Review Article

Mechanisms of Laser-Tissue Interaction: I. Optical Properties of Tissue

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Abstract:

Today, lasers are widely used in biology and medicine, and the majority of health centers and hospitals utilize modern laser systems for diagnosis and therapy applications. Researchers have introduced different medical applications for different lasers used in surgeries and other medical treatments. Medical lasers can be categorized in both diagnosis and therapy branches. Main difference between diagnosis and therapy applications is the type of laser-tissue interactions. In diagnosis, one tries to arrange a noninvasive method to study the normal behavior of tissue without any damage or clear effect on tissue. But in therapy, such as surgery, a surgeon uses laser as a knife or for affecting a specific region. So, the medical laser applications are defined by the interaction type between laser light and tissues. The knowledge of laser-tissue interaction can help doctors or surgeons to select the optimal laser systems and modify the type of their therapy. Therefore, we seek to review the mechanisms of laser- tissue interaction. In this paper, the optical properties of biological tissue such as absorption, scattering, penetration and fluorescence are reviewed. Also, the effects of these properties on laser penetration in tissue have been explained.
Keyword: medical optics; lasers; scattering; absorption; fluorescence

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Introduction

After the invention of laser, many researches were performed investigating potential interaction on tissue by means of all types of lasers and biological tissues (1-24). While the number of feasible combinations for the experimental parameters is unlimited, mainly five groups of interaction types are categorized. These are: photochemical interactions, thermal interactions, ablative photodecomposition, plasma-mediated ablation, and photo- disruption (25). Before focusing on these interactions, it is important to study the optical properties of biological tissues. The importance is due to the dependency of light penetration inside biological tissues on laser parameters and optical properties of tissues (26). Therefore, each biological tissue has individual impulse response functions when irradiated by laser light. This impulse response is complicated and many groups around the world work in this field (27-32). This scientific subject is called medical optics and has important role in laser surgery, optical imaging, and photodynamic therapy (33). Each of the interaction mechanisms will be carefully discussed in the next sections of this review in later volumes. Emphasis is placed on microscopic mechanisms controlling various processes of laser energy conversion. Each type of interaction will be introduced in separate papers by common macroscopic observations including

typical experimental data and/or histology of tissue samples after laser exposure.

In this review, we will talk about basic phenomena occurring when biological tissue is irradiated by laser light. In principle, four phenomena exist which govern on undistributed propagation of light in tissue: reflection, scattering, absorption and fluorescence. Reflection can be studied by Fresnel's law (34). Most part of laser energy penetrates into biological tissue. The penetration of laser light in biological tissue depends on optical properties of biological tissue, such as index of refraction, scattering and anisotropic factor, and also the absorption of laser light in tissue. These optical properties determine the mechanism of laser-tissue interaction in that special case. So, first, we study the optical properties of biological tissue, followed by the study of the effect of these properties on penetration of laser light.

Mainly, the behavior of laser in its interaction with tissue can be classified by its wavelength. Today, there are several lasers with wavelengths between x-ray and infra-red (IR). Famous lasers like CO_2, neodymium-doped yttrium aluminium garnet (Nd: YAG), fiber laser, and dye lasers are frequently applied in medicine. The most important difference that can be used to classify lasers is their wavelength, because the molecular absorption depends on this important parameter. For example, the 200 nm laser light is absorbed only slightly by viruses; more is seen by bacteria cells, and an entire absorption by mammalian cells. This absorption is mainly due to the presence of endogenous molecules that absorb heavily near 200 nm such as DNA, genetic material and proteins. Oxygen consumption is activated by illuminating with light at 365 nm. It is believed that mitochondria are the absorber of 630 nm (35). Therefore, in medical optics, the wavelength of laser has an important role due to the absorption peaks of bio-molecules and tissues.

Medical optics

400-1100 nm spectral region is called optical window. Most biological tissues are classified by strong optical scattering in this region. So, they are referred to as turbid media (Figure 1). In other words, the photons (The laser light can be simultaneously assumed as electromagnetic wave and particle beam of photon.) of lasers diffuse and attenuate in biological tissues.

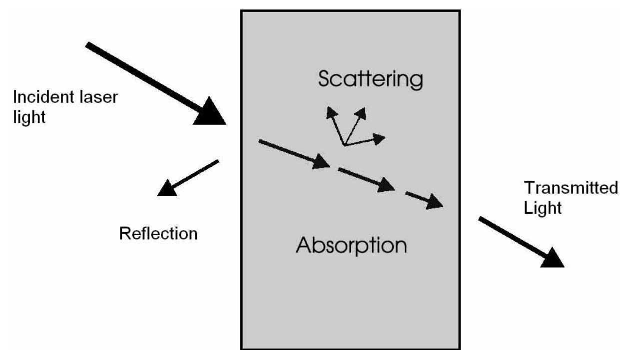

Figure 1. Schematic of scattering in turbid media (15).

Scattering of laser light by cells, nuclei, mitochondria, lysosome, macromolecules, membranes and other components, results in diffusion of light in biological tissues. Optical scattering originates from light interaction with biological structures ranging from cell membranes to whole cells. The size of this scattereres varies from 10 nm to 10 microns. These scattereres are distributed randomly in biological tissue; photons usually encounter multiple scattering events. The scattering coefficient σ is defined as the probability of photon scattering in a medium per unit path length. The scattering mean free path (spatial interval between two adjacent scatterings) is the reciprocal of scattering coefficient σ. The scattering coefficient of biological tissues depends on the wavelength of laser, e.g. the scattering coefficient of liver for lambda of 515, 800 and 1064 nm is 285,200 and 150 cm^{-1}, respectively. The scattering mean free path of liver for these wavelengths is 35, 50 and 66 microns, which shows that the spatial interval between two scatterings increases for longer wavelengths.

The probability of no scattering after a photon propagates over path length x can be written by Beer's law (36):

$$T(x) = \exp(-\sigma x) \qquad (1)$$

In most biological tissues, the majority of scattered light travels in forward direction. So, these biological tissues have anisotropy which is convenient to define a phase function $p(\theta)$ of a photon to be scattered by an angle θ. If $p(\theta)$ is a constant and not dependent on θ, the media is called isotropic, otherwise, it is called anisotropic medium. Experiments show the mean value of

phase function g is a number between -1 and +1. Where $g = 1$ denotes purely forward scattering and $g = -1$ purely backward scattering, and $g = 0$ isotropic scattering. Most biological tissues have $g > 0.7$ (37).

The absorption coefficient α is defined as the probability of photon absorption in a medium per unit path length. The reciprocal of α is referred to at the mean absorption length. Optical absorption in biological tissue originates from water, melanin and hemoglobin (Hb and HbO_2). Figure 2 depicts the molar extinction coefficient of oxy and deoxyhemoglobin vs. wavelength. To convert the molar extinction coefficient to absorption coefficient in (cm^{-1}), multiplied by the molar concentration and 2.303 (38):

$$a = \frac{2.303 .e.x}{64500} \quad (2)$$

Where e and x are molar extinction coefficient (cm^{-1}/M) and number of gram per liter, a typical value of x for whole blood is $x = 150$ g Hb/liter. 64500 (g Hb/mole) is gram molecular weight of hemoglobin.

The absorption coefficient of natural water is shown in Figure 3 (38). Melanin is a chromophore that exists in the human epidermal layer of skin responsible for protection from harmful UV radiation. When melanocytes are stimulated by solar radiation, melanin is produced (39). Melanin is one of the major absorbers of light in some biological tissue (although its contribution is smaller than other components). There are two types of melanin: eumelanin which is black-brown and pheomelanin which is red-yellow (39). The molar extinction coefficient spectra corresponding to both types are shown in Figure 4. Melanin absorbs ultraviolet strongly.

As an example, the absorption coefficients of biological tissue at two wavelengths $\lambda_{1,2}$ can be used to estimate the concentrations of Hb and HbO_2 as in the following method (36):

$$a(\lambda_1) = \ln(10)e_{ox}(\lambda_1)C_{ox} + \ln(10)e_{ode}(\lambda_1)C_{de}$$
$$a(\lambda_2) = \ln(10)e_{ox}(\lambda_2)C_{ox} + \ln(10)e_{de}(\lambda_2)C_{de} \quad (3)$$

Here, e_{ox} and e_{dx} are the known molar extinction of oxy-and deoxyhemoglobin, respectively; C_{ox} and C_{dx} are the molar concentrations of oxy- and deoxy-hemoglobin, respectively, in tissue. The oxygen saturation (SO_2) and the total concentration (C_{Hb}) of hemoglobin can be computed as follows:

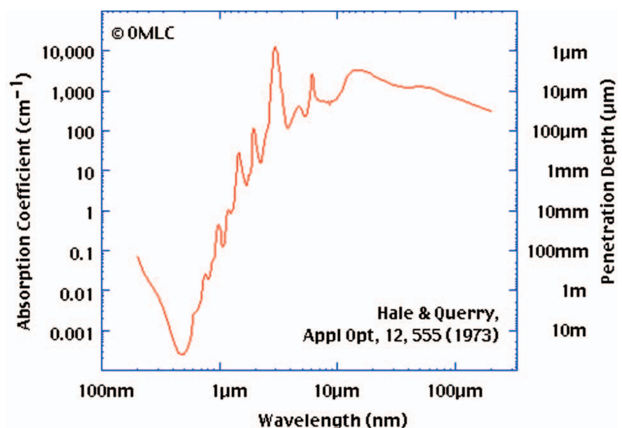

Figure 3. Absorption coefficient of natural water with penetration depth (38).

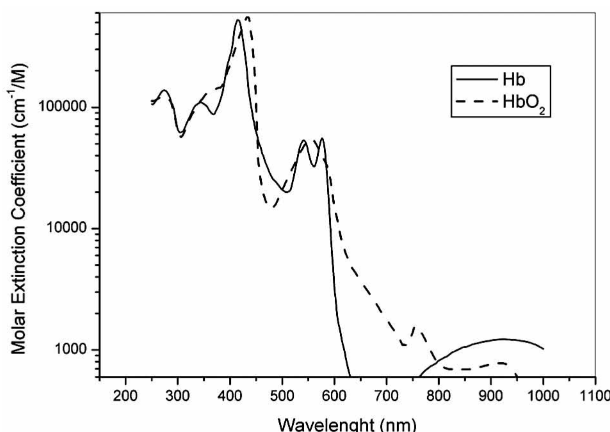

Figure 2. Molar extinction coefficient of oxy and deoxyhemoglobin v.s. wavelength (38).

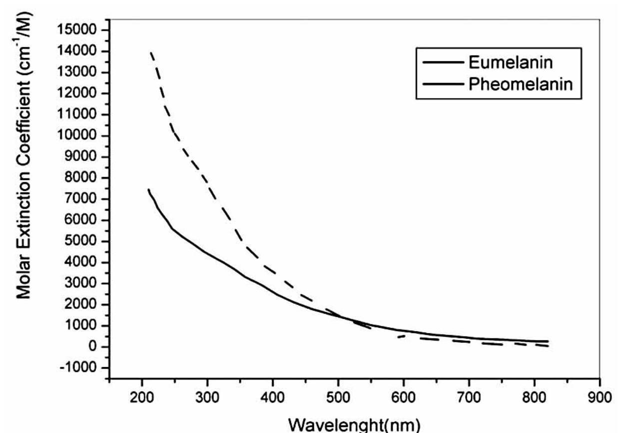

Figure 4. The molar extinction coefficient of eumelanin and pheomelanin v.s. wavelength (38).

$$SO_2 = \frac{C_{ox}}{C_{ox} + C_{de}} \qquad (4)$$
$$C_{Hb} = C_{ox} + C_{de}$$

These parameters are essential for oximetry and functional imaging.

Molecular absorption of laser light

When tissue is irradiated by laser light, a small fraction of light is reflected as shown in Figure 1, but most of laser light penetrates into tissue, where it is either absorbed or scattered by the molecules. As it can be seen in the previous figures, water has two regions of strong absorption, one in UV and one in the IR region. The absorption peak in the case of aromatic rings of proteins and the nuclide acids is in the UV region between 260 and 280 nm. Hence, in the UV region, the laser light is strongly absorbed by water and proteins in the tissue, resulting in a poor light penetration into the tissue. The same is true in IR region starting at about 1.3 microns. Blood absorbs light in a broad wavelength region up to red light (630 nm), and above 600 nm, the absorption of blood is weak. Melanin absorbs light in a region from UV to near IR. Between 600 nm and 1.3 microns, the absorption coefficient of the tissue molecules is small, resulting an interesting optical window to allow penetration of laser light into tissue.

When tissue is irradiated by laser light, most of the energy of light is absorbed by tissue molecules, and they are excited. Laser-excited molecules can return to ground state by emitting fluorescence or phosphorescence light, depending on the lifetime of excited electron. The lifetime of fluorescence is on the order of nanosecond, but the lifetime of phosphorescence is longer (millisecond or longer). In Table 1, the properties of endogenous fluorescence at physiologic PH are classified (where λ_a denotes maximum absorption wavelength; e denotes molar extinction coefficient; where λ_x denotes maximum excitation wavelength; where λ_m denotes maximum emission wavelength) (36). Fluorescence can provide data about the structure, and interaction of bimolecular structures. For example, mitochondrial fluorophore NADH (nicotinamide adenine dinucleotide) is an important sign in cancer detection. The emission spectra of some biological components are shown in Figure 5.

Table 1. Properties of endogenous fluorescence at physiologic PH.

Fluoresence	$\lambda_a(nm)$	$e(cm^{-1}M^{-1})$	$\lambda_x(nm)$	$\lambda_m(nm)$
NAD^+	260	18×103	-	-
NADH	260	14.4×103	290	440
	340	6.2×103	340	450
Phenylalanine	260	0.2×103	-	280
Tryptophan	280	5.6×103	280	350
Tyrosine	275	1.4×103	-	300
Ceriod	-	-	340-395	430-460
Collagen, elastin	-	-	325	400
Lipofusion	-	-	340-395	430-460

Effects of optical properties on penetration of laser light into biological tissue

The study of laser penetration in different biological tissues is one of the aims in medical optics. For example the laser light propagation in skin is important for hair removal and other usage of laser in dermatology. In references number (42) the laser light transport in Asian and Caucasian skins has been studied. Normalized reflectivity variation of Caucasian and Asian skins vs. volume fraction of melanosome for wavelength of 694 nm of ruby laser is illustrated in Figure 6a-b. The level of melanosome is assumed to vary from 1.3 to 5.5% and from 10 to 15.5% for Caucasian and Asian skins, respectively (38). The concentration of hemoglobin in Caucasian and Asian skins is assumed to be 5% and 2%, respectively. The figures illustrate that reflectivity of both types of skins decreases for larger volume fraction of

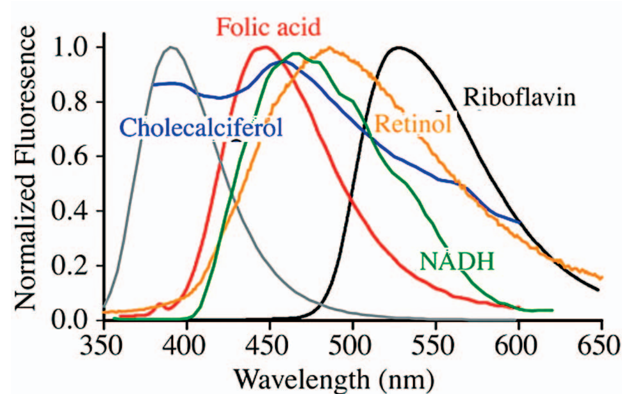

Figure 5. Emission spectra of some biological components. All compounds were measured in buffered (pH 7.2) saline solution, except retinol and cholecalciferol (vit D), which were measured in EtOH. Riboflavin, cholecalciferol, and NADH were measured at 100 μM; retinol, folic acid, phylloquinone, pyridoxine, and nicotinamide were measured at 500 μM. (b) Emission spectra of the compounds shown in a (measured in the same solvents) (41).

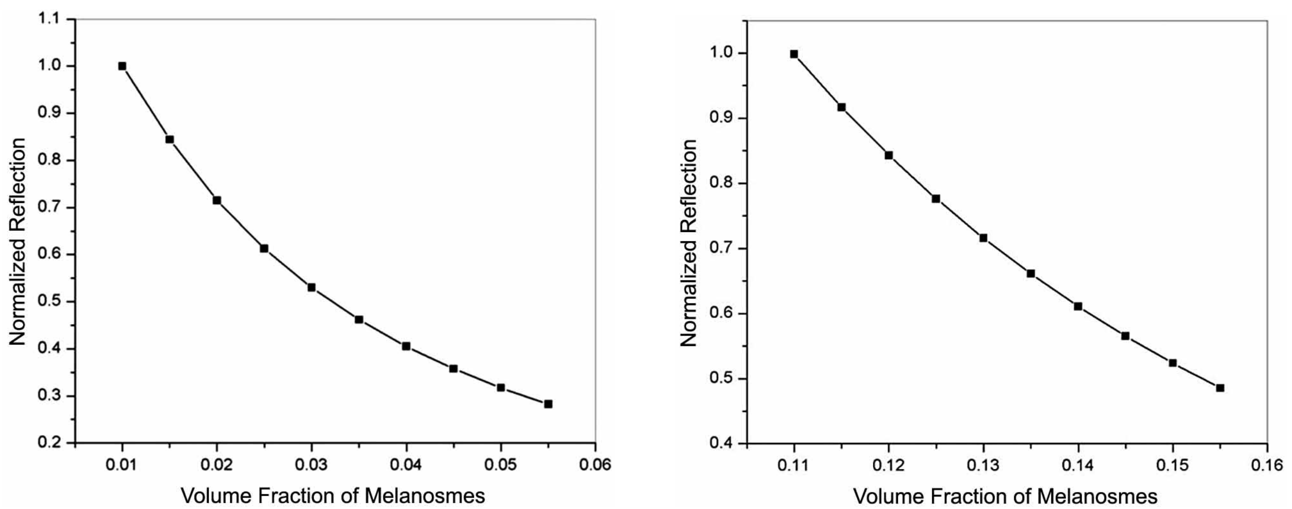

Figure 6. Variation of normalized reflectance vs. volume fraction of melanosome from skin with hemoglobin volume fraction of 5% (a) and 2% (b) (42)

melanosomes. But, for Caucasian skin, normalized reflection reduces down to 51% by increasing volume fraction of melanosome while, for Asian skin, this reduction is more pronounced and is about 71.8%. Similar trends are observed for other famous wavelengths, i.e. 775 (Alexanderit laser) and 1064 nm (Nd:YAG laser).

To study the effect of hemoglobin concentration on light propagation, the blood flow is assumed to be uniformly distributed in the dermis layer (38). Figure 7 shows variation of normalized reflectance of skin vs. blood volume fraction for Caucasian and Asian skins with melanosome volume fraction of 1 and 10%, respectively. One can observe that the reduction of reflectivity is not significant for different values of hemoglobin concentrations. Based on Mie theory, scattering cross section depends on geometrical shape of scattering centers and the wavelength of incident light and its dependence on blood volume fraction can be neglected (38, 43). Therefore, blood volume fraction only changes absorption coefficient of dermis layer. As the blood is assumed to be uniformly distributed in dermis layer, its absorption coefficient, due to hemoglobin concentration, is expected to increase for larger blood volume fractions. But, hemoglobin absorption coefficient at 694 nm is about $0.2mm^{-1}$ and, therefore, variation of blood volume fraction does not significantly change dermis absorption of light.

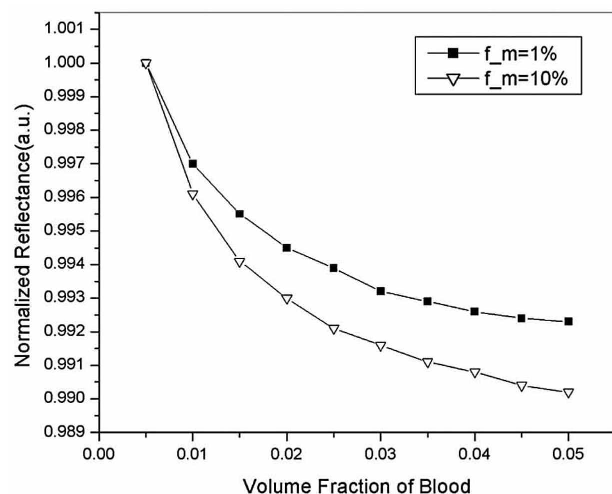

Figure 7. Normalized reflectance variation vs. hemoglobin volume fraction for two different values of melanin volume fraction (42).

Also transverse scattering of light from tissues is studied in references number (42). Scattering of light arises because of density variation. The effect is due to the presence of different types of molecules in tissue (36). Figure 8 illustrates Maximum Scattered Beam Width (MSBW), i.e. distance where fluence of the beam in transverse direction reduces to 0.001% of its initial value for Asian and Caucasian skins for different wavelengths (optical properties of different skin are mentioned in Table.2). The Figure shows that MSBW parameter increases for longer wavelengths for both skin types. That is because for longer wavelengths, both scattering cross section and reduced scattering coefficient decrease (44-36). Furthermore, in NIR region absorption of melanin, as the most important absorbing element, decreases

Table 2. Optical properties of Asian and Caucasian skins

λ(nm)	694	755	1064
Type	**Cau. / Asian**	**Cau. / Asian**	**Cau. / Asian**
Absorp.of epi. (mm^{-1})	0.063 / 2.29	0.054 / 1.7	0.035 / 0.57
Absorp. of derm. (mm^{-1})	0.028 / 0.033	0.027 / 0.029	0.026 / 0.028
Scatt. of epi. (mm^{-1})	40 / 38	35 / 26	26 / 24
Scat. of derm. (mm^{-1})	20 / 19	17.5 / 13	13 / 12

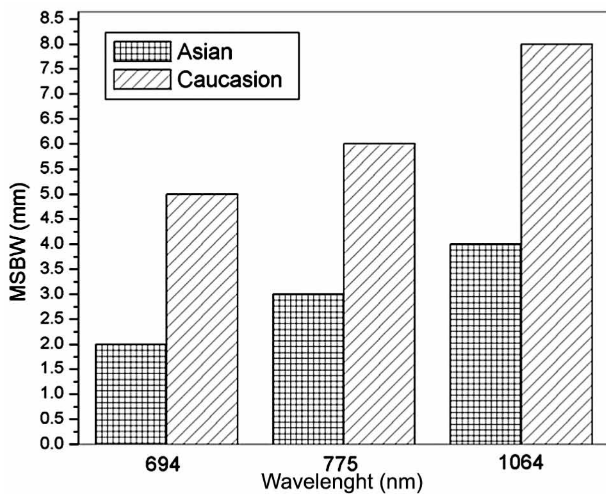

Figure 8. Maximum Scattered Beam Width (MSBW) for three different wavelengths (42).

for longer wavelengths (36). Therefore, moving toward longer wavelengths results in simultaneous reduction of absorption coefficient and reduced scattering coefficient and, consequently, increase in magnitude of diffusion coefficient. On the other hand, mean free path of tissue is proportional to diffusion coefficient (26). Therefore, for longer wavelengths, mean free path in transverse plane and, consequently, MSBW, increase.

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