Published in final edited form as:

Proc SPIE Int Soc Opt Eng. 2006 January 21; 6139: . doi:10.1117/12.646251.

Study of light fluence rate distribution in photodynamic therapy using finite-element method

Jun Li, Timothy C. Zhu*, and Jarod C. Finlay

Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA 19104

Abstract

In photodynamic therapy (PDT), it is desirable to determine the light fluence distribution accurately for treatment planning. Earlier studies have shown heterogeneous distribution of optical properties in patients' prostates. Finiteelement method (FEM) is suitable for dealing with heterogeneous media and irregular geometries. Cylindrical diffusing fibers (CDFs) were modeled as linear sources of finite lengths, using the same parameters as those used in the treatments. Meshes were generated in the three-dimensional (3D) prostate geometry, reconstructed using transrectal ultrasound images of the prostate. Heterogeneous optical properties measured in the prostate were applied in the calculation and the refractive-index mismatch boundary condition was studied. Compared with the measurements, the FEM calculations using heterogeneous optical properties show better agreements than those using homogeneous optical properties.

Keywords

finite-element method; photodynamic therapy; light fluence rate; 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. Laser at wavelength of 732 nm is used to activate MLu.

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.

*tzhu@mail.med.upenn.edu; phone 1 215 662-4043; fax 1 215 349-5978.

Light fluence delivered to the tumor volume is an important dosimetry quantity to ensure the efficacy of the treatment. It is desirable to accurately predict light fluence distribution in prostate. Light propagation in biological tissue experiences absorption and scattering and the latter is usually dominant in near infrared region. This phenomenon can be modeled using the diffusion equation. The fact that tissue optical properties are heterogeneously distributed makes it necessary to solve the diffusion equation directly to predict light fluence rate distribution. There have been studies using the finite element method (FEM) to model light transport in biological tissues using light sources located outside the tissue.^{3,4} In this paper, we applied FEM to study light transport in a prostate for linear light sources placed inside the prostate, taking into account real prostate geometry, boundary conditions, and most importantly, optical heterogeneity. The calculation was implemented with Comsol Multiphysics (Comsol Inc., Burlington, Massachusetts).

2. METHOD

2.1 Diffusion equation and boundary conditions

For continuous-wave light source, the steady-state diffusion equation was used to describe light propagation in a prostate, which was expressed as³

$$-\nabla \cdot D \nabla \phi + \mu_a \phi = q, \quad (1)$$

where ϕ is the light fluence rate, $D (=1/3 \mu_s')$ is the diffusion coefficient, μ_a is the optical absorption coefficient, and q is the source strength. μ_s' is the reduced optical scattering coefficient. In the calculation, the CDFs were modeled as linear sources using weak forms.

Four kinds of boundary conditions were considered for the boundary between prostate and outside medium:³ Dirichlet boundary ($\phi = 0$), prostate (tissue)-air boundary, prostate-nonscattering medium boundary (i.e., matched-nonscattering boundary), and prostate-tissue (scattering medium) boundary. The second and the third boundary conditions were described with the modified Robin boundary condition, i.e., $\phi + 2AD \vec{n} \cdot \nabla \phi = 0$, where $A = [2/(1-R_0) - 1 + |\cos \theta_c|^3] / [1 - |\cos \theta_c|^2]$, and $R_0 = (n-1)^2/(n+1)^2$. n is the ratio of the refractive indices between the prostate $n_{prostate}$ and outside medium (n_{out}): $n = n_{prostate} / n_{out}$. $\theta_c = \arcsin(1/n)$ is the critical angle. Figure 2 shows the results of calculations using the Dirichlet boundary (solid line), tissue-air boundary (dotted line), and matchednonscattering boundary (dashed line) in a 3-cm (in z direction) prostate with a 5-cm long source. The Dirichlet boundary condition represents a perfect absorbing medium surrounding the tissue. Photons are absorbed when crossing the boundary. For the tissue-air boundary condition, we applied $n_{prostate} = 1.4$ and $n_{out} = 1$ for air. For the matched nonscattering boundary condition, we assumed that $n_{out} = n_{prostate} = 1.4$. The calculations show that for these three boundary conditions, the light fluence rates decrease dramatically towards zero at locations close to the boundary. Since we did not see this phenomenon in our measurements, we think the fourth boundary condition, i.e., the prostate (tissue)-tissue boundary, is more reasonable.

We assumed that there was a scattering medium surrounding the prostate (Fig. 3) and the calculation was performed using a layer structure in the calculation. Refractive-index match and mismatch were considered. A strict expression for the refractive-index mismatch

boundary condition has been derived by Faris.⁵ For simplicity, we used the approximation given by Dehghani *et al.*,⁶ which is expressed by

$$\phi_{prostate}/\phi_{out} \approx (n_{prostate}/n_{out})^2, \quad (2)$$

and

$$\vec{n} \bullet D_{prostate} \nabla \phi_{prostate} = \vec{n} \bullet D_{out} \nabla \phi_{out}, \quad (3)$$

where $\phi_{prostate}$ and ϕ_{out} are light fluence rates in prostate and outside medium, respectively. Eq. (2) and (3) describes such a boundary condition: fluence rate is discontinuous whereas flux is continuous. When $n_{prostate}=n_{out}$, Eq. (2) and (3) describes refractive-index match boundary condition. In the study of boundary effects, we used a simple geometry, a cylindrical geometry. All the calculations were based on this boundary condition.

The prostate geometry was reconstructed using the ultrasound images of a treated prostate, with which the study of light fluence rate distribution was carried out. In the calculation, linear sources were placed inside the geometry with the same arrangements as those in the treatment. Three-dimensional distribution of optical properties which had been measured in the prostate was used in the calculation. The optical properties outside of prostate beyond the region of measurement were estimated to obtain the best agreement between the calculation and measurement.

2.2 Mesh generation for light fluence rate calculation

Figure 4 shows a two-cylinder geometry with meshes. The 3D geometry was partitioned into tetrahedrons and the boundary was partitioned into triangular elements. In the geometry of 2.5 cm-radius and 7-cm height, the meshes included 35917 nodes. The elements were Langrange quadratic. Because the linear source has large gradient at locations close to it, to obtain accurate results at those locations, finer meshes were generated around the source. In the case of heterogeneous optical properties, optical properties at the nodes were obtained by interpolating the measured optical properties. In the calculation using actual prostate geometry, the meshes had 140696 nodes.

3. RESULTS AND DISCUSSION

Figure 5 shows the results of the study of the refractive-index mismatch boundary condition. Cylindrical geometry (Fig. 4) was used to avoid the affect of irregular shape on results. A smaller cylinder, which was 2 cm in radius and 3 cm in height, mimicked a prostate placed inside a larger cylinder, which was 2.5 cm in radius and 7 cm in height, simulated a scattering layer surrounding the prostate. The lateral dimension of the layer was selected to be large enough to ensure that there is no boundary effect from the outer layer. Two source lengths (3 cm and 5 cm) were studied. The sources were located at the center of the cylinders in the radial direction and were along the axial direction, i.e., z direction. The 5-cm source extrudes outside the 3-cm cylinder (prostate) at each end by 1 cm, which were in the larger cylinder (the layer). To study the effects of different boundary conditions, we assumed the optical properties in the two cylinders were the same and homogeneous: $\mu_a =$

0.3 cm⁻¹ and $\mu_s' = 14$ cm⁻¹. These optical properties are the average values of the optical properties measured in 14 patients.¹ Figure 5(a) shows the light fluence rate distributions along z at a distance of 0.5 cm away from the 3-cm long source in the radial direction. The dotted-dashed line is the result for the layer with the same refractive-index as the prostate and the solid line is that with the refractive-index mismatch, where we assumed the refractive indices for the prostate and the layer were 1.4 and 1.0, respectively. It is seen that the fluence rate was discontinuous at the boundaries in the mismatch case: there was an abrupt jump in the fluence rate. On the other hand, it is smooth in the match case. Figure 5(b) shows the result of the 5-cm source. The parts of the source, which were located in the layer, brought remarkable difference between the mismatch and match cases. In our experiments, we had never seen such discontinuous distributions in the measured fluence rates. So we hypothesize that in reality prostate and outside media have similar refractive index, i.e., the refractive indices are matched. This is applied to all subsequent calculations in the paper. In Fig. 5(b), the square symbols show the results of an analytic model, which was based on infinite medium. One can see that the result of the match case is the same as that of the infinite medium if the optical properties of the prostate and the layer are the same. We will see later that the result of the match case changes with the optical properties of the outer layer.

Figure 6(a) is an ultrasound image of a patient's prostate, in which the contour of the prostate and the source locations are shown. With seven slices of images, a 3D geometry of the patient's prostate was reconstructed, which is shown in Fig. 6(b). The geometry was used in the calculations.

The optical properties of the patient's prostate had been measured during the treatment. The 3D data is composed of data obtained in six planes with separation of 0.5 cm. Figure 7 shows the optical properties measured in one of the planes ($z=0.5$ cm). The optical properties were heterogeneous. In the plane shown in Fig. 7, absorption coefficients varied from less than 0.1 to 1 cm⁻¹, and scattering coefficients varied from 5 to over 45 cm⁻¹.

Figure 8(a) shows the mesh of the prostate geometry with a cylindrical layer surrounding outside. Figure 8(b) shows the calculation result: a surface plot of the fluence rate distribution at $z = 1.5$ cm. In this calculation, measured heterogeneous optical properties were applied for twelve linear sources using the lengths, strengths (150 mW/cm), retraction, and locations used in the treatment. The calculation time is about 400 seconds. In the prostate, for the locations where there were no measured optical properties, interpolations were taken. Optical properties ($\mu_a = 0.3$ cm⁻¹ and $\mu_s' = 14$ cm⁻¹) were assumed for the outer layer. The fluence rates in this plane were ranged between 0-4500 mW/cm². High fluence rates were found at locations close to the sources. Similar calculations were carried out for the case assuming the prostate having homogeneous optical properties ($\mu_a = 0.3$ cm⁻¹ and $\mu_s' = 14$ cm⁻¹).

To study the effect of optical heterogeneity on the light fluence distribution, we compared the isodose lines obtained using heterogeneous optical properties and using homogeneous optical properties ($\mu_a = 0.3$ cm⁻¹ and $\mu_s' = 14$ cm⁻¹) for the prostate. Figure 9(a) shows the 150 mW/cm² isodose surface of calculated fluence rate in three-dimension using

heterogeneous optical properties. Figures 9(b)-(h) show the isodose lines for heterogeneous optical properties and homogeneous optical properties in each slice. The solid line is the prostate contour, the dashed line is the isodose lines for the homogeneous optical properties, and the dotted lines are the isodose lines for the heterogeneous optical properties. The calculation using homogeneous optical properties shows similar coverage as the calculation using measured heterogeneous optical properties except for a region in the upper part of the prostate. This indicates that the homogeneous assumption and the application of the average optical properties ($\mu_a = 0.3 \text{ cm}^{-1}$ and $\mu_s' = 14 \text{ cm}^{-1}$) to the prostate sometimes can be applied to obtain approximate light fluence distribution. However, such approximations are not accurate. The heterogeneity does have effects on the fluence rate distribution. Lower fluence rates, compared to the homogeneous case, are found in the upper part region of the prostate in the heterogeneous case, corresponding to the high absorption region shown in Fig. 7. In other words, optical absorption coefficients in that region were underestimated when using the average optical properties. Calculation using heterogeneous optical properties can provide more accurate results.

We compared the calculations with measurements in several linear tracks inside prostate, *in vivo*. Light fluence rate distributions had been measured during the treatment. For this patient, we had measured fluence rates in four quadrants, which were defined as right upper quadrant (RUQ), left upper quadrant (LUQ), right lower quadrant (RLQ), and left lower quadrant (LLQ) (Fig. 10(a)). We did comparisons only in three quadrants because the measured data in one quadrant (RUQ) was not reliable. Figure 10(b)-(d) show the fluence rate distributions at the detector positions, along the z direction. The measurement results were plotted with solid lines. The calculation results were plotted with dashed and dotted lines. According to the ultrasound images, the z coordinates of the prostate in LUQ, RLQ, and LLQ were between 0 and 1 cm, 0 and 2.2 cm, and 0 and 2.5 cm. It was found that the optical properties of the outer layer affected the fluence rate distribution. In the calculations, we assumed that the layer had homogeneous optical properties, i.e., the average optical properties $\mu_a = 0.3 \text{ cm}^{-1}$ and $\mu_s' = 14 \text{ cm}^{-1}$. In LUQ, the distribution (dotted line) calculated using the average optical properties had smaller amplitudes than the measurement. In the other two quadrants, the amplitudes were larger than the measurements. We also searched for the optimal optical properties for the layer for each quadrant using iterative method within optical property ranges: $\mu_a = 0 \sim 2 \text{ cm}^{-1}$ and $\mu_s' = 0.01 \sim 60 \text{ cm}^{-1}$. The results were plotted in dashed lines, which showed better agreements with the measurements in both amplitude and profile, compared to the calculations using the average optical properties for the layer. We found that the optimal optical properties for the outer layer were different for each quadrant and were close to the measured optical properties at that quadrant. For example, the optimal optical properties for the layer in LUQ calculation are $\mu_a = 0.01 \text{ cm}^{-1}$ and $\mu_s' = 46 \text{ cm}^{-1}$, and the optical properties in the prostate at the boundary of LUQ are $\mu_a = 0.07 \text{ cm}^{-1}$ and $\mu_s' = 46.6 \text{ cm}^{-1}$. Overestimated absorption in the layer, e.g., the average optical properties for LUQ, caused lower fluence rates in the prostate in the calculation, and vice versa (the average optical properties for RLQ and LLQ). Since the optical property measurements in the z direction were in the range of 0-2.5 cm, the optical properties outside this range were not available. The search for the optimal optical properties can do

compensation to find the optical properties which were unknown. This result implies the potential of reconstructing optical property distribution by the optimization search.

4. CONCLUSIONS

Finite element method was applied to study the light fluence rate distribution in a treated prostate. A layer structure, in which the prostate was surrounded by scattering-medium layer, was proposed. Boundary conditions incorporating refractive-index mismatch was studied. Calculations considering boundary conditions, real prostate geometry, and heterogeneous optical properties were carried out. The calculations using the measured heterogeneously-distributed optical properties showed more accurate results, compared to those using homogeneous optical properties. With the optimal search for the unknown optical properties, the calculation provided the capability to obtain accurate results (compared with measurements) and showed the possibility of reconstructing optical properties.

Acknowledgments

This work is supported by grants from Department of Defense (DOD) DAMD17-03-1-0132 and National institute of health (NIH) P01 CA87971 and R01 CA109456.

References

1. Zhu TC, Dimofte A, Finlay JC, Stripp D, Busch T, Miles J, Whittington R, Malkowicz SB, Tochner Z, Glatstein E, Hahn SM. Optical properties of Human Prostate at 732nm Measured *in vivo* during motexafin lutetium-mediated photodynamic therapy. *Photochem photobiol.* 2005; 81:96–105. [PubMed: 15535736]
2. 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: Biol.* 2005; 79:231–241.
3. Schweiger M, Arridge SR, Hiraoka M, Delpy DT. The finite element method for the propagation of light in scattering media: Boundary and source conditions. *Med Phys.* 1995; 22(11):1779–1792. [PubMed: 8587533]
4. Lee JH, Kim S, Kim YT. Finite element method for diffusive light propagations in index-mismatched media. *Opt Express.* 2004; 12(8):1727–1740. [PubMed: 19474999]
5. Faris, Gregory W. Diffusion equation boundary conditions for the interface between turbid media: a comment. *J Opt Soc Am.* 2002; A19(2):519–520.
6. Dehghani, Hamid; Brooksby, Ben; Vishwanath, Karthik; Pogue, Brian W.; Paulsen, Keith D. The effects of internal refractive index variation in near-infrared optical tomography: a finite element modelling approach. *Phys Med Biol.* 2003; 48:2713–2727. [PubMed: 12974584]

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

Figure 2.

Fluence rate distributions calculated using different boundary conditions in a 3-cm (in the z direction) prostate with a 5-cm light source.

Figure 3.
Prostate with surrounding medium.

Figure 4.
Two-cylinder geometry with meshes, linear source is at the center, along the longitudinal direction (z direction)

Figure 5.

(a) Fluence rate distribution along z for the 3-cm source, at 0.5 cm away; and (b) fluence rate distribution along z for the 5-cm source, at 0.5 cm away fluence rate

(a)

(b)

Figure 6.

(a) Ultrasound image of a patient's prostate. (b) Prostate geometry reconstructed using ultrasound images.

Figure 7. Measured optical properties in the plane of $z=0.5$ cm. (a) Optical absorption coefficients. (b) Optical scattering coefficients.

Figure 8.

(a) Mesh plot of the prostate geometry with a cylindrical layer. (b) Calculation result. A surface plot at the plane of $z = 1.5$ cm. Color bar shows the range of fluence rate (mW/cm^2) distribution in this plane.

Figure 9.

(a) Isodose surface of 150 mW/cm^2 obtained in the calculation using heterogeneous optical properties. (b)-(h). Isodose lines in each slice. Solid line: prostate contour; dashed line: isodose line for the calculation using homogeneous optical properties; dotted line: isodose line for the calculation using heterogeneous optical properties.

Figure 10.

(a) Locations of the sources and detectors in four quadrants (RUQ, LUQ, RLQ, and LLQ). Comparisons of fluence rate distributions between measurements and calculations at the detector positions, along z direction, in (b) LUQ, (c) RLQ, and (d) LLQ. Solid line: measurement; dashed line: calculations using certain optical properties indicated in the figure; dotted line: calculation using the average optical properties ($\mu_a = 0.3 \text{ cm}^{-1}$ and $\mu_s' = 14 \text{ cm}^{-1}$).