Effects of refractive index on near-infrared tomography of the breast

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Near infrared (NIR) optical tomography is an imaging technique in which internal images of optical properties are reconstructed with the boundary measurements of light propagation through the medium. Recent advances in instrumentation and theory have led to the use of this method for the detection and characterization of tumors within the female breast tissue. Most image reconstruction approaches have used the diffusion approximation and have assumed that the refractive index of the breast is constant, with a bulk value of approximately 1.4. We have applied a previously reported modified diffusion approximation, in which the refractive index for different tissues can be modeled. The model was used to generate NIR data from a realistic breast geometry containing a localized anomaly. Using this simulated data, we have reconstructed optical images, both with and without correct knowledge of the refractive-index distribution to show that the modified diffusion approximation can accurately recover the anomaly given a priori knowledge of refractive index. But using a reconstruction algorithm without the use of correct a priori information regarding the refractive-index distribution is shown as recovering the anomaly but with a degraded quality, depending on the degree of refractive index mismatch. The results suggest that provided the refractive index of breast tissue is approximately 1.3–1.4, their exclusion will have minimal effect on the reconstructed images. © 2005 Optical Society of America

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1. Introduction

Near-infrared (NIR) optical tomography, is a noninvasive imaging modality in which images of internal optical properties are reconstructed by use of measured transmission data. More specifically, a number of optical fibers are placed around the surface of the tissue to be imaged and light is transmitted from one fiber at a time, while all other fibers are used to measure the exiting light at discrete locations around the tissue. The recovery of the interior optical properties is treated as a nonlinear inverse problem based on measurements at the exterior of the domain to be imaged. The light source can be operated in continuous-wave (cw) pulsed or intensity-modulated modes, giving rise to output measurements of light intensity, temporal point-spread function, or phase and amplitude, depending on the strategy adopted. Typically light sources are applied at a number of NIR wavelengths, each, in turn, giving rise to additional spectrally independent boundary measurements. The time-resolved or frequency-domain data allows for reconstruction of internal optical property distributions of absorption (μ_a) and/or reduced scatter (μ_s') for each wavelength, which can in turn be used to calculate images of the concentrations of the dominant chromophores, including oxyhemoglobin, deoxyhemoglobin and water, as well as scattering power and amplitude. These images are the end results of NIR tomography, and they may complement other imaging modalities, potentially defining NIR tomography as a functional imaging technique.

For image reconstruction with the measured boundary data, several different algorithms can be used, depending on datatype, number of measurements, and domain under investigation. Many imaging algorithms rely on a numerical model, whereby the process for iteratively updating the internal distribution of absorption and scatter is to match the measured data to model-based predictions. Assuming that the tissue scatter dominates absorption and that the imaging domain is large enough so that the smallest source–detector fiber distance is greater than a few mean scattering lengths, the diffusion approximation (DA) models the light propagation effectively.
Recently, advances have been made in representing bulk internal refractive-index (RI) variation in tissue within the numerical model. Jiang and Xu have used a higher-order DA that also takes into account the RI as a spatially varying property and have presented reconstructed images of internal absorption, reduced scatter, and refractive index using cw data. Our earlier study showed the implementation of RI spatial variation within the DA using a finite-element modeling approach. Specifically, we defined an internal boundary condition that allows for discontinuous internal variations of RI between regions of contrast (or slowly varying) optical properties. This approach provided a good match between three-dimensional finite-element model results and Monte Carlo simulations, as well as controlled experimental measurements, suggesting that the technique is a valid approximation.

The absolute values of RI for breast tissue types are still a subject under investigation. Estimates are difficult to obtain accurately in vivo, but some data have been reported for various tissue types. Although adipose tissue (fatty layer) has been measured to be 1.455, to the best of our knowledge no results exist for fibroglandular tissue. Nonetheless, the RI of glandular tissue is believed to be lower than that of adipose tissue. The rationale for a lower value is sound in that estimates of the composition of fibroglandular tissue place its water content (greater than 1%) to be high, indicating that its bulk RI is likely close to that of water.

In this paper, we have investigated at the effect of variation of RI within a realistic two-dimensional model of a female breast, by assuming distinct values for the adipose and glandular tissue compartments. Using our current dual modality magnetic resonance imaging (MRI)-NIR system, we can collect NIR and MRI data simultaneously allowing accurate a priori information regarding the tissue structure under investigation. Specifically, we have generated NIR data from a two-dimensional model of the female breast, obtained from MRI, within which we have assumed RI variation for the two main types, namely, adipose and glandular tissue. Within the glandular layer, we have inserted an abnormality with absorption and scatter-only contrast. Using the modeled NIR data perturbed by noise, we have reconstructed images of internal absorption and reduced scatter and have shown the effect on RI variation within reconstructed images for the cases of either no a priori or exact information on the RI values.

2. Theory

A. Forward Model

It is generally accepted that if the magnitude of the isotropic fluence rate within tissue is significantly larger than the directional flux magnitude, the light field is diffuse, which occurs when the scattering interaction dominates over absorption in a region of interest. Mathematically, this assumption allows a simplification of the Boltzmann transport equation, by converting the description of an anisotropic light field into a diffusion equation approximation. The diffusion approximation in the frequency domain is given by

\[- \nabla \cdot (\mu_a(r) + \frac{i\omega}{c_m(r)}) \nabla \Phi(r, \omega) + \frac{i\omega}{c_m(r)} \Phi(r, \omega) = q_0(r, \omega),\]

where \(\mu_a\) and \(\mu_s\) are absorption and reduced scattering, respectively; \(q_0(r, \omega)\) is an isotropic source; \(\Phi(r, \omega)\) is the photon fluence rate at position \(r\);

\[\kappa = \frac{1}{3(\mu_a + \mu_s)},\]

is the diffusion coefficient; and \(c_m(r)\) is the speed of light in the medium at any point, defined by \(c/n(r)\), where \(n(r)\) is the index of refraction at the same point and \(c\) is the speed of light in a vacuum.

The best description of the air–tissue boundary, is reported through an index-mismatched type III condition, in which the fluence at the edge of the tissue exits and does not return. The flux leaving the external boundary is equal to the fluence rate at the boundary weighted by a factor that accounts for the internal reflection of light back into the tissue. This relation is described in

\[\Phi(\xi, \omega) + 2A\hat{n} \cdot \kappa(\xi)\nabla \Phi(\xi, \omega) = 0,\]

where \(\xi\) is a point on the external boundary \(\partial\Omega_i\), and \(A\) depends on the relative RI mismatch between tissue \(\Omega_i\) and air. \(A\) can be derived from Fresnel’s law, \(\theta_0 = \arcsin(n_{\text{AIR}}/n_1)\), the angle at which total internal reflection occurs for photons moving from region \(\Omega_i\) with RI \(n_1\) to air with RI \(n_{\text{AIR}}\), and

\[R_0 = \frac{(n_1/n_{\text{AIR}} - 1)^2}{(n_1/n_{\text{AIR}} + 1)^2}.\]

At the external boundaries, \(n_{\text{AIR}} = 1\), the RI of free space.

At interior nodes, which lie on an interface between two media with different indices of refraction, we apply the conditions used by Schmitt et al., Taka-tani and Graham, and Paris:

\[\hat{n} \cdot D_i \nabla \Phi_1(\xi, \omega) = \hat{n} \cdot D_j \nabla \Phi_2(\xi, \omega),\]

\[\frac{\Phi_1(\xi, \omega)}{\Phi_2(\xi, \omega)} = \left(\frac{n_1}{n_2}\right)^2.\]
These equations enforce continuity in the flux across a step change in RI ($n$), and establish a corresponding discontinuity in the fluence on the basis of the two RIs defining the regions separating the boundary.

B. Inverse Model

The data is represented by a nonlinear operator $y^* = F[\mu_a, \kappa]$, where $y^*$ is a complex vector having a real and imaginary components, which are mapped to log amplitude and phase in measurement. Then the image reconstruction method seeks a solution to

$$\min_{\hat{\mu}_a, \hat{\kappa}} \| y^* - F(\hat{\mu}_a, \hat{\kappa}) \|_{H^1},$$

where $\| \|_{H^1}$ is the weighted L2-norm, representing the square root of the sum of the squared elements. The magnitude of this is sometimes referred to as the projection error and provides a value for determining the convergence of the iterative reconstruction algorithm.

The finite-element method is used as a general and flexible method for solving the forward problem in arbitrary geometries. In the inverse problem, in which the aim is to recover internal optical property distributions from boundary measurements, we assume that $\mu_a(\mathbf{r})$ and $\kappa(\mathbf{r})$ are expressed in a basis with a limited number of dimensions (less than the dimension of the finite-element system matrices). A number of different strategies for defining reconstruction bases are possible; in this paper we use a linear pixel basis. To find $(\hat{\mu}_a, \hat{\kappa})$ in Eq. (7), we used a Levenberg–Marquardt algorithm in which is repeatedly solved

$$a = J^T(JJ^T + \rho I)^{-1}b,$$

where $b$ is the data vector, $b = (y^* - F[\mu_a, \kappa])^T$; $a$ is the solution update vector, $a = [\delta\kappa; \delta\mu_a]$; $\rho$ is the regularization factor; and $J$ is the Jacobian (sensitivity or weight) matrix for the DA model that is calculated with the Adjoint method.

3. Simulation Methods

An MRI of a female subject, Fig. 1(a), was used to create a two-dimensional mesh Fig. 1(b). The mesh contained 2306 nodes corresponding to 4042 linear triangular elements and has a major and minor axis diameter of 101 and 82 mm, respectively. For this subject, experimental data was collected with an MRI-NIR system. We combined the NIR measurements with a priori anatomical information from the MRI (assuming no RI variation) to estimate the optical absorption and reduced scatter for each tissue type. These procedures generated estimates of the adipose layer as having an absorption of 0.003 mm$^{-1}$ and a reduced scatter of 0.95 mm$^{-1}$, whereas the glandular tissue resulted in an absorption of 0.006 mm$^{-1}$ and a reduced scatter of 1.1 mm$^{-1}$. Alternatively, assuming a single tissue type within the breast, we calculated bulk properties for the breast as having an absorption of 0.0056 mm$^{-1}$ and a reduced scatter of 1.125 mm$^{-1}$. Assuming an RI of 1.455 for the adipose tissue and an RI of 1.2, 1.3, or 1.4 for glandular tissue, we calculated data with the presence of an anomaly within the breast, for two separate cases:

1. Assuming a homogenous distribution of absorption and reduced scatter of 0.0056 and 1.125 mm$^{-1}$, respectively, it was assumed that the RI varied between each layer with a value of 1.455 for the adipose tissue and 1.2, 1.3, or 1.4 for glandular tissue. The modeled anomaly, as shown in Fig. 2 (top row) had a contrast in absorption and reduced scatter only and
was assumed to have the same RI as glandular tissue.

2. The adipose layer had an absorption of 0.003 mm\(^{-1}\) and a reduced scatter of 0.95 mm\(^{-1}\), whereas the glandular tissue had an absorption of 0.006 mm\(^{-1}\) and a reduced scatter of 1.1 mm\(^{-1}\). The RI varied between each layer with a value of 1.455 for the adipose tissue and 1.2, 1.3, or 1.4 for glandular tissue. The modeled anomaly, as shown in Fig. 5 below, (top row) had a contrast in absorption and reduced scatter only and was assumed to have the same RI as glandular tissue.

Boundary data was modeled for 16 equally spaced sources and detectors arranged on the external periphery of the model, with added Gaussian noise of 1\% in amplitude and 1° in phase. For each set of data, two types of reconstruction were investigated: (i) correct (a priori) information on RI variation and (ii) a constant RI of 1.455. In all cases images were reconstructed on a 20 × 20 uniform grid basis by use of an initial regularization [Eq. (8)] of \(\rho = 10\), and the number of iterations was continued until the projection error [Eq. (7)] changed by less than 1\% from the previous iteration.\(^1\)

4. Results

In each of the cases described in Section 3, the simulated data were calibrated with methods described elsewhere\(^1,27,28\) to provide an estimate of the bulk optical properties of absorption and reduced scatter for initiating the reconstruction algorithm.

Figure 2 shows the exact (top row) and the reconstructed images for the model, which has a homogeneous absorption and reduced scatter of 0.0056 and 1.125 mm\(^{-1}\), respectively, except within the anomaly that was assigned values of 0.012 and 2 mm\(^{-1}\). The RI is 1.455 for the adipose tissue and 1.4 for the glandular and the anomaly tissues. Images were reconstructed assuming either correct values of RI for each layer (middle row) or a constant RI distribution of 1.455 (bottom row). In each case, images of absorption and reduced scatter were recovered simultaneously by use of log amplitude and phase of the NIR data.

Figures 3 and 4 present exact (top row) and reconstructed images in which the model is identical to that in Fig. 2, except for the RI of the glandular and the anomaly tissues, which was set to 1.3 and 1.2, respectively.

Figure 5 shows exact (top row) and reconstructed images in which the adipose layer had an absorption of 0.003 mm\(^{-1}\) and a reduced scatter of 0.95 mm\(^{-1}\) whereas the glandular tissue had an absorption of 0.006 mm\(^{-1}\) and a reduced scatter of 1.1 mm\(^{-1}\). The anomaly within the glandular tissue had an absorption of 0.012 mm\(^{-1}\) and a reduced scatter of 2 mm\(^{-1}\). The RI was 1.455 for the adipose tissue and 1.4 for the glandular and the anomaly tissues. As in Fig. 2, images were produced assuming either the correct values for the RI in each layer (middle row) or a homogeneous RI distribution of 1.455 (bottom row). Figures 6 and 7 show analogous results to those in Figure 5, except for the RI of the glandular and the
anomaly tissues, which was set to 1.3 and 1.2, respectively.

5. Discussion
In cases in which the tissue is optically (absorption and reduced scatter) homogenous (except for an anomaly) but has different RIs for different tissue types, the recovered optical properties are very similar to the expected values, yielding a peak value of the anomaly for absorption and reduced scatter of approximately 0.0087 and 2.0 mm$^{-1}$, respectively, when correct a priori information on RI distribution is applied throughout the model. Assuming that the model is also uniform in RI, the quality of the reconstructed images varies, depending on the degree of deviation from the true values of RI as expected. For small deviations of RI, that is, when the glandular tissue has an RI of 1.455 but is assumed to be 1.4, the anomaly...
reconstructed images are very similar to the case in which correct RI is assumed, Fig. 2. As the deviation is increased (Figs. 3 and 4), the quality of the reconstructed images is reduced. For example, in Fig. 4 (an assumed value of 1.2 for glandular tissue RI), the amount of background noise in absorption and scatter is increased, and the recovered anomaly is blurred and overly smoothed. Interestingly, the peak value of absorption has increased to 0.01 mm$^{-1}$.

When the tissue is heterogeneous in both optical properties and RI, correct information on the RI distribution improves the reconstruction. Fig. 6 shows the same scenario as Fig. 5 except that the glandular tissue (and the anomaly) has an RI of 1.3.
throughout the model generates recovered optical properties that are very similar to the expected values, yielding a peak value in the anomaly for absorption and reduced scatter of approximately 0.0086 and 2.0 mm\(^{-1}\), respectively. If the reconstruction assumes a uniform RI, the quality of the reconstructed images again varies, depending on the level of deviation from the true distribution of RI. For small deviations, the reconstructed images are similar to the case in which correct RI is used (Fig. 5). As the deviation of the assumed RI increases (Figs. 6 and 7), the quality of the reconstructed images is reduced, but the peak value of recovered absorption increases. In Fig. 7, for example, the RI of the glandular tissue is 1.2, whereas the assumed value for the homogenous reconstruction is 1.455 (bottom row). As in the homogenous case, the amount of background noise in absorption and scatter is increased; however, the recovered anomaly is blurred and overly smoothed, and the peak value of absorption has increased to 0.01 mm\(^{-1}\).

Figure 8 shows the sensitivity map (Jacobian matrix) of log amplitude and absorption for a single source and detector, where the RI distribution is assumed to be either homogeneous at 1.455 or heterogeneous with an adipose layer of RI = 1.455 and a glandular layer of RI = 1.2. From this figure, it evident that a decrease in RI of the glandular tissue reduces the sensitivity deep within the breast. This reduction in sensitivity may explain the increased errors observed when a homogenous assumption of RI is used for image reconstruction. A lower sensitivity within the glandular region will give rise to overly smoothed reconstructed images. However, note that an assumption for the glandular tissue RI of 1.2 is probably not realistic and is only included here for bracketing the effects on image reconstruction.

The recovery of the reduced scatter images seems to have been less affected by the variation of the RI. Although only the sensitivity maps of log amplitude and absorption are only shown, similar trend is seen for other available data types and optical properties (log amplitude or phase versus absorption and scatter). However, it is important to note that the magnitude of the reduced sensitivity for scatter and log amplitude or phase (not shown) is much smaller than that seen for log amplitude and absorption.

6. Conclusion
The effect of discrete RI changes within breast tissue upon NIR image reconstruction has been investigated. Previous studies\(^{11}\) reported our results in modeling the effect of RI on the forward model. In our current results, the initiative was advanced to investigate the effect of RI variation on NIR image reconstruction, either by assumption of correct knowledge of the RI of each tissue or by application of a homogenous value throughout the model.

Synthetic measurement data have been generated from a realistic two-dimensional breast MRI, exhibiting two distinct layers of adipose and glandular tissue. Published values exist for the RI of adipose tissue but not for the glandular tissue. However, it is generally accepted that glandular tissue has a lower RI, and we have assumed a value of 1.4.\(^{16}\) Nonetheless, to illustrate the effects of RI variation with NIR image reconstruction, we have generated data assuming an RI of glandular tissue of 1.4, 1.3, or 1.2. Furthermore, we have also modeled two distinct...
cases in which each layer had either the same or different absorption and reduced scatter properties, allowing us to separate the effects of absorption and reduced scatter from RI variation. In either case, we modeled an anomaly deep within the breast and reconstructed images assuming either correct information on the RI or simply assuming it to be homogenous.

The reconstructed images show that providing the RI of the glandular tissue, when it is not far from the value of adipose tissue, has little effect on the qualitative and quantitative accuracy of the results. For the layered model (Figs. 5–7) the difference in contrast of the reconstructed anomaly (between use of the correct RI or a homogenous value) is 3.5% when the actual glandular tissue RI is 1.4 (but assumed to be 1.455) and increases to 16% when the actual glandular tissue RI is 1.2. If the RI variation is not modeled, the background noise in the reconstructed images increases, and the reconstructed anomaly exhibits a more blurred character, which can be as large as 200% in the absorption images. This increase in noise and in blurriness can be understood by examination of the sensitivity functions in Fig. 8, which show that as the RI of the glandular tissue decreases with respect to adipose tissue, the sensitivity within the glandular tissue also decreases. Another interesting and very important point to note here is that when the RI distribution is not correctly modeled within the reconstruction algorithm, the effects of the data mismatched owing to the RI are exhibiting themselves within the reconstructed absorption images, clearly seen in Figs. 3 and 4. Also, images were reconstructed (not shown) assuming a homogeneous RI of 1.3 and 1.2 in all of the presented results (depending on the RI of the glandular tissue), and similar results were found, as presented, when a homogeneous RI of 1.455 was assumed.

Our research has considered only the reconstruction of absorption and reduced scatter with data generated by a model with RI variation. Assuming the RI of the whole breast is similar, for example, the RI is 1.455 for adipose and 1.4 for glandular tissue, reconstructed images of absorption and scatter can be obtained that ignore the effect of RI with modest degradation in the recovery of information about an abnormality. However, it is also important to note that this analysis was completed under the assumption that the abnormality (i.e., tumor) has the same RI as its background tissue and is most typically located in the fibroglandular tissue. Although, a study by Jiang and Xu12 has reported large variations in the RI of tumors relative to the background, little other pathologic or in vivo data exists on the RI of glandular tissue or the various types of tumor. Further studies are needed to establish the RI variation for different types of tumor and to investigate how such variations might alter NIR tomography.

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References