Tissue optics

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The article provides a brief overview of light propagation in tissue. The application of tissue optics for medical diagnosis and phototherapy is also discussed.

THERE exists considerable current interest in the use of optical methods for medical imaging, diagnosis and therapy[1]. This is motivated by the growing maturity of lasers, fiber optics and associated technologies because of which practical realization of the considerable potential of the optical approaches has now become feasible. Encouraging results have already been obtained for use of optical techniques for *in situ* monitoring of tissue parameters, discrimination of diseased tissue from normal, mammography, and several therapeutic applications. For most of these applications, in particular for the use of light in therapy, it is important to be able to predict the spatial distribution of light in the target tissue. This is rather involved because the biological tissue is inhomogeneous and the presence of microscopic inhomogenities (macromolecules, cell organelles, organized cell structure, interstitial layers etc.) makes it turbid. Multiple scattering within a turbid medium leads to spreading of a light beam and loss of directionality. Therefore, much of the results of the optics of homogenous, nonscattering media (like the Beer Lambert's law, used widely to work out the spatial variation of light in a nonscattering medium) are not applicable to light propagation in tissue. A rigorous, electromagnetic theory based approach for analysing light propagation in tissue will need to identify and incorporate the spatial/temporal distribution and the size distribution of tissue structures and their absorption and scattering properties. Clearly this is a formidable task. Therefore, heuristic approaches with different levels of approximations have been developed to model light transport in tissues. An effort for modelling light transport also requires accurate values for the optical transport parameters of the tissue. Measurement techniques, different from those used for homogeneous nonscattering media are required for this purpose.

The term tissue optics encompasses modelling of the light transport in tissues, measurement of tissue optical transport parameters, and development of models which can explain the optical properties of tissue and their dependence on the number, size and arrangement of the tissue elements. In this article we provide a brief overview of these aspects and also discuss some representative applications of tissue optics for biomedical applications.

Tissue optical parameters

An exact modelling of the inhomogeneous and turbid tissue is not presently feasible. The tissue is therefore generally represented as an absorbing bulk material with scatterers randomly distributed over the volume. Further, it is usually assumed to be homogenous, even though this is not a true representation. The parameters used to characterize the optical properties of the tissue are, the absorption coefficient (μ_i), single scattering coefficient (μ_s), the transport coefficient ($\mu_t = \mu_a + \mu_s$) and the phase function $p(s, s')$ (refs 2, 3). The linear optical coefficients μ_i are defined so that $l_a = \mu_a^{-1}$, $l_s = \mu_s^{-1}$, and $l_t = \mu_t^{-1}$ give the absorption, scattering, and transport mean free paths, respectively. The function $p(s, s')$ is the probability density function giving the probability of photon scatter from an initial propagation direction s to a final direction s'. The linear optical coefficients are related to the absorption and scattering cross-sections (σ_a and σ_s respectively) by $\mu_a = \rho\sigma_a$ and $\mu_s = \rho\sigma_s$. Here ρ is the particle density and independent scatterer approximation is implicit. The integral of phase function (or the differential cross-section) over $4\pi sr$ may be normalized to one or more frequently to the ratio $\mu_s/(\mu_a + \mu_s)$. This quantity is the transport albedo (a) and will be unity for a nonabsorbing scattering material. The first moment of the phase function is the average cosine of the scattering angle, denoted by g. It is also referred to as the anisotropy parameter. The value of g ranges from -1 to $+1$, where $g = 0$ corresponds to isotropic scattering, $g = +1$ corresponds to ideal forward scattering and $g = -1$ corresponds to ideal backward scattering. A photon acquires random direction after about $1/(1 - g)$ scattering events, which is only five for $g = 0.8$. Typical values of g for biological tissues vary from 0.7 to 0.99. Another parameter frequently used is $\mu_s' = \mu_s (1 - g)$. This is referred to as the reduced scattering coefficient. It defines the probability of photon to be scattered in path length z when the scattering is described by an isotropic function. The use of μ_s' assumes that the reflection and transmission for a slab of tissue with optical parameters μ_a, μ_s, and $g \neq 0$ are the same as those for the

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same slab with optical parameters μ_a, μ'_s and $g = 0$. This so called similarity principle, is not exact and holds if $\mu'_s \gg \mu_a$ and if the light distribution is studied far enough away from the light source and boundaries, typically at a distance greater than the effective mean free path $(\mu'_s + \mu_a)^{-1}$. An exact calculation of the cross-sections for the poorly characterized absorbing and scattering centers located in a biological tissue is not feasible. The average optical constants of relatively homogeneous tissues can be calculated from experimental data by fitting the experimental results with appropriate models. This will be discussed later in the article.

Development of optical models that explain the observed scattering properties of soft biological tissues is also of considerable interest[4]. Such modelling can provide insight into how the scattering properties are influenced by the numbers, sizes and arrangements of the tissue elements. Single scattering of collimated light is used widely to study cells and subcellular structures in suspensions. This approach is not directly applicable for tissues due to multiple scattering. Nevertheless, diffusely scattered light from tissue contains information about its underlying structures. Measurements on the diffusely scattered light have recently been used to get estimates for scatterer size in tissues[5]. Further, the extrapolation of the results obtained from cell suspensions to tissues suggest that a majority of scattering from a tissue takes place from organelles within the cell[6] and that the cell shape has little effect. Therefore, scattering from tissue should contain information on changes in organelle structure and number. Recently[7] the density and size distribution of the epithelial cell nuclei have been estimated by analysis of the reflectance from a mucosal tissue. This could have valuable application in clinical diagnosis since these quantities are important indicators of neoplastic precancerous changes in biological tissues.

Tissue optic theories

Theoretical formulations based on the electromagnetic theory, though rigorous, in that it is possible to include all the multiple scattering, diffraction and interference effects, do not lead to solvable equations for any case of practical interest in tissue optics. The heuristic radiative transfer (RT) theory has been the most successful in modelling light transport in tissues[2,3,8]. In this approach, originally developed by Chandrasekhar[9] to explain light propagation in stellar atmosphere, light propagation in a tissue is described by transport of energy by the motion of photons through a medium containing discrete scattering and absorption centres. The time-independent equation for the net change of radiance $L(\mathbf{r}, \mathbf{s})$ at position $\mathbf{r}$ in the direction of unit vector $\mathbf{s}$ can be written as:

$$(\mathbf{s}\cdot\nabla_t)L(\mathbf{r},\mathbf{s}) = -\rho\sigma_t L(\mathbf{r},\mathbf{s}) + \frac{\rho\sigma_t}{4\pi}\int_{4\pi} p(\mathbf{s},\mathbf{s}')L(\mathbf{r},\mathbf{s}')\mathrm{d}\Omega' + \varepsilon(\mathbf{r},\mathbf{s}). \quad (1)$$

The first and the second term on the right hand side represent the depletion and increase of $L(\mathbf{r}, \mathbf{s})$ respectively. The last term specifies the contribution to $L(\mathbf{r}, \mathbf{s})$ of sources located within the medium. This equation called the equation of transfer is equivalent to the Boltzman equation used in the kinetic theory of gases and in neutron transport theory.

There are no exact general solutions to the transport equations in a tissue. For tissues, tenuous scattering approximation (volume density of scattering particles $< 10^{-3}$) rarely applies. Tissues are therefore usually modelled either as intermediate scattering media or dense media (volume density $> 10^{-2}$). The intermediate scattering case is the most difficult to handle rigorously. Several approaches like the Kubelka–Munk model have been employed[2,3]. The range of validity of these models is not well established and the formulation cannot be generalized to most cases of practical interest. For weakly absorbing, dense media, in which scattering predominates ($(1-g)\ \mu_s \gg \mu_a$), the integro–differential equation of radiation transfer reduces to a simpler photon diffusion equation[2,3,8] whose time-independent form can be expressed as[2,3]:

$$\nabla^2\phi_d(\mathbf{r}) - \frac{\mu_a}{D}\phi_d(\mathbf{r}) = -\frac{S(\mathbf{r})}{D}, \quad (2)$$

where D is the diffusion constant, given by $D = 1/3[\mu_a + \mu_s(1-g)]$, $S(\mathbf{r})$ is the 'source' term and ϕ is the radiant energy fluence rate or 'space irradiance'. It is defined as the radiant flux incident from all directions on a small sphere divided by the cross-sectional area of the sphere. When the medium does not contain actual light sources, the 'apparent' source consists of unscattered photons. In order to solve the diffusion equation for a given problem an appropriate choice of the phase function and the boundary condition are required. The choice of phase function is arbitrary due to the diversity and the unknown nature of the inhomogenities. Several approximations have therefore been used[2,3,8]. The exact boundary condition for diffuse intensity is that at the surface there should be no diffuse intensity entering the medium from outside because the diffuse intensity is generated only within the medium. In the diffusion approximation this cannot be satisfied exactly and approximate boundary conditions are used[2,8,10]. One such approximation, valid for matched boundaries, is that at the surface the total diffuse flux directed inwards be zero. For unmatched boundaries this will be the part of the outwardly directed flux reflected

by the surface. A typical tissue–air boundary reflects more than 50% of the outwardly directed isotropic diffuse fluence[10]. Therefore, boundary reflections have a significant influence on the distribution of light, particularly near the surface. It is pertinent to note that the diffusion approximation itself holds only for the region far from the boundary and the source, where the incident photons have lost all of their initial directionality. Time resolved measurements on the transport of photons[11] through a slab of random media (with thickness l) have confirmed that the prediction of the time-dependent diffusion approximation deviates monotonically from the measured scattered pulse as the value of l/l_t decreases or the anisotropic scattering increases. For $l/l_t = 6$ and $l = 10$ mm, the average time of arrival was about 0.9 times that predicted by diffusion theory[11]. For a uniformly illuminated optically dense slab, far away from boundary so that $S(\mathbf{r}) = 0$, eq. (2) can be integrated to give the following expression for the diffuse flux density $\phi_d(z)$:

$$\phi_d(z) = \phi_d(z=0)\exp(-\mu_{\text{eff}} z). \tag{3}$$

Here, μ_{eff} is the effective attenuation coefficient for diffuse flux deep into the tissue, and is related to the optical constants by:

$$\mu_{\text{eff}}^2 = 3\mu_a[\mu_a + \mu_s(1-g)]. \tag{4}$$

The diffusion approximation is a fair representation for light transport, in a soft tissue, in the visible and near-infrared spectral region and has therefore been applied to many cases of interest for laser applications in medicine. The other widely used method for modelling light transport in tissues is the Monte-Carlo simulation. In this statistical approach to radiative transfer, the multiple scattering trajectories of individual photons are determined using random numbers to predict the probability of each microscopic event. The superposition of many photon paths approaches the actual photon distribution in time and space. Although Monte-Carlo simulations may require lengthy computation time they can be performed for any experimental geometry and are considered the 'gold standard' of tissue optics calculations.

Measurement of tissue optical parameters

Measurements of tissue optical parameters are made complicated by multiple scattering. In this section we provide a brief overview of the techniques developed for *in vitro* and *in vivo* measurements. For details the reader is referred to the excellent review provided by Wilson[12].

Direct measurement of optical parameters of a resected tissue

An obvious approach to eliminate multiple scattering effects is to use tissue sample with thickness $d << 1/\mu_s$. The absorption coefficient can then be determined by measuring all the photons transmitted or scattered by the sample, so that the only loss is due to absorption. Similarly, for the typical situation, where $\mu_a << \mu_s$, the scattering coefficient can be determined by filtering out the collimated photons using a suitable aperture and detecting all the scattered photons. Measurement of phase function requires determination of the angular distribution of the scattered photons. All the three measurements are most conveniently done using a integrating sphere. This approach, however, has a fundamental limitation. Because the typical value of μ_s for soft tissues is in the range 100–1000 cm^{-1}, the samples thickness must be less than about 10 μm. The methods used for the preparation of these thin sections may alter the tissue optical properties. Further, the signals are weak. For example, for soft tissues in the visible wavelength range, $\mu_a \sim \mu_s/100$. Therefore, the loss of photons due to absorption in sample thickness $d << 1/\mu_s$ is very small. The weak signal may easily be swamped by several artifacts like unavoidable fluctuations in incident light flux, nonuniformity of response of the integrating spheres etc. Although methods have been developed to minimize these effects this approach may not provide very accurate measurements.

Indirect measurements on a resected tissue

A more practical approach for determining tissue optical parameters is to work with an optically thick tissue section and measure its optical characteristics like the diffuse reflectance (R_d), the diffuse transmittance (T_d), the transmitted collimated light (T_c), spatial distribution of fluence, etc. Approximate analytical models or the Monte-Carlo simulation can then be used to determine the tissue optical parameters through their relationship with the measured parameters. It is pertinent to note that for measurement of T_c, the tissue has to be thin and therefore measured R_d and T_d may not correspond to the completely diffused light. If only R_d and T_d are measured, then it is not possible to determine all the three parameters (μ_a, μ_s and g). With these measurements one can estimate μ_a and the reduced scattering coefficient μ'_s under the assumption that the similarity principle holds.

The analytical models, even where applicable, have not yet provided a closed form equation for the tissue optical parameters in terms of the measured parameters. Therefore, for both the analytical and Monte-Carlo methods it is necessary to either (i) forward calculate the

measured parameters over the expected range of values for the tissue optical parameters and interpolate or (ii) use an iterative procedure. The right choice of model to derive the optical properties involves a trade off between accuracy, speed and flexibility.

Several other approaches have also been developed. In the 'added absorber' method, μ_{eff} for the tissue is measured as a function of the concentration of a dye of known extinction coefficient which is uniformly distributed in the tissue. From these measurements, μ_a and μ_s' can be worked out using a suitable theoretical model under the assumption that the tissue scattering remains unchanged with the addition of dye. The angular peak shape of the coherently backscattered light has also been used for estimating the optical parameters of a tissue[13–15]. Photothermal and photoacoustic techniques can also be used. However, very little published information exists in this regard. We had used photoacoustic spectroscopy to estimate the wavelength dependence of breast tissue absorption[16]. The values for μ_a measured at several wavelengths were in reasonable agreement with the values reported using other techniques.

In vivo measurements

Some of the techniques discussed above can in principle be used for *in vivo* measurements also. This however may require positioning of appropriate fiber probes in the tissue to be investigated. For clinical applications a noninvasive approach will clearly be more appropriate. A great deal of effort is being put in to exploit the diffuse reflectance from a tissue for this purpose. Though, both spatially integrated and spatially resolved diffused reflectance measurements have been used the latter are usually more convenient in practice. The basic arrangement for spatially resolved measurements involves illuminating a small area of the sample by a monochromatic light. The relative radiance $R(r)$ (defined as the ratio of the detected radiance to the incident radiant flux) is determined, as a function of distance r between the centres of the spot of illumination and detection, using appropriate fiber probes. The measurements can be made in steady state or time resolved mode. Both have been used for measurements of tissue parameters. The rationale for the use of $R(r, t)$ in tissue parameter measurements is straightforward. Both the spatial and temporal distribution of the diffuse radiance are influenced by μ_a and μ_s. The lower the value of μ_s', larger will be the spatial extent over which photons will be distributed and consequently the steady state relative radiance curve $R(r)$ will be less steep. Similarly with increasing absorption the radiance at larger distances will be affected more than at shorter distances leading to a lower and steeper $R(r)$ curve. Mismatched boundaries lead to surface reflection because of which the $R(r)$ curve becomes less steep. Similar considerations apply to temporal broadening of an incident light pulse due to multiple scattering. For $r >> 1/\mu_s'$, a relationship between $R(r, t)$ and μ_a, μ_s' is provided by Patterson *et al.*[17] using time-dependent diffusion theory for a semi-infinite optically homogenous medium. It also follows from this theory that

$$\mu_a = -\frac{n}{c}\lim_{t\to\infty}\frac{\partial \ln R(\mathbf{r},t)}{\partial t},$$

where n is the average refractive index for tissue. Thus the final slope of local reflectance time curve gives μ_a directly. However, for finite geometries the slope also depends on the tissue geometry and source-detector separation. The time resolved measurements can be done in both time and frequency domain. The time domain measurements have the potential to yield μ_a and μ_s' directly. However, since time resolution of tens of ps is required, sophisticated and expensive lasers are needed for pursuing this approach. Frequency domain measurements by themselves and in combination with steady state measurements have also been explored for determination of $\mu_s\mu_a'$ (ref. 12).

In vivo measurements of tissue parameters using the steady state spatial radiance profile is receiving a lot of attention. This is motivated by the fact that this approach, due to the simpler technology involved, holds considerable promise for the design of a low cost, portable equipment. This approach was first elaborated by Groenhuis *et al.*[18,19] who also provided an expression for $R(r)$ using diffusion theory. The parameters μ_s', and μ_a could be estimated using diffusion theory when applicable and Monte-Carlo simulations when necessary. It has also been shown[20] that the slope of the ln $R(r)$ versus r curve is strongly correlated to the reduced transport coefficient $\mu_t' = \mu_a + \mu_s'$ for smaller values of r and to the effective attenuation coefficient μ_{eff} for larger values of r. This provides a convenient approach to measure μ_a and μ_s'. The sensitivity, defined as the ratio between a relative variation of the measured quantity, i.e. the slope of $\ln|R(r)|$, and a relative variation of a tissue parameter (μ_{eff} or μ_s') when the other is kept constant, depends on the value of r at which measurements are made[21]. For good sensitivity in the measurement of μ_s', slope of $\ln|R(r)|$ should be measured as close to the point of illumination as possible. Another advantage of small fiber separations is that it is expected to enhance sensitivity to high-angle scattering. This is because photons must turn around by way of high-angle scattering events to get detected. It has been shown[22] that high-angle scattering can lead to better differentiation of morphological features of the tissue. However, for the validity of the similarity principle, the separation between the detector and the point of illumination should be greater than

$1/\mu_s'$. To improve the sensitivity of μ_{eff}, the second measurement position should be selected as far away as possible from the point of illumination. The maximum distance that can be used in practice will be limited by the signal to noise ratio and the size of the probe. Design considerations for a practical system have been investigated[21,23]. *In vivo* clinical measurements of tissue optical parameters during endoscopic procedures in hollow organs, have been reported using this approach[21]. A large variation was observed in the estimated values of μ_{eff} and μ_s' for human esophagus from *in vivo* measurements on 11 patients[21]. While this may represent real variance in tissue optical properties, measurement errors, in particular, those induced by tissue inhomogeneities are also expected to contribute.

It is pertinent to note here that for modelling light transport in tissue, usually a homogenous tissue is assumed. However, many tissues of interest, especially skin, cannot be considered homogeneous and are in fact multilayered. Application of semi-infinite homogeneous algorithms to a layered tissue architecture can introduce serious artifacts in the measured optical properties[24]. The artifacts result from forcing the algorithm to fit data, which correspond primarily to the upper layer for smaller values of r and to the lower layer for larger values of r, to a model that uses the same optical properties at all distances. Therefore, while for some applications the averaged information provided by the homogeneous single layer model may be sufficient, more demanding applications require multilayered photon propagation models. Efforts are therefore being made to develop such algorithms[24,25]. Clinical applications also require rapid estimation of optical parameters from the measured reflectance profile. This aspect is also being addressed to[23,26].

Representative clinical applications

Measurement of tissue optical properties and determination of light transport in a tissue can be of immense value for several clinical applications. As an example, for any phototherapy, the induced effect will depend on the chromophore concentration and the light flux at the target site. The determination of these parameters is therefore crucial for the success of any phototherapy. Similarly, a change in biochemical composition or morphology of tissue will result in a change in the spectral dependence and magnitude of μ_a and μ_s, respectively. Such changes also get reflected in the inelastic scattering (fluorescence/Raman) from the tissue. Measurements on tissue optical parameters and inelastic scattering, can therefore be used to discriminate a diseased tissue from a normal one as well as for *in situ* monitoring of metabolic activity[27]. The differences in the optical parameters of a normal tissue and tumour are also being exploited for optical imaging of tumours embedded in soft tissue. Very encouraging results have been reported on optical mammography, a noninvasive imaging modality that employs visible and near infrared light to detect breast cancer[28]. The application of tissue optics for imaging is discussed elsewhere in this issue. Here, we discuss briefly two representative applications of tissue optics in (i) photodynamic therapy and (ii) laser induced fluorescence diagnosis of cancer.

Photodynamic therapy

Photodynamic therapy (PDT) is a promising approach for cancer therapy. It involves systemic administration of a drug like haemotoporphyrin derivative (HPD) which over a period of two to three days is excreted by the healthy tissue but is selectively retained by the tumour. The drug is inert in dark but when photoexcited at an appropriate wavelength, it leads to generation of singlet oxygen which is toxic to the host tissue cell. Selective destruction of cancerous tissue with minimal effect on healthy tissue can thus be achieved. The technique is now being used for treatment of lung, endobronchial, esophageal cancer and superficial bladder cancer[29]. Its use in other cancerous conditions is also being actively researched.

The therapeutic effect at the tumour site depends on the drug concentration and the radiant energy density at the site which together determine the energy absorbed per unit volume at the target site. Knowledge of these two parameters is therefore required in determining light dose for safe and effective treatment. Tissue optics methods have been developed for this purpose and are being constantly refined to meet clinical requirement[30–32]. A convenient dosimetry model for PDT is based on the assumption[3] that tumour eradication requires the absorption of a minimum energy density (w^*) by the localized drug in every region of the tumour. The energy density absorbed by the photosensitizer localized at position $\mathbf{r}$ for an exposure time t equals $\gamma_d\, c_{d_0}\, \phi(\mathbf{r})t$. Here γ_d is the specific absorption coefficient of the drug at the irradiation wavelength, c_{d_0} is the drug concentration and $\phi(\mathbf{r})$ the diffuse energy fluence rate. This is under the assumption that $\phi(\mathbf{r})$ remains constant during PDT and the drug concentration is uniform throughout the tumour and constant in time. The PDT dosimetry condition is taken as $w(\mathbf{r}_n) > w^*$ where $\mathbf{r}_n$ is the tumour location where PDT induces necrosis. The corresponding energy fluence threshold q^* is $\phi(\mathbf{r}_n)t$. Thus knowing $\phi(\mathbf{r})$, the depth of necrosis can be worked out. The value of $\phi(\mathbf{r})$ will depend on the mode of light delivery. For the typical irradiation geometries used, dosimetry relations, which relate the depth of necrosis to the power delivered at the tissue surface and the optical parameters of the tissue are provided by Grossweiner[3].

Generally the light dose and the drug dose do not show reciprocity, i.e. to achieve the same PDT response halving the drug dose requires more than twice the light dose[3]. Therefore, *in vivo* measurements of the localized drug concentration are also highly desirable. The drug concentration can be estimated by determining μ_a for the target tissue wherein it is localized, by following the principle of added absorber method discussed earlier. This will require knowledge of the native tissue optical parameters, the extinction coefficient of the drug in tissue environment and the assumption that localization of drug does not affect tissue scattering. *In vivo* estimation of drug concentration can also be made from quantitative measurement of drug fluorescence. The uncertainty in these estimates can result from the fact that the fluorescence quantum yield is a strong function of the local microenvironment. Such measurements have also to contend with the problem of multiple scattering to be discussed next in the article.

Laser induced fluorescence diagnosis for cancer

The use of laser induced fluorescence for discriminating malignant tissue from benign tumour or normal tissue is receiving considerable attention[27]. This is because it offers the promise of a sensitive, *in situ*, near real time diagnosis without any adverse side effects, making it particularly attractive for mass screening. Most often diagnosis is done exploiting the differences in the steady state spectra of normal and diseased tissues. Some of the observed differences are expected to be due to the biochemical changes in tissue that are associated with the onset and progression of the disease. However, the measured spectra also has artifacts due to wavelength-dependent absorption and scattering of excitation and emission photons during their propagation through the tissue. For example, significant differences have been observed in the 337 nm excited fluorescence intensity in the blue spectral region from malignant and normal human tissues from breast[33] and oral cavity[34]. These can be caused by several factors like changes in the contribution of blood absorption owing to changes in neovascularization of the tissue, changes in tissue morphology or due to change in nicotinamide adenine dinucleotide fluorescence[27,33,34]. Although excitation/emission spectroscopy can provide some understanding of the likely causes[35], extraction of true fluorescence spectrum from the observed spectrum is required to quantify these effects. Several studies have been made with this objective[36–38]. Extraction of true fluorescence spectra will not only generate biochemical information on the tissue but also help in the design of systems with enhanced sensitivity to the specific biochemical features of the tissue.

Conclusions

One of the cherished dreams of mankind has been to develop techniques to 'peep' inside the body noninvasively and with no ill effects. The persistent march towards this objective has seen the development of a wide variety of biomedical imaging techniques such as computed tomography, magnetic resonance imaging etc. which have in turn resulted in a substantial improvement in the quality of health care. The latest step in this endeavour is the exploration of the use of lasers and optical techniques for the realization of the challenging goal. The other dream is to correct for, with a high selectivity and precision, any potential risk factor detected during routine periodic health checkup. One strategy that has a lot of promise in this respect is the use of drugs that are activated by light. Because these drugs are inert until photoexcited by radiation with the right wavelength, the clinician can target the tissue selectively by exercising the control on light exposure (only the tissue exposed to both drug and light will be affected). A good example is the fast developing photodynamic therapy of cancer. There are indications that selective photoexcitation of native chromophores in the tissue may also lead to therapeutic effects[39] . Tissue optics has to play a crucial role in the realization of both the dreams. An understanding of light transport in tissue and the information content of the elastically or inelastically scattered light from tissues is mandatory for a successful realization of the potential of these optical approaches for achieving quality health care.

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