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Characterization of tissue optical properties for prostate PDT using interstitial diffuse optical tomography

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Abstract

Photodynamic therapy (PDT) is an important treatment modality for localized diseases such as prostate cancer. In prostate PDT, light distribution is an important factor because it is directly related to treatment efficacy. During PDT, light distribution is determined by tissue optical property distributions (or heterogeneity). In this study, an interstitial diffuse optical tomography (iDOT) method was used to characterize optical properties in tissues. Optical properties (absorption and reduced scattering coefficients) of the prostate gland were reconstructed by solving the inverse problem using an adjoint model based on diffusion equation using a modified matlab public user code NIRFAST. In the modified NIRFAST method, linear sources were modeled for the reconstruction. Cross talking between absorption coefficients and reduced scattering coefficients were studied to have minimal effect, and a constrained optical property method (set either absorption coefficient or reduced scattering coefficient to be homogeneous) is also studied. A prostate phantom with optical anomalies was used to verify the iDOT method. The reconstructed results were compared with the known optical properties, and the spatial distribution of optical properties for this phantom was successfully reconstructed.

Keywords

Photodynamic therapy; optical property; diffuse optical tomography

1. INTRODUCTION

Photodynamic therapy (PDT) is an important treatment modality for cancer and other localized diseases [1]. During the treatment, photosensitizers excited by light react with ground state oxygen $^3\text{O}_2$, which leads to generation of the major cyto-toxic agent – singlet oxygen $^1\text{O}_2$ - to kill the surrounding tissues and cells [2, 3]. In this process, tissue optical properties are of great significance since they determines how the light reacts with photosensitizers. Therefore, an interstitial diffuse optical tomography (iDOT) system has been developed to characterize the optical properties of tissues, prostate gland for instance, during PDT [4]. DOT is an optical imaging modality that utilizes light to measure physiological-based tissue contrasts noninvasively [5]. Based on these DOT measurements,

three-dimensional spatial map of tissue optical properties such as absorption coefficient or reduced scattering coefficient can be obtained using diffusion model based reconstruction algorithms.

During the iDOT data acquisition, linear sources and detectors controlled by a motorized system were inserted into the prostate gland phantom sequentially. Optical signals were recorded from the detectors, which were illuminated by the continuous-wave linear sources. From the measurements, 3D spatial distributions of light fluence rate can be described and optical properties (absorption and reduced scattering coefficients) of the prostate gland were reconstructed by solving the inverse problem with the use of an adjoint model based on the diffusion equation [6]. After iDOT, the same linear sources can be used for deliver expected PDT treatments. In this study, a prostate phantom including anomalies with known optical properties was prepared. iDOT was used to reconstruct the 3D optical properties of the phantom, and the results were compared with pre-known phantom parameters.

2. MATERIALS AND METHODS

2.1 Materials

Solid silicone phantoms were prepared for this study mimicking human prostate. Carbon black ((Raven 5000 Ultra II, Columbian Chemistry Company) ink and Titanium Dioxide (TiO_2) (T-8141, Sigma) were added to room-temperature-vulcanizing (RTV) solutions to mimic the variations of optical absorption coefficient and reduced scattering coefficient, respectively, with different concentrations. After adding the ink and TiO_2 , the solution was cured after 24-72 hours under room temperature in molds with designated shapes. Anomalies with different optical properties but made with the same material were prepared and inserted to a base phantom to test the iDOT reconstruction algorithm, as shown in Fig. 1.

2.2 Experimental geometry

Once the solid phantom was prepared, catheters were inserted into the phantom parallel to each other, as shown in Figure 1b. Linear light sources and isotropic detectors were inserted into the catheters for the iDOT measurement. Light fluence rate profiles were measured and recorded from the detector channels by scanning the isotropic detectors along the catheter for each linear light source, when connected to the laser with a known power. The scanning and recording functions of the detectors are implemented by a motorized system controlled by a home-made program written in Visual Basic.

The geometric contour of the prostate phantom was determined by ultrasound images as shown in Figure 2a taken one week prior to the experiments. The phantom contours were then used to build the geometry of the finite element model. Once the light fluence rate profiles were recorded, a home-made program in Matlab was used to determine the relative positions of the linear light sources to the prostate phantom, as shown in Figure 2c.

2.3 iDOT algorithm

The iDOT reconstruction algorithm has been discussed in our previous publications [7-9]. Briefly, continuous wave (CW) light is modeled by steady state light diffusion equation when propagating in highly-scattered media:

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

where Φ is the light fluence rate, S is an isotropic source distribution, and $\kappa = 1/3(\mu_a + \mu'_s)$ is the diffusion coefficient. The reconstruction algorithm includes an iterative process, in which a set of initial values of optical properties were used to calculate the light fluence rate spatial distribution for the first iteration using finite element method. Once the fluence rate distribution is calculated, the Jacobian matrix was constructed in CW mode, which represents the change of the calculated fluence rate to a small change of optical properties at each mesh node in the finite element model.

$$\left(J^T J + \frac{1}{\lambda} I \right)^{-1} J^T \delta \Phi = \delta \mu, \quad (2)$$

where J is the Jacobian matrix, I is the identity matrix, $\delta \Phi$ is the difference between calculated fluence rate and measured fluence rate at each iteration, $\delta \mu$ is the update for the optical properties, and $\frac{1}{\lambda}$ is monotonically decreased over the iteration procedure. An adjoint model was used in this process for calculation efficiency. The projection error was then estimated between calculated fluence rate and measured fluence rate. Once the projection error reaches preset criterion, iterations stop and optical properties are determined. In our model, the geometric model was implemented in COMSOL, and solving the diffusion equation was implemented by a modified version of NIRFAST [10] for continuous wave problems.

2.4 Manual adjustment

For some experiments, the light fluence rate profiles may not be correctly recorded, including in-air light profile instead of in-media light profile, or detector scanning misalignment etc. In those cases, the current iDOT algorithm could not reconstruct the light fluence rate profile accurate enough and human decision need to be made in order to correctly reconstruct the optical properties. Manual adjustments include two aspects, namely excluding data and changing optical properties. The first aspect will exclude the data that was recorded in a wrong way, while the second aspect includes manually adjusting reconstructed optical properties so that calculated light fluence matches better with measured light fluence, as there is still room to improve the iDOT reconstruction algorithm. The second aspect manual adjustment includes applying a correction factor to the absorption coefficient within a region of interest, as shown in Figure 3. The correction factor was determined by observation of the difference between reconstructed light fluence rate measured light fluence rate.

3. RESULTS AND DISCUSSIONS

3.1 iDOT reconstruction results

The iDOT reconstruction algorithm was applied to an example data set taken from the prostate phantom measurements. 12 linear light source channels and 5 detector channels were used for the reconstruction, as illustrated in Figure 2b. Figure 4 shows the reconstructed the spatial distribution of the absorption coefficients and reduced scattering coefficients on cross sections of the prostate phantom, as well as the prostate phantom contour at the depths and the corresponding light source/detector channels positions. Three optical anomalies are reconstructed in the absorption coefficient maps, with an initial estimation of homogeneous optical properties ($\mu_a = 0.3 \text{ cm}^{-1}$, and $\mu'_s = 15 \text{ cm}^{-1}$) used as for the background value. According to Figure 1b, the optical properties are ($\mu_a = 0.3 \text{ cm}^{-1}$, and $\mu'_s = 15 \text{ cm}^{-1}$) for anomaly A, ($\mu_a = 0.9 \text{ cm}^{-1}$, and $\mu'_s = 7.55 \text{ cm}^{-1}$) for anomaly B, and ($\mu_a = 0.9 \text{ cm}^{-1}$, and $\mu'_s = 15 \text{ cm}^{-1}$) for anomaly C. The reconstruction results recovered the location of the three anomalies with acceptable accuracy. The reconstruction results were produced by the iDOT reconstruction algorithm for 23 iterations, which took ~58 minutes on a PC with 2.40 GHz CPU and 2.0 GB RAM.

The spatial distributions of reconstructed optical properties are also shown in 3D, in which absorption coefficient distribution is shown in Figure 5a, while the reduced scattering coefficient distribution is shown in Figure 5b. The three anomalies can be easily discerned in Figure 5a (denoted by the arrows, where anomaly A has the same optical properties as the background). Some reconstruction artifacts can also be found in Figure 5a on the top of the prostate phantom, which may mainly due to the light fluence rate profile being out of the phantom.

The reconstructed light fluence rate profiles for light source – detector pairs are also shown in Figure 6 in blue color, as well as the measured light fluence rate profiles from the same source-detector pairs, to test the accuracy of the reconstruction results.

3.2 Manual adjustment results

Figure 7 and 8 shows an example of manual adjustment results. In this example, 12 linear light source channels and 6 detector channels were used for the reconstruction, but some of the light fluence rate profiles were not correctly recorded, which caused inaccuracy of the iDOT reconstruction algorithm. Those pairs (included A6, F8, and E11 as demonstrated in Figure 3) were then discarded for better reconstruction accuracy, as aspect one in manual adjustment. Then the iDOT algorithm was applied the date set, and the reconstructed light fluence rate profiles are shown in Figure 7, compared with the measured ones. There are some discrepancies between the reconstructed ones and the measured ones, which demonstrated the room of improvement for the iDOT algorithm. To make the reconstructed optical properties more accurate, we performed the second aspect of the manual adjustment on light fluence rate profiles A2, A5, D10, E10, B6, D5, C7, C3, F3, and F12 to make the data match better with the measured light fluence rate profiles. After manual adjustment, the reconstructed light fluence rate profiles are shown in Figure 8, as compared with the measured ones. One can notice that after manual adjustment, the reconstructed data have

been improved in terms of matching with measured light fluence rate profiles, which provides better accuracy for the reconstruction.

Figure 9 shows the reconstructed the spatial distribution of the absorption coefficients and reduced scattering coefficients on cross sections of the prostate phantom after both manual adjustment aspects. Three optical anomalies are reconstructed in the absorption coefficient maps, with an initial estimation of homogeneous optical properties ($\mu_a = 0.2 \text{ cm}^{-1}$, and $\mu'_s = 15 \text{ cm}^{-1}$) used as for the background value. According to Figure 1b, the optical properties are ($\mu_a = 0.1 \text{ cm}^{-1}$, and $\mu'_s = 15 \text{ cm}^{-1}$) for anomaly A, ($\mu_a = 0.5 \text{ cm}^{-1}$, and $\mu'_s = 15 \text{ cm}^{-1}$) for anomaly B, and ($\mu_a = 0.9 \text{ cm}^{-1}$, and $\mu'_s = 15 \text{ cm}^{-1}$) for anomaly C. The reconstruction results recovered the location of the three anomalies with acceptable accuracy.

4. CONCLUSION

In this study, an interstitial diffuse optical tomography technique is introduced, which was implemented using finite element model and performed by NIRFAST. The iDOT method was applied to reconstruct optical properties from a solid prostate phantom. The optical properties were successfully reconstructed in 3D, compared with pre-known conditions of the phantom construction, and the reconstructed light fluence rate profiles were compared with the measured ones to validate the reconstruction algorithm accuracy. A manual adjustment method was also applied to improve the optical property reconstruction, in the cases when the light fluence rate was not correctly recorded.

The manual adjustment improves the reconstruction accuracy, and also demonstrated the potential for the iDOT algorithm for improvement. Reducing cross-talking between absorption coefficients and reduced scattering coefficients and regional reconstructions are both current effort to improve the iDOT reconstruction algorithm. Potential clinical applications are also of great interest as future directions of this study.

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Figure 1. Schematic of silicone prostate phantom in (a) 3D and (b) 2D cross section. A, B, and C show the anomalies with different optical properties. Crosses demonstrate the position of linear sources, while circles represent positions of detectors.

Figure 2.

Experimental geometry for iDOT. (a) Ultrasound image of the prostate phantom at depth of 3.5 cm. (b) Extracted phantom contour at depth of 3.5 cm, with positions of linear light sources (red cross) and detectors (green circle). (c) Linear light source positions and prostate phantom contour in 3D.

Figure 3. Demonstration of manual adjustment. The region of interest showing in the schematic was chosen to be the region between light source 5 and detector A.

Figure 4.
iDOT reconstruction results of spatial distribution of absorption coefficient and reduced scattering coefficient on cross sections of the prostate phantom.

Figure 5.
iDOT reconstruction results of 3D spatial distribution of absorption coefficient and reduced scattering coefficient.

Figure 6.
Reconstructed light fluence rate profile (blue) from 20 light source – detector pairs compared with the measured light fluence rate profiles (red).

Figure 7.

Reconstructed light fluence rate profile (blue) from 21 light source – detector pairs compared with the measured light fluence rate profiles (red) before second aspect of manual adjustment.

Figure 8.

Reconstructed light fluence rate profile (blue) from 21 light source – detector pairs compared with the measured light fluence rate profiles (red) after second aspect of manual adjustment.

Figure 9.

iDOT reconstruction results of spatial distribution of absorption coefficient and reduced scattering coefficient on cross sections of the prostate phantom after manual adjustment for example shown in Figure 7 and 8.