determined for different geometries in a way that first-degree burns do not occur in the skin while the vein wall exposes to fourth-degree burn [22]. The volume of spheroid can be derived as below:

$$V = \frac{4}{3} \pi a^2 b \quad (6)$$

In this equation, "a" and "b" are the semi-minor and -major axes of the spheroid. The major axis of the spheroid was considered on the center of the vein; therefore, the amount of "b" was 10 mm. Moreover, the amount of "a" should be less than 0.75 of the distance between the skin and the vein to prevent skin burns. Accordingly, the maximum acceptable volume of thermal damage was determined for different cases.

$$V_{max} = \frac{15}{2} \pi h^2 \quad (7)$$

Table 1. Optical and thermal parameters used in the numerical simulation extracted from references [12, 25]

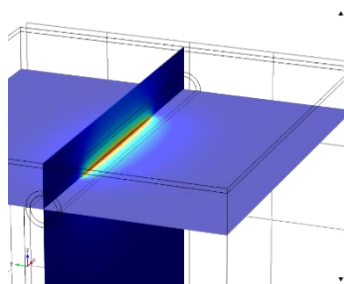
Parameter	Skin	tissue	Vessel Wall	Blood
$\mu_a (mm^{-1})$	0.1	0.03	0.1	0.28
$\mu'_s (mm^{-1})$	0.81	1.0	2	0.6
$\mu_{eff} (mm^{-1})$	0.52	0.3	0.79	0.86
$C (J \cdot g^{-1} \cdot K^{-1})$	2.87	3.78	3.78	3.82
$\rho (g \cdot mm^{-3})$	0.86×10^{-3}	1.05×10^{-3}	1.05×10^{-3}	1.05×10^{-3}
$K (W \cdot mm^{-1} \cdot K^{-1})$	3.02×10^{-4}	5.6×10^{-4}	5.6×10^{-4}	5.6×10^{-4}
$A_f (s^{-1})$	3.1×10^{98}	5.6×10^{63}	5.6×10^{63}	7.6×10^{66}
$E_a (J \cdot mole^{-1})$	6.28×10^5	4.3×10^5	4.30×10^5	4.48×10^5

Skin-vein distance

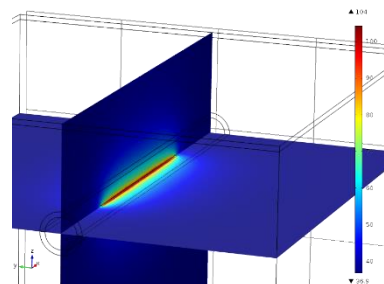
5 mm

10 mm

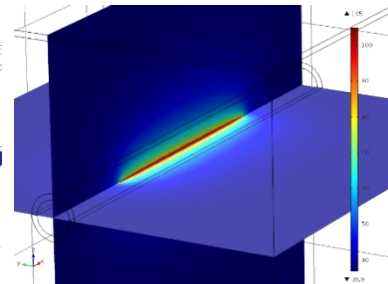
15 mm

Pullback Speed =
1 mm/s

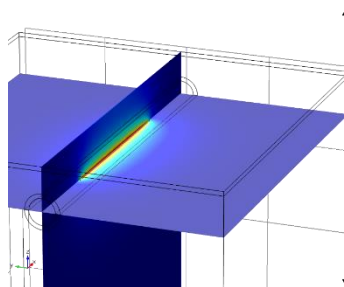
(a)



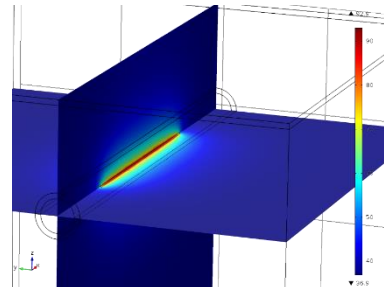
(b)



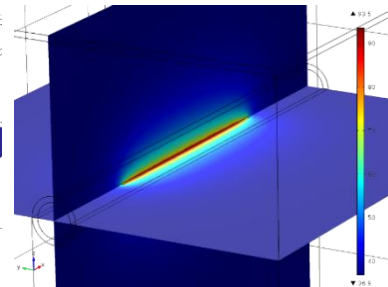
(c)

Pullback Speed =
2 mm/s

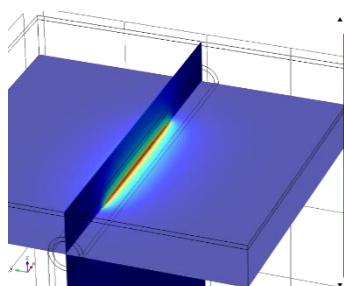
(d)



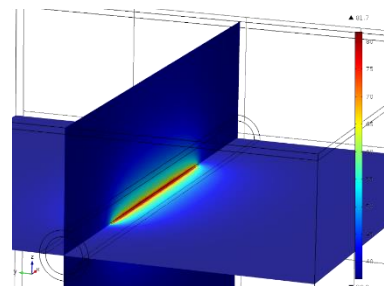
(e)



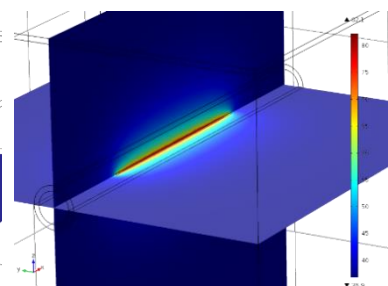
(f)

Pullback Speed =
4 mm/s

(g)



(h)



(i)

Figure 2. The temperature distribution within the domain for different laser pullback speeds and skin-vein distances.

In this formula, “h” was considered to be the distance between the skin and vein. Furthermore, to obtain complete vein ablation, the extension of thermal tissue damage should be more than $\frac{4}{3}$ of the volume of vein in the irradiated region. Therefore, the minimum acceptable volume of thermal damage can be determined as follows:

$$V_{\min} = \frac{4}{3} \pi r^2 (2b).$$

By considering $b=10$ mm and $r=2.5$ mm (the radius of vein), the minimum volume of thermal damage would be equal to $V_{\min}=523.3$ mm³ for all cases.

Table 2. Performing mesh independency analysis to achieve accurate results with minimum computational cost

	Number of elements	Vein wall temperature (°C)	Percentage of difference	Skin temperature (°C)	Percentage of difference	Thermal damage volume (mm ³)	Percentage of difference
1	19156	52.2		39.7		1245	
2	30267	55.1	0.052%	41.5	0.043%	1288	0.033%
3	42560	56.8	0.030%	42.1	0.014%	1321	0.025%
4	56342	57	<0.01%	42.2	<0.01%	1327	<0.01%

Numerical solution

The numerical model was implemented using finite element method in commercially available COMSOL Multiphysics v4.4 software. The defined geometries, partial differential equations, and boundary conditions are specified in this software. The domain was discretized into approximately 42000 tetrahedral elements. Mesh analysis was performed until differences between solutions from two consecutive meshes were less than 2%.

Three different parameters were considered for mesh analysis including skin temperature, vein wall temperature, and the extension of thermal-induced tissue damage. The suitable grid was selected in a way that by increasing the number of elements, the percentage of alternations of calculated values for these parameters were less than 2%. The numerical data obtained from the mesh independency analysis for one of the cases are represented in Table 2 (vein depth from the skin=10 mm and laser pullback speed=2 mm/s).

Time steps and convergence tolerance were computed to be 0.1 s and 10^{-3} , respectively. After running the models, temperature field inside the blood, vein wall, perivenous tissue, and skin were achieved. For better examining the thermal ablation of varicose vein with laser, the Arrhenius model was used and the extension of thermal-induced tissue damage corresponding to the temperature field was determined for different cases. The optimized laser pullback speeds for different geometries were selected in a way that the skin remained intact and the complete ablation of the vein wall was achieved.

Results

The duration of the laser radiation was 20 s, 10 s, and 5 s for the models with the laser pullback speed of 1 mm/s, 2 mm/s, and 4 mm/s, respectively. The temperature field for different geometries and laser pullback speeds after the completion of the irradiation are demonstrated in Figure 2. According to the results, the temperature field within the varicose veins with different geometries and the same laser pullback speeds was approximately the same.

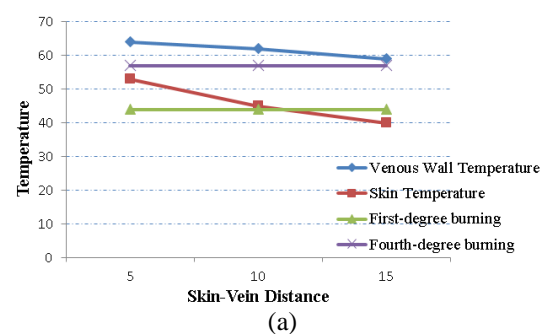
However, the maximum temperature in the models decreased by increasing the laser pullback speed. In fact, the increase of laser pullback speed led to the reduction of the duration of laser emission and the amount of diffused energy to the blood and other tissues was diminished.

The post-irradiation temperature of the skin and vein that was dependent on the vein depth from the skin and

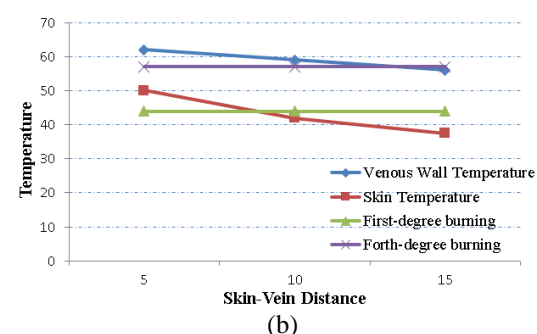
laser pullback speed is shown in Figure 3. As the results of the present study indicated, at a specific laser pullback speed, the vein temperature is approximately the same for different geometries; however, the skin temperature significantly increased by the reduction of the depth of the varicose vein from the skin.

Moreover, for the same geometry, the reduction of laser pullback speed led to the increase of temperature in both the vein and skin. Based on the results of the current study, if the vein was located in a depth of 5 mm from the skin and the pullback speed of laser was 1 mm/s, the temperatures of vein and skin would reach to 64°C and 55°C, respectively, which result in irreversible tissue denaturation in the vein wall as well as skin burn.

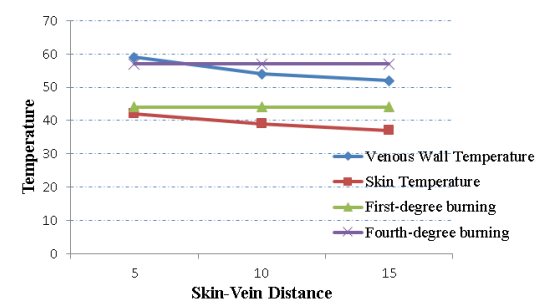
Pullback Speed of Laser= 1 mm/s



Pullback Speed of Laser= 2 mm/s



Pullback Speed of Laser= 4 mm/s



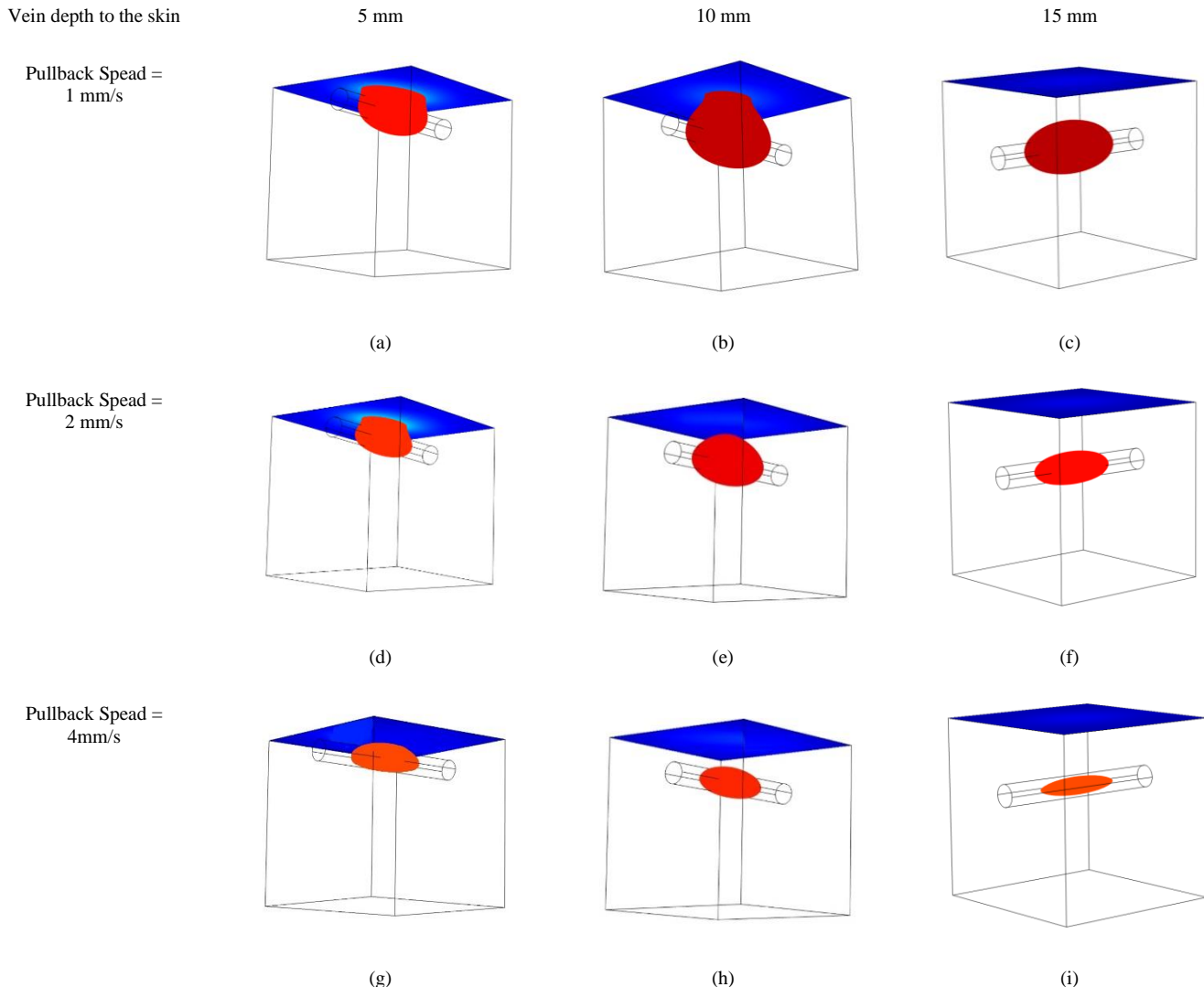
(c)

Figure 3. The temperature of venous wall and skin as a function of vein depth and laser pullback speed

The skin temperature significantly decreased with the increase of the vein depth from the skin and laser pullback speed.

For example, when the vein depth from the skin reached to 10 mm and the laser pullback speed increased to 2 mm/s, the temperature of the skin became lower

than 44°C; nevertheless, no skin burn was occurred. In addition, no significant change was observed in the skin at different laser pullback speeds in the vein depth of 15 mm. In this case, when the laser pullback speed was higher than 1 mm/s, the vein temperature was lower than 57°C (the required temperature for fourth-degree burn) and consequently the treatment was incomplete.

**Figure 4.** Thermal damage volume after endovascular laser treatment for different laser pullback speed and vein depth.

The extension of thermal-induced damage for different cases is demonstrated in Figure 4. As demonstrated in this figure, the solution shape was like a spheroid with a principal axis corresponding to the center of the vein. In Figure 5, the extension of thermal-induced damage was compared to defined suitable ranges for different geometries in different cases. If the distance between the vein and skin was 5 mm and the laser pullback speed was 1 mm/s or 2 mm/s, the extension of damage would be greater than the suitable range and consequently the skin burn would occur.

On the other hand, when the distance between the varicose vein and skin was 15 mm and the laser pullback speed was 2 mm/s or 4 mm/s, the extension of damage was lower than the suitable range and consequently the treatment was not performed completely. Accordingly, complete ablation and the prevention of skin burn could be achieved at the optimal laser pullback speed of 4 mm/s, 2 mm/s, and 1 mm/s for the veins located in a depth of 5 mm, 10 mm, and 15 mm from the skin surface, respectively.

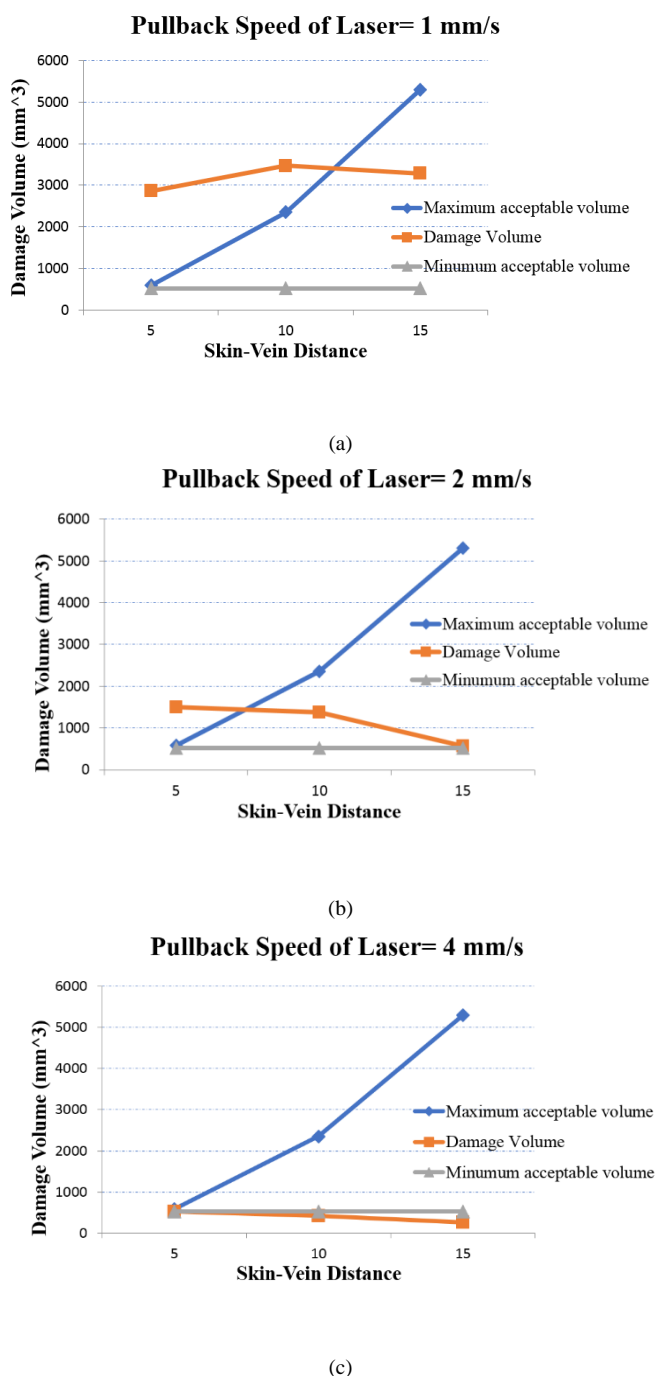


Figure 5. Comparing the suitable ranges of thermal damage volume and the thermal damage volume achieved by ELT as a function of skin-vein distance and laser pullback speed.

Discussion

In this study, numerical simulation was performed to estimate temperature distribution inside the vein and surrounding tissues in the continuous mode of ELT. Regarding the results of the current study, the efficiency of ELT depends on the laser pullback speed in addition to the distance between the skin and the vein. ELT in deep veins induced higher temperature to the skin surface. Moreover, the total energy required for ELT amplified by the increase of vein depth from the skin.

Additionally, the increase of laser pullback speed decreased the duration of laser emission and absorbed energy within the tissue. Consequently, the possibility of skin burn reduced by increasing the vein depth from the skin and laser pullback speed.

In this study, we focused on the laser pullback speed; however, laser power is the other parameter which can be investigated easily. It seems that the increase of laser pullback speed and reduction of laser power can lead to similar results. To shorten the surgical time and maximize the efficiency of laser treatment, Hernandez-Osma et al. suggested to use cold air for skin protection. Nonetheless, the necessity of using surface cooling system together with ELT was not examined completely [25].

We found that the probability of skin burn was high in the cases in which the veins are located in the depth of less than 5 mm from the skin surface or when laser pullback speed was low. Therefore, the utilizing of surface cooling system was recommended to prevent skin burns in these cases. However, when the distance between the skin and the vein was long enough or the laser pullback speed was selected properly, the surface cooling system can be omitted. The effect of using surface cooling system can be considered in the future studies. Our results were consistent with those reported by Marqa et al., who examined the effect of different geometries on the efficiency of pulsed mode of ELT [13, 23].

Strengths and Limitations of the Study

The main limitation of this study was due to the inaccuracy of the optical and thermal properties of the tissue, which play a key role in the accuracy of the results. This problem was intensified by considering the nonlinearity and dependence of these properties to different variables like temperature [13]. It was assumed that optical and thermal properties of perivenous tissues are the same that may not be accurate. Many methods have been tried to determine these properties; however, there are significant differences between the values presented by different groups that reflect the difficulty of measuring these properties.

In addition, parallel with numerical simulation, experimental studies should be used to identify certain treatment protocols that lead to effective collagen denaturation, vein wall thickening, and reduction of vein lumen diameter with minimal perivascular injury [26, 27]. The optimization of the laser power and laser pullback speed for different patients suffering from varicose veins can improve the efficacy of ELT and decrease the risks associated with damage of perivenous tissues during ELT.

Conclusion

In this study, we proposed a numerical simulation to evaluate the effect of vein depth from the skin and laser pullback speed on the efficiency of ELT. The aim of a successful ELT was the prevention of skin burn and complete ablation of the vein wall. Considering the results of this study, the efficiency of ELT depends on

the distance between the skin and vein, as well as laser pullback speed. It was concluded that laser pullback speed in the ELT should be determined considering the geometry of varicose veins. These results can be helpful to perform ELT more efficiently.

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