Published in final edited form as:

Proc SPIE Int Soc Opt Eng. 2008 January 19; 6845: . doi:10.1117/12.762340.

Interstitial diffuse optical tomography using an adjoint model with linear sources

Xiaodong Zhou and Timothy C. Zhu

Department of Radiation Oncology, University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104

Abstract

An improved interstitial diffuse optical tomography (iDOT) system has been developed to characterize the optical properties of prostate gland during the photodynamic therapy (PDT). Multiple cylindrical light diffusers with different lengths (instead of point sources used in an earlier version) and isotropic detectors are introduced interstitially in the prostate gland in-vivo. During the data acquisition, linear sources and detectors are stepping into prostate sequentially controlled by a motorized system. A computerized multi-channel attenuator system is developed to automatically control the power strength of each linear source and on times to speed up data acquisition. Three dimensional optical properties are obtained by solving the inverse problem of steady-state diffusion equation based on an adjoint model with Moore-Penrose scheme. The convergence, accuracy and the speed of the algorithms are tested in mathematical phantoms and in prostate simulating phantoms with known optical properties. For comparison, the optical properties of tissue simulating phantoms are also reconstructed using iDOT with multiple isotropic point sources. Data acquisition time in iDOT using linear sources is at least 10 times faster than using the point sources with the total data acquisition time to be less than 1 minutes. Reconstruction results showed both algorithms can successfully recover the optical properties. Reconstruction using linear sources/detectors acquisition mode is 20 times faster than the point sources/detectors method (30 minutes vs. 4 hours on a 3.4 GHz Pentium PC with 4 GB memory). We have demonstrated that linear-source/detector acquisition mode out-performs the point-source mode, and is more practical to be implemented in the clinical settings.

Keywords

diffuse optical tomography; linear source; prostate; photodynamic therapy

1. INTRODUCTION

Diffuse optical tomography (DOT) is a new imaging modality with potential applications in functional imaging of the brain and breast cancer detection [1-5]. This imaging technique seeks to recover the optical parameters of tissue from boundary measurements of transmitted near-infrared or visible light. Instrumentation for optical tomography system is relatively less expensive and is portable for the clinical settings[1]. It has been proved that DOT system can provide a viable alternative to current available functional imaging systems such as functional magnetic resonance imaging[1]. A typical DOT system often consists of a light source (lasers, white light), illuminating the biological tissue from the surface at different

source positions in succession[1]. The photons which propagate through tissue are then collected at multiple detector positions on the tissue surface[1]. Three measurement schemes are used for these measurements: time domain, frequency domain and continuous wave (cw). Of these three measurement types, the cw method is the simplest and least expensive, and can provide fastest data acquisition and greatest signal-to-noise level[6].

One of the applications of cw DOT system is the light dosimetry for interstitial prostate photodynamic therapy (PDT). The effectiveness of PDT treatment largely depends on the number of photons absorbed by the photosensitizers located in the tumor tissue [7]. Thus the light and photosensitizer dosimetry are essential for PDT treatments [8]. In our prostate PDT protocol, optical properties of prostate are first determined before the treatment, so that a real-time modeling and monitoring of photons deposition in the prostate can be achieved. Prostate optical properties are determined via an interstitial DOT system where light sources and detectors are interstitially inserted in the prostate tissue [9].

In the earlier version of this interstitial diffuse optical tomography system, multiple point sources are used and the measurements are obtained by sequentially scanning the multiple point sources and detectors along the axial direction. In this update version of iDOT, multiple linear sources are used as light sources. The lengths and locations of the placement of these linear light sources are according to the pre-treatment plan. The advantages of using multiple linear sources instead of point sources are three folds. First, using linear sources placed at the planned treatment locations with specific lengths greatly reduces the preparation time. Since the optical property characterization and PDT treatment use the same linear source setup, there is no need to replace the point sources used in the traditional iDOT measurements with the linear treatment fibers for the light treatment. This is essential for the clinical PDT treatment and dosimetry in the operating room, where the patients are under general anesthesia. Secondly, using multiple linear sources instead of multiple point sources reduces the data acquisition time. In the traditional iDOT with point sources, both the sources and detectors are scanned along the prostate axial direction. At least five scans for each source layer separated at 5mm apart are needed to cover the whole prostate. However, in the linear source data acquisition scheme, the linear sources are placed still at the treatment positions and no scans are needed. Last, iDOT with linear sources has less computational cost. The number of sources is greatly reduced compared to the scanning point sources scheme, thus the size of the Jacobian matrix is much smaller.

In this study, we present a 3D inverse model with multiple linear sources that can recover the heterogeneous optical properties of the prostate tissue. These models are built in the COMSOL Multiphysics / MATLAB environment, where the partial differential equations are solved in COMSOL Multiphysics and the heterogeneous equation coefficients are updated via Levenberg-Marquardt algorithm written in MATLAB. We have validated these proposed models by reconstructing the optical properties of the 3D mathematical phantoms with the numerically simulated data and the measured optical phantom data. We demonstrated that the reconstruction algorithm with multiple linear sources algorithm outperforms the 3D point source algorithm in terms of accuracy/computation cost ratio.

2. MATERIALS AND METHODS

2.1 Theory and Computation Methods

The propagation of near-infrared light through highly scattering media (such as biological tissues) is often modeled as a second order elliptic partial differential equation [10]. For continuous-wave diffuse optical tomography system, steady-state attenuation measurements are made, and the light fluence rate can be calculated using steady-state diffusion approximation to the radiation transfer equation:

$$-\nabla \cdot \kappa \nabla \Phi + \mu_a \Phi = q \quad (1)$$

where Φ is the isotropic photon density and q is an isotropic source distribution. The model is characterized by two spatially varying functions μ_a (absorption coefficient) and $\kappa = 1/3(\mu_a + \mu'_s)$ (diffusion coefficient) (μ'_s : scattering coefficient), which gives rise to the dual parameter search space nature of the optimization problem. We use the modified Robin boundary condition $\Phi + 2\kappa/\alpha \vec{n} \cdot \nabla \Phi = 0$, where $\alpha = (1 - |\cos \Theta_c|^2)/(2(1 - R_0) - 1 + |\cos \Theta_c|^3)$ and $R_0 = (n-1)^2/(n+1)^2$, $n = n_{\text{tissue}}/n_{\text{outside}}$ is the ratio of refraction index between tissue (n_{tissue}) and outside medium (n_{outside}), and $\Theta_c = \arcsin(1/n)$ is the critical angle. In prostate tissue, a matched non-scattering boundary: $\Phi + 2\kappa \vec{n} \cdot \nabla \Phi = 0$ is used where $n_{\text{tissue}} = 1.4$, $n_{\text{outside}} = 1.4$ and $\alpha = 1$.

Newton-Raphson iterative method is used to minimize the objective function:

$$\Psi = \frac{1}{2} \sum_{i=1}^{n_{\text{source}}} \sum_{j=1}^{n_{\text{detector}}} \left(\Phi_{i,j}^{(m)} - P_{i,j}[\mu_a \quad \kappa] \right)^2 \quad (2)$$

where $\Phi_{i,j}^{(m)}$ is the data for the j -th measurements from i -th source. Use the subscript i to represent the data for a single source i , $\vec{P}_i[\mu_a \quad \kappa]$ is the projection operator for source i , $\vec{\Phi}_i^{(c)}$ is the projection data obtained by sampling $\vec{P}_i[\mu_a \quad \kappa]$ at the discrete measurements positions $\{\vec{r}_{i,1}, \vec{r}_{i,2}, \dots, \vec{r}_{i,n_{\text{detector}}}\}$ [10].

Following the L-M scheme, the parameter update can be obtained by:

$$\Delta x^k = \left(\mathbf{J}^T \mathbf{J} + \lambda \mathbf{I} \right)^{-1} \mathbf{J}^T \left(\ln \Phi^{(m)} - \ln \Phi^{(c)}(x^k) \right) \quad (3)$$

where

$$\mathbf{J} = \begin{bmatrix} \frac{\partial \ln \Phi_1}{\partial \kappa_1} & \dots & \frac{\partial \ln \Phi_1}{\partial \kappa_N} & ; & \frac{\partial \ln \Phi_1}{\partial \mu_{a1}} & \dots & \frac{\partial \ln \Phi_1}{\partial \mu_{aN}} \\ \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ \frac{\partial \ln \Phi_M}{\partial \kappa_1} & \dots & \frac{\partial \ln \Phi_M}{\partial \kappa_N} & ; & \frac{\partial \ln \Phi_M}{\partial \mu_{a1}} & \dots & \frac{\partial \ln \Phi_M}{\partial \mu_{aN}} \end{bmatrix} \quad (4)$$

is the Jacobian matrix at i -th iteration, representing the sensitivity between the field distribution with respect to the perturbations of optical properties [10]. The Jacobian matrix contains the first derivatives of the log of the amplitude of the i -th measurements with

respect to the optical properties at the j -th nodes, and is calculated using the adjoint method in this study:

$$\frac{\partial \phi_{j,i}}{\partial \kappa_k} = - \frac{\langle \nabla G(\vec{r}_k, \vec{r}_i) \cdot \nabla \phi(\vec{r}_j, \vec{r}_k) \rangle}{\phi(\vec{r}_j, \vec{r}_i)} \quad (5)$$

$$\frac{\partial \phi_{j,i}}{\partial \mu_{a,k}} = - \frac{\langle G(\vec{r}_k, \vec{r}_i) \cdot \phi(\vec{r}_j, \vec{r}_k) \rangle}{\phi(\vec{r}_j, \vec{r}_i)} \quad (6)$$

Since only the cw measurements are used, the Jacobian matrix presented here only contains the amplitude sensitivity sub-matrices, where the phase sensitivity sub-matrices are eliminated. Examples of individual rows in the Jacobian matrix plotted as images are shown in the Fig. 2. These maps relate small changes in the log amplitude of the measurements for a given source-detector configuration, due to the small perturbations in the optical absorption and diffusing properties at all nodal locations.

2.2 Simulation and Phantom Studies

The synthetic measurement cw data were calculated for a cubic phantom as shown in Fig. 1, containing a single μ_a anomaly and a single μ_s' anomaly. The cube has a dimension of 40mm by 50 mm and a height of 60mm centered at (25mm,15mm,0mm). The model has a background $\mu_a=0.03\text{mm}^{-1}$ and $\mu_s'=1.4\text{mm}^{-1}$. The μ_a anomaly has absorption coefficient of 0.09mm^{-1} and positioned at (17.5mm,27.5mm,0mm) and has a radius of 2.5mm. The μ_s' anomaly has a scattering coefficient of 4.2mm^{-1} , and is at position (32.5mm,27.5mm,0mm) and has a radius of 2.5mm. The third anomaly is positioned at (17.5mm,12.5mm, 0mm), with a radius of 2.5mm, and $\mu_a=0.09\text{mm}^{-1}$, $\mu_s'=4.2\text{mm}^{-1}$. A total of 12 linear sources and 54 detector sites spanned at $z=0\text{mm}$, $z=\pm 5\text{mm}$, $z=\pm 10\text{mm}$, $z=\pm 15\text{mm}$, $z=\pm 20\text{mm}$ are used for reconstruction.

Experiments were performed on one optical phantom with three heterogeneities, as depicted in Fig. 2. Silicon based solid phantom was fabricated with RTV12A and RTV12C (RTV-141, Medford Silicone, Medford, New Jersey). Carbon black (Raven 5000 Ultra II, Columbian Chemistry Company) is used as absorbers. The mean particle size of the carbon black is $\sim 8\text{nm}$. Titanium Dioxide (TiO_2) (T-8141, Sigma) is used as the scatterers. After the homogeneous phantom was made, three holes were drilled at the positions shown in Fig.2, and were filled with mixture of RTV12A and RTV12C with different carbon black and TiO_2 concentrations. The homogeneous phantom has absorption coefficient of 0.03mm^{-1} , and reduced scattering coefficient of 1.4mm^{-1} . Three heterogeneities are absorption anomaly only ($\mu_a=0.09\text{mm}^{-1}$, $\mu_s'=1.4\text{mm}^{-1}$), scattering anomaly only ($\mu_a=0.03\text{mm}^{-1}$, $\mu_s'=4.2\text{mm}^{-1}$) and both absorption and scattering anomaly ($\mu_a=0.09\text{mm}^{-1}$, $\mu_s'=4.2\text{mm}^{-1}$). All the anomalies are cylindrical with a diameter of 5mm, and are separated 120° apart. (Fig. 2)

3. RESULTS AND DISCUSSIONS

Fig. 3 shows an example of modeled data from interstitial DOT with linear sources (a) and point sources (b). In linear source case, one linear source and four most adjacent detector scan positions (21 detector positions) are used, giving a total number of 84 measurements to cover a 10mm by 10mm by 40mm region. In point source case, to cover the same region, five point sources are used to replace the linear source, while the detectors positions remain the same as linear source case, giving a total number of 420 measurements. The log amplitudes of the modeled data are significant higher in the iDOT linear source model compared to the point source model with the same equivalent source strength. This implies that the Jacobian sensitivity matrix in the linear iDOT model is more sensitive to the measurements, since the number of useful measurements (number of Jacobian matrix elements larger than the noise level) is larger in the linear iDOT[11]. Fig. 4 shows the cross-section of a subset of the Jacobian matrix calculated from the iDOT with linear source (a) and with point sources (b). The magnitude of the Jacobian matrix in the linear iDOT are two times larger than the point source model in the imaging region.

Two categories of reconstruction results are presented in this paper. 3D data generated from the finite element forward model of a cubical phantom containing a single absorption heterogeneity and a single scattering heterogeneity. These data are used to test the performance of the iDOT reconstruction algorithm with application of multiple linear sources, such as convergence and accuracy. 3D data acquired with cw interstitial DOT system from a prostate phantom containing single absorption, single scattering and absorption and scattering heterogeneities. These data are used to test the capability of the system when noisy data are used.

3.1 Reconstruction from simulated data

Figure 5 shows the reconstructed absorption (1st row) and reduced scattering (2nd row) images for the target medium. The source detector positions are depicted in Figure 1, with 12 linear sources and 18 detectors, lead to total 216 measurements. The forward mesh contains 10456 tetrahedral elements and 2474 nodes. The mesh density is much finer around the linear source positions and detector positions to ensure the accuracy of the forward calculation of rapid change field. The reconstruction mesh is uniformly constructed in the medium with a size of 10 by 8 by 10, giving to total 800 unknowns. Three optical anomalies are reconstructed with a initial estimation of homogeneous optical properties used as for the background value. The images reported here are results of 25 iterations with about 7 minutes per iteration for reconstruction on a Pentium D 3Ghz PC with 4G memory. The reconstruction with linear sources can recover the location and the size of the anomaly with acceptable accuracy. The crosstalk between the absorption anomaly and the scattering anomaly are greatly reduced when a Jacobian normalized scheme is used. Shown in Fig.5, are the absorption and scattering images for 5 different cut: $z=0\text{mm}$, $z=\pm 2.5\text{mm}$, $z=\pm 5\text{mm}$.

3.2 Reconstructed from measured phantom data

In the reconstruction from the simulated data study, the emission profiles of the linear light diffusers are assumed uniform. However, in order to get the accurate optical properties of

the optical phantoms, exact knowledge of the spatial light source emission characteristics has to be implemented in the forward FEM model. Thus the in-air emission profiles of twelve linear sources are measured. Fig. 6 shows the emission profiles of the 12 linear sources; the raw fluence rate measurements are presented as a function of the distance. Channel 3, 6, 9 and 12 are 3cm log cylindrical light diffusers, while the other channels are 4cm. The placement and the length of the linear light sources are determined via the PDT treatment planning program.

In the phantom study, similar geometry is used for the iDOT reconstruction program with linear sources. 12 linear sources and 18 detectors, lead to total 216 measurements. The forward mesh contains 8413 tetrahedral elements and 6221 nodes. The reconstruction mesh is uniformly constructed in the medium with a size of 10 by 8 by 10, giving to total 800 unknowns. Fig. 7 shows the reconstruction results from the phantom measurements. The locations and sizes of the optical anomalies are poorly recovered. This might be due to the fact that the actual source and detector positions are different than the positions in the treatment plan. The linear sources or detectors might deviate from the planned tracks, resulting in a different source detector distance for the reconstruction.

4. CONCLUSION

In this paper, we have presented a DOT reconstruction algorithm using multiple linear light diffusers. This algorithm is modified from the conventional iDOT algorithm with point sources based on Levenberg-Marquardt algorithm. We have presented simultaneous reconstruction of absorption and scattering from mathematical simulated data for three dimension cases and measurements data from optical phantoms. We have demonstrated that the new reconstruction algorithm can reconstruct multiple planes from multi-plane measurements, and requires less computational costs. The proposed linear iDOT system outperforms the conventional point source iDOT system in system setup, data acquisition and numerical computations.

ACKNOWLEDGEMENTS

This work is supported by Department of Defense Grant DAMD 17-03-1-0132 and National Institute of Health (NIH) R01 CA109456 and PO1 CA87971.

REFERENCES

1. Gibson AP, Hebden JC, Arridge SR. Recent advances in diffuse optical imaging. *Phys Med Biol.* 2005; 50(4):R1–43. [PubMed: 15773619]
2. Bamett AH, et al. Robust inference of baseline optical properties of the human head with three-dimensional segmentation from magnetic resonance imaging. *Appl Opt.* 2003; 42(16):3095–108. [PubMed: 12790461]
3. Boas DA, Dale AM. Simulation study of magnetic resonance imaging-guided cortically constrained diffuse optical tomography of human brain function. *Appl Opt.* 2005; 44(10):1957–68. [PubMed: 15813532]
4. Custo A, et al. Effective scattering coefficient of the cerebral spinal fluid in adult head models for diffuse optical imaging. *Appl Opt.* 2006; 45(19):4747–55. [PubMed: 16799690]
5. Bluestone AY, et al. Three-dimensional optical tomographic brain imaging in small animals, part 1: hypercapnia. *J Biomed Opt.* 2004; 9(5):1046–62. [PubMed: 15447026]

6. Franceschini MA, Boas DA. Noninvasive measurement of neuronal activity with near-infrared optical imaging. *Neuroimage*. 2004; 21(1):372–86. [PubMed: 14741675]
7. Wilson BC. Photodynamic therapy for cancer: principles. *Can J Gastroenterol*. 2002; 16(6):393–6. [PubMed: 12096303]
8. Dougherty TJ, et al. Photodynamic therapy. *J Natl Cancer Inst*. 1998; 90(12):889–905. [PubMed: 9637138]
9. Zhu TC, Finlay JC, Hahn SM. Determination of the distribution of light, optical properties, drug concentration, and tissue oxygenation in-vivo in human prostate during motexafin lutetium-mediated photodynamic therapy. *J Photochem Photobiol B*. 2005; 79(3):231–41. [PubMed: 15896650]
10. Arridge SR, Hebden JC. Optical imaging in medicine: II. Modelling and reconstruction. *Phys Med Biol*. 1997; 42(5):841–53. [PubMed: 9172263]
11. Yalavarthy PK, et al. Critical computational aspects of near infrared circular tomographic imaging: Analysis of measurement number, mesh resolution and reconstruction basis. *Optics Express*. 2006; 14(13):6113–6127. [PubMed: 19516784]

Figure. 1.

Schematic for the setup of interstitial diffuse optical tomography (iDOT) with multiple linear sources for simulation study (a) and phantom study (b). The lines are the linear sources with a length of 3cm, the dots are the detector scanning positions. 12 linear sources and 6 scanning positions are shown here, along the scanning track, 9 detector positions are used ($z=0\text{mm}$, $z=\pm 5\text{mm}$, $z=\pm 10\text{mm}$, $z=\pm 15\text{mm}$, $z=\pm 20\text{mm}$) giving 12×54 total measurements.

Figure. 2.
Schematic of the optical phantom used for the phantom study, three heterogeneities are included with diameters of 5mm inserted as shown in 3D plot (a) and cross-section plot (b).

Figure. 3.

Plots of modeled data from interstitial DOT with linear source (a) and with point source (b) for homogeneous mathematical phantom ($\mu_a=0.03\text{mm}^{-1}$, $\mu_s'=1.4\text{mm}^{-1}$) as shown in Fig.1. Log amplitudes of data are shown.

Figure 4.

Plots of the cross-section of the Jacobian matrix (absorption sub-matrix) from iDOT with linear source and with point source for homogeneous mathematical phantom ($\mu_a=0.03\text{mm}^{-1}$, $\mu_s'=1.4\text{mm}^{-1}$).

Figure 5.

Cross-sections of 3D reconstruction for absorption and scattering images. Slice locations are $z=0\text{mm}$, $z=\pm 2.5\text{mm}$, $z=\pm 5\text{mm}$. The regions outside the source-detector covered area has been set as the background optical properties with $\mu_a=0.09\text{mm}^{-1}$, $\mu_s'=1.4\text{mm}^{-1}$.

Figure 6.

Emission profiles of 12 linear light diffusers used for the optical phantom study. Channel 3,6,9 and 12 are 3cm long light diffusers, and the others are 4cm long diffusers. Data shown are raw fluence rate data.

Figure 7.

Reconstruction of the optical phantom for absorption coefficient only. The regions outside the source-detector covered area has been set as the background optical properties with $\mu_a=0.09\text{mm}^{-1}$, $\mu_s'=1.4\text{mm}^{-1}$. Results shown here are the reconstruction images for different cuts along the z-axis: $z=0\text{mm}$, $z=\pm 5\text{mm}$, $z=\pm 10\text{mm}$, $z=\pm 15\text{mm}$, and $z=\pm 20\text{mm}$. Only the absorption images are shown.