

INFLUENCE OF OPTICAL AND THERMOPHYSICAL CHARACTERISTICS OF BIOLOGICAL TISSUE ON ITS THERMAL CONDITIONS UNDER LASER IRRADIATION

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On the basis of the developed analytical method of solving the heat conduction equation in a multicomponent biological tissue, its thermal conditions under laser irradiation have been investigated. Quantitative data on the temperature fields under a wide variation of the optical and thermophysical parameters in the tissue in the 400–700-nm range of wavelengths are given. The steady-state regime of the field in the tissue at various depths has been investigated. Estimates of the possible use of the time dependence of temperature under tissue cooling to solve the inverse problem — determine the heat-conductivity coefficient, the parameter of heat exchange with the medium, and the depth attenuation coefficient of light — are given.

In recent years, to treat a number of diseases and perform surgical operations, irradiation of human biological tissues has been actively used. In so doing, along with the biochemical processes proceeding in the body, heating of the tissues occurs. Depending on the problem being solved, it can play a positive or a negative role, but in any event adequate estimates are needed.

The calculation of the thermal conditions and their analysis have been the subject of many works. As applied to biological tissues, one uses, as a rule, numerical procedures based on finite-difference [1–3]] and finite-element schemes [4, 5] or the Green function approach [6–8]. Taking into account that the problem of investigating the thermal conditions is multiparametric, it is a good idea to use an engineering apparatus that permits one to obtain results that are physically visual and available for practice and *a priori* reveal important and unimportant parameters and thus create prerequisites for easier use of the known numerical procedures in investigating fine effects. In [9–11], an analytical method for calculating the thermal fields in two-component biological tissues illuminated by a laser beam was proposed. It is based on the analysis of the characteristic times [12] of the thermal processes determining the temperature conditions of the tissue — the heat conductivity in the tissue depth and in the radial direction and the heat exchange of the surface with the environment and of the blood vessels with the tissue-base surrounding them. It has been shown [10, 11] that 0.1–10 msec after the beginning of irradiation the temperatures of the components (blood and tissue-base) equalize and the medium, in terms of heat, can be considered as a one-component medium. The concrete value of the instant of time at which such equalization occurs is proportional to the squared mean diameter of the vessel and inversely proportional to the thermal diffusivity of the tissue.

The aim of the present paper is quantitative analysis of the laws of tissue heating and cooling under a wide variation of the irradiation parameters and optothermophysical characteristics of the tissue.

We first give some initial conditions of works [9–11]. For a one-component medium, we have the following heat-conduction equation:

$$\frac{\partial T}{\partial t} = \eta \left(\frac{\partial^2 T}{\partial z^2} + \frac{\partial^2 T}{\partial r^2} + \frac{1}{r} \frac{\partial T}{\partial r} \right) + S(t, z, r) - \nu T \quad (1)$$

with the initial and boundary conditions

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TABLE 1. Some Model Optical and Thermophysical Parameters of the Biological Tissue

λ	C_v														
	0.01					0.05					0.1				
	k	β	z_0	$R, \%$	τ_η	k	β	z_0	$R, \%$	τ_η	k	β	z_0	$R, \%$	τ_η
418	20.4	7.56	0.132	24.9	0.125	94.9	17.2	0.0581	5.89	0.0241	188	25.1	0.04	2.13	0.011
575	2.36	1.53	0.655	45.2	3.1	10.2	3.18	0.315	19.2	0.706	20	4.41	0.227	9.65	0.367
600	0.575	0.71	1.41	65.8	14.2	1.5	1.13	0.888	50.5	5.64	2.65	1.47	0.68	39.6	3.3
700	0.289	0.41	2.43	69.4	42.5	0.382	0.462	2.17	65.4	33.5	0.497	0.519	1.93	61.2	26.5

$$T(t=0, z, r) = 0, \quad T(t, z=\infty, r) = 0, \quad T(t, z, r=\infty) = 0, \quad \left. \frac{\partial T(t, z, r)}{\partial z} \right|_{z=0} = hT(t, z=0, r),$$

$$\left. \frac{\partial T(t, z, r)}{\partial r} \right|_{r=0} = 0. \tag{2}$$

Here T is the temperature excess over the initial temperature of the tissue. Note that from the fourth condition of relations (2) it follows at first glance that the initial temperature of the tissue is equal to the ambient temperature, but this is not so. In [9, 12], it was shown that if one approximately (by estimating the asymptotics) takes into account the thermal reaction of the organism to the temperature growth due to the action of light, then the solution of Eq. (1) under conditions (2) will correspond to the initial conditions of the tissue (about 36°C) rather than of the environment. Naturally, such an account is rather rough, but it gives correct asymptotics and, as is shown in [9], preserves the analyticity of the solution. The source function that is due to the action of external radiation is of the form

$$S(t, z, r) = E_0 u(t) \frac{k(1-R_1)(1+R)}{c\rho(1-RR_2)} \exp(-\beta z) \exp(-2r^2/r_0^2), \tag{3}$$

and the temporal form of an irradiation pulse of duration t_p has the form

$$u(t) = \begin{cases} 1 & \text{at } t \leq t_p, \\ 0 & \text{at } t > t_p. \end{cases} \tag{4}$$

The last term of Eq. (1) describes the intratissue (perfusion) heat exchange, where ν is the perfusion rate or the volume of blood flowing through a unit volume per unit time.

We shall consider a model medium reflecting, on average, the main trends of change in the thermophysical and spectral optical properties of soft biological tissues, e.g., muscles or derm. The model data were obtained by analyzing a large number of publications [9, 12]. They represent a convenient estimate of the properties of real tissues. In [9], the principles of constructing the model are described in detail and a comparison of its results with the experimental data obtained by different authors is made. It was shown that the character of the spectral change in the optical properties agrees with the experimental data. The quantitative values sometimes show a discrepancy by a factor of 2–3, but this is not surprising taking into account the diversity of tissues, their changeability, and many other fairly apparent factors.

Soft tissues consist mainly of water, so that the above two components have practically equal thermal diffusivities $\eta = 1.4 \cdot 10^{-7} \text{ m}^2/\text{sec}$ and the values of the product of the specific heat capacity by the density $c\rho = 4.2 \cdot 10^6 \text{ J}/(\text{m}^3 \cdot \text{K})$ [9, 12]. As is seen from (3), the radial structure of the light beam is assumed to be Gaussian with a characteristic radius r_0 at the $1/e^2$ level. The optical characteristics of the tissue entering into (3) — the absorption coefficients and the depth attenuation coefficients of light, as well as the reflection coefficients $R, R_1,$ and R_2 of the

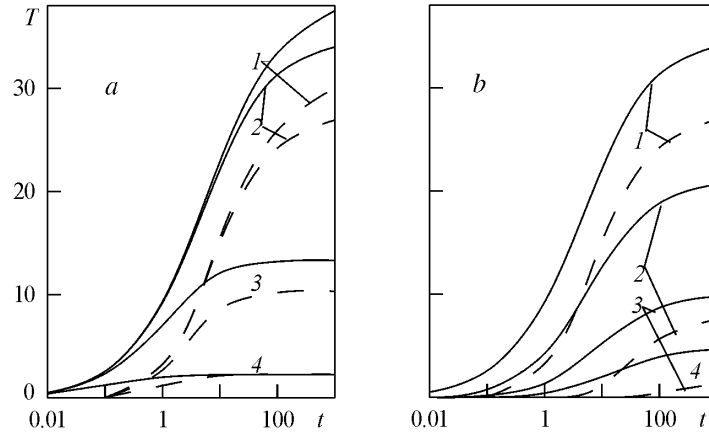


Fig. 1. Time dependence of the tissue temperature excess at $h = 0.01$ (curves 1), 40 (2), 1000 (3), $10,000 \text{ m}^{-1}$ (4), $\lambda = 418 \text{ nm}$ — a and $\lambda = 418 \text{ nm}$ (1), 572 (2), 600 (3), 700 nm (4), $h = 40 \text{ m}^{-1}$ — b; $z = 0$ (solid curves) and $10z_0$ (dashed curves), $C_v = 0.1$, $r_0 = 0.25 \text{ cm}$, $E_0 = 2 \text{ W/cm}^2$.

layer bulk and the tissue surface under various illumination conditions — were investigated in detail in [9, 11, 12]. Note that at a refractive index of the tissue $m = 1.33$ $R_1 = 0.02$ and $R_2 = 0.47$. The values of R in the 400–700-nm range of wavelengths are given in Table 1. As wavelengths λ , the characteristic points of the spectral absorption curve of blood were chosen [13, 14].

The solution of (1), (2) is of the form

$$T(t, z, r) = \int_0^t u(t - \tau) T_{\delta}(\tau, z, r) d\tau, \quad (5)$$

where

$$T_{\delta}(t, z, r) = T_{\delta, \infty}(t, z) \frac{r_0^2 \exp\{-r^2/[4(r_0^2/8 + \eta t)]\}}{8(r_0^2/8 + \eta t)}. \quad (6)$$

Here $T_{\delta}(t, z, r)$ and $T_{\delta, \infty}(t, z)$ represent the solution under irradiation of the medium by a δ -pulse of finite [9–11] and infinite [12, 15] width, respectively:

$$T_{\delta, \infty}(t, z) = \frac{E_0 k (1 - R_1) (1 + R)}{c\rho (1 - RR_2)} \left[\frac{F(t, z)}{2} - F_1(t, z) \frac{\sqrt{\tau_{\eta}}}{\sqrt{\tau_{\eta}} - \sqrt{\tau_h}} \right] \exp(-vt), \quad (7)$$

$$F(t, z) = \exp\left(\frac{t}{\tau_{\eta}}\right) \left[\exp(-\beta z) \operatorname{erfc}\left(\sqrt{\frac{t}{\tau_{\eta}}} - \frac{z}{2\sqrt{t\eta}}\right) + \exp(\beta z) \operatorname{erfc}\left(\sqrt{\frac{t}{\tau_{\eta}}} + \frac{z}{2\sqrt{t\eta}}\right) \right], \quad (8)$$

$$F_1(t, z) = \exp\left(\frac{t}{\tau_{\eta}}\right) \exp(\beta z) \operatorname{erfc}\left(\sqrt{\frac{t}{\tau_{\eta}}} + \frac{z}{2\sqrt{t\eta}}\right) - \exp\left(\frac{t}{\tau_h}\right) \exp\left(\frac{z}{\sqrt{\tau_h \eta}}\right) \operatorname{erfc}\left(\sqrt{\frac{t}{\tau_h}} + \frac{z}{2\sqrt{t\eta}}\right). \quad (9)$$

Formulas (7)–(9) contain the time parameters having a clear physical meaning: $\tau_{\eta} = 1/(\beta^2 \eta)$ — the characteristic time of temperature equalization in the tissue thickness, and $\tau_h = 1/(h^2 \eta)$ — the characteristic time of heat exchange between the tissue surface and the environment.

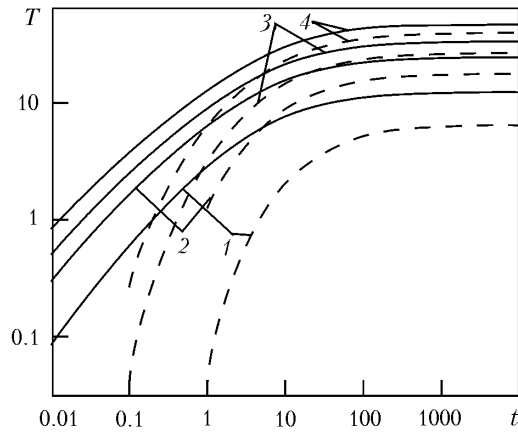


Fig. 2. Time dependence of the tissue temperature excess at $C_v = 0.01$ (curves 1), 0.05 (2), 0.1 (3), and 0.2 (4), $z = 0$ (solid curves) and $10z_0$ (dashed curves). $\lambda = 418 \text{ nm}$, $h = 40 \text{ m}^{-1}$, $r_0 = 0.25 \text{ cm}$, $E_0 = 2 \text{ W/cm}^2$.

We now proceed to the quantitative consideration of the mechanisms of heating and cooling of a biological tissue. To determine the absorption coefficient of blood, we assume the hematocrit to be equal to 0.4, the fraction of erythrocytes in the blood to be equal to 0.25, and the degree of oxygenation — to 0.75. Precisely for this case Table 1 gives the optical parameters used in the calculations. We also assume that $E_0 = 2 \text{ W/cm}^2$, $r_0 = 0.25 \text{ cm}$, and $\nu = 0$. The temperature values will be given on the beam axis at $r = 0$.

Figure 1 shows the tissue heating curves for various heat-release parameters h at the tissue–environment interface and attenuation coefficients in the depth regime β . It will be recalled that these parameters correspond to their equivalent characteristic times of heat release into the environment τ_h and the tissue depth τ_η (Table 1). Note that $h = 0.01 \text{ m}^{-1}$ ($\tau_h = 7.1 \cdot 10^{10} \text{ sec}$) corresponds to an almost heat-insulated medium, 40 m^{-1} ($4.5 \cdot 10^3 \text{ sec}$) — to dry air, 1000 m^{-1} (7.1 sec) — to water, and $10,000 \text{ m}^{-1}$ (0.071 sec) — to a good heat conductor. The above minimum and maximum values of h are practically not realized; however, the corresponding dependences are given in Fig. 1 for completeness of the picture. They are close to the mathematically limiting cases and are of purely academic interest. In a living organism, such a situation is impossible. Figure 1 shows the dependence for $z = 0$ and $10z_0$, where $z_0 = 1/\beta$ is the effective depth of light penetration into the tissue. At the initial instants of time t the surface temperature is always higher than in the tissue depth. With increasing t the heating process is retarded and the curves tend to their asymptotic values, which are the larger, the smaller the h (Fig. 1a) and the larger the β (Fig. 1b). At very large values of h the temperature inside the medium in the steady-state regime can become equal to T on the surface (curve 4 in Fig. 1a) or even higher than the latter. Note that when $t \ll \tau_h$, the temperature is independent of τ_h because the mechanism of heat release into the environment does not yet manifest itself. At large times, however, the temperatures tend to their asymptotic values, which are the higher, the smaller the h . In Fig. 1b, $\tau_\eta \ll \tau_h$ at all λ . This indicates that the heating is determined by τ_η alone. It is seen that the practically asymptotic regime appears at times much smaller than τ_h .

Above, the perfusion rate ν was assumed to be equal to zero. Strictly speaking, this assumption holds only at small times after the beginning of irradiation. For example, at the perfusion rate characteristic of skin such values of t measure about 60 sec [16]. Would the account for the perfusion at large times lead to the same changes in the data of Fig. 1 (and all the following figures)? Actually the respective temperatures will be somewhat lower. For example, the calculations by formulas (5)–(9) with allowance for the perfusion ($\nu = 0.00165 \text{ sec}^{-1}$ [16]) show that the maximum values of T for the solid curves 1 and 2 in Fig. 1 become equal to 34.9 and 32.1 K, respectively, instead of 37.5 and 34 K. If "saturation" of the temperature (or its steady-state regime) occurs, as for curves 3 and 4 in Fig. 1, then the perfusion does not influence the presented results at all. Therefore, the intratissue heat exchange as a result of the blood microcirculation is not taken into account hereinafter.

Figure 2 illustrates the influence of the concentration C_v of blood vessels on the heating at $z = 0$ and $10z_0$. The quantity C_v is the portion of the tissue unit volume occupied by blood. Sometimes it is also called the relative blood filling. Although the concentration C_v can vary with increasing temperature because of the discovery of new

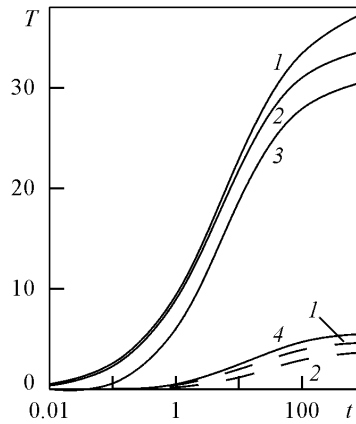


Fig. 3. Time dependence of the tissue temperature excess at $z = 0$ (curves 1), z_0 (2), $5z_0$ (3), and $10z_0$ (4), $\lambda = 418$ (solid curves) and 700 nm (dashed curves). $h = 10 \text{ m}^{-1}$, $C_v = 0.1$, $r_0 = 0.25 \text{ cm}$, $E_0 = 2 \text{ W/cm}^2$.

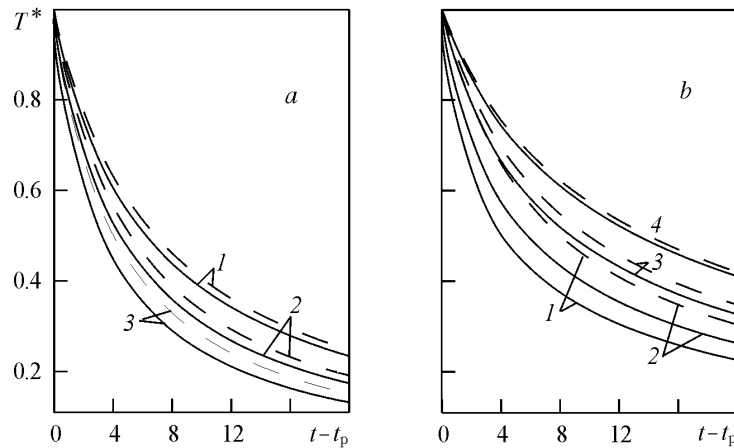


Fig. 4. Time dependence of the tissue temperature excess (in relative units) at $h = 500$ (curves 1), 1000 (2), 2000 m^{-1} (3), $\lambda = 700 \text{ nm}$ — a and $\lambda = 418$ (1), 575 (2), 600 (3), 700 nm (4), $h = 40 \text{ m}^{-1}$ — b; $z = 0$ (solid curves) and 0.5 mm (dashed curves) $C_v = 0.05$; $r_0 = 0.25 \text{ cm}$, $E_0 = 2 \text{ W/cm}^2$, $t_p = 300 \text{ sec}$.

capillaries, this effect is difficult to describe quantitatively in analytical form and is not considered here. The range of $C_v = 0.01\text{--}0.2$ covers the changes in the volume concentration of blood in the majority of normal and pathological tissues [17, 18]. The C_v values determine the absorption coefficient k of the elementary volume of the tissue and, consequently, the parameter β . Thus, C_v influences both the quantity of absorbed energy and the depth of penetration of light into the tissue. Obviously, with increasing C_v there is also an increase in the temperature. This is clearly seen from Fig. 2. Despite the fact that the light practically does not reach the depth $z = 10z_0$ (dashed curves) heating of deep tissue layers occurs due to the effective heat transfer from the near-surface regions.

Figure 3 illustrates the tissue heating at various depths z . Here $h = 40 \text{ m}^{-1}$ (contact with air), i.e., the heat release into the environment is small. Apparently, in this case the temperature decreases with increasing depth. A decrease in the absorption coefficient of the tissue at the wavelength $\lambda = 700 \text{ nm}$ (dashed curves) also leads to a drop in T compared to $\lambda = 418 \text{ nm}$ (solid curves).

Consider now the process of tissue cooling upon termination of irradiation. The absolute temperature values will not be given here, since they were given in Figs. 1–3 for various values of the medium parameters. The results on the time dependences $T(t - t_p)$ presented below have been normalized to the temperature at the moment the pulse ceases $T(t_p)$. Plotted on the abscissa is the time passed since the instant t_p .

TABLE 2. Estimates of the Instant of Time (sec) at Which the Stable Thermal Regime Sets in (Upper Number) and of the Temperature Excess (K) in This Regime (Lower Number) at Various Depths in the Tissue

λ	$h = 40$ at r_0				$h = 1000$ at r_0			
	0.05	0.1	0.2	0.5	0.05	0.1	0.2	0.5
	$z = 0$							
418	8	23	64	233	1.7	3.6	7.6	20
	4.7	9.9	20	45.1	3.2	5.5	8.4	12
575	16	36	83	262	3.1	5.7	11	27
	2.1	5	11	28	1.3	2.6	4.5	7.4
600	34	63	120	320	5.7	9.7	18	41
	0.66	1.8	4.4	12	0.38	0.87	1.7	3.2
700	74	120	200	440	10	17	30	68
	0.26	0.76	2	6.5	0.14	0.34	0.73	1.6
	$z = z_0$							
418	8.9	24	66	240	1.8	3.8	7.9	20
	4.4	9.6	19	45	3	5.4	8.5	13
575	23	44	94	280	4.4	7.3	13	30
	1.7	4.4	10	27	1.2	2.6	4.8	8.4
600	61	93	160	370	11	16	26	54
	0.46	1.4	3.7	11	0.33	0.87	2	4.2
700	160	210	310	560	32	43	61	110
	0.16	0.52	1.6	5.6	0.12	0.36	0.95	2.6
	$z = 5z_0$							
418	21	39	86	270	3.9	6.2	11.2	26
	2.7	7.1	16	42	1.7	3.8	7	12
575	160	180	240	450	27	31	40	69
	0.46	1.6	5.3	19	0.23	0.79	2.2	5.9
600	630	700	760	990	130	140	160	210
	0.08	0.3	1.1	5.4	0.04	0.14	0.47	1.9
700	1900	2300	2400	2700	580	620	660	780
	0.02	0.02	0.28	1.6	0.01	0.04	0.13	0.65

Figure 4a presents the tissue cooling curves on the surface (solid curves) and at a depth of 0.5 mm (dashed lines) upon irradiation by light with a wavelength $\lambda = 700$ nm ($\tau_\eta = 33.5$ at $C_v = 0.05$). The environment is water. In this case, the values of h can vary over the range of 500–2000 m^{-1} ($\tau_h = 28.6$ –1.8 sec). Here, at large h the tissue cooling is largely determined by the heat release into the environment. Naturally, with increasing h cooling occurs faster. With increasing z this process is retarded. In practice, the parameter h (or τ_h) is difficult to measure experimentally, since the heat withdrawal from the surface depends also on many other factors. However, data like those given in Fig. 4a open up a fundamental possibility of determining h , e.g., by superimposing the experimental curve on the theoretical ones.

Figure 4b corresponds to the case where $\tau_h \gg \tau_\eta$ and the cooling mechanisms are largely determined by τ_η . The different values of τ_η are due to the tissue irradiation by light of different wavelengths (see Table 1). It is seen that dramatic spectral changes in the blood absorptivity lead to marked differences in the cooling rate. With increasing k (decreasing τ_η) the temperature drops faster. As in Fig. 4a, where comparison of experimental and theoretical data permits, in principle, determination of τ_h and, therefore, h or η (depending on which of these parameters is known in advance), in this case the possibility of finding β or η opens up. However, the question of concrete methods of solving the above inverse problems requires additional studies.

This paper does not present results of the analysis of the influence of t_p , r_0 , and C_v on the medium cooling rate. The developed analytical method of investigating the thermal fields in biological tissues, briefly described at the beginning of the article, permits easy quantitative analysis. It is clear that with increasing irradiation pulse width the tissue is heated more uniformly in depth. An increase in the beam dimensions leads to the fact that the mechanism of heat outflow in the radial direction manifests itself at later instants of time after the onset of irradiation, and at certain durations t_p it may not begin working at all until irradiation is terminated. Then the tissue heating is described by simple formulas [10, 11] for an infinitely wide beam containing no integration operations. These formulas resulted from the analytical calculation of the integral in (5) of functions (7)–(9). This issue was investigated in [10, 11].

From Figs. 1–3 it is seen that in the course of time under continuous irradiation the temperature tends to a stationary value. In so doing, the mechanisms of heat withdrawal into the tissue depth and in the radial direction, as well as into the environment, balance the energy delivery from the light source. Table 2 gives the quantitative data on the moment of onset of the stable regime (upper number in each square) and the temperature excess (lower number) at this instant of time at $C_v = 0.05$, $E_0 = 2 \text{ W/cm}^2$. As a stationary temperature criterion, its value equal to $0.9T(\infty, z, t)$ was taken. Two cases have been considered — the tissue in air and in water. From Table 2 it is seen that the stable regime sets in faster for the near-surface layers of the medium than for the deep ones, since for the heat to reach a certain depth time is needed. With increasing λ the stationary temperature decreases and is realized later. Obviously, this is associated with the corresponding spectra of the absorption coefficient and the values of the parameter τ_η (see Table 1). The moment of onset of the stable regime strongly depends on the parameter of heat exchange h with the environment. For instance, in water it is much faster than in air, and the temperature values are somewhat lower.

In conclusion, note that in this work only some examples of the influence of the optical and thermophysical parameters of a biological tissue on its thermal conditions under laser irradiation have been illustrated. The proposed analytical method for calculating the temperature fields permits their investigations in a specific instance as applied to the optical, biological or medical problem being solved. In so doing, it is necessary to resort to a complicated mathematical apparatus or awkward computer programs.

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NOTATION

c , specific heat capacity, J/(kg·K); C_v , volume concentration of blood vessels; E_0 , surface power density, W/cm²; F , F_1 , auxiliary functions (8), (9); h , parameter of the heat exchange between the tissue and the environment, m⁻¹; k , absorption coefficient of the two-component tissue, cm⁻¹; m , refractive index of the tissue; r , current radial coordinate, cm; r_0 , effective beam radius, cm; R , reflection coefficient of the layer bulk; R_1 , reflection coefficient of the tissue surface under external irradiation; R_2 , reflection coefficient of the tissue surface under irradiation from the inside of the medium; S , source function, K/sec; t , current time, sec; T , temperature, K; T^* , normalized temperature; u , temporal pulse form; ν , perfusion rate, sec⁻¹; z , depth, mm; z_0 , depth of penetration of light into the tissue, mm; β , depth attenuation coefficient of the tissue, mm⁻¹; δ , delta-pulse; η , thermal diffusivity, m²/sec; λ , wavelength, nm; ρ , density, kg/m³; τ , integration variable; τ_h , characteristic time of heat exchange with the environment, sec; τ_η , characteristic time of heat transfer into the depth of the tissue, sec. Subscripts: 0, laser-beam parameter; ∞ , infinitely wide irradiation beam; p, pulse; v, volume; δ , delta-pulse; η , heat transfer in the tissue depth; *, normalization.

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