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Analytical solution for light propagation in a two-layer tissue structure with a tilted interface for breast imaging

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Abstract

Reflectance measurement of breast tissue is influenced by the underlying chest wall, which is often tilted as seen by the detection probe. We develop an analytical solution of light propagation in a two-layer tissue structure with tilted interface and refractive index difference between the layers. We validate the analytical solution with Monte Carlo simulations and phantom experiments, and a good agreement is seen. The influence of varying the tilting angle of the interface on the reflectance is discussed for two types of layered structures. Further, we apply the developed analytical solution to obtain the optical properties of breast tissue and chest wall from clinical data. Inverse calculation using the developed solution applied to the data obtained from Monte Carlo simulations shows that the optical properties of both layers are obtained with higher accuracy as compared to using a simple two-layer model ignoring the interface tilt. This is expected to improve the accuracy in estimating the optical properties of breast tissue, thus enhancing the accuracy of optical tomography of breast tumors.

1. Introduction

Accurate evaluation of optical properties of embedded lesions from surface reflectance measurements is important and challenging in optical tomography.^{1–4} The biological tissues often contain layered structures, which contribute to the total reflectance measurements. A two-layer light propagation model is a simple and sufficiently accurate approximation to the imaging medium in most of the biomedical applications. Various numerical and analytical methods have been developed to study the time domain and frequency domain reflectance from layered tissue structures.^{5–12} Most of these methods were intended to analyze cases where the upper skin layer was relatively thinner (of the order of a few millimeters) such as skin above the subcutaneous fat layer or skin overlying the skull. In such applications the reflectance measured on the surface would be mostly influenced by the properties of the thicker second layer, which could then be easily retrieved. Several practical applications require imaging of two-layer structures where the upper layer is in general thicker (1–2 cm) and the interface between the layers may be tilted. Light-reflectance measurement from breast tissue is an example where the breast tissue and chest wall may have a titled interface with respect to the imaging probe. In such cases the reflectance measured at the upper tissue surface might have equal contributions from both layers or dominant contributions from either one of the layers, depending entirely on the layer thickness or tilt of the interface and the optical properties of the layers. Unlike in the case of imaging biological tissue underneath thin skin, any simple approximation here would lead to large errors in analysis. Clinical results have shown that for patients whose breast tissue thickness is less than 1.5 to 2 cm, depending on average optical properties, the frequency domain reflectance measurement of both amplitude and phase acquired at a larger distance from a source often deviate from expected linear curves due to the presence of the chest wall.^{13,14} This is common for patients with smaller breasts when measurements are made in the supine

position. A systematic analysis of the effects of the different layer properties and the tilted interface on the reflectance measured at the tissue surface is necessary for developing any new image reconstruction techniques to account for the chest-wall-induced distortion effect.

Analytical solutions are preferred over numerical methods such as Monte Carlo calculations, which require intensive computation. Analytical solutions developed for frequency domain reflectance in two-layer tissue structure usually assume an average refractive index (RI) for both layers. It has already been shown that the estimated values of absorption and reduced scattering coefficients could be erroneous if the RI mismatch between layers were not considered.¹⁵ The RI mismatch changes the balance of energy inside the medium determining a temporal and spatial redistribution of light energy. The effect of RI mismatch for two-layer structures with a thinner upper layer has been investigated using the finite element method by Deghani *et al.*¹⁶ To the best of our knowledge, a simple analytical solution for a two-layer tissue structure with a thicker upper layer considering both RI mismatch and tilt of the interface does not exist in the literature. In this paper, we introduce such an analytical solution, which derives the basic methodology from the two-layer analytical solution developed by Dayan *et al.*⁶ and Kienle *et al.*⁵ However, the boundary conditions have been modified to incorporate the RI mismatch and the tilt at the interface of the layered structure, and the solutions are derived accordingly. To the best of our knowledge, there has been no prior work on the analysis of multilayer structures with a tilted interface. This is done as part of our efforts to understand and improve the clinical imaging of breast tissue where the reflectance measured at the surface is influenced by the chest-wall layer properties and the chest-wall layer may not be parallel to the imaging probe.^{13,14}

The application of a two-layer model is mainly in estimating the average optical properties of tissue layers with improved accuracy compared to the semi-infinite approximation. The accurate optical properties would in turn enhance the quantification of functional imaging of tumors buried in such a medium. While this has been shown by several authors previously,^{5,7–11} all of them used signals detected at smaller source-detector separations that were sufficient for two-layer models with extremely thin upper layers. The property estimation of the second layer was more important for these studies since the tumors would be lying in the lower layer. For breast imaging where the upper layer (breast tissue) is typically between 1 and 4 cm, the signals detected at source-detector separations larger than 2 cm are of more relevance and hence any tilt at the interface between the breast tissue and the underlying chest wall is also of relevance for breast imaging as compared to the studies on layered structures with thinner upper layers of the order of a few millimeters.

This paper is organized as follows. In Section 2 we show the analytical derivation for light propagation in a two-layer tissue structure with a tilted interface. In Section 3 we discuss computational and numerical methods and experimental methods used to validate our newly developed solution. Results are presented in Section 4, and a summary is given in Section 5.

2. Theory

In this section, we present the derivation of an analytical solution for light propagation in a two-layer tissue structure, which could have an arbitrary tilt at the interface and refractive index mismatch between the layers.

Diffusion equations are solved for a two-layer turbid medium considering the most general case of an arbitrary tilted interface and also considering the refractive index difference between the two layers. The layer structure is shown in Fig. 1. An infinitely thin beam of frequency-modulated light is assumed to be incident perpendicularly on the top surface of a two-layer turbid medium, which would be diffused isotropically in the top layer at a depth of $z = z_0$. The diffusion equation for the fluence rates ($\text{mm}^{-2} \text{s}^{-1}$) is given as

$$D_1 \nabla^2 \Phi_1(r, \omega) - \left(\mu_{a1} + j \frac{\omega}{v_m} \right) \Phi_1(r, \omega) = -\delta(x, y, z - z_0) \exp\left(j \frac{\omega}{v_i} r\right), 0 \leq z \leq 1, \quad (1)$$

$$D_2 \nabla^2 \Phi_2(r, \omega) - \left(\mu_{a2} + j \frac{\omega}{v_m} \right) \Phi_2(r, \omega) = 0, l \leq z, \quad (2)$$

where $r = (x^2 + y^2 + z^2)^{1/2}$; $D_i = (1/3)(\mu_{ai} + \mu_{si})^{-1}$ are the diffusion coefficients; μ_{ai} and μ_{si} are the absorption and reduced scattering coefficients, respectively; and $z_0 = 1/(\mu_{a1} + \mu_{s1})$ and j are the fluence rates for the layers $i = 1$ and 2 , respectively. The modulation frequency of the source is $\omega = 2\pi f$; v_i is the speed of light in the medium.

The boundary conditions used are

$$\Phi_1(z = -z_b, r) = 0, \quad (3)$$

$$\Phi_1(r \rightarrow \infty) = 0, \quad (4)$$

$$\frac{\Phi_1(l, r)}{\Phi_2(l, r)} = \frac{n_1^2}{n_2^2}, \quad (5)$$

$$D_1 \frac{\partial \Phi_1(z)}{\partial z} \Big|_{z=l^-} \cos(\theta_1) = D_2 \frac{\partial \Phi_2(z)}{\partial z} \Big|_{z=l^+} \cos(\theta_2). \quad (6)$$

Equation (3) refers to the extrapolated boundary condition assumed at the free surface. z_b is the extrapolated distance¹⁷ given by $(1 + R_{\text{eff}}/1 - R_{\text{eff}})2D_1$. R_{eff} depends on the refractive indices of the tissue layer and represents the fraction of photons total internally diffused at the boundary. The RI mismatch at the interface of the two layers causes discontinuity of photon fluence, for which an approximate boundary condition is given by Eq. (5). This has been shown to be valid for layers with RI mismatch up to 1.4.¹⁵ Equation (6) represents the continuity condition for the normal component of the flux at the tilted interface, expressed in terms of the tilting angle of the interface. Here θ_1 represents the tilt of the interface with respect to the top surface of the tissue. From Fig. 1, we can see that θ_1 also represents the angle between the direction in which the diffused light is directed and the normal to the interface. θ_2 is the corresponding angle of refraction, considering the material difference between the two media with n_1 and n_2 being the refractive indices of layers 1 and 2, respectively.

Further, to solve diffusion equations (1) and (2) using these boundary conditions, we follow the spatial inversion approach used by Kienle *et al.*,⁵ where Eqs. (1) and (2) transform into ordinary differential equations. The boundary conditions in the spatially transformed domain corresponding to Eq. (3)–(6) are then used to solve them. The fluence rate $\phi_i(z, s_1, s_2)$ in the spatially transformed domain is obtained for each region in the structure at the tissue surface where

$$\phi_i(z, s_1, s_2) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \Phi_i(x, y, z) \times \exp[i(s_1 x + s_2 y)] dx dy. \quad (7)$$

At the surface of the tissue, $\phi_1(z, s)$ can be obtained by using the boundary conditions for this tilted interface structure to solve the transformed diffusion equation and is given by

$$\phi_1(z, s) = \frac{\sinh[\alpha_1(z_b + z_0)]}{D_1\alpha_1} \frac{D_1\alpha_1\phi \cosh[\alpha_1(l - z)] + (n_2/n_1)^2 D_2\alpha_2 \sinh[\alpha_1(l - z)]}{D_1\alpha_1\phi \cosh[\alpha_1(l - z_b)] + (n_2/n_1)^2 D_2\alpha_2 \sinh[\alpha_1(l - z_b)]} - \frac{\sinh[\alpha_1(z_0 - z)]}{D_1\alpha_1}, 0 \leq z < z_0, \quad (8)$$

where $s^2 = s_1^2 + s_2^2$, $f^2 = (D_f s^2 + \mu_{af} + j/v_f)/D_f$ and $\phi = \cos(\theta_1)/\cos(\theta_2)$.

Fluence rate at the surface of the tissue ($z = 0$) can be obtained by spatial Fourier inversion

$$\Phi_1(\rho, z=0) = \frac{1}{2\pi} \int_0^\infty \phi_1(z=0) s I_0(s\rho) ds, \quad (9)$$

where I_0 is the Bessel function of zero order and ρ is the source-detector separation. Spatial reflectance $R(\theta)$ can be calculated as the integral of the radiance over the backward hemisphere⁵

$$R(\rho) = \int_{2\pi} d\Omega [1 - R_{\text{fres}}(\theta)] \frac{1}{4\pi} \left[\Phi_1(\rho, z=0) + 3D_1 \frac{\partial \Phi_1(\rho, z=0)}{\partial z} \cos(\theta_1) \right] \cos(\theta), \quad (10)$$

where $R_{\text{fres}}(\theta)$ is the Fresnel reflection coefficient of light at an incident angle θ with respect to the normal of the boundary. It should be noted that the quantity l in the fluence rate equation is actually a function of θ due to the tilt of the interface between the two layers and is given as $l(\theta) = l_0 - \tan(\theta_1)$, where l_0 is the maximum thickness of the layer. The analysis considers only uniform tilt in any one direction. More complex analysis would be required to consider an arbitrary interface.

3. Methods

Here we discuss the numerical and computational methods followed by the experimental methods that we used to validate the solution developed in Section 2.

A. Forward and Inverse Methods

The newly developed analytical solution needs to be validated with an established method. In this section we discuss the forward simulations using the Monte Carlo method for light propagation in a two-layer tissue structure with a tilted interface and a nonlinear regression technique (inverse method) that will be used later in the paper to obtain the optical coefficients of the layered structure from measured reflectance or calculated reflectance from a two-layer tissue structure.

1. Monte Carlo Simulations—The Monte Carlo (MC) method for light propagation in layered structures was used to validate our analytical model.^{18–20} The layered structure is chosen as shown in Fig. 1. The general methodology used here is the same as reported in Ref. ¹⁴, except for the introduction of a tilt at the interface between the layers. In addition, time domain computation is adopted to obtain a reflectance measurement at the modulation frequency through the Fourier transform used in phantom and clinical experiments. In our simulation, 100 million photons were generated at a source location and the scattering angle was calculated using the Henyey–Greenstein function. The anisotropy factor g was chosen to be 0.9 in this simulation. The weight of this photon was decreased due to the absorption and scattering processes. For every scattering event where the calculated step size (s) (along a particular direction) caused a photon to cross the boundary between two layers, the photon

was first propagated to the point where its trajectory intersected the boundary via a shortened step size (s_1). When the boundary was parallel with the incident surface, the angle of incidence was computed with respect to the $\pm z$ axis and used to determine whether the photon experienced total internal reflection (from Snell's law). If the photon was internally reflected, then the z component of the photon's travel direction was reversed and the photon completed the remainder of the step ($s - s_1$) in the same layer. Otherwise, the reflection coefficient from Fresnel's equations was computed and compared against a uniformly generated random number. If the random number was less than the reflection coefficient, the photon experienced total internal reflection; otherwise it was transmitted to the next layer. On transmission into a different layer, the final spatial location of the photon was calculated by propagating the photon with a distance of $s - s_1$ that was adjusted in length according to the difference in total interaction coefficients between the two layers, and its direction was corrected to consider refraction by Snell's law. When the boundary is tilted, the propagation principle at the boundary is the same as the parallel boundary; however, the computation is more complex. For example, the angle of incidence, the angle of reflection, and the angle of refraction are all calculated based on the normal line of the titled interface in three dimensions. First, a plane A is established by the normal line of the titled interface and the incident photon direction. Then Snell's Law is applied to calculate the reflection or refraction angle in plane A. The calculated reflection or refraction angle is then converted to the azimuthal angle in the original (x, y, z) coordinates.

This MC simulation was performed in the time domain and the resulting data was Fourier transformed to provide amplitude and phase profiles at multiple modulation frequencies as a function of source-detector distance. A spatial resolution of 1 mm is chosen and the temporal resolution varies with the distance to the source, d . When d is less than 1 cm, between 1 and 2 cm, between 2 and 5 cm, or larger than 5 cm, the temporal resolution is chosen as 1, 3, 7, and 10 ps, respectively. The computation error in the simulation can be approximated as $1/\sqrt{n}$, where n is the number of received photons. For different temporal resolution ranges, the corresponding errors are 0.1%–0.5%, 0.5%–1.5%, 1.5%–7.0%, and 7%–15%, respectively.

2. Nonlinear Regression Method—To obtain the optical coefficients μ_{a1} , μ_{s1} , μ_{a2} , and μ_{s2} , a nonlinear regression method based on the Nelder–Mead simplex algorithm^{21,22} was used to simultaneously fit the amplitude and phase obtained from the MC simulations with the analytical solution. The Nelder–Mead simplex method is a widely used direct searching method for multidimensional unconstrained minimization. It tries to minimize a scalar-valued nonlinear function of multiple independent parameters by using only the function values. This algorithm has been previously used for estimation of tissue properties from layered tissue structure models⁹ and has been chosen due to its simplicity and good convergence in spite of the slow convergence rate. The thickness of the upper layer and the tilt angle are assumed to be known. In our experiments and clinical studies using the combined ultrasound and optical probe, the upper layer thickness and the interface tilting angle can be estimated with sufficient accuracy using the ultrasound image. The data collected between source-detector separations of 2.0 to 6.5 cm were used to perform the fitting. For each case, various initial values were used to avoid any local minima and to estimate the correctness of the converged value.

B. Experimental Methods

1. Phantom Experiments—The experimental validation of the analytical solution was performed using an existing frequency domain near-infrared (NIR) system. This system was a modified version of the system reported in Ref. ²³. It consisted of a triwavelength laser diode source of 660, 780, and 830 nm wavelengths. The outputs of the laser diodes were

amplitude modulated at 140 MHz. A single detector fiber coupled to one photomultiplier tube (PMT) detector was placed at multiple locations from 2 to 6.5 cm away from the source. Solid silicone phantoms were used to emulate the second layer over which intralipid solution was used to emulate the top layer. In phantom experiments, the layer depth and tilting angle are known, unlike in the case of clinical studies where coregistered ultrasound is used to estimate breast tissue thickness and chest-wall orientation.

2. Clinical Studies—The study protocol was approved by a local Institutional Review Board. Signed informed consent was obtained from all patients who agreed to participate in the study. In clinical experiments, NIR optical source fibers, detector fibers, and a commercial ultrasound transducer were integrated on a handheld probe.^{24,25} The handheld probe is circular in shape and 10 cm in diameter. Twelve dual-wavelength (780, 830 nm) laser diodes were used to sequentially illuminate the breast, and eight parallel PMT detectors were used to simultaneously detect the reflected light. Patients were scanned in a supine position while multiple sets of optical reflectance measurements were made with coregistered ultrasound images at lesion locations and symmetric locations of the contralateral normal breast. The measurements obtained at normal locations were used to estimate background optical properties, which were used to compute a weight matrix for imaging. Thus accurate estimation of background optical properties is important for improving the accuracy of tumor imaging. The geometry used for a clinical experiment is not quite the same as the configuration used in deriving the analytical solution. However, since our combined probe has 75% of the sources distributed on one side of the central ultrasound probe,²⁵ this portion of the source-detector pair configuration approximates better the configuration used in analytical and MC simulations. The corresponding amplitude and phase profiles were used to estimate the background optical properties reported in Subsection 4.E.

The optical properties of the chest wall are not available in the literature. The only available data are the optical properties of muscles and bones. Muscle was reported to have a large absorption and medium scattering coefficients with μ_a in the range of 0.12 to 0.25 cm^{-1} and μ_s in the range of 3 to 10 cm^{-1} .^{26–31} Bone is a highly absorbing and scattering medium. The reported optical properties of bone are $\mu_a = 0.23 \text{ cm}^{-1}$ and $\mu_s = 21.4 \text{ cm}^{-1}$.^{32,33} By assuming various ratios of muscle and bone components as representations of the chest wall, we choose optical properties of μ_a in the range of 0.12 to 0.23 cm^{-1} and μ_s in the range of 3 to 22 cm^{-1} in the reported studies. Throughout this paper, a range of second layer μ_a values was chosen for the purpose of investigating the possible effects of different types of chest-wall layers (more muscular or bony), which may vary from patient to patient.

4. Analysis and Results

In this section we first validate the analytical solution derived in Section 2 using MC simulations (in Subsection 4.A) and phantom measurements (in Subsection 4.B). In Subsection 4.C we discuss the influence of varying the tilting angle at the interface on the reflectance measured at the tissue surface. In Subsection 4.D we show the inverse calculations using the analytical solution to simultaneously obtain average optical properties of both tissue layers. In Subsection 4.E, we demonstrate the use of the analytical solution to obtain the average optical properties of breast tissue and chest-wall layers from *in vivo* clinical data.

A. Comparison of Analytical Solution with Monte Carlo Results

We chose a set of tissue parameters to validate our analytical results with MC simulations of two-layer tissue structures with tilted or flat interfaces and present representative cases here. A linear array of source-detector arrangements chosen was the same as that used in

obtaining the analytical solution. Figures 1 and 2 show a comparison of the analytical solution and MC simulations for different second-layer absorption coefficients μ_{a2} and reduced scattering coefficients μ_{s2} for both tilted and nontilted interfaces. For tilted cases, the maximum layer thickness was 2 cm (where the source is positioned), and the thickness of the layer reduces to 0.38 cm for the detector placed at 7 cm. Data were obtained from source-detector separation from 0.5 to 7 cm. Of the two cases chosen, the first case was assumed to have upper-layer properties (μ_{a1} and μ_{s1}) that are typically obtained from dense breast tissues and lower-layer properties, which could represent the chest-wall layer with significant bone components (relatively lower μ_{a2} and higher μ_{s2}). The second case has the same μ_{a1} and μ_{s1} as the first case but with higher μ_{a2} and μ_{s2} , which could represent a chest-wall layer with significant muscle and bone components. Good agreement has been obtained for both methods. The MC calculation for case 1 with the tilted interface has used a uniform resolution of 5 ps for all source detector separations. This is because the resolution of 10 ps chosen for larger source-detector separation used for other cases seemed to be insufficient for this case with an extremely low absorption of the chest-wall layer when it is very close to the surface at larger source-detector separation (due to the tilt). Higher resolution and larger photon numbers chosen for better accuracy would result in a long computation time.

B. Experimental Validation of the Analytical Solution

Experimental measurements of the two-layer phantoms were made with and without tilt at the interface to validate the analytical results. The solid phantom used for the second layer had calibrated optical properties of $\mu_a = 0.01 \text{ cm}^{-1}$ and $\mu_s = 14 \text{ cm}^{-1}$ and a refractive index of 1.55. Intralipid solution was used as the top layer, thus making it easy to change the layer thickness whose refractive index is close to that of water ~ 1.33 . The top layer had optical properties of $\mu_a = 0.11 \text{ cm}^{-1}$ and $\mu_s = 8.3 \text{ cm}^{-1}$ and a refractive index of 1.33. Figure 3 shows the reflectance measured at 780 nm for the two-layer phantom with and without a tilted interface. In the absence of tilt, the upper layer thickness was 1.5 cm. The tilted case shown is for a tilting angle of 10° for which the layer thickness reduces to 0.35 cm for a source-detector separation of 6.5 cm. When the interface is tilted, the second layer comes closer to the tissue surface for larger source-detector separation. Here the amplitude measured at larger source-detector separation is higher for the tilted case compared with the flat interface case, mainly because of the lower absorption of the second layer ($\mu_a = 0.01 \text{ cm}^{-1}$) compared to that of the first layer ($\mu_a = 0.11 \text{ cm}^{-1}$). The phase measurements at larger distances increase faster for the tilted case compared with the flat interface mainly because of the higher scattering of the second layer.

C. Change in Reflectance with Varying Tilt at the Interface

In this subsection we show the effect of varying the interface tilting angle on the measured reflectance obtained from a two-layer tissue structure. We have analyzed two types of layered structures. The first case has a lower and the second has a higher absorbing second layer in comparison with the absorption coefficient of the first layer. A typical case of a maximum layer thickness of 1.5 cm is chosen with varying tilting angles from 0° to 11° . Here a maximum source-detector separation of 6.5 cm is chosen for which the upper-layer thickness would be as small as 0.24 cm for an 11° tilt. In case 1, the tissue parameters chosen are close to those used in the phantom experiment, which was discussed in Subsection 3.B. From Fig. 4, we can see that when the second layer is of relatively lower absorption (case 1, $\mu_{a2} < \mu_{a1}$), the effect of tilt is more prominent on the measured reflectance phase, and when the second layer is of relatively higher absorption (case 2, $\mu_{a2} > \mu_{a1}$), the effect of tilt is more prominent on the reflectance amplitude. This is because when the second layer is less absorbing, the light diffusing into this layer accumulates phase difference due to the longer optical path it takes, resulting in a higher phase difference when

the tilting angle is larger. For a higher absorbing second layer, most of the light penetrating into this layer gets absorbed resulting in a relatively lower amplitude with increasing tilt. In this case, the major part of the detected signal is from the photons that have traveled only in the top layer, showing smaller change in a measured phase with a varying tilting angle. Thus it is important that both the amplitude and the phase data are simultaneously used for fitting while reconstructing the optical properties of a two-layer structure with a tilted interface.

D. Estimation of the Optical Coefficients Using the Analytical Solution

In this subsection we use the analytical solution derived in Section 2 and nonlinear regression to estimate the two-layer tissue optical properties from the data obtained from the MC simulations. Figure 5(a) shows a plot of the estimated absorption coefficient of the first layer versus the actual absorption coefficient of the second layer, which is varied from 0.02 to 0.11 cm^{-1} . Figure 5(b) shows the estimated absorption coefficient of the second layer versus the actual values for the same cases as in Fig. 5(a). For all the cases in Fig. 5, the absorption coefficient of the first layer is chosen as 0.05 cm^{-1} , the reduced scattering coefficients of the first layer and the second layer are 5 and 10 cm^{-1} , respectively. It can be seen that when the tilting effect is ignored in the estimation process, the error in calculating the absorption coefficient of the first layer increases by at least 15% and could be as large as 80% depending on the optical properties of both layers, whereas the error in estimating the absorption coefficient of the second layer is seen to increase by at least 10% and could be as high as 60% when the tilting effect is neglected. For inverse calculation neglecting the tilting effect, the first layer thickness is chosen as the average layer thickness as seen by the detection probe, which seems to yield the best results if the tilting is being ignored. Figure 6(a) shows the estimated reduced scattering coefficient of the first layer with and without considering the tilting effect versus the actual reduced scattering coefficient of the second layer, which is varied from 8 to 14 cm^{-1} . Figure 6(b) shows the estimated reduced scattering coefficient of the second layer with and without considering tilt versus the actual reduced scattering coefficient for the cases shown in Fig. 6(a). In all the cases shown in Figs. 5 and 6, the angle of tilt is 7° and the maximum thickness of the first layer is 1.2 cm, which would reduce to 0.34 cm for the maximum source-detector separation at 7 cm. It can be seen that, in comparison to the inverse calculation considering the tilting effect at the interface, the error in estimating the scattering coefficient of the first layer increases by at least 8% and could be as high as 20% when the effect of tilt is neglected, whereas the error in estimating the second-layer reduced scattering coefficient increases by at least 15% and could be as high as 40% when the effect of tilt is ignored. The data obtained at source-detector separations above 2 cm is used for fitting. The first-layer absorption coefficient is usually obtained accurately when the tilt is considered and with a higher estimation error when the tilting effect is ignored. The error is larger for the cases when the absorption or reduced scattering coefficient of the second layer is relatively lower.

Estimation error in the scattering coefficient of the second layer is less than 20% and that of the absorption coefficient is less than 15% when the tilting effect is considered. We have noticed that these percentages may vary slightly, with one of the coefficients estimated with higher accuracy, whereas the accuracy of the other coefficient is reduced.

E. Use of the Analytical Solution to Estimate Average Tissue Optical Properties From Clinical Data

In this subsection we show the use of the two-layer model to estimate the background tissue optical properties from clinical data. We present the inverse calculations to the data obtained from one 52-year-old patient and another 21-year-old patient under study. Figure 7 shows an ultrasound image obtained from the normal breast of the first patient. The breast tissue thickness is about 1.25 cm, and the data collected from both wavelengths were used to

obtain the optical properties of the breast tissue and the chest-wall layer at 780 and 830 nm. Table 1 shows the estimated average optical properties of the breast tissue (μ_{a1} and μ_{s1}) and those of the chest wall (μ_{a2} and μ_{s2}). The optical properties were reasonable and consistent at both wavelengths. Figure 8 shows the ultrasound image obtained from the second patient in which the tilted chest wall can be seen clearly. The tilt is about 6° with a maximum breast tissue layer thickness of 1.75 cm reducing to as small as 1 cm.

Table 2 shows the average optical properties estimated from measurements using the average layer thickness of 1.4 cm with the tilting angle ignored, whereas Table 3 shows the average properties estimated by using the measured 6° tilt. It is interesting to note that after considering the tilt, the average absorption and reduced scattering coefficients seem to follow the general trend that we have observed from many normal breasts: The average absorption coefficient measured at 830 nm is in general higher than that obtained at 780 nm, but the reduced scattering coefficient is in general lower than that obtained at 780 nm.

5. Discussion and Summary

We have developed an analytical solution for light propagation in two-layered tissue structures with a tilted interface and validated it using MC calculations and phantom experiments with good agreement in the results. Using this solution, we have analyzed the effect of varying the interface tilting angle on the reflectance measurements of two-layer structures. We have observed that the effect of tilt results in increased deviation in phase or amplitude measurements as compared to the nontilted case depending on whether the lower layer has lower or higher optical absorption. A nonlinear regression method has been used to estimate the two-layer optical properties from the MC data. Our results show that ignoring the tilting effect could result in errors in the estimation of optical properties of both tissue layers. For the typical cases that we considered, where the maximum upper layer thickness was about 1.5 cm or less, we have observed higher errors in the estimation of the upper-layer optical properties when the tilt is ignored. This could be crucial in imaging smaller breasts where the chest-wall interface may be tilted with respect to the measurement probe.

Coregistered ultrasound images can provide the breast–chest interface depth and tilting angle in real time. The probe geometry used to collect data was not exactly the same as the geometry used in deriving the analytical solution, but the consistent background optical properties obtained from two optical wavelengths from each patient indicate the robustness of the two-layer model and the nonlinear regression method. Further studies are planned to obtain more data sets from selected patients with smaller breasts at multiple locations of different breast tissue–chest wall orientations to validate the technique. With the better accuracy in estimating tissue background optical properties for two-layer structures with tilted interfaces, the next step is to develop robust image reconstruction algorithms using either an analytical solution or a numerical method for the layered medium. Currently, we are working in this direction.

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Fig. 1. Schematic of a two-layer tissue structure with tilted interface. RM is the normal to the tilted surface, and we assume $n_2 > n_1$.

Fig. 2.

Comparison of analytical and MC calculations for a two-layer structure. (a) Amplitude plots and (b) phase plots for case 1, $\mu_{a1} = 0.05 \text{ cm}^{-1}$, $\mu_{s1} = 6 \text{ cm}^{-1}$, $\mu_{a2} = 0.02 \text{ cm}^{-1}$, $\mu_{s2} = 15 \text{ cm}^{-1}$, and case 2, $\mu_{a1} = 0.05 \text{ cm}^{-1}$, $\mu_{s1} = 6 \text{ cm}^{-1}$, $\mu_{a2} = 0.08 \text{ cm}^{-1}$, $\mu_{s2} = 30 \text{ cm}^{-1}$. For the tilted case the first layer maximum thickness is 2 cm with a 13° tilting angle at the interface.

Fig. 3. Phantom measurements compared with analytical results for tilted and nontilted interface. (a) Amplitude plots and (b) phase plots.

Fig. 4. Simulated (a) amplitude and (b) phase plots for two-layer structures with varying tilting angles (circle, 4°; star, 8°; diamond, 11°) for case 1, $\mu_{a1} = 0.1 \text{ cm}^{-1}$, $\mu_{s1} = 6$, $\mu_{a2} = 0.01 \text{ cm}^{-1}$, $\mu_{s2} = 14 \text{ cm}^{-1}$, and case 2, $\mu_{a1} = 0.05 \text{ cm}^{-1}$, $\mu_{s1} = 6 \text{ cm}^{-1}$, $\mu_{a2} = 0.09 \text{ cm}^{-1}$, $\mu_{s2} = 14 \text{ cm}^{-1}$. The dashed line and the solid line represent reflectance at zero-degree tilt for case 1 and case 2, respectively.

Fig. 5.

Estimated absorption coefficient of (a) the first layer (μ_{a1}) and (b) the second layer (μ_{a2}) determined by nonlinear regression of the analytical solution to MC data plotted versus the true value of the absorption coefficient of the second layer (μ_{a2}). Parameters chosen for MC simulations are a maximum layer thickness of 1.2 cm, an interface tilt of 7° , $\mu_{a1} = 0.05 \text{ cm}^{-1}$, $\mu_{s1} = 5 \text{ cm}^{-1}$, $\mu_{s2} = 10 \text{ cm}^{-1}$, and μ_{a2} varying from 0.02 to 0.11 cm^{-1} . The solid line indicates the true value, stars represent the estimated values considering the interface tilt, and squares represent the estimated values ignoring the interface tilt.

Fig. 6.

Estimated reduced scattering coefficient of (a) the first layer (μ_{s1}) and (b) the second layer (μ_{s2}) determined by nonlinear regression of the analytical solution to MC data plotted versus the true value of reduced scattering coefficient of the second layer (μ_{s2}). Parameters chosen for MC simulations are a maximum layer thickness of 1.2 cm, an interface tilt of 7° , $\mu_{a1} = 0.05 \text{ cm}^{-1}$, $\mu_{s1} = 5 \text{ cm}^{-1}$, $\mu_{a2} = 0.08 \text{ cm}^{-1}$, and μ_{s2} = varying from 8 to 14 cm^{-1} . The solid line indicates the true value, stars represent the estimated values considering the interface tilt, and squares represent the estimated values ignoring the interface tilt.

Fig. 7.
(Color online) Ultrasound image obtained from a 52-year-old patient with an effective breast tissue thickness of 1.25 cm at the breast tissue–chest wall interface marked by the array of white arrows.

Fig. 8.

Ultrasound image obtained from a 21-year-old patient showing a maximum breast tissue thickness of about 1.75 cm reducing to 1 cm with a tilt angle of 6° . The breast tissue–chest wall interface is marked by the array of white arrows. The horizontal scale is 6.5 cm.

Table 1
Estimated Background Absorption and Reduced Scattering Coefficient of Breast Tissue and Chest Wall^a

Measurement	μ_{a1} (cm ⁻¹)	μ_{s1} (cm ⁻¹)	μ_{a2} (cm ⁻¹)	μ_{s2} (cm ⁻¹)
780 nm	0.0797	4.21	0.182	17.66
830 nm	0.070	4.07	0.179	18.31

^aTaken from the optical reflectance measurement of the first patient with the corresponding ultrasound image shown in Fig. 7.

Table 2
Estimated Background Absorption and Reduced Scattering Coefficient of Breast Tissue and Chest Wall^a

Measurement	μ_{a1} (cm ⁻¹)	μ_{s1} (cm ⁻¹)	μ_{a2} (cm ⁻¹)	μ_{s2} (cm ⁻¹)
780 nm	0.0426	9.799	0.0768	15.556
830 nm	0.0420	10.04	0.0799	11.578

^aTaken from the optical reflectance measurement of the second patient with the corresponding ultrasound image shown in Fig. 8. The results shown are from using an average layer thickness of 1.4 cm.

Table 3
Estimated Background Absorption and Reduced Scattering Coefficient of Breast Tissue and Chest Wall^a

Measurement	μ_{a1} (cm ⁻¹)	μ_{s1} (cm ⁻¹)	μ_{a2} (cm ⁻¹)	μ_{s2} (cm ⁻¹)
780 nm	0.052	9.75	0.079	12.4
830 nm	0.073	6.8	0.13	9.93

^aTaken from the optical reflectance measurement of the second patient with the corresponding ultrasound image shown in Fig. 8. The results shown are from using measured tilt from the ultrasound image.