

Simple “Digital Phantom” for Testing Attenuation-Imaging Methods in Optical Coherence Tomography

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Abstract. The manuscript describes a simple but realistic and efficient method for generation of OCT scans with fairly correct accounting for optical signal attenuation dominated by scattering. The strong domination of scattering in the optical attenuation coefficient (OAC) is typical of OCT where the illuminating-beam wavelength is intentionally chosen in optical transparently windows with minimal absorption. At the same time the scattering-dominated OAC may strongly differ for various types/states of biological tissues, so that the diagnostic value of OCT examinations can be significantly increased due to spatially-resolved estimation of OAC. However, the results of OAC-reconstruction may be strongly degraded by the “speckle noise” intrinsic to OCT scans, various measurement noises, and some other factors. Verification of OAC-reconstruction accuracy in physical experiments is challenging since controllable variation in the parameters of physical phantoms and OCT systems is often difficult or even impossible. In view of this, realistic numerical simulations may open unprecedented possibilities for testing and comparison of various OAC methods in highly controllable and flexibly variable conditions. Here, we describe a method enabling generation of realistic “digital phantoms” and present instructive examples demonstrating their usefulness for testing OAC-reconstruction approaches. © 2024 Journal of Biomedical Photonics & Engineering.

Keywords: optical coherence tomography; OCT-scan formation modeling; speckle pattern; optical attenuation imaging.

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1 Introduction

Development of new modalities beyond conventional structural imaging has become one of the main trends in Optical Coherence Tomography (OCT) [1]. In particular, this concerns such actively developing modalities as Optical Coherence Angiography in various forms [2–4], as well as various approaches to realization of Optical Coherence Elastography [5–7]. Also diagnostic approaches are known which are based on deep analysis of speckle-pattern parameters in OCT (e.g. [8, 9]).

Another active direction is the development of approaches aimed at assessment of optical attenuation coefficient (OAC) based on the analysis of signal decay

in OCT scans. Various methods of OAC visualization are discussed in several recent reviews, e.g. [10, 11]. Although optical-signal attenuation for forward propagation is described by a simple exponential factor, for estimation of the attenuation coefficient by analyzing OCT scans, the situation is less trivial. For formation of OCT scans, besides attenuation in the medium, there are other factors that also affect the signal amplitude (in particular, there is such an evident factor as the influence of OCT-beam focusing, as well as the so-called roll-off effect intrinsic to the most widely spread spectral-domain OCT devices). Furthermore, even if these factors are eliminated or corrected, the depth dependence of signal decay in OCT scans may be exponential only for spatially

uniform attenuation coefficient in the studied medium. At the same time, for diagnostic purposes in biomedical applications of OCT, the most interesting is spatially-resolved mapping of the spatially-inhomogeneous attenuation rather than obtaining of only spatially-averaged estimates assuming the decay described by a single exponential function. It can also be pointed out that methods of spatially-resolved OAC estimation are interesting not only for differentiation of various types of biotissues (e.g. cancerous tissues from normal ones which may differ by the OAC values [12]). Namely, one of active fields in biophotonics is the development of technologies of artificial reduction of OAC values for biological tissues, also termed optical clearing methods in studying of which pioneering results were obtained by the research group of professor Valery Tuchin from Saratov State University [13, 14]. For optical clearing, tissues usually are impregnated with a clearing agent which gradually diffuses into the tissue bulk from the surface leading to gradual, initially spatially inhomogeneous reduction of OAC, so that the possibility to perform monitoring of OAC variations with one-side OCT examination represents an evident interest.

In view of this, in the recent decade, significant attention has been paid to the development of OCT-based methods allowing for spatially-resolved attenuation imaging. An important step in solving this problem was the work by Vermeer et al. [15], where an approach to spatially-resolved OAC estimation from OCT scans was proposed for the case of strong domination of contribution of scattering to the OCT-signal decay. This assumption about the scattering dominance is usually quite reasonable; however, there are some other factors that may significantly worsen the operability of method [15]. For example, among these factors are incomplete decay of the OCT signal within the visualized depth or the influence of various noises, including the reception noise, as well as the “speckle noise” intrinsic to OCT scans. Consequently, there are quite many studies devoted to mitigation of the above-mentioned negative factors in approach [15], for example [16, 17]. Certainly, other OCT-based methods proposed for OAC estimation using are also susceptible to various degrading factors.

For verification of operability and accuracy of various OCT modalities quite often various experimental tests on specially prepared phantoms with *a priori* known properties are used. Phantom-based tests were used for verification various OCT-based diagnostic methods, for example, for determining the density of scattering centers based on estimation of speckle contrast [18], for OCT-based flow-velocity estimation [19], as well as in the context of OCT-based OAC estimation [15]. Properly prepared phantoms were considered for imitating various properties of biotissues, including mechanical, optical, and structural ones [20]. However, creation of sufficiently controllable properties of physical phantoms is a rather difficult problem. Furthermore, maybe even more difficult is to provide in physical experiments the possibility of flexible variation of experimental

parameters, which concerns parameters of both the imitated tissues and the used OCT-systems.

In this regard, from the first years OCT development till present, significant attention is paid to creation of convenient and at the same time sufficiently realistic models describing formation of OCT signals. Using such models various OCT-based methods can be tested. In particular, much attention was paid to modeling speckles in OCT scans [21]. For example, such modeling was helpful for understanding the degrading role of OCT speckles for quality of structural OCT images [21], or for understanding limitations of speckle tracking in OCT-based elastography [22]. Numerous other studies were focused of the diagnostic value of assessment of OCT-speckle characteristics rather than on their degrading role. For example, along with earlier models like work [21] based on summation of several phasors with random phases in individual pixels or more complex heuristic models (e.g. [23]), a number of other methods were proposed for fairly accurate simulation of speckles in OCT scans. Some of them used the Monte-Carlo approach to description of propagation of OCT-beam photons in a turbid scattering material [24].

Other approaches used the wave description of OCT signals, either in an approximate form [25] or using fairly accurate simulations of focused OCT beams utilizing either formalism of Gaussian beams represented in spatial domain [26] or a rather general angular-spectrum description [27]. In the context of testing attenuation imaging methods it can be stated that despite fairly accurate accounting for the interference nature of OCT speckles such models quite often did not consider the decay of OCT beams. Obviously, in the case of spatially uniform non-zero attenuation its influence could be modeled by applying a simple depth-dependent exponential factor to simulated OCT images. However, the assumption about spatially-uniform attenuation is oversimplified and does not look adequate for solving diagnostic problems using analysis of OCT scans in application to real biological tissues.

In what follows we describe a rather simple but efficient numerical approach to creation of fairly realistic OCT scans that can be used as “digital phantoms” for testing various methods of OCT-based optical attenuation imaging. The proposed approach readily allows one to account for main features of OCT scans. In particular, it correctly takes into account the interference nature of OCT speckles (i.e., the “speckle noise” intrinsic to OCT scans), as well as naturally describes the point-spread function shape and the influence of inter-pixel signal leakage without making additional assumptions. The proposed “digital phantom” allows one to introduce arbitrary spatial dependences of the OAC. It is generally accepted and confirmed by numerous studies that in OCT the signal attenuation is dominated by the optical wave scattering rather than absorption as was an essential assumption for the approach to OAC estimation proposed in Ref. [15] and subsequent related studies. Besides the “speckle noise”, other measurement noises can also be controllably introduced in the proposed “digital

phantom". Other main parameters of the simulated tissue (first of all, density and brightness of scatterers), as well as key parameters of the OCT setup (first of all, the illuminating beam spectrum), can also be very flexibly varied. In the following section we describe the proposed model and, using real OCT scans for comparison, demonstrate the possibility to simulate a number of characteristic situations of spatial distributions of OAC. Then the developed "digital phantom" is used to give some instructive examples demonstrating the usefulness of the proposed simulation method for development of spatially-resolved mapping of OAC.

2 Simulation of Basic OCT Scans

For simulating basic OCT scans we apply the approach described in Refs. [28, 29]. We briefly recall that such a model corresponds to the most widely used in OCT case of weakly focused beams, for which the variation in the illuminating beam radius is insignificant within the visualized depth. The illuminating-beam spectrum of a spectral-domain OCT setup is characterized by the spectral shape $S(k_n)$, where k_n are the discrete wavenumbers localized around the central wavenumber k_0 . For each lateral position of the beam it illuminates discrete scatterers with axial coordinates z_j and scattering amplitudes A_j . The illuminated scatterers emit backscattered waves, the complex amplitudes of which are summed at the reception. The phases of the received waves are determined by the phase angles acquired during the forth-and-back propagation. Summation of a discrete number of spectral components yields a pixilated 1D scan (A-scan) with the pixel amplitudes $A(q)$ given by the following expression [28]:

$$A(q) = \sum_j \sum_n S(k_n) A_j \exp(i2k_n z_j) \exp(-i \frac{2\pi n}{H} z_q). \quad (1)$$

In Eq. (1) the maximal unambiguously imaged depth H is determined by the distance δk between the neighboring spectral component in the source spectrum $S(k_n)$, such that $\delta k = k_{n+1} - k_n = \pi/H$. The axial positions z_j of the scatterers are random and continuous, whereas coordinates z_q of pixels in the pixilated A-scan are discrete and equidistantly located within the imaged depth H . It was demonstrated in Refs. [27, 29] that for weakly focused beams, one may take into account the amplitude shape of the beam cross section to describe how the scatterers enter and leave the illuminating beam when the latter is scanned laterally. The scattered-signal amplitude A_j takes into account the lateral position of the scattering particle within the illumination beam cross section. At the same time the neglect of phase variation within the beam cross section does not appreciably affect the simulated scans [27]. Such a method of OCT-scan simulation correctly takes into account the interference of waves backscattered by scattering particles located within every sample volume, the sizes of which are determined by the beam diameter and the coherence length that in turn is determined by the total spectral

width and form of the source spectrum $S(k_n)$. The interference nature of speckles in OCT in earlier models (e.g. [21]) was simulated via summation of a number of phasors with random phases. However, unlike simple summation of several phasors, the discussed here approach fairly rigorously considers interference of waves scattered by individual scatterers, so that speckle properties can be fairly correctly found for a chosen set of OCT-system parameters (illuminating-beam geometry and spectral properties of the optical source, density of scattering centers and statistics of their scattering amplitudes). The point-spread-function shape, including the effects of signal leakage among neighboring pixels are naturally obtained for both axial and lateral directions. In the lateral direction this is determined by the illuminating beam diameter and the degree of self-overlapping during the lateral scanning. The degree of independence of pixels in axial and lateral directions is important for spatial averaging procedures that will be used in the following sections.

Fig. 1 shows the results of OCT-scan modeling based on Eq. (1). The 2D scan (B-scan in Fig. 2(a)) with sizes 256×256 pixels is simulated for an OCT system with a central wavelength of $1 \mu\text{m}$ in a tissue with the refraction coefficient $n = 1.3$. This corresponds to the often used OCT sources with the wavelength of $1.3 \mu\text{m}$ in vacuum, the spectral width is 100 nm . The physical sizes of the simulated B-scan are $1000 \mu\text{m}$ axially and $2000 \mu\text{m}$ laterally. The lateral step between the neighboring A-scans is $8 \mu\text{m}$ and the half-width of the illuminating beam with a Gaussian profile is $10 \mu\text{m}$. The number of scatterers distributed over the scan area is $128 \cdot 10^3$, which imitates a typical density of biological cells in biological tissues. A single amplitude profile shown in Fig. 1(b) corresponds to the axial direction shown by the dashed line in Fig. 1(a). The histogram of the pixel amplitudes for the B-scan shown in Fig. 1(a) is presented in Fig. 1(c), where the dashed line shows the histogram approximation by a Rayleigh distribution expected for the developed speckle pattern [21]. If necessary, a desired level of measurement noise can readily be imitated in the simulated complex-valued B-scans by adding to every pixel random complex quantities, for example, with Gaussian distribution of real and imaginary parts.

An important issue that should be pointed out is that the so-simulated speckle patterns still do not imitate the influence of attenuation, as well as other factors affecting the OCT-signal amplitude in real B-scans. Among the latter factors the most important are the influence of the so-called roll-off effect intrinsic to spectral domain OCT devices and the illuminating beam focusing/divergence. The latter somewhat affects the signal amplitude even in OCT systems with fairly weakly focused illuminating beams. Although the origin of these effects and the corresponding approximating equations for the roll-off effect and focusing are well understood [10, 11, 30], for real OCT systems, the parameters entering these equations usually are not known.

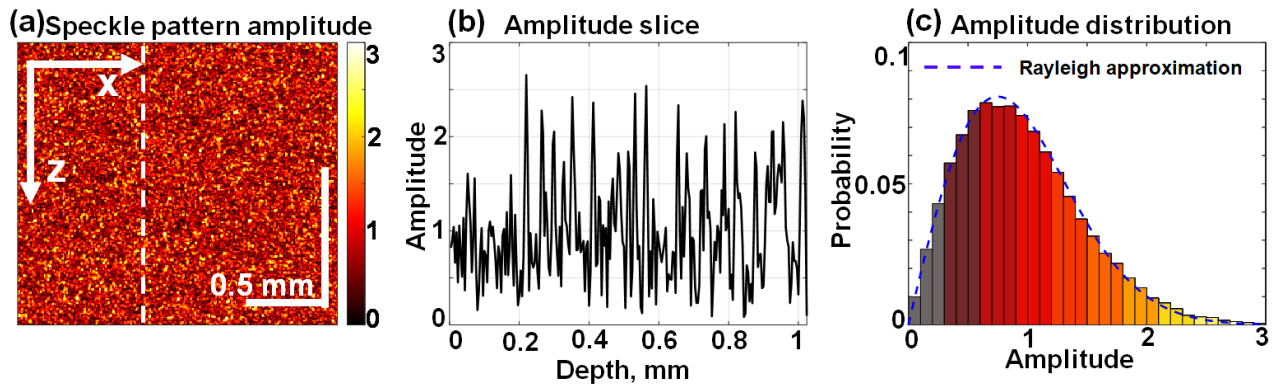


Fig. 1 Demonstration of speckle pattern, representative depth profile and speckle-amplitude statistics for the generated OCT scan. (a) Structural OCT scan shown in a linear scale. (b) Representative depth profile along the dashed line in panel (a). (c) Histogram of amplitude distribution.

In view of this, the corresponding correcting depth-dependent factors for a particular system can be determined experimentally. For example, the amplitude of the OCT-signal scattered from a plane boundary of a scattering phantom can be measured as a function of the boundary depth. Bearing in mind that the focus position depends on the optical wavelength dependent on the refraction index, one may place a layer of a transparent immersion liquid above the calibration sample. In such a case, one should verify that the illuminating-beam absorption in the immersion layer is either negligibly small or known from independent measurements. In what follows we assume that such preliminary calibration measurements are made and the depth-dependent correcting factor are applied to the OCT scan, so that in the absence of signal attenuation in the studied sample the OCT signal should have in average uniform amplitude like in the scan shown in Fig. 1(a). In the next sections we first consider how various depth-dependences of attenuation can be introduced in the formed “digital phantom” based on initially simulated B-scans with spatially uniform amplitude like in Fig. 1(a) and then the developed “digital phantom” is used to give some instructive examples demonstrating the usefulness of the proposed simulation method for development of spatially-resolved mapping of OAC.

3 Introducing Various Depth-Dependences of Attenuation in the Digital Phantom

There are two main significantly different reasons of optical signal decay for which numerous data can be found in literature. One reason is the optical signal absorption usually characterized by the absorption coefficient μ_a . The other reason is the signal decay caused by scattering and characterized by coefficient μ_s . For spatially uniform media, both attenuation mechanisms cause exponential signal decay described by factors $\exp(-\mu_a z)$ and $\exp(-\mu_s z)$, where z is the propagation distance. It is also assumed that other factors affecting the amplitude (like the above-mentioned influence of focusing or the roll-off effect) are absent or are duly compensated. In biological tissues the attenuation essentially depends on the optical wavelength. This fact

is taken into account when choosing the operating wavelength of OCT signals, so that the so-called transparency windows are chosen to increase the imaging depth. In particular, near infrared range is often chosen for creation OCT devices, e.g., one of often used wavelengths in OCT is 1300 nm. Numerous independent studies of optical signal attenuation in various media consistently indicate that in biological tissues the optical signal attenuation is strongly dominated by scattering rather than absorption, see, e.g., [13, 31, 32]. The statement about strong dominance of scattering over absorption is also related to OCT-signal attenuation. This fact is generally accepted and is used as an essential basic assumption for OAC-reconstruction methods widely used in recent years [15]. In terms of the above introduced attenuation coefficients μ_a and μ_s , the condition of strong dominance of scattering means that for most biological tissues one may consider that $\mu_s \gg \mu_a$, so that the energy loss during the forth-and-back propagation of the illuminating OCT beam is mostly caused by scattering.

Then following Ref. [15] to account for the attenuation process of the received OCT signal due to scattering, the following expression can be used:

$$I(z) = I_0 F(z) S(z) \theta(z) \cdot \mu_s(z) \cdot \exp[-2 \int_0^z \mu_s(z') dz'], \quad (2)$$

where $I(z)$ is the received intensity of the OCT signal; I_0 is the signal intensity incident on the biological tissue; $F(z)$ is the depth-dependent function describing focusing (confocal function); and $S(z)$ is the so-called roll-off function describing the depth-dependent sensitivity of the receiving array of detectors. Factor $\theta(z)$ is a coefficient characterizing the portion of total scattered radiation propagated back from scatterers and collected by the receiving array of OCT detectors. In some works, it is assumed that this portion should be constant in order to consider that the observed decay of the received OCT signal can be attributed to the scattering losses. However, it is clear that the influence of the unknown factor $\theta(z)$ is very similar to the effects of factors $F(z)$ and $S(z)$, so that the calibration measurement described in the previous

section can be used to determine and compensate the total effect of the product $F(z)S(z)\theta(z)$. Consequently, after such calibration and compensation the effective received signal acquires the simple form

$$I(z) = I_0 \cdot \mu_s(z) \cdot \exp[-2 \int_0^z \mu_s(z') dz'], \quad (3)$$

as if $F(z)S(z)\theta(z) = 1$. This equation still retains the depth-dependence of the received signal caused by the influence of the sought function $\mu_s(z)$.

Eq. (3) can be understood as the smoothed depth-dependence of each A-scan. The initial simulated 2D scan shown in Fig. 1 on the contrary is depth-independent corresponding to the absence (compensation) of all factors responsible for depth-dependence (including attenuation, sensitivity roll-off typical of spectral-domain OCT systems and both geometrical factors $F(z)$ and $\theta(z)$).

Consequently, for simulation of the influence of OAC dominated by signal scattering, one may take a depth-independent B-scan initially simulated as shown in Fig. 1. Initially this file is simulated in the complex-valued form (with both amplitude and phase), so that for obtaining the intensity, the complex-valued scan should be pixel-by-pixel multiplied by its complex-conjugated value. Then in the so-obtained intensity image, the intensity of each A-scan must be multiplied by the factor

given by Eq. (3) for a chosen desired distribution $\mu_s(z)$ of the optical attenuation coefficient. In such a way, however, one obtains only intensity images, whereas the described simulation procedure allows for obtaining complete complex-valued scans affected by the signal attenuation. To this end, one should again take the scan shown in Fig. 1 in the full complex-valued form and multiply it by the square root of $I(z)$ given by Eq. (3). Certainly, the intensity of the so-obtained files is exactly the same. However, the complex-valued scan opens additional possibilities, for example, for introducing arbitrary motions of scatterers to imitate a series of OCT scans affected by tissue motions, or for applying of coherent methods of OCT-scans processing, combining of OAC mapping with other OCT-modalities, e. g. elastography and angiography, etc.

Figs. 2 and 3 show examples of intensity distribution for the so-simulated OCT scans corresponding to two characteristic forms of $\mu_s(z)$. Fig. 2 shows the B-scan corresponding to a uniform distribution of OAC for $\mu_s(z) = 5 \text{ mm}^{-1}$ with the monotonically decaying signal intensity as is clearly seen from Figs. 2(a) and 2(b), in which the depth-dependence for the logarithm of intensity is shown. This dependence in average exhibits invariable slope determined by the exponential function in Eq. (3). Figs. 2(c) and 2(d) illustrate the same behavior in the linear scale.

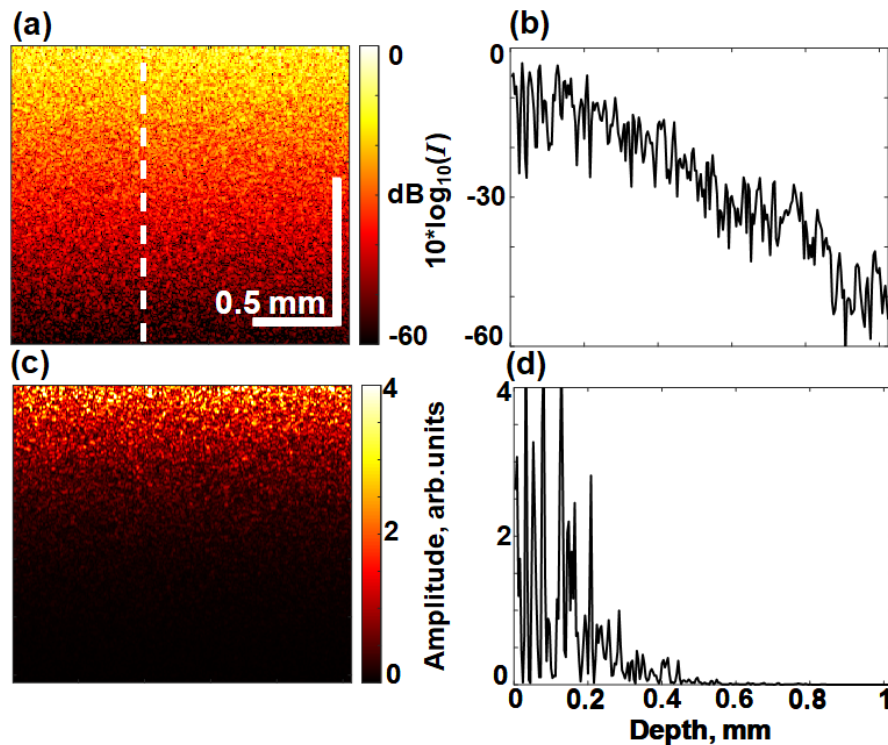


Fig. 2 Simulated OCT scans for spatially homogeneous OAC distribution with $\mu_s(z) = 5 \text{ mm}^{-1}$. (a) Structural OCT scan shown in a logarithmic scale. (b) Representative depth profile along the dashed line shown in panel (a). (c) The same scan as in panel (a) showing the OCT-signal amplitude in a linear scale. (d) The same depth profile as in panel (b) represented in a linear scale.

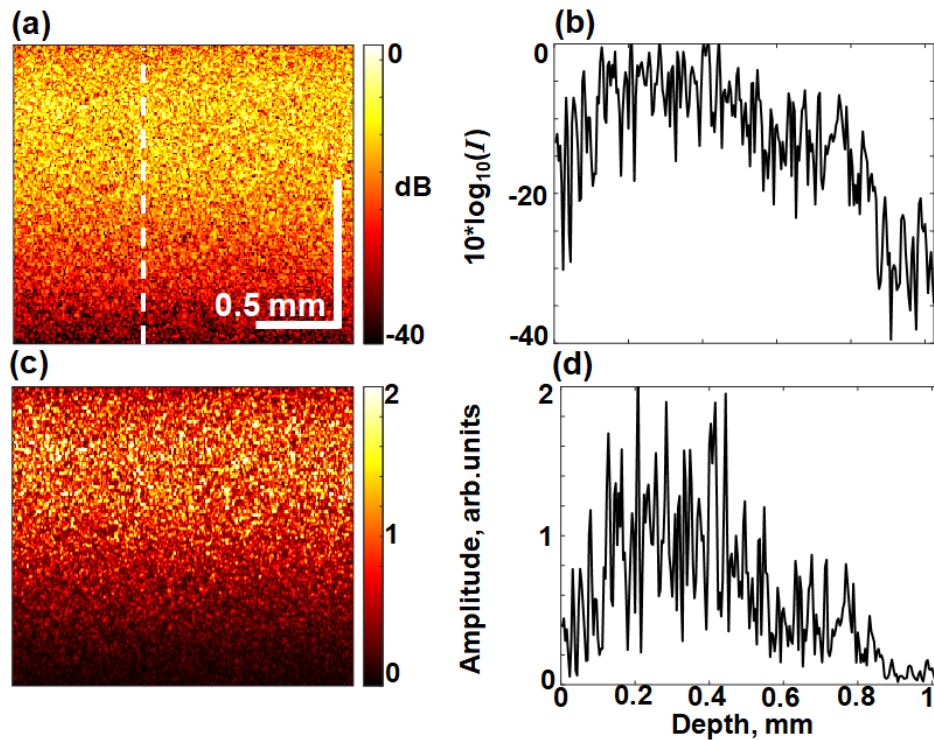


Fig. 3 Simulated OCT scans for spatially inhomogeneous OAC distribution with initial $\mu_s(0) = 0.25 \text{ mm}^{-1}$ and gradient $d\mu_s(z)/dz = 6.25 \text{ mm}^{-2}$ for which the received signal intensity demonstrates initial increase. (a) Structural OCT scan shown in a logarithmic scale ; (b) representative depth profile along the dashed line shown in panel (a); (c) the same scan as in panel (a) showing the OCT-signal amplitude in a linear scale; (d) the same depth profile as in panel (b) represented in a linear scale.

The next Fig. 3 demonstrates another characteristic form of $\mu_s(z)$. Namely, it is clear from Eq. (3) that the depth-dependence of the intensity is determined by the combined influence of the exponential factor and the pre-factor $\mu_s(z)$. It is clear that if this pre-factor sufficiently rapidly increases with the depth, such that

$$d\mu_s(z)/dz > 2\mu_s^2(z), \quad (4)$$

then intensity $I(z)$ may even increase with increasing depth. Fig. 3 illustrates such a situation and corresponds to coefficient $\mu_s(z)$ that linear growth as a function of z with the invariable rate $d\mu_s(z)/dz = 6.25 \text{ mm}^{-2}$ starting from $\mu_s(0) = 0.25 \text{ mm}^{-1}$. Figs. 3(a) and 3(b) are presented in logarithmic scale and show the intensity of the simulated B-scan and the depth dependence of intensity for a single A-scan. Figs. 3(c) and 3(d) show the same plots in the linear scale.

Note further that noise is always present in real OCT devices, and its presence introduces a bias in the received signal intensity, which should be adequately taken into account when estimating OAC [15, 16]. In the simulated complex-valued scans, a realistic measurement noise may readily be introduced by adding random, e.g., Gaussian quantities to the real and imaginary parts of the pixel amplitudes. Usually it makes sense to compare the mean noise intensity with the maximal intensity OCT B-scan usually occurred in the upper part of the scan. In

the following examples in Fig. 4, the so-defined signal-to-noise ratio amounts to $\sim 30 \text{ dB}$ in the upper part of the scans.

Notice further that by setting $\mu_s(z)$ to zero, it is possible to model an empty space above the studied sample, which is typical for non-contact imaging. Adjusting the simulated level and spatial distribution of attenuation, as well as the level of simulated noises one can imitate various types of real OCT scans of biological tissues. Some of such instructive real examples are presented in Fig. 4.

In Fig. 4 we use real OCT scans of homogeneous cartilage samples observed before and after 10 min of impregnation with an optical clearing agent (glycerol) like in works [33, 34]. For simulating scans, the attenuation and noise parameters were chosen to reproduce main features of the real scans. By applying a glycerol solution, the optical clearing effect was achieved in the upper layers of the cartilage sample, resulting in the formation of a gradient of the attenuation coefficient with the reduced scattering in the near surface layers and more intense scattering localized at an intermediate depth. This situation corresponds to sufficiently fast growth of $\mu_s(z)$ with increasing depth (as formulated in Eq. (4) and illustrated in the simulated Fig. 3) and is in contrast with the character of scattering before application of glycerol, when the brightest signal was localized near the sample surface.

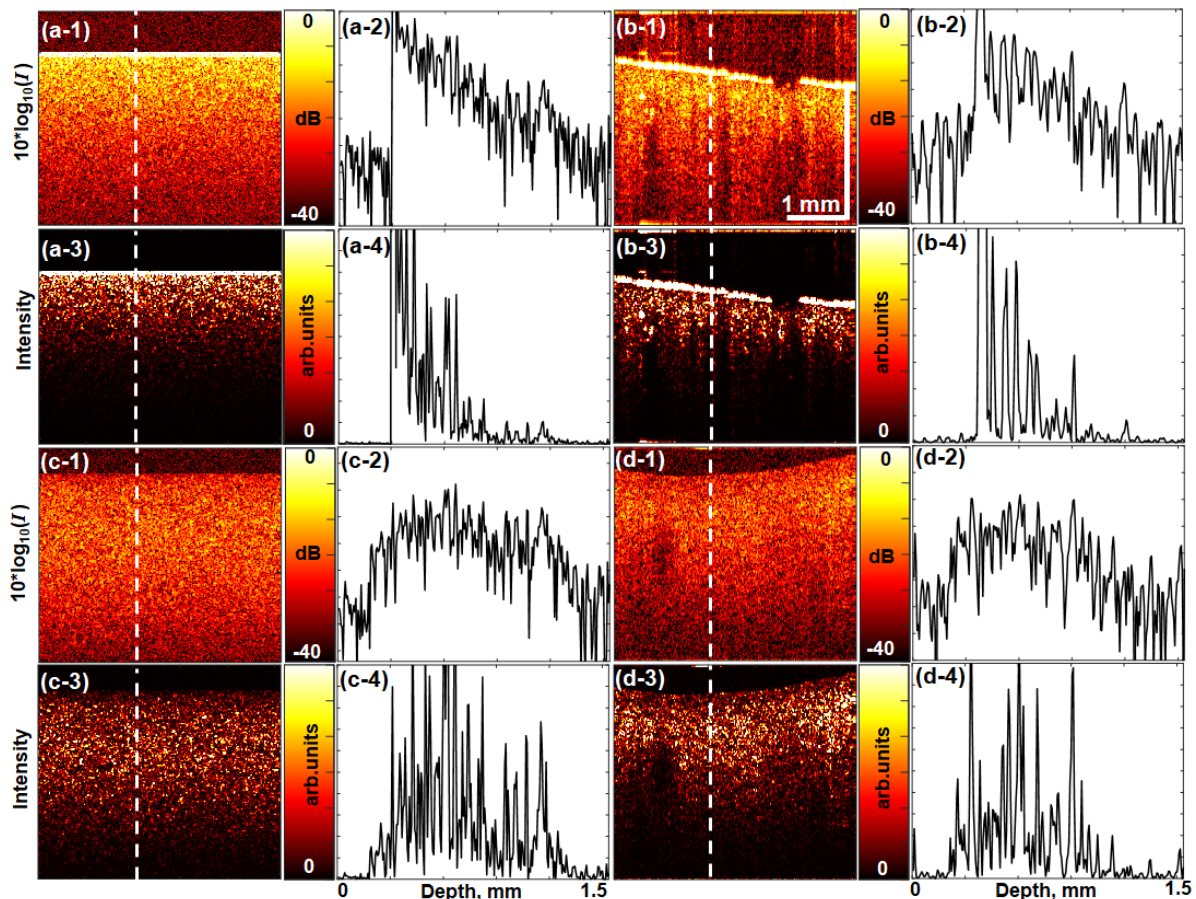


Fig. 4 Demonstration of similarity of the simulated (left column) and real (right column) OCT scans obtained for homogeneous cartilage samples before and after 10 min of impregnation with glycerol, respectively. Panel (a-1) is real OCT scan obtained before impregnation and (b-1) is the corresponding simulated scan shown in logarithmic scale. Panels (a-2) and (b-2) are the corresponding depth profiles along the dashed lines shown in panels (a-1) and (b-1). Panels (a-3), (a-4) and (b-3), (b-4) – the same plots as in panels (a-1), (b-1) and (a-2), (b-2) in the upper row but shown in the linear scale. Panels (c-1), (c-2) and (d-1), (d-2) are the same set of plots obtained after impregnation and the corresponding simulated plots shown in logarithmic scale. The bottom row shows a similar set of simulated and real post-impregnation plots shown in linear scale. Notice that initially the most intense signal occurred near the sample surface, whereas after impregnation with glycerol, the most intense scattering occurs at an intermediate depth.

4 Examples Illustrating Adequacy and Usefulness of the Described Model for Testing OAC-Estimation Methods

For OCT application in various biomedical problems it is of key importance to enable sufficiently reliable spatially resolved estimation of OCT-scan parameters. This requirement is common for various OCT modalities – OCT-based elastography [35–37], OCT-based angiography [38, 39], or parameters of speckle texture [8, 9, 40]. In this context, much attention in recent years has also been paid to the development of spatially-resolved methods for estimating the attenuation coefficient. A significant portion of such studies were stimulated by the appearance of paper [15] by Vermeer et al., where a formula for spatially-resolved estimation of OAC was proposed for usage in OCT. This formula is exact under certain conditions which are not always perfectly satisfied for real OCT scans. However, when these conditions are fairly well fulfilled,

method [15] of OAC reconstruction can be used as a reference one. By this reason for verification of adequacy of the described “digital phantom”, in the following section we demonstrate the results of OAC reconstruction by method [15] applied to the simulated OCT scans.

4.1 Correspondence between the Optical Attenuation Coefficient Adopted in the Simulated “Digital Phantoms” and Vermeer’s Reconstruction

In this section, compare the $\mu_s(z)$ profile adopted in the procedure of OCT-scan simulation using the procedure described in Section 3 with OAC reconstructed from the simulated scans using method [15] under nearly ideal conditions of the method operability. We emphasize once again that, when performing such a comparison, we assume that the geometrical factors and sensitivity roll-off entering Eq. (2) have already been compensated by

performing the calibration test as described at the end on Introduction. After such compensation the intensity profile can be affected only by the OCT-signal losses due to optical-signal scattering and eventual absorption in the tissue. Then the only remaining condition of the validity of approach [15] to reconstruction of OAC after the above-mentioned compensation procedures is that the OCT-signal attenuation is strongly dominated by scattering. This is precisely the case when the depth-dependence of the OCT-signal intensity reduces to Eq. (3).

Then in the absence of additive measurement noises and in the case of complete decay of the observed signal intensity $I(z)$ within the visualized region, for arbitrary form of $\mu_s(z)$, the following rigorously valid expression was derived in Ref. [15]:

$$\mu_s(z) = \frac{I(z)}{2 \int_z^\infty I(z') dz'}. \quad (5)$$

Physically Eq. (5) reflects the fact that the optical-beam energy passed through the depth coordinate z is equal to the energy loss caused by scattering during the optical-beam propagation from the current depth z to infinite depth.

It is important that Eq. (5) is written in the continuous form and is rigorously valid only at a semi-infinite interval. However, OCT scans are always acquired withing a finite depth interval $z \leq H$ and have a pixelated form. Thus, the discretized counterpart of Eq. (5) can be written as:

$$\mu_s(z_i) \approx \frac{I(z_i)}{2\Delta \sum_{j=i+1}^{j_H} I(z_j)}, \quad (6)$$

where index j_H corresponds to the maximal imaged depth H in the OCT scan and Δ is the axial inter-pixel distance (for brevity, in what follows called pixel size). Depth H is always finite, which leads to an unpleasant consequence intrinsic to Eq. (6). Namely, when $z \rightarrow H$ the estimate of $\mu_s(z)$ in Eq. (6) tends to a very big value $\mu_s(z) \rightarrow 1/(2\Delta)$ corresponding to a decay scale of the order of pixel size.

An important feature of both Eq. (5) for continuous representation and Eq. (6) written in the discretized form, is that the so-obtained spatially-resolved estimate of the attenuation coefficient $\mu_s(z)$ depends on the local values of $I(z)$. Therefore, when analyzing OCT scans characterized by the very strong variability of speckle intensities $I(z_i)$ like in the examples of speckle patterns shown in Figs. 3 and 4, function $\mu_s(z_i)$ reconstructed by Eq. (6) should also demonstrate strong variability. Consequently, more stable estimates of $\mu_s(z_i)$ can be obtained only using appropriately performed spatial averaging. The corresponding examples are shown in Fig. 5 using a simulated OCT image in which a spatially homogeneous distribution of $\mu_s(z)$ in the tissue was assumed as shown in Fig. 5(a-1). In the simulations shown in Fig. 5 for the moment we do not introduce additive measurement noises to show in the most clear form the influence of the “speckle noise”, i.e. the variability of speckle amplitudes intrinsic to OCT scans. Fig. 5(a-2) shows the corresponding simulated structural B-scan in which the pronounced “speckle noise” is visible. The corresponding very noisy map of OAC reconstructed using Eq. (6) without any averaging is shown in Fig. 5(b-1). Fig. 5(b-2) demonstrates a single vertical profile along the dashed line shown in Fig. 5(b-1).

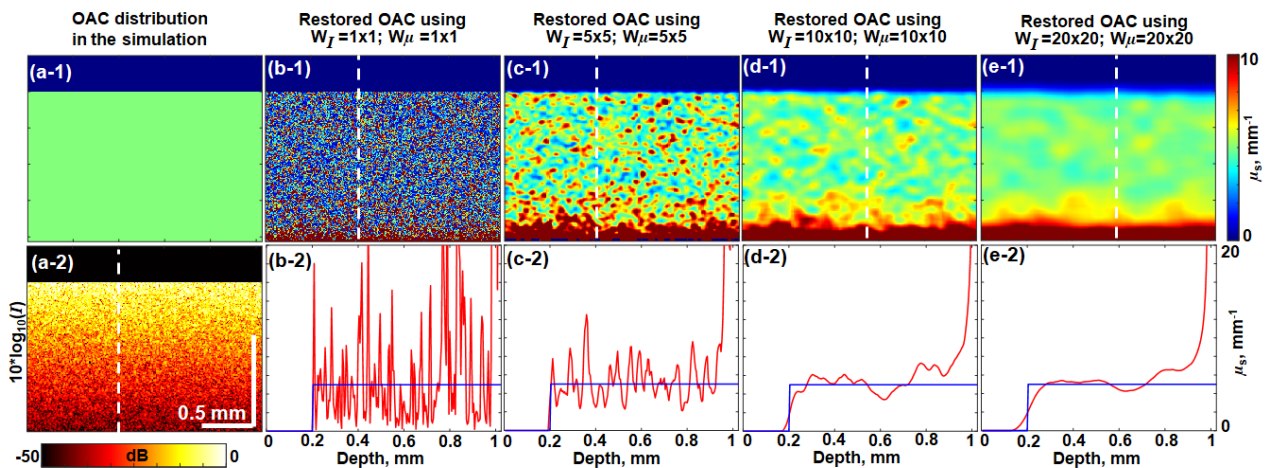


Fig. 5 Demonstration of OAC reconstruction using method [15] for several variants of preliminary averaging of intensity and subsequent averaging of reconstructed $\mu_s(z)$ using sliding windows 1×1 , 5×5 , 10×10 , and 20×20 pixels. (a-1) Distribution of OAC adopted in the model. (a-2) The corresponding simulated structural OCT scan. (b-1) Reconstructed OAC without averaging. Panels (c-2), (d-2), and (e-2) show reconstructed OAC using averaging windows with the sizes indicated above the plots, the white dashed lines indicate the positions of the depth profiles shown in panels (b-2)–(e-2). The OAC value inside the simulated tissue is $\mu_s(z_i) = 5 \text{ mm}^{-1}$.

The unaveraged profile of $\mu_s(z_i)$ reproduces the strong variability of intensity of individual speckles inherited from the structural OCT scan shown in Fig. 5(b-2), so that the adopted in the simulation depth-independent profile of $\mu_s(z_i)$ is almost completely masked by the speckle noise. To improve the quality of the obtained OAC maps one may use spatial averaging. In the examples shown in Fig. 5 the two-step averaging was used: (i) averaging over window W_l was first applied to the intensity of structural OCT-scan shown in Fig. 5(b-2); (ii) then averaging over window W_μ was applied to the attenuation coefficient $\mu_s(z)$ initially estimated using the previously averaged intensity for every pixel via Eq. (6). The results of such two-step averaging are shown for several sizes of averaging windows 5×5 , 10×10 , and 20×20 pixels. The same window sizes $W_l = W_\mu$ were used both in steps (i) and (ii).

The maps of $\mu_s(z)$ and representative profiles shown in columns (c), (d), and (e) in Fig. 5 demonstrate that with the appropriately performed averaging, the method based on Eq. (6) demonstrates a good correspondence of the OAC distribution adopted in the simulations and estimated attenuation coefficient over the most part of the scans not too close to the scan bottom. At the same time Fig. 5 also clearly demonstrates the above mentioned artefactual feature intrinsic to the discretized Eq. (6). Namely, closer to the bottom of the OCT scan, the estimated OAC demonstrates the artefactual growth that was mentioned in the discussion of Eq. (6). Nevertheless, for the main portion of the imaged region, the assumed in the simulation distribution of $\mu_s(z)$ and the results of its reconstruction from the simulated “digital phantom” using Eq. (6) proposed in Ref. [15] demonstrate a very good coincidence. Increase in the averaging-window size on the one hand eliminates noisy deviations of the reconstructed OAC profile from $\mu_s(z)$ adopted in the simulation, but on the other hand the averaging smoothens high gradients of $\mu_s(z)$ as is clear from Figs. 5(d-2) and 5(e-2).

This coincidence confirms that the simulated “digital phantom” is quite adequate. Among the distorting factors, which may introduce biases in the OAC estimate by Eq. (6), the most important is the influence of various measurement noises (unrelated to the speckle variability that is already captured in the examples shown in Fig. 5). These noises affect both the numerator and denominator in Eq. (6). Another important factor is the influence of incorrect estimation of the denominator in Eq. (6) because of incomplete decay of the OCT signal withing the visualized depth. The influence of these distorting factors on the OAC reconstruction was discussed in a number of studies (e.g., [16, 17, 41–43]) starting from work [15] itself. These distorting factors can readily be introduced in the simulated digital phantom so that the efficiency and accuracy of the corresponding modifications of method [15] and possibly alternative methods can be studied in detail in highly controllable conditions with the possibility of flexible variations of all parameters.

4.2. Demonstration of the Speckle Noise Role in Estimation of Essentially Inhomogeneous $\mu_s(z)$ Distribution

The above-considered examples were related to $\mu_s(z)$ reconstruction in the simplest case of spatially homogeneous distribution of OAC. However, it is ability of spatially-resolved reconstruction which is usually considered as the main advantage of Vermeer’s approach [15] and its modifications. Although the basic Eq. (5) is formally exact, it was already demonstrated in Fig. 5 that the strong random spatial variability of the speckle pattern intrinsic to OCT scans may very strongly mask the regular character of the $\mu_s(z)$ even in the simplest case when OAC is in average invariable within the visualized region.

Fig. 6 shows a more complex spatial distribution of $\mu_s(z)$ which is characterized by presence of several layers by analogy with the example discussed in Ref. [15]. Here, we still do not introduce additive measurement noise to demonstrate in the most clear form the degrading role of OCT speckles in the reconstruction of OAC, for which the discretized Eq. (6) is used. To compare with the case of absence of speckles, we first generate the structural OCT image and then normalize to unity amplitude or all pixels, so that the scan remains pixelated, but variation in speckle amplitudes become completely eliminated.

The layered OAC distribution adopted in the simulations is shown in Fig. 6(a-1). The step-wise profiles of $\mu_s(z)$ are also shown by the blue solid line in Figs. 6(b-2), 6(c-2), and 6(d-2). The corresponding structural OCT scan is shown in Fig. 6(a-2). In the right part of panel (a-2) the speckle pattern is retained. The left part of this panel shows the image obtained by applying the influence of attenuation described by Eq. (3) to the initial scan with normalized speckle amplitudes. The results of the OAC reconstruction via discretized Eq. (6) are shown as color coded maps in Figs. 6(b-1), 6(c-1), and 6(d-1). The left part in these maps corresponds to the left part of the structural image Fig. 6(a-2) with eliminated speckle-amplitude variability and the right parts are obtained with retaining of OCT speckles. The respective representative profiles of OAC reconstructed using Eq. (6) are shown in Figs. 6(b-2), 6(c-2), and 6(d-2) for three variants of spatial averaging similarly to Fig. 5. The profiles obtained with retaining of speckles are shown by solid red lines and the profiles found after elimination of the speckle variability are given by dashed black lines. It is clear that pixel-to-pixel reconstruction without averaging similarly to Fig. 5 yields OAC distributions strongly degraded by the speckle influence. The profiles of $\mu_s(z)$ obtained with normalization of speckle amplitudes are much closer to the profile adopted in the model with a clear step-wise structure even without averaging.

However, even for the OCT image with eliminated speckle noise, the finite depth used for reconstruction of $\mu_s(z)$ in the discrete Eq. (6) leads to appearance of deviation of the reconstructed OAC from the actual $\mu_s(z)$ distribution adopted in the simulations.

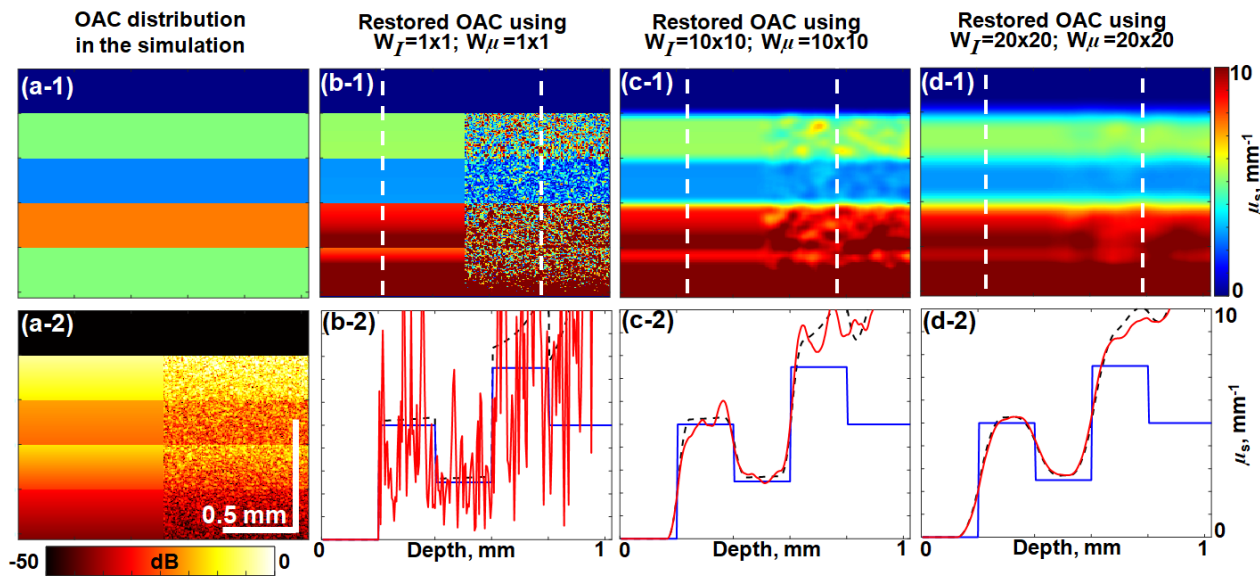


Fig. 6 Influence of the “speckle noise” on the reconstruction of spatially-inhomogeneous distribution $\mu_s(z)$ using approach [15] in the absence of additive measurement noises. Panels (a-1) and (a-2) show the OAC distribution adopted in the simulations and the simulated OCT scan, respectively. The OAC values in the five layer in panel (a-1) in the direction downward are 0, 5, 2.5, 7.5, and 5 mm^{-1} . The reconstructed 2D distributions of OAC are shown in panels (b-1), (c-1), and (d-1) without averaging, with averaging window 10×10 pixels and 20×20 pixels, respectively. The corresponding depth profiles of OAC for the positions marked by dashed lines in the 2D scans, are shown in panels (b-2), (c-2), and (d-2) by red lines. The blue lines in panels (b-2), (c-2), and (d-2) show the stepwise OAC profile adopted in the simulation.

This deviation is due to underestimation of the denominator in the discretized Eq. (6) in comparison with the exact continuous form of Eq. (5). Close to the image bottom this underestimation becomes especially strong causing rather strong deviations of the reconstructed and actual $\mu_s(z)$. Various modifications of Eq. (5) are discussed in the literature to eliminate this underestimation of the denominator (e.g. [16]). Such modified methods can also be tested using the “digital phantom” described here and the corresponding comparison of various modified approaches may be presented elsewhere. Returning to the present consideration, we emphasize once again that the speckle noise strongly degrades the quality of the spatially-resolved reconstruction of $\mu_s(z)$ as demonstrated in Fig. 6(b-2) and the right half of OAC map in Fig. 6(b-1). Averaging may help to significantly suppress this speckle-induced degradation, but this suppression is attained at the expense of reduction in the spatial resolution. The described “digital phantom” also makes it possible to quantitatively estimate the detectable contrast in the variable $\mu_s(z)$ for various sizes of averaging windows.

One may also mention that even if the reconstructed OAC distribution without averaging is rather noisy, the regions with significantly reduced OAC (more transparent regions in structural scans) are reconstructed with a better contrast. In practice, obtaining of maximal resolution in the reconstructed OAC maps is important when the spatially-resolved OAC reconstruction is used for detection of lymphatic vessels in OCT scans. It is known that these regions are characterized by reduced scattering [44, 45]. Besides fairly evident discrimination

of such regions by reduced amplitude of signal, the spatially-resolved mapping of OAC can also be used for imaging lymphatic vessels [43]. The proposed “digital phantom” can be used for testing and assessment of ultimate possibilities of this approach. For illustration, we present Fig. 7 in which the adopted distribution of OAC comprises local regions in which the scattering is reduced by various degrees. These regions imitate fragments of lymphatic-vessel cross sections (small circles) and elongated segments of such vessels that are more typical for *en face* images, but here they are presented in B-scans for illustration.

The reconstructed 2D maps of OAC demonstrate that fairly small regions, in which the scattering coefficient is reduced by a factor of 2 and greater, can be rather clearly singled out even in the presence of the speckle noise and even without averaging. The moderate averaging, for the window sizes $W_l = W_\mu = 5 \times 5$ pixels, improves the contrast between the background tissue and “lymphatic vessels” almost without the resolution loss. However, too large averaging window $W_l = W_\mu = 20 \times 20$ pixels on the contrary completely degrades the resolution of the visualization of the vessels. In these examples the addition measurement noise is not introduced and for OAC reconstruction we use Eq. (6). Certainly the additive noises can readily be introduced, the background OAC can easily be varied in the simulated OCT scans. Thus, the efficiency of visualization of regions with reduced OAC can be tested for various modifications of Eq. (6) discussed in the literature to account for the noise floor and the influence of incomplete signal decay, the degree of OAC contrast, etc.

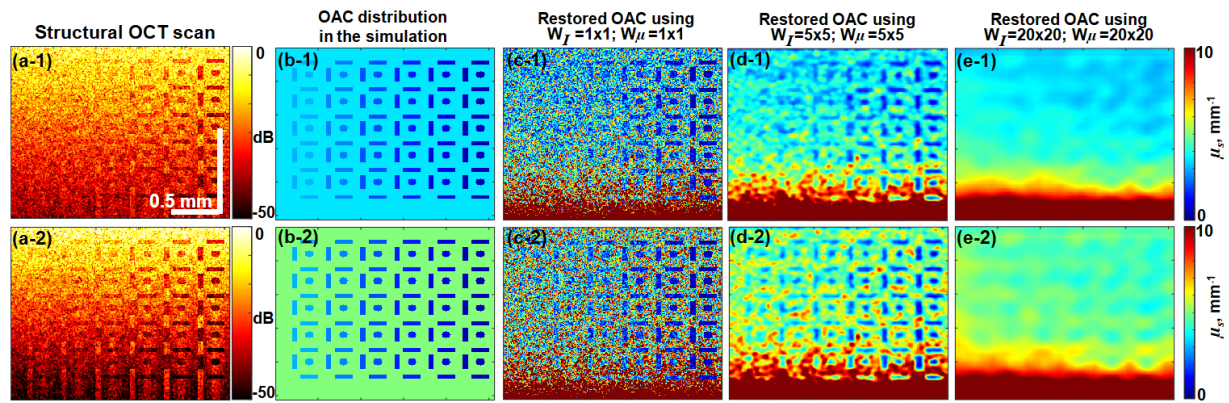


Fig. 7 Imitation of visualization of lymphatic vessels characterized by pronouncedly reduced scattering using spatially-resolved reconstruction of OAC. Column (a) shows the simulated structural scans, for which the adopted in simulation OAC distributions are shown in column (b). Columns (c), (d), and (e) show the OAC reconstruction based on Eq. (6) without averaging, for the averaging window $W_l = W_\mu = 5 \times 5$ pixels and $W_l = W_\mu = 20 \times 20$ pixels, respectively. The two rows correspond to the two different background values of the scattering coefficient of 3.5 mm^{-1} and 5 mm^{-1} , respectively. In the regions imitating the lymphatic vessels, for both rows the OAC value decreases from 3 down to 0.5 mm^{-1} in steps by 0.5 mm^{-1} .

Here, we limit ourselves to the above-presented examples illustrating the convenience of the developed digital phantom. Results of its application for detailed comparative tests of OAC-reconstruction methods will be presented elsewhere.

5 Discussion

In the previous sections we described a fairly simple although reasonably realistic model of OCT-image formation corresponding to widely used weakly focused Gaussian beams that enable approximately depth-independent lateral resolution within the visualized depth of 1–2 mm typical for OCT. In such beams, even the neglect of lateral curvature of the phase front is fairly reasonable as demonstrated in Ref. [27]. However, for more rigorous (although somewhat more computationally demanding) representation of weakly focused beams, the influence of the Gaussian-beam phase-front curvature can also be taken into account, for example, using the approach described in Ref. [26]. Method [26] is convenient for simulating two-dimensional B-scans in the form of adjacent individually generated A-scans. If simulations of 3D stacks of B-scans are required, approach [27] can be efficiently applied. Furthermore, it is noteworthy that approach [27] allows one to simulate arbitrary types of OCT beams, including Gaussian ones with arbitrary focusing, as well as Bessel beams or other beam types if necessary. This flexibility of approach [27] is due to utilization of the angular-spectrum approach which is very universal and applicable to description of various types of OCT beams.

The above-mentioned methods described in Refs. [26–29] similarly to the method used in this study generate OCT scans in which initially losses of the illuminating beam are neglected, so that accounting for scattering-induced attenuation can be made using the procedures described above in Section 3. In principle, besides the OCT-signal losses due to scattering, one may also introduce additional exponential factor describing

the optical-signal losses caused by absorption during the forth-and-back propagation. However, in such a case the elegant approach to spatially-resolved OAC imaging proposed in Ref. [15] would not be applicable because it is based on the assumption of strong dominance of scattering-related losses.

Certainly, the possibilities of approaches [26–29] to OCE-signal formation are not limited to testing methods of OAC imaging, but can readily be used for developing other OCT modalities. In particular, simulation methods presented in Refs. [26–29] have already been efficiently used for perfection of OCT-based elastography [46–48]. Similar modeling was used for testing various OCT-based approaches to angiographic imaging, see e.g. [27, 29, 49]. Regarding simulations of elastographic and angiographic processing, of key importance is that methods [26–29] readily enable generation of large series of OCT scans with arbitrary displacements of scatterers from one scan to another. Such displacements may be either regular corresponding to a desirable form of strain distribution or caused by regular flows, as well as may relate to random Brownian-like motions or arbitrary combinations of regular and random displacements (see, e.g., [29, 47, 49]). For alternative approaches to OCT-signal modeling, such generation of multiple OCT scans with accounting for interframe scatterer displacements is not always feasible or may require very high computational costs like for Monte-Carlo methods. However, the advantage of Monte-Carlo methods is that they may rather naturally account for effects of multiple scattering, consideration of which is problematic for methods [26–29]. In the present form these methods are based on consideration of ballistic single-scattered signal in the backward direction as is assumed by the very principle of OCT operation. In this regard, multiple scattering is a degrading effect in OCT. However, there also other important (in many cases even more important) degrading factors intrinsic to OCT scans, such as speckle

noise, as well as typical of many situations effects related to decorrelation of OCT scans due to translational or strain-induced displacement of scatterers. Such factors can readily be accounted for in the wave-based approaches [26–29]. Understanding of those multi-factor effects (both degrading and information-bearing ones) is very important for development of such OCT modalities as elastography or angiography, OAC imaging, speckle-contrast analysis of OCT scans, etc. Possibilities of purely analytical description of the respective effects are strongly limited by simplest situations. Consequently, utilization of the modeling method discussed in this study, as well as related methods [26–29] open very convenient in the context of developing not only OAC imaging possibilities, but also for studying a broad range of other OCT modalities for application in both educational and research problems.

6 Conclusions

In the previous sections we presented a simple but efficient method to simulate “digital phantom” which can be conveniently used for comparative studies of performance of various methods proposed for OAC estimation using OCT-scan analysis. The described approach makes it possible to realistically simulate both speckle noises and other additive noises affecting OCT images. Besides, unlike the simple summation of several phasors with random phases, the described “digital phantom” correctly accounts for the effects of signal leakage among neighboring pixels due to the final axial size of the point-spread-function determined by the optical-signal bandwining, as well as the finite lateral size of speckles. The latter is determined by the illuminating beam diameter and the degree of self-overlapping during the lateral scanning. These factors are also realistically accounted in the so-formed “digital phantom” and determine the degree of statistical independence of

neighboring pixels. The degree of this independence is important for choosing adequate sizes of averaging window because the results of averaging procedures strongly depend on the amount of independent averaged elements. The simulated OCT scans realistically imitate speckle structure of OCT scans, which makes it possible to assess the degrading role of speckles in various situations. Besides correctly reproducing variability of intensity, phase properties of both the signal from scatterers and additive measurement noise can also be reproduced in the described model, so that both coherent and incoherent methods of OCT-scan processing can be comparatively tested using the presented simulation approach.

A very important advantage of simulations is extremely high flexibility allowing one to controllably vary all important parameters in the considered problems, including both properties of the simulated tissue and parameters of the OCT setup used to image this tissue. In physical experiments such flexible and precise control of experimental conditions is much more difficult and expensive and may be even unfeasible. Thus the proposed approach and above presented demonstrations of its usage can be used for further perfection of OAC estimation methods in optical coherence tomography.

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Disclosures

The authors declare that they have no conflict of interest.

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