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Optical Properties of Intralipid: A Phantom Medium for Light Propagation Studies

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Intralipid℠ is an intravenous nutrient consisting of an emulsion of phospholipid micelles and water. Because Intralipid is turbid and has no strong absorption bands in the visible region of the electromagnetic spectrum, and is readily available and relatively inexpensive, it is often used as a tissue simulating phantom medium in light dosimetry experiments. In order to assist investigators requiring a controllable medium that over a finite range of wavelengths is optically equivalent to tissue, we have compiled previously published values of the optical interaction coefficients of Intralipid, most of which were measured at a wavelength of 633 nm. We have extended the measurements of the absorption and reduced scattering coefficients from 460 to 690 nm and the total attenuation coefficient from 500 to 890 nm. These measurements show that, for stock 10% Intralipid, the absorption coefficient varies from 0.015 to 0.001 cm^{-1} between 460 and 690 nm, the reduced scattering coefficient varies from 92 to 50 cm^{-1} between 460 and 690 nm, the total attenuation coefficient varies from 575 to 150 cm^{-1} between 500 and 890 nm, and the average cosine of scatter varies from 0.87 to 0.82 between 460 and 690 nm. With these data, we discuss the design of an optically tissue-equivalent phantom consisting of Intralipid and black India ink.

Key words: intralipid, light-dosimetry, optical-interaction-coefficients, phantom, radiative-transfer, similarity

INTRODUCTION

Knowledge of the degree to which tissue scatters and absorbs light is important for understanding the physical processes manifested by the interaction of light and tissue. For example, in photodynamic therapy [1], red light is often used for photosensitizing dye activation because it is only weakly absorbed in tissue [2] and consequently is relatively penetrating compared to the 10.6-μm wavelength laser beam produced by a CO_2 laser which is strongly absorbed [3] and consequently is useful for precise surgical cutting.

When investigating the underlying mechanisms of a particular laser-tissue interaction, it is

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sometimes necessary to quantify the energy fluence rate ψ [W/m^2]. While measurements of the energy fluence rate in tissue are possible, for example, with an isotropic collector at the tip of an optical fiber [4], they are often impractical in tissue layers only a few millimeters or less in thickness. Nevertheless, such measurements [5,6], or measurements of the diffuse reflectance of tissue [7], can be used to determine the optical interaction coefficients. Once the coefficients of the tissue are known, forward calculations of the energy fluence rate or diffuse reflectance can be done [8,9].

Intralipid™ (Kabivitrum Inc., CA), a phospholipid emulsion used as an intravenous nutrient, is a useful phantom medium for light dosimetry studies because, like tissue, it is turbid at visible wavelengths. Furthermore, it has no strong absorption bands in the visible region of the spectrum. Intralipid's practicality is a result of its low cost, relatively inert chemical nature, and wide availability as either a 10% or 20%-solids suspension. Consequently, it is sometimes used as a tissue simulating (i.e. phantom) medium in studies of light dosimetry [2,5,6,8].

In this paper we have compiled, from the literature, measurements of the total attenuation, reduced scattering and absorption coefficients and the asymmetry parameter of Intralipid at a wavelength of 633 nm. We have extended the measurements of the absorption and reduced scattering coefficients and asymmetry parameter from 460 to 690 nm, and the total attenuation coefficient from 500 to 890 nm. The experimental techniques we used to measure these coefficients will be discussed. Finally, using the measured optical interaction coefficients, we will show how one can produce a phantom, consisting of Intralipid and an added absorber, that will exhibit a diffuse reflectance and effective penetration depth similar to a selected tissue with known interaction coefficients.

MATERIALS AND METHODS

Definitions

The propagation of light in turbid media (e.g., tissues or Intralipid) can be modelled using radiative transfer theory [8–12]. In radiative transfer theory, the wave nature of light is ignored and only the flow of radiant energy is considered. With this theory, it is possible to calculate optical features of turbid media; features such as the diffuse reflectance, R_d, which for plane parallel media, semi-infinite in extent, is the radiance external to the media integrated over 2π steradians, and the energy fluence rate, ψ, which is the radiance within the media integrated over 4π steradians. Within the context of radiative transfer theory, these optical features are usually a function of three optical interaction coefficients: the scattering coefficient, μ_s[cm^{-1}], the absorption coefficient, μ_a[cm^{-1}], and the (single scattering) phase function, $p(\theta)$, where θ is the deflection angle for a single scattering event. In some approximate solutions for R_d and ψ derived from radiative transfer theory, the details of the scattering phase function are ignored and only the average cosine of scatter, $g = \langle\cos\theta\rangle$, also called the anisotropy or asymmetry parameter, is considered. With models of radiative transfer, it is often possible to calculate the energy fluence rate and diffuse reflectance of highly scattering media ($\mu_s >> \mu_a$) with knowledge of only the absorption and reduced scattering coefficient, μ_s', where $\mu_s' = \mu_s(1-g)$.

Phantom Solutions

Stock 10%-solids Intralipid™ was used as the scattering medium in this study while black India ink (Faber-Castell, TN) at a concentration of 0.1% by volume, was used as the absorbing medium. The absorption coefficient of the ink was measured in a standard spectrophotometer. While it was originally thought that India ink was entirely absorbing and non-scattering, recent evidence [13] has shown this not to be the case. Therefore, in our data analysis, the reduced scattering coefficient of our India ink was assumed to be the average of three values measured [13] at 594 nm for two other brands of India ink; the value used was $\mu_s' = 4.03$ cm^{-1}. We shall assume this value to be constant from 460 to 690 nm.

The presence of an index of refraction mismatch at an interface at the surface of, or within, tissue can significantly affect the energy fluence rate and diffuse reflectance of the tissue [10–12,14–16]. A 10%-solids solution of Intralipid consists of approximately 90% water, and 10% fatty micelles with indices of refraction only slightly greater than water. The index of refraction of Intralipid, $n_{Intralipid}$, over the range of wavelengths utilized in these experiments was assumed to be equivalent to water [17], that is, 1.33.

Measuring the Optical Interaction Coefficients

The techniques used to measure μ_s, μ_a, and g of Intralipid are described below. Note that these

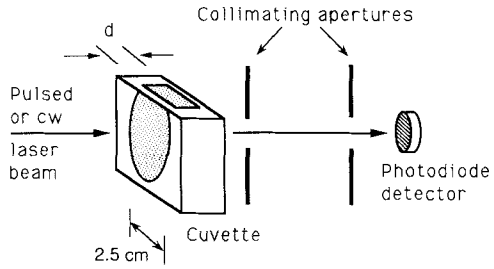

Fig. 1. The experimental arrangement used to measure the total attenuation coefficient of Intralipid. The field of view of the photodiode is 3×10^{-5} sr, and the cuvette is made of glass which provides a sample thickness, d, of 0.83 mm.

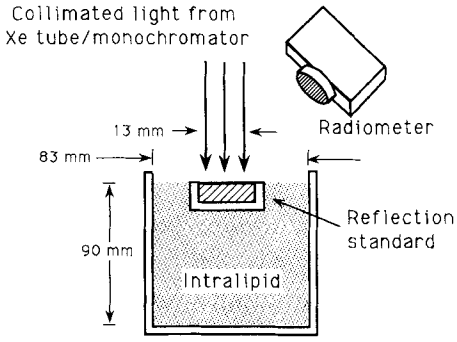

Fig. 2. The experimental arrangement used to measure the diffuse reflectance of Intralipid. The reflection standard (Spectralon™) was in position only for the normalization measurement. The Intralipid (or Intralipid and ink) was held in a glass 500 ml beaker and the radiometer was positioned so as to avoid specular reflection off the surface of the sample.

techniques can also be used to measure the interaction coefficients of tissues.

Method 1: Narrow Beam Attenuation. In Intralipid, the attenuation of a collimated beam of light is due to both absorption and scattering. We used a classical narrow-beam [18] experimental arrangement (Fig. 1) to measure the total attenuation coefficient, μ_t, where $\mu_t = \mu_a + \mu_s$. In this experimental arrangement, the collimating apertures which restricted the field of view of the photodiode detector to a solid angle of 3×10^{-5} sr, were necessary to prevent most of the scattered photons from reaching the detector. The stock 10% Intralipid was diluted in distilled water to one part in 50 and the resulting sample was held in a cuvette with a pathlength, d, of 0.83 mm. The total attenuation coefficient was calculated from the measured data using

$$\mu_t = \left(\frac{1}{d}\right) \ln\left(\frac{I_o}{I}\right) \qquad (1)$$

where I is the signal measured when light is transmitted through a cuvette filled with Intralipid and I_o is the signal measured when light is transmitted through the same cuvette filled with water. Water was used in the latter measurement in order to compensate for specular reflection losses of the incident light off the cuvette interfaces. The source of incident light was a pulsed nitrogen pumped dye laser (PRA Inc., Ontario, Canada), and the value for I and I_o was the average of several pulses. The use of three different dyes made measurements possible over intervals in the range of 500 to 890 nm. The laser pulses had a temporal width of about 200 ps, an energy of approximately 250 μJ with negligible pulse-to-pulse variation, and a repetition rate of about 1 Hz. To demonstrate that non-linear optical effects due to the high peak power were negligible, measurements at wavelengths of 633 and 595 nm were done with 5-mW HeNe continuous-wave lasers.

Method 2: Diffuse Reflectance From a Semi-infinite Medium. The optical feature of Intralipid (or tissues) perhaps easiest to measure is the diffuse reflectance from a semi-infinite sample, R_∞. Ignoring specular reflection and assuming $\mu_s(1-g)>>\mu_a$, radiative transfer theory can be used to show that the diffuse reflectance of a normally incident collimated beam from a semi-infinite medium with an index of refraction mismatch at the surface, can be expressed as [10]

$$R_\infty = \frac{a'}{1 + 2k(1 - a') + \left(1 + \frac{2k}{3}\right)\sqrt{3(1 - a')}} \qquad (2)$$

where $a' = \mu_s'/(\mu_s' + \mu_a)$, $k = (1+r)/(1-r)$, and the internal diffuse reflectance, r, is obtained from $r = -1.44n_{rel}^{-2} + 0.71n_{rel}^{-1} + 0.668 + 0.0636n_{rel}$ [19], where $n_{rel} = n_{Intralipid}/n_{air}$. This equation is accurate to better than 10% for $\mu_s' > 19\mu_a$ [10]. Measurements of the diffuse reflectance were obtained using the experimental arrangement shown in Figure 2. The light from a xenon lamp and monochromator was delivered by a liquid-core light guide and collimated by a lens to produce a 1.3-cm diameter beam projected down onto the surface of an Intralipid solution held in a 500-ml beaker (8.3-cm diameter). No light could be seen leaking out the sides of the beaker, therefore

TABLE 1. The Optical Interaction Coefficients of 10% Intralipid at 633 nm*

μ_t (cm^{-1})	Method	$\mu_s(1-g)$ (cm^{-1})	Method	μ_a (cm^{-1})	Method	g	Method	References
344 ± 2	a	105 ± 1	b	0.11 ± 0.01	b	0.675	e	2
386 ± 4	a	—		0.57 ± 0.15	b	0.71 ± 0.03	b	5
—		150	b	0.16	b	—		6
365 ± 2	a	—		—		0.69	e	18[g]
476 ± 9	a	—		0.149 ± 0.004	b	0.768 ± 0.006	b	27
420 ± 30		185 ± 1	b	0.0261 ± 0.0008	c	—		29
550	a	—		0.095	b	0.83	b	30
417 ± 22	a	—		0.49	c	0.55	e	31
—		—		0.0100 ± 0.0025	d	—		32
—		145 ± 2	b	0.53 ± 0.03	b	—		33
400 ± 10	a	—		0.01	b	0.667 ± 0.015	b	34
400 ± 20	a	—		0.52	b	0.698 ± 0.024	b	35
—	a	119 ± 4	c	0.007 ± 0.002	c	—		36[h]
344 ± 28	a	60 ± 8	f	0.0029 ± 0.0134	c	0.826 ± 0.177	f	(i)
362 ± 53		144 ± 9		0.027 ± 0.154		0.75 ± 0.18		(j)

*Methods: a) Narrow beam attenuation; b) Energy fluence rate profile/added absorber; c) Diffuse reflectance & transmittance; d) Time resolved reflectance; e) Goniometry; f) Diffuse reflectance/added absorber; g) Media used was Nutralipid™; h) Media used was Liposyn™; i) This work, Figures 3, 5, and 7C; j) Weighted mean of tabulated data (see text).

it was effectively a semi-infinite phantom. A calibrated radiometer was angled approximately 5° from the vertical and positioned over the sample in such a way as to avoid detecting the specular reflection of the incident beam off the surface of the Intralipid solution. The reflection readings were normalized to the signal obtained when a standard Spectralon™ 99.4% reflector (Labsphere Inc., NH) was positioned at the surface of the phantom. The manufacturer states that the reflectance from 400 to 900 nm of this standard is 99.4% and varies by only 0.2% at most. We assumed that differences in the angular dependence of the reflectance of the Intralipid sample and Spectralon standard were negligible, since diffuse reflectance from turbid media is generally assumed to be Lambertian [20].

Measurements of R_∞ were taken over a wavelength range from 460 to 690 nm for two different solutions; one solution consisted of 10%-solids Intralipid alone while the other consisted of 10%-solids Intralipid and black India ink. The settling of the ink in the Intralipid was negligible over the several minutes it took to do the measurements. In the second solution, enough ink was added (0.1% by volume) so that the absorption coefficient of the mixture was dominated by the ink ($\mu_{a,ink}$ = 2.75 cm^{-1} at 460 nm). Measurements of R_∞ exhibited by the ink/Intralipid solution were analyzed with equation 2 with the μ_a set to the spectrophotometrically measured values for the added ink and the μ_s' set to the sum of the value for ink (4.03 cm^{-1}) and Intralipid (unknown). From this, the calculated μ_s' of Intralipid was considered, along with measurements of R_∞ of the Intralipid solution, in Equation 2, which was then used to calculate the μ_a of Intralipid.

Calculating the Anisotropy Factor

While it is possible to measure the phase function of Intralipid by goniometry [18,21] or measurements of radiance, $L(z,\Omega)$ [$Wcm^{-2}sr^{-1}$] [22,23], or g, from time-resolved or phase-modulated reflectance [24], such measurements are difficult in practice or require somewhat specialized apparatus. We calculated the anisotropy factor of Intralipid from the measured data of μ_s', μ_t, and μ_a, using

$$g = 1 - \frac{\mu_s'}{\mu_t - \mu_a} \qquad (3)$$

RESULTS AND DISCUSSION

Previously Published Measurements at 633 nm

Table 1 shows a list of the previously published measurements of the interaction coefficients of 10%-solids Intralipid at 633 nm. Note that in two of the cases, solutions (Nutralipid [18], Phamacia, Quebec, and Liposyn [36], Abbot Labs, Montreal) similar to Intralipid were used. The weighted means (each datum being weighted by the inverse of the square of its quoted error; data without quoted errors are ignored) and standard deviation of the quoted values give the following

results: $\mu_s' = (144 \pm 9)$ cm^{-1}, $\mu_a = (0.027 \pm 0.154)$ cm^{-1} and $g = (0.75 \pm 0.18)$. Note, however, that the mean of the measured μ_s', and $\mu_s(1-g)$ calculated from the means of the measured μ_t, μ_a and g, that is (90.4 ± 7.9) cm^{-1}, are significantly different. The source of this discrepancy is not known.

While the inconsistencies in the data for each interaction coefficient might be due to the different techniques used to measure them, the relatively large errors in the results obtained for the experimentally simple to measure μ_t, suggests an intersample variation probably arising from inconsistencies in the manufacturing process; Intralipid is not manufactured to be a standard optical scattering medium.

Despite the large variation in the data, it is apparent from Table 1 that (1) the absorption coefficient of Intralipid at 633 nm is quite low (by comparison, the absorption coefficient of water at 633 nm [17] is about 0.0028 cm^{-1}); (2) scattering dominates absorption by a factor of about 13,400 times, and (3) that the values for g consistently show that Intralipid micelles will, on the average, scatter a photon preferentially in the forward direction. The phase function of Nutralipid™ (an intravenous nutrient purportedly identical to Intralipid) has been directly measured [18] and an analytic expression consisting of a weighted sum of a Henyey-Greenstein phase function [8] and an isotropic phase function is a good approximation to it.

New Measurements

Figure 3 shows the measured total attenuation coefficient as a function of wavelength for 10%-solids Intralipid. The least-squares fitted (reduced chi-square = 0.78) power curve ($C\lambda^{-2.33}$, where C is a constant and λ is the wavelength) is intended to make interpolation easier. The value of μ_t measured at 633 nm (i.e. 344 ± 28 cm^{-1}) is consistent with the mean of the results shown in Table 1 (i.e., 362 ± 53 cm^{-1}). The continuous-wave measurements at 595 and 633 nm are consistent with the pulsed laser measurements, and so we can infer that the high peak power of the nitrogen/dye laser pulses do not cause any significant non-linearities in the optical properties of the Intralipid. The spectral behavior of the attenuation coefficient of Intralipid is similar to the behavior of tissues [25,26] in that the attenuation coefficient decreases with increasing wavelength. Since the size distribution and index of refraction of the micelles in Intralipid is known [27], Mie

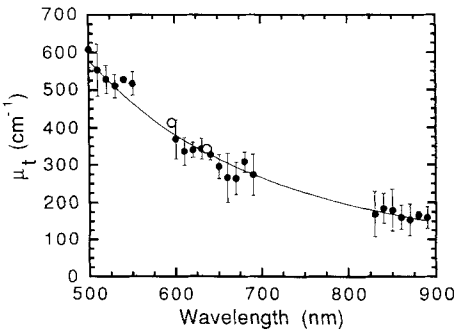

Fig. 3. Results of the measurement of the total attenuation coefficient. Measurements were done on samples drawn from three different bottles of Intralipid: the points are the means and the error bars are the standard deviation of three measurements. The line, intended to ease interpolation, is a least squares fit of a power function, $C\lambda^{-x}$, where C is a constant, to the data. The fitting procedure resulted in $x = 2.33$. The open circles (single measurements) are the data obtained when continuous-wave 5-mW HeNe lasers were used as the source of irradiance.

theory [28] can be used to predict the spectral behavior of the interaction coefficients. A Mie theory analysis of Intralipid predicts that μ_t should depend on wavelength approximately as λ^{-2}, which is in relatively good agreement with the measurements shown in Figure 3. Such a Mie theory analysis has also been done on tissue [37] for the purpose of explaining the temperature induced changes in the optical properties of tissues.

Figure 4 shows the diffuse reflectance of two different media, one (A) being Intralipid alone and the other (B) being Intralipid with 0.1% of black India ink added. The lines, which are weighted least-squares linear fits to the data, are justified because the results of the fits shows that the probability that the reflectance is linearly correlated to the wavelength is greater than 90% (linear correlation coefficient = 0.557) and 99% (linear correlation coefficient = −0.876) for Figure 4A and B, respectively.

Figure 5 shows the μ_s' and μ_a extracted from the fitted lines shown in Figure 4. The error bars are calculated from the experimental errors in the measurements of the diffuse reflectance; the lower half of the error bars are indefinite. Intralipid consists of 10.8% soybean oil, 1.8% glycerin, and 1.2% lecithin [27]. The results of spectrophotometric measurements of pure samples of these media showed that glycerin and lecithin have negligible absorption from 450 to 820 nm, but soybean oil (Fig. 6), scaled to an effective 10% concentration, exhibits an absorption coefficient of

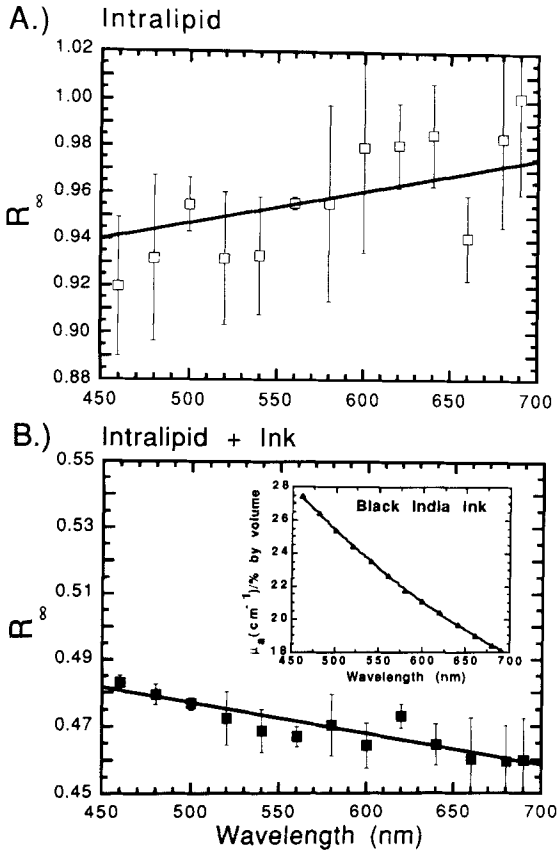

Fig. 4. The diffuse reflectance of (A) stock 10% Intralipid and (B) 10% Intralipid with 0.1% black India ink added. The data points are the means, and the error bars are standard deviations, of measurements done on three samples, each drawn from a different bottle of Intralipid. The straight lines are weighted least squares linear fits to the data. The graph inset in Figure 4B is the spectral absorption coefficient of the ink measured in a standard spectrophotometer.

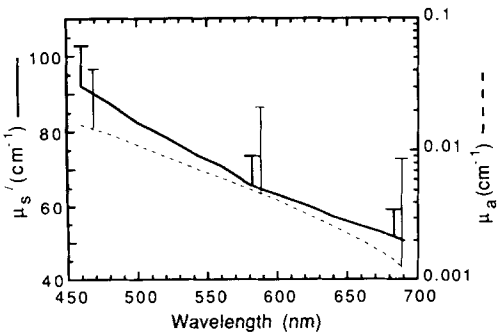

Fig. 5. The reduced scattering and absorption coefficients of Intralipid obtained using equation 2 and the linear fits to the measurements of R_∞ shown in Figure 4. The error bars are calculated from the errors in the measurements R_∞. The bottom half of the error bars could not be calculated from the experimental data and so these data represent an upper bound to the absorption coefficient.

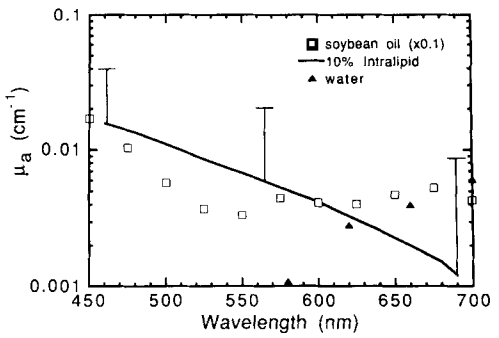

Fig. 6. The absorption coefficient of soybean oil, measured with a standard spectrophotometer, Intralipid (see Figure 5), and water [17]. The absorption coefficient of water below 570 nm is less than 0.001 cm^{-1} and so does not appear on the graph. The absorption coefficient of soybean oil was divided by 10 in order to be able to compare it to the Intralipid used in these experiments, which was a 10% solids suspension.

about 0.2 cm^{-1} at 450 nm decreasing to about 0.04 cm^1 at 550 nm and is approximately constant out to 800 nm. The absorption coefficient of soybean oil is consistent with the values of the measured absorption coefficient of Intralipid. It has been stated [27,29] that water is the primary absorber of light in Intralipid. We have found that in the red region of the spectrum, both water and soybean oil contribute to the absorption while in the blue region, the absorption is due primarily to soybean oil. We are currently trying to improve and extend the measurements of μ_a and μ_s' using a different experimental arrangement involving measurements of diffuse reflectance and total transmittance of collimated light (450–1100 nm) through a sample of Intralipid positioned at the port of an integrating sphere. The details of this experimental technique can be seen elsewhere [38].

The absorption coefficient (from Fig. 5) and the scattering coefficient (from Fig. 3, with μ_a subtracted) are plotted in Figure 7, along with measurements done by others at discrete wavelengths (shown as open circles). The fitted curve for μ_s was extended out beyond the Nd-YAG wavelength of 1,064 nm; this extrapolation is justified since the μ_t between 500 and 890 nm is described well by the fit of $C\lambda^{-2.33}$ and because the μ_a of water contributes insignificantly to μ_t over this range (the maximum abosorption of water between 500 and 890 nm is 0.45 cm^{-1} at 970 nm [17]). The curve for μ_a was not extended beyond it's measured range since it predicted unre-

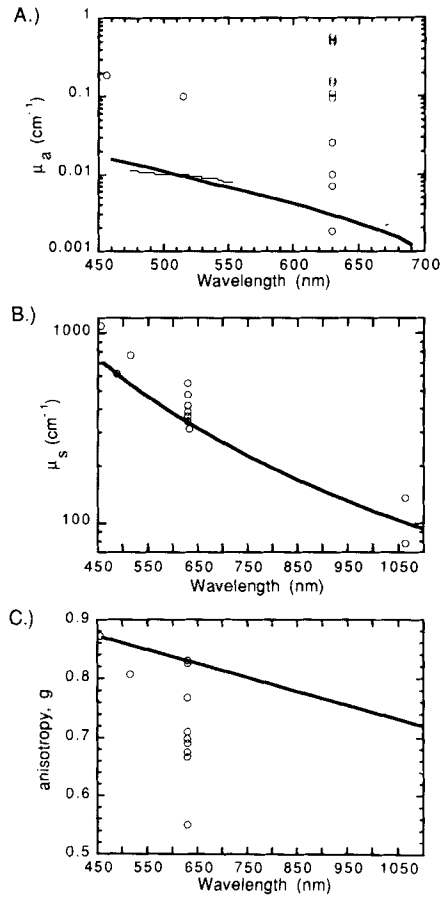

Fig. 7. The (**A**) absorption coefficient (**B**) scattering coefficient and (C) anisotropy parameter of stock 10% Intralipid. The solid lines are the data obtained in this study, and in the case of B and C are extrapolated out to 1100 nm from data spanning 500 to 890 and 460 to 690 nm, respectively. The open circles are the data from Table 1, while the values at 458, 514, and 1064 nm are after van Staveren et al. [27].

alistically low values in the infrared where it is well known that water has absorption bands. The anisotropy factor of Intralipid, shown in Figure 7C, was calculated using equation 3 (assuming μ_a to be negligible) and the data in Figures 3 and 5; the curve was also extrapolated out to 1,100 nm. This result for g is consistent with Mie theory, which predicts a linear decrease in g with increasing wavelength over this range of wavelengths. Because Mie theory predicts a decrease in the scattering coefficient with increasing wavelength, one might expect the reflectance of Intralipid to decrease with wavelength. As shown in Figure 4A, this is not the case; this is probably a result of the decreasing absorption coefficient and anisotropy factor with increasing wavelength.

Designing a Tissue Equivalent Phantom Consisting of Intralipid and a Non-Scattering Absorber

Having established estimates of the optical interaction coefficients of Intralipid, it remains to show how one can make use of this medium in an experiment requiring a tissue-simulating phantom. We will make use of the similarity relations [12,20,39,40], which can be formulated to show that two media (labelled with subscripts 1 and 2) will exhibit "similar" diffuse reflectance if

$$\frac{\mu_{s,1}(1-g_1)}{\mu_{a,1}} = \frac{\mu_{s,2}(1-g_2)}{\mu_{a,2}} \qquad (4)$$

As an example, these relations predict that a medium with $g=0$, $\mu_a=1$ mm^{-1} and $\mu_s=9.5$ mm^{-1} will exhibit a similar reflectance to a medium with $g=0.5$, $\mu_a=0.5$ mm^{-1}, and $\mu_s=9.5$ mm^{-1}. We can see from Van de Hulst's [20] exact solutions to the radiative transfer problem, that the diffuse reflectance for semi-infinite media (ignoring effects of the surface interface) is 0.478 and 0.486 for each of these media respectively, while diffusion theory (Eq. 2, with $n_{rel}=1$) gives 0.434. For Equation 4 to be valid, it is necessary that $\mu_s(1-g)>>\mu_a$, for both media; this limitation is because in the derivation of equation 4, it is assumed that the radiance within the medium is linearly anisotropic [12]. We will now make use of Equation 4 to show how it is possible to make a tissue-like optical phantom medium consisting of Intralipid and a purely absorbing medium.

In the red to infrared region of the spectrum (650–1,100 nm), the scattering coefficients of tissue have been shown to be on the order of 200–1,000 cm^{-1}, the absorption coefficients are on the order of 0.01–1 cm^{-1}, and the scattering is forward peaked with asymmetry parameters on the order of 0.7–0.95 [26]. To make a tissue-like phantom out of Intralipid and a non-scattering absorbing medium, consider the following example: let us take the μ_s and g of 10% Intralipid at 633 nm to be the weighted mean of those shown in Table 1, $\mu_s=362$ cm^{-1} and $g=0.75$, and say we want to optically simulate bovine muscle with $\mu_s=330$ cm^{-1}, $\mu_a=0.5$ cm^{-1} and $g=0.95$ [18]. Using Equation 4, and assuming $n_{rel}=1.33$, we can see that if we add absorber (Fig. 8) to the Intralipid to bring the absorption coefficient up to 2.742 cm^{-1} from the mean in Table 1 of $\mu_a=0.027$ cm^{-1}, the similarity relation will hold. We will use the example of black India ink as the pure absorber,

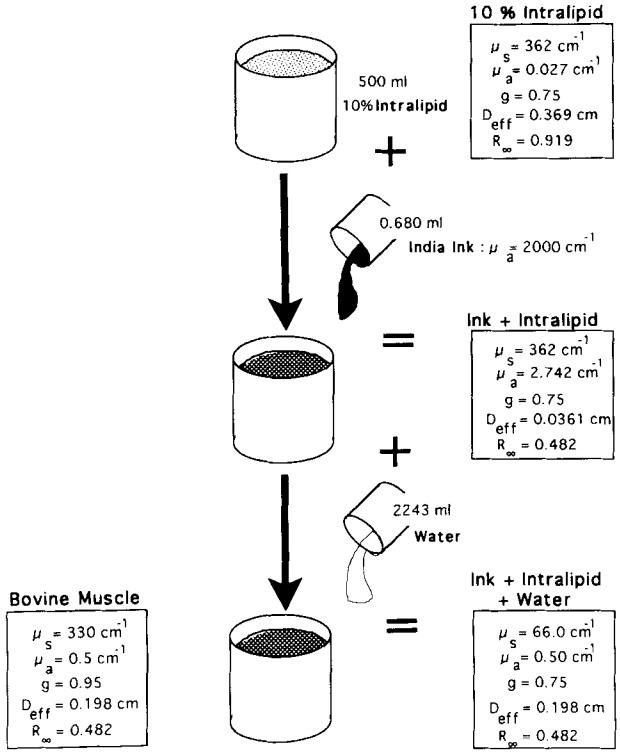

Fig. 8. A diagrammatic representation of the design of a phantom using 10% Intralipid and black India ink that will exhibit a diffuse reflectance, R_∞, and effective penetration depth, D_{eff}, like that of bovine muscle at 633 nm. For the calculations done to be valid, the phantom must be effectively infinite in size; that is, the walls of the phantom should extend at least 12 effective penetration depths beyond the edges of the incident beam and the depth of the phantom should extend at least 12 effective penetration depths from the surface of the medium.

although a non-scattering medium such as a molecular dye would be better. We can see from the insert in Figure 4B that by adding 0.136% by volume of the black India ink we used in these experiments to 10% Intralipid, the final absorption coefficient will be 2.742 cm^{-1}. The resulting phantom medium will exhibit a diffuse reflectance similar to bovine muscle.

From diffusion theory [12], it can be shown that the (effective) penetration depth, D_{eff}, that is the depth over which the energy fluence rate in a medium falls by a factor of e (i.e., 2.718), is [10]:

$$D_{eff} = \frac{1}{\sqrt{3\mu_a[\mu_a + \mu_s(1 - g)]}} \quad (5)$$

This equation is valid when $\mu_s' >> \mu_a$ and the volume being considered is far from sources and boundaries. In the phantom described above, D_{eff} would be on the order of 0.036 cm. For the phantom to be effectively "infinite" in size (i.e., insignificant light leakage out the sides or bottom of the phantom), it is necessary that the medium extend unperturbed at least 12 penetration depths in thickness and in distance away from the edges of the incident beam [41]. If, for example, we wish to construct the phantom to have the same effective penetration depth as bovine muscle, the phantom can be diluted with water. A dilution factor, x (x = [initial volume + volume of water added]/initial volume) will scale μ_a and μ_s down by a factor x, resulting in an increase in D_{eff} by a factor x (see Fig. 8). The total diffuse reflectance will be unaffected as long as the container holding the phantom is effectively infinite in size. Note, however, that the diluted medium may appear darker to the eye than the undiluted medium. This is because the source of diffusely reflected photons, in the case of pure 10% Intralipid, is to a large degree near the surface of the medium where the incident beam impinges while the source of diffusely reflected photons becomes more extended throughout the volume of the phantom when the phantom becomes more dilute, and thus appears less intense.

CONCLUSIONS

Intralipid consists of water and an emulsion of fatty micelles, polydisperse in size. Purportedly because of inconsistencies in the manufacturing process, the optical interaction coefficients of a particular sample of Intralipid can not be precisely known without being measured, but the values plotted in Figure 7 are useful for providing the best currently available estimates. At 633 nm, the mean of the independently measured values for the interaction coefficients show that $\mu_s' = (144 \pm 9)$ cm^{-1}, $\mu_a = (0.027 \pm 0.154)$ cm^{-1} and $g = (0.75 \pm 0.18)$. Intralipid at 633 nm, like tissue, is highly scattering, weakly absorbing, and scatters preferentially in the forward direction. Both the scattering and absorption coefficients, as well as the anisotropy parameter, decrease with increasing wavelength in the visible region of the spectrum, as predicted by Mie theory. The scattering properties of Intralipid are manifested by the particulate nature of the medium while the absorption is hypothesized to be due to both water and soybean oil.

With knowledge of the optical interaction coefficients of Intralipid and a non-scattering ab-

sorber, one can use the similarity relation to design a phantom out of these materials that will exhibit a tissue-like diffuse reflectance. The effective penetration depth of the phantom can be made tissue-like by diluting the phantom with water.

If the interaction coefficients of a phantom medium need to be known with more precision, polystyrene microspheres [18], while relatively expensive, would likely prove to be a superior scattering component. Recent evidence [13] showed that black India ink particles mixed in Intralipid aggregate to particles about 1 μm in size and consequently scatter 633 nm light to a significant degree. Lipophobic molecular dyes might prove to be simpler to use when building optical phantoms consisting of Intralipid and an added absorber.

REFERENCES

1. Wilson BC, Jeeves WP: Photodynamic therapy of cancer. In Ben-Hur E, Rosenthal (eds): "Photomedicine: Volume II." Boca Raton: CRC Press, 1987, pp 127–177.
2. Flock ST: "The Optical Properties of Tissues and Light Dosimetry at 633 Nm." Ph.D. Dissertation, McMaster University, Hamilton, Ontario, Canada, 1988.
3. Boulnois JL: Photophysical processes in recent medical laser developments: A review. Lasers Med Sci 1986; 1: 47–66.
4. Marijnissen JPA, Star WM: Quantitative light dosimetry in vitro and in vivo. Lasers Med Sci 1986; 2:235–242.
5. Moes CJM, van Gemert MJC, Star WM, Marijnissen JPA, Prahl SA: Measurements and calculations of the energy fluence rate in a scattering and absorbing phantom at 633 nm. Appl Opt 1989; 28:2292–2296.
6. Wilson BC, Patterson MS, Burns DM: Effect of photosensitizer concentration in tissue on the penetration depth of photoactivating light. Lasers Med Sci 1986; 1:235–244.
7. Patterson MS, Wilson BC, Feather JW, Burns DM, Pushka W: The measurement of dihematoporphyrin ether concentration in tissue by reflectance spectrophotometry. Photochem Photobiol 1987; 46:337–343.
8. Flock ST, Patterson MS, Wilson BC: Monte Carlo modelling of light propagation in highly scattering tissue II: Comparison with measurements in phantoms. IEEE Trans Biomed Eng 1989; BME 36:1169–1173.
9. Jacques SL, Prahl SA: Modeling optical and thermal distributions in tissue during laser irradiation. Lasers Surg Med 1987; 6:494–503.
10. Flock ST, Wilson BC, Patterson MS, Wyman DR: Monte Carlo modelling of light propagation in highly scattering tissue I: Model predictions and comparison with diffusion theory. IEEE Trans Biomed Eng 1989; BME 36:1162–1168.
11. Star WM, Marijnissen JPA, van Gemert MJC: New trends in photobiology (invited review). Light dosimetry: Status and prospects. J Photochem Photobiol B 1987; 1:149–167.
12. Patterson MS, Wilson BC, Wyman DR: The propagation of optical radiation in tissue, Part I: Models of radiation transport and their applications. Lasers Surg Med 1991; 6:155–168.
13. Madsen SJ, Patterson MS, Wilson BC: The use of india ink as an optical absorber in tissue-simulating phantoms, Phys Med Biol 1992; in press.
14. Groenhuis RAJ, Bosch JJ, Ferwenda HA: Scattering and absorption of turbid materials determined from reflection measurements I: Theory. Appl Opt 1977; 22:2465–2462.
15. Motamedi M, Rastegar S, LeCarpentier G, Welch AJ: Light and temperature distributions in laser irradiated tissue: The influence of anisotropic scattering and refractive index. Appl Opt 1989; 28:2230–2237.
16. Hemenger RP: Optical properties of turbid media with specularly reflecting boundaries: Applications to biological problems. Appl Opt 1977; 16:2007–2012.
17. Hale GM, Querry MR: Optical constants of water in the 200-nm to 200-μm wavelength region. Appl Opt 1973; 12:555–563.
18. Flock ST, Wilson BC, Patterson MS: Total attenuation coefficients and scattering phase functions of tissues and phantom materials at 633 nm. Med Phys 1987; 14:835–841.
19. Egan WG, Hilgeman TW: "Optical Properties of Inhomogeneous Materials." New York: Academic Press, 1979:
20. van de Hulst HC: "Multiple Light Scattering Tables, Formulas and Applications," Vol. I and II. New York: Academic Press, 1980:
21. Jacques SL, Alter CA, Prahl SA: Angular dependence of HeNe laser light scattering by human dermis. Lasers Life Sci 1987; 1:309–333.
22. Herman M, Lenoble J: Asymtotic radiation in a scattering and absorbing medium. J Quant Spect Radiat Trans 1968; 8:355–367.
23. Elliot TA, Duraez T, McCormick NJ, Bossert DJ: Experimental test of a time-dependent inverse radiative transfer algorithm for estimating scattering parameters: Addendum. J Opt Soc Amer 1989; 6:603–606.
24. Patterson MS, Moulton JD, Wilson BC, Chance B: Applications of time-resolved light scattering measurements to photodynamic therapy dosimetry. In Dougherty T (ed): "Photodynamic Therapy: Mechanisms II." Proc SPIE 1203, 1990, pp 62–75.
25. Parsa P, Jacques SL, Nishioka NS: Optical properties of rat liver between 350 and 2200 nm. Appl Opt 1990; 28: 2325–2330.
26. Cheong WF, Prahl SA, Welch AJ: A review of the optical properties of biological tissues. IEEE J Quant Elect 1990; 26:2166–2185.
27. van Staveren HJ, Moes CJM, van Marle J, Prahl SA, van Gemert MJC: Light scattering in intralipid-10% in the wavelength range of 400–1100 nanometers. Appl Opt 1991; 30:4507–4514.
28. Bohren CF, Huffman DR: "Absorption and Scattering of Light by Small Particles." New York: J Wiley and Sons, 1983:
29. Driver I, Feather JW, King PR, Dawson JB: The optical properties of an aqueous suspension of intralipid, a fat emulsion. Phys Med Biol 1989; 12:1927–1930.
30. Star WM, Marijnissen JPA, Jansen H, Keijzer M, van Gemert MJC: Light dosimetry for photodynamic therapy for whole bladder wall irradiation. Photochem Photobiol 1987; 46:619–624.

31. Jacques S: personal communication/unpublished results, 1988.
32. Jacques S, Flock ST: Effect of surface boundary on time-resolved reflectance: Measurements with a prototype endoscopic catheter. In Chance B, Katzir A (eds): "Time-Resolved Spectroscopy and Imaging of Tissues." Proc SPIE 1431, 1991, pp 12–20.
33. Patterson MS, Moulton JD, Wilson BC, Chance B: Applications of time resolved light scattering measurements to photodynamic therapy dosimetry. In Dougherty TJ (ed): "Photodynamic Therapy: Mechanisms II." Proc SPIE 1990; 1203:pp 62–75.
34. Marijnissen JPA: personal communication/unpublished results, 1988.
35. Moes C: personal communication/unpublished results, 1988.
36. Farrel T: personal communication/unpublished results, 1991.
37. Thomsen SL, Jacques SL, Flock ST: Microscopic correlates of macroscopic optical property changes during thermal coagulation of myocardium. In Jacques SL (ed): "Laser-Tissue Interaction." Proc SPIE 1990; 1202:2–11.
38. Saidi IS, Jacques SL, Tittel FK: The optical properties of neonatal skin versus gestational age, 1992; submitted to J Invest Derm.
39. Wyman DR, Patterson MS, Wilson BC: Similarity relations for the interaction parameters in radiation transport: Appl Opt 1989; 28:5243–5249.
40. Yoon G, Prahl SA, Welch AJ: Accuracies of the diffusion approximation and its similarity relations for laser irradiated biological media. Appl Opt 1989; 28:2250–2255.
41. Wilson BC, Jacques SL: Optical reflectance and transmittance of tissues: Principles and applications. IEEE J Quant Elec 1990; 26:2186–2199.