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An improved analytic function for predicting light fluence rate in circular fields on a semi-infinite geometry

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Abstract

Accurate determination of *in-vivo* light fluence rate is critical for preclinical and clinical studies involving photodynamic therapy (PDT). This study compares the longitudinal light fluence distribution inside biological tissue in the central axis of a 1 cm diameter circular uniform light field for a range of *in-vivo* tissue optical properties (absorption coefficients (μ_a) between 0.01 and 1 cm^{-1} and reduced scattering coefficients (μ_s') between 2 and 40 cm^{-1}). This was done using Monte-Carlo simulations for a semi-infinite turbid medium in an air-tissue interface. The end goal is to develop an analytical expression that would fit the results from the Monte Carlo simulation for both the 1 cm diameter circular beam and the broad beam. Each of these parameters is expressed as a function of tissue optical properties. These results can then be compared against the existing expressions in the literature for broad beam for analysis in both accuracy and applicable range. Using the 6-parameter model, the range and accuracy for light transport through biological tissue is improved and may be used in the future as a guide in PDT for light fluence distribution for known tissue optical properties.

Keywords

MC; PDT; semi-infinite medium; analytical expression

1. INTRODUCTION

When treating the surface lesions with PDT, it is often necessary to treat a lesion size as small as 1-cm in diameter, e.g., all our mice studies for treatment response to PDT use a collimator field of such a circular field [1, 2]. The light fluence rate for 1 cm circular field reduces significantly from that for an infinite large field because of the reduced photon scattering by tissue [3, 4]. The purpose of this study is to determine the longitudinal distribution of light fluence rate for the 1 cm diameter field and expressed the results as an analytical function of tissue optical properties (μ_a , μ_s'). We used Monte-Carlo simulation because the diffusion theory is not valid when the lateral dimension of beam geometry becomes comparable to the mean-free-path of the photons or when the region of interest is near the air-tissue interface. Literature search reveals only analytical expression for broad

beams, when the lateral dimension is much larger than the mean-free path [5]. For broad beams, dependence on the two dimensional tissue optical properties (μ_a , μ_s') can be simplified as a one-dimensional function of albedo, $a' = \mu_s' / (\mu_a + \mu_s')$, or diffuse reflectance, R_d , so long as all spatial dimensions are scaled by the mean-free path ($I = 1/(\mu_a + \mu_s')$) [5].

2. MATERIALS AND METHODS

2.1 MC simulation

The setup geometry to be calculated by Monte-Carlo simulation for a semi-infinite medium with uniform optical properties, i.e. the absorption coefficient μ_a , the scattering coefficient μ_s , the scattering anisotropy g ($= 0.9$), and the index of refraction n (1.4 for tissue) is shown in Fig. 1a. The outside medium is air ($n_0=1$). The light field is parallel and uniform inside a circle with radius R and incident toward the air-tissue interface. ($R = 0.5$ cm or 10 cm for broad beam except for when $\mu_a = 0.01$ and $\mu_s' = 2$ cm $^{-1}$, where $R = 30$ cm was used.) Most tissues have a preferential scattering in the forward direction with a scattering anisotropy $g = 0.90$ [6]. In the diffusion approximation, the tissue scattering is converted to isotropic conditions ($g = 0$) and the tissue scattering property is described by a reduced scattering coefficient $\mu_s' = \mu_s (1-g)$. To improve the scoring efficiency, Monte-Carlo simulation is performed for a pencil-beam incident on a semi-infinite tissue phantom (Fig. 1b). Details of the Monte-Carlo simulation process are described elsewhere [3]. The range of tissue optical properties (μ_a between 0.01 and 1 cm $^{-1}$ and μ_s' between 2 and 40 cm $^{-1}$) is based on a review on the *in-vivo* tissue optical properties [7].

2.2 Analytical expression and fitting algorithm

For 1-cm diameter circular fields, we found that Eq. (1) can fit the resulting MC data very well, typically to a depth of at least 0.5 cm or a few mean-free-path, I , whichever is larger. This fitting equation is termed 6-parameter fit since it includes 6 fitting parameters: λ_1 , λ_2 , λ_3 , b , C_2 , C_3 :

$$\phi/\phi_{\text{air}} = (1 - b \cdot e^{-\lambda_1 d})(C_2 e^{-\lambda_2 d} + C_3 e^{-\lambda_3 d}), \quad (1)$$

where $\phi_{\text{air}} = P/A$, $A = \pi R^2$ is called in-air fluence rate that can be calculated using the total power, P (in mW), and the treatment area, A , of the collimated beam. For a broad beam, existing literature shows that a 4-parameter fit (λ_1 , λ_2 , b , C_2) is sufficient to fit the MC data [5]:

$$\phi/\phi_{\text{air}} = (1 - b \cdot e^{-\lambda_1 d}) \cdot C_2 e^{-\lambda_2 d}. \quad (2)$$

We have modified the original form ($\phi / \phi_{\text{air}} = C_2 e^{-\lambda_2 d} - C_1 e^{-\lambda_1 d}$) [5] to be Eq. (2) because the term $(1 - b \cdot e^{-\lambda_1 d})$ that fits the buildup region only can be taken out of the final results, and one will automatically get the analytical expression for diffusion approximation, i.e., C_2 is the backscattering coefficient and $\lambda_2 = \mu_{\text{eff}}$ is the effective attenuation coefficient.

The non-linear optimization routine was performed in Matlab by minimizing a standard deviation according to:

$$f = \sqrt{\frac{\sum_{i=1}^N \left(1 - \frac{\varphi_{\text{fit}}(z_i, \text{params})}{\varphi_{MC}(z_i)}\right)^2}{N(N-1)}}. \quad (3)$$

Where φ_{fit} is based on either Eq. 1 and/or Eq. 2 to result in either 6 or 4 parameters as the results of optimization. φ_{MC} is the MC simulation result as a function of discrete depth z_i , $i = 1, 2, \dots, N$. Typical value of z_i is between 0 and 2 cm in 0.01 cm steps, i.e., $N = 200$. Multi-variable optimization algorithm uses a deferential convolution algorithm described elsewhere [8].

2.3 Relationship between fitting parameters and the tissue optical properties

For broad beams, we have found that all four fitting parameters are a function of R_d (or a') as used by Jacques [5]. The two fitting parameters (λ_1 and λ_2) should be proportional to μ_{eff} . We have found the following relationships:

$$b = 1.154 - 1.025 \cdot R_d^{0.1823}, \quad (4)$$

$$\frac{\lambda_1}{\mu_{\text{eff}}} = 1.596 \cdot e^{3.547 \cdot R_d}, \quad (5)$$

$$C_2 = 5.996 \cdot R_d + 2.931, \quad (6)$$

$$\frac{\lambda_2}{\mu_{\text{eff}}} = 3.039 \cdot R_d^5 - 8.023 \cdot R_d^4 + 8.342 \cdot R_d^3 - 4.306 \cdot R_d^2 + 1.144 \cdot R_d + 0.865. \quad (7)$$

For 1-cm diameter beam, we found that that it is still possible to express the parameters λ_1 as a function of R_d and the parameters $\lambda_2/\mu_{\text{eff}}$ as a function of μ_{eff} but the λ_2 value is larger than the corresponding values for the broad beam. It is not possible to express the other fitting parameters as a function of R_d alone. We have found the following relationship between them to optical properties (μ_a, μ_s') as a two-dimensional function:

$$b = \frac{0.672 + 0.6675 \cdot e^{-9.72 \cdot \mu_a} - 0.533 \cdot e^{-4.68 \cdot \mu_a}}{\mu_s'^{0.3185} - 0.3172}, \quad (8)$$

$$\frac{\lambda_1}{\mu_{\text{eff}}} = 0.00355 \cdot e^{10.04 \cdot R_d} + 1.549 \cdot e^{2.441 \cdot R_d}, \quad (9)$$

$$C_2 = \frac{4.613 \cdot \mu_s'^{0.2713} + 6.924}{\mu_a^{0.5983} + 2.268}, \quad (10)$$

$$\lambda_2 = 0.8859 \cdot (\mu_a \cdot \mu_s')^{0.6251} + 2.399, \quad (11)$$

$$C_3 = \frac{0.6031 \cdot e^{-9.622 \cdot \mu_a}}{\mu_s'^{4.275 \cdot \mu_a}}, \quad (12)$$

$$\lambda_3 = (0.0224 \cdot \mu_s' + 1.141) \cdot (1.159 \cdot \mu_a + 0.5668). \quad (13)$$

3. RESULTS AND DISCUSSIONS

Tables 1 and 2 show the summary results of fitting the MC simulation results for a board beam (10 cm diameter for all tissue optical properties except for $\mu_a = 0.01 \text{ cm}^{-1}$ and $\mu_s' = 2 \text{ cm}^{-1}$, where a 30 cm diameter circular beam was used) and a 1-cm diameter beam, respectively, for depth up to 3.5 cm deep. For 1-cm diameter circular beam, C_3 approaches zero for a subset of data ($\mu_a = 0.1 \text{ cm}^{-1}$) so that only a 4-parameter fit is necessary. In this case, the value of λ_3 is unnecessary and its value is expressed as “—” in Table 2.

Figure 2 show the fitting results for the 4-parameters used for broad beam and Eqs. 4 – 7. The fitting is performed using the curve fitting tool from Matlab global optimization toolbox (cftool.m). R^2 of the fitting results are all very good ($R^2 > 0.98$). For broad beam, as pointed out in previous publication [5], the diffuse reflectance can be used in place of the pairs of optical properties (μ_a, μ_s'). The R_d values are obtained from MC simulation [3, 4] and are listed in Table 1 and Figure 3. An analytical expression based on the same form as a diffusion approximation [9] can be determined between R_d and the albedo, a' as:

$$R_d = 0.4843a' \cdot (1 + e^{-4.428 \sqrt{1-a'}}) \cdot e^{-2.65 \sqrt{1-a'}}, \quad (14)$$

$$a' = \frac{\mu_s'}{\mu_s' + \mu_a}. \quad (15)$$

Figure 3 shows the goodness of the fit between R_d and $a'/(1-a')$ using Eq. 14.

Figure 4 shows the fitting results for the 6-parameters used for the 1-cm diameter circular beam and Eqs. 8–13. Notice that the scaling theorem is no longer in existence so that most of the parameters have to be expressed as a function of two dimensional function of μ_a and μ_s' . R^2 of the fitting results are also very good ($R^2 > 0.97$). It is also found that 6 parameters are necessary to fit the data instead of 4 parameters for some tissue optical properties, particularly those with low absorption coefficients ($\mu_a < 0.1 \text{ cm}^{-1}$). We actually started with 4 parameter fitting to the MC data and then introduce the two additional parameters (C_3, λ_3) in Eq. 1 to improve fitting results to the MC data.

A comparison between the 4 parameters between 1-cm diameter beam and the broad beam for the same optical properties shows that λ_2 is always larger for 1-cm beam than that for the

broad beam. C_2 is quite similar between 1-cm beam and broad beam for most tissue optical properties except for $\mu_a = 0.01 \text{ cm}^{-1}$. We used a different expression (Eq. 10) for the 1-cm diameter circular beam than that for the broad beam (Eq. 6).

Figure 5 shows the comparison between MC simulation results of ϕ/ϕ_{air} for (a) broad beam and (b) 1-cm diameter beam using the fitting parameters in Tables 1 and 2, respectively, as well as Eqs. 4–7 and Eqs. 8–13. For comparison, we have also included the fitting results from Ref.[5] for the broad beam.

Figure 6 shows the relative deviation of the fitting and the MC simulation results for (a) broad beam and (b) 1-cm diameter beam, defined as the difference between the fit and the MC result relative to the maximum fluence rate.

For broad beam, Eqs. 4–7, fits all MC data to a maximum error of $\pm 2\%$ for all depths, while parameters from Table 1 fits the MC data to within 1% for all depths. Parameters from Ref. [5] fit most of the data except for $\mu_a = 0.01 \text{ cm}^{-1}$, where 20% error is observed. Among the difference between our MC data and Jacques's fit, 3% can be attributed to difference in the value of index of refractions used for the MC simulation: 1.4 and 1.38 between us and Jacques, as well as other subtle differences in MC simulation. For the 1-cm diameter circular beam, the 6 parameter fitting using Eqs. 8–13, can fit the MC data to a maximum error of $\pm 8\%$ for depth up to 3.5 cm for all optical properties considered in this study, while parameters from Table 2 fits the MC data to a maximum error of $\pm 2\%$. It is clear that 4 parameter fits (Eqs. 4 – 7) cannot fit the MC data very well for 1-cm diameter beams for low absorption coefficients, yielding a maximum error of over 22% for $\mu_a = 0.01 \text{ cm}^{-1}$ and $\mu_s' = 2 \text{ cm}^{-1}$.

One additional advantage of our expression (Eq. 1) is that the fitting based on diffusion approximation is automatically obtained by dividing it by $(1 - be^{-\lambda_1 d})$. The results are shown in Fig. 7 for (a) broad beam and (b) 1-cm diameter circular beam, respectively. For broad beam, Eqs. 4 – 7 without the buildup region fits the data very well. For 1-cm circular beam, the buildup region term have a larger impact on the light fluence rate distribution on the central axis, extending up to 0.5 cm depth. The fit is not good for low absorption coefficients ($\mu_a = 0.01 \text{ cm}^{-1}$, see Fig. 7b)

Figure 8 shows the relative deviation between the fit and the MC simulation, normalized to the maximum MC calculated fluence rate. Beyond the buildup region, the maximum error is 1% for the broad beam and 12% for the 1-cm circular beam for depth up to 1 cm. Within the buildup region, the maximum error is 23% for the broad beam and 120% for the 1-cm circular beam.

4. CONCLUSION

We have performed MC simulation for air-tissue interface and provided an expression for the longitudinal light fluence rate distribution on the central axis with an accuracy of better than a relative standard deviation of 2% for broad beams and 8% for the 1-cm diameter circular beams for the full range of the *in-vivo* tissue optical properties studied. An analytical expression is provided to determine the parameters as a function of tissue

properties. We have also independently validated the analytical fitting result for broad beams.

Acknowledgments

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Figure 1.

(a) Setup geometry for Monte-Carlo simulation for a semi-infinite turbid medium. The light fluence rate is calculated along the central-axis on the center of the field. (b) Pencil beam setup is actually used for the Monte Carlo simulation. The ring scoring voxel has radius width dr and thickness dz at depth z and radius r in a cylindrical geometry.

Figure 2.

Fitting results between the 4 parameters (b , C_2 , $\lambda_1/\lambda_{\text{eff}}$, $\lambda_2/\mu_{\text{eff}}$) and the diffuse reflectance (R_d) for broad beams. Solid lines are Eqs. 4–7 for their respective parameters, black circles represent fitting results using 4 parameters from Table 1, and red triangles represent parameters using formulas from Ref. [5]. R^2 refers to the goodness of fit between the fitting results of each parameter to their respective equation.

Figure 3.

Relationship between R_d and $a'/(1-a')$, where the albedo $a' = \mu_s' / (\mu_a + \mu_s')$. R^2 refers to the goodness of fit between the R_d and Eq. 14.

Figure 4.

Fitting results between the 6 parameters (b , C_2 , C_3 , $\lambda_1/\mu_{\text{eff}}$, λ_2 , λ_3) and the optical properties (μ_a and μ_s') for 1-cm circular beam. Solid lines are Eqs. 8–13 for their respective parameters, black circles represent fitting results using 6 parameters from Table 2. R^2 refers to the goodness of fit between the fitting results of each parameter to their respective equation.

Figure 5. ϕ/ϕ_{air} for (a) broad beam and (b) 1-cm diameter beam for three tissue optical properties $(\mu_a, \mu_s') = (i) (1, 40), (ii) (0.1, 10), \text{ and } (iii) (0.01, 2) \text{ cm}^{-1}$.

Figure 6.

Relative deviation of the fitting results to the MC simulation data for (a) broad beam and (b) 1-cm beam for three tissue optical properties $(\mu_a, \mu_s') =$ (i) (1, 40), (ii) (0.1, 10), and (iii) (0.01, 2) cm^{-1} . Data for (i) and (ii) are vertically shifted for clarity: +25% for (ii) and +30% for (i) for (a) and +25% for (ii) and +30% for (i) for (b), respectively.

Figure 7.

(a) ϕ/ϕ_{air} for broad beam with MC simulation and 4-parameter fitting using Eqs. 4 – 7 without the buildup term and (b) ϕ/ϕ_{air} for 1-cm diameter beam with MC simulation and 6-parameters fitting using Eqs. 8 – 13 without the buildup region for three tissue optical properties $(\mu_a, \mu_s') = (i) (1, 40), (ii) (0.1, 10), \text{ and } (iii) (0.01, 2) \text{ cm}^{-1}$.

Figure 8.

(a) Relative deviation of the 4-parameter fitting using Eq. 2 without the buildup region to the MC simulation data for broad beam, (b) Relative standard deviation of the 6-parameter fitting using Eq. 1 without the buildup region to the MC simulation data for 1-cm beam.

Table 1

Summary of the 4 fitting parameters ($b, \lambda_1, \lambda_2, C_2$) using Eq. 2 to the MC calculated ϕ/ϕ_{air} for broad beam for optical properties (μ_a, μ_s). MC calculated diffuse reflectance R_d is also listed.

μ_a	μ_s	R_d	b	λ_1	λ_2	C_2
0.1	2	0.6907	0.23	4.82	0.25	7.10
	10	0.8317	0.16	16	0.55	7.89
	23.5	0.8777	0.16	30	0.85	8.2
0.01	34.5	0.8936	0.15	38	1.03	8.24
	40	0.8991	0.14	42	1.12	8.27
0.1	2	0.3589	0.29	4.21	0.79	5.1
	10	0.6042	0.2	22.3	1.74	6.54
	23.5	0.7084	0.2	52.6	2.67	7.19
0.1	34.5	0.7475	0.18	80.6	3.23	7.36
	40	0.7611	0.18	89.7	3.48	7.46
0.5	2	0.1334	0.45	3.81	1.86	3.69
	10	0.3589	0.29	22.1	3.93	5.08
	23.5	0.4947	0.25	52.9	5.98	5.93
0.5	34.5	0.5518	0.24	77.4	7.23	6.30
	40	0.5730	0.24	90.62	7.78	6.43
1	2	0.0710	0.52	3.74	2.78	3.25
	10	0.2520	0.36	21.66	5.63	4.42
	23.5	0.3848	0.3	52.95	8.5	5.29
1	34.5	0.4463	0.29	76.26	10.28	5.71
	40	0.4694	0.25	89.21	11.04	5.77

Table 2

Summary of the 6 fitting parameters ($b, \lambda_1, \lambda_2, C_2, \lambda_3, C_3$) using Eq. 1 to the MC calculated ϕ/ϕ_{air} for 1-cm diameter circular beam for optical properties (μ_s, μ_a, μ_t).

μ_t	μ_s'	b	λ_1	λ_2	λ_3	C_2	C_3
0.01	2	0.844	3.23	2.74	0.684	5.27	0.494
0.01	10	0.4271	16.8	2.67	0.749	6.591	0.467
0.01	23.5	0.33785	31.05	2.76	0.964	7.849	0.496
0.01	34.5	0.2486	42.3	2.85	1.11	8.163	0.505
0.01	40	0.2293	46.9	2.89	1.162	8.254	0.49
0.1	2	0.6785	2.22	2.55	0.811	5.149	0.178
0.1	10	0.2904	16.6	3.22	0.98	5.927	0.118
0.1	23.5	0.2302	33.8	3.86	1.149	7.231	0.0735
0.1	34.5	0.19	44.4	4.27	—	7.535	0.00122
0.1	40	0.1803	50.7	4.4	—	7.614	0.00117
0.5	2	0.6638	2.85	3.14	—	4.26	0.00485
0.5	10	0.357	17.4	4.87	—	5.19	0.00115
0.5	23.5	0.2618	34	6.57	—	6.175	0.002819
0.5	34.5	0.2354	48.2	7.66	—	6.525	0.000385
0.5	40	0.2252	55.2	8.15	—	6.64	0.000172
1	2	0.6986	3.25	3.79	—	3.876	0.000543
1	10	0.4081	16.5	6.33	—	4.699	0
1	23.5	0.3068	40	8.84	—	5.472	0
1	34.5	0.2812	58.1	10.5	—	5.845	0
1	40	0.2513	69.8	11.2	—	5.887	0