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Monte Carlo simulation of light fluence calculation during pleural PDT

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Abstract

A thorough understanding of light distribution in the desired tissue is necessary for accurate light dosimetry in PDT. Solving the problem of light dose depends, in part, on the geometry of the tissue to be treated. When considering PDT in the thoracic cavity for treatment of malignant, localized tumors such as those observed in malignant pleural mesothelioma (MPM), changes in light dose caused by the cavity geometry should be accounted for in order to improve treatment efficacy. Cavity-like geometries demonstrate what is known as the “integrating sphere effect” where multiple light scattering off the cavity walls induces an overall increase in light dose in the cavity. We present a Monte Carlo simulation of light fluence based on a spherical and an elliptical cavity geometry with various dimensions. The tissue optical properties as well as the non-scattering medium (air and water) varies. We have also introduced small absorption inside the cavity to simulate the effect of blood absorption. We expand the MC simulation to track photons both within the cavity and in the surrounding cavity walls. Simulations are run for a variety of cavity optical properties determined using spectroscopic methods. We concluded from the MC simulation that the light fluence inside the cavity is inversely proportional to the surface area.

Keywords

Photodynamic therapy; photon transport; intracavitary treatment planning; Monte Carlo Simulations

1. INTRODUCTION

Photodynamic therapy (PDT) is a cancer treatment modality well suited for treating localized cancers, such as malignant pleural mesothelioma (MPM). MPM has no standard treatment protocol and patient outlook is on average, 6–17 months. Traditional cancer treatments do not consistently improve patient outlook, and PDT is one treatment option that shows promise. PDT uses a photosensitizing drug that is administered to the patient at a prescribed time before surgery. Once this time has elapsed, the treatment area is illuminated by a laser of a drug-specific wavelength. This illumination generates singlet oxygen that, in

turn, causes localized cell death and tissue necrosis. Thus it is critical to understand and monitor the amount of light delivered to the desired tissue to optimize treatment efficacy. The more uniform and consistent light is delivered will lead to greater treatment accuracy and patient outlook.

Current PDT MPM protocol at the University of Pennsylvania involves the surgical debulking of tumor in the thoracic cavity, followed by illumination from a laser that is monitored by seven isotropic detectors, sutured at several different locations in the patient's thoracic cavity. The clinician uses the real time read out of the detectors as a guide for the regions of the cavity being treated. The pleural treatment program at Penn treats patients with MPM or pleural effusion. The photosensitizing drug, HPPH®, is administered 24–48 hours before irradiation. Once this illumination time is complete, the patient under goes surgical tumor debulking and irradiation. The irradiation is applied using a laser of wavelength 661 or 665 nm at 15–60 J/cm. Within the thoracic cavity, the light delivery is continuously administered by a moving point source directed by the clinician. It is at this point in the PDT treatment where real-time dosimetry guidance becomes most critical. As the clinician applies the light source, the knowledge of how greatly each particular area of the thoracic cavity is being irradiated will make the entire treatment process more effective and efficient.

The clinician uses a real time read out of the fluence from the isotropic detectors, measured in mW/cm², as guide to treat the thoracic cavity uniformly. This treatment protocol is not customized to each patient's specific thoracic cavity geometry. The geometry of the treatment volume is an important consideration. We know from Star[1] that when a spherical cavity is illuminated, the overall fluence is higher than it would be for a semi-infinite plane. This phenomenon, known as the integrating sphere effect (IS effect) results from photons scattering multiple times into the cavity. For treatment planning purposes then, it is important to consider the IS effect. Monte Carlo simulations of cavities with varying shape and optical properties provide a method to better understand total fluence in a cavity. We present the results of a series of Monte Carlo (MC) simulations, considering the fluence at the cavity wall for spherical and ellipsoidal cavities. In the future, this work can be used to improve treatment planning for cavity-like geometries such as the thoracic cavity or bladder.

2. THEORY

We follow the work of Willem Star[1] to calculate analytically the fluence in a spherical cavity. The diffusion approximation is applied to a spherical geometry to model the cavities we hope to work with in a clinical setting. The diffusion approximation can be expressed as,

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

where $D=(1/3 \mu_s')$, μ_s' is the reduced scattering coefficient (cm⁻¹), μ_a is the absorption coefficient (cm⁻¹), ϕ is the fluence rate, and S is the source term. Since we are working in spherical geometry, ϕ is a function of position r and independent of angle by symmetry. To solve for the fluence, we need to apply boundary conditions both within the medium surrounding the cavity and within the cavity[2],

$$\hat{n} \cdot \nabla \phi = 0, \text{ (inside medium)} \quad (2)$$

$$\phi + A' D \hat{n} \cdot (\nabla \phi) = 0, \text{ (inside cavity)} \quad (3)$$

To solve for the fluence within the medium we assume that all back-scattered photons re-enter the medium[1]. Applying equation (2) to equation (1) we can find an expression for the fluence in the surrounding medium by approximating the solution to Eq. (1) with a linear combination of exponential integrals[2],

$$\phi(r) = \frac{3S}{4\pi} \left\{ \frac{\mu_{tr} e^{-\mu_{eff}(r-r_0)}}{r(1+\mu_{eff}r_0)} - \frac{2}{3} \frac{e^{-\mu_t(r-r_0)}}{r^2} \right\}, \quad (4)$$

where $\mu_{eff} = (3\mu_a\mu_{tr})^{1/2}$, $\mu_t = \mu_a + \mu_s$, $\mu_{tr} = \mu_a + \mu_s(1-g)$, and r_0 = cavity radius. This solution holds only for an isotropic source and is independent of refractive index mismatch. Solving Eq. (3) for Eq. 1 for fluence within the cavity gives:

$$\phi(r)_{total,cavity} = \frac{S}{4\pi r^2} + \frac{S \cdot \beta}{4\pi r_0^2}, \quad (5)$$

where β is a function of optical properties and refractive index,

$$\beta = \left(\frac{\mu_{eff}}{\mu_a} - 3 \right) t, \quad (6)$$

$$t = \int_0^\theta 2t_{fresnel} \cos\theta \sin\theta d\theta, \quad (7)$$

where $t_{fresnel} = 1 - R_{fresnel}$, which is expressed as:

$$\frac{1}{2} \left(\left(\frac{n \cos\theta' - n_{tissue} \cos\theta}{n \cos\theta + n_{tissue} \cos\theta'} \right)^2 + \left(\frac{n \cos\theta - n_{tissue} \cos\theta'}{n \cos\theta + n_{tissue} \cos\theta'} \right)^2 \right), \quad (8)$$

where n is index of refraction of the cavity, n_{tissue} is the index of refraction of the surrounding medium, θ is the angle of incidence, and θ' is the angle of refraction. This solution is for a centrally located, isotropic light source with homogeneous optical properties in a spherical cavity with no attenuation present in the cavity.

The solution presented here accounts for the effects of backscattered light but only holds for symmetric geometries where angular dependence can be ignored. To account for attenuation at the cavity wall Eq. 5 becomes:

$$\phi(r)_{total,cavity} = \left(\frac{S}{4\pi r^2} + \frac{S \cdot \beta}{4\pi r_0^2} \right) e^{-\mu_{eff}r}. \quad (9)$$

Equation (9) demonstrates that, for a spherical cavity, the total fluence is inversely proportional to the surface area of the cavity. We consider a spherical as well an ellipsoidal cavity in this study. Our MC results for the ellipsoidal cavity are compared to Eq. (9) where the surface area is given by:

$$SA = 2\pi a^2 + \pi \frac{c^2}{e} \ln \left(\frac{1+e}{1-e} \right), \quad (10)$$

where e is a function of the semi-principal axes, a and c , of the cavity,

$$e^2 = 1 - \frac{c^2}{a^2}. \quad (11)$$

In this way, we begin perturb the spherical cavity and observe, via MC simulation, how the total fluence is affected by this loss of symmetry.

3. METHODS

2.1 Monte Carlo Simulation and Photon Transport

To model photon transport in different cavities, MC simulations are a widely used method. The MC simulation developed here is a modified version of the code developed in C by Boas et al. [3]. Their simulation, whose photon transport method is described in detail by Wang and Jacques[4], is able to track photons as they travel through a grid laid over the entire geometry in different regions of optical properties. This tracking methods is particularly useful for our purposes, where the simulation cavity has either no absorption or scattering (no attenuation) or minimal absorption (attenuating). In our previous work[5], we did not track the photons in the cavity, only those in the surrounding medium. By tracking the photon at any point in the geometry we again further knowledge of how photon transport is affected by different geometries.

A brief description of how the MC simulation handles photon migration follows. A photon is launched in a user-specified direction from a given location. To achieve an isotropic point source, each photon is launched in a random direction from ranging from 0 to 2π from the center of the cavity (determined by using a uniformly distributed random number). The length to the first scattering event is calculated using an exponential distribution. Photon absorption is determined by decreasing the photon weight by $e^{(-\mu_a L)}$ where L is the length the photon travels[4]. The Henyey-Greenstein phase function is used to determine the scattering angle. The new scattering length of the photon is then determined from an exponential distribution as before. The photon is propagated this new length in the new direction. This propagation process continues until the photon exits the medium or the photon traveled for 10 ns, which at this point, its weight can be regarded as negligible[3]. When a photon encounters a medium boundary, the probability of reflection is calculated using Fresnel's equation[4]. If the photon is reflected back into the cavity, our multiple scattering treatment (described below) determines the photon's path.

The MC simulations presented here were performed for a spherical cavity of radius 10 cm and an ellipsoid of semi-major axis 10 cm and semi-minor axis of 5 cm (this is by definition an oblate ellipsoid). 10^8 photons were run for each simulation. The absorption coefficient of the surrounding medium ranged from 0.01 to 0.05 and 0.1 cm^{-1} , while the reduced scattering coefficient was kept constant at 5 cm^{-1} . Simulations were run for an air cavity ($\mu_a=\mu_s'=0$) and an attenuating cavity ($\mu_a=0.005 \text{ cm}^{-1}$). The voxel size of the geometry was 1 mm^3 .

3.2 Multiple Scattering

The MC simulation code developed by Boas et al. [3] does not account for the multiple scattering observed in large cavities. To accurately simulate the photon migration the cavity size of interest, we added a treatment of multiple scattering to the existing simulation. The multiple scattering treatment is based on previous work[5] and is described schematically in Fig. 1. We consider multiple scattering first for a sphere, whose complete symmetry allow the calculation of scattering angles to be simplified. As the cavity loses axes of symmetry the calculation of scattering angles off the inner cavity wall becomes more complicated and approximations are made for the scattering angle.

3. RESULTS

3.1 Spherical Cavity

The MC simulations for a spherical cavity were performed on a sphere with two different tissue layers (see Fig. 2). The inner sphere, of radius 10 cm was assigned either a $\mu_a=\mu_s'=0$ (air cavity) or a $\mu_a=0.005 \text{ cm}^{-1}$ (attenuating cavity). The outer spherical shell had an inner radius of 10 cm and outer radius of 20 cm. The reduced scattering coefficient was kept constant while the absorption coefficient was varied (as described earlier). The volume was broken up into voxels, each 1 cm^3 in size. Photon positions were tracked voxel by voxel. The results from the simulations are presented in Fig. 3a–d.

3.2 Ellipsoidal Cavity

4. DISCUSSION AND CONCLUSION

Our results demonstrate that despite the loss of symmetry in an ellipsoidal cavity, the total fluence in the cavity is inversely proportional to the surface area of the cavity. When comparing the fluence as a function of distance from the center of the cavity to the analytic solution given by Star, there is good agreement for an air cavity. When the cavity is filled with an attenuating medium, however, the analytic solution overestimates the fluence. A modified solution, then, is needed to model the fluence in an attenuating cavity accurately. This modification is important, as we look to simulations that simulation conditions in the clinic more closely. The treatment cavity is rarely just filled with air. Instead, blood and an Intralipid™ solution are present, both scattering and absorbing photons. Furthermore, homogeneous optical properties were used in this study. In reality, the optical properties of the thoracic cavity are highly variable. In the future, *in-vivo* optical property data can be used to create a more realistic simulation geometry.

Acknowledgments

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Fig. 1.

Schematic of how attenuation is accounted for in our MC simulation. The point p_0 is the point where two photons interact a distance r_0 from the cavity center. The photon which hits the cavity wall with direction u_0 , a distance r_2 from the cavity center and then travels a distance l and is incident on the cavity wall with an angle β and then refracts at an angle α .

Fig. 2.

Visualization of the spherical cavity generated in MATLAB[™]. For plotting purposes the volume's size was normalized by the outermost radius. Photons were launched from the center of this volume. The code used allows the user to track photons at any location in the geometry. For this study, photons were tracked at different locations along the cavity-medium boundary (where the red and green spheres meet).

Fig. 3.

(a) Fluence as a function of position from the cavity center, normalized to the cavity radius (10 cm) for a centrally located source in an air cavity. The solid line represents analytic solution where line color indicates different μ_a (red=0.01 cm⁻¹, green=0.05 cm⁻¹, blue=0.1 cm⁻¹). MC results are represented by circles, with same color representation indicating the respective μ_a as before. (b) Total fluence at the cavity wall for varying total cavity surface area for an air cavity, where **x** represents the MC results and **o** represents the analytic solutions. Overall, for the air cavity, there is good agreement between analytic and MC results for total fluence as a function of surface area. (c) Fluence as a function of position from the cavity center normalized to cavity radius (10 cm) for a centrally located source in an attenuating cavity ($\mu_{att}=0.005$ cm⁻¹). The same representation scheme used in (a) is applied here. (d) Total fluence at the cavity wall for varying total cavity surface area in an attenuation cavity. Again, the same representation schema used in (b) is applied here. Note that, compared to (b), the analytic solution tends to overestimate the total fluence in the presence of an attenuating medium in the cavity.

Fig. 4.

(a) Visualization of the ellipsoidal cavity used for simulation, with the geometry normalized to outer semi-major axis (20 cm). (b) The ellipsoidal cavity used in this study is an oblate ellipsoid, where the two semi-major axes are equal with the semi-minor axis < semi-major axes. A cross section of the ellipsoidal cavity is depicted here along the semi-minor axis. (c) Cross section of the cavity along the semi-major axis.

Fig. 5.

(a) Fluence as a function of position from the cavity center, normalized to the cavity semi-major axis (10 cm) for a centrally located source in an air cavity. The solid line represents analytic solution whewith $\mu_a=0.01 \text{ cm}^{-1}$. Circles represent MC results. (b) Total fluence at the cavity wall for varying total cavity surface area for an air cavity, where $\times$ represents the MC results and $\circ$ represents the analytic solutions and different μ_a are indicated by color (red= 0.01 cm^{-1} , green= 0.05 cm^{-1} , blue= 0.1 cm^{-1}). Overall, for the air cavity, there is good agreement between analytic and MC results for total fluence as a function of surface area. (c) Fluence as a function of position from the cavity center normalized to cavity semi-major axis (10 cm) for a centrally located source in an attenuating cavity ($\mu_{\text{att}}=0.005 \text{ cm}^{-1}$). The same representation scheme used in (a) is applied here. (d) Total fluence at the cavity wall for varying total cavity surface area in an attenuation cavity. Again, the same representation schema used in (b) is applied here. Compared to the results in Fig. 3, the analytic solution systematically overestimates the total fluence. This overestimation becomes more pronounced in the presence of an attenuating cavity medium.