Tomographic reconstruction of layered tissue structures

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ABSTRACT

In recent years the interest in the determination of optical properties of layered tissue structure has resurfaced. Applications include, for example, studies on layered skin tissue and underlying muscles, imaging of the brain underneath layers of skin, skull, and meninges, and imaging of the fetal head in utero beneath the layered structures of the maternal abdomen. In this work we approach the problem of layered structures in the framework of model-based iterative image reconstruction schemes. These schemes are currently developed to determine the optical properties inside tissue from measurement on the surface. If applied to layered structure these techniques yield substantial improvements over currently available semi-analytical approaches.

Keywords: Image reconstruction techniques, layered structures, tomography; turbid media

1. INTRODUCTION

Most biological tissues consist of layers that have different optical properties. For example, layered tissue structure can be found in the skin, the esophagus, or the human head. Layers can be as thin as a few microns, such as the endothelial cell layer that covers the interior of arteries, and as thick as a centimeter, such as the skull that encapsulates the brain. Understanding how light propagates in layered tissue structures is important in many diagnostical and therapeutical applications and several researchers have sought an understanding of how light propagates. In 1979, Takatani and Graham [1] first presented theoretical results based on diffusion theory for the steady-state diffuse reflectance from a two-layer system. Keijzer *et˚al* [2] approached the problem of layers with different refractive indices. Nossal and Taitelbaum [3,4] developed a three-dimensional lattice random-walk algorithm to study systems whose top layer has either a higher or lower absorption coefficient than the underlying medium. Schmitt *et˚al* [5] generalized the approach of Takatanis and Graham [1] to a multilayer model of photon diffusion in skin by including reflections from boundaries. Cui and Ostrander [6] developed a three-dimensional photon-diffusion finite-difference model to study steady-state photon-migration in layered tissues. Hielscher et al [7] theoretically and experimentally investigated time-resolved photon emission from layered turbid media. More recently several researchers have tried to develop algorithms that allow for the determination of optical properties of layered structures from backscattering measurements. [8,9,10,11,12,13] All these works assume knowledge of the thickness of the layers and often derive analytical or semi-analytical solutions for semi-infinite layered structures.

In this work we approach the problem of layered tissues within the framework of a model-based iterative image reconstruction scheme (MOBIIR). [14,15,16,17,18,19] These schemes are currently widely applied in the field of diffuse optical tomography (DOT). In this field one tries to obtain optical properties of large tissues, such as the breast, brain, or limbs, from measurements taken on the circumference. Surprisingly no studies have been performed so far that use these optical-tomographic methods for layered tissue structures. In this work we implemented and tested an optical tomographic image reconstruction scheme for layered media. It is shown that with the information of layered structures the optical properties of multi layered tissues can be determined with high accuracy, often even when no knowledge of the number and thickness of layers is available.

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2. METHODS

In general, model-based iterative image reconstructions schemes [14-19] consist of three major parts: (1) a forward model that predicts the detector readings based on a given spatial distribution of optical properties, (2) an objective function Φ that compares the predicted with measured signals and (3) an updating scheme that uses the gradient of the objective function with respect to the optical properties to provide optical parameters for subsequent forward calculations.

As a forward model to predict the detector readings we employ for this study the time-resolved diffusion equation,

$$\frac{\partial \Phi(\mathbf{r},t)}{\partial t} = \frac{\partial}{\partial x}\left(D(\mathbf{r}) \frac{\partial \Phi(\mathbf{r},t)}{\partial x} \right) + \frac{\partial}{\partial y}\left(D(\mathbf{r}) \frac{\partial \Phi(\mathbf{r},t)}{\partial y} \right) + \frac{\partial}{\partial z}\left(D(\mathbf{r}) \frac{\partial \Phi(\mathbf{r},t)}{\partial z} \right) - c\mu_a(\mathbf{r})\Phi(\mathbf{r},t) + S(\mathbf{r},t). \tag{1}$$

Here $\Phi(\mathbf{r},t)$ is the fluence [Wcm^{-2}] and $S(\mathbf{r},t)$ is the source strength at position $\mathbf{r} = (x,y,z)$ and time t. The position-dependent absorption and diffusion coefficients are denoted by $\mu_a(\mathbf{r})$ and $D(\mathbf{r})$ respectively. The speed of light in the medium is represented by c. The diffusion coefficient is defined as $D(\mathbf{r}) = c[3\mu_a(\mathbf{r}) + 3(1-g(\mathbf{r}))\mu_s(\mathbf{r})]^{-1}$, where g is the scattering anisotropy value, equal to the average value of the cosine of the angle through which photons are scattered.[20] The coefficient $\mu_s'(\mathbf{r}) = (1-g(\mathbf{r}))\mu_s(\mathbf{r})$ is called the effective or transport scattering coefficient.

We use a finite-difference discretization scheme to numerical solve Eq. 1. [15] For this numerical study we chose zero boundary condition, however other boundary conditions are also available (e.g. Robin boundary conditions). The solution of the forward model for a given distribution of optical properties, $\mu_a(\mathbf{r})$ and $D(\mathbf{r})$, provide the predicted detector readings $P_{s,d,t} := P_{s,d,t}(\mu_a(\mathbf{r}), D(\mathbf{r}))$ for a given source s, detector d, and time point t, on the surface of the medium. These predictions are compared to measurements $M_{s,d,t}$ through an objective function defined by

$$\Theta(\mu_a(\mathbf{r}), D(\mathbf{r})) = \sum_s \sum_d \sum_t \left(\frac{M_{s,d,t} - P_{s,d,t}(\mu_a(\mathbf{r}), D(\mathbf{r}))}{M_{s,d,t}} \right)^2 . \tag{2}$$

Starting with an initial guess ($\mu_a(\mathbf{r})$, $D(\mathbf{r})$), the values of ($\mu_a(\mathbf{r})$, $D(\mathbf{r})$) are iteratively updated, by calculating the gradient of the objective function Θ with respect to each unknown $\mu_a(\mathbf{r})$ and $D(\mathbf{r})$,

$$\begin{aligned} \frac{\partial \Theta(\mu_a(\mathbf{r}), D(\mathbf{r}))}{\partial(\mu_a(\mathbf{r}), D(\mathbf{r}))} &= \left(\frac{\partial \Theta(\mu_a(\mathbf{r}), D(\mathbf{r}))}{\partial \mu_a(\mathbf{r})}, \frac{\partial \Theta(\mu_a(\mathbf{r}), D(\mathbf{r}))}{\partial D(\mathbf{r})} \right) \\ &= \left(\frac{\partial \Theta}{\partial \mu_a(r_1)}, \frac{\partial \Theta}{\partial \mu_a(r_2)}, \ldots, \frac{\partial \Theta}{\partial \mu_a(r_K)}, \frac{\partial \Theta}{\partial D(r_1)}, \frac{\partial \Theta}{\partial D(r_2)}, \ldots, \frac{\partial \Theta}{\partial D(r_K)} \right) \end{aligned} \tag{3}$$

(K = number of unknowns in problems). This is most efficiently done by the method of adjoint differentiation [15,17,18,21,22]. Once the gradient (Eq. 3) is known a line-minimization along the direction of the gradient is performed within the K-dimensional search space. Once a minimum of Θ along this direction is found a new gradient is calculated and a new search direction for the line-minimization is determined using well know conjugated gradient schemes. This procedure is repeated until a minimum of Θ is found. A more detailed description concerning this method was previously presented by Hielscher et al [15].

When layered tissue structures are considered the MOBIIR scheme can be adjusted as follows. Consider a 2-dimensional medium which is discretized into NxN pixels (Fig. 1a). In the most general case this problem has 2xNxN unknows, because each pixel can take on different values of μ_a and D. Therefore the gradient (Eq. 3) of the objective function is a vector of length 2xNxN. The values of μ_a and D are updated for each pixel separately. If one knows that the medium is layered one can combine all N pixels in one row to one large "row-pixel" (Fig. 1b). In this way the number of unknowns is reduced by a factor of N. The gradient (Eq. 3) of the new problem is now a vector of length 2xN. Therefore the optical properties are updated for an entire row in the same way. Further simplification of the problem can be achieved, when the number of layers and their respective thicknesses are known. In this case all rows belonging to one layer can be combined to one "layer-pixel" (Fig. 1c), and the number of unknowns is further reduced to 2xM < 2xN. Therefore, the knowledge about a layered structure of the medium results in a reduction of the dimensionality of the minimization problems.

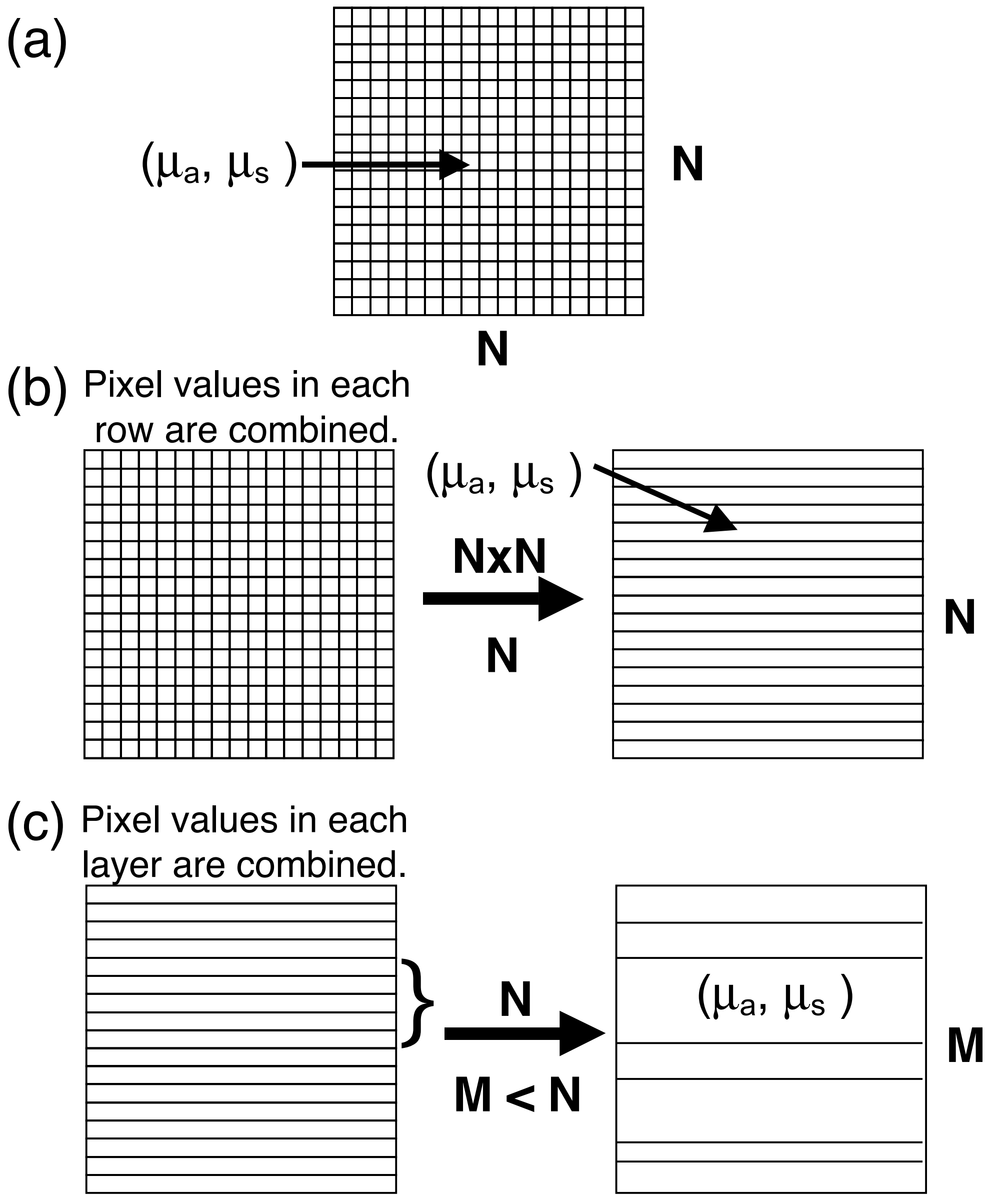

Fig. 1: Illustration of how knowledge about layered tissue structure reduces dimensionality of minimization problem in model-based iterative image reconstruction (MOBIIR) schemes. (a) In the most general case, the medium needs to be discretized into NxN pixels. Each pixel can take on different values for μ_a and D, which lead to 2xNxN unknowns. (b) If it is *a priori* known that medium is layered, the number of unknowns reduces by a factor of N. (c) When the number and position of layers are known, the problem reduces further to 2xM<2XN variable parameters. Therefore instead of iteratively updating 2xNxN parameters, the problem reduces to updating 2xM parameters.

In practice, the calculation of a gradient with 2xNxN unknowns does not slow down the image reconstruction process compared to a gradient calculation for 2xM unknowns. In gradient-based MOBIIR schemes that employ a line-minimization step, most of the computational effort lies in the numerous forward calculations. Because convergence criteria require a small enough mesh size, the forward calculation has to be performed on a NxN grid even when M layers with only 2xM optical parameters are considered. Therefore, instead of calculating the gradient for 2xM parameters, it is also possible to calculate all 2xNxN components of the gradient vector, average the gradient components belonging to one layer, and update the optical properties for each pixels belonging to that layer in the same way. The results shown in this work were obtained in this fashion.

3. RESULTS

To show how this scheme can be employed for the reconstruction of layered media, we first generated synthetic data using the exact distribution of optical properties. Then we started the iterative reconstruction algorithms with a homogeneous distribution of optical properties as a first guess. Three different updating procedures were used to recover the original distribution of optical properties. First, the optical properties in each pixel of the image were updated independently (Fig. 1a). Therefore no information about the layered structure of the tissue was used. Second, we updated

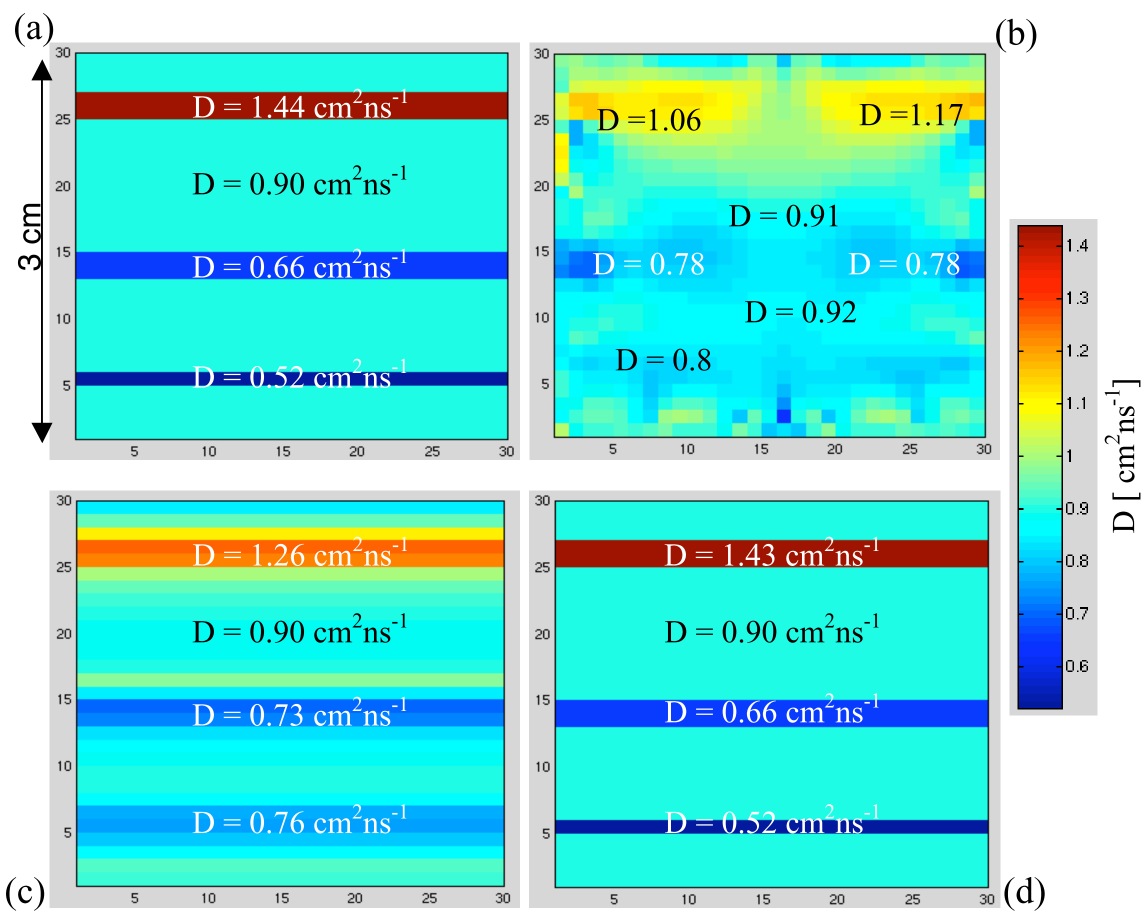

Fig. 2. Reconstruction results assuming different degrees of knowledge about medium. a) Original distribution of optical properties. The gray and black dots on the circumference indicate source and detector positions, respectively. b) Image reconstruction result assuming no knowledge about layered structure. Starting from an initial guess of D = 1 cm^2ns^{-1}. Each of the 30x30 = 900pixel is updated independently. c) Image reconstruction result assuming knowledge that medium is layered. All pixels in one row are updated simultaneously. d) Image reconstruction result assuming knowledge about position and thickness of layers. Therefore only 7 different values are updated in MOBIIR scheme using the gradient of the objective function (Eq. 3).

the optical properties of all the pixels in one row together (Fig. 1b). This is equivalent to assume that the medium has a layered structure, but no information about the number of layers or layer thickness is available. Third, we assumed that the number of the layers and the exact thickness of each layer is known (Fig. 1c). In this case the optical properties within each layer were updated.

Figure 2 shows the results for an example of a layered structure. Given is a cube of 3x3x3cm, which contains 7 layers. Four layers have the same diffusion coefficient $D = c/(3\mu_a + 3\mu_s') = 0.9$ cm^{2}ns^{-1}, while the values of the other layers are D = 1.44 cm^{2}ns^{-1}, D = 0.66 cm^{2}ns^{-1}, and D = 0.52 cm^{2}ns^{-1}. The absorption coefficient is considered constant μ_a = 0.1 cm^{-1}. The medium is surrounded by one source on each side and 24 equally spaced detectors (Fig. 2a) The MOBIIR scheme is started with an initial guess of D = 1.00 cm^{2}ns^{-1}. Fig. 1b, 1c, and 1d show the reconstruction result for the three different cases after 10 iterations. It can be seen that the more information is available the better the reconstruction results. If the number and thickness of the layers are known, almost perfect reconstructions of the optical properties can be achieved. In this case the number of unknowns is reduced from 30x30=900 pixel values in Fig. 2b to the 7 different D values in Fig. 2d. Even when we don't know the exact number of layers the reconstruction results are reasonable (Fig. 2c). In this case we have 30 unknowns. Similar results are obtained if layered variations in μ_a are considered.

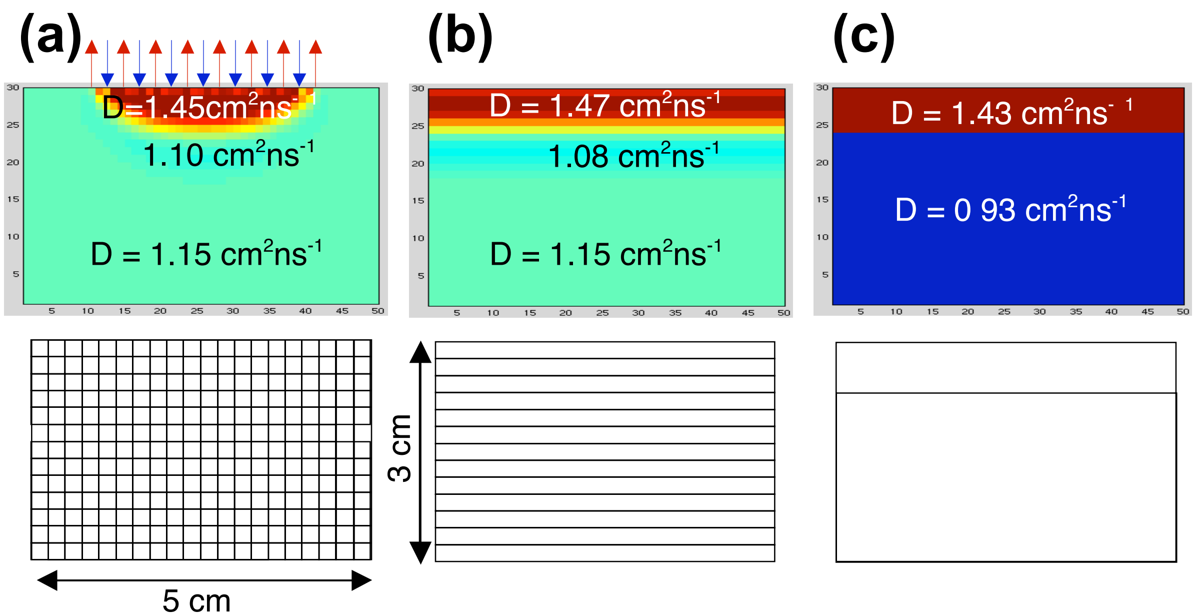

Fig.3: Reconstruction of a layered medium using only backscattering data. Shown is a cross-section through a 5x3cm medium, which consists of a 0.6-cm-thick top layer and a 2.4-cm-thick bottom layer. (a) Image reconstruction result assuming no knowledge about layered structure. Each of the 30x50 = 1500 pixels are updated independently. (Also shown are positions of 8 source and 7 detectors on the top of the medium.) (b) Image reconstruction result assuming knowledge that medium is layered. All pixels in one row are updated simultaneously. (c) Image reconstruction result assuming knowledge about thickness of layers. Therefore only 2 different values are updated.

In biomedical application on often encounters the situation that only backscattered data is available. Therefore, we also studied how our approach performs in this case. As an example we considered a 5x5x3cm medium, which consist of a 0.6 cm top layer with D = 1.44 cm^{2}ns^{-1} and a 2.4 cm bottom layer with D = 0.90 cm^{2}ns^{-1}. The absorption coefficient was considered constant μ_a = 0.1˚cm^{-1}. Eight source and 7 detectors where placed along a line on the surface of the medium (Fig. 3a). The MOBIIR reconstruction scheme was started with a value of D = 1.15 cm^{2}ns^{-1}, which lies inbetween the value for the top layer and the value for the bottom layer. Figure 3a shows the reconstruction result for the case of now information about the layers. The optical property of the top layer, just underneath the sources and detectors, is reconstructed with high accuracy. However, the D value of the lower layer is not recovered. Here the value stays very close to or equal to the initial guess, which indicates that the gradient (Eq. 3) in this area is very small and changes of these pixels values do not influence the objective function (Eq. 2). The image reconstruction improves slightly when a layered structure is assume (Fig. 3b). Now we find good *D*-values for the entire width of the top layer, however, values for the lower layer are still very close to the initial guess. When the thickness of the top layer is known, and the problem reduces to 2 unknowns, the MOBIIR algorithm recovers the optical properties with high accuracy (Fig. 3c).

Different measurement geometries may also aid in the recovery of optical propertied from layered media. This is illustrated in Fig. 4, where a layered medium with a 2-cm-thick top layer and a 4-cm-thick bottom layer is considered. The absorption coefficient of the top layer is μ_a = 0.08 cm^{-1}, and the bottom layer has a μ_a = 0.15 cm^{-1}. In this example μ_s' was kept constant at μ_s' = 8 cm^{-1}. The reconstruction problem is approached in two steps. First, only source-detector pairs with separation smaller than 5 cm are used (Fig. 4a) to define the objective function in Eq. 2. The iterative reconstruction process is started with an initial guess of μ_a = 0.12 cm^{-1} for all pixels in the image. The properties of the top layer are recovered with high accuracy, while the optical properties of the lower layer remain close or equal to the initial guess. The gradient (Eq. 3) for pixels in the lower layer is almost zero, which indicates that these points have little influence on the value of the objective function (Eq. 2). In a second step, the optical properties of the top layer are set to the value found in the first step and detector reading from source and detectors further apart are used to define the objective function (Eq. 2). The iterative reconstruction process is started with the result from the first step. In this second step the new objective function depends strongly on the optical properties of the lower layer, the gradient with respect to these parameters is large, and the optical properties of the lower layer are recovered nicely (Fig. 4b).

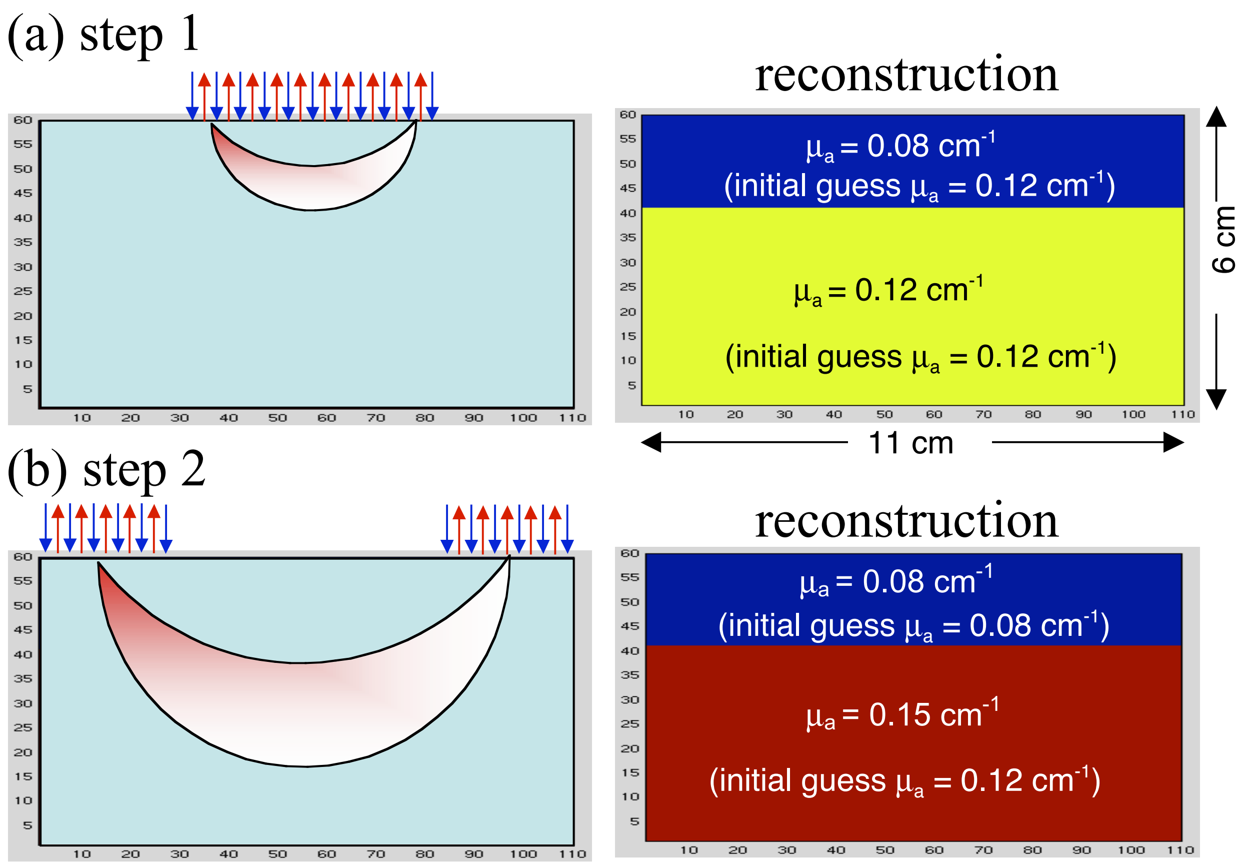

Fig.4: Reconstruction of optical properties of layered media by using different source-detector geometries. First the optical properties of the top layer are recovered by using data from source-detector pairs with small separations (step 1). In a second step the properties of the top layer are fixed to values found in the first step, and the optical properties of the lower layer are determined from source-detector pairs with large separations.

4. SUMMARY

The determination of optical properties of layered tissues remains an important problem, since many tissues display a layered structure. In this work we approach this problem within the framework of model-based iterative image reconstruction schemes (MOBIIR). These schemes are currently widely applied in the field of diffuse optical tomography (DOT), in which one attempts to find the distribution of optical properties in large tissue volumes, such as the breast, brain, or limbs from measurements on the circumference. Employing a MOBIIR scheme, image reconstruction can be interpreted as a nonlinear optimization problem, in which a scalar objective function is minimized. The objective function is, for example, given by the least-square error norm between measured and predicted data. The predicted data is obtained by using an appropriate model for light propagation in tissue, such as the time-dependent diffusion equation with zero boundary or Robin boundary conditions. This model depends on the optical properties at set of discrete points (pixels) inside the medium, which are the variables of the optimization problem. Starting with an initial guess of the optical properties, the properties are updated by calculating the gradient of the objective function with respect to these variables and performing a series of line-minimization within a conjugated gradient scheme.

In this work we showed that information about layered structures can be incorporated into MOBIIR schemes, by updating the values of each pixels that belong to one layer in the same fashion, rather than updating the values for all pixels independently. This is achieved by averaging the gradient of the objective function with respect to all pixel in one layer, and updating all pixel values in that layer accordingly. We distinguished two cases: First we updated in the same way the optical properties of all the pixels in one row parallel to the surface of the medium. This is equivalent to the assumption that the medium has a layered structure, but no information about the number of layers or layer thickness is available. Second, we assumed that the number of the layers and the exact thickness of each layer are known. In this case the optical properties within each layer were updated in the same way. We found that the more information about the nature of the layered structure is available, the better the image reconstruction results. Especially when the number and thickness of layers is known a priori, the optical properties can be recovered with high accuracy.

When only backscattered data is available, attention has to be paid to the exact source-detector configurations. Multi-step MOBIIR algorithms, which use source and detectors at different distance in each step, may be best suited to determine optical properties of layers at different depth.

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