Effect of image reconstruction bias upon spectroscopy-based quantification of chromophores in near-infrared tomography

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Abstract: Accuracy of chromophore concentrations in near-infrared tomography is affected by negative bias in the recovery of absorption coefficients and availability of limited wavelengths. The effect of these factors has been studied with suitable error models.

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1. Introduction

Near-infrared imaging applied in breast cancer allows functional information to be obtained that may be used to diagnose tumors based on their metabolic and functional status represented through vascularization, oxygenation and water content. Light absorption is caused by different absorbing chromophores in tissue like hemoglobin, oxy-hemoglobin and water. Knowing the spectral features of these chromophores in the wavelength band of interest, and by obtaining the absorption coefficients through measurements on the breast and through image reconstruction, it is possible to quantitatively determine the hemoglobin, oxygen saturation and water maps of the breast[1].

One of the limitations of near infrared imaging is that spatial resolution is limited by the dominance of scattering[2, 3], and though several advances in experimental and model-based theory have permitted modest separation of absorption and scattering, there is potentially a limit to this resolution in terms of quantitative accuracy. The general trend in recovery of absorption properties is an underestimation, where the magnitude of underestimation depends on the tumor size [4] [1] [5]. Since, any inaccuracy in quantification of absorption coefficient affects the resultant chromophore concentrations, the ability to quantify hemoglobin, oxygen saturation and water suffers, and this poses a limit on the reliability and diagnostic capability of optical tomography. The work in this paper performs a systematic evaluation of the propagation of the error in transforming absorption into chromophore information, by incorporating a random error model (simulating the random error due to limited wavelength availability) and a systematic error model (simulating the negative bias observed in reconstruction).

2. Methods

Obtaining hemoglobin, oxygen saturation and water images of the breast using diffuse optical tomography is a three stage process: 1) obtaining measurements of light reflectance from the breast; 2) applying a model of light propagation to recover the bulk optical properties of the breast such as absorption and reduced scattering coefficients; 3) estimating concentrations of the underlying molecular chromophores in the tissue using their known spectral signatures. These stages have been described briefly below.

Data Acquisition and Image Reconstruction: The frequency domain data acquisition system at Dartmouth has been described in detail elsewhere [6]. The system is designed for cross sectional imaging of the pendant breast in three planes, spaced 1cm apart to allow interrogation of up to 4cm of tissue. A radial configuration of fiber optics with 16 source-detector positions in each plane has been implemented with horizontal and vertical movement of fibers to accommodate different sized breasts. Tissue probing at six wavelengths between 660 and 850nm is possible and light detection is achieved using high gain photo-multiplier tubes (PMTs) with heterodyning for appropriate signal conversion. The measurements consisting of amplitude and phase undergo calibration to account for any offsets or model-data mismatch, and the calibrated data is reconstructed to yield absorption and reduced scattering coefficient maps. The image reconstruction is based on the frequency domain diffusion equation used to model light propagation in highly scattering media[7]. The core of the reconstruction scheme is a Newton-Raphson minimization method for

iteratively updating the optical property parameters based on minimization of the standard sum of squared differences between the measured and calculated optical radiance at specific detector locations.

Obtaining Chromophore Concentration: Using absorption coefficients and the molar absorption spectra (ε), the concentration of the chromophores (oxyhemoglobin-[HbO_2], de-oxyhemoglobin-[Hb] and water-[H_2O]) can be obtained by a linear least squares constrained fit to the equation

$$[\mu_a] = [\varepsilon]\,[c] \qquad (1)$$

where μ_a is a vector consisting of the absorption coefficients at six wavelengths for each point, and c is a vector of the concentrations of the three chromophores to be determined. ε is a 6x3 matrix containing the molar absorption spectra of the three chromophores at the six wavelengths. The total hemoglobin (Hb_T) is given by ([Hb_T] = [HbO_2] + [Hb]) and oxygen saturation (S_tO_2) is given by (S_tO_2 = ([HbO_2] /[Hb_T]) x 100 %).

3. Results

The quantitative reliability of chromophore concentration estimation depends significantly on the accuracy of the spectral optical property estimates. Studies have shown that optical properties are recovered to within 15% of true value in cases of anomalies of size 25mm [1], and 25% for heterogeneities of size 17mm[4]; however, for an object of 10mm, the error limit can be much higher.

To evaluate these error trends in a systematic manner, simulations were carried out where the boundary data at modulation frequency 100MHz was generated using the finite element based forward model for a single absorbing heterogeneity with a 2-D mesh of diameter 86mm (1785 nodes) [5]. The model had a background μ_a = 0.005 mm^{-1} and μ_s' = 1 mm^{-1}. Additional data sets were also generated for various embedded circular objects of diameter 10mm, 15mm and 20mm, for differing contrasts in the anomaly. 1% random Gaussian-distributed noise was also added to the data. Figure 1(a) shows the results for the average value for absorption coefficient recovered in the region of interest: as is evident, quantitative accuracy suffers as the diameter of the anomaly decreases, and the mean error with respect to the true value used to generate the data, has increased from 28% for a 20mm object, to 38% for a 15mm object, to 47.3%for a 10mm object.

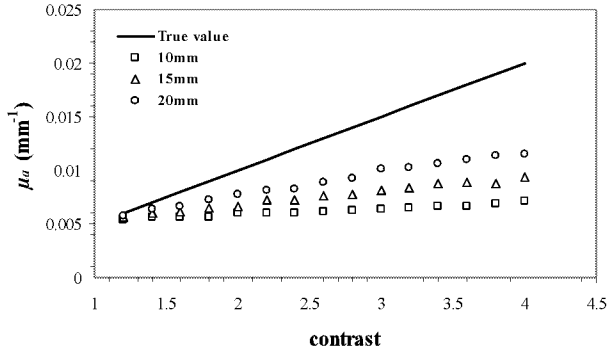
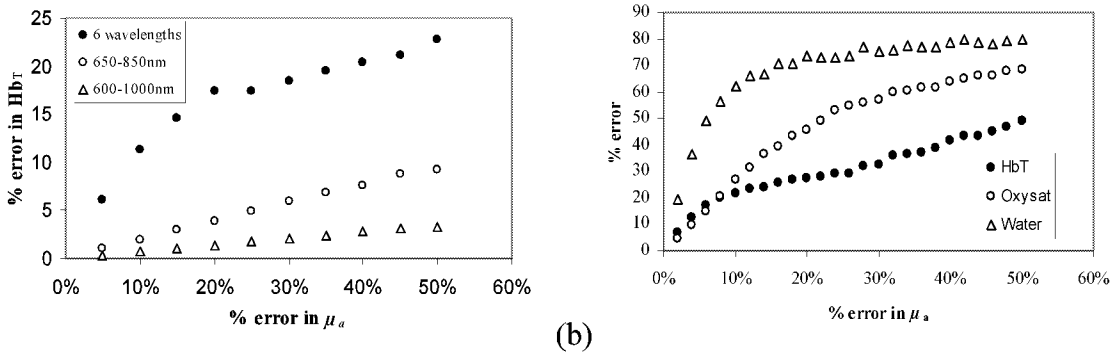


Figure 1. Reconstructed absorption coefficient for different sized inclusions, as a function of the contrast relative to the background absorption. These are simulated data with region of interest values taken from the final images.

It is useful to analyze how the absorption coefficient error projects onto the estimation of the chromophore concentrations. Towards this end, a systematic error propagation analysis was carried out by starting with a known set of chromophore concentrations (known Hb_T, S_tO_2 and water) and obtaining the absorption coefficients corresponding to these concentrations using a simple matrix multiplication (equation 1). In the random error model, a random noise level was added to the set of μ_a values at the 6 wavelengths, and the concentrations were recovered using a constrained linear least-squares fit, so that the error manifested in the concentrations occurred as a result of error in the absorption coefficients. This analysis was carried out for a starting concentration of total hemoglobin=30μM, oxygen saturation=60% and water=60% (typical concentrations found in breast tissue [8]), where the error in the final chromophore concentrations retrieved was the mean from 1000 such runs of adding random noise. Figure 2a shows the results for error propagation in hemoglobin for 6 wavelengths, 101 wavelengths (650-850nm in 2nm spacing) and 201 wavelengths (600-1000nm in 2nm spacing).

A random error model is representative of a homogeneous estimate of μ_a; however, clinically observed images are closer to heterogeneous test objects. Taking into account the observed results which indicate that error in recovery of absorption spectra is systematic with a negative bias, instead of having random fluctuations, a systematic error model was devised. This error model was derived from results of simulations carried out on anomalies of different sizes and with varying contrasts, and a consistent parabolic relationship was observed. This parabolic indication was implemented in an error model which adds error in μ_a based on the contrast available in the anomaly versus background. The systematic model when implemented gives a more complete description of the quantification of chromophores, as shown in figure 2b.



(a) (b)

Figure 2(a) The percent error in the calculated total hemoglobin value is estimated based upon spectral fitting with random errors assumed in the absorption coefficient. Results show how the error would change when different numbers of wavelengths are used in the measurements. In (b) the same error propagation calculation is shown with a bias error model demonstrating how this error is amplified for the same error in absorption.

4. Discussion

The accuracy in functional parameters such as hemoglobin, oxygen saturation and water content is a key factor in developing NIR tomography and the error propagation analysis presented here shows how important it is to have quantitative accuracy in the optical absorption coefficient. When information from the entire wavelength spectrum is incorporated, the levels of error drop as expected, signifying that chromophore information is more immune to accuracy in quantification of μ_a in the presence of many wavelengths. The parabolic error model is representative of the general trend observed in reconstruction, and may be different for other types of reconstruction depending on the error observed. Further studies are being completed to decrease the systematic bias effects by use of zoning approaches to provide apriori information[5] and address the random error factor by increases in the number of wavelengths (white light spectroscopy) for interrogation, after obtaining a region of interest using near-infrared tomography.

5. Acknowledgements

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6. References

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