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OPTICAL PROPERTIES OF SKIN, SUBCUTANEOUS, AND MUSCLE TISSUES: A REVIEW

ALEXEY N. BASHKATOV*,‡, ELINA A. GENINA*
and VALERY V. TUCHIN*,†
*Institute of Optics and Biophotonics
Saratov State University,
Saratov 410012, Russia
†Institute of Precise Mechanics and Control
of RAS, Saratov 410028, Russia
‡a.n.bashkatov@mail.ru

The development of optical methods in modern medicine in the areas of diagnostics, therapy, and surgery has stimulated the investigation of optical properties of various biological tissues, since the efficacy of laser treatment depends on the photon propagation and fluence rate distribution within irradiated tissues. In this work, an overview of published absorption and scattering properties of skin and subcutaneous tissues measured in wide wavelength range is presented. Basic principles of measurements of the tissue optical properties and techniques used for processing of the measured data are outlined.

Keywords: Absorption coefficient; scattering coefficient; anisotropy factor; reduced scattering coefficient; refractive index.

1. Introduction

Recent technological advancements in the photonics industry have spurred real progress toward the development of clinical functional imaging, surgical, and therapeutic systems. The development of the optical methods for medicine in the areas of diagnostics, surgery, and therapy has stimulated the investigation of optical properties of human tissues, since the efficacy of optical probing of the tissues depends on the photon propagation and fluence rate distribution within irradiated tissues. Monitoring of blood oxygenation and tissue metabolism, detection of skin malignancies, and skin optical imaging are examples of light diagnostic applications in dermatology. Therapeutic optical technologies mostly include photothermal and photodynamic therapy.

For these applications, knowledge of optical properties of skin and subcutaneous tissues is of great importance for interpretation and quantification of the diagnostic data, and for prediction of light distribution and absorbed energy for therapeutic and surgical use. In this review, we are presenting an overview of optical properties of skin and subcutaneous (including muscle) tissues measured in a wide range of wavelengths.

‡Corresponding author.

2. Basic Principles of Measurements of Tissue Optical Properties

Methods for determining the optical parameters of tissues can be divided into two large groups, direct and indirect methods.[1−12] Direct methods include those based on some fundamental concepts and rules such as the Bouguer−Beer−Lambert law, the single-scattering phase function for thin samples, or the effective light penetration depth for slabs. The parameters measured are the collimated light transmission T_c and the angular dependence of the scattered light intensity, $I(\theta)$ (W/cm^2 sr) for thin samples or the fluence rate distribution inside a slab. The normalized scattering angular dependence is equal to the scattering phase function $I(\theta)/I(0) \equiv p(\theta)$, 1/sr. These methods are advantageous in that they use very simple analytic expressions for data processing and reconstruction of optical parameters of tissue: μ_a, μ_s, and g, where μ_a is the absorption coefficient, μ_s is the scattering coefficient, and g is the anisotropy factor of scattering. Their disadvantages are related to the necessity to strictly fulfill experimental conditions dictated by the selected model (single scattering in thin samples, exclusion of the effects of light polarization and refraction at cuvette edges, etc.; in the case of slabs with multiple scattering, the recording detector (usually a fiber light guide with an isotropically scattering ball at the tip end) must be placed far from both the light source and the medium boundaries).

Indirect methods obtain the solution of the inverse scattering problem using a theoretical model of light propagation in a medium. They are, in turn, divided into iterative and non-iterative models. The former uses equations in which the optical properties are defined through parameters directly related to the quantities being evaluated. The latter are based on the two-flux Kubelka−Munk model and multi-flux models. In indirect iterative methods, the optical properties are implicitly defined through measured parameters. Quantities determining the optical properties of a scattering medium are enumerated until the estimated and measured values for reflectance and transmittance coincide with the desired accuracy. These methods are cumbersome, but the optical models currently in use may be even more complicated than those underlying non-iterative methods (examples include the diffusion theory, inverse adding-doubling (IAD), and inverse Monte Carlo (IMC) methods).

The optical properties of a tissue could be measured by different methods. The single- or double-integrating sphere method combined with collimated transmittance measurements is most often used for *in vitro* studies of tissues. This approach implies either sequential or simultaneous determination of three parameters: collimated transmittance $T_c = I_c/I_0$ (I_c is the intensity of transmitted light measured using a distant photodetector with a small aperture, W/cm^2, and I_0 is the intensity of incident radiation, W/cm^2), total transmittance $T_t = T_c + T_d$ (T_d being diffuse transmittance), and diffuse reflectance R_d. The optical parameters of the tissue are deduced from these measurements using different theoretical expressions or numerical methods (two-flux and multi-flux models, the IMC or IAD methods) relating μ_a, μ_s, and g to the parameters being investigated.

Any three measurements from the following five are sufficient for the evaluation of all three optical parameters[2]:

- Total (or diffuse) transmittance for collimated or diffuse radiation;
- Total (or diffuse) reflectance for collimated or diffuse radiation;
- Absorption by a sample placed inside an integrating sphere;
- Collimated transmittance (of unscattered light); and
- Angular distribution of radiation scattered by the sample.

Iterative methods normally take into account discrepancies between refractive indices at sample boundaries as well as the multilayer nature of the sample. The following factors are responsible for the errors in the estimated values of optical coefficients and need to be borne in mind in a comparative analysis of optical parameters obtained from different experiments[2,13−18]:

- The physiological conditions of tissues (the degree of hydration, homogeneity, species-specific variability, frozen/thawed or fixed/unfixed state, *in vitro*/*in vivo* measurements, smooth/rough surface);
- The geometry of irradiation;
- The matching/mismatching interface refractive indices;

- The angular resolution of photodetectors;
- The separation of radiation experiencing forward scattering from unscattered radiation; and
- The theory used to solve the inverse problem.

To analyze light propagation under multiple scattering conditions, it is assumed that absorbing and scattering centers are uniformly distributed across the tissue. Ultraviolet-A (UV-A), visible, or near-infrared (NIR) radiation is normally subjected to anisotropic scattering characterized by a clearly apparent direction of photons undergoing single scattering, which may be due to the presence of large cellular organelles (mitochondria, lysosomes, Golgi apparatus, etc.).[1−4,7−12,19]

When the scattering medium is illuminated by unpolarized light and/or only the intensity of multiple scattered light needs to be computed, a sufficiently strict mathematical description of continuous wave (CW) light propagation in a medium is possible in the framework of the scalar stationary radiation transfer theory (RTT).[1−4,7−12,19,20] This theory is valid for an ensemble of scatterers located far from one another and has been successfully used to work out some practical aspects of tissue optics. The main stationary equation of RTT for monochromatic light has the form

$$\frac{\partial I(\vec{r},\vec{s})}{\partial s} = -\mu_t I(\vec{r},\vec{s}) + \frac{\mu_s}{4\pi}\int_{4\pi} I(\vec{r},\vec{s})p(\vec{s},\vec{s}')d\Omega' \qquad (1)$$

where $I(\vec{r},\vec{s})$ is the radiance (or specific intensity)-average power flux density at point $\vec{r}$ in the given direction $\vec{s}$, W/cm^2 sr; $p(\vec{s},\vec{s}')$ is the scattering phase function, 1/sr; $d\Omega'$ is the unit solid angle about the direction $\vec{s}'$, sr, and $\mu_t = \mu_a + \mu_s$ is the total attenuation coefficient. It is assumed that there are no radiation sources inside the medium.

The scalar approximation of the radiative transfer equation (RTE) gives poor accuracy when the size of the scattering particles is much smaller than the wavelength, but provides acceptable results for particles comparable to and larger than the wavelength.[21,22]

The phase function $p(\vec{s},\vec{s}')$ describes the scattering properties of the medium and is, in fact, the probability density function for scattering in the direction $\vec{s}'$ of a photon traveling in the direction $\vec{s}$; in other words, it characterizes an elementary scattering act. If scattering is symmetric relative to the direction of the incident wave, then the phase function depends only on the scattering angle θ (angle between directions $\vec{s}$ and $\vec{s}'$), i.e., $p(\vec{s},\vec{s}') = p(\theta)$. The assumption of random distribution of scatterers in a medium (i.e., the absence of spatial correlation in the tissue structure) leads to normalization: $\int_0^\pi p(\theta)2\pi\sin\theta d\theta = 1$. In practice, the phase function is usually well approximated with the aid of the postulated Henyey−Greenstein function (HGF)[1−4,7−11,15,16,23−62]:

$$p(\theta) = \frac{1}{4\pi}\frac{1-g^2}{(1+g^2-2g\cos\theta)^{3/2}} \qquad (2)$$

where g is the scattering anisotropy parameter (mean cosine of the scattering angle θ)

$$g \equiv \langle\cos\theta\rangle = \int_0^\pi p(\theta)\cos\theta\cdot 2\pi\sin\theta d\theta.$$

The value of g varies in the range from -1 to 1; $g = 0$ corresponds to isotropic (Rayleigh) scattering, $g = 1$ to total forward scattering (Mie scattering at large particles), and $g = -1$ to total backward scattering.[1−4,7−11,20,21]

3. Integrating Sphere Technique

One of the indirect methods to determine optical properties of tissues *in vitro* is the integrating sphere technique.[2,11,13−18,27−40,42−50,53−58,60−83] Diffuse reflectance R_d, total T_t, and/or diffuse transmittance T_d, and collimated transmittance T_c are measured. In general, the absorption and scattering coefficients and anisotropy factor can be obtained from these data using an inverse method based on the radiative transfer theory. When the scattering phase function $p(\theta)$ is available from goniophotometry, g can be readily calculated. In this case, for the determination of μ_a and μ_s it is sufficient to measure R_d and T_t only. Sometimes in experiments with tissue and blood samples, a double-integrating sphere configuration is preferable, since in this case both reflectance and transmittance can be measured simultaneously and less degradation of the sample is expected during measurements. Nevertheless, in the case of a double-integrating sphere arrangement of the experiment in addition to the single-integrating sphere corrections of measured signals, multiple exchange of light between the spheres should be accounted for.[29,37,74]

Some tissues (e.g., melanin-containing) and blood have high total attenuation coefficients in the visible and NIR spectral range. Therefore, the collimated transmittance measurement for such samples (e.g., the undiluted blood layer with a moderate thickness ≈ 0.1 mm is a technically difficult task.[56] To solve this problem, a powerful light source combined with a sensitive detector must be used.[75] Alternatively, it is possible to collect the collimated light together with some forward-scattered light using the third integrating sphere.[76] In this case, the collimated transmittance is separated from the scattered flux on the stage of the data processing in use, e.g., a MC technique[60] or a small angle approximation.[79] Another approach was exactly the same as was used in Refs. 43, 67, 69, 70. In these studies, the diffuse reflectance, total and diffuse transmittance have been measured, and IMC algorithm, taking into account geometry of the measurement, has been used for treatment of the experimental data.

4. Kubelka–Munk and Multi-Flux Approach

To separate the light beam attenuation due to absorption from the loss due to scattering the one-dimensional (1D), two-flux Kubelka–Munk (KM) model can be used as the simplest approach to solve the problem. This approach has been widely used to determine the absorption and scattering coefficients of biological tissues, provided the scattering is significantly dominant over the absorption.[2,11,20,24,63,64,73,85–87] The KM model assumes that light incident on a slab of tissue because of interaction with the scattering media can be modeled by two fluxes, counterpropagating in the tissue slab. The optical flux, which propagates in the same direction as the incident flux, is decreased by absorption and scattering processes and is also increased by backscattering of the counterpropagating flux in the same direction. Changes in counterpropagating flux are determined in an analogous manner. The fraction of each flux lost by absorption per unit path length is denoted as K, while the fraction lost due to scattering is called S. The main assumptions of the KM model include: K and S parameters are assumed to be uniform throughout the tissue slab; all light fluxes are diffuse; and the amount of light lost from the edges of the sample during reflectance measurements is negligible. Basic KM model does not account for reflections at boundaries at which index of refraction mismatches exist.

Following the KM model and diffusion approximation of the RTE, the KM parameters were expressed in terms of light transport theory: the absorption and scattering coefficients and scattering anisotropy factor.[2,86] Thus, when scattering significantly prevails during absorption, a simple experimental method using modified KM model expressions can be successfully employed as

$$S = \frac{1}{bd} = \ln\left[\frac{1 - R_d(a-b)}{T_t}\right];$$
$$K = S(a-1); \quad a = \frac{1 - T_t^2 + R_d^2}{2R_d}; \quad b = \sqrt{a^2 - 1};$$
$$K = 2\mu_a; \quad S = \frac{3}{4}\mu_s(1-g) - \frac{1}{4}\mu_a;$$
$$\mu_t = \mu_a + \mu_s; \quad \mu_s' = \mu_s(1-g) > \mu_a, \tag{3}$$

where μ_t is determined based on Bouguer–Beer–Lambert law ($T_c = \exp(-\mu_t l)$) from measured values of collimated transmittance T_c, where l is tissue sample thickness. Thus, all three parameters (μ_a, μ_s, and g) can be found from the experimental data for total transmittance T_t, diffuse reflectance R_d, and collimated transmittance T_c of the sample.

Often, such simple methods as the KM model[13,15,16,28,30–44,47,56,62,67–70] or diffusion approximation[57,60,61,88,89] are used as the first step of the inverse algorithm for estimation of the optical properties of tissues and blood. The estimated values of the optical properties are then used to calculate the reflected and transmitted signals, employing one of the more sophisticated models of light propagation in tissue or blood. At the next step, the calculated values are compared with the measured ones. If the required accuracy is not achieved, the current optical properties are altered using one of the optimization algorithms. The procedures of altering the optical properties and calculating the reflected and transmitted signals are repeated until the calculated values match the measured values with the required accuracy.

5. IAD Method

The IAD method provides a tool for the rapid and accurate solution of inverse scattering

problem.[15,16,25–40,42,44,62,66,77,78] It is based on the general method for the solution of the transport equation for plane-parallel layers suggested by van de Hulst[90] and introduced to tissue optics by Prahl.[30,78,91] An important advantage of the IAD method when applied to tissue optics is the possibility of rapidly obtaining iterative solutions with the aid of up-to-date microcomputers; moreover, it is flexible enough to take into account anisotropy of scattering and the internal reflection from the sample boundaries. The method includes the following steps:

(1) The choice of optical parameters to be measured;
(2) Counting reflections and transmissions;
(3) Comparison of calculated and measured reflectance and transmittance; and
(4) Repetition of the procedure until the estimated and measured values coincides with the desired accuracy.

In principle, the method allows for any intended accuracy to be achieved for all the parameters being measured, provided the necessary computer time is available. An error of 3% or less is considered acceptable.[30] Also, the method may be used to directly correct experimental findings obtained with the aid of integrating spheres. The term "doubling" in the name of the method means that the reflection and transmission estimates for a layer at certain ingoing and outgoing light angles may be used to calculate both the transmittance and reflectance for a layer twice as thick by means of superimposing one upon the other and summing the contributions of each layer to the total reflectance and transmittance. Reflection and transmission in a layer having an arbitrary thickness are calculated in consecutive order, first for the thin layer with the same optical characteristics (single scattering), then by consecutive doubling of the thickness, for any selected layer. The term "adding" indicates that the doubling procedure may be extended to heterogeneous layers for modeling multilayer tissues or taking into account internal reflections related to abrupt change in refractive index.[30]

The adding-doubling technique is a numerical method for solving the 1D transport equation in slab geometry.[30,78,86] It can be used for media with an arbitrary phase function and arbitrary angular distribution of the spatially uniform incident radiation. Thus, finite beam size and side losses of light cannot be taken into account. The method is based on the observation that for an arbitrary incident radiance angular distribution $I_{\text{in}}(\eta_c)$, where η_c is the cosine of the polar angle, the angular distribution of the reflected radiance (normalized to an incident diffuse flux) is given by Prahl *et al.*[30,78,86]:

$$I_{\text{ref}}(\eta_c) = \int_0^1 I_{\text{in}}(\eta'_c) R(\eta'_c, \eta_c) 2\eta'_c d\eta'_c, \tag{4}$$

where $R(\eta'_c, \eta_c)$ is the reflection redistribution function determined by the optical properties of the slab.

The distribution of the transmitted radiance can be expressed in a similar manner, with obvious substitution of the transmission redistribution function $T(\eta'_c, \eta_c)$. If M quadrature points are selected to span over the interval $(0, 1)$, the respective matrices can approximate the reflection and transmission redistribution functions:

$$R(\eta'_{ci}, \eta_{cj}) \to R_{ij}; \quad T(\eta'_{ci}, \eta_{cj}) \to T_{ij}. \tag{5}$$

These matrices are referred to as the reflection and transmission operators, respectively. If a slab with boundaries indexed as 0 and 2 is comprised of two layers, (01) and (12), with an internal interface 1 between the layers, the reflection and transmission operators for the whole slab (02) can be expressed as

$$\begin{aligned}
\mathbf{T}^{02} &= \mathbf{T}^{12}(\mathbf{E} - \mathbf{R}^{10}\mathbf{R}^{12})^{-1}\mathbf{T}^{01}, \\
\mathbf{R}^{20} &= \mathbf{T}^{12}(\mathbf{E} - \mathbf{R}^{10}\mathbf{R}^{12})^{-1}\mathbf{R}^{10}\mathbf{T}^{21} + \mathbf{R}^{21}, \\
\mathbf{T}^{20} &= \mathbf{T}^{10}(\mathbf{E} - \mathbf{R}^{12}\mathbf{R}^{10})^{-1}\mathbf{T}^{21}, \\
\mathbf{R}^{02} &= \mathbf{T}^{10}(\mathbf{E} - \mathbf{R}^{12}\mathbf{R}^{10})^{-1}\mathbf{R}^{12}\mathbf{T}^{01} + \mathbf{R}^{01},
\end{aligned} \tag{6}$$

where $\mathbf{E}$ is the identity matrix defined in this case as

$$\mathrm{E}_{ij} = \frac{1}{2\eta_{ci} w_i} \delta_{ij}, \tag{7}$$

where w_i is the weight assigned to the ith quadrature point and δ_{ij} is a Kronecker delta symbol, $\delta_{ij} = 1$ if $i = j$, and $\delta_{ij} = 0$ if $i \neq j$.

The definition of the matrix multiplication also slightly differs from the standard. Specifically

$$(\mathbf{AB})_{ik} \equiv \sum_{j=1}^{M} A_{ij} 2\eta_{cj} w_j B_{jk}. \tag{8}$$

Equation (6) allows one to calculate the reflection and transmission operators of a slab when those of the comprising layers are known. The idea of method is to start with a thin layer for which the RTE can be simplified and solved with relative ease, producing the reflection and transmission operators for the thin layer, then to proceed by doubling the

thickness of the layer until the thickness of the whole slab is reached. Several techniques exist for layer initialization. The single-scattering equations for reflection and transmission for the HGF are given by van de Hulst[90] and Prahl.[78] The refractive index mismatch can be taken into account by adding effective boundary layers of zero thickness and having the reflection and transmission operators determined by Fresnel's formulas. The total transmittance and reflectance of the slab are obtained by straightforward integration of Eq. (4). Different methods of performing the integration and the IAD program provided by Prahl[30,78,91] allows one to obtain the absorption and the scattering coefficients from the measured diffuse reflectance R_d and total transmittance T_t of the tissue slab. This program is the numerical solution to the steady-state RTE [Eq. (1)] realizing an iterative process, which estimates the reflectance and transmittance from a set of optical parameters until the calculated reflectance and transmittance match the measured values. Values for the anisotropy factor g and the refractive index n must be provided to the program as input parameters.

It was shown that using only four quadrature points, the IAD method provides optical parameters that are accurate to within 2−3%,[30] as was mentioned earlier; higher accuracy, however, can be obtained by using more quadrature points, but it would require increased computation time. Another valuable feature of the IAD method is its validity for the study of samples with comparable absorption and scattering coefficients,[30] since other methods based on only diffusion approximation are inadequate. Furthermore, since both anisotropic phase function and Fresnel reflection at boundaries are accurately approximated, the IAD technique is well suited to optical measurements of biological tissues and blood held between two glass slides. The adding-doubling method provides accurate results in cases when the side losses are not significant, but it is less flexible than the MC technique.

The IAD method has been successfully applied to determine optical parameters of blood[92]; human and animal dermis[16,39,40,77,93]; brain tissues[28,94]; colon tissues[36]; bronchial tissue[31]; ocular tissues such as retina,[33,34] choroids, sclera, conjunctiva, and ciliary body[16,44,62]; mucous tissue[38]; muscle tissue[93]; subcutaneous tissue[39,40]; cranial bone[42]; aorta[16]; and other soft tissues in the wide range of the wavelengths.[2,11]

6. IMC Method

Both the real geometry of the experiment and the tissue structure may be complicated. Therefore, IMC method should be used if reliable estimates are to be obtained. A number of algorithms to use the IMC method are available now in the literature.[5,11,13,41,43,45−49,51−61,67−70,95−113] Many researchers use the MC simulation algorithm and program provided by Jacques and Wang.[59,111,112] Among the first designed IMC algorithms, a similar algorithm for determining all the three optical parameters of the tissue (μ_a, μ_s, and g) based on the *in vitro* evaluation of the total transmittance, diffuse reflectance, and collimated transmittance using a spectrophotometer with integrating spheres, can be also mentioned.[5,13,43,45−49,53−58,60,61,67−71,95,98,102,103,108] The initial approximation (to speed up the procedure) was achieved with the help of the Kubelka−Munk theory, specifically its four-flux variant.[13,43,45,47,54−56,67−70] The algorithms take into consideration the sideways loss of photons, which becomes essential in sufficiently thick samples. Similar results were obtained using the condensed IMC method.[5,46,49,53,71,102,103]

The MC technique is employed as a method to solve the forward problem in the inverse algorithm for the determination of the optical properties of tissues and blood. The MC method is based on the formalism of the RTT, where the absorption coefficient is defined as a probability of a photon to be absorbed per unit length, and the scattering coefficient is defined as the probability of a photon to be scattered per unit length. Using these probabilities, a random sampling of photon trajectories is generated.

The basic algorithm for the generation of photon trajectories can be shortly described as follows.[59,74,111,112] A photon described by three spatial coordinates and two angles (x, y, z, θ, ϕ) is assigned its weight $W = W_0$ and placed in its initial position, depending on the source characteristics. The step size s of the photon is determined as $s = -\ln(\xi)/\mu_t$, where ξ is a random number between 0 and 1. The direction of the photon's next movement is determined by the scattering phase function substituted as the probability density distribution. Several approximations for the scattering phase function of tissue and blood have been used in MC simulations. These include the two empirical phase functions widely used to approximate the scattering phase

function of tissue and blood, Henyey−Greenstein phase function (HGPF) [see Eq. (2)], the Gegenbauer kernel phase function (GKPF),[113−115] and theoretical Mie phase function.[116] The HGPF has one parameter g that may be represented as the infinite series of Legendre polynomials $P_n^1(\cos\theta)$,

$$p_{\mathrm{HG}}(\theta) = \frac{1}{4\pi}\sum_{n=0}^{\infty}(2n+1)f_n P_n^1(\cos\theta), \qquad (9)$$

where $f_n = g^n$ is the nth order moment of the phase function.

The GKPF has two variable parameters, α and g:

$$p_{\mathrm{GK}}(\theta) = K[1+g^2-2g\cos(\theta)]^{-(\alpha+1)}, \qquad (10)$$

where

$$K = \alpha g\pi^{-1}(1-g^2)^{2\alpha}[(1+g)^{2\alpha}-(1-g)^{2\alpha}]^{-1},$$
$$\alpha > -1/2, \quad |g| \le 1.$$

The GKPF is a generalization of the HGPF and can be reduced to HGPF by setting $\alpha = 0.5$. The GKPF may be represented as the infinite series of Gegenbauer polynomials, C_n^{α}[114,115]:

$$p_{\mathrm{GK}}(\theta) = \frac{2K}{(1-g^2)}\sum_{n=0}^{\infty}\left(1+\frac{n}{\alpha}\right)C_n^{\alpha}[\cos(\theta)]g^n. \qquad (11)$$

The HGPF and GKPF are widely employed in radiative transport calculations for the description of the single-scattering process in whole blood[56,67−70,74,75,92,113] and tissues[5,13,15,16,25,28−49,53,57−62,77,93−98,100,101,103,106−109,117] because of their mathematical simplicity. However, it is clear that the HGPF and GKPF cannot be used for accurate calculations of the angular light distribution scattered by a single particle. For some calculations, theoretical Mie phase function may be useful[116]:

$$p(\theta) = \frac{1}{k^2r^2}(|S_1|^2+|S_2|^2), \qquad (12)$$

where S_1 and S_2 are functions of the polar scattering angle and can be obtained from the Mie theory as

$$S_1(\theta) = \sum_{n=1}^{\infty}\frac{2n+1}{n(n+1)}\{a_n\pi_n(\cos\theta)+b_n\tau_n(\cos\theta)\},$$
$$S_2(\theta) = \sum_{n=1}^{\infty}\frac{2n+1}{n(n+1)}\{b_n\pi_n(\cos\theta)+a_n\tau_n(\cos\theta)\}. \qquad (13)$$

The parameters π_n and τ_n represent

$$\pi_n(\cos\theta) = \frac{1}{\sin\theta}P_n^1(\cos\theta),$$
$$\tau_n(\cos\theta) = \frac{d}{d\theta}P_n^1(\cos\theta), \qquad (14)$$

where $P_n^1(\cos\theta)$ is the associated Legendre polynomial. The following recursive relationships are used to calculate π_n and τ_n:

$$\pi_n = \frac{2n-1}{n-1}\pi_{n-1}\cos\theta - \frac{n}{n-1}\pi_{n-2},$$
$$\tau_n = n\pi_n\cos\theta - (n+1)\pi_{n-1}, \qquad (15)$$

and the initial values are

$$\begin{cases}\pi_1 = 1, & \pi_2 = \cos\theta,\\ \tau_1 = \cos\theta, & \tau_2 = 3\cos 2\theta.\end{cases} \qquad (16)$$

The coefficients a_n and b_n are defined as:

$$a_n = \frac{\psi_n(\alpha)\psi_n'(m\alpha) - m\psi_n(m\alpha)\psi_n'(\alpha)}{\zeta_n(\alpha)\psi_n'(m\alpha) - m\psi_n(m\alpha)\zeta_n'(\alpha)}$$
$$b_n = \frac{m\psi_n(\alpha)\psi_n'(m\alpha) - \psi_n(m\alpha)\psi_n'(\alpha)}{m\zeta_n(\alpha)\psi_n'(m\alpha) - \psi_n(m\alpha)\zeta_n'(\alpha)} \qquad (17)$$
$$m = n_p/n_0, \quad \alpha = 2\pi a n_0/\lambda_0$$

where a is the radius of spherical particles, λ_0 is the light wavelength in vacuum, ψ_n, ζ_n, ψ_n', and ζ_n' are the Riccati−Bessel functions of the first and second kind, n_0 is the refractive index of the ground material, and n_p is the refractive index of scattering particles.

For the HGPF, the random scattering angle θ_{rnd}^{HG} is given by

$$\theta_{rnd}^{HG} = \arccos\left\{\frac{1}{2g}\left[1+g^2-\left(\frac{1-g^2}{1-g+2g\xi}\right)^2\right]\right\}. \qquad (18)$$

For the GKPF, the random scattering angle θ_{rnd}^{GK} is determined as[113]

$$\theta_{rnd}^{GK} = \arccos\left[(1+g^2-1/\sqrt[\alpha]{\zeta_{rnd}})/2g\right], \qquad (19)$$

where $\zeta_{rnd} = 2\alpha g\xi/K + (1+g)^{-2\alpha}$, and α and K are defined in Eq. (10).

If experimental scattering phase function is known for the discrete set of scattering angles θ_i, $f(\theta) = f(\theta_i)$, it can be determined in the total angular range using the spline-interpolation technique. Then, the value of the function $F_n = \int_0^{\theta_n} f(\theta)d\theta$ can be calculated numerically for any value of θ_n. It is easy

to see that F_n is a non-decreasing function that is mapping the interval $(0, 1)$. Therefore, when random value γ is sampled, $\theta_{rnd}^{\exp}$ is determined by setting $F_n = \xi$.

The Mie phase function can be tabulated and treated in the same way as the experimental phase function.[113] In most cases, azimuthal symmetry is assumed. This leads to $p(\phi) = 1/2\pi$ and, consequently, $\phi_{rnd} = 2\pi\xi$. At each step, the photon loses part of its weight due to absorption: $W = W(1 - \Lambda)$, where $\Lambda = \mu_s/\mu_t$ is the albedo of the medium.

When the photon reaches the boundary, part of its weight is transmitted according to the Fresnel equations. The amount transmitted through the boundary is added to the reflectance or transmittance. Since the refraction angle is determined by the Snell's law, the angular distribution of the outgoing light can be calculated. The photon with the remaining part of the weight is specularly reflected and continues its random walk.

When the photon's weight becomes lower than a predetermined minimal value, the photon can be terminated using the "Russian roulette" procedure.[59,60,111,112,118,119] This procedure saves time, since it does not make sense to continue the random walk of the photon, which will not essentially contribute to the measured signal. On the other hand, it ensures that the energy balance is maintained throughout the simulation process.

The MC method has several advantages over the other methods because it may take into account mismatched medium-glass and glass−air interfaces, losses of light at the edges of the sample, any phase function of the medium, and the finite size and arbitrary angular distribution of the incident beam. If the collimated transmittance is measured, then the contribution of scattered light into the measured collimated signal can be accounted for.[11,59,60] The only disadvantage of this method is the long time needed to ensure good statistical convergence, since it is a statistical approach. The standard deviation of a quantity (diffuse reflectance, transmittance, etc.) approximated by MC technique decreases proportionally to $1/\sqrt{N}$, where N is the total number of launched photons.

It is worthy of note that stable operation of the algorithm was maintained by generation of 10^5 to 5×10^5 photons per iteration. Two to five iterations were usually necessary to estimate the optical parameters with approximately 2% accuracy. The computer time required can be reduced not only by the condensed IMC method[46] but also by means of graphical solution of the inverse problem[99−101] or by means of generating a look-up table[5,49,53,71,102,103,105] following a preliminary MC simulation. In the last case, a linear or spline interpolations[120] between the data points can be used to improve the accuracy of the selection process.

In general, *in vivo* μ_a and μ_s' values for human skin proved to be significantly smaller than those obtained *in vitro* (about 10 and two times, respectively).[11,46,53,58,95,121,122] For μ_a, the discrepancy may be attributed to the low sensitivity of the double-integrating sphere, and goniometric techniques have been applied for *in vitro* measurements at weak absorption combined with strong scattering ($\mu_a \ll \mu_s$) and the sample preparation methods. For μ_s', the discrepancy may be related to the strong dependence of the method on variations in the relative refractive index of scatterers and the ground medium of the tissue m, $\mu_s' \sim (m-1)^2$, which can be quite different for living and sampled tissue.[99,123] The *ex vivo* measurements using the integrating sphere technique with corresponding IMC models, and very carefully prepared human tissue samples allow for accurate evaluation of μ_a and μ_s', which are very close to *in vivo* measurements.[13,14,53,58,95,121,122,124]

7. Direct Measurement of the Scattering Phase Function

Direct measurement of the scattering phase function $p(\theta)$ is important for the choice of an adequate model for the tissue being examined.[5,8,11,74,113,125] The scattering phase function is usually determined from goniophotometric measurements in relatively thin tissue samples.[3,5,11,24,32−34,71,92,102,113,126−141] The measured scattering angular dependence can be approximated either by the HGPF[24,32−34,76,128,129,136,138,139] [see Eq. (2)] or by a set of HGPFs, with each function characterizing the type of scatterers and specific contribution to the angular dependence [see Eq. (9)].[11,127] In the limiting case of a two-component model of a medium containing large and small (compared with the wavelength) scatterers, the angular dependence is represented in the form of anisotropic and isotropic components.[19,24,39,43,102,124,129,132,133,137,139] Other approximating functions are equally useful, e.g., those obtained from the Rayleigh−Gans

approximation,[124] ensuing from the Mie theory,[96,97,134,138] or a two-parameter GKPF [HGPF is a special simpler case of this phase function, see Eq. (10)].[72,113,128] Some of these types of approximations were used to find the dependence of the scattering anisotropy factor g for dermis and epidermis on the wavelengths in the range from 300 to 1,300 nm, which proved to coincide fairly well with the empirical formula,[86]

$$g_e \sim g_d \sim 0.62 + \lambda \times 0.29 \times 10^{-3}, \qquad (20)$$

on the assumption of a 10% contribution of isotropic scattering (at wavelength 633 nm).[139] The wavelength λ is given in nanometers. Another form of the spectral dependence of anisotropy factor can be presented as

$$g(\lambda) = A + B(1 - \exp(-(\lambda - C)/D)), \qquad (21)$$

where A, B, C, D are some of the empirical constants.

The experimental values of anisotropy factor g for many types of human and animal tissues are presented in Tables 1–3 and approximated using Eq. (21).

It should be noted that the correct prediction of light transport in tissues depends on the exact form of the phase function used for calculations.[5,11,67,74,101,113] Simulations performed with different forms of $p(\theta)$ (HGPF, Mie, and GKPF) with the same value of $\langle\cos(\theta)\rangle$ result in the collection of significantly different fractions of the incident photons, particularly when small numerical-aperture delivery and collection fibers (small source-detection separation) are employed.[72,74,97,113]

Moreover, for media with high anisotropy factors, precise measurements of the scattering phase function in the total angle range from 0 to 180 degrees is a difficult technical task, demanding an extremely large dynamic range of measuring equipment. Most of the scattered radiation lies in the range from 0 to

Table 1. Optical properties of human and animal skin tissues measured *in vitro* and *ex vivo* (root mean square (RMS) values are given in parentheses) (IS, single integrating sphere; DIS, double integrating sphere).

Tissue	λ, nm	μ_a, cm^{-1}	μ_s, cm^{-1}	g	μ_s', cm^{-1}	Remarks
Caucasian skin ($n = 21$)	400	3.76 (0.35)	—	—	71.8 (9.4)	IS, IAD; whole skin; in the spectral range of 400–2,000 nm: $\mu_s' = 1.1 \times 10^{12}\lambda^{-4} + 73.7\lambda^{-0.22}$, [$\lambda$] in nanometers[39]
	500	1.19 (0.16)	—	—	32.5 (4.2)	
	600	0.69 (0.13)	—	—	21.8 (3.0)	
	700	0.48 (0.11)	—	—	16.7 (2.3)	
	800	0.43 (0.11)		—	14.0 (1.9)	
	900	0.33 (0.02)	—	—	15.7 (2.1)	
	1,000	0.27 (0.03)	—	—	16.8 (2.8)	
	1,100	0.16 (0.04)	—	—	17.1 (2.7)	
	1,200	0.54 (0.04)	—	—	16.7 (2.9)	
	1,300	0.41 (0.07)	—	—	14.7 (2.6)	
	1,400	1.64 (0.31)	—	—	14.3 (3.7)	
	1,500	1.69 (0.35)	—	—	14.4 (3.8)	
	1,600	1.19 (0.22)	—	—	14.2 (3.4)	
	1,700	1.55 (0.28)	—	—	14.7 (3.5)	
	1,800	1.44 (0.22)	—	—	13.4 (2.9)	
	1,900	2.14 (0.28)	—	—	12.2 (3.1)	
	2,000	1.74 (0.29)	—	—	12.0 (2.9)	
Caucasian skin ($n = 3$)	400	13.48	—	—	34.28	IS, IAD; whole skin; in the spectral range of 400–1,800 nm: $\mu_s' = 2.85 \times 10^{7}\lambda^{-2.311} + 209.311\lambda^{-0.518}$, [$\lambda$] in nanometers, data from graphs of Ref. 16
	500	6.19	—	—	25.05	
	600	3.77	—	—	18.67	
	700	2.41	—	—	14.82	
	800	1.94	—	—	12.42	
	900	1.76	—	—	10.57	
	1,000	1.55	—	—	9.23	
	1,100	1.33	—	—	7.91	
	1,200	1.76	—	—	7.11	
	1,300	1.76	—	—	6.60	
	1,400	10.29	—	—	6.21	

Table 1. (*Continued*)

Tissue	λ, nm	μ_a, cm^{-1}	μ_s, cm^{-1}	g	μ_s', cm^{-1}	Remarks
	1,500	16.21	—	—	5.47	
	1,600	5.44	—	—	5.87	
	1,700	4.11	—	—	5.59	
	1,800	6.05	—	—	5.68	
Caucasian skin ($n = 22$)	1,000	0.98	—	—	12.58	DIS, IAD; whole skin; data from graphs of Ref. 77; in the spectral range of 1,000−1,250 nm: $\mu_s' = 7.59 \times 10^7 \lambda^{-2.503} + 165.86\lambda^{-0.402}$, [$\lambda$] in nanometers
	1,100	0.98	—	—	11.77	
	1,200	1.87	—	—	11.08	
	1,300	1.77	—	—	10.69	
	1,400	7.94	—	—	11.39	
	1,500	13.1	—	—	11.38	
	1,600	5.2	—	—	10.10	
	1,700	4.85	—	—	9.96	
	1,800	6.5	—	—	9.96	
	1,900	13.0	—	—	10.63	
Rabbit skin (epidermis + dermis)	630	0.94 (0.13)	213 (21)	0.812 (0.017)	40 (2.2)	DIS, IAD[93]
	632.8	0.33 (0.02)	306 (12)	0.898 (0.007)	31.6 (2.2)	
	790	0.70 (0.07)	321 (8)	0.94 (0.003)	18.4 (0.5)	
Piglet skin (epidermis + dermis)	632.8	1.0 (0.1)	492 (17)	0.953 (0.001)	22.7 (0.8)	DIS, IAD[93]
	790	2.4 (0.2)	409 (14)	0.952 (0.001)	19.3 (0.6)	
	850	1.6 (0.1)	403 (20)	0.962 (0.005)	14.3 (1.5)	
Stratum corneum	350	25.92	500	0.902	48.99	Data from graphs of Ref. 154 (with reference to Refs. 86, 139, 141); in the spectral range of 400−700 nm: $g = 0.918 + 0.304$ $(1 - \exp(-(\lambda - 507.4)/2404))$
	400	17.28	500	0.903	48.44	
	450	11.63	500	0.910	45.24	
	500	10.47	500	0.916	41.93	
	550	9.83	500	0.923	38.69	
	600	8.67	500	0.93	35.02	
	650	8.21	500	0.936	32.21	
	700	8.15	500	0.942	28.93	
Epidermis (lightly pigmented/ medium pigmented/ highly pigmented)	350	9.99/30.16/69.8	210.4	0.702	—	Data from graphs of Ref. 154 (with reference to Refs. 86, 139, 141); in the spectral range of 350−700 nm: $g = 0.745 + 0.546$ $(1 - \exp(-(\lambda - 500)/1806))$; $\mu_s = 1.752 \times 10^8 \lambda^{-2.33} + 134.67\lambda^{-0.494}$, [$\lambda$] in nanometers
	400	6.77/20.2/46.67	156.3	0.712	—	
	450	4.41/13.5/31.52	121.6	0.728	—	
	500	2.58/9.77/21.82	93.01	0.745	—	
	550	1.63/6.85/16.13	74.70	0.759	—	
	600	1.47/5.22/12.35	63.76	0.774	—	
	650	1.2/3.68/9.15	55.48	0.787	—	
	700	1.06/3.07/7.11	54.66	0.804	—	
Human epidermis ($n = 10$)	400	26.36	—	—	31.73	IS, 1D diffusion approximation; Caucasian skin; in the spectral range of 400−800 nm: $\mu_s' = 1.175 \times 10^3 \lambda^{-0.6}$, [$\lambda$] in nanometers; data from graphs of Ref. 50
	450	13.84	—	—	30.11	
	500	7.79	—	—	28.27	
	550	5.73	—	—	26.82	
	600	3.01	—	—	25.29	
	650	1.58	—	—	24.14	
	700	0.89	—	—	22.97	
	750	0.49	—	—	22.09	
	800	0.35	—	—	21.27	
Human epidermis ($n = 7$)	400	12.96 (1.44)	—	—	106.2 (11)	IS, IMC, in the spectral range of 370−1,400 nm: $\mu_s' = 1.08 \times 10^8 \lambda^{-2.364} + 135.71\lambda^{-0.267}$, [$\lambda$] in nanometers[57]
	500	7.07 (0.66)	—	—	70.6 (7)	
	600	3.08 (0.76)	—	—	51.4 (5.0)	
	700	2.58 (0.77)	—	—	42.7 (4.1)	
	800	1.71 (0.59)	—	—	36.8 (3.6)	

Table 1. (*Continued*)

Tissue	λ, nm	μ_a, cm^{-1}	μ_s, cm^{-1}	g	μ'_s, cm^{-1}	Remarks
	900	0.80 (0.45)	—	—	33.6 (3.5)	
	1,000	0.45 (0.28)	—	—	30.6 (3.4)	
	1,100	0.17 (0.14)	—	—	29.2 (3.2)	
	1,200	0.71 (0.44)	—	—	26.5 (3.1)	
	1,300	0.71 (0.42)	—	—	25.7 (3.1)	
	1,400	15.53 (2.5)	—	—	27.5 (3.6)	
	1,500	23.69 (3.5)	—	—	28.3 (4.2)	
	1,600	7.49 (1.64)	—	—	23.0 (3.3)	
Human dermis	350	20.74	212.7	0.715	—	Data from graphs of Ref. 154 (with reference to Refs. 86, 139, 141); in the spectral range of 350−700 nm: $g = 0.715 + 3.8 \times 10^{-4}(1 - \exp(-(\lambda - 542)/1129))$; $\mu_s = 1.752 \times 10^8 \lambda^{-2.33} + 134.67\lambda^{-0.494}$, $[\lambda]$ in nanometers
	400	13.82	159.9	0.715	—	
	450	9.31	124.1	0.715	—	
	500	8.37	92.24	0.715	—	
	550	7.86	77.22	0.715	—	
	600	6.94	63.09	0.715	—	
	650	6.57	55.98	0.715	—	
	700	6.52	53.62	0.715	—	
Human dermis ($n = 8$)	400	9.13 (1.18)	—	—	76.8 (11)	IS, IMC, in the spectral range of 370−1,400 nm: $\mu'_s = 1.19 \times 10^8 \lambda^{-2.427} + 71.476\lambda^{-0.258}$, $[\lambda]$ in nanometers[57]
	500	3.36 (0.43)	—	—	46.2 (4.6)	
	600	1.72 (0.24)	—	—	32.2 (2.9)	
	700	1.53 (0.25)	—	—	26.4 (2.5)	
	800	1.22 (0.21)	—	—	22.5 (2.3)	
	900	0.83 (0.17)	—	—	20.1 (2.3)	
	1,000	0.79 (0.18)	—	—	18.6 (2.2)	
	1,100	0.46 (0.17)	—	—	17.6 (2.1)	
	1,200	1.33 (0.22)	—	—	16.6 (2.0)	
	1,300	1.19 (0.24)	—	—	16.2 (2.0)	
	1,400	11.7 (1.14)	—	—	18.6 (1.9)	
	1,500	17.5 (1.48)	—	—	19.9 (2.0)	
	1,600	6.63 (0.57)	—	—	15.9 (1.8)	
Caucasian dermis ($n = 12$)	633	0.32	—	—	26.99	IS, IMC; data from graphs of Ref. 58; in the spectral range of 620−1,000 nm: $\mu'_s = 1.66 \times 10^5 \lambda^{-1.356}$, $[\lambda]$ in nanometers
	700	0.12	—	—	23.02	
	750	0.09	—	—	20.62	
	800	0.02	—	—	18.80	
	850	0.01	—	—	17.41	
	900	0.03	—	—	16.18	
	950	0.22	—	—	15.10	
	1,000	0.39	—	—	14.68	
Negroid dermis ($n = 5$)	633	2.45	—	—	32.29	IS, IMC; data from graphs of Ref. 58; in the spectral range of 620−1,000 nm: $\mu'_s = 3.33 \times 10^5 \lambda^{-1.438}$, $[\lambda]$ in nanometers
	700	1.51	—	—	27.24	
	750	1.12	—	—	24.02	
	800	0.80	—	—	21.26	
	850	0.61	—	—	19.70	
	900	0.46	—	—	18.55	
	950	0.49	—	—	17.67	
	1,000	0.49	—	—	16.83	
Caucasian bloodless dermis	450	5.13	134.9	0.054	—	IS, IAD; data from graph of Ref. 78; in the spectral range of 450−800 nm: $\mu_s = 2.97 \times 10^5 \lambda^{-1.257}$, $[\lambda]$ in nanometers; in the spectral range of 500−800 nm: $g = 0.334 + 0.217(1 - \exp(-(\lambda - 567)/90.76))$, $[\lambda]$ in nanometers
	500	3.45	119.9	0.120	—	
	550	2.28	108.1	0.288	—	
	600	1.81	97.38	0.410	—	
	650	1.44	87.89	0.461	—	
	700	1.16	78.48	0.50	—	
	750	1.03	72.29	0.519	—	
	800	0.88	65.89	0.531	—	

Table 1. (*Continued*)

Tissue	λ, nm	μ_a, cm^{-1}	μ_s, cm^{-1}	g	μ_s', cm^{-1}	Remarks
Caucasian bloodless dermis ($n = 5$)	633	2.7	187	0.82	33.66	IS, 1D-diffusion approximation[139]
Caucasian bloodless dermis ($n = 30$)	350 400 450 633	23.2 9.5 6.3 2.7	147.2 136.1 130.8 90.3	0.14 0.22 0.38 0.62	127.2 106.7 81.2 33.9	IS, 1D-diffusion approximation; data from graphs of Ref. 158 (with references to Zrakit D.: unpublished Masters report, Massachusetts Institute of Technology, 1986); in the spectral range of 350−650 nm: $g = 0.438 + 0.475(1-\exp(-(\lambda-494.6)/282.15))$, $\mu_s' = 5.86 \times 10^5 \lambda^{-1.391} - 18.66\lambda^{0.115}$, $[\lambda]$ in nanometers
Piglet skin dermis	632.8 790 850	0.89 (0.1) 1.8 (0.2) 0.33 (0.03)	289 (7) 254 (5) 285 (5)	0.926 (0.002) 0.945 (0.001) 0.968 (0.001)	21.1 (0.4) 13.9 (0.3) 9 (0.2)	DIS, IAD[93]
Porcine skin dermis ($n = 44$)	900 1,000 1,100 1,200 1,300 1,400 1,500	0.06 0.12 0.17 1.74 1.04 9.11 7.32	282.6 270.4 267.2 263.9 262.8 246.2 259.6	0.904 0.904 0.904 0.903 0.903 0.872 0.873	— — — — — — —	IS, IMC; post-mortem time 2 ∼ 10 h; data from graphs of Ref. 98; in the spectral range of 1,000−1,300 nm: $\mu_s = 440.2\lambda^{-0.072}$, $[\lambda]$ in nanometers
Porcine skin dermis ($n = 40$)	325 442 532 633 850 1,064 1,310 1,557	5.6 1.9 1.4 0.7 1.6 3.1 6.2 10.4	220 89 69 58 90 26 40 21	0.38 0.36 0.64 0.72 0.88 0.86 0.87 0.82	— — — — — — — —	IS, IMC; data from graphs of Ref. 150; in the spectral range of 325−1,557 nm: $g = 0.653 + 0.219(1-\exp(-(\lambda-530.2)/242.8))$; $\mu_s = 3.286 \times 10^8 \lambda^{-2.487} + 80.454\lambda^{-0.215}$, $[\lambda]$ in nanometers

Table 2. Optical properties of human and animal subcutaneous tissues measured *in vitro* and *ex vivo* (RMS values are given in parentheses) (IS, single integrating sphere).

Tissue	λ, nm	μ_a, cm^{-1}	μ_s, cm^{-1}	g	μ_s', cm^{-1}	Remarks
Subdermis (primarily globular fat cells) ($n = 12$)	633 700 750 800 850 900 950 1,000	0.12 0.09 0.09 0.08 0.09 0.12 0.15 0.12	— — — — — — — —	— — — — — — — —	12.58 12.10 11.75 11.40 11.17 10.95 10.81 10.71	IS, IMC; data from graphs of Ref. 58; in the spectral range of 620−1,000 nm, $\mu_s' = 139.24\lambda^{-0.373}$, $[\lambda]$ in nanometers
Human subcutaneous adipose tissue ($n = 6$)	400 500 600	2.26 (0.24) 1.49 (0.06) 1.18 (0.02)	— — —	— — —	13.4 (2.8) 13.8 (4.0) 13.4 (4.7)	IS, IAD; in the spectral range of 600−1,500 nm: $\mu_s' = 1.05 \times 10^3 \lambda^{-0.68}$, $[\lambda]$ in nanometers[39]

Table 2. (*Continued*)

Tissue	λ, nm	μ_a, cm^{-1}	μ_s, cm^{-1}	g	μ_s', cm^{-1}	Remarks
	700	1.11 (0.05)	—	—	12.2 (4.4)	
	800	1.07 (0.11)	—	—	11.6 (4.6)	
	900	1.07 (0.07)	—	—	10.0 (3.4)	
	1,000	1.06 (0.06)	—	—	9.39 (3.3)	
	1,100	1.01 (0.05)	—	—	8.74 (3.3)	
	1,200	1.06 (0.07)	—	—	7.91 (3.2)	
	1,300	0.89 (0.07)	—	—	7.81 (3.2)	
	1,400	1.08 (0.03)	—	—	7.51 (3.3)	
	1,500	1.05 (0.02)	—	—	7.36 (3.4)	
	1,600	0.89 (0.04)	—	—	7.16 (3.2)	
	1,700	1.26 (0.07)	—	—	7.53 (3.3)	
	1,800	1.21 (0.01)	—	—	7.50 (3.48)	
	1,900	1.62 (0.06)	—	—	8.72 (4.2)	
	2,000	1.43 (0.09)	—	—	8.24 (4.0)	
Human subcutaneous adipose tissue ($n = 10$)	400	15.98 (3.2)	—	—	49.5 (6.5)	IS, IMC, in the spectral range of 370−1,300 nm: $\mu_s' = 1.08 \times 10^8 \lambda^{-2.525} + 157.494\lambda^{-0.345}$, [$\lambda$] in nanometers[57]
	500	5.50 (0.69)	—	—	35.4 (4.5)	
	600	1.89 (0.40)	—	—	27.0 (3.2)	
	700	1.27 (0.24)	—	—	23.0 (2.5)	
	800	1.08 (0.23)	—	—	20.2 (2.1)	
	900	0.95 (0.22)	—	—	18.5 (1.8)	
	1,000	0.89 (0.25)	—	—	17.4 (1.7)	
	1,100	0.74 (0.22)	—	—	16.6 (1.5)	
	1,200	1.65 (0.30)	—	—	16.1 (1.5)	
	1,300	1.05 (0.27)	—	—	15.8 (1.4)	
	1,400	6.27 (0.88)	—	—	16.8 (1.6)	
	1,500	8.52 (1.46)	—	—	17.6 (1.8)	
	1,600	3.60 (0.61)	—	—	15.7 (1.6)	
Rat subcutaneous adipose tissue ($n = 10$)	400	2.25 (1.34)	—	—	19.8 (6.3)	IS, IAD; in the spectral range of 600−1,400 nm: $\mu_s' = 25.51\lambda^{-0.12}$, [$\lambda$] in nanometers[40]
	500	0.64 (0.34)	—	—	14.3 (4.1)	
	600	0.64 (0.33)	—	—	12.2 (3.5)	
	700	0.75 (0.36)	—	—	11.4 (3.2)	
	800	1.05 (0.47)	—	—	11.0 (3.1)	
	900	1.25 (0.55)	—	—	10.8 (3.0)	
	1,000	1.43 (0.61)	—	—	10.9 (3.0)	
	1,100	1.43 (0.61)	—	—	10.6 (2.8)	
	1,200	2.07 (0.99)	—	—	11.2 (2.9)	
	1,300	1.43 (0.64)	—	—	10.5 (2.8)	
	1,400	2.29 (1.20)	—	—	10.7 (3.0)	
	1,500	2.03 (1.07)	—	—	10.3 (3.0)	
	1,600	1.40 (0.72)	—	—	9.33 (2.7)	
	1,700	3.04 (1.69)	—	—	11.6 (3.4)	
	1,800	2.67 (1.43)	—	—	10.8 (3.2)	
	1,900	4.55 (2.65)	—	—	13.8 (4.5)	
	2,000	3.99 (2.28)	—	—	12.7 (4.2)	
	2,100	2.76 (1.53)	—	—	11.3 (3.6)	
	2,200	2.65 (1.48)	—	—	12.2 (3.6)	
	2,300	6.92 (3.67)	—	—	22.7 (6.0)	
	2,400	6.54 (3.52)	—	—	24.0 (6.1)	
	2,500	5.58 (3.04)	—	—	23.9 (6.4)	

Table 3. The optical properties of muscle tissues measured *in vitro* and *ex vivo* (RMS values are given in parentheses).

Tissue	λ, nm	μ_a, cm^{-1}	μ_s, cm^{-1}	g	μ_s', cm^{-1}	Remarks
Muscle ($n = 1$)	633	1.23	—	—	8.94	IS, IMC; data from graphs of Ref. 58; in the spectral range of 620−1,000 nm: $\mu_s' = 7.67 \times 10^3 \lambda^{-1.045}$, [$\lambda$] in nanometers
	700	0.48	—	—	8.18	
	750	0.41	—	—	7.71	
	800	0.28	—	—	7.04	
	850	0.3	—	—	6.67	
	900	0.32	—	—	6.21	
	950	0.46	—	—	5.9	
	1,000	0.51	—	—	5.73	
Muscle	630	1.4 (0.2)	110 (5)	0.846 (0.009)	16.5 (0.7)	Rabbit; DIS, IAD[93]
	632.8	0.74 (0.06)	140 (6)	0.968 (0.002)	4.4 (0.3)	
	790	2.3 (0.2)	157 (11)	0.95 (0.005)	6.8 (0.7)	
Muscle	630	1.2 (0.1)	239 (16)	0.732 (0.013)	62.1 (2)	Piglet; DIS, IAD[93]
	632.8	0.59 (0.01)	179 (12)	0.858 (0.012)	24.7 (0.7)	
Muscle ($n = 9$)	500	1.17	89.2	0.903	—	Rat; IS, IMC
	550	1.66	88.2	0.909	—	Data from graphs of Ref. 152; in the spectral range of 550−800 nm, $\mu_s = 2.39 \times 10^7 \lambda^{-2.215} + 376.94 \lambda^{-0.274}$; $g = 0.883 + 0.051\ (1 - \exp(-(\lambda - 469.3)/84.11))$, [$\lambda$] in nanometers
	600	0.95	83.3	0.926	—	
	650	0.56	79.0	0.930	—	
	700	0.52	73.56	0.930	—	
	750	0.52	71.30	0.931	—	
	800	0.54	66.70	0.930	—	
Beef muscle	450	1.41	—	—	7.17	Spatial resolved reflectance, diffusion approximation; data from graphs of Ref. 177; in the spectral range of 600−950 nm: $\mu_s' = 3.65 \times 10^4 \lambda^{-1.341}$, [$\lambda$] in nanometers
	500	1.49	—	—	8.22	
	550	1.43	—	—	5.55	
	600	1.39	—	—	6.72	
	650	0.41	—	—	6.11	
	700	0.16	—	—	5.56	
	750	0.11	—	—	5.11	
	800	0.09	—	—	4.71	
	850	0.11	—	—	4.35	
	900	0.15	—	—	4.09	
	950	0.26	—	—	3.57	

30 degrees, counting from the direction of the incident beam. In addition, measurements at angles close to 90 degrees are strongly affected by scattering of higher orders, even for the samples of moderate optical thickness.[142]

8. Optical Properties of Tissues

The above-discussed methods and techniques were successfully applied for estimation of optical properties of a wide number of tissues. Evidently, many types of animal and human tissues may have very close optical properties, but some specificity is expected. Early published data on optical properties of both human and animal tissues are presented in Refs. 2, 13−19, 28, 31−44, 47, 50−58, 61−64, 66−84, 86−88, 92−99, 102, 103, 122, 124, 139, 141, 143−158.

Measurements of skin and subcutaneous tissues optical properties taken *in vitro* and *ex vivo* by different research groups are summarized in Tables 1−3. Data presented in the tables reflect well the situation in the field of the tissue optical parameters measurements. It is clearly observed that major attention was paid to investigations of optical properties of skin tissues because of great importance and perspectives of optical tomography of subcutaneous tumors and optical monitoring and treatment of cutaneous diseases. Nevertheless, in general, not many data for optical transport parameters are available in the literature. Moreover, these data are dependent on the tissue preparation technique, sample storage procedure, applied measuring method

and inverse problem-solving algorithm, measuring instrumentation noise, and systematic errors.

8.1. *Skin tissues optical properties*

Skin presents a complex heterogeneous medium where blood and pigment content are spatially distributed variably in depth.[159,160] Skin consists of three main visible layers from surface: epidermis (100−150 μm thick, the blood-free layer), dermis (1−4 mm thick, vascularized layer), and subcutaneous fat (hypodermis or adipose tissue) (from 1 mm to 6 mm thick, depending on the body site).

The randomly inhomogeneous distribution of blood and various chromophores and pigments in skin produces variations of average optical properties of skin layers. Nonetheless, it is possible to define the regions in the skin, where the gradient of skin cells structure, chromophores, or blood amounts changing with a depth equals roughly zero.[161] This allows subdividing these layers into sublayers regarding the physiological nature, physical and optical properties of their cells, and pigments content. The epidermis can be subdivided into the two sublayers: non-living and living epidermis, and consist of four distinct cell types: keratinocytes (produce keratin), melanocytes (produce melanin), Langerhans cells, and Merkel cells. The predominant cells are the keratinocytes and they are arranged in five strata: the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale. The non-living epidermis or stratum corneum ($\sim$20 μm thick) consists of only dead squamous cells, which are highly keratinized with a high lipid ($\sim$20%) and protein ($\sim$60%) content, and has a relatively low ($\sim$20%) water content.[159−162] Living epidermis ($\sim$100 μm thick) contains most of the skin pigmentation, mainly melanin, which is produced in the melanocytes occurring in the stratum basale, and it is found in membranous particles called melanosomes.[163] There are two types of this pigment: the red/yellow phaeomelanin and a brown/back eumelanin.[163] The ratio between the concentration of phaeomelanin and eumelanin present in human skin varies from individual to individual, with much overlap between skin types. Parsad *et al.*[164] reported the values between 0.049 and 0.36. The melanin absorption level depends on how many melanosomes per unit volume are in epidermis. The volume fraction of the epidermis occupied by melanosomes varies from 1.3% (lightly pigmented specimens) to 43% (darkly pigmented specimens).[19] A basal lamina separates the epidermis from the dermis.

Dermis is a vascularized layer and the main absorbers in the visible spectral range are the blood hemoglobin, β-carotene (0.22−0.63 nmol/g[165]) and bilirubin. In the IR spectral range, absorption properties of skin dermis are defined by absorption of water. The scattering properties of the dermis are mainly defined by the fibrous structure of the tissue, where collagen fibrils are packed in collagen bundles and have lamellae structure. The light scatters on both single fibrils and scattering centers, which are formed by the interlacement of the collagen fibrils and bundles. The dermis consists of two structurally different layers, papillary and reticular, which differ principally by the size of collagen fibers and blood content. The small size of the collagen fibers in the papillary dermis (diameter of an order of magnitude less than visible light wavelength) makes this layer highly backscattering. Within the reticular dermis, the large size of collagen fiber bundles causes highly forward-directed scattering. Thus, any light which reaches this layer is passed on deeper into the skin and contributes to some extent to the spectrum reflected from the skin.[166] The blood volume fraction in the skin varies from 0.2%[19] to $\sim$4%.[167] The volume fraction of water in the dermis is estimated as 70%,[77] 75%,[168] 65%,[169] and 65.1−75.8%,[170] which, on average, yields 70.2 $\pm$ 5.2%. To sum up, the average scattering properties of the skin are defined by the scattering properties of the dermis because of relatively big thickness of the layer (up to 4 mm) and comparable scattering coefficients of the epidermis and the reticular dermis. Absorption of hemoglobin and water of skin dermis, and melanin and lipids of skin epidermis define absorption properties of the whole skin.

The *in vitro* and *ex vivo* skin tissues' optical properties have been measured with integrating sphere technique in the visible and NIR spectral ranges[16,39,50,57,58,77,78,86,93,98,139,141,150,154,158] and the results are summarized in Table 1.

8.2. *Subcutaneous adipose tissue optical properties*

The subcutaneous adipose tissue is formed by aggregation of fat cells (adipocytes) containing

stored fat (lipids) in the form of a number of small droplets for lean or normal humans and a few or even single big drop in each cell for obese humans; and the lipids are mostly presented by triglycerides.[171,172] The diameters of the adipocytes are in the ranges from 15 μm to 250 μm[173] and their mean diameter varied from 50 μm[171] to 120 μm.[172] In the spaces between the cells, there are blood capillaries (arterial and venous plexus), nerves, and reticular fibrils connecting each cell and providing metabolic activity of fat tissue.[171,172] Absorption of the human adipose tissue is defined by absorption of hemoglobin, lipids, and water ($\sim 10.9 \pm 1.4\%$).[174] The main scatterers of adipose tissue are spherical droplets of lipids, which are uniformly distributed within adipocytes.

The adipose tissue optical properties have been measured with integrating sphere technique in the visible and NIR spectral ranges[39,40,57,58] and the results are summarized in Table 2.

8.3. *Muscle optical properties*

Muscle is one of the most abundant tissues in the human body and knowledge of its optical properties is very important for therapeutic and diagnostic applications. It is well understood that muscle is made up of individual components known as muscle fibers. These fibers are made from myofibrils, which are long cylinders of about 1−2 μm diameter.[175] The term "muscle" refers to multiple bundles of muscle fibers held together by connective tissue. The gap among the myofibrils is full of sarcoplasma consisting of cellular organelles. Absorption of the muscle tissue is defined by absorption of hemoglobin and water ($52.0 \pm 0.3\%$[174] or $73 \pm 0.5\%$[176]). The optical properties of muscle tissue have been measured in the visible and NIR spectral ranges[58,93,152,177] and these data are summarized in Table 3.

9. Refractive Index Measurements

Measuring refractive indices in tissues and their constituent components is an important focus of interest in tissue optics because the index of refraction determines light reflection and refraction at the interfaces between air and tissue, detecting fiber and tissue, and tissue layers; it also strongly influences light propagation and distribution within tissues, defines the speed of light in tissue, and governs how the photons migrate.[3,4,7−11,19,21,111,115,116] Although these studies have a rather long history, the mean values of refractive indices for many tissues are missing in the literature. According to Ref. 11, most of them have refractive indices for visible light in the 1.335−1.620 range (e.g. 1.55 in the stratum corneum, 1.620 in enamel, and 1.386 at the lens surface). It is worthwhile noting that *in vitro* and *in vivo* measurements may differ significantly. For example, the refractive index in rat mesenteric tissue *in vitro* was found to be 1.52 compared with only 1.38 in the *in vivo* study. This difference can be accounted by the decreased refractivity of ground matter, n_0, due to impaired hydration. Indeed, the optical properties of tissues, including refractive indices, are known to depend on water content. The refractive indices of water over a broad wavelength range from 200 nm to 200 μm have been reported in Ref. 178.

To model tissue by a mixture of water and a bioorganic compound of a tissue is more adequate. For instance, the refractive index of human skin can be approximated by a 70/30 mixture of water and protein.[77] Assuming that a protein has a constant refractive index value of 1.5 over the entire wavelength range, the authors of Ref. 77 have suggested the following expression for estimation of skin index of refraction:

$$n_{\text{skin}}(\lambda) = 0.7(1.58 - 8.45 \times 10^{-4}\lambda + 1.1 \times 10^{-6}\lambda^2 - 7.19 \times 10^{-10}\lambda^3 + 2.32 \times 10^{-13}\lambda^4 - 2.98 \times 10^{-17}\lambda^5) + 0.3 \times 1.5, \quad (22)$$

where wavelength λ is in nanometers.

For different parts of a biological cell, values of refractive index in the NIR range can be estimated as follows: extracellular fluid, $n = 1.35$−1.36; cytoplasm, 1.360−1.375; cell membrane, 1.46; nucleus, 1.38−1.41; mitochondria and organelles, 1.38−1.41; and melanin, 1.6−1.7.[11,146,147] Scattering arises from mismatches in refractive index of the components that make up the cell. Organelles and subcomponents of organelles having refractive indices different from their surroundings are expected to be the primary sources of cellular scattering. In tissues where cells are surrounded by other cells or tissue structures of similar index, certain organelles become the important scatterers.[9−11] Mitochondria (0.5−1.5 μm in diameter), lysosomes (0.5 μm), and peroxisomes (0.5 μm) are very important scatterers whose size, relative to the wavelength of light, suggests that

they must make a significant contribution to backscattering. Granular melanin, traditionally thought of as an absorber, must be considered an important scatterer because of its size and high refractive index.[32,41,179] Structures consisting of membrane layers, such as the endoplasmic reticulum or Golgi apparatus, may prove significant because they contain index fluctuations of high spatial frequency and amplitude. Besides cell components, fibrous tissue structures such as collagen and elastin fibers must be considered as important scatterers.

Refractivity measurements in a number of strongly scattering tissues at 633 nm performed with a fiber-optic refractometer.[180] The method is based on a simple concept: that the cone of light originating from an optical fiber is dependent on the refractive indices of the cladding material, core material (quartz), and air into which the cone of light emerges. The cladding on a 1 mm-core-diameter optical fiber was stripped from the fiber, and the tissue for which the index is to be measured was substituted for the cladding. With the index for air (n_0) and the quartz fiber (n_q) known, along with the emitted angular light distribution (θ) measured at the optical fiber's output, the following equation for the determination of tissue index of refraction (n) can be derived from the expression for the fiber numerical aperture (NA)[180]:

$$n = (n_q^2 - [n_0 \sin\theta]^2)^{1/2}. \tag{23}$$

Using this simple and sensitive technique, it was found that fatty tissue has the largest refractive index (1.455), followed by kidney (1.418), muscular tissue (1.41), and then blood and spleen (1.4).[180] The lowest refractive indices were found in lungs and liver (1.38 and 1.368, respectively).[180]

The principle of total internal reflection at laser beam irradiation is also used for tissue and blood refraction measurements.[181,182] A thin tissue sample is sandwiched between two right-angled prisms that are made of ZF5 glass with a high refractive index, $n_0 = 1.70827$, and angle, $\alpha = 29°55'41.4''$. For an incident laser beam polarized in the S-plane, for the determination of the mean refractive index of tissues, Eq. (24) is valid:[181]

$$n = \sin i_t \times \cos\alpha + \sin\alpha \times [n_0^2 - \sin^2 i_t]^{1/2} \tag{24}$$

where the incident angle of total reflectance i_t is a measurable parameter.

Measurements for fresh animal tissues and human blood at four laser wavelengths of 488 nm, 632.8 nm, 1079.5 nm, and 1341.4 nm and room temperature were presented in the form of Cauchy dispersion equation[181]

$$n(\lambda) = A + B\lambda^{-2} + C\lambda^{-4} \tag{25}$$

with λ in nanometers; values of the Cauchy coefficients are presented in Table 4.

Because the refractive index of tissue and blood components defines their scattering properties, measured scattering parameters may have an advantage to evaluate the refractive index of tissue and blood components and their mean values. For a monodisperse system of spherical scatterers, the reduced scattering coefficient can be described by the following expression

$$\mu_s' = N_0 \pi a F(f_s) Q_s(n_s, n_0, a, \lambda)(1 - g), \tag{26}$$

where N_0 is the number of scatterers in a unit volume, a is their radius, $F(f_s)$ is the function accounting for the density of particle packing, f_s is the volume fraction of scatterers, n_s is the refractive index of the scatterers, n_0 is the refractive index of the ground material, λ is the wavelength, and Q_s and g are factors of scattering efficiency and anisotropy, which are calculated from Mie theory.[116]

Determination of the reduced scattering coefficient of a tissue sample using integrating sphere or spatially resolved techniques and corresponding algorithms for extraction of the scattering coefficient, such as IAD or IMC methods, the knowledge of the refractive indices of the scatterers and the ground material at one of the wavelengths, as well as experimental or theoretical estimations for mean radius of the scatterers, allows one to solve the inverse problem and reconstruct the spectral dependence of the refractive index of the scatterers

Table 4. Values of Cauchy coefficients of dispersion in Eq. (25).[181]

Tissue sample	A	$B \times 10^{-3}$	$C \times 10^{-9}$
Porcine muscle$_\parallel$	1.3694	0.073223	1.8317
Porcine muscle$_\perp$	1.3657	1.5123	1.5291
Porcine adipose	1.4753	4.3902	0.92385
Ovine muscle$_\parallel$	1.3716	5.8677	0.43999
Ovine muscle$_\perp$	1.3682	8.7456	−0.16532

for a given spectral dependence of the refractive index of the ground material. Similar measurements and theoretical estimations done for a tissue sample before and after its prolonged bathing in saline or other biocompatible liquid with known optical characteristics allow one to evaluate the spectral dependencies of the refractive index of the scatterers and the ground material.[183,184]

Let us consider a few examples. The major scatterers in human sclera are long collagen fibers with a wide range of diameters and a mean value of 100 nm.[11] Fibers are arranged quasi-randomly in the bundles.[11,185] Due to the characteristic structure sizing and multiple crossings of bundles, this system can be approximated by a monodisperse system of spherical scatterers with similar spectral properties. In that case, the Mie-equivalent scatterer radius is equal to 250 nm.[183] Using experimental spectral dependence for the reduced scattering coefficient and accounting for a scleral sample that has been placed into a physiological solution for a long time, the interstitial fluid was therefore replaced by a physiological solution whose refractive index is close to water, and the spectral dependence for refractive index of the scatterers was reconstructed. The following approximated formula for the refractive index of the material of effective scatterers of scleral tissue valid within the spectral range from 400 nm to 800 nm was obtained as a final result of the reconstruction[183]:

$$n_c(\lambda) = 1.4389 + 1.588 \times 10^4\lambda^{-2} - 1.4806 \times 10^9\lambda^{-4} + 4.3917 \times 10^{13}\lambda^{-6}, \quad (27)$$

where λ is in nanometers.

In fact, this dispersion relation should be close to the spectral dependence of the index of refraction of hydrated collagen because 75% of sclera's dry weight is due to collagen. The estimated value of the refractive index of normally hydrated scleral collagen (68% of hydration for a whole tissue) of $n = 1.474$, corresponding to direct refraction measurements for whole sclera at a wavelength of 589 nm, is well fitted to the value calculated from this semiempirical relation.[11]

The similar analysis of experimental data of the scattering properties of normal and immersed rat skin in the spectral range from 400 nm to 700 nm allows one to reconstruct spectral dependences of both refractive indices for material of effective scatterers $n_{ss}(\lambda)$ and ground (interstitial liquid) material $n_{si}(\lambda)$ as[184]

$$n_{ss}(\lambda) = 1.4776 - 1.7488 \times 10^4\lambda^{-2} + 6.727 \times 10^9\lambda^{-4} - 3.339 \times 10^{14}\lambda^{-6} \quad (28)$$

$$n_{si}(\lambda) = 1.351 + 2.1342 \times 10^3\lambda^{-2} + 5.7893 \times 10^8\lambda^{-4} - 8.1548 \times 10^{13}\lambda^{-6} \quad (29)$$

Using the law of Gladstone and Dale (which states that resulting value of refractive index of mixed substance represents as average of the refractive indices of the components related to their volume fraction, i.e., $n = \sum_{i=1}^{N} n_i f_i$; $\sum_{i=1}^{N} f_i = 1$, where n_i and f_i are the refractive index and volume fraction of the individual components, respectively, and N is the number of the components[142]), and using these expressions, one can derive the dispersion formula for a whole skin as[184]

$$n_{\text{skin}}(\lambda) = 1.309 - 4.346 \times 10^2\lambda^{-2} + 1.6065 \times 10^9\lambda^{-4} - 1.2811 \times 10^{14}\lambda^{-6}. \quad (30)$$

This is a more precise formula for describing the refractive index of skin than Eq. (22), which was obtained from the simplest suppositions for a skin model as a mixture of water and proteins with a constant refractive index.

For tissue optics, this is of great importance to know the dispersion properties of melanin, which is present in skin, hairs, eye sclera, and iris, and other tissues. Melanin granules are the major back-reflecting particles in optical coherence tomography (OCT) and small-scale spatially resolved spectroscopy of skin. The above-described spectroscopic studies of water suspensions of natural melanin, where the mean radius of particles was determined using electronic microscopy, allow us to solve the inverse problem and to reconstruct the wavelength dependence of the refractive index of melanin particles in the range from 350 nm to 800 nm as[179]

$$n_{\text{mel}} = 1.684 - 1.8723 \times 10^4\lambda^{-2} + 1.0964 \times 10^{10}\lambda^{-4} - 8.6484 \times 10^{14}\lambda^{-6} \quad (31)$$

The OCT is a newly developed modality that allows one to evaluate the scattering and absorption properties of tissue *in vivo* within the limits of an OCT penetration depth of 1–3 mm. The principles and applications of OCT are described in detail in Refs. 11, 186–191. In its simplest form, this method assumes that backscattered light from a tissue

decreases in intensity according to

$$I_b \cong I_0 \exp[-2(\mu_a + \mu_s)z] \tag{32}$$

where $(\mu_a + \mu_s)$ is the total attenuation coefficient and $2z$ is the round-trip distance of light backscattered at a depth z. For most tissues in the NIR, $\mu_a \ll \mu_s$; thus, μ_s can be estimated as

$$\mu_s \approx \frac{1}{2z(\ln[I_b(z)/I_0])} \tag{33}$$

or as the slope of a graph $\ln[I_b(z)/I_0]$ versus z. Experimental data for tissue OCT images show that the logarithmically scaled average for multiple in-depth scans' backscattered intensity, $\ln(I_b(z))$, decays exponentially; thus, by performing a linear regression on this curve, the scattering coefficient can be determined. More comprehensive algorithms pertaining to multiple scattering effects and properties of a small-angle scattering phase function are available in the literature.[192−195]

The OCT dynamic and spatially confined measurements of refractive index and scattering coefficients of tissue and blood are very important for the monitoring of physiological changes in living tissues. The OCT provides simple and straightforward measurements of the index of refraction both *in vitro* and *in vivo*.[193,194,196−199] The in-depth scale of OCT images is determined by the optical path length Δz_{opt} between two points along the depth direction. Because a broadband light source is used, the optical path length is proportional to the group refractive index n_g and geometrical path length Δz as

$$\Delta z_{\text{opt}} = n_g \Delta z. \tag{34}$$

Usually, $n_g \cong n$. This simple relation is valid for a homogeneous medium and can be used in *in vitro* studies when geometrical thickness of a tissue sample Δz is known.

Sometimes both the refractive index and thickness of a tissue sample should be measured simultaneously. In that case, a two-step procedure can be applied.[197,198] First, a stationary mirror is placed in the sample arm of an interferometer to get the geometric position of the mirror supposing that the group refractive index of air is 1 (z_1). Then, a tissue sample with unknown index n_g and thickness d should be placed before the mirror in the sample arm. Two peaks from the anterior (z_2) and the posterior (z_3) surfaces of the sample will appear with the distance between them equal to a sample optical thickness [see Eq. (34)], and the position of the mirror (z_4) will be shifted by $(n_g - 1)d$ due to the sample whose group refractive index is greater than that of air. Thus, the calculation of the geometrical thickness and the group refractive index proceeds as follows:

$$d = (z_3 - z_2) - (z_4 - z_1), \quad n_g = \frac{z_3 - z_2}{d}. \tag{35}$$

For *in vivo* measurements of the index of refraction, a focus-tracking method that uses the OCT to track the focal-length shift that results from translating the focus of an objective along the optical axis within a tissue was introduced[198] and further developed.[193,194,199] For the refractive index evaluation, the coincidence of the maxima of the interference pattern and spatial focus, registered as a signal maximum, is needed. At least two points along the depth direction have to be probed to estimate a mean value of the refractive index between them. Usually, a multistep measurement is provided. The geometric average refractive index for a fiber/lens focus tracking system is defined by the following expression[193,194]

$$\bar{n} = \sqrt{n_g n} = \frac{n_{\text{obj}}}{\sqrt{1 - \frac{\Delta z_{L1}}{\Delta z_{\text{fiber}}}}} \tag{36}$$

where n_{obj} is the refractive index of the objective in the sample arm, Δz_{L1} is the change of position of the first objective lens, and Δz_{fiber} is the fiber tip position in the sample arm. The difference between both refractive indices is usually small, only a few percent, and can be ignored in practice. For a piecewise homogeneous medium along the depth direction, the slope $\Delta z_{L1}/\Delta z_{\text{fiber}}$ has to be evaluated at the focus tracked condition.

A bifocal optical coherence refractometer, which is based on the measurements of the optical path length difference between two foci simultaneously, was recently suggested.[200,201] The main advantage of this technique is that it avoids the need to physically relocate the objective lens or the sample during an axial scan. At employment of a relatively low NA objective lens in the sample arm, the ratio of the optical path length difference between two foci, measured in the medium, $\Delta z_{f\text{-opt}}$, and in air,

Δz_f, is described by the expression[200]

$$\frac{\Delta z_{f\text{-opt}}}{\Delta z_f} \approx n_g n\left[1+\frac{1}{2}(NA)^2\left(1-\frac{1}{n^2}\right)\right]. \quad (37)$$

For a typical value of tissue index of refraction $n = 1.4$ and $NA = 0.2$, the second term in the square parentheses is of only 1% of the magnitude of the ratio. Accounting for this estimation and that $n_g \cong n$, a much simpler relation, as used in Ref. 193, can be found as

$$\Delta z_{f\text{-opt}} \approx n^2 \Delta z_f. \quad (38)$$

Results of *in vitro* and *in vivo* measurements of phase and group refractive indices of skin and subcutaneous tissues using the technique discussed and some other techniques are summarized in Table 5.

Table 5. Experimental values of phase or group refractive indices of skin and subcutaneous tissues measured *in vitro* and *in vivo* (RMS values are given in parentheses).[3,55,150,180–182,193,194,198,200,201,209]

Tissue	λ, nm	n, n_g	Remarks
Human subcutaneous fat	456–1,064	1.44	Ref. 55
Porcine adipose	632.8	1.4699 (0.0003)	Ref. 205, total internal reflection
Porcine adipose	632.8	1.464	Ref. 206, total internal reflection, 12 samples
Porcine adipose	650	1.382 (0.006)	Ref. 209, total internal reflection
Bovine adipose	650	1.396 (0.004)	Ref. 209, total internal reflection
Chicken fat	1,310	1.450 (0.014)	Ref. 207, OCT
Porcine muscle	632.8	1.381	Ref. 206, total internal reflection, 12 samples; tissue striations-oriented parallel to interface with cap-glass
Porcine muscle	632.8	1.410	Ref. 206, total internal reflection, 12 samples; tissue striations-oriented perpendicular to interface with cap-glass
Chicken muscle	1,310	1.399 (0.013)	Ref. 207, OCT
Human muscle	456–1,064	1.37	Ref. 55
Canine muscle	633	1.400 (0.006)	Ref. 180
Bovine muscle	633	1.412 (0.006)	Ref. 180
Bovine muscle	592	1.382 (0.004)	Ref. 208, confocal microscopy
Bovine muscle$_{\parallel}$	650	1.377 (0.003)	Ref. 209[a], total internal reflection
Bovine muscle$_{\perp}$	650	1.414 (0.003)	Ref. 209[a], total internal reflection
Ovine muscle$_{\parallel}$	488	1.404 (0.003)	Ref. 181[a], total internal reflection
	632.8	1.389 (0.002)	
	1079.5	1.378 (0.004)	
	1341.4	1.375 (0.003)	
Ovine muscle$_{\perp}$	488	1.402 (0.002)	Ref. 181[a], total internal reflection
	632.8	1.389 (0.002)	
	1079.5	1.375 (0.003)	
	1341.4	1.373 (0.003)	
Porcine muscle$_{\parallel}$	488	1.402 (0.002)	Ref. 181[a], total internal reflection
	632.8	1.381 (0.002)	
	1079.5	1.372 (0.003)	
	1341.4	1.370 (0.003)	
Porcine muscle$_{\perp}$	488	1.399 (0.002)	Ref. 181[a], total internal reflection
	632.8	1.379 (0.002)	
	1079.5	1.370 (0.002)	
	1341.4	1.367 (0.003)	
Porcine muscle$_{\parallel}$	632.8	1.380 (0.007)	Ref. 182[a], total internal reflection
Porcine muscle$_{\perp}$	632.8	1.460 (0.008)	Ref. 182[a], total internal reflection
Porcine muscle$_{\parallel}$	650	1.387 (0.005)	Ref. 209[a], total internal reflection
Porcine muscle$_{\perp}$	650	1.418 (0.003)	Ref. 209[a], total internal reflection
Stratum corneum of human skin	400–700	1.55	Ref. 3
Stratum corneum of human skin	1,300	1.51 (0.02)	Ref. 198, OCT, optical path length measurements

Table 5. (*Continued*)

Tissue	λ, nm	n, n_g	Remarks
Stratum corneum of human skin (palm of hand)	1,300	$(nn_g)^{1/2} = 1.47$ (0.01)	Ref. 193, OCT
Stratum corneum of human skin (dorsal surface of a thumb)	980	$(nn_g)^{1/2} = 1.50$ (0.02)	Ref. 201, bifocal OCT refractometer
Stratum corneum/epidermis interface (volar side of a thumb)	980	$(nn_g)^{1/2} = 1.34$	Ref. 200, bifocal OCT refractometer
Epidermis of human skin (palm of hand, granular layer)	1,300	$(nn_g)^{1/2} = 1.43$ (0.02)	Ref. 193, OCT
Epidermis of human skin (palm of hand, basal layer)	1,300	$(nn_g)^{1/2} = 1.34$ (0.02)	Ref. 193, OCT
Epidermis of human skin (volar side of lower arm)	1,300	$(nn_g)^{1/2} = 1.36$ (0.01)	Ref. 193, OCT
Epidermis of human skin	1,300	1.34 (0.01)	Ref. 198, OCT, optical path length measurements
Dermis of human skin	1,300	$n_g = 1.41$ (0.03)	Ref. 198, OCT, optical path length measurements
Dermis of human skin	1,300	$n_g = 1.4$ (0.007)	Ref. 198, OCT, optical path length measurements
Upper dermis of human skin (palm of hand)	1,300	$(nn_g)^{1/2} = 1.41$ (0.03)	Ref. 193, OCT
Upper dermis of human skin (volar side of lower arm)	1,300	$(nn_g)^{1/2} = 1.43$ (0.02)	Ref. 193, OCT
Pig skin	1,300	$(nn_g)^{1/2} = 1.415$	Ref. 194, OCT
Rat skin	456−1,064	1.42	Ref. 55
Mouse skin	456−1,064	1.40	Ref. 55
Porcine skin (dermis)	325	1.393	Refs. 150, 202, prism laser refractometer
	442	1.376	
	532	1.359	
	633	1.354	
	850	1.364	
	1,064	1.360	
	1,310	1.357	
	1,557	1.361	
Human skin epidermis	325	1.489 (S) 1.486 (P)	Ref. 203, prism laser refractometer with an incident beam of S- or P-polarization
	442	1.449 (S) 1.447 (P)	
	532	1.448 (S) 1.446 (P)	
	633	1.433 (S) 1.433 (P)	
	850	1.417 (S) 1.416 (P)	
	1,064	1.432 (S) 1.428 (P)	
	1,310	1.425 (S) 1.421 (P)	
	1,557	1.404 (S) 1.400 (P)	
Human skin epidermis	1,300	1.3884 (0.0013)	Ref. 204, forearm of 20 Caucasian volunteers, OCT
Human skin dermis	325	1.401 (S) 1.403 (P)	Ref. 203, prism laser refractometer with an incident beam of S- or P-polarization
	442	1.4395 (S) 1.400 (P)	
	532	1.378 (S) 1.381 (P)	
	633	1.396 (S) 1.393 (P)	
	850	1.384 (S) 1.389 (P)	
	1,064	1.375 (S) 1.385 (P)	
	1,310	1.358 (S) 1.364 (P)	
	1,557	1.363 (S) 1.367 (P)	

Note: [a]Tissue sample labeled as $\parallel$ and $\perp$ are the same sample with the tissue fibers oriented in parallel and perpendicular to the interface, respectively.

10. Summary

We believe that this overview of tissue optical properties will provide users a possibility to predict optical properties of tissues under their interest and evaluate light distribution in the organ under examination or treatment. We have tried to collect as complete as possible data on optical properties of skin and subcutaneous tissues and presented some of these data in the form of approximation formulas as a function of the wavelength for easy use. In spite of this and availability of other reviews,[1−7,10,11,55] evidently, the data collection and measurements should be continued in order to have more complete and precise information about different tissues in norm and pathology, to recognize age-related, disease-related, and treatment-related changes of optical properties. Data on blood optical properties can be found in the following Refs. 10−12, 54−56, 67−70, 72, 74, 75, 113, 128, 130, 131, 134, 181.

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