The Propagation of Optical Radiation in Tissue. II: Optical Properties of Tissues and Resulting Fluence Distributions

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Abstract. This paper is the second of two reviewing the propagation of electromagnetic radiation of wavelength 0.25–10 μm in tissue. This part begins with a discussion of how the fundamental optical interaction coefficients of tissue may be measured. Both direct methods, in which the coefficients are measured for optically thin samples, and indirect methods, in which the coefficients are inferred from measurements on bulk samples are described. The difficulties inherent in both types of measurement are outlined. Next the wavelength dependence of the scattering and absorption coefficient is discussed, both from a heuristic point of view and by illustration from current literature. We illustrate how the optical spectrum can be divided into regions where the propagation of light is dominated by absorption or scattering effects. Finally we show how the distribution of light fluence in these spectral regions is dramatically different and illustrate the important features of these distributions.

INTRODUCTION

In the first part of this review (1) we stated three requirements for calculating the light field in tissue. These were:

(i) a mathematical description of the interaction of optical radiation with tissue;
(ii) information about the optical properties of the irradiated tissue; and
(iii) workable solutions of the mathematical equations to provide calculations of sufficient accuracy.

The first and third of these requirements were discussed in some detail in Part I. This paper deals with the optical properties of tissues and the features of light fluence distributions in these tissues.

We begin with a description of experimental techniques which have been used to obtain the absorption and scattering coefficients of tissues. These can be divided into two classes: direct methods in which the coefficients are calculated from measurements on excised, optically thin samples, and indirect methods in which the interaction coefficients must be deduced from measurements of some dependent parameter, such as the diffuse reflectance. After consideration of the advantages and limitations of these techniques we explore the variation of absorption and scattering with wavelength. Three wavelength regimes are identified—those in which absorption is the dominant process, those in which scattering is dominant, and those in which both processes must be considered. The fluence distributions which result in these different regimes are radically different and their important features are discussed.

DETERMINATION OF TISSUE OPTICAL PROPERTIES

As discussed by Wilson et al (2) there are two distinct strategies which can be used to obtain information about the absorption and scattering coefficients of tissue. In the so-called 'direct method', experiments are devised to measure the fundamental properties under conditions which correspond to their definition and which are independent of any mathematical model of radiative transfer. For example, if a thin tissue sample can be prepared in which single scattering is the only significant process, then the phase function can be measured by rotating a suitable detector around the sample. The technical difficulties inherent in such direct measurements will be discussed below. The

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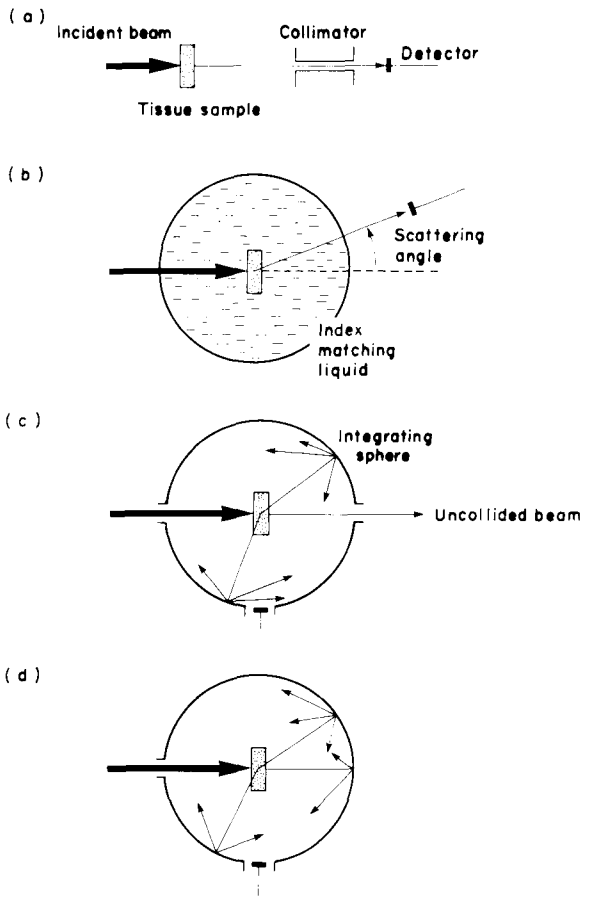

Fig. 1. Methods for the direct measurement of fundamental optical properties of tissue. (a) Direct measurement of the total attenuation coefficient, μ_t. (b) Measurement of the scattering phase function, $f(\hat{\Omega}'\cdot\hat{\Omega})$. (c) Measurement of the scattering coefficient, μ_s. (d) Measurement of the absorption coefficient, μ_a.

second strategy is to deduce the fundamental optical properties from measurement of a set of dependent parameters. These 'indirect methods' fall into the general category of inverse problems in physics. The technique most often used has been to deduce the interaction coefficients from measurements of diffuse reflectance and transmittance of tissue slabs. As will be explained in more detail, there is no accepted way to work 'backward' from such measurements and van de Hulst (3) has commented that this is not a well determined inverse problem.

Direct methods of measuring tissue optical properties

By definition, the absorption and scattering coefficients apply to infinitesimally thin samples. In practice, a sample which is thin enough so that multiple scatter can be ignored will meet this criterion. This requires that the sample thickness x meets the condition that $\mu_t x \ll 1$, where μ_t is the total attenuation coefficient. As a result, direct measurements are not generally possible in vivo, although one exception is noted below.

In principle, μ_t can be determined even for relatively thick samples and its determination establishes the 'thin sample' criterion stated above. A measurement of μ_t can be performed as illustrated in Fig. 1(a). A well-collimated beam, such as that from a laser, is incident on the tissue sample, and directly transmitted (i.e. unscattered) light is measured by a detection method which is insensitive to scattered radiation. If the incident fluence rate is ψ_0 and the detected fluence rate is ψ, then the total attenuation coefficient can be determined from the sample thickness by

$$\mu_t = \frac{1}{x} \log_e \frac{\psi_0}{\psi} \qquad (1)$$

Measurements of this sort have been reported for tissue slabs by Flock et al (4), Jacques and Prahl (5), Marchesini et al (6), Peters et al (7) and Key et al (8). In addition, Marijnissen and Star (9) have reported in situ results where a collimated fibre optic detector was placed within the tissue. It is likely, however, that the collimation was inadequate to provide an accurate measure of μ_t. Such in situ measurements might be successfully performed by using some other form of scatter rejection. For example, sub-picosecond laser pulses and time-of-flight optical gating, as described by Martin et al (10), would allow the rejection of scattered light because of its longer pathlength through the tissue. Alternatively, depolarization of polarized incident light might be used to measure μ_t by implanting a polarization preserving fibre in the tissue as described by Svaasand and Gomer (11).

The most detailed results for μ_t have been reported at the helium neon laser wavelength of 633 nm but it is likely that at all wavelengths in our range of interest μ_t is very high, typically 10–100 mm^{-1}. This implies that very little unscattered light will penetrate more than a few tenths of a millimetre so that detector noise will

be a limitation on measurements with thicker samples. It is also clear that optically thin samples are physically thin as well. If $\mu_t = 10\,\text{mm}^{-1}$ and we wish to have $\mu_t x = 0.1$, then the sample thickness should be only 0.01 mm. Preparation of such thin samples is feasible using a freezing microtome but this introduces the possibility of changes due to freezing. Thin smears of tissue can be used (4) if the tissue is first mechanically ground, but this may well alter the scattering structure. Such thin preparations must also be mechanically supported, usually on glass slides, and care must be taken to avoid dehydration. An additional problem is that thin samples may be quite heterogeneous, and that several measurements may be necessary to determine the 'average' optical properties.

Leaving these technical questions aside, we will examine how the fundamental coefficients may be obtained if appropriate samples are available. Figure 1(b) illustrates the method used by Flock et al (4) to measure the scattering phase function at 633 nm. The sample, held between glass slides, is immersed in a cylindrical water tank to minimize distortions in the measured phase function caused by refraction at the tissue boundaries. Similar experiments have been reported by Jacques et al (12) and Key et al (8). Bruls and van der Leun (13) have used a glass hemisphere to match refractive indices with epidermal samples and have measured the phase function at several wavelengths between 254 and 546 nm. All observed phase functions have been very forward peaked, which is consistent with scattering by inhomogeneities of a size comparable to, or larger than, the wavelength of light.

This technique can be extended to obtain the absolute differential scattering coefficient if the measurement at a given angle is properly normalized to the incident fluence. An assumption of azimuthal symmetry then allows the total scattering coefficient to be computed by numerical integration. These experiments are tedious to perform, however, and an alternative is to use an integrating sphere to collect the scattered radiation as shown in Fig. 1(c). As discussed by Wilson et al (2), the detector signal is measured with the sample present, (S_s), and without the sample present, (S_0). It is necessary to ensure that the directly transmitted (uncollided) beam is not included in S_s, so for this measurement it must be allowed to pass out of the sphere or be absorbed in a beam stop. For an optically thin sample of thickness x, μ_s is given by

$$\mu_s = \frac{1}{x}\,\frac{S_s}{S_0} \tag{2}$$

If the scattering is very forward peaked, it is difficult to avoid losing some scattered radiation in the beam stop or exit port but this can be minimized by using a larger sphere and placing the stop or port farther from the sample. In a regime where $\mu_s \gg \mu_a$ there may be no need to measure μ_s independently but instead μ_s is given by a direct measurement of μ_t. While the wavelength dependence of tissue optical properties is not yet well known, the scattering coefficient is probably much larger than the absorption coefficient over the range 600–1500 nm for most soft tissues.

The absorption coefficient can also be measured directly as described by Wilson et al (2) and Marchesini et al (6) and illustrated in Fig. 1(d). Again, using an integrating sphere, measurements are made of the signal with the sample, (S_a), and without the sample, (S_0), but in this case S_a includes both scattered and directly transmitted radiation. The difference between S_a and S_0 is due only to absorption so that

$$\mu_a = \frac{1}{x}\,\frac{S_0 - S_a}{S_0} \tag{3}$$

This measurement should work well when $\mu_a \sim \mu_s$ but if $\mu_a \ll \mu_s$ the change in signal due to absorption in an optically thin sample will be relatively small compared to S_0—perhaps one part in a thousand. Wilson et al (2) have proposed a modification of the method in which the sample and a water standard are placed side-by-side within the integrating sphere. The incident beam is periodically switched between the two and a lock-in amplifier is used to detect the synchronous absorption signal. (It should be noted that these simple descriptions of integrating sphere techniques have ignored many technical difficulties in the measurements. The reader is referred to the original publications for discussion of these.)

It may also be feasible to measure the absorption coefficient directly by non-optical methods. Recall that the local absorbed energy rate is the product of the absorption coefficient, μ_a, and the energy fluence rate ψ. Since almost all of this absorbed energy is converted to thermal energy, measurement of the local heating and knowledge of ψ should allow deduction of μ_a. Two non-invasive techniques have been used to measure the local heating in tissue: photoacoustic spectroscopy (14) and photothermal

radiometry (15). The first technique is based on the detection of acoustic waves generated in the tissue by thermal gradients, while the second relies on measurement of the infrared radiation emitted from the heated tissue. Because of the difficulty in measuring or calculating ψ, the methods have so far been used only to measure relative changes in the absorption coefficient as a function of wavelength or other factors, but the potential exists for absolute determination of μ_a.

From the preceding description, it is evident that the direct measurement of tissue optical properties is a challenging experimental problem. It may be that such direct methods are not the best way to determine optical properties and their application in vivo or in situ is clearly limited. Nonetheless these measurements are important in that they establish the range of expected values for μ_a, μ_s and $f(\hat{\Omega}'\cdot\hat{\Omega})$ and may guide the design of the various indirect or inverse methods which will be discussed next.

Indirect methods of measuring tissue optical properties

A wide range of optical measurements can be made on tissue to provide data for an inverse estimation of the fundamental optical properties. Wilson et al (2) have divided these into three categories:

(i) external, in which light detectors are situated outside the tissue volume and properties such as diffuse reflectance and transmittance are measured;
(ii) internal, in which detectors are located within the tissue to measure parameters such as μ_{eff}; and
(iii) perturbation methods, in which internal or external measurements are made after the addition to the tissue of a substance with known optical properties.

Table 1 lists, under these three categories, measurements which have been used in indirect

Table 1. Measurable optical parameters which depend on the fundamental optical properties of tissue. Subsets of this list can be used for indirect calculation of the interaction coefficients as described in the text. Measurements marked with an asterisk have been performed in vivo

Measured parameter	Representative references
(a) External	
* Scattered reflectance	Jacques and Prahl (5) Anderson et al (19) Peters et al (7)
* Spatial dependence of scattered reflectance	Bonner et al (33) Groenhuis et al (24) Wilson et al (34)
Angular dependence of scattered reflectance	Wilksch et al (35) Barbour (36)
* Temporal dependence of scattered reflectance	Chance et al (37) Patterson et al (25)
* Scattered transmittance	Jacques and Prahl (5) Peters et al (7)
Spatial dependence of scattered transmittance	Langerholc (38)
Angular dependence of scattered transmittance	Wilksch et al (35)
* Temporal dependence of scattered transmittance	Delpy et al (39)
(b) Internal	
* Effective attenuation coefficient	Wilson et al (22)
Radiance (angular dependence)	Doiron et al (40) Marijnissen and Star (9)
* Absolute energy fluence rate	Star et al (29)
Temporal dependence of fluence rate	Jacques (41)
(c) Perturbation	
Change in effective attenuation coefficient with added absorber	Profio and Sarnaik (42) Wilson et al (43)
* Change in scattered reflectance with added absorber	Patterson et al (44)

methods along with representative references which describe the methodology in detail. Methods which have been applied in vivo are indicated by an asterisk in Table 1. Rather than discuss these various methods in detail, we will indicate some problems common to all indirect methods. The most obvious of these is that the mathematical model used in the derivation may be inadequate. For example, the simple Kubelka–Munk 2-flux model has been used in the past under inappropriate conditions of highly anisotropic radiance. Other problems pertain to the lack of a stable inversion procedure that provides a unique solution. Except for the 2-flux models, which allow arithmetic calculation of S and K from the reflectance and transmittance, there is no simple procedure to determine optical properties from a set of measurements. It is usual to use a number of 'forward' calculations to iteratively estimate the optical properties that would generate the measurements obtained. While there is a large amount of published literature on forward calculations, especially for the slab geometry, there is often insufficient data for proper interpolation. Thus, it is necessary to set up a computer program to perform such iterative calculation using one of the models discussed in Part I of this review (1).

The problem of uniqueness is tied to the principle of similarity discussed below. It is possible for two media of substantially different optical properties to yield very similar optical measurements, for example, the diffuse reflectance and transmittance. Given the limited accuracy of such experimental measurements, it may be impractical to find a set of measurements sufficient to resolve such ambiguities. The range of possible solutions may be considerably restricted, however, by making some specific direct measurement. Jacques et al (12) and Peters et al (7), for instance, have used a narrow beam transmission measurement of μ_t to aid in the derivation of μ_a, μ_s, and g from reflectance and transmittance measurements.

The last problem is the related one of instability. As discussed by van de Hulst (3), it is possible in principle to derive the entire scattering phase function from a measurement of μ_{eff} and the angular dependence of the radiance in the diffusion region. This has been attempted by Herman and Lenoble (16) but, as they indicate, the accuracy of experimental measurements is such that it is impossible to distinguish between phase functions which differ in the third or higher Legendre expansion coefficient.

Despite these difficulties, it is likely that progress in tissue optics will rely largely on indirect measurements of optical properties because of the potential of these techniques for characterizing intact, or even living tissue. Further research is required to determine the most suitable methods, and the results of direct methods should help guide this work.

Summary of optical properties and wavelength dependence

In this section we will review the currently accepted values for the fundamental tissue optical properties and their wavelength dependence. Before discussing the experimental data, it is worth speculating on the wavelength behaviour of the absorption and scattering processes. Considering first absorption, we expect that in the ultra-violet part of the spectrum μ_a would be very large due to the high u.v. absorption characteristic of many biomolecules such as proteins and nucleic acids. As the wavelength increases, this absorption falls off and absorption due to specific chromophores such as haemoglobin, myoglobin, bilirubin and melanin dominates. In this wavelength range, we might expect to see large differences in μ_a among different tissue types as their content of such chromophores will vary considerably. Once the wavelength increases beyond 1000 nm, infrared absorption by water becomes the dominant mechanism and we might expect the absorption coefficient of most tissues to be largely water-like. For reference, the absorption spectra of melanin, haemoglobin and water are shown in Fig. 2.

The spectral behaviour of the scattering coefficient is not easy to predict. While the scattering of light by isolated dielectric particles has been the subject of intense study (17) the application of this work to tissue is not established because of the complex nature of this biological medium. As discussed in Part I (1), it is probably more valid to think of tissue as a medium with random dielectric fluctuations than as a distribution of scattering particles in a homogeneous matrix. Nevertheless, this second naive model may give valid clues as to the size of dominant scattering inhomogeneities in tissue. For particles much smaller than the wavelength of incident light, λ, the phase function is proportional to $[1 + (\hat{\Omega}' \cdot \hat{\Omega})^2]$ and the scattering coefficient is proportional to λ^{-4}. This scattering is referred to as Rayleigh scattering after Lord Rayleigh who first studied it. Light

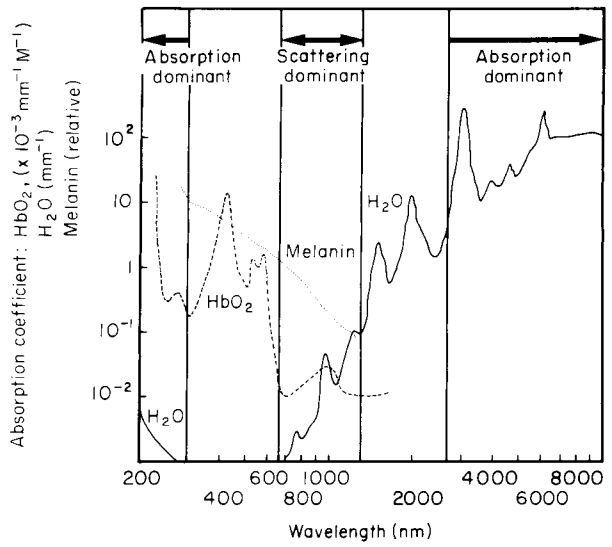

Fig. 2. The absorption spectra of water, oxyhaemoglobin and melanin (after Boulnois (45)) and Hale and Querry (46). Also shown are approximate boundaries of regions where absorption is dominant or scattering is dominant for light propagation in soft tissue.

scattering by larger homogeneous spheres was first described by Mie (18) and scattering by particles of size comparable to, or larger than the wavelength of incident light is generally referred to as Mie scattering. The phase function in this case can be very complex with many nulls and maxima. In general the scattering coefficient and anisotropy factor, g, increase with particle size. Observed phase functions for tissue are quite forward-peaked, consistent with Mie scattering by particles of micron scale—cells and major organelles are of this order of magnitude. Given the range of potential scatterer size in tissue, we would not expect to observe much structure in the phase function but rather a general decrease in μ_s and g with increasing wavelength.

Experimental data are still quite limited but a reasonably consistent picture, not at odds with the simple arguments above, is beginning to emerge. The skin has been the most extensively studied tissue to date because of its importance in photobiology but, with the growth of laser surgery and photodynamic therapy, data are becoming available for other soft tissues. As an example of skin data we show in Fig. 3 the absorption and scattering coefficients of human dermis as determined by Anderson et al (19).

These investigators used Kubelka–Munk theory to derive S and K from reflectance and transmittance measurements. We have used Eqs (29) and (30) in Part I (1) to calculate μ_a and $\mu_s(1 - g)$ from their data and have replotted it in this form. As discussed above, the results are probably quantitatively unreliable at wavelengths where $\mu_a \geq (1 - g)\mu_s$. The absorption coefficient is remarkably flat over the central wavelength range but does show peaks at 1430 and 1890 nm, consistent both in position and amplitude with water absorption. There is also an increase in μ_a at short wavelengths as expected. The absence of any specific features in the absorption spectrum from 500–1200 nm in dermis can be attributed to the lack of specific chromophores, including haemoglobin, in the excised samples studied. The absorption spectrum of epidermis, on the other hand, has been shown to correlate well with the behaviour of melanin (19). The transport scatter coefficient falls by more than an order of magnitude from 300–2400 nm. Again, this decrease is anticipated but the separate behaviour of μ_s and g is not known. Measurements by Jacques and Prahl (5) showed for mouse skin (dermis and epidermis) that g = 0.74 at 488 nm, and Bruls and van der Leun (13) measured the epidermal phase function from 254–546 nm. However, to

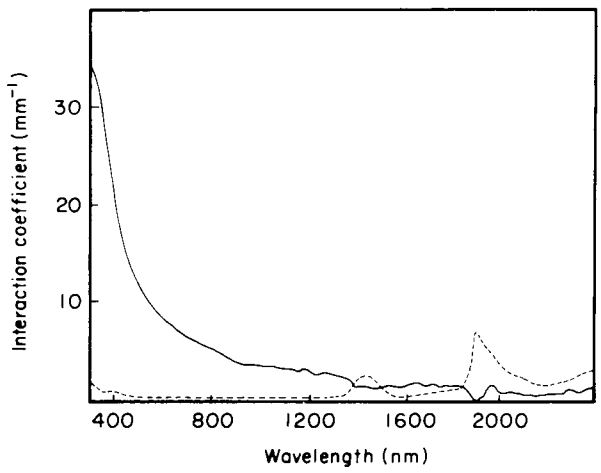

Fig. 3. The absorption coefficient, μ_a, and transport scattering coefficient, $(1 - g)\mu_s$, versus wavelength for human dermis as determined by Anderson et al (19). The data are most accurate where $(1 - g)\mu_s \gg \mu_a$ because they were derived using a simple 2-flux model of light propagation. —— $\mu_s(1 - g)$; ---- μ_a.

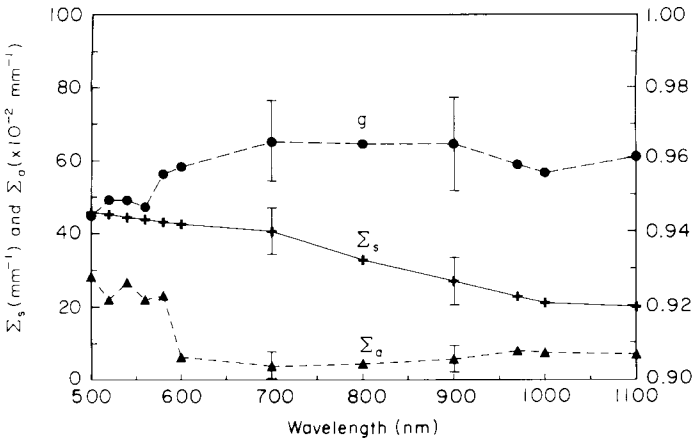

Fig. 4. The absorption coefficient (denoted by Σ_a in this graph), scattering coefficient (Σ_s) and anisotropy parameter (g) for a sample of normal human glandular breast tissue as measured by Peters et al (7).

our knowledge, no systematic study of the phase function for skin over a broad wavelength range has been conducted.

As mentioned, there has been little work to date on the optical properties of other soft tissues over a wide wavelength range as effort has been concentrated on the 630 nm region important in current photodynamic therapy. Results at this wavelength have been summarized by Wilson and Patterson (20). As an example of the observed behaviour with wavelength, the absorption coefficient, scattering coefficient and anisotropy parameter for human glandular breast tissue are shown in Fig. 4. These data were obtained by Peters et al (7) in the following manner. Thin slices (10–30 μm) were prepared from a gross sample and the total attenuation coefficient was directly measured as a function of wavelength as described earlier. One millimetre slices were also prepared and the transmittance and reflectance were measured using standard integrating sphere techniques. A Monte Carlo simulation of the transmittance and reflectance measurement geometry was then applied in an iterative fashion to estimate μ_a, μ_s and g using the fixed value of $\mu_a + \mu_s$ determined by the narrow beam transmission experiments. These results are therefore not dependent on any approximation to the radiative transfer equation.

The absorption coefficient shows two main features—a double peak at about 540 and 580 nm characteristic of oxyhaemoglobin and a much smaller peak at 970 nm due to water. The scatter coefficient shows a smooth decrease with wavelength, falling by about a factor of two from 500 to 1100 nm. The anisotropy factor shows no significant changes over this wavelength range, remaining at about 0.96. While data such as that illustrated here is now appearing in the literature for a variety of tissue types (21), there is still a need for more extensive measurements of the fundamental optical properties over the wavelength range useful for medical applications.

One problem which has been touched on above is the relationship between optical properties determined for tissue samples in vitro and the same tissue in vivo. Wilson et al (22) have shown that over the wavelength range where haemoglobin contributes significantly to the absorption, large changes may be caused by blood drainage and deoxygenation. Other workers (13) have measured the effects of dehydration on light scattering by skin samples and other artifacts can be introduced by freezing and storage (23). A reliable method of determining the fundamental optical properties of tissue in situ and in vivo is clearly desirable. We are some way from satisfying that goal, but recent advances based on both steady-state (24) and time resolved (25) measurements of scattered light are very promising.

The principle of similarity

The idea that media with different fundamental optical properties might have similar fluence distributions has been mentioned previously in this paper but a more complete discussion was deferred to this section because the idea is important in both the determination of fluence distributions and the measurement of optical properties. The concept is depicted in Fig. 5 where photon paths are traced through two slabs—one has a high scattering coefficient and a forward-peaked phase function, the other has a lower scattering coefficient but an isotropic phase function. From the net 'equivalence' of photon paths we might postulate that these two slabs would exhibit similar dependent characteristics.

This principle has been explored extensively by van de Hulst (3) and has been discussed in the context of tissue optics by Wilson and Patterson (20), Flock et al (4) and Star et al (26)

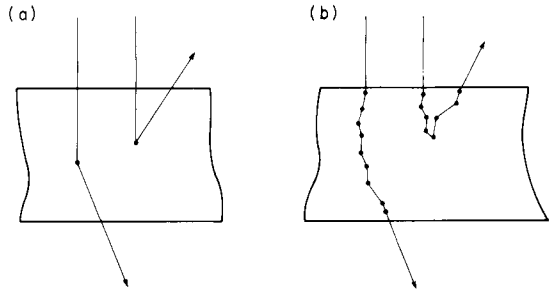

Fig. 5. Schematic illustration of the principle of similarity. Slab (a) has a low scattering coefficient and an istotropic phase function whereas slab (b) has a high scattering coefficient and a forward-peaked phase function. As shown, dependent optical properties such as reflectance and transmittance may be similar for the two media despite their different fundamental optical properties.

among others. The conclusion of these studies was that two media will have similar fluence distributions if

$$\mu_{a1} = \mu_{a2} \tag{4}$$

$$(1 - g_1)\mu_{s1} = (1 - g_2)\mu_{s2} \tag{5}$$

where the subscripts 1, 2 refer to the two media. Wyman and Patterson (27) have shown that this relation is exact only if the radiance is linearly anisotropic and Star et al (26) have illustrated this for materials with tissue-like characteristics. Wyman et al (28) went on to generalize similarity relations, showing that if the radiance were Nth order anisotropic then similarity of two sets of optical properties could be exactly achieved if the first N Legendre moments of the two phase functions were appropriately matched.

The idea of similarity is important for two reasons. One is that modelling of light transport is considerably simplified for isotropic scattering and a considerable number of results have been published for this case. The second reason is that similarity presents itself as ambiguity in the inverse determination of optical properties as discussed earlier. These two aspects of similarity suggest an interesting question: does it matter if experimental measurements yield the wrong optical properties (because of similarity) if, by using this incorrect set, we can nonetheless, accurately predict the fluence distribution (again because of similarity)? It is difficult to answer this question rigorously except to note that the adequacy of the incorrect or reduced set of parameters depends on how accurately the fluence distribution must be known. As indicated by Star et al (26) and explained above, the equivalence will tend to break down at sources and boundaries and the edge of fields. The reduced set of parameters might be adequate, however, to predict the fluence at depth, say along the central axis of a large external beam.

THE NATURE OF THE LIGHT FIELD IN TISSUE

Having discussed the mathematical modelling of light propagation in tissue, mathematical solutions of the problem and the determination of tissue optical properties, we can address our overall goal and discuss the resulting distribution of fluence in tissue. We will confine our remarks to the most commonly encountered situation of external beams. We know that the optical interaction coefficients, especially μ_a, are wavelength dependent so that the resulting distribution will also depend strongly on wavelength. We can identify three regimes: those in which absorption dominates, in which scattering dominates and in which scattering and absorption are comparable.

The simplest case is that in which absorption is the dominant process. If we somewhat arbitrarily define this region as that where $\mu_a > 10(1 - g)\mu_s$, and if we assume that $(1 - g)\mu_s \sim 1\,\text{mm}^{-1}$, we see from Fig. 2 that water absorption alone would imply that this criterion is met for wavelengths greater than 2700 nm. Absorption of u.v. by biopolymers would impose a lower limit and certainly the clinically important cases of excimer and CO_2 laser irradiation fall into this absorption dominated category. In this case the fluence falls off (for external beam irradiation) as

$$\psi = \psi_0 e^{-\mu_a x} \tag{6}$$

Because scatter is relatively unimportant, lateral spreading of the beam will also be negligible, as will energy losses due to scattering out of the tissue. The radiance will remain very forward-peaked even at depth.

The other extreme, where scattering dominates absorption, probably applies to most tissues in the wavelength range 650–1300 nm if we use the criterion $\mu_a < 0.1(1 - g)\mu_s$. Diffusion theory can be successfully used to model the interaction of light with tissue in this regime with the limitations noted in Part I (1). The scattering dominated propagation creates a

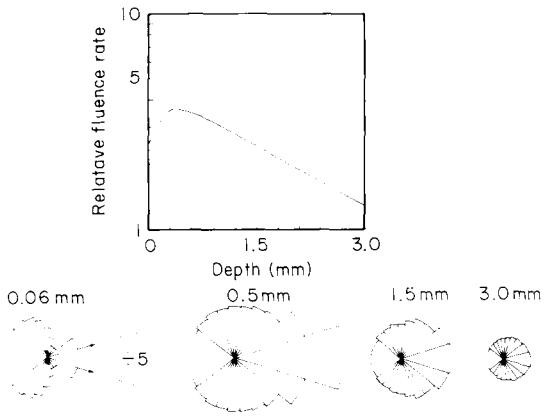

Fig. 6. Fluence rate versus depth in a highly scattering tissue. The results, obtained by Monte Carlo simulation, show the build-up of the fluence rate to a value 3.6 times higher in the tissue than in the incident beam. The tissue is considered to be a semi-infinite medium irradiated by an infinite collimated beam of normal incidence. Polar plots of the radiance at different depths show the transition from a highly forward-peaked angular dependence near the surface to a stable diffusion pattern at depth. The simulation did not include a mismatch in the index of refraction at the surface. $\mu_s = 33\,mm^{-1}$, $\mu_a = 0.033\,mm^{-1}$, $g = 0.95$.

number of interesting features which are summarized below and illustrated in Fig. 6. In general we note the following.

(i) At sufficient depth the fluence vs depth curve obeys a single exponential behaviour, $e^{-\mu_{eff}x}$, where μ_{eff} is approximately $[3\,\mu_a(\mu_a + (1 - g)\mu_s)]^{\frac{1}{2}}$.

(ii) At sufficient depth the radiance assumes a fixed angular dependence. There is a transition zone from this depth to the surface where the radiance can undergo large changes in angular dependence, especially if the incident radiation is collimated. It is a misconception that the radiance becomes isotropic at sufficient depth. This is true only if there is no absorption—even media with high single scattering albedos may have significantly anisotropic diffusion patterns. This has important implications for in situ measurements of fluence and shows the necessity for using a detector with isotropic response such as that described by Star et al (29).

(iii) The fluence rate in tissue may be several times that in the incident beam. This counter-intuitive feature may appear to violate the conservation of energy. This is not the case, however, because the fluence rate is merely proportional to the number of photons passing through an infinitesimal spherical volume per unit time. In a highly scattering medium a given photon can contribute to the fluence rate at many locations and several times at one location before it is absorbed. In a non-scattering medium, each photon can contribute to the fluence only at locations along a straight line and only once at each location. The fluence rate in tissue can therefore exceed that in the incident beam. Of course we still require that energy be conserved. If we recall that the local rate of energy absorption is $\mu_a\,\psi$, the total rate of energy absorption in the tissue is $\int \mu_a\,\psi\,dV$. It can be shown for the case in Fig. 6, where the fluence rate in tissue exceeds that in the beam by a factor of up to 3.6, that only 32% of the incident energy is absorbed in the tissue, the remainder being lost by scatter out of the tissue surface. We note also from Fig. 6 that the fluence cannot be predicted from a measurement of only μ_{eff} and ψ_0. Some investigators have used the approximation $\psi = \psi_0\,e^{-\mu_{eff}x}$, which may be in error by typically a factor of 3.

(iv) In a highly scattering tissue it may also be necessary to consider the effect on the fluence distribution of a boundary mismatch in the index of refraction. Tissue is usually assumed to have an index of refraction a few per cent higher than water (30), whereas that of air is, of course, close to unity. Light which is incident on such a tissue/air boundary from within the tissue will be internally reflected, thereby increasing the local fluence rate. Such effects have been shown theoretically by Star et al (26), Flock et al (31) and Jacques and Prahl (5), and experimentally by Moes et al (32). The magnitude of this effect for typical tissue parameters is illustrated in Fig. 7, where we have assumed that the tissue air interface is perfectly smooth.

(v) The geometric extent of the source may also significantly affect the fluence distribution. In Fig. 8 the central axis fluence profile is shown for circular beams of different diameters. Because of scatter from the periphery, a larger beam will be more penetrating. For a beam of sufficient size, this profile will have the shape characteristic of an infinite beam because photons from the edges are absorbed before they reach the central axis. Marijnissen and Star (9) have shown that for lightly pigmented muscle tissue at 633 nm this critical diameter is a few centimetres. This effect has not been fully appreciated by investigators who have attempted to apply formulas appropriate for infinite source geometries to irradiation with small diameter beams.

(vi) As shown in Fig. 9, for irradiation of a

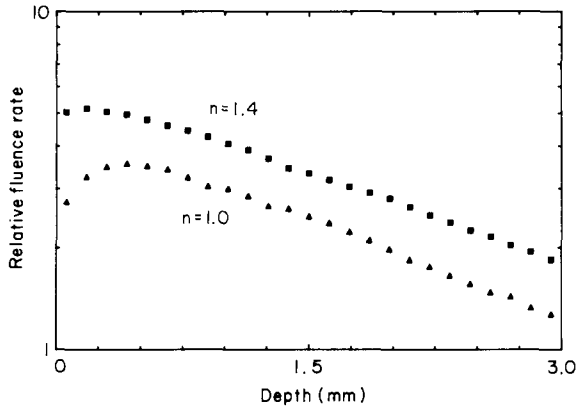

Fig. 7. Influence of a mismatch in index of refraction at the tissue boundary. The tissue properties and irradiation conditions are the same as in Fig. 6. For the lower curve, and all other figures, the index of refraction of tissue is assumed to be identical to that of the external medium whereas for the upper curve the index of refraction is 1.4 times that of the external medium. The results were obtained by a Monte Carlo simulation. $\mu_s = 33\,mm^{-1}$, $\mu_a = 0.033\,mm^{-1}$, $g = 0.95$.

scattering medium with a normally incident 'pencil' beam there is considerable lateral spread of the light fluence. This effect is very important in therapeutic Nd-YAG laser irradiation and also contributes to significant dose inhomogeneity in photodynamic therapy (PDT).

In the third regime, where scatter and absorption are both significant it is difficult to make any general comments regarding the fluence distribution. This case, for which $0.1(1 - g)\mu_s < \mu_a < 10(1 - g)\mu_s$, applies to two zones, one extending from roughly 300–650 nm and the other from 1300–2700 nm. A simple exponential fall-off and stable radiance pattern are still established at sufficient depth and some of the other features due to scatter may be present. This is the most difficult case to model and one of the more accurate methods such as discrete ordinates, many flux or Monte Carlo should be used in this case.

CONCLUSIONS

In this paper we have illustrated how the light fluence distribution in tissue depends strongly on the relative magnitude of the scattering and absorption coefficients. The resulting distribution will depend not only on the type of tissue irradiated but also on the wavelength of irradiation. The prediction of these fluence distributions requires useful models of light propagation and also information about the fundamental optical properties of tissue in vivo.

We are some way from having a reliable, non-invasive method of obtaining this information especially in a clinical setting. Nonetheless, considerable progress has been made by a number of groups in recent years. Experiments on excised tissue samples have shown in broad detail the magnitude of scattering and absorption coefficients and their dependence on wavelength. This information has been valuable in indicating which radiation propagation models can be applied in different circumstances. Fibre optic based measurements of diffusely reflected light, both steady-state and time resolved, show great promise for non-invasive tissue characterization. Much work needs to be done to establish which techniques and models are superior under different circumstances with respect to accuracy, cost and clinical utility. Photoacoustic and photothermal methods may also prove to be useful in vivo probes of tissue optical properties.

The use of optical radiation in medicine continues to grow at a rapid pace. In surgery we have seen the advent of pulsed u.v. lasers whose non-linear interaction with tissue requires complex mathematical modelling. In photodynamic therapy the interaction of light with exogenous photosensitizers is proving to be both

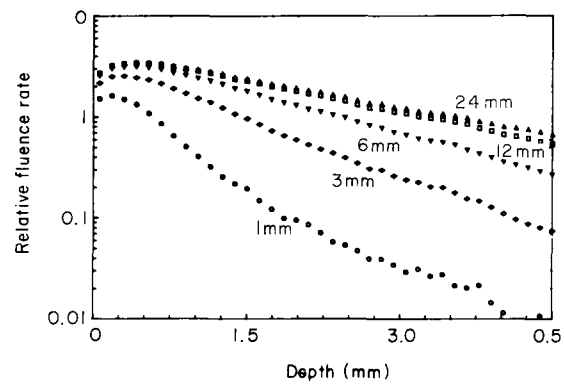

Fig. 8. Monto Carlo calculations of influence of beam diameter on the fluence rate along the central axis in a highly scattering tissue. The beam is normally incident on a semi-infinite tissue slab. $\mu_s = 33\,mm^{-1}$, $\mu_a = 0.033\,mm^{-1}$, $g = 0.95$.

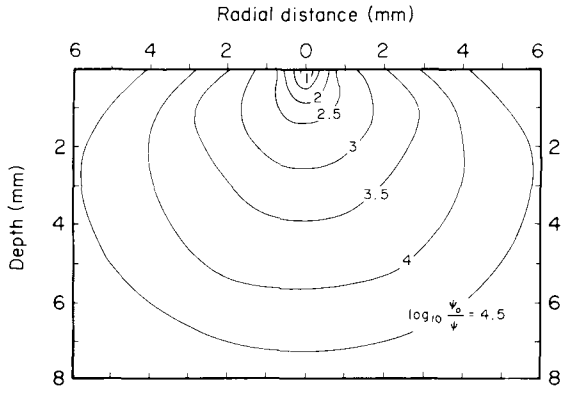

Fig. 9. Plot of iso-fluence rate contours for a 0.12 mm beam normally incident on a highly scattering semi-infinite tissue slab. Despite the initial collimation of the beam, the light is rapidly diffused in all directions. The results were obtained by a Monto Carlo simulation. $\mu_s = 33\,mm^{-1}$, $\mu_a = 0.033\,mm^{-1}$, $g = 0.95$.

a useful tool and a challenging problem in dosimetry. In vivo optical spectroscopic techniques are also expanding and the exploitation of time-of-flight information may add the potential of spatially resolved spectroscopy and imaging. All of these techniques raise difficult experimental and theoretical questions which must be answered if they are to be developed to their full potential.

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