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Modeling light fluence rate distribution in optically heterogeneous prostate photodynamic therapy using a kernel method

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Abstract

To accurately calculate light fluence rate distribution for light dosimetry in prostate photodynamic therapy (PDT), heterogeneity of optical properties has to be taken into account. Previous study has shown that a finite-element method (FEM) can be an efficient tool to deal with the optical heterogeneity. However, the calculation speed of the FEM is not suitable for real time treatment planning. In this paper, two kernel models are developed. Because the kernels are based on analytic solutions of the diffusion equation, calculations are much faster. We derived our extensions of kernel from homogeneous medium to heterogeneous medium assuming spherically symmetrical heterogeneity of optical properties. The kernel models are first developed for a point source and then extended for a linear source, which is considered a summation of point sources uniformly spaced along a line. The kernel models are compared with the FEM calculation. In application of the two kernel models to a heterogeneous prostate PDT case, both kernel models give improved light fluence rate results compared with those derived assuming homogeneous medium. In addition, kernel model 2 predicts reasonable light fluence rates and is deemed suitable for treatment planning.

Keywords

photodynamic therapy; light fluence rate; kernel method; heterogeneity; prostate

1. INTRODUCTION

Photodynamic therapy^{1,2} is a treatment modality employing light of certain wavelength in the presence of oxygen to activate a photosensitizer which then causes localized cell death or tissue necrosis. In treatment of large bulky tumors in solid organs such as prostate, this technique faces challenges because of limited light penetration into tissue. Currently, interstitial light delivery is an efficient illumination scheme for such tumors, whereby optical fibers are placed directly into the bulky tumors or organs. Based on the results of a preclinical study in canines, we have initiated a protocol for motexafin lutetium (MLu)-mediated PDT of the prostate in patients at the University of Pennsylvania.^{3,4} Laser at wavelength of 732 nm is used to activate MLu.

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In our prostate PDT, cylindrical diffusing optical fibers (CDFs) with active lengths between 1 and 5 cm were used as light sources (Fig. 1). Catheters were inserted in parallel into the prostate with the guidance of an ultrasound unit and a template. The CDFs were placed in the catheters, which had lengths larger than the prostate size to ensure the prostate was completely covered during treatment.

Light fluence delivered to the tumor volume is an important dosimetry quantity to ensure the efficacy of a treatment. Accurate and fast predication of light fluence distribution is desirable for real-time treatment planning for prostate PDT. In previous studies, based on a homogeneous assumption, we developed a kernel method for light fluence rate calculation,⁵ which has the advantage of fast calculation. Our clinical study showed that optical properties are heterogeneous in a prostate. Figure 2 shows measured absorption coefficient map and reduced scattering coefficient map in a slice, which are superimposed on the prostate contour.⁶ The optical absorption coefficients vary from 0.1 to 1 cm⁻¹ and the reduced scattering coefficients vary from 5 to 45 cm⁻¹. Figure 3 shows light fluence rates (150 mW/cm² isodose lines) calculated using homogeneous and heterogeneous optical properties, respectively. The mean optical properties were used in the homogeneous calculation. The calculation using heterogeneous optical properties shows different fluence rate distribution (the dotted line) in the upper part of the prostate. This result indicates that optical heterogeneity needs to be taken into account in light fluence rate calculation. We have developed a finite element method (FEM),⁷ which can deal with optical heterogeneity. However, the FEM calculation is not fast enough for real-time treatment planning. The study in this paper is aimed to develop a kernel method, which is fast in calculation and can deal with optical heterogeneity. Two kernel models, which take into account of optical heterogeneity, have been developed and the calculation results have been compared with those of FEM.

2. METHOD

Because light scattering dominates absorption, the transport of near-infrared light in biological tissue is often described by a diffusion equation,^{7,8}

$$-\nabla \cdot (D(\mathbf{r})\nabla\phi) + \mu_a(\mathbf{r})\phi = S \quad (1)$$

where the diffusion coefficient $D=1/3\mu_s'$ (μ_s' is the reduced scattering coefficient), μ_a is the absorption coefficient, and S is the source power (in units of mW or W). For heterogeneous medium, i.e., when D and μ_a are spatially dependent, Eq. 1 can only be solved numerically. We use finite-element method to solve this equation and use the solution as our gold standard to evaluate the accuracy of our kernel models. In regions where the light source is sufficient far away from the point of interest, the diffusion approximation is sufficiently accurate to predict the light fluence rate. In near field region, Monte Carlo simulation will be necessary to obtain accurate results.

For homogeneous medium, Eq. 1 can be solved analytically for a point source:⁹

$$\phi = \frac{3S\mu_s'}{4\pi r} \cdot e^{-\mu_{eff}r}, \quad (2)$$

where $\mu_{eff} = \sqrt{3\mu_a\mu_s'}$ is the effective attenuation coefficient,¹⁰ and r is the distance between source and detector.

2.1 Heterogeneous kernel model 1

A heterogeneous kernel model is developed by extending the result of the homogeneous kernel model (Eq. 2) by taking into account of optical heterogeneity. We assume that optical heterogeneity is made of spherically symmetrical regions of homogeneous optical properties. We also assume that the expression for light fluence rate for the homogeneous region at the light source has exactly the same form as Eq. 2. For other regions of homogeneous optical properties, we require the relative distribution of light fluence rate follows Eq. 2 and the weight changes as a function of location. In addition, at the boundary of the different regions, the light fluence rate has to be continuous. One can prove that the light fluence rate can be expressed as,

$$\phi = \frac{3S\mu_s'(0)}{4\pi r} \cdot e^{-\int \mu_{eff} dr}, \quad (3)$$

where $\mu_{eff}(r)$ is heterogeneous along the ray line r that connects source and detector. For three-dimensional (3D) heterogeneous medium, this model can be further extended by replacing $\mu_{eff}(r)$ by $\mu_{eff}(r, \theta, \phi)$ and the integration is performed along the ray line. Considering that a linear source is composed of multiple point sources (segments), the light fluence rate for a linear source (Fig. 4) can be expressed as a superposition of the solution for a point source, i.e.,

$$\phi = \sum_{i=1} \frac{3\mu_s' \cdot s \cdot \Delta x_i \cdot e^{-\int_0^{r_i} \mu_{eff} \cdot dr}}{4\pi r_i}, \quad (4)$$

where s is the source strength of each segment along the linear source, x_i is the division along the direction parallel to the orientation of the linear source, and r_i is the distance between the i th source segment and the detector. The summation in Eq. 4 is over all the segments composing the linear source. The fluence rate at a point in a prostate is the summation of the fluence rates generated by each linear source.

2.2 Heterogeneous kernel model 2

We develop another heterogeneous kernel model for a point source, which is suitable for spherical-shell distribution of optical properties. For a point source located at $r=0$, optical properties are assumed to be homogeneous in each shell surrounding the source and are different from shell to shell. Figure 5 shows the spherical shell geometry. Light fluence rates in each shell are expressed as

$$\phi_1 = C \left(\frac{p_1 \mu_{s,1}}{4\pi r} e^{-\mu_{eff,1} r} + \frac{q_1 \mu_{s,1}}{4\pi r} e^{\mu_{eff,1} r} \right), (r < r_1) \quad (5)$$

$$\phi_2 = C \left(\frac{p_2 \mu_{s,2}}{4\pi r} e^{-\mu_{eff,2} r} + \frac{q_2 \mu_{s,2}}{4\pi r} e^{\mu_{eff,2} r} \right), (r_1 < r < r_2) \dots \quad (6)$$

$$\phi_N = C \left(\frac{p_N \mu_{s,N}}{4\pi r} e^{-\mu_{eff,N} r} + \frac{q_N \mu_{s,N}}{4\pi r} e^{\mu_{eff,N} r} \right), (r_{N-1} < r < r_N) \quad (7)$$

and

$$\phi_{N+1} = C \frac{p_{N+1} \mu_{s,N+1}}{4\pi r} \cdot e^{-\mu_{eff,N+1} r}, (r_N < r < \infty) \quad (8)$$

Boundary conditions between two shells are⁶

$$\phi_i = \phi_{i+1} |_{r=r_i}, \quad (9)$$

$$\vec{n} \bullet D_i \nabla \phi_i = \vec{n} \bullet D_{i+1} \nabla \phi_{i+1}, \quad (10)$$

In addition, the total energy released by the light source has to be conserved

$$\int \mu_{a,i} \phi_i \cdot dV = S. \quad (11)$$

Fluence continuity and flux continuity are considered in the boundary conditions. In Eq. 11, energy absorbed in the medium is equal to the source power S . The coefficients C , p_i , and q_i are derived using Eqs. 5–11.

$$p_i = \frac{1}{2D_i r_i \mu_{eff,i} \mu_{s,i}} \cdot [(D_i(-1 + r_i \mu_{eff,i}) - D_{i+1}(-1 - r_i \mu_{eff,i+1})) p_{i+1} \mu_{s,i+1}' e^{(\mu_{eff,i} - \mu_{eff,i+1}) r_i} + (D_i(-1 + r_i \mu_{eff,i}) - D_{i+1}(-1 + r_i \mu_{eff,i+1})) q_{i+1} \mu_{s,i+1}' e^{(\mu_{eff,i} + \mu_{eff,i+1}) r_i}], \quad (12)$$

$$q_i = \frac{1}{2D_i r_i \mu_{eff,i} \mu_{s,i}} \cdot [(D_i(1 + r_i \mu_{eff,i}) - D_{i+1}(1 + r_i \mu_{eff,i+1})) p_{i+1} \mu_{s,i+1}' e^{-(\mu_{eff,i} + \mu_{eff,i+1}) r_i} + (D_i(1 + r_i \mu_{eff,i}) - D_{i+1}(1 - r_i \mu_{eff,i+1})) q_{i+1} \mu_{s,i+1}' e^{-(\mu_{eff,i} - \mu_{eff,i+1}) r_i}], \quad (13)$$

$$C = \left(\sum_{i=1}^{N+1} A_i \right)^{-1}, \quad (14)$$

where

$$\begin{aligned}
A_i = \frac{\mu_{a,i}}{\mu_{eff,i}^2} \cdot [& -p_i \mu_{s,i}' ((1+r_i \mu_{eff,i}) e^{-\mu_{eff,i} r_i} - (1+r_{i-1} \mu_{eff,i}) e^{-\mu_{eff,i} r_{i-1}}) \\
& + q_i \mu_{s,i}' ((-1+r_i \mu_{eff,i}) e^{\mu_{eff,i} r_i} + (1-r_{i-1} \mu_{eff,i}) e^{\mu_{eff,i} r_{i-1}})] \\
& (\text{for } i=1, r_{i-1}=0)
\end{aligned} \tag{15}$$

For $i=N+1$ (i.e., the outmost shell), $r_{N+1}=\infty$ and $q_{N+1}=0$. In the study, we assume $p_{N+1}=1$.

For arbitrary 3D distribution of optical properties, we expanded the expressions for light fluence rate to keep the forms to be the same as those expressed in Eqs. 5–8 and Eqs. 12–15, and optical properties along a ray line between a source and a detector were used, i.e., $\mu_{eff}(r)$ was replaced by $\mu_{eff}(r, \theta, \phi)$.

3. RESULTS AND DISCUSSION

The point-source solution of the heterogeneous model 1 was first tested with spherical shell optical property distribution (Fig. 5). The radii of the shells are 0.3, 0.7, 1.1 and 4 cm, respectively. Figure 6 shows the comparison of light fluence rates calculated using FEM and the kernel model, which are along a line (in the z direction) located at 0.5 cm away from the source. The absorption coefficients in the shells (from inner to outer) are 1.4, 1.1, 0.7, and 0.3 cm^{-1} , respectively. And the reduced scattering coefficients are 14 cm^{-1} . The ratios show that the deviations of the kernel from the FEM are within 15% in the data range of $-0.5 \sim 0.5$ cm. The data beyond the range was not compared because the values were small, which may cause errors in the ratio.

Comparison between FEM and kernel model 1 were made in a prostate PDT case using measured 3D distribution of optical properties. Figure 7 shows the source and detector arrangement in the PDT case. We usually divide a prostate into four regions: right upper quadrant (RUQ), left upper quadrant (LUQ), right lower quadrant (RLQ), and left lower quadrant (LLQ). Light fluence rates were calculated at the detector positions in each quadrant along the direction z , which is perpendicular to the paper.

Calculated fluence rates using FEM and kernel model 1 are shown in Fig. 8. In the figure, fluence rates calculated using the homogeneous model (Eq. 2) are also presented for comparison. In the homogeneous calculation, optical properties were assumed to be homogeneous in a quadrant and mean optical properties of a quadrant were used. The fluence rate distributions calculated using the heterogeneous model show similar features as the FEM results and those calculated using the homogeneous model have larger discrepancies from FEM than the heterogeneous kernel model 1, especially in the quadrant LUQ and RLQ.

However, substantial errors were still present using heterogeneous kernel model 1 for the test case. Deviations of the fluence rates calculated using the kernel models from those using FEM were calculated at each data point. Figure 9 shows histograms of the deviations of the

heterogeneous kernel results in each quadrant. The vertical axis represents the number of data points compared. The maximum deviation in four quadrants is 72%, which is smaller than that of the homogeneous kernel model (128%).

Significant improvements were observed using the heterogeneous kernel model 2 for both point and linear sources. Different optical property distributions were applied in test of the point source solution, which were varied from shell to shell, e.g., optical absorption coefficients were increased (or decreased) from inner shell to outer shell, or optical scattering coefficients were increased (or decreased) from inner shell to outer shell. Figure 10 compares calculated fluence rates and the ratios between kernel model 2 and FEM results for a point source. The fluence rates calculated using the kernel model 2 agree very well with those of the FEM.

The heterogeneous kernel model 2 was also applied for linear source, in the same prostate PDT case as shown in Fig. 7. Fluence rates were calculated in each quadrant, using the measured heterogeneous optical properties. The results are shown in Fig. 11, which show significant improvements over the results of the heterogeneous kernel model 1 (Fig. 8). The maximum deviation in four quadrants is reduced to 31%.

4. CONCLUSIONS

Two heterogeneous kernel models were tested for light fluence calculation in heterogeneous prostate PDT, and the calculation results were compared with those of FEM. Calculation accuracy was improved by using the heterogeneous kernel models. The calculation using the heterogeneous kernel model 2 agrees better with that using the FEM than kernel model 1. In the study of a prostate PDT case, the maximum deviations were reduced from 128% (using homogeneous kernel model) to 71% (using the heterogeneous model 1) to 31% (using the heterogeneous kernel model 2). For the particular prostate test case, we have demonstrated that the heterogeneous kernel model 2 is sufficiently accurate for purpose of treatment planning. Further tests with additional cases are needed to verify this conclusion.

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Figure 1.
Schematics of prostate PDT. CDF: cylindrical diffusing fiber.

Figure 2. Measured optical properties. (a) Optical absorption coefficients (b) Optical scattering coefficients.

Figure 3.
Isodose lines calculated using homogeneous (dashed line) and heterogeneous (dotted line) optical properties, respectively.

Figure 4.
Linear source model.

Figure 5.
Spherical shell distribution of optical properties.

Figure 6.

(a) Light fluence rates calculated using FEM and the heterogeneous kernel model 1, respectively. (b) Ratio of light fluence rates between the kernel and FEM.

Figure 7.
Source and detector arrangement in a prostate PDT case.

Figure 8.

Comparison of light fluence rates in four quadrants for kernel model 1, which were calculated using FEM, heterogeneous kernel (Eq. 3), and homogeneous kernel (Eq. 2), respectively.

Figure 9.

Histograms of the deviations of light fluence rates calculated using the heterogeneous kernel model 1 from those calculated using FEM.

Figure 10.

Fluence rates calculated using the heterogeneous kernel model 2 and the FEM, respectively, and the ratios between the kernel and the FEM. Optical properties were varied from inner shell to outer shell in such sequences: optical absorption coefficients were (a) increased and (b) decreased; Optical scattering coefficients were (c) increased and (d) decreased.

Figure 11.

Comparison of light fluence rates in four quadrants, which were calculated using the FEM and the heterogeneous kernel model 2 (Eqs 5 – 15), respectively.