Does the photon-diffusion coefficient depend on absorption?

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We investigate the controversy over the precise form of the photon diffusion coefficient and suggest that it is largely independent of absorption, i.e., \( D_0 = v/3\mu'_a \). After presentation of the general theoretical arguments underlying this assertion, Monte Carlo simulations are performed and explicitly reveal that the absorption-independent diffusion coefficient gives better agreement with theory than the traditionally accepted photon diffusion coefficient, \( D_m = v/3(\mu'_a + \mu_s) \). The importance of resolving this controversy for the proper characterization of the material optical properties is discussed. © 1997 Optical Society of America [S0740-322X(97)01912-1]

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1. INTRODUCTION

Human tissues are turbid media wherein the transport of near-infrared photons is modeled quite well by the diffusion equation. Recently, there has been substantial interest in using near-infrared light to probe human tissues for localized heterogeneities such as breast and brain tumors, and several algorithms based on the photon diffusion equation for detecting and characterizing tumors have been developed.\(^1\)\(^-\)\(^11\)

Nevertheless, there has been some confusion in the community about the exact form of the light diffusion constant in media with both absorption and scattering. Specifically, in most derivations of the diffusion equation from the transport equation, the diffusion coefficient \( D \) is found to be \( D_m = v/3(\mu'_a + \mu_s) \),\(^4\)\(^-\)\(^17\) where \( \mu'_a \) is the medium reduced scattering coefficient, \( \mu_a \) is its absorption coefficient, and \( v \) is the speed of light in the medium. Recently, however, it has been suggested that \( D \) should be independent of absorption, i.e., \( D_0 = v/3\mu'_a \).\(^18\)\(^,\)\(^19\) Resolution of this problem is important for accurate determination of optical properties, particularly in media wherein absorption is large.

In this paper we use Monte Carlo techniques to suggest that the photon diffusion coefficient is independent of absorption. A theoretical discussion similar to that given by Furutsu and Yamada\(^18\) is first developed to illustrate the differences in a particular transformation property of the photon transport equation and the photon diffusion equation. In this case it is argued that the transformation property should be preserved, and this is possible only when \( D = D_0 \). This analysis provides some reasons to reject the traditional photon diffusion coefficient. We then develop a Monte Carlo program to simulate the propagation of photons in infinite, homogeneous, and isotropic media with optical properties resembling those of human tissues. Comparing the Monte Carlo results and photon diffusion theory by using the two different diffusion coefficients, we quantitatively demonstrate that agreement between experiment and theory is improved when \( D = D_0 \).

Characterization of tissue optical properties is an important goal of diffuse optical tomography.\(^6\)\(^,\)\(^20\)\(^-\)\(^22\) In some cases the agreement between diffusion theory and observation will depend on the exact nature of the diffusion coefficient. For example, reconstruction methods based on perturbation theory will have different dependencies on the variations in \( \mu_a \) and \( \mu'_a \). We demonstrate that the characterization is accurate to better than 1% when \( D = D_0 \) and \( \mu_a \sim 0.1\mu'_a \); when \( D = D_0 \), characterization errors are approximately 10% for \( \mu_a = 0.1\mu'_a \).

2. THEORY

The photon diffusion equation is an approximation of the photon transport equation [Eq. (1)], which is known to describe accurately the propagation of photons through random, turbid, highly scattering media.\(^1\)\(^,\)\(^12\)\(^,\)\(^13\) We will first consider some general properties of the transport equation. The transport equation is...
\[
\frac{1}{v} \frac{\partial L(r, \hat{\Omega}, t)}{\partial t} + \nabla \cdot L(r, \hat{\Omega}, t) + \mu_s L(r, \hat{\Omega}, t) = \mu_s \int L(r, \hat{\Omega}', t) f(\hat{\Omega}, \hat{\Omega}') d\hat{\Omega}' + S(r, \hat{\Omega}, t), \tag{1}
\]

where \(L(r, \hat{\Omega}, t)\) is the radiance at position \(r\) traveling in direction \(\hat{\Omega}\) at time \(t\) with units of \(\text{W m}^{-2} \text{sr}^{-1}\) (sr=steradian=unit solid angle), \(f(\hat{\Omega}, \hat{\Omega}')\) is the normalized phase function representing the probability of scattering into a solid angle \(\hat{\Omega}'\) from angle \(\hat{\Omega}\), \(v\) is the speed of light in the medium in \(\text{cm s}^{-1}\), \(\mu_s\) is the scattering coefficient in \(\text{cm}^{-1}\), \(\mu_a\) is the absorption coefficient in \(\text{cm}^{-1}\), \(\mu_s = \mu_s + \mu_a\) is the transport coefficient, and \(S(r, \hat{\Omega}, t)\) is the spatial and angular distribution of the source in \(\text{W m}^{-3} \text{sr}^{-1}\).

This equation has an interesting transformation property for the case of homogeneous turbid media:

\[
L(r, \hat{\Omega}, t) = \exp(-v\mu_a t) L_0(r, \hat{\Omega}, t). \tag{2}
\]

Here \(L(r, \hat{\Omega}, t)\) is the solution of the transport equation in the absorbing media, and \(L_0(r, \hat{\Omega}, t)\) is the solution in the same medium, but with zero absorption. The validity of this transformation is checked by substituting Eq. (2) into Eq. (1) and assuming that the source \(S(r, \hat{\Omega}, t)\) is zero for \(r \neq 0\). After substitution we obtain the following absorption-independent transport equation for \(L_0(r, \hat{\Omega}, t)\):

\[
\frac{1}{v} \frac{\partial L_0(r, \hat{\Omega}, t)}{\partial t} + \nabla \cdot L_0(r, \hat{\Omega}, t) + \mu_s L_0(r, \hat{\Omega}, t) = \mu_s \int L_0(r, \hat{\Omega}', t) f(\hat{\Omega}, \hat{\Omega}') d\hat{\Omega}'. \tag{3}
\]

We see that the time-dependent impulse response of a homogeneous medium has two separable parts: one that is determined by the scattering coefficient \([L_0(r, \hat{\Omega}, t)]\), and one that is determined by the medium absorption \([\exp(-v\mu_s t)]\). This property has been shown to apply for photon propagation in turbid media and has been further exploited by others.\(^{23-26}\)

In light of this observation, diffusion theory might be expected to have the same transformation property. This follows because the diffusion theory is derived from transport theory, and thus its solutions are a subset of the solutions of the transport equation [Eq. (1)]. The traditional time-dependent photon diffusion equation is\(^{1,12}\)

\[
\nabla^2 U(r, t) - \frac{v \mu_a}{D_{\mu_a}} U(r, t) - \frac{1}{D_{\mu_a}} \frac{\partial U(r, t)}{\partial t} = -\frac{1}{D_{\mu_a}} S(r, t), \tag{4}
\]

where \(U(r, t)\) is the photon density at position \(r\) and time \(t\), \(v\) is the speed of light in the medium, \(S(r, t)\) is the source term, and \(D_{\mu_a}\) is the traditional diffusion coefficient

\[
D_{\mu_a} = v/3(\mu'_s + \mu_a), \tag{5}
\]

in which \(\mu_a\) is the absorption coefficient and \(\mu'_s = \mu_s(1 - g)\) is the reduced scattering coefficient, where \(g\) is the scattering anisotropy. In analogy with the solutions of the transport equation [Eq. (2)], we might expect that

\[
U(r, t) = U_0(r, t) \exp(-v \mu_s t), \tag{6}
\]

\[
J(r, t) = J_0(r, t) \exp(-v \mu_s t), \tag{7}
\]

where \(U_0(r, t) [J_0(r, t)]\) is the photon density (photon flux) with absorption and \(U_0(r, t) [J_0(r, t)]\) is the photon density (photon flux) satisfying Eq. (4) without absorption \((\mu_a = 0)\). When these transformations [Eqs. (6) and (7)] are inserted into the traditional diffusion equation [Eq. (4)], we obtain the following equation for \(U_0(r, t)\):

\[
\nabla^2 U_0(r, t) - \frac{1}{D_{\mu_a}} \frac{\partial U_0(r, t)}{\partial t} = 0. \tag{8}
\]

Notice that \(U_0(r, t)\) depends on the sample absorption; the independence of the absorption and scattering parts of the solution is unrealized, i.e., the general transformation property is no longer valid.

Now let us review the derivation of the diffusion equation [Eq. (4)] from the transport equation [Eq. (1)] to gain a better understanding of the approximations that led to the breakdown of this transformation property. We start with the following coupled differential equations:

\[
\frac{\partial}{\partial t} U(r, t) + \mu_a v U(r, t) + \nabla \cdot J(r, t) = S_0(r, t), \tag{9}
\]

\[
\frac{1}{v} \frac{\partial}{\partial t} J(r, t) + (\mu'_s + \mu_a) J(r, t) + \frac{v}{3} \nabla U(r, t) = S_1(r, t). \tag{10}
\]

These equations are obtained from the transport equation [Eq. (1)] by expanding the radiance and the source term,\(^{13,27}\) i.e.,

\[
L(r, \hat{\Omega}, t) = \frac{v}{4\pi} U(r, t) + \frac{3}{4\pi} J(r, t) \cdot \hat{\Omega}, \tag{11}
\]

\[
S(r, \hat{\Omega}, t) = \frac{1}{4\pi} S_0(r, t) + \frac{3}{4\pi} S_1(r, t) \cdot \hat{\Omega}. \tag{12}
\]

The expansions are substituted into Eq. (1). Integrating Eq. (1) over \(\hat{\Omega}\), we obtain Eq. (9). Multiplying Eq. (1) by \(\hat{\Omega}\) and integrating over \(\hat{\Omega}\), we obtain Eq. (10). This is equivalent to the so-called \(P_1\) approximation of the transport equation.\(^{12,13,15}\)

At this point it is straightforward to show that the transformations still hold for Eqs. (9) and (10) for a homogeneous, turbid medium. The substitution of the transformation equations (6) and (7) into Eqs. (9) and (10) yields coupled equations for \(U_0(r, t)\) and \(J_0(r, t)\) that are still independent of absorption, i.e.,

\[
\frac{\partial}{\partial t} U_0(r, t) + \nabla \cdot J_0(r, t) = 0, \tag{13}
\]

\[
\frac{1}{v} \frac{\partial}{\partial t} J_0(r, t) + \mu'_s J_0(r, t) + \frac{v}{3} \nabla U_0(r, t) = 0. \tag{14}
\]
The next step in the derivation of the diffusion equation is to decouple Eqs. (9) and (10). This is done by using the following substeps: (1) Solve Eq. (9) for \( \mathbf{V} \cdot \mathbf{J}(r, t) \), (2) then take the divergence of Eq. (10), and finally (3) substitute \( \mathbf{V} \cdot \mathbf{J}(r, t) \) from Eq. (9) into Eq. (10). These substeps produce the telegrapher’s equation for \( U(r, t) \) (Ref. 28):

\[
-D_{\mu_a} \nabla^2 U(r, t) + v \mu_a U(r, t) + \frac{\partial U(r, t)}{\partial t}
\]

\[
+ \frac{3D_{\mu_a}}{v} \left[ \mu_a \frac{\partial U(r, t)}{\partial t} + \frac{1}{v} \frac{\partial^2 U(r, t)}{\partial t^2} \right]
\]

\[
= S_0(r, t) + \frac{3D_{\mu_a}}{v^2} \frac{\partial S_0}{\partial t} - \frac{3D_{\mu_a}}{v} \nabla \cdot \mathbf{S}_1(r, t).
\]

Inserting the separable form for \( U \) [transformation equation (6)] into Eq. (15) and canceling terms, we arrive at an equation for \( U_0(r, t) \) that is still independent of absorption:

\[
-\nabla^2 U_0(r, t) + \frac{3}{v} \mu_s' \frac{\partial U_0(r, t)}{\partial t} + \frac{3}{v^2} \frac{\partial^2 U(r, t)}{\partial t^2} = 0.
\]

Equation (15) is not yet the photon diffusion equation, and the transformation property is still valid. It is interesting to note that for the static case (i.e., no time dependence), the telegrapher’s equation [Eq. (15)] reduces to a time-independent diffusion equation with \( D = D_{\mu_a} \); however, we will show in Section 3 that this is inconsistent with Monte Carlo results, even for the time-independent case (see Fig. 6 below).

The final step in the derivation of the diffusion equation requires some assumptions in order to drop the underlined terms in Eq. (15).\(^4,27\) The dipole source term \( S_1(r, t) \) is dropped by assuming an isotropic source; this is justified, since collimated sources can be treated as isotropic sources displaced one transport mean free path into the scattering medium from the collimated source. The condition for dropping the remaining terms is most easily understood in the frequency domain. Here the time dependence of the source and the photon density is \( \exp(-i\omega t) \), and the time derivatives can be replaced by \(-i\omega \). The remaining underlined terms are then negligible when\(^4,27\)

\[
3\omega D \ll v^2 \Rightarrow w/\mu_s' \ll 1.
\]

In essence, the photon scattering frequency must be much larger than the source modulation frequency. Furthermore, the albedo should be close to unity for the diffusion approximation to be valid, that is,

\[
\mu_s'/\left(\mu_s + \mu_a\right) = 1,
\]

or

\[
\mu_a'/\left(\mu_s' + \mu_a\right) \ll 1.
\]

Thus we are left with Eq. (4). We can no longer separate the absorption and scattering effects [Eqs. (6) and (7)] by using this time-dependent diffusion equation. The transformation property of the transport equation has now been lost! There is no clear physical reason evident from the derivation alone that reveals why these transformations should be lost.

We note, however, that there is an inconsistency in this traditional derivation. When terms of order \( \mu_a'/\left(\mu_s' + \mu_a\right) \approx 1 \) [relation (19)] are dropped, then, for the nearly isotropic case (which is a requirement of \( P_1 \) expansion), \( \mu_a \ll \mu_s' \) and terms of order \( \mu_a/\mu_s' \) should also be dropped; hence

\[
D_0 = v/3\mu_s'.
\]

This has been discussed in detail by Furutsu and Yamada\(^18\) and Furutsu.\(^19\) The new diffusion coefficient [Eq. (20)] preserves the transformation (6) for the time-dependent diffusion equation (4).\(^26\) We also note that this new result is in agreement with derivations based on the continuum limit of the lattice random-walk theory by Gandjbakhe and Weiss.\(^29\)

This is the status of the current controversy in the literature. Rather than considering further the details of the theoretical derivations of the diffusion coefficient, we present Monte Carlo results that exhibit substantially better agreement with diffusion theory when an absorption-independent diffusion coefficient \( D = D_0 \); Eq. (20) is used. The absorption-independent diffusion coefficient thus makes possible characterization of the optical properties of homogeneous media.

3. MONTE CARLO SIMULATIONS

In our Monte Carlo simulations we placed an isotropic photon source at the origin. Concentric spherical detectors were placed around the origin at intervals of 0.2 cm. For each scattering event, a check is made to see if the photon has crossed a detector. If the photon has crossed a spherical shell in the radially outward direction, then the outward flux for that detector at that time is scored. If the crossing was in the inward direction, then the same is done for the inward flux. Photon flux inward and photon flux outward are thus recorded for each detector as a function of time. Figure 1 shows a simple two-dimensional sketch of the setup.

Analytical equations for the diffusion approximation for the inward and outward components of the flux are\(^13,14,17\)

\[
J_- = \frac{\nu}{4} U(r, t) + \frac{D}{2} \frac{\partial U(r, t)}{\partial r},
\]

\[
J_+ = \frac{\nu}{4} U(r, t) - \frac{D}{2} \frac{\partial U(r, t)}{\partial r},
\]

where \( J_- \) and \( J_+ \) are the radially inward and outward components of the flux, respectively.

Photons are propagated through the medium by using appropriate optical properties and phase functions.\(^30–32\) The Heney–Greenstein phase function gives the cosine of the scattering angle as

\[
\cos \theta = \frac{1}{2g} \left[ 1 + g^2 - \left( 1 - g^2 \right)^{2} \left( 1 - g + 2g \xi \right)^{2} \right],
\]
4. RESULTS AND DISCUSSION

Photon density at time \( t \) and distance \( r \) from the source provides an elegant way to examine the absorption dependence of the photon diffusion coefficient \( D \). For an infinite medium, the solution of the photon diffusion equation [Eq. (4)] is\(^\text{\textsuperscript{1,34}}\)

\[
U(r, t) = (4\pi D t)^{-3/2} \exp(-r^2/4Dt - \mu_a vt). \tag{24}
\]

If we consider two measurements of \( U(r, t) \) for the same geometry, source–detector position, \( \mu_a \), and \( g \), but for different \( \mu_a \), then

\[
\begin{align*}
\ln \left[ \frac{U_1(r, t)}{U_2(r, t)} \right] &= \frac{r^2}{4t} \left[ \frac{1}{D_2^2} - \frac{1}{D_1^2} \right] + (\mu_{a,1} - \mu_{a,2})vt \\
&+ \ln \left[ \frac{D_2}{D_1} \right]^{3/2},
\end{align*}
\tag{25}
\]

where the subscripts 1 and 2 distinguish between the two different media. If \( D = D_{\mu_a} \) [Eq. (5)], a plot of Eq. (25) is curved at early time. If \( D = D_0 \) [Eq. (20)], a plot of Eq. (25) is linear all the time. Figure 2 illustrates this point for the two different diffusion coefficients; the dotted curves indicate the result with \( D = D_{\mu_a} \), and the solid line indicates the \( D = D_0 \) result.

Applying the same analysis to the photon density obtained from the Monte Carlo results, we see that the Monte Carlo simulations indicate clearly that \( D = D_0 \) as in Eq. (20). Figure 3 shows the Monte Carlo results for \( \mu_{a,2} = 0.05, 0.1, \) and \( 0.5 \) \text{cm}^{-1} \) compared with those for \( \mu_{a,1} = 0.005 \text{cm}^{-1} \), with a source–detector separation of \( 1 \) cm. In all three cases, the plots are straight lines.

\[
U(r, t) = 2(J_\perp + J_\parallel)/vA\Delta t, \tag{23}
\]

where \( A \) is the detector surface area \( 4\pi d^2 \) (\( d \) is the source–detector separation), \( v \) is the speed of light in that medium, and \( \Delta t = 20 \times 10^{-12} \) s is the width of the time channel. The photon density is normalized by dividing it by the detector surface area and the width of the time bins. The results are saved in a text file and analyzed by using photon migration imaging software for comparisons with diffusion theory.\(^\text{\textsuperscript{33}}\)
The plots in Fig. 4 show the modulation frequency dependence of the fractional amplitude residuals for an infinite, homogeneous medium with $\mu_s = 10 \text{ cm}^{-1}$ and source–detector separation of 1 cm for $\mu_a = 0.05, 0.1, 0.5,$ and $1.0 \text{ cm}^{-1}$. Figure 4(a) plots the residuals for diffusion theory with the use of $D = D_{\mu_a}$. We see that the agreement between diffusion theory and Monte Carlo results becomes worse with increasing absorption coefficient. Comparing Fig. 4(a) with Fig. 4(b), where $D = D_0$, we see that the residuals are substantially smaller for the latter case.

From Fig. 4 we see that when $D = D_{\mu_a}$, the diffusion theory underestimates the amplitude, whereas, when $D = D_0$, diffusion theory overestimates the amplitude. These differences between theory and experiment result from the diffusion approximation. However, the observed trend suggests that the diffusion approximation can be modified by choosing a diffusion coefficient ($D$) that has a $\mu_a$ dependence but with different weights for the absorption and scattering coefficients. The residuals are flat for all frequencies; therefore they can be corrected by weighting the absorption coefficient, i.e., $D = \frac{1}{3} \mu_s^2 + k \mu_a$ (where $k$ is a scalar coefficient). Figure 4(a) shows that when $D = D_{\mu_a}$, the diffusion approximation is underestimating the amplitude, and from Fig. 4(b) we see that the diffusion approximation overestimates the amplitude when $D = D_0$. This suggests that with $k < 1$ the diffusion approximation can be corrected to match the Monte Carlo results better. However, as we see in Fig. 5, the dependence of the residuals on source–detector separation indicates that a distance-dependent correction is required, and this correction is smaller at large separations when $k = 0$. Such a correction is also inconsistent with the notion that $D$ should be a property of the medium; i.e., it should not be a function of the source–detector separation.

The plots in Fig. 5 show the dependence of the fractional amplitude residuals on the source–detector separation for an infinite, homogeneous medium with $\mu_s = 10 \text{ cm}^{-1}$ and modulation frequency of 200 MHz for $\mu_a = 0.05, 0.5,$ and $1.0 \text{ cm}^{-1}$. Solid curves indicate $D = D_0$, and dotted curves indicate $D = D_{\mu_a}$. It can be seen from these plots that the agreement between diffusion theory and Monte Carlo simulations gets worse with increasing absorption coefficient, as expected. When $D = D_{\mu_a}$, amplitude residuals increase quickly with larger source–detector separations when $\mu_a/\mu_s > 1/20$. For example, looking at the case with $\mu_a = 1 \text{ cm}^{-1}$, we can see an error that jumps to more than 20% after 1 cm when $D = D_{\mu_a}$, in comparison with errors that are always less than $10\%$ for $D = D_0$. These plots also indicate the breakdown of the diffusion theory near the source. The residuals are not flat anymore, indicating that the photon diffusion coefficient is not a function of absorption, and the correction discussed above is not allowed.

We now consider the effect that the form of the photon diffusion coefficient will have on our ability to characterize accurately the optical properties of turbid media. To this end we have used a least-squares-fitting algorithm to fit for the optical properties obtained by two different methods. We first fit data from a given source–detector separation.
separation as a function of modulation frequency. We next fit data for a given modulation frequency over a range of source–detector separations, which is shown in Fig. 6.

When fitting data from a range of modulation frequencies at a given source–detector separation, we see that the reduced scattering coefficient is characterized more accurately when $D = D_m$. However, the absorption coefficient is determined with approximately the same accuracy with either $D_0$ or $D_m$. This behavior is expected.

When fitting data that cover a range of modulation frequencies, one is essentially performing an analysis in the time domain. In the time domain, the absorption coefficient is determined at long times, where the decay of the photon density is dominated by $\exp(-\nu \mu_a t)$. The determination of $\mu_a$ is thus independent of $D$. Furthermore, the determination of the reduced scattering coefficient using the two different $D$’s differs by the value of $\mu_a$, and $D = D_0$ is more accurate. Here the fitting is accomplished by minimizing the $\chi^2$ value over the range of modulation frequencies for each source–detector separation.

We fit simultaneously for the initial amplitude of the source $S_0(r, t)$ in Eq. (4), to cancel the systematic errors that are observed in Figs. 4 and 5, and for the initial time for the injection of the pulse of light, to cancel systematic errors that are due to temporal binning as explained previously. Both $\mu_s$ and $\mu_a$ are also simultaneously fitted for.

When we fit data from a range of source–detector separations for a given frequency (Fig. 6), we see that the
breakdown of the diffusion approximation near sources plays a role in the comparison of the fit results from two different $D_s$. We overcome this problem by choosing a fitting range from 1 cm to 2 cm, where the diffusion theory breakdown region is avoided. Both $\mu'_s$ and $\mu_a$ are fitted simultaneously at each modulation frequency except for $w = 0$ (i.e., dc case). In the latter case, $\mu_a$ is assumed to be known, and we fit for $\mu'_s$. For low $\mu_a$'s, i.e., $\mu_a \leq 0.1$ cm$^{-1}$, we obtain fits for $\mu'_s$ accurate to within 1% by using both $D_0$ and $D_{\mu_a}$. In Fig. 6 we see that for $\mu_a \geq 0.5$ cm$^{-1}$ the accuracy for $D = D_0$ is better than that for $D = D_{\mu_a}$ (i.e., <2% versus >10%). Thus we also note that even for the time-independent case we find that $D = D_0$ gives better accuracy. When we fitted for $\mu_a$, the form of $D$ did not change the fitting accuracy, as expected.

The data shown in the figures are results from simulations with anisotropy constant $g = 0$. However, they describe different values of $g$ equally well. In our simulations, anisotropy constants of 0.001, 0.2, 0.5, and 0.9 all produced similar results.

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**REFERENCES AND NOTES**


**Fig. 6.** $\mu_s$ fitting results through a range of source–detector separations (1 cm to 2 cm) versus modulation frequency is shown for different absorption coefficients. Both $\mu'_s$ and $\mu_a$ are fitted simultaneously at each modulation frequency, except for $w = 0$ (i.e., dc case). In the latter case, $\mu_a$ is assumed to be known, and we fit for $\mu'_s$. Solid (dotted) lines indicate results for $D = D_0$ ($D = D_{\mu_a}$). $\mu'_s = 10$ cm$^{-1}$; $\mu_a = 0.05$ and 1.0 cm$^{-1}$ in (a) and (b), respectively. Dashed lines are used to indicate the expected $\mu'_s$. We see that for $\mu_a = 0.5$ and 1.0 cm$^{-1}$ the accuracy for $D = D_0$ is within 2%, whereas when $D = D_{\mu_a}$, the discrepancy is as large as more than 10%.

We also note that, even for the time-independent case, $D = D_0$ gives better accuracy. For low $\mu_a$ values investigated, such as $\mu_a = 0.05$ and 0.1 cm$^{-1}$, we obtain results accurate within 1%, which is under the expected noise level. The discrepancies and the comparison of the results for two different $D_s$'s are not significant. Here, once again, the details of $D$ do not play a role, and hence the plots for the $\mu_a$ fits are not shown here. The details are discussed in the text.


33. The photon migration imaging software and the Monte Carlo modeling of light transport in multi-layered tissues are available upon request from the authors.


36. Information on independence of the diffusion coefficient from absorption is available from Dr. G. Nishimura, Biophysics Laboratory, Research Institute for Hokkaido University, Sapporo 060 Japan; e-mail: gnishi@imdes.hokudai.ac.jp.