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Analysis of the tomographic contrast during the immersion bleaching of layered biological tissues

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Abstract. **The control of optical properties of biological tissues irradiated by a cw laser source is considered. Within the framework of the stationary model of the radiation transfer, basic factors affecting the tomographic contrast of a layered medium are revealed theoretically and numerically, when immersion liquids, decreasing the radiation scattering level in a medium, are used.**

Keywords: *immersion bleaching of biological tissues, optical tomography, radiation transfer equation, Monte Carlo method.*

1. Introduction

One of the important directions in modern biomedical diagnostics is the development of methods aimed at improving the visualisation quality of the biotissue structure [1, 2]. The main problem of the optical tomography is related to the peculiarities of the light propagation in biological tissues: the light field propagated through an object is characterised by a significant predominance of the multiply scattered component over the unscattered (ballistic) component. Quite often, it is the latter component that is the carrier of useful information in the visualisation of the internal structure of the medium. This problem can be solved by increasing the penetration depth of ballistic photons in the object under study. To do this, the solutions of glucose, glycerine, and other immersion liquids are applied on the skin surface. The liquid diffusion into the tissue depth leads to equalization of the refractive indices of the main tissue and the scatterers, which results in a controlled decrease in the scattering coefficient and an increase in the ballistic components in a propagating signal [1–4].

Usually, due to the presence of the epidermal barrier, the penetration depth of the immersion liquid does not exceed 150–250 μm. This depth can be increased with the help of intracutaneous injections of a solution, which is localised for some time in the tissues of a patient. Despite the fact that from the medical point of view the use of the cutaneous

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introduction of the agent is more preferable, the efficiency of the optical immersion is significantly higher in the case of the intracutaneous injection [3]. Another technique allowing one to increase the penetration depth of the immersion liquid through the epidermal barrier is based on the formation of penetrability islets by limiting the thermal action of the corneous layer [5].

There is an opinion that the best visualisation quality of the medium under study is achieved in the case of complete equalization of the refractive indices of the basic substance and scatterers, leading to the disappearance of scattering. Indeed, in most cases, this statement is justified because it is confirmed by numerical simulations and physical experiments [1–5]. However, much depends on the formulation of the problem, the choice of the diagnostic methods, the medium structure and its characteristics. In this paper, we study analytically and numerically the control problems of optical properties of biological tissues in order to increase the tomographic contrast of the medium. It is shown that the complete equalization of the refractive indices does not always lead to an increase of that fraction of the ballistic component of the measured signal, which is caused by the presence of a foreign inclusion in the medium.

2. Formulation of the problem

We assume that the inhomogeneous medium where radiation propagates has a plane geometry, fills the spatial region $G = \{z : z \in (z_0, z_p)\}$, and consists of p layers $G_i = \{z : z \in (z_{i-1}, z_i)\}$, $i = 1, ..., p$. For each G_i layer, we specify the refractive index n_i as well as the attenuation and scattering coefficients $\mu(z) = \mu_i$ and $\mu_s(z) = \mu_{s,i}$, $z \in G_i$.

The radiation propagation in the layer can be described using the stationary transfer equation, which, in the absence of internal radiation sources, can be written in the form [1, 6, 7]

$$vf_z(z, v) + \mu(z)f(z, v) = \mu_s(z)\int_{-1}^{1} S(z, v, v')f(z, v')\mathrm{d}v'. \quad (1)$$

The function $f_z(z, v)$ means the radiation flux density at point $z \in G$ in the direction making with the positive direction of the symmetry axis of the medium an angle whose cosine is equal to v. The phase scattering function $S(z, v, v')$ determines the character of the photon scattering in the medium.

At the boundary of the region G, the densities of the radiation fluxes entering the medium are specified:

$$f(z_0, v) = h(v),\ v > 0, \quad f(z_p, v) = h(v),\ v < 0. \quad (2)$$

At the contact boundaries $z = z_i$ $(i = 1, ..., p-1)$, the matching conditions [8–11] are laid down, which reflect the relations between the incident, mirror reflected and refracted fluxes:

$$f(z_i + 0, v) = R_i(v) f(z_i + 0, -v) + T_i(v) \times f(z_i - 0, \psi_i), \quad v \in [-1, 0),$$
$$f(z_i - 0, v) = R_i(v) f(z_i - 0, -v) + T_i(v) \times f(z_i + 0, \psi_i), \quad v \in (0, 1]. \tag{3}$$

Here

$$f(z_i \pm 0, v) = \lim_{\varepsilon \to 0, \varepsilon > 0} f(z_i \pm \varepsilon, v)$$

are the limiting values of the function $f(z, v)$ at the medium interfaces z_i. The coefficients $R_i(v)$ and $T_i(v)$ characterise the reflectivity and transmittivity of the interface surface $z = z_i$ and for unpolarised radiation are determined by the expressions:

$$R_i(v) = \frac{1}{2}(R^2_{\parallel,i} + R^2_{\perp,i}), \quad T_i(v) = 1 - R_i(v),$$

where

$$R_{\parallel,i}(v) = \frac{\tilde{n}_i(v)\psi_i(v) - v}{\tilde{n}_i(v)\psi_i(v) + v}; \quad R_{\perp,i}(v) = \frac{\psi_i(v) - \tilde{n}_i(v)v}{\psi_i(v) + \tilde{n}_i(v)v};$$

$$\tilde{n}_i(v) = \begin{cases} n_{i+1}/n_i & \text{for} \quad 0 < v \leqslant 1, \\ n_i/n_{i+1} & \text{for} \ -1 \leqslant v < 0 \end{cases}$$

is the relative refractive index of the boundary z_i; the quantity $\psi_i = \psi_i(v)$ is related to v by the known Snell law [12]:

$$\psi_i(v) = \begin{cases} \operatorname{sgn} v[1 - \tilde{n}_i^2(v)(1 - v^2)]^{1/2} & \text{for } 1 - \tilde{n}_i^2(v)(1 - v^2) \geqslant 0, \\ 0 & \text{for } 1 - \tilde{n}_i^2(v)(1 - v^2) < 0. \end{cases}$$

One can easily see that at all v so that $1 - \tilde{n}_i^2(v)(1 - v^2) \leqslant 0$, the equalities $R_i(v) = 1, T_i(v) = 0$ are fulfilled, which corresponds to the case of the total internal reflection [12].

We will consider the problem of the optical tomography of the skin layer *in vivo* under the following characteristic experimental conditions. The source and the detector are located at one boundary, for example, at $z = z_0$, and the characteristics of the medium are determined not in transmission but by reflected and scattered radiation: $f(z_0, v)$, $-1 \leqslant v < 0$. The authors of papers [10, 11] considered similar formulations of the problems. The searched-for parameters in these problems were the relative refractive indices and the optical thicknesses of the layers, which were found by solving the transfer equation known only at the boundary z_0.

It was noted in [10, 11] during the computer experiments that the error in the layer reconstruction increases with increasing the layer depth. Therefore, by bleaching the entire medium or its part, we decrease the total optical thickness of the inhomogeneous layer and can expect the better visualisation of the medium structure. Our further aim is to formalise the formulation of the problem and give a qualitative and quantitative description of the dependence of the optimal refractive index of the bleaching liquid on the characteristics of the biological tissue.

Let the refractive index in the jth layer be

$$n_j = c_j n_{c,j} + (1 - c_j) n_{0,j}, \tag{4}$$

where $n_{c,j}$, $n_{0,j}$ are the refractive indices of scattering microinhomogeneities and the basic substance in the jth layer, and c_j is the relative concentration of scattering particles. We assume for simplicity that the scattering coefficient $\mu_{s,j}$ of the jth layer is related to $n_{c,j}/n_{0,j}$ by the expression [2]

$$\mu_{s,j} = \sigma_j \left(1 - \frac{n_{c,j}}{n_{0,j}}\right)^2, \tag{5}$$

and the absorption coefficient $\mu_a = \mu - \mu_s$ is independent of $n_{c,j}/n_{0,j}$. The quantity σ_j in (5) is determined by the density and dimensions of the scatterers in the layer G_j [1].

In many important practical cases, the phase scattering function $S(z, v, v')$ in a separate jth layer depends only on the angle θ between the incident and scattered photons and is well approximated by the Henyey–Greenstein function [1]:

$$S_j(\theta) = \frac{1}{2} \frac{1 - g_j^2}{(1 + g_j^2 - 2g_j \cos\theta)^{3/2}}. \tag{6}$$

The scattering anisotropy parameter g_j is determined by the characteristics of the scattering centres in the jth layer. The case $g_j = 0$ corresponds to isotropic scattering and $g_j = 1$ – to the total forward scattering.

For many biological tissues, the scattering indicatrix S has an elongated shape and the values of g lie in the range from 0.6 to 0.9, and in some cases, for example for blood, they can achieve 0.995 [1]. It is known that the introduction of the immersion agent into the tissue leads, along with a decrease in the scattering coefficient, to an increase in the scattering anisotropy [13]. Usually, this dependence is manifested significantly weaker. Thus, for example, paper [13] presents analytic expressions of the linear dependence of μ_s and g on the glucose concentration C in the intralipid solution, the function gradient $\mu_s(C)$ exceeding by several orders of magnitude the corresponding gradient $g(C)$ in the absolute quatity. Obviously, this is explained by the fact that the dependence of the scattering anisotropy on the immersion liquid concentration is sometimes neglected.

In the first approximation, we can restrict our consideration by the case when g_j linearly depends on $n_{0,j}$:

$$g_j(n_{0,j}) = g_j^{(0)} + (g_j^{(c)} - g_j^{(0)}) \frac{n_{c,j} - n_{0,j}}{n_{c,j} - n_{0,j}^{(0)}},$$
$$n_{0,j}^{(0)} \leqslant n_{0,j} \leqslant n_{c,j}, \tag{7}$$

where $n_{0,j}^{(0)}$ and $g_j^{(0)}$ is the refractive index of the basic substance and the scattering anisotropy factor before the introduction of the immersion liquid, respectively; $g_j^{(c)}$ is the anisotropy parameter at $n_{0,j} = n_{c,j}$.

We assume that in our problem the layer $G_j = (z_j, z_{j+1})$ is bleaching and contains one foreign inclusion. Thus, instead of one layer G_j we obtain three: $G_j^- = (z_j, z_j^*)$, $G_j^* = (z_j^*, z_{j+1}^*)$ and $G_j^+ = (z_{j+1}^*, z_{j+1})$ (the region G_j^* is interpreted as an inclusion or a microinhomogeneity). We will use f and f^* to designate the solutions of boundary problem (1)–(3) for the sets of inhomogeneous media $\{G_1, G_2, ..., G_p\}$ and $\{G_1, ..., G_{j-1}, G_j^-, G_j^*, G_j^+, G_{j+1}, ..., G_p\}$, respectively, the functions h and h^* from conditions (2) (for f and f^*) being equal to each other, while the attenuation and scattering coefficients and the refractive index in all the layers, except for G_j^*, for the function f^* coinciding with the corresponding coefficients for f.

If the difference $f^* - f$ at $z = z_0$ and $v \in [-1, 0)$ is equal to zero, this, in fact, means that the use of G_j^* does not influence the radiation emerging from the medium; in other words, it is invisible in the light reflected and scattered by the medium. From the mathematical point of view, this can be interpreted as nonuniqueness of the inverse problem solution which involves the determination of the characteristics of the microinhomogeneities G_j^* by the solution of direct problem (1)–(3) known at the boundary z_0. If at this boundary $f_b^* - f_b = 0$, where f_b^*, f_b are the corresponding ballistic components of the measured signals, then the inclusion is invisible for the tomographic systems detecting the unscattered part of the photons, which was formed due to reflection (and re-reflection) from the internal boundaries of the medium interface z_i. The increase in the fraction of unscattered photons caused by the presence of microinhomogeneity G_j^* violates the condition $f_b^* - f_b = 0$ and should favourably affect the reconstruction of the inclusion in the medium.

There naturally appears the following extremal problem (control problem).

Problem 1. It is required to find the optimal refractive index $n_{0,j}$ of the basic substance in the medium $G_j^- \cup G_j^+$ from relations (1)–(3) and the extremal condition

$$J_1(n_{0,j}) = \frac{|f_b^*(z_0 - 0, v) - f_b(z_0 - 0, v)|}{f^*(z_0 - 0, v)} \to \max, \qquad (8)$$

if n_j, $\mu_{s,j}$, S_j and g_j in $G_j^- \cup G_j^+$ are determined by relations (4)–(7), while the function $h(v)$ and all other parameters of the medium G are known.

The direction determined by v in condition (8) can be chosen from different assumptions, in particular, using the experimental technique for determining the medium structure.

For example, in optical coherence tomography [3] taking into account additional interference effects of the measured field, using the required devices information on the term, whose quantity is proportional to the change in the refractive index at the boundary $z = z_i$, is extracted from the ballistic signal with the direction $v = -1$.

It was shown in papers [10, 11] that under some conditions, the function $\partial f_b^*(z_0, v)/\partial v$, $v < 0$ increases infinitely when v tends to the value $v_i = -[1-(n_i/n_1)^2]^{1/2}$. This condition allows one to determine the corresponding refractive indices n_i/n_1 without knowing the scattering characteristics of the medium because the non-ballistic component in the output signal, having a large smoothness with respect to the angular variable, is filtered by the differentiation operation. Because v_1 is known in advance, it is obviously worth considering such formulations of problem 1 when at the boundary $z = z_0$ the radiation flux density averaged in the directions $v \in [-1, 0)$ serves as target function J_1.

3. Analytic solution of the auxiliary problem

Below, we will restrict our analysis to the case when $v = -1$ in (8) and consider some auxiliary problem.

Problem 2. It is necessary to find the optimal refractive index $n_{0,j}$ of the basic substance in the medium $G_j^- \cup G_j^+$ from relations (1)–(3) and the extremal condition

$$J_2(n_{0,j}) = \frac{|f_b^*(z_j - 0, -1) - f_b(z_j - 0, -1)|}{f_b^*(z_j + 0, 1)} \to \max, \qquad (9)$$

if n_j, $\mu_{s,j}$ in $G_j^- \cup G_j^+$ are determined from (4) and (5), while all other parameters of the media G_j^-, G_j^*, and G_j^+ are known.

For a medium with the microinhomogeneity G_j^* and without it, the functional J_2 represents a difference of the ballistic fluxes emerging from the layer G_j. In this case, for convenience, this difference is normalised to the quantity $f_b^*(z_j + 0, 1)$. Problem 2 has a local character making it possible to consider it for each layer separately, independently of other layers. In addition, the function J_2 in extremal condition (9) contains only the ballistic component. In this case, problem 2 is simpler than problem 1 and allows analytic solution under the assumptions made below.

Let $f_b(z_{j+1} - 0, -1) = f_b^*(z_{j+1} - 0, -1) = 0$. The last assumption is often justified, for example, at a rather large optical thickness of the medium G_j^+, i.e. $\mu_j|z_{j+1} - z_{j+1}^*| \gg 1$. Taking this into account, we have $f_b(z_j - 0, -1) = 0$ and

$$f_b^*(z_j - 0, -1) \approx f_b^*(z_j + 0, 1) R_j^* \exp(-2\mu_j|z_j^* - z_j|) \times \left(1 + \frac{(1 - R_j^*)^2}{\exp(2\mu_j^*|z_{j+1}^* - z_j^*|) - R_j^{*2}}\right). \qquad (10)$$

We use μ_j^* and n_j^* to designate the attenuation coefficient and the refractive index of the inclusion G_j^* and R_j^* to designate the reflection coefficient at the medium interface G_j^-, G_j^* in the direction corresponding to $v = 1$. We will consider the case most difficult and interesting for tomography, when the searched-for inclusion is small, i.e. its optical thickness $\mu_j^*|z_{j+1}^* - z_j^*|$ tends to zero. Then, taking into account (10), target function (9) has a relatively simple form:

$$J_2(n_{0,j}) \approx \tilde{J}_2(n_{0,j}) = 2\exp(-2\mu_j|z_j^* - z_j|)\frac{R_j^*}{1 + R_j^*}. \qquad (11)$$

The solution of problem 2 with the target function $\tilde{J}_2$, where $\mu_{s,j}$ is given by relation (5), is finally reduced to determining the roots of the quintic equation with respect to the variable $n_{0,j}$. One of the roots of this equation, $n_{0,j} = (n_j^* - c_j n_{c,j})/(1 - c_j)$ corresponds to the vanishing coefficient R_j^*, and, hence, to zero and the minimum of the function $\tilde{J}_2$. Only two roots from other four roots are real. They are the local maxima of the function $\tilde{J}_2$ and can be expressed in radicals.

To analyse vividly the dependence of the optimal solution of extremal problem 2 on the medium characteristics, we will write the asymptotic expression for the root of equation $\tilde{J}_2'(n_{0,j}) = 0$, which is in the vicinity of $n_{c,j}$ and yields the maximum of the function $\tilde{J}_2(n_{0,j}) = 0$. By neglecting the terms of the second-order smallness with respect to the quantity inverse to the layer thickness G_j^-, we have

$$n_{0,j} = n_{c,j} + \frac{n_{c,j}^2 n_j^* (n_{c,j} + n_j^*)(1-c)}{2(n_{c,j} - n_j^*)(n_{c,j}^2 + n_j^{*2})\sigma_j |z_j^* - z_j|}, \tag{12}$$

where σ_j is determined in (5).

A simple analysis of expression (12) shows that when $|z_j^* - z_j|$ increases, the optimal value of the refractive index of the basic substance, as was expected, tends to the quantity of the refractive index of scattering particles. However, the difference $n_{c,j} - n_j^*$, which is in the denominator of the second term in expression (12), can substantially affect the proximity of $n_{0,j}$ and $n_{c,j}$. In this case, if this difference is greater than zero, the optimal refractive index of the basic substance is larger than the refractive index of scattering microinhomogeneities of the medium, and if the difference is smaller than zero, we correspondingly have $n_{0,j} < n_{c,j}$.

In section 4 in computer experiments, we will use the results of the solution of the auxiliary problem and show that although the target function J_1 significantly differs quantitatively from the function $\tilde{J}_2$, the optimal solutions of problems 1 and 2 are rather close in a broad range of variations in the parameters of the medium.

4. Numerical solution of extremal problem 1

To solve extremal problem 1, we should know the solution $f(z_0 - 0, v)$ of boundary problem (1)–(3). The main problem consists in the fact that the mentioned boundary problem does not have an analytic solution; therefore, we will need, first of all, a numerical method for determining the function f. For these purposes, we will use one of the modifications of the weight Monte Carlo methods, the so-called method of conjugate directions [14]. As is known, the main idea of the Monte Carlo method consists in the simulation of a rather large number of photon trajectories in order to accumulate some statistical information on the required quantities. The main feature of the method used in our paper is the fact that in numerical simulations, the whole tree of trajectories is at once constructed and not each branch separately. At each top, the tree is branched into three branches corresponding to the effects of photon refraction, reflection, and scattering. If we trace N acts of the photon–medium interaction, 3^N linear (physical) trajectories correspond to this tree. In this case, only scattering introduces a statistical error in the algorithm. The reflection and refraction effects, except the errors of the round-off and restriction in the number of acts of interaction with the interface, are exactly taken into account.

The main scheme of the method is as follows. For the given point z, for example in the region G_i, and the fixed direction determined by v, we estimate the contribution of the photons f_N, which experienced no more than N acts of scattering, reflection, and refraction in the medium. A photon with this direction can get to point z from the same region during the acts of scattering or reflection from the boundary or from an adjacent region during refraction from the interface. If one of the region boundaries is external, photons can arrive directly from the radiation source.

Thus, the contributions of photons flying directly from the external radiation source, which are either reflected from the medium interface or refracted at this boundary, are determined by the following quantities:

$$f_0(z, v) = \exp\left[-\frac{\mu_i}{v}(z - z_\xi)\right] h(z_\xi, v), \tag{13}$$

$$[R_\xi(v) f_{N-1}(z_\xi, -v) + T_\xi(v) f_{N-1}(z_\xi, \psi_\xi)] \times \exp\left[-\frac{\mu_i}{v}(z - z_\xi)\right]. \tag{14}$$

Here

$$\xi = \xi(v) = \begin{cases} i, & v < 0, \\ i-1, & v > 0, \end{cases}$$

$$h(z_\xi, v) = \begin{cases} h(v), & \xi = 0 \text{ or } \xi = p, \\ 0, & \text{otherwise}, \end{cases}$$

and the function f_{N-1} describes a flux of particles experiencing no more than $N-1$ acts of interaction with the medium. The contribution of a scattered photon is estimates by the quantity

$$\lambda_i \left\{1 - \exp\left[-\frac{\mu_i}{v}(z - z_\xi)\right]\right\} f_{N-1}(z'_k, v'_k), \tag{15}$$

where $\lambda_i = \mu_{s,i}/\mu_i < 1$ is the single scattering albedo; z'_k are the random points of the photon scattering distributed with the probability densities

$$\frac{\mu_i \exp[-\mu_i(z - z'_k)/v]}{v\{1 - \exp[-\mu_i(z - z_\xi)/v]\}};$$

v'_k are the directions of the photon motion distributed with the density $S_i(v, v'_k)$, which is determined by expression (6) at the corresponding anisotropy parameter g_i. In this case, the probability of the particle escape from the region G_i and its absorption are taken into account with the help of the weight multiplier $\lambda_i\{1 - \exp[-\mu_i(z - z_\xi)/v]\}$. Its use allows one to simulate most informative trajectories, thereby increasing the calculation accuracy.

The total intensity at point (z, v) produced by the particles, which experienced no more than N acts of interaction with the medium, is estimated using the corresponding summations over the M trees. Naturally, if scattering is absent in the medium, it is sufficient to construct one tree ($M = 1$). Thus, the basic calculation expression has the form:

$$f_j(z, v) = [R_\xi(v) f_{j-1}(z_\xi, -v) + T_\xi(v) f_{j-1}(z_\xi, \psi_i)] \times \exp\left[-\frac{\mu_i}{v}(z - z_\xi)\right] + \frac{\lambda_i}{M}\left\{1 - \exp\left[-\frac{\mu_i}{v}(z - z_\xi)\right]\right\} \times \sum_{k=1}^{M} f_{j-1}(z'_k, v'_k) + f_0(z, v), \quad j = 1, \ldots, N. \tag{16}$$

This approach presents, in fact, the solution by the method of successive approximations of the integral equation equivalent to boundary problem (1)–(3) [7, 8, 11]. The software realisation of recurrent relations (16) is easily performed using recursive procedures. This feature of the

Table 1. Optical properties of the biological tissue.

Layer	Layer thickness/mm	Refractive index	Scattering coefficient/mm^{-1}	Absorption coefficient/mm^{-1}	Scattering anisotropy factor
Epidermis (G_1)	0.1	1.35	45	0.15	0.8
Derma (G_2^-)	l	1.4	20	0.073	0.76
Glass (G_2^*)	0.2	n_2^*	0.22	0.18	0
Derma (G_2^+)	$1.2 - l$	1.4	20	0.073	0.76

algorithm poses additional requirements to the random-access memory of the computer. In addition, the use of the recursion decreases the statistical error of the algorithm because it does not allow one to perform a random selection of reflection and refraction events of a photon.

In computer simulations of the experiments, we will consider a 1.5-mm-thick two-layer medium consisting of 0.1-mm-thick epidermis (G_1) and 1.4-mm-thick derma (G_2) layers, respectively. It is assumed that the immersion agent is introduced into the derma, which contains a foreign inclusion G_2^* – a glass with the specified refractive index and the scattering and absorption coefficients. Thus, the medium to be bleached contains in fact four layers: G_1, G_2^-, G_2^* and G_2^+.

The parameters of the layers G_1, G_2^-, G_2^*,and G_2^+ before bleaching had the values typical of human skin in the spectral region 600 – 700 nm [3, 15, 16] (Table 1).

In the derma, the concentration of scattering particles is usually 30 % [16], and the refractive index corresponding to them is equal to 1.46, i.e. $c_2 = 0.3$, $n_{c,2} = 1.46$. According to data of Table 1, $n_2 = 1.4$; therefore, due to assumption (4), the refractive index $n_{0,2}^{(0)}$ of the basic substance before bleaching should be equal to $(n_2 - c_2 n_{c,2})/(1 - c_2) \approx 1.37$.

The numerical experiments were performed using the following scheme. The refractive index $n_{0,2}$ varied from $n_{0,2}^{(0)}$ to $n_{c,2}$ with a step 0.005. In accordance with relations (4) – (7), this lead to a change in other parameters of the layers G_2^- and G_2^+, the parameters of the media G_1, G_2^* being invariable. On a discrete mesh of the values $n_{0,2}$, we first calculated the solution of the direct problem f^* at point $(z, v) = (z_0, -1)$ and then, the target function $J_1(n_{0,2})$ in which the ballistic components $f_{\rm b}$ and $f_{\rm b}^*$ were found analytically. Solving the direct problem, we assumed that radiation weakly collimated in the direction $v = 1$ enters the medium G only through the boundary $z = z_0$:

$$h(v) = \begin{cases} \exp[-2(1 - v)^2], & v > 0, \\ 0, & v < 0. \end{cases}$$

The number of trajectories simulated by the Mote Carlo method, depending on the complexity of the experiment, varied within $M = 20000 - 100000$.

From the obtained discrete set of the values of the function J_1, we selected the maximal one and refractive index of the basic substance of the bleaching layer corresponding to this value was taken as an approximate solution of problem 1.

We performed two series of experiments. In the first series, the position of the foreign inclusion G_2 in the medium varies so that the thickness l of the layer G_2^- increases, being 0.05, 0.1, and 0.5 mm, while the thickness of the layer G_2^+, on the contrary, decreases: $1.2 - l = 1.15, 1.1$, and 0.7 mm. The refractive index of the microinhomogeneity n_2^* was chosen equal to 1.48. The scattering indicatrix in each layer was calculated by expression (6), the anisotropy parameter $g_2(n_{0,2})$ in the bleaching layer varying from $g_2^{(0)} = 0.76$ to $g_2^{(c)} = 0.8$.

Figure 1a presents the dependences of $J_1(n_{0,2})$ at $n_{0,2} \in [1.37, 1.47]$ and different l. One can easily see that when l is increased, the maximum of the target function is displaced to the right and tends to the refractive index of scattering particles, $n_{c,2} = 1.46$, in agreement with the qualitative behaviour of asymptotic expression (12) for the optimal solution. The specific optimal values of the refractive index of the basic substance in the bleaching layer, obtained in this series of the experiments, proved close to the corresponding approximate solutions of the auxiliary extremal problem 2 with the target function $\tilde{J}_2$ (Table 2).

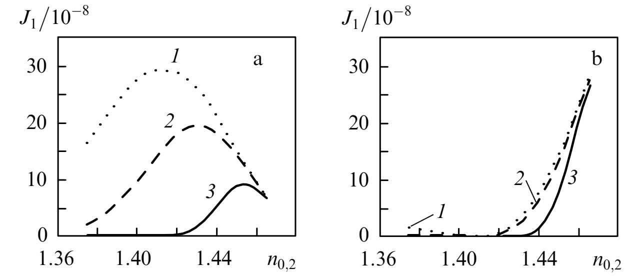

Figure 1. Target function $J_1(n_{0,2})$ for the refractive indices of the foreign inclusion $n_2^* = 1.48$ (a) and 1.42 (b) at different positions of the inclusion in the bleaching layer: $l = 0.05$ (*1*), 0.1 (*2*), and 0.5 mm (*3*).

Table 2. Results of the numerical experiment at $n_2^* = 1.48$.

Burial depth of the inclusion in the bleaching layer/mm	Point of the function maximum $J_1(n_{0,2})$	Point of the function maximum $\tilde{J}_2(n_{0,2})$
0.05	1.410	1.417
0.1	1.430	1.426
0.5	1.455	1.449

The second series of the experiments was similar to the first series. The only difference is that the refractive index n_2^* of the inclusions was smaller than the refractive index $n_{c,2}$ of the scattering particles and was equal to 1.42. In this case, according to the results of the solution of the auxiliary problem, the optimal refractive index should be higher than $n_{c,2}$ but due to physical assumptions with respect to the anisotropy parameters and the scattering coefficient, the solution of the problem is searched for in the interval $[n_{0,2}^{(0)}, n_{c,2}]$. Therefore, one can see from Fig. 1b that the maximum of the function $J_1(n_{0,2})$ is achieved at the end of the interval at point $n_{0,2} = n_{c,2}$ for all three cases ($l = 0.05, 0.1$, and 0.5 mm).

Note that the expansion of the possible variation range of the anisotropy parameter $g_2(n_{0,2})$ from [0.76, 0.8] to [0.76, 1] and, hence, the change in the scattering phase function (6) almost did not change the plot of the target function $J_1(n_{0,2})$. Although one should expect that the increase in the number of forward scattered photons should lead to an increase in the ballistic component in the reflected signal. In our opinion, one of the reasons consists in the fact that in the formulation of the problem under study, the first layer is not bleaching and the anisotropy parameter in it does not change. This leads to a noticeable suppression of the ballistic component of radiation in the epidermis.

To confirm this assumption, we performed a series of experiments with a model medium whose optical parameters are presented in Table 1 in the case when the epidermis (the layer G_1) is excluded from it. The burial depth of the glass in the derma was assumed equal to 0.1 mm.

In this case, an increase in the fraction of the ballistic component is really observed with increasing the anisotropy parameter (Fig. 2). Nevertheless, the position of the point of the function maximum $J_1(n_{0,2})$ remains virtually invariable.

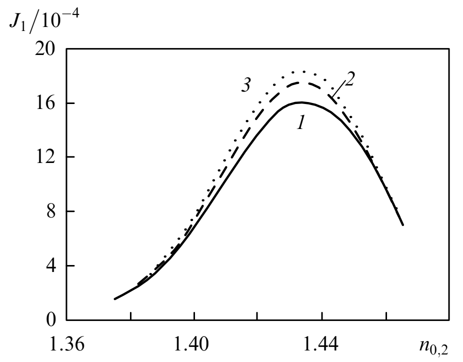

Figure 2. Target function $J_1(n_{0,2})$ for the medium without epidermis at the depth of the foreign inclusion $l = 0.1$ mm and the variation range of the scattering anisotropy parameter in the derma $0.76 \leqslant g \leqslant 0.8$ (*1*), $0.76 \leqslant g \leqslant 0.9$ (*2*), and $0.76 \leqslant g \leqslant 1$ (*3*).

Therefore, the results of the experiments showed that the optimal refractive index of the bleaching liquid significantly depends on the parameters of the searched for micro-inhomogeneity and is not obligatory close to the refractive index of the radiation scatterers in the medium.

5. Conclusions

The experiments performed in this paper allow us to make the following conclusions.

The results of tomographic investigations of biological tissues with the help of bleaching liquids should be treated with a certain degree of caution because in some cases their use can lead to deterioration of the reconstruction quality of the medium structure.

Obviously, reliable visualisation of the medium internal structure can be achieved in experiments with different immersion liquids including those whose refractive indices are smaller or greater than the refractive indices of the scatterers in the medium; in addition, it is necessary, if possible, to performed tomographic measurements during the time of the immersion liquid diffusion into the tissue. In principle, this is often done to estimate the rate of diffusion processes [3].

Another way is the use of *a priori* information about the parameters of the required inclusions when choosing this or that immersion liquid. In this case, to determine the optimal bleaching liquid, it is possible to use the results of computer simulations in solving problem 1 or analytic solutions of simplified problem 2.

One of the serious assumptions of this paper is the hypothesis about the medium stratification, including a quite unrealistic hypothesis about the plane shape of the inclusion. It is clear that such theoretical and numerical investigations can be also performed for the general three-dimensional case, which will be done elsewhere. However, for real physical experiments this refinement of the model is not always reasonable because in solving the extremal problems of type 1 and 2, we cannot expect the high accuracy of the *a priori* information on the structure of the irradiated medium. This, in particular, can explain our restriction to the quantity of foreign inclusions and bleaching layers. The latter assumption has also allowed us to obtain quite easily the analytic solution of problem 2 and to compare it with the solution of problem 1. Note that for the numerical algorithm determining the solution of problem 1, the above restriction is not fundamental.

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