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A Physical Model of Laser-Assisted Blocking of Blood Flow: I. Rectangular Radiation Pulses

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Abstract—A method for the calculation of blocking blood flow upon treatment of vessel pathologies by laser irradiation at a wavelength of 530 nm are considered. The model is based on the assumption that blood-vessel occlusion is a consequence of preceding photothermal coagulation of internal layers of the vessel wall. The irradiation regimes are determined that provide homogeneous coagulation of the vessel wall at a minimal energy consumption and high selectivity of action upon irradiation by rectangular laser pulses.

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INTRODUCTION

Theoretical analysis of the destructive action of high-intensity optical radiation on biological structures is an important stage in the development of scientific principles for the application of lasers in medicine. Among these structures, skin and pathological subcutaneous formations of vessels play a special role. A large number of studies have been devoted to the investigation of propagation of radiation in these objects, formation and evolution of the temperature field in them, as well as to the investigation of destructive changes in these objects [1–16]. Various models were considered in these studies: a model of skin as a set of plane layers with different optical and physical properties (epidermis, dermis, blood layer) [1–9], a similar model containing a single infinite cylindrical blood vessel [10, 11], and more complex models including both numerous blood vessels in a semi-infinite medium and analogues of real histological specimens [12–14]. The propagation of radiation and subsequent formation of thermal sources in these model structures were considered in terms of the transport theory [8, 15], Kubelka–Munk theory [1, 7], and Monte Carlo method [2–4, 13]. Some studies considered the conditions of thermal denaturation of vessel walls upon laser heating [1, 4, 6, 15]. Along with the study of the thermal action of smooth laser pulses [1–14], significant attention is paid to the investigation of the response of tissues to pulse-periodic irradiation [4, 6, 16, 17]. The study of the destructive action of laser radiation on these biological structures made it possible to solve a number of problems connected with the choice of the radiation wavelength and optimization of regimes of irradiation of vessel pathologies in the course of their treatment [1, 6, 9, 12].

This study is a continuation of investigations discussed above. It is aimed at solving a practically important problem of laser-assisted blocking of the blood flow in a vessel under conditions of minimal damage to adjacent healthy tissues. The necessity of local blocking of the blood flow arises, e.g., upon dissection of tissues (stanching blood flow), upon treatment of vascular malformations (including those of diabetic origin), varicose veins, cosmetic skin defects, and so on.

The method of analysis proposed is based on the effect of contraction of blood vessels upon their heating to some critical temperature T_{cr} [18].

Comparing the results obtained in [1, 15, 18], we suggested that the blocking (occlusion) of a blood vessel in this case is a consequence of preceding thermal denaturation (coagulation) of internal layers of vessel walls. This suggestion is equivalent to the following relation:

$$T_{cr} = T_{thr}, \tag{1}$$

where T_{thr} is the so-called threshold coagulation temperature. Usually, this term is taken to mean such an increase in the temperature of the tissue under given irradiation conditions at which the degree of thermal denaturation of the tissue corresponds to a decrease in the relative concentration f of intact molecules that constitute the tissue to the level $f = e^{-1}$.

Then, to solve the problem posed taking into account equality (1), it seems logical to require that the temperature of heating T at any point of the perimeter of a blood vessel would satisfy the condition

$$T_{thr} \le T < T_{vap}, \tag{2}$$

where T_{vap} is the temperature of the vaporization phase transition.

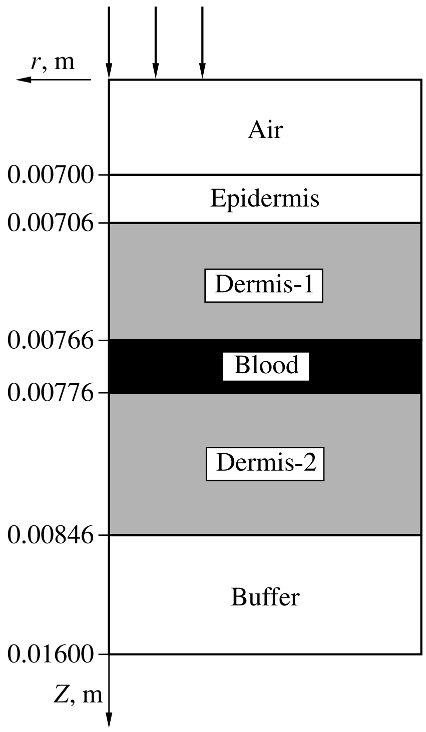

Fig. 1. Geometric configuration of a model of skin. The coordinates of the layer boundaries are given on the Z axis. The model configuration is adequate to the structure of skin considered in [4].

On the one hand, condition (2) eliminates inhomogeneous coagulation and, according to (1), inhomogeneous local shrinkage of the blood vessel. On the other hand, this condition decreases the probability of mechanical damage of tissues upon vaporization.

In this study, we will simulate the processes of heating and denaturation of tissues at the boundary of a blood vessel upon irradiation of skin at the wavelength 530 nm and, taking into account (2), determine, to a first approximation, the rational irradiation conditions for the blocking of the vessel.

MATHEMATICAL MODEL

The model of skin is analogous to that considered in [4]. It is represented by a multilayer cylinder along axis of which a light beam with a Gaussian radial intensity distribution propagates. The thicknesses of the layers are given in Fig. 1, and the optical and physical properties of the layers are presented in Table 1. In order for the conditions at the outer boundaries of the model structure to remain unperturbed, the radius of the cylinder is chosen to be much greater than the radius of the light beam. The buffer layer shown in Fig. 1 serves the same purpose. In turn, the radius of the light beam is chosen to be greater than the thickness of the main absorbing layer (the blood layer). This makes it possible to retain the calculation scheme close to those used in [1–6] and to simplify the subsequent comparison of results.

The temperature field is determined from the solution of the nonstationary heat conduction equation in the cylindrical region with the axial symmetry [19, 20],

$$\rho(z)C_p(z)\frac{\partial T}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}\left[r\chi(z)\frac{\partial T}{\partial r}\right] + \frac{\partial}{\partial z}\left[\chi(z)\frac{\partial T}{\partial z}\right] + Q(t)q(r, z, k, s). \tag{3}$$

Here, $T(r, z, t)$ is the temperature excess over the physiological norm (36.7°C); $\rho(z)$, $C_p(z)$, and $\chi(z)$ are the density, heat capacity, and thermal conductivity, respectively; $Q(t)$ is the time dependence of the intensity of the incident radiation; $q(r, z, k, s)$ is the volumetric power of the heat evolution; and k and s are the absorption and scattering coefficients.

The heat conduction equation was solved numerically using a locally one-dimensional economic difference scheme. To this end, the partial differential equation was separated into a set of one-dimensional difference problems. The difference scheme has the second approximation order and is absolutely stable. The boundary conditions have the following form:

$$T(r, z, 0) = T(r_{\max}, z, t) \equiv 0,$$
$$\frac{\partial T}{\partial r}(0, z, t) = \frac{\partial T}{\partial z}(r, 0, t) = \frac{\partial T}{\partial z}(r, l, t) \equiv 0. \tag{4}$$

The absorption of the radiation in tissue layers was determined according to the small-angle approximation of the transport theory [21]. The volumetric power of the heat evolution in the ith layer was sought taking into

Table 1. Optical and physical properties of structural elements of a model of skin

Skin layer	k, m^{-1}	s, m^{-1}	g	χ, W m^{-1} K^{-1}	C_p, J kg^{-1} K^{-1}	ρ, kg m^{-3}	ΔZ*, m
Air	10^{-6}	10^{-8}	1.0	2.7×10^2	1.01×10^3	1.17	7×10^{-3}
Epidermis	2.3×10^3	3.6×10^3	0.775	0.21	3.6×10^3	1.2×10^3	6×10^{-5}
Upper dermis	2.4×10^2	8.8×10^2	0.775	0.53	3.8×10^3	1.2×10^3	6×10^{-4}
Blood	2.7×10^4	4.7×10^2	0.995	0.55	3.6×10^3	1.1×10^3	10^{-4}
Lower dermis	2.4×10^2	8.8×10^2	0.775	0.53	3.8×10^3	1.2×10^3	6×10^{-4}

* Layer thickness.

account the scattering of the radiation and the divergence of the laser beam,

$$q_i(r, z) = \frac{E_{i-1}(k_i + s_i)R_{i-1}^2}{r_s^2}\exp\left[-k_i(z - z_i) - \frac{r^2}{r_s^2}\right],$$

$$r_s^2 = R_{i-1}^2 + \frac{2z}{k_i}\left[1 - \frac{\tanh\vartheta}{\vartheta(1 + 2\theta\tanh\vartheta)}\right], \qquad (5)$$

$$\vartheta = \sqrt{s_i k_i(1 - g_i)}, \quad E_{i-1} = E(z = z_{i-1}, r = 0),$$

$$i = 1, 2, 3.$$

Here, q_i is the volumetric power of the heat evolution in the ith layer; E_i is the irradiance (W/m^2) of the front boundary of the ith layer on the laser beam axis; R_0 (i = 1) is the radius of the light spot in the Z plane at the intensity level e^{-1} with respect to the maximal intensity; 2θ is the divergence angle of the light beam; and g is the factor that characterizes the shape of the scattering indicatrix in the Henyey–Greenstein representation [21]. The numerical values of the basic parameters of the layers (Fig. 1) for the laser radiation wavelength λ = 530 nm are given in Table 1. At all stages of the calculations, it is assumed that the optical and physical parameters of the vessel wall are close to the properties of surrounding tissues (dermis).

As in [1, 4, 6, 15], the thermal denaturation of the tissues is described by the kinetic equation of an irreversible first-order chemical reaction. The rate constant K of this reaction changes with temperature according to the Arrhenius law,

$$\frac{df}{dt} = -K(T)f,$$

$$K(T) = \frac{kT}{h}\exp\left(-\frac{\Delta H - T\Delta S}{RT}\right). \qquad (6)$$

Here, f is the relative concentration of intact molecules at the point (r, z); ΔH is the difference of the enthalpies of the initial and activated states (the activation enthalpy); ΔS is the corresponding entropy difference (the activation entropy); R is the universal gas constant; k is the Boltzmann constant; and h is Planck's constant. According to [15], the values of the parameters of the reaction ΔH and ΔS for the tissues of the vessel walls amount to 430000 J/mol and 940 J/(mol K).

By solving Eq. (3) simultaneously with Eqs. (6) for the specified action conditions (for the given parameters of the laser beam and irradiation time) at the point (r, z), we can easily determine the value of the irradiance E, W/m^2 (or of the radiant exposure H, J/m^2) at which the residual (after the pulsed heating and subsequent cooling) relative concentration f of intact molecules of the medium will decrease from 1 to e^{-1}. In what follows, we will term this value of the irradiance (radiant exposure) the threshold irradiance (radiant exposure).

To analyze the results obtained below, two parameters are used: the thermal relaxation time τ_z and the characteristic size Δz_0. The quantity τ_z is defined as the time during which the temperature at the inner surface of the absorbing layer (at the interface blood–dermis 2, Fig. 1) reaches a maximum under the action of a radiation pulse with the duration $t \ll \tau_z$ on the outer surface of the absorbing layer (on the interface blood–dermis 1, Fig. 1). The value of τ_z calculated according to (3) was 2.7×10^{-2} s. This is close to the estimate yielded by the approximate formula from [6],

$$\tau_z = \frac{1}{a}\left(\frac{2\Delta z}{\pi}\right)^2,$$

where $a = \chi/(c\rho)$ is the thermal diffusivity, which, in our case, is equal to 1.4×10^{-7} m^2/s (Table 1).

Physically, the characteristic size Δz_0 represents the penetration depth of radiation into the light absorbing layer. The value of this parameter can be found from the following relation [6]:

$$\Delta z_0 = \frac{2}{k + (1 - g)s}.$$

In our case, for the blood layer, $\Delta z_0 = 7.4 \times 10^{-5}$ m.

Because we consider the effective coagulation of the vessel walls, in addition to condition (2), it is logical to require that the radiation energy that is reached on the outer surface of the blood vessel would be completely transformed into heat and spent for the subsequent tissue coagulation. In other words, the layer thickness Δz should be approximately equal to the characteristic size Δz_0:

$$\Delta z \approx \Delta z_0. \qquad (7)$$

The model structure shown in Fig. 1 corresponds to this condition.

IRRADIATION WITH RECTANGULAR LASER PULSES: RESULTS AND DISCUSSION

As seen from Figs. 2 and 3, the temperature distribution over the layer thickness is essentially nonuniform. If the exposure time is smaller than ~10^{-3} s, the heating temperatures of the outer T_o and inner T_{in} boundaries of the blood layer differ by more than an order of magnitude. In this case, condition (2) cannot be simultaneously satisfied for both boundaries. As the increasing exposure time exceeds τ_z, the temperature field becomes more uniform due to the presence of heat exchange (Fig. 3). In our case, the temperature ratio T_o/T_{in} decreases to 1.4–1.5 (Fig. 4) and reaches saturation at exposure times in the range (2–4)τ_z.

Further increase in the exposure time significantly reduces the selectivity of the thermal laser action (curve *5* in Fig. 2 for t = 1 s) due to deep dissipation of thermal energy into dermal tissues.

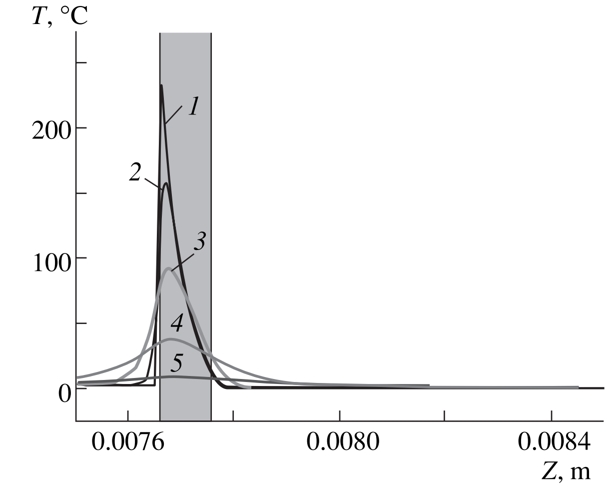

Fig. 2. Fragment of the axial temperature distribution in a model structure irradiated by rectangular laser pulses with the duration τ = (*1*) 10^{-5}, (*2*) 10^{-3}, (*3*) 10^{-2}, (*4*) 0.1, and (*5*) 1 s. The position of the blood layer is shaded. The radiant exposure H in all cases is 5×10^4 J/m^2.

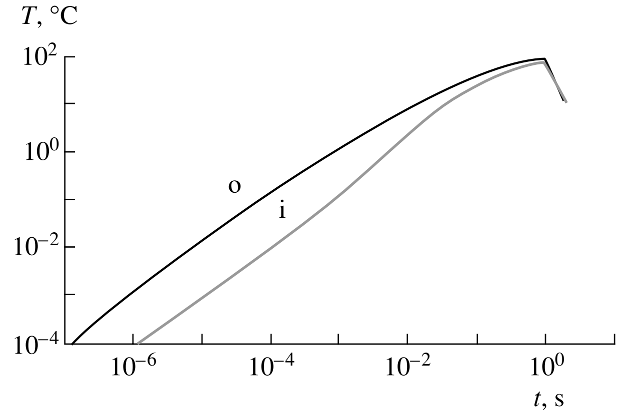

Fig. 3. Heating kinetics of the outer (o) and inner (i) surfaces of the absorbing layer at the irradiance on the laser beam axis 5×10^5 W/m^2.

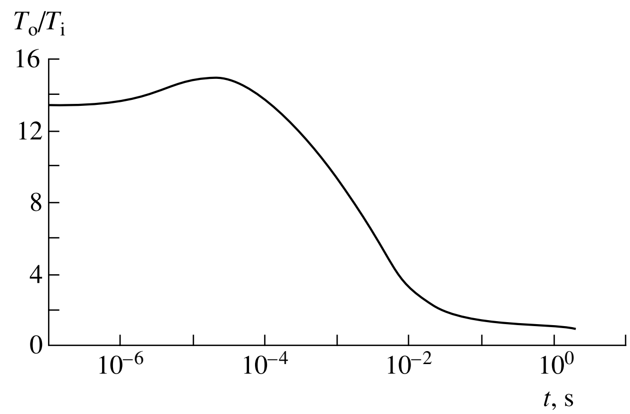

Fig. 4. Ratio of the heating temperatures of the outer (o) and inner (i) surfaces of the absorbing layer in relation to the irradiation time at the irradiance on the laser beam axis 5×10^5 W/m^2.

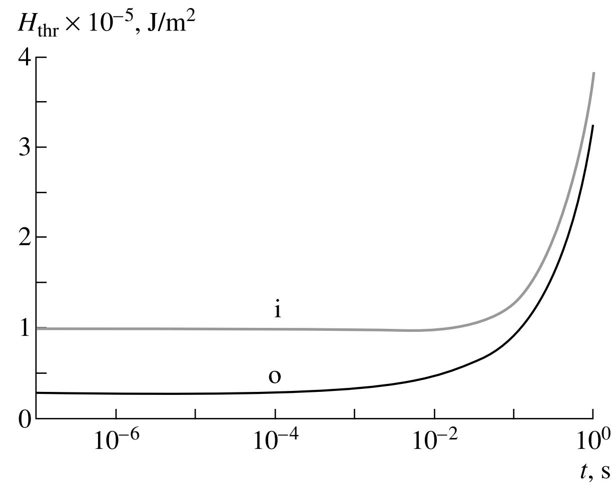

Fig. 5. Threshold radiant exposure (H, J/m^2) of the inner (i) and outer (o) surfaces of the absorbing blood layer in relation to the laser pulse duration.

More correctly, the criteria for the choice of the exposure time can be determined from the calculation of the threshold coagulation conditions of the vessel walls. As was indicated above, these conditions are determined from the simultaneous solution of Eqs. (3) and (6). The calculated values of the threshold temperature excess T_{thr} over the physiological norm (36.7°C) on the laser beam axis are presented in Table 2 for a number of exposure times.

Note that the threshold temperature of vessel shrinkage measured in [17] for heating times about several seconds amounted to 90°C. This value corresponds to our estimate: $T = T_{thr} + 36.7 \approx 90$°C. This confirms the assumption on the interrelation of thermal coagulation of vessel walls with subsequent occlusion of the blood vessel.

Figure 5 shows calculated dependences of the threshold radiant exposures H_{thr}(on) and H_{thr}(in) on the irradiation time. It is seen that, as the increasing exposure time exceeds 0.1 s ($\approx 6\tau_z$), the amount of energy necessary to create threshold coagulation conditions sharply increases. This phenomenon is caused by the reasons mentioned above: the temperature field diffusion, the loss of the action selectivity, and, as a consequence, the increase in the heating volume.

Table 2. Threshold heating temperature T_{thr} (°C) for the coagulation of tissues near the outer (o) and inner (i) boundaries of the blood layer

t, s	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}	1.0	10
T_{thr}(o)	79.5	78.4	74.7	72.2	64.2	56.5	48.6
T_{thr}(i)	63.1	63.1	63.1	63.1	62.5	54.6	48.6

We also note that, to ensure simultaneous coagulation of tissues at the inner and outer surfaces of the absorbing layer, the radiation energy should correspond to the greater of the two threshold radiant exposures shown in Fig. 4, i.e., to H_{thr}(in). In this case, taking into account the temperature of the medium T_0 (36.7°C), the heating temperature of the outer surface T*(o) will reach the value

$$T^*(\mathrm{o}) = \frac{T(\mathrm{o})}{T(\mathrm{i})}T_{\mathrm{thr}}(\mathrm{i}) + T_0. \qquad (8)$$

The dependence of the ratio T(o)/T(i) on the exposure time is shown in Fig. 5, and the values of T_{thr} are given in Table 2. The corresponding behavior of T*(o) is shown in Fig. 6.

The data presented above indicate that, from the viewpoint of energy efficiency, homogeneous coagulation of the vessel walls can be obtained in the range of exposure times $t \approx (1–5)\tau_z$, and, under more stringent requirements to the locality of the thermal action, at $t \approx (1–3)\tau_z$. If the temperature of the vaporization phase transition T_{vap} is estimated as the water boiling temperature, condition (2) proves to be unrealizable for the model chosen in the above-indicated interval of t (Fig. 5). In our opinion, however, such an estimate is too rough for a number of reasons.

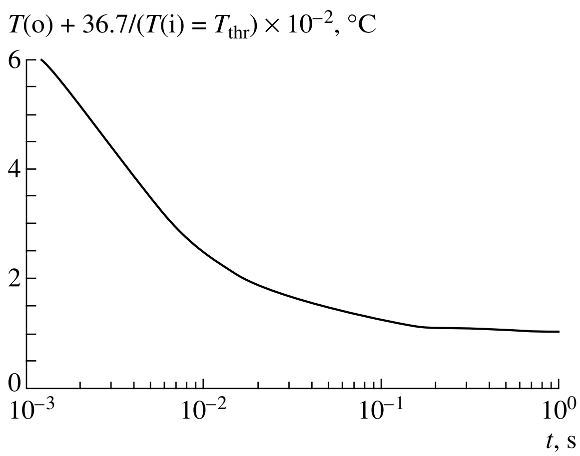

Fig. 6. Maximal temperature of the outer surface of the absorbing layer corresponding to the threshold coagulation conditions of the inner surface plotted as a function of the exposure time.

If the conditions of formation of boiling centers in water are considered, the interval of heating times of the order of 10^{-2}–10^{-1} s is characteristic of the vaporization regime that is intermediate between the stationary vaporization phase transition (occurring at 100°C with the heating time being in a matter of seconds or longer) and the explosive vaporization regime (taking place at ~300°C with the heating time being less than 10 μs) [22]. For water, which is in a bound state in biological structures, these parameters have not been studied yet. However, according to indirect data, it is expected that, under real conditions, these temperatures should be higher. In this connection, one can refer to the data in [23], which indicate that the energy spent for the formation of microbubble seeds in tissues of internal organs is more than two times higher as compared to model media (water, gelatin gel). It is also necessary to take into account that, by the moment of reaching a maximal temperature, the tissue on the outer wall is already at the primary coagulation stage, because its temperature exceeds T_{thr}.

In connection with the above, it seems that it would be more correct not to deny the fundamental possibility of efficient blocking the blood vessel under conditions considered but to suggest that there is a risk factor for mechanical damage of tissues which is connected with the possibility of formation of gas–vapor bubbles near the outer boundary of the blood vessel. The degree of this risk will increase in cases of radiation energy overdose in the course of therapeutic action.

A possible way to reduce the risk of mechanical damage of vessel walls is to use the regime of pulse modulation of radiation. This regime will be considered in the second part of our investigation.

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