

Dual-wavelength laser system with optical feedback for the treatment of cutaneous vascular diseases

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An original optical scheme of a dual-wavelength laser system with feedback for the treatment of vascular skin diseases is proposed. The system operates at wavelengths of 450 and 980 nm. A control algorithm for the dual-wavelength laser system has been developed to improve the treatment efficiency of vascular skin lesions. The algorithm is based on measuring skin reflectance at wavelengths that are both sensitive to the concentration of oxyhemoglobin, deoxyhemoglobin, and methemoglobin in skin vessels and insensitive to changes in blood composition. Using the Monte Carlo method, the influence of human blood oxygenation and methemoglobin content on the reflectance spectra of human skin in the wavelength range of 400–1100 nm was numerically investigated. Within the framework of a seven-layer model of human skin, the reflectance of normal skin, skin with an enlarged vessel, and skin with a coagulated vessel was studied. It was found that to monitor the $\text{HbO}_2 \rightarrow \text{Hb}$ transformation, it is necessary to analyze the intensity of light reflected from the skin at wavelengths near the isosbestic points of deoxyhemoglobin and methemoglobin (e.g., at 660 nm). To monitor the $\text{Hb} \rightarrow \text{MetHb}$ transformation, the intensity of reflected light should be analyzed at wavelengths near the isosbestic points of oxyhemoglobin and deoxyhemoglobin (e.g., at 810 nm).

Keywords: spectrum, reflection, algorithm, skin, blood vessels, laser, blood, oxyhemoglobin, deoxyhemoglobin, methemoglobin, feedback, dual-wavelength laser system.

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Introduction

Blood vessel diameter in normal human skin generally varies with types of vessels. Typical capillary diameter is approximately 8–12 μm . Arterioles (precapillary and terminal) generally have a diameter of 17–26 μm , and a diameter of deeper arterioles reaches 40 μm [1]. Cutaneous vascular disorders, including telangiectasia, port-wine stains (nevus flammeus) and rosacea, are a group of malformations associated with structural damage and impairment of dermal blood vessels. These diseases are characterized by various depths, diameters and types (capillary, venous or arterial) of vascular lesions and blood flow properties [2–9].

Effective laser treatment of cutaneous vascular diseases (laser sclerotherapy) is based on a selective photothermolysis concept where the energy of selected laser radiation wavelengths is absorbed by hemoglobin in vascular lesions, causing coagulation of blood vessels with minimized damage of surrounding tissues, collapse, absorption and replacement with dermal tissue with a normal capillary network [10–12]. Single-wavelength laser exposure is mainly used for treatment of various cutaneous vascular malformations. For rosacea treatment, 532 nm (neodymium lasers with second harmonic generation, KTP), 585–595 nm (pulsed dye laser, PDL), 980 and 1064 nm (diode and Nd:YAG lasers) lasers and intense pulsed light (IPL) in a wavelength range of 500–1200 nm are used [10,13,14]. Laser radiation with wavelengths of 532 nm and 585 nm

effectively acts on superficial blood vessels, reducing redness and rosacea severity, while diode and Nd:YAG lasers provide deeper penetration of laser energy and are used for treatment of large and deep blood vessels, and in patients with dark skin (Fitzpatrick skin types V and VI) [10,15]. For port-wine stain treatment, sclerotherapy by pulsed dye laser (PDL, 585–595 nm) radiation optimally absorbed by oxyhemoglobin is the most clinically effective method that allows selective photothermolysis of vascular lesions without damaging surrounding tissues [16,17]. For resistant or deep lesions, Nd:YAG lasers (1064 nm) and alexandrite lasers (755 nm) are used to act on blood vessels at a depth of more than 1 mm [18,19]. Telangiectasia treatment involves exposure of abnormal superficial vessels to laser radiation absorbed by hemoglobin to cause selective destruction of the vessels. KTP lasers, pulsed dye lasers, diode lasers (980 nm) and Nd:YAG lasers (1064 nm) are used. Short-wavelength lasers (532, 595 nm) are most effective for superficial telangiectasia, and long-wavelength lasers (980, 1064 nm) are used for sclerotherapy of deeper blood vessels of the lower limb. In most cases, more than one laser sclerotherapy session are required for full removal of a vessel [20]. Note that single-wavelength exposure is ineffective for deep-seated vessels treatment and in some cases leads to negative implications for tissues surrounding the vessel.

Dual-wavelength exposure allows for considerable increase in efficiency and reduction of possible negative

effects of laser treatment of cutaneous vascular diseases [21]. Dual-wavelength laser systems constitute one of the most promising areas in treatment of cutaneous vascular diseases due to combined therapeutic action of two different laser wavelengths on blood vessels of various types, diameters and depth. Unlike single-wavelength lasers which are only effective on blood vessels with limited localization, dual-wavelength systems provide deeper and controlled photothermolysis adapted to anatomic and physiological properties of lesions. Modern systems can be fitted with a skin surface cooler designed to reduce the burning risk significantly and increase the laser sclerotherapy safety [21–23]. Dual-wavelength laser systems most commonly consist of a combination of 532 nm and 1064 nm radiation wavelengths and provide simultaneous action on superficial and deeply-seated blood vessels, ensuring a more pronounced clinical effect and reducing the number of required procedures [24]. Other systems combine PDL and Nd:YAG lasers where the radiation pulse of the former (585–595 nm) is absorbed by oxyhemoglobin, heats the blood in vessels and transforms hemoglobin into methemoglobin having a higher absorption coefficient for near IR radiation. The second pulse of Nd:YAG laser (1064 nm) effectively completes coagulation of the blood vessel, while the energy density used for vessel coagulation is reduced, thus, reducing thermal injury of epidermis [21,22]. There are other combinations of laser radiation wavelengths: for example, 532 nm and 940 nm, where the former acts on capillary and arterial formations, and the latter acts on larger venous vessels [25], as well as 980 nm and 1470 nm [26] or 450 nm and 980 nm [27]. At the same time, to gain the best therapeutic effect in terms of high efficiency and low injury rate, the action of radiation with both wavelengths shall be controlled by changing radiation properties on a timely basis. Therefore, it is apparent that an increase in the efficiency of dual-wavelength laser action on cutaneous vessels is only possible through a development of a feedback system with an adequate operation algorithm, which is, in particular, based on the measurement of optical characteristics of biotissue.

Laser systems with temperature feedback from a heated end of a waveguide tool are currently the best-known. The feedback provides real-time detection of tissue overheating and automatic correction of laser properties or complete termination of the action [28–30]. However, the temperature feedback doesn't make it possible to detect exactly what kind of biotissue structure is exposed to laser, and current condition of the biotissue, therefore, it cannot detect whether the desired effect is achieved in the structure which is required for the best treatment [31]. For this purpose, it is important to create feedback that can track a change of optical properties in biotissues in real time on the basis of a marker state analysis. Marker is a substance, changes of optical properties of which are indicative of the processes taking place in the biotissue exposed to laser radiation [31]. Monitoring of intensity of light reflected from the biotissue at wavelengths at which the greatest change of optical properties of the biotissue is induced by laser heating of

the biotissue can be taken as a basis of such feedback mechanism.

It is known that heating of hemoglobin, including laser heating, leads to hemoglobin transformation [32, 33] which starts from transformation of oxyhemoglobin (HbO₂) into deoxyhemoglobin (Hb) when blood reaches 46–48°C [34], and further heating to 65–70°C leads to formation of methemoglobin (MetHb). During heating up to approximately 80°C, irreversible reactions take place and cause hemoglobin denaturation and coagulation [35]. Having unique optical properties, HbO₂, Hb and MetHb will change blood reflection, absorption and transmission in the course of transformation. Earlier within the developed optical blood model, it has been shown that when HbO₂ is replaced with Hb (reduction of oxygen saturation), absorption increases in the wavelength range of 590–780 nm and decreases in the wavelength range of 780–1100 nm, replacement of Hb with MetHb leads to an increase in absorption at 590–1100 nm, and to a decrease in absorption at 520–590 nm. The observed changes indicate that the reflectance and transmittance of human blood are inversely proportional to its absorbance. [36].

A set of reflection measurement experiments for whole blood [31, 33], human skin [37] and animal skin [38] has shown that a change in spectral ranges typical of HbO₂ transformation into Hb and MetHb was observed after single-wavelength and dual-wavelength laser exposure. However, numerical justification of results of these studies are still not available.

Thus, the purpose of this study was to develop a numerical optical model allowing for estimating the reflection from normal skin, skin with a dilated blood vessel and skin with a coagulated blood vessel, and to study numerically by the Monte Carlo method the effect of human blood oxygenation and methemoglobin content on the human skin reflection spectra at 400–1100 nm, to propose an optical circuit of a dual-wavelength laser system with laser wavelengths of 450 nm and 980 nm with feedback on the basis of this numerical simulation for treatment of cutaneous vascular diseases, and to develop a control algorithm for this dual-wavelength laser system.

Materials and methods

Parameters of the dual-wavelength laser system with optical feedback for treatment of cutaneous vascular diseases were selected on the basis of numerical simulation of interaction between laser radiation and human skin considering a change in optical properties of blood during oxyhemoglobin transformation into deoxyhemoglobin and methemoglobin. Simulation results were used to choose an active laser wavelengths to be used directly for therapeutic treatment of a vessel to make it coagulated and a diagnostic laser wavelengths to be used for estimating the change in oxyhemoglobin, deoxyhemoglobin and methemoglobin

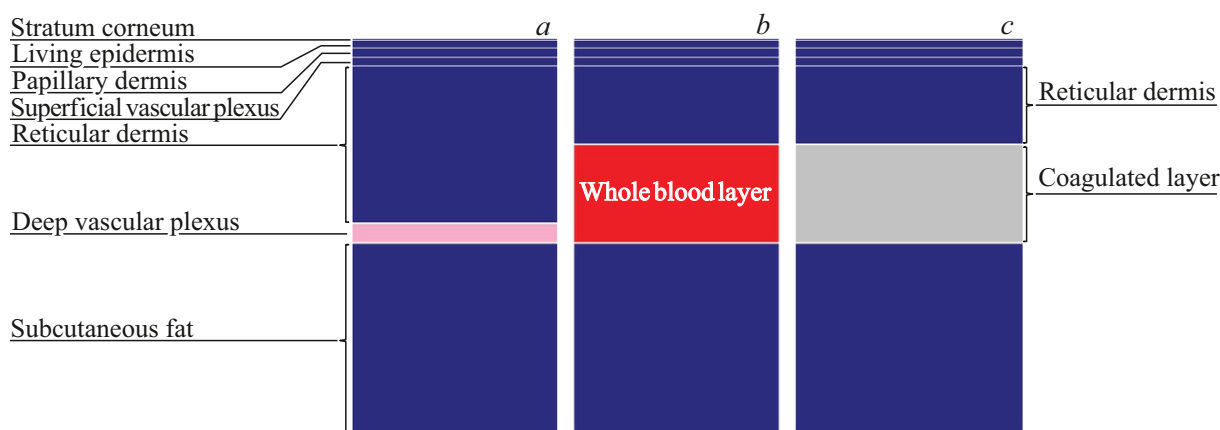


Figure 1. Seven-layer computer model: normal human skin (*a*), human skin with a dilated vessel in the dermis (*b*), human skin with a coagulated vessel (*c*).

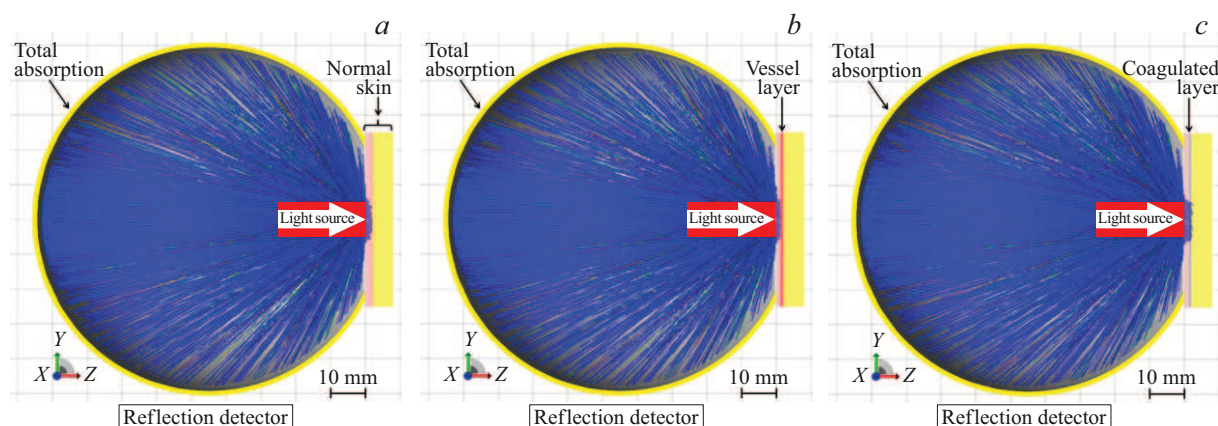


Figure 2. Example of beam paths in computer simulation of a bench for estimating the power of light reflection from the normal human skin layer (*a*), human skin with a dilated vessel (*b*) and skin with a coagulated vessel (*c*) (calculation was performed for combination № 1 according to Table 1, light source radiation wavelength is 532 nm). Red rays — for each such ray, the fraction of 1/10000 of the source power ranges from 100.0% to 66.6%; green rays — from 66.6% to 33.3%; blue rays — from 33.3% to 0.1%, respectively.

concentration in vessels to optimize the vessel sclerosis process by the therapeutic laser radiation.

To simulate the interaction between light and normal skin, a numerical optical model of normal human skin consisting of seven layers as described in [39] was used (Figure 1, *a*). Based on the details of vessel structure and depth in telangiectasia [2,3], a numerical optical model of skin with a dilated vessel (Figure 1, *b*) was proposed where the deep vascular plexus layer is replaced with the 1000 μm whole blood layer, which is comparable with sizes of large telangiectasia in human skin [20]. The total skin thickness remained unchanged and was equal to 2100 μm , while the reticular dermis decreased to 820 μm . Vessel coagulation (Figure 1, *c*) was simulated by replacing the optical properties of the whole blood layer in the numerical optical model of human skin with a dilated vessel with the optical properties of a coagulated chicken breast [40].

Absorption and scattering coefficients, and anisotropy factor of blood contained in blood-filled skin layers (pap-

illary dermis, superficial vascular plexus, reticular dermis and whole blood layer) varied with oxyhemoglobin, deoxyhemoglobin and methemoglobin concentrations in blood (Table 1 and [36]).

Computer models of the bench for estimating the power of reflected light flux from normal human skin, human skin with a dilated vessel and skin with a coagulated vessel are shown in Figure 2.

Numerical 3D simulation was performed in Trace-Pro 7.0.1 (Lambda Research Corporation, USA) using the Monte Carlo method. Light source emitted in the wavelength range of 400–1100 nm. It was a circle of 10 mm in diameter placed at a distance of 20 mm from the skin surface facing it (Figure 2). The source produced a collimated beam with a diameter of 10 mm, which was directed perpendicularly onto the surface of the skin area 50 mm in diameter. The beam diameter was selected in accordance with the data on radiation parameters for laser telangiectasia sclerosis presented in Ref. [20]. The spectral

Table 1. Combinations of oxyhemoglobin (C_{HbO_2}), deoxyhemoglobin (C_{Hb}) and methemoglobin (C_{MetHb}) concentrations in blood used for numerical simulation

№	$C_{HbO_2}, \%$	$C_{Hb}, \%$	$C_{MetHb}, \%$
1	100	0	0
2	80	20	0
3	60	40	0
4	40	60	0
5	20	80	0
6	0	100	0
7	0	80	20
8	0	60	40
9	0	40	60
10	0	20	80
11	0	0	100

and spatial distribution of radiation in the source beam was uniform. The simulation used 10,000 rays with a total power of 1 W. The light flux reflected after interacting with the skin layer was intercepted by a receiver (the Total Absorption sphere of 100 mm in diameter, Figure 2) and embedded TracePro 7.0.1 tool was used to estimate the light power via area integration of the spatial power distribution of the light flux that had reached and had been fully absorbed by the receiver.

Numerical simulation provided light power spectra $R(\lambda)$ of light reflected from a skin area in a wavelength range of 400–1100 nm with various combinations of oxyhemoglobin, deoxyhemoglobin and methemoglobin concentrations. $dR(\lambda)$ was further defined:

$$dR(\lambda)_{var} = R(\lambda)_{var} - R(\lambda)_1, \quad (1)$$

where $R(\lambda)_{var}$ is the calculated power of light reflected from skin, the blood contained in which had the concentrations C_{HbO_2} , C_{Hb} and C_{MetHb} as shown in Table 1, $R(\lambda)_1$ is the calculated power of light reflected from skin for combination № 1.

To control the HbO_2 , Hb and $MetHb$ concentrations in skin in terms of the dual-wavelength laser system algorithm with optical feedback chosen for treatment of cutaneous vascular diseases, it is proposed to measure the power of light reflected from skin in wavelength ranges meeting the following criteria: criterion № 1 I — reflected light power changes insignificantly (less than 5%) during the $HbO_2 \rightarrow Hb \rightarrow MetHb$ transformation; criterion № 2 — reflected light power changes insignificantly (less than 10%) during the $HbO_2 \rightarrow Hb$ transformation and significantly (more than 25%) during the $Hb \rightarrow MetHb$ transformation; criterion № 3 — reflected light power changes significantly (more than 25%) during the $HbO_2 \rightarrow Hb$ transformation and insignificantly (less than 10%) during the $Hb \rightarrow MetHb$ transformation.

Wavelength ranges meeting Criterion № 1 were defined as

$$S_I(\lambda) \leq 0.05 \times S_{I\max}, \quad (2)$$

where $S_I(\lambda) = \sum_{var=1}^{11} |dR_{var}(\lambda)|$ for $500 \text{ nm} \leq \lambda \leq 1100 \text{ nm}$, $S_{I\max}$ is the maximum value of $S_I(\lambda)$.

Wavelength ranges meeting Criterion № 2, were defined as

$$S_{II}(\lambda) \leq 0.1 \times S_{II\max}, \quad (3)$$

where $S_{II}(\lambda) = \sum_{var=1}^6 |dR_{var}(\lambda)|$ for $500 \text{ nm} \leq \lambda \leq 1100 \text{ nm}$, $S_{II\max}$ is the maximum value of $S_{II}(\lambda)$.

$$S_{III}(\lambda) \geq 0.25 \times S_{III\max}, \quad (4)$$

where $S_{III}(\lambda) = \sum_{var=6}^{11} |R_{var}(\lambda) - R_6(\lambda)|$ for $500 \text{ nm} \leq \lambda \leq 1100 \text{ nm}$, $S_{III\max}$ is the maximum value of $S_{III}(\lambda)$.

Wavelength ranges meeting Criterion № 3 were defined using equations (5) and (6):

$$S_{II}(\lambda) \geq 0.25 \times S_{II\max}, \quad (5)$$

$$S_{III}(\lambda) \leq 0.1 \times S_{III\max}. \quad (6)$$

Results and discussion

Figure 3 shows spectra $R(\lambda)_{1-11}$, $dR(\lambda)_{1-11}$ for normal skin (Figure 3, *a*), skin with a dilated vessel and various oxyhemoglobin, deoxyhemoglobin and methemoglobin concentrations, and $R(\lambda)_{12}$, $dR(\lambda)_{12}$ for skin with a coagulated vessel (Figure 3, *b*). The spectra demonstrate the behavior of $R(\lambda)$ and $dR(\lambda)$ of skin related to a change of forms of hemoglobin in skin. We didn't estimate the behavior of spectra $R(\lambda)_{var}$ and $dR(\lambda)_{var}$ within 400–500 nm because exposure to radiation with these wavelengths induces intense biotissue fluorescence [41] which can hinder the analysis of the contribution of changes of forms of hemoglobin to the reflected light spectrum.

Reflected light wavelength ranges for normal skin and skin with a dilated vessel meeting Criteria № 1–3 were defined using equations (1)–(6) and are listed in Table 2. Note that within the wavelength ranges meeting Criteria № 1–3, replacement of oxyhemoglobin with deoxyhemoglobin in blood-filled layers of normal skin and skin with a dilated vessel at 530 nm, 571 nm, 584 nm and 798 nm, $R(\lambda)_{var}$ and $dR(\lambda)_{var}$ results in only minor changes (less than 5%), which adequately correlates with previously reported data for isobestic points of blood [42,43]. The observed difference between the wavelengths of these points in spectra as shown in Figure 3 and the corresponding wavelengths from [42,43] results from consideration of the light scattering contribution in skin layers. Also, when deoxyhemoglobin is replaced with methemoglobin, $R(\lambda)_{var}$ and $dR(\lambda)_{var}$ change insignificantly (less than 5%) near the known isobestic points of methemoglobin [44,45], i.e. at 516 nm, 603 nm, 660 nm and 764 nm.

As previously found in [36], the above-mentioned reflection trends during the $HbO_2 \rightarrow Hb$ transformation are associated with a decrease in absorption and increase in

Table 2. Wavelength ranges (nm) of light reflected from skin meeting criteria № 1–3

Biotissue	Criterion № 1	Criterion № 2	Criterion № 3
Normal human skin	520–550	786–816	598–607 658–666 739–764
Human skin with a dilated blood vessel	522–532	810–820	594–610 654–676 710–774

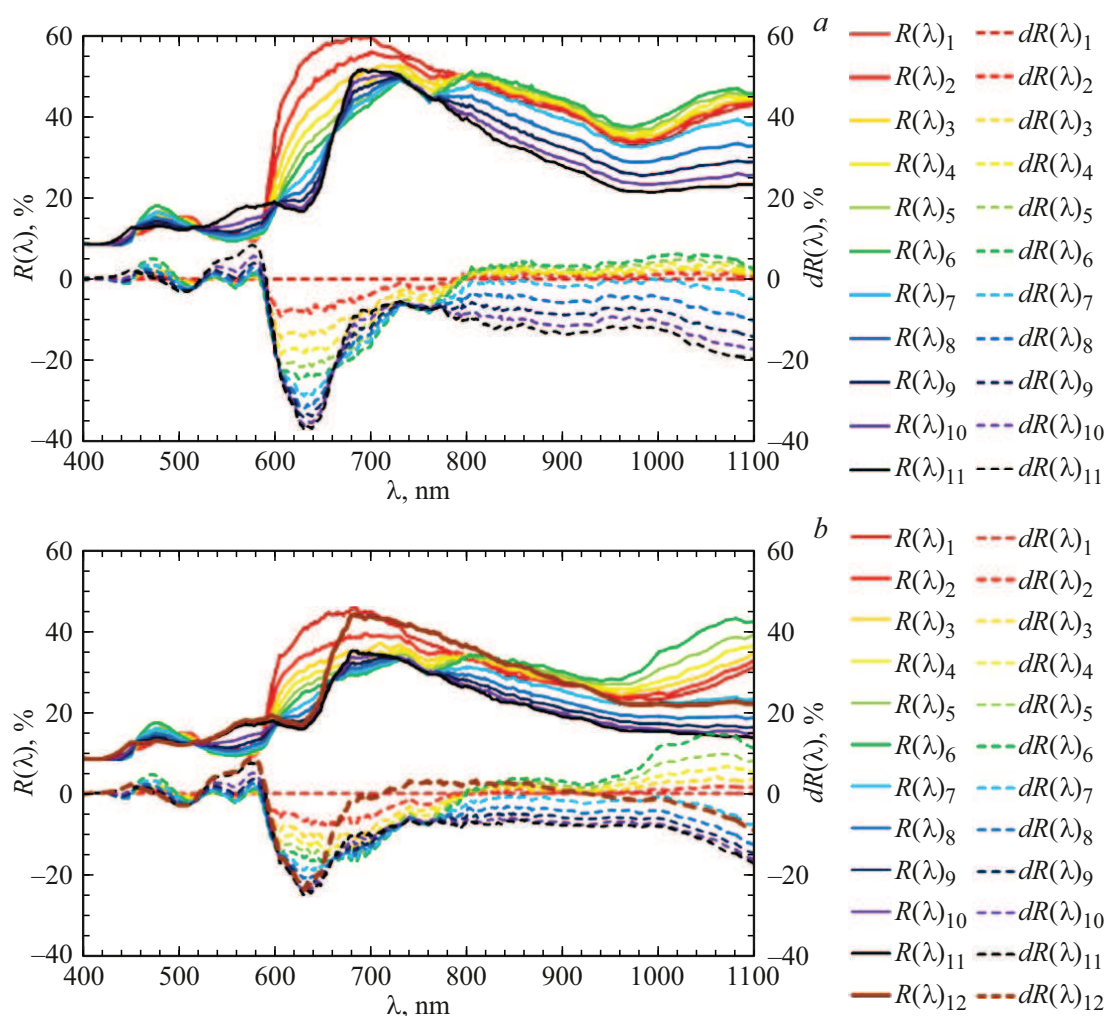


Figure 3. Spectra $R(\lambda)_{var}$ and $dR(\lambda)_{var}$ of normal human skin (a), human skin with a dilated vessel with various oxyhemoglobin, deoxyhemoglobin and methemoglobin concentrations, and skin with a coagulated vessel (b), index var is the combination No. as listed in Table 1, $R(\lambda)_{var}$ — solid lines, $dR(\lambda)_{var}$ — dashed lines.

transmission at 780–1100 nm of both whole blood and blood-filled biotissues, and with an increase in absorption and decrease in transmission in the same wavelength range during the Hb→MetHb transformation. This correlation can be used for optimizing laser sclerotherapy of skin vessels by initiating the HbO₂→Hb transformation under the action of green-blue laser radiation (for example, with an active

wavelength of 450 nm) to increase near IR transmission (for example, with an active wavelength of 980 nm).

Therefore, according to the numerical simulation data, it has been found that the diagnostic wavelength ranges most suitable for estimating the chromophore composition of blood should correspond to the isobestic points of blood. Thus, to determine the HbO₂→Hb transformation (Crite-

tion № 3), use radiation wavelengths near the isobestic points of deoxyhemoglobin and methemoglobin, for example, 660 nm. To determine the Hb→MetHb transformation (Criterion № 2), use the radiation wavelengths near the isobestic points of oxyhemoglobin and deoxyhemoglobin, for example, 810 nm.

To avoid the skin relief effect and work tool positioning inaccuracy on $R(\lambda)$, provide the feedback system with a reference signal with a radiation wavelength at which $R(\lambda)_{var}$ and $dR(\lambda)_{var}$ change insignificantly during the HbO₂→Hb→MetHb transformation (Criterion № 1 I), for example, 532 nm. The reference signal is always taken to be constant and equal to 1 regardless of the chromophore concentration, tool position and skin surface relief.

Behavior of $R(\lambda)$ depending on the concentration of blood chromophores in normal skin, skin with a dilated vessel and skin with a coagulated vessel at 660 nm, 810 nm and 532 nm is shown in Figure 4, a. Normalization of $R(660\text{ nm})$, $R(810\text{ nm})$ and $R(532\text{ nm})$ to $R(532\text{ nm})$ gave similar dependences of reduced $R_{532}(660\text{ nm})$, $R_{532}(810\text{ nm})$ and $R_{532}(532\text{ nm})$ (Figure 4, b) which are used as a basis for the control algorithm of the dual-wavelength laser system with active laser radiation at 450 nm and 980 nm.

Based on the above-mentioned simulation results and experience of laser sclerotherapy of skin vessels summarized during review of the literature [13,18,20], operating algorithm of the laser system with optical feedback for sclerotherapy of dilated cutaneous vessels can consist of the following steps.

Step 1. Calibration Detection of dilated vessels in skin. At this step, OS_1 (oxygen saturation) and MS_1 (methemoglobin saturation) are determined for skin without dilated vessels equal to reduced $R_{532}(660\text{ nm})$ and $R_{532}(810\text{ nm})$, respectively:

$$OS_1 = R_{532}(660\text{ nm}), \quad (7)$$

$$MS_1 = R_{532}(810\text{ nm}). \quad (8)$$

OS_1 shall be in the range from 5.3 to 5.7, and MS_1 shall be in the range from 4.3 to 4.7. If the values of these variables meet the above-mentioned conditions, then there are no dilated vessels in skin and laser treatment is not initiated. Values of OS_1 and MS_1 are stored in the feedback memory as values corresponding to normal skin.

Step 2. Search for a dilated vessel The system doesn't initiate laser treatment with active laser radiation until a dilated vessel is detected. Detection of a dilated vessel is matched by a decrease in OS_1 and MS_1 to 4.2 ± 0.2 and 3.1 ± 0.2 whose values at this step are stored in the device in the form of OS_2 and MS_2 as values corresponding to skin with a dilated vessel. After detecting a dilated vessel, treatment with 450 nm active laser radiation is initiated.

Step 3. Skin optical clearing Being effectively absorbed by blood, 450 nm therapeutic laser radiation initiates the process of blood saturation reduction and according to [36] results in an increase in transmission at 980 nm, leading to skin optical clearing. During exposure to the 450 nm therapeutic laser radiation, OS_3 and MS_3 (Figure 5) are continuously measured and calculated as

$$OS_3 = \frac{R_{532}(660\text{ nm})}{OS_2}, \quad (9)$$

$$MS_3 = \frac{R_{532}(810\text{ nm})}{MS_2}. \quad (10)$$

When $OS_3 = 0.6$ is reached, 450 nm therapeutic laser exposure stops and 980 nm therapeutic laser exposure starts, while $MS_3 \approx 1$ during the 450 nm active laser exposure. At this step, if reflection coefficients at 660 nm and 810 nm reach the initial values of OS_1 and MS_1 (meaning that normal skin is affected), laser exposure stops immediately.

Step 4. Dilated vessel coagulation During exposure to the 980 nm therapeutic laser radiation, MS_3 is measured continuously. When $MS_3 = 0.6$, a temperature necessary for vessel coagulation is reached, and a further increase in MS_3 to 0.85 indicates that coagulation is successful. In this case, the 980 nm laser radiation action stops because the dilated vessel is considered to be successfully coagulated.

When developing laser systems with optical feedback, an urgent question arises about increasing the signal-to-noise ratio. Therefore, three main configurations of optical circuits for effective signal detection can be distinguished. Each of these configurations is based on different physical principles of separation of powerful therapeutic laser radiation and low-power effective feedback signal from the target biotissue.

The most versatile optical circuit of such device implies separation of therapeutic laser radiation and optical feedback signal paths [46]. Active laser radiation is delivered to the target biotissue via an optical system (for example, an optical fiber with a focusing attachment) and the feedback signal is collected via the second independent optical system (a separate optical fiber) placed at an angle to the first one and directed to the receiver. Note that this circuit was used in an experimental setup proposed in [33]. There is a considerable difficulty with accurate combination of optical axes for systems with separate channels. This causes a space resolution constraint where feedback signal collection cannot be strictly localized in the laser exposure zone. This constraint becomes critical for targeting small and anatomy-/morphology-variable structures, for example, skin vessels.

Combination/separation of the optical axes of therapeutic laser and optical feedback signal can be achieved in systems with a spectrum splitter which is used for spectral separation of the optical feedback signal from the therapeutic laser radiation (option 1) [47]. In this configuration, therapeutic laser radiation is directed, for example, to a

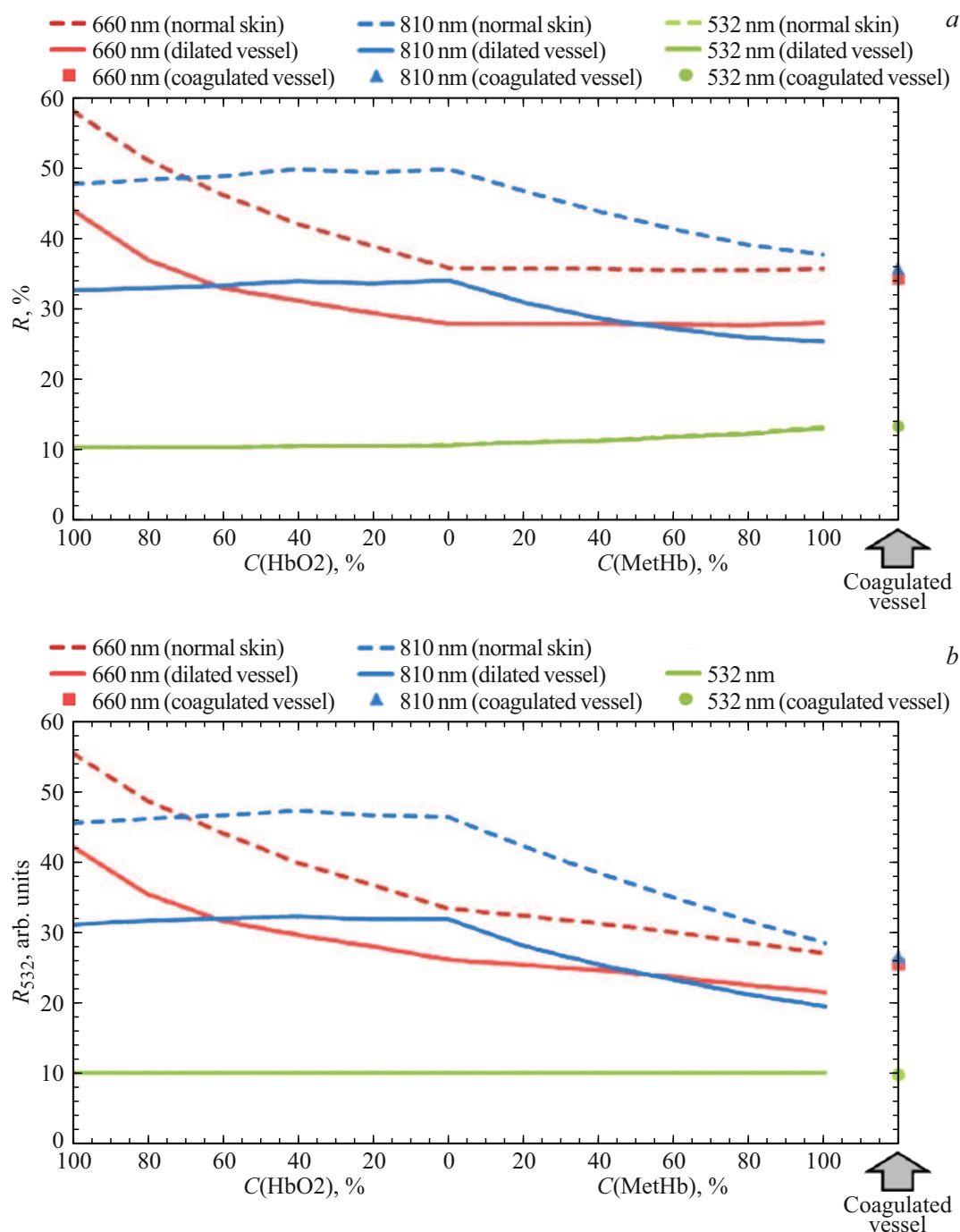


Figure 4. Behavior of $R(660 \text{ nm})$, $R(810 \text{ nm})$, $R(532 \text{ nm})$ (a) and $R_{532}(660 \text{ nm})$, $R_{532}(810 \text{ nm})$, $R_{532}(532 \text{ nm})$ (b) depending on blood chromophore concentration in normal skin and skin with a dilated vessel, and skin with a coagulated vessel.

dichroic mirror having a high reflection coefficient at the therapeutic laser wavelength and low reflection coefficient at the optical feedback signal wavelengths (diagnostic wavelengths). Therapeutic laser radiation reflected from such mirror through a delivery system is directed to the target biotissue, and the feedback signal returns via the same way. This system will be will function properly, if the optical feedback signal wavelength is within the mirror transparency range. A configuration option is possible

where the dichroic mirror has a high transmission coefficient at the therapeutic laser wavelength, and the feedback signal is in the high reflection coefficient region of this mirror. However, application of this method is restricted in multi-wavelength laser systems, which is associated with a problem of matching reflection and transmission bands of several active wavelengths and optical feedback signal, especially in systems with a broadband illumination source.

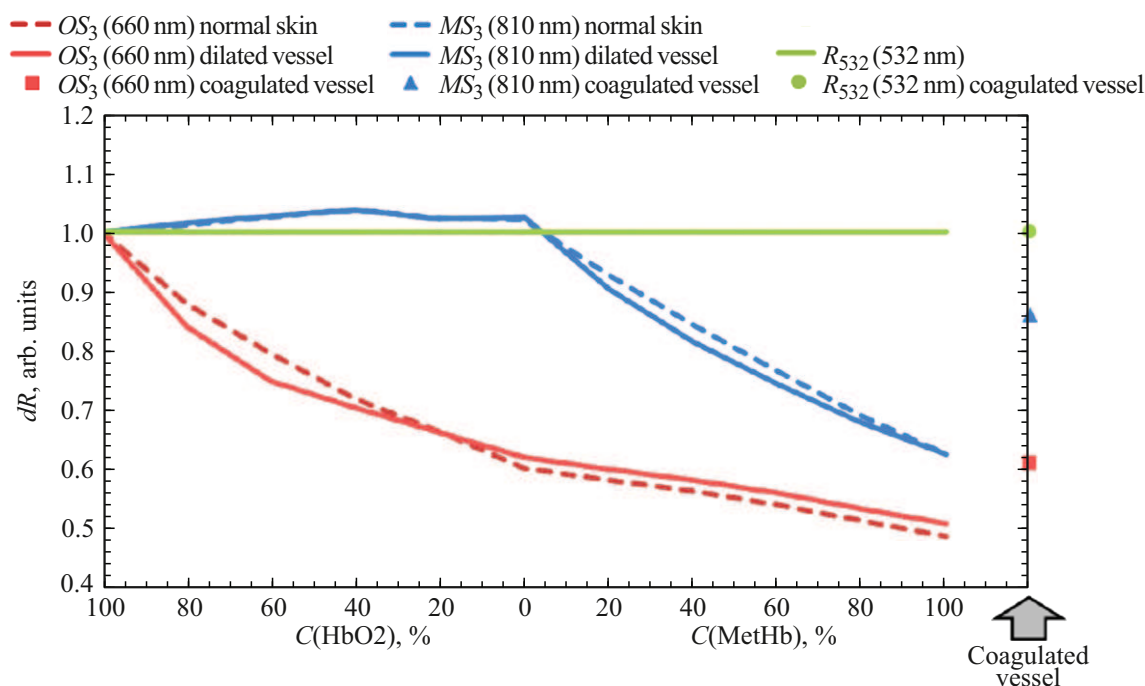


Figure 5. Behavior of OS_3 , MS_3 and $R_{532}(532\text{ nm})$ depending on the blood chromophore concentration in normal skin, skin with a dilated vessel and skin with a coagulated vessel.

Configuration with aperture separation which uses a mirror with an axial bore (option 2) is another option of combination/separation of the therapeutic laser radiation and optical feedback signal [48]. Here, several therapeutic laser wavelengths and optical feedback signal go directly through a small bore in the center of such mirror and are introduced into an optical fiber with incompletely filled numerical aperture. Light reflected and scattered from the target biotissue goes back via the optical fiber, filling the whole numerical aperture of the optical fiber, and then, being reflected from the mirror surface, reaches the receiver (for example, a photodiode) placed outside the bore, passing through an optical filter where the effective feedback signal, is separated from the active laser radiation reflected from the biotissue. This and previous approaches ensure that analysis is performed exactly in the laser exposure point. The main disadvantage is in inevitable optical loss where a part of effective optical signal is lost and doesn't reach the receiver.

According to the above-mentioned analysis, the following configuration of the dual-wavelength laser system with optical feedback is proposed to implement the operating algorithm of the laser system with optical feedback for sclerotherapy of dilated cutaneous vessels. In the system, the $980 \pm 10\text{ nm}$ active laser radiation is combined with the 532 ± 10 , 660 ± 10 and $810 \pm 10\text{ nm}$ diagnostic (optical feedback signal) radiation of laser diodes in the first beam combining unit (Figure 6, 1) and introduced into the intermediate optical fiber (Figure 6, 2). In the second beam combining unit (Figure 6, 3), the $450 \pm 10\text{ nm}$ therapeutic

laser radiation is added to the $980 \pm 10\text{ nm}$ therapeutic laser radiation and diagnostic laser radiation and then is introduced into the operating optical fiber (Figure 6, 4) by a lens with an aperture smaller than the numerical aperture of this optical fiber. From the output, the therapeutic and diagnostic radiations are directed to skin. The therapeutic and diagnostic radiations reflected from skin return into the operating optical fiber, completely filling its numerical aperture. Radiation with larger aperture reflected from skin strikes the feedback mirror unit (Figure 6, 5) placed in the second beam combining unit, gets reflected from them, goes through narrow-band light filters (Figure 6, 6) that transmit only the diagnostic radiation for each wavelength individually, and strikes the receives (Figure 6, 7) that also detect a signal individually for each wavelength. Optical feedback operation is provided by a microcontroller with the recorded above-mentioned operating algorithm of the laser system with optical feedback for sclerotherapy of dilated cutaneous vessels.

For the purpose of the study, a numerical model of the dual-wavelength laser system with feedback was created in TracePro 7.0.1 (Lambda Research Corporation, USA), and the Monte Carlo method was used to calculate the beam path. Figure 7 shows the 660 nm diagnostic radiation beam path in this model with various options of combination/separation of the active laser radiation and optical feedback signal.

Numerical simulation results were used to calculate the signal-to-noise ratio for options 1 and 2 of combination/separation of the active laser radiation and optical

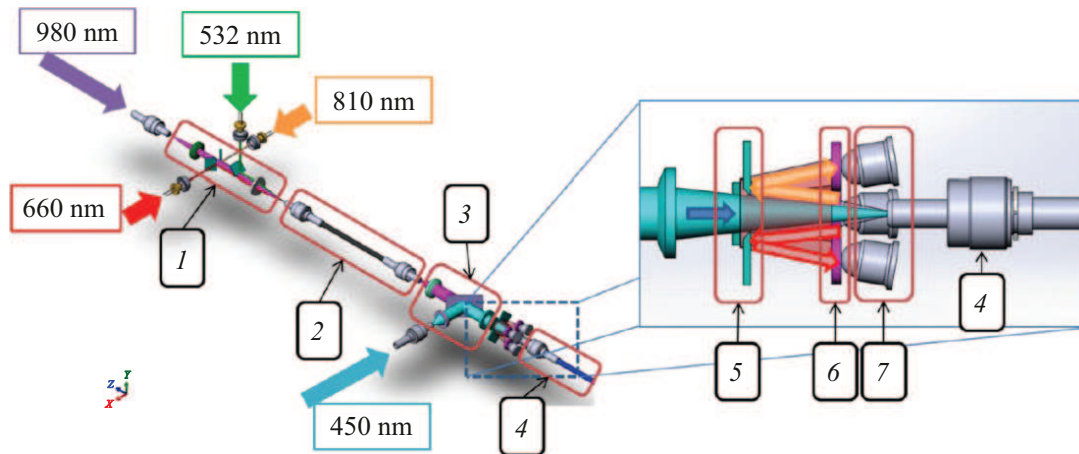


Figure 6. Schematic diagram of a dual-wavelength laser system with optical feedback for treatment of cutaneous vascular diseases: 1 — the first beam combining unit; 2 — intermediate optical fiber; 3 — the second beam combining unit; 4 — operating optical fiber; 5 — feedback mirror unit; 6 — narrow-band optical filters; 7 — receivers; 450 nm, 980 nm — therapeutic laser sources; 532 nm, 660 nm, 810 nm — diagnostic laser sources (patent application №2025126305).

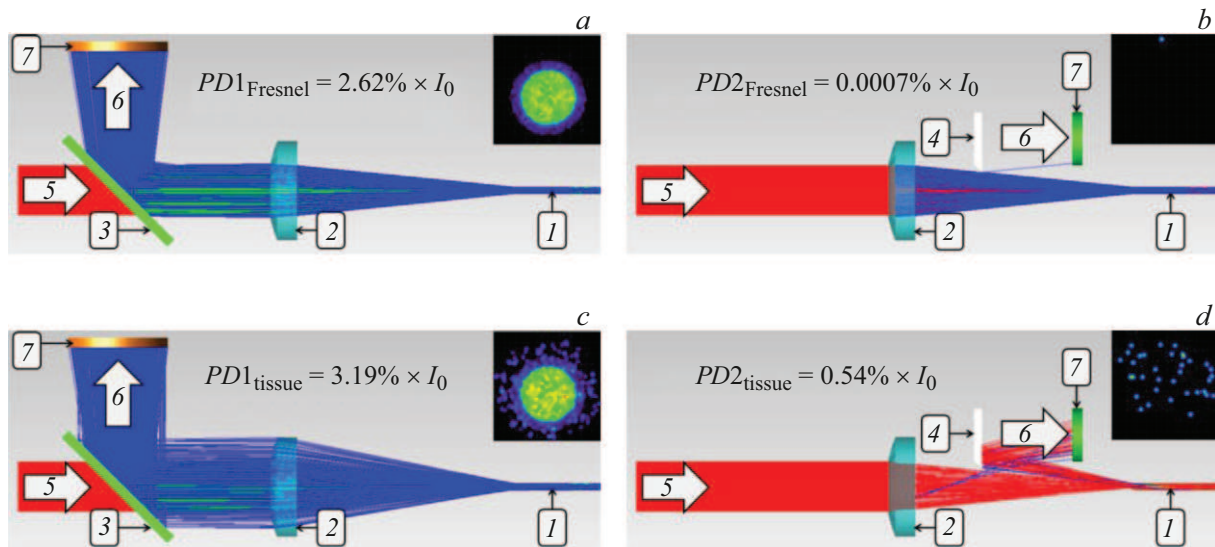


Figure 7. Path of 660 nm diagnostic laser beams in the numerical model of the dual-wavelength laser system with feedback for treatment of cutaneous vascular diseases with various options of combination/separation of active laser radiation and optical feedback signal: (a) option 1, the waveguide output end is oriented into air; (b) option 1, the waveguide output end is oriented into normal skin (chromophore combination № 1 as shown in Table 1); (c) option 2, the waveguide output end is oriented into air; (d) option 2, the waveguide output end is oriented into normal skin (chromophore combination № 1 as shown in Table 1). Red rays - for each such ray, the fraction of 1/10000 of the source power ranges from 100.0% to 66.6%; green rays - from 66.6% to 33.3%; blue rays - from 33.3% to 0.1%, respectively. The upper right quadrant in each figure shows a spatial distribution of light flux power on the receiver. 1 — operating optical fiber, 2 — lens, 3 — spectrum splitter, 4 — mirror, 5 — therapeutic or diagnostic laser beam (I_0), 6 — radiation reflected both from optical surfaces (noise) and biotissue (signal), 7 — receiver.

feedback signal (N_1 and N_2 , respectively):

$$N_1 = \frac{PD1_{\text{tissue}}}{PD1_{\text{Fresnel}}} = 1.23, \quad (11)$$

where $PD1_{\text{Fresnel}}$ is the power of light flux reflected from optical surfaces and striking the receiver (noise) (Figure 7, a), $PD1_{\text{tissue}}$ is the power of light flux striking the receiver and reflected both from optical surfaces and biotissue (signal)

(Figure 7, b).

$$N_2 = \frac{PD2_{\text{tissue}}}{PD2_{\text{Fresnel}}} = 771.43, \quad (12)$$

where $PD2_{\text{Fresnel}}$ is the power of light flux reflected from optical surfaces and striking the receiver (noise) (Figure 7, c), $PD2_{\text{tissue}}$ is the power of light flux striking the receiver and

reflected both from optical surfaces and biotissue (signal) (Figure 7, d).

Comparison of N_1 and N_2 shows that the configuration with aperture separation of direct and reflected (option 2) has a manifold better signal-to-noise ratio.

Conclusion

Thus, this study has investigated the effect of human blood oxygenation and methemoglobin concentration on human blood reflection spectra. It has been found that to control the $\text{HbO}_2 \rightarrow \text{Hb}$ transformation in skin, intensity of light reflected from skin shall be analyzed at wavelengths near the isobestic points of deoxyhemoglobin and methemoglobin, for example, at 660 nm, and to control the $\text{Hb} \rightarrow \text{MetHb}$ transformation, reflected light intensity shall be analyzed at wavelengths near the isobestic points of oxyhemoglobin and deoxyhemoglobin, for example, 810 nm. A dual-wavelength laser system with optical feedback is proposed. The system is designed for selective photocoagulation of dilated vessels in skin and tracking the state of these vessels via analysis of light reflection at key wavelengths for laser-induced hemoglobin transformation. The system uses 450 nm and 980 nm active laser radiation sources and diagnostic radiation sources with wavelengths which are „sensitive“ (660, 810 nm) and „insensitive“ (532 nm) to a change in the oxyhemoglobin, deoxyhemoglobin and methemoglobin concentrations in cutaneous vessels. A control algorithm has been developed for this dual-wavelength laser system to improve the efficacy of treatment of cutaneous vascular lesions. The algorithm involves the measurement of skin reflection at wavelengths both sensitive to the oxyhemoglobin, deoxyhemoglobin and methemoglobin concentrations in cutaneous vessels and insensitive to a change in blood composition. Options of combination/separation of the active laser radiation and optical feedback signal are analyzed. It is shown numerically that when diagnostic radiation receivers that control the oxyhemoglobin, deoxyhemoglobin and methemoglobin concentrations in skin are placed in the annular zone adjacent to the operating optical fiber inlet in a region with an aperture larger than the therapeutic laser radiation input aperture, but not larger than the numerical aperture of this operating optical fiber, a signal-to-noise ratio greater than 700 can be achieved and, thus, a negative effect of radiation reflected from the system's optical surfaces on signals detected by receivers can be virtually avoided. Numerical simulation results described in this work and based on the widely known literature data need additional experimental verification, which is planned by the authors for the near future.

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Declaration of competing interest

The authors declared that they had not any conflict of interests.

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