Optical Characterization of Breast Tumors by Frequency-Domain Optical Mammography

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Abstract

We present a method aimed at the non-invasive optical characterization of breast tumors. This method is based on using diffusion theory to model the propagation of intensity-modulated light in breast tissue. The tumor is assumed to be a spherical inhomogeneity. We report our first results obtained in the laboratory on a tissue-like phantom, and in the clinic on a patient affected by breast cancer. The \textit{in vivo} result indicates that the malignant tumor considered has a higher absorption and a higher reduced scattering coefficient than healthy tissue.

Keywords

Medical optics instrumentation, Medical and biological imaging, Optical diagnostics for medicine, Imaging systems.

\textit{OCIS codes}: 170.3830, 300.0300, 300.1030, 290.0290.

1. Introduction

Near-infrared light is a potentially effective probe to detect breast tumors non-invasively. By transilluminating the slightly compressed breast with intensity modulated light, we have found promising results in tumor detection \cite{1}. Optical methods can proceed beyond the simple detection of optical inhomogeneities by providing information about the optical properties of such inhomogeneities. This article presents an approach aimed at the optical characterization of breast tumors by non-invasive optical methods in the frequency-domain.

2. Theory

Diffusion theory has been successfully employed to describe light propagation in turbid media such as tissue. The analytical solution of the diffusion equation for the photon density has been reported for homogeneous media \cite{2}, and for the case of media containing spherical \cite{3} or cylindrical \cite{4} inhomogeneities. We propose to use the analytical solution for one spherical object embedded in a uniform slab to extract information on the optical properties of breast tumors detected by frequency-domain optical mammography. This result is achieved by fitting the photon-density-wave amplitude and phase to the analytical solution. We performed the fit using the PMI (photon migration imaging) code \cite{5}.

3. Methods

Laboratory experiment

The basic features of the frequency-domain spectrometer are described in detail in Ref. \cite{6}. Briefly, the light source is a laser diode emitting at 750 nm, whose intensity is modulated at a frequency of 120 MHz. The laser diode is coupled to a silica optical fiber 1 mm in core diameter. A second fiber (also 1 mm in core diameter) is used to collect the light signal. The two fibers, separated by 4.8 cm, are deeply immersed in a TiO\textsubscript{2} suspension having optical properties ($\mu_a = 0.020$ cm$^{-1}$; $\mu_s' = 8.7$ cm$^{-1}$) that match those of breast tissue in the near-infrared. The optical detector is a photomultiplier tube. Amplitude and phase of the modulated intensity at 120 MHz are obtained by heterodyning methods and digital filtering. An approximately spherical object (radius 0.6 cm, $\mu_a = 0.30$ cm$^{-1}$, $\mu_s' = 7.2$ cm$^{-1}$) made of hot melt glue was placed in between the source and detector fibers, at distances of about 1.9 and 2.9 cm, respectively. Frequency-domain data were taken while the source and detector fibers were scanned in tandem, always being collinear, along a line perpendicular to the source-detector direction (see Fig. 1(a)). The sample geometry is shown in Fig. 1(a). Figure 1(b) shows the amplitude and phase measured along the scanning line.
Clinical case

We acquired a frequency-domain optical mammogram on a 55-year-old woman affected by breast cancer. The light mammography apparatus (LIMA) developed at Carl Zeiss, Oberkothen (Germany) and currently tested at the Robert Roessle Hospital and Tumor Institute, Berlin (Germany), is described in detail in Refs. [1,7,8]. It employs intensity modulated (110 MHz) laser diodes to acquire a two-dimensional projection image (corrected for edge effects) of the slightly compressed breast. The laser beam and the detector optical fiber, always kept collinear, are scanned in tandem. Fig. 2(a) shows the particular scanning line (the one showing the largest effect of the tumor on the optical data) considered in our analysis. By contrast with the laboratory experiment, where the data in the absence of the inhomogeneity are constant over the scanning line, the optical data on the breast show significant edge effects (larger amplitude, and smaller phase in locations closer to the breast edge, because of a reduced tissue thickness and other geometrical effects [8]). These edge effects must be accounted for, before the amplitude and phase data can be fitted with the analytical solution to the sphere-in-slab problem. We do that by fitting a smooth curve to the data out of the tumor region. This curve is shown in Fig. 2(b) for both the amplitude and the phase collected at 690 nm along the selected scanning line. These curves should be interpreted as being representative of the data we would have collected in the absence of the tumor (but in the presence of the edge effects). For this reason, we call them “background curves.” We use the background curves to normalize the experimental data to account for the edge effects. Specifically, we divide the measured amplitude by the background amplitude, and we subtract the background phase from the measured phase. The resulting normalized data are shown in Fig. 2(c).

4. Results

The result of the fits of the diffusion equation solution to the experimental data are shown by the lines in Figs. 1(b) and 2(c). The fit in Fig. 1(b) has employed the solution for a sphere in an infinite medium,
whereas the fit in Fig. 2(c) is based on the solution for a sphere in an infinite slab of thickness 4 cm. In both cases, the fitted parameters are the radius ($a$), the position ($x$ along the scanning line, $z$ along the source-detector line), the absorption ($\mu_a$) and the reduced scattering ($\mu_s'$) coefficients of the sphere. In doing the fits, we have assumed no refractive index mismatch between the sphere and the surrounding medium, and we have used measured (for Fig. 1(c)) or literature [9] (for Fig. 2(c)) values for the host medium optical coefficients. The comparison between the values of the parameters recovered from the fit and the expected values is reported in Table I for the phantom experiment, and in Table II for the clinical case.

![Diagram of frequency-domain light mammography unit](image)

Figure 2. (a) Vertical cross-section of the slightly compressed breast and schematic diagram of the frequency-domain light mammography unit. The breast compression is $L = 4$ cm in the case reported here. (b) The symbols are the amplitude and the phase measured along the selected scanning line. The continuous lines are smooth curves through the points out of the tumor area. (c) The symbols are the normalized data. The lines are the best fit of diffusion theory to the data. The parameters obtained from the fit are reported in Table II.

**Table II. Clinical case**: comparison between the expected values of various parameters and the corresponding values recovered from the fit. The background optical properties are $\mu_a = 0.03$ cm$^{-1}$ and $\mu_a' = 12$ cm$^{-1}$ (from Ref. [9]).

<table>
<thead>
<tr>
<th>$a$ (cm)</th>
<th>$x$ (cm)</th>
<th>$z$ (cm)</th>
<th>$\mu_a$ (cm$^{-1}$)</th>
<th>$\mu_s'$ (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
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<td>expected</td>
<td>fit</td>
<td>expected</td>
<td>fit</td>
<td>expected</td>
</tr>
<tr>
<td>0.8</td>
<td>1.1</td>
<td>4.9</td>
<td>4.9</td>
<td>0.5-1.0</td>
</tr>
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</table>
5. Discussion

The results of the phantom experiments show that diffusion theory can be successfully employed to optically characterize inhomogeneities embedded in turbid media. The relatively small deviations between the predicted values and the fitted values of the parameters cannot be justified in terms of the instrumental uncertainties. Rather, they may be attributed to the non-perfect spherical shape of our inhomogeneity, and to a refractive index mismatch between the inhomogeneity \((n \sim 1.5)\) and the background medium \((n_0 \sim 1.33)\).

The results of the clinical case show that our non-invasive method is applicable on human breasts \textit{in vivo}. The tumor size, the only fitted parameter on which we had knowledge (from the pathologist report), is in reasonable agreement with the size obtained from the fit. The tumor coordinate along the source-detector line (depth) deviates by several millimeters from the expected value estimated from the optical mammogram in the perpendicular projection. It may be more effective to obtain the depth coordinate by other methods (for instance by use of an off-axis detector fiber, or by perpendicular views of the breast), and take this value as a fixed parameter in our fit. The absorption and the reduced scattering coefficient of this malignant tumor (papillary cancer) are both greater than those of the surrounding healthy tissue.

It is worth stressing two points: (1) Our method does not provide a spatial reconstruction of the breast optical properties, but rather it takes a simplified approach based on dividing the breast into a spherical inhomogeneity (the tumor), and a uniform background (healthy tissue). (2) On the basis of recent studies [10,11], we expect that the simultaneous assessment of the optical properties and the size of tumors smaller than about 1 cm in diameter is not feasible. However, a parameter proportional to the tumor absorption coefficient can be obtained also for small tumors. Consequently, by using two or more wavelengths, it should always be possible to quantify the hemoglobin saturation of the tumor area, which is a physiologically relevant parameter.

6. Conclusions

We have presented a non-invasive method to obtain information on the optical properties of breast tumors \textit{in vivo}. This approach has the potential to add specificity to frequency-domain optical mammography, which has already shown promising results in breast tumor detectability.

7. Acknowledgments

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8. References


