Laser-tissue interaction principles: tissue optical properties in the light therapeutic window (invited review)

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ABSTRACT

The ability of light to penetrate a tissue and deposit energy in tissues is key to therapeutic applications. In this context, the knowledge of the optical properties of the various biological tissues is mandatory, since the efficacy of laser treatment depends on photon propagation and fluence rate distribution within irradiated tissues. Photon propagation in biological tissue is characterized by the basic optical properties of absorption, scattering and refractive index variations. These properties govern the numbers of photons that are transmitted between points on the tissue surface and deep into the tissue. Even for thin, sub-millimeter sections of tissue, injected photons are likely to be scattered several times before they reach the boundary. As a consequence a coherent, collimated input laser beam will be effectively incoherent and isotropic after traversing a few tissue millimeters, as scattering does not generally preserve coherence.

1. Introduction to tissue optical properties

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 scattering particles randomly distributed over the volume. Further, it is usually assumed to be homogenous (e.g. with constant density), even if this is approximation is not always a good model. The parameters used to characterize the optical properties of the tissue are: the absorption coefficient (μ_a), the single scattering coefficient (μ_s), the transport coefficient $\mu_t = \mu_a + \mu_s$ and the phase function p(s, s'). For the interpretation of μ_a, μ_s and μ_t we refer the reader to previous articles [1,2]. We remind also that units for μ_t , μ_a and μ_s are usually cm^{-1}.

The function p(s, s') is the probability density function, giving the probability that a photon undergoes scattering from an initial propagation direction s to a final direction s'.

The optical coefficients μ_a and μ_s are related to the absorption and scattering cross-sections (σ_a and σ_s respectively) by $\mu_a = \rho\ \sigma_a$ and $\mu_s = \rho\ \sigma_s$. We remind that σ is proportional to the probability that a photon undergoes an absorption (σ_a) and scattering (σ_s) event respectively, while ρ is the particle volume density. In this context independent scatterer approximation is implicit. This corresponds to the assumption that scattering from one particle is not influenced by scattering from other particles, so that the so called "multiple scattering" is neglected.

The average cosine of the scattering angle is denoted by g. It is also referred to as the anisotropy parameter, and represents the average propagation direction of a photon after one scattering event. The value of g ranges from –1 to +1, where g = 0 corresponds to isotropic scattering (i.e. all scattering directions have equal probability), g = +1 corresponds to ideal forward scattering (i.e. the beam continues propagating straightforward) and g = –1 corresponds to ideal backward scattering (i.e. the beam is back-reflected). The coefficients μ_a , μ_s and g may be interpreted as follows. The absorption and scattering coefficients equal the average number of absorption and scattering events per unit path length of photon travel in the tissue, respectively. Any additional scattering event tends to randomize the photon direction, according to the value of g. For example, it can be found that 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, so that 3-100 scattering events are necessary to obtain photons with random directions if a collimated beam penetrates into the tissue. 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. The scattering seen in tissue is mainly due to cells and is dependent on the cell morphology. Scattering can be caused by the cell nuclei, mitochondria, lysosomes, and the Golgi apparatus. At small incident angles the cells themselves are responsible for scattering, whereas at larger incident angles the nuclei of cells may be responsible for it. Cell refraction indices must be considered to apply the scattering theory. To model this, Mie theory is often used, treating the scattering particles as individual spheres distributed either monodispersely or polydispersely with an incident planar electromagnetic wave as a function of the distance between the observer and the particles, the scattering angle, the refractive index and the diameter of the particles.

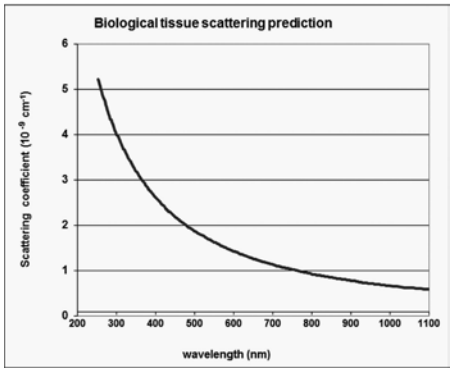

Figure 1: Theoretical prediction for the scattering coefficient of a human tissue, mean values.

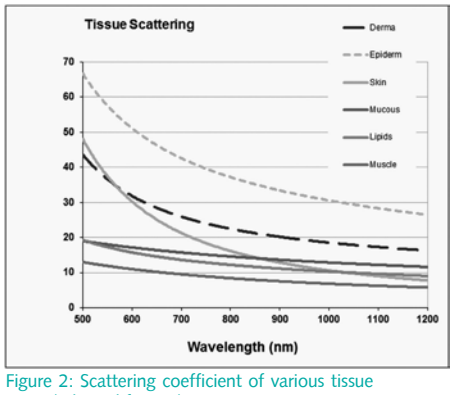

Figure 2: Scattering coefficient of various tissue types (adapted from 3).

The absorption coefficient varies greatly over the visible spectrum, while the scattering coefficient of tissue decreases monotonically as the wavelength increases (Figures 1,2). The presence of chromophores affects the absorption coefficient. There are a variety of chromophores, both natural and exogenously supplied, which can contribute to μ_a. Usually, blood and water will dominate the absorption. In relation to the visible part of the spectrum, melanin, fat, bilirubin and beta-carotene must be considered. Other chromophores present minor contributions. If one is interested in spectroscopic detection, then the minor contributions are important. If one is interested in understanding light penetration into a tissue for some therapeutic protocol, then the minor contributions usually do not significantly perturb the light transport.
Let us conclude this part by analyzing the most important tissue chromophores and their contribution to μ_s and μ_a.

Blood

The major contribution to blood optical absorption is due to hemoglobin, both in its oxygenated and deoxygenated forms. The absorption spectrum for deoxy-hemoglobin and oxy-hemoglobin are distinctly different, thus resulting in difference in total absorption as a function of oxygen saturation. The absorption spectrum of oxy-hemoglobin peaks between 400 nm and 600 nm and deoxy-hemoglobin peaks between 400 nm and 850 nm. The absorption coefficient of whole blood is represented in Fig. 3, which shows fully oxygenated and deoxygenated blood. Reliable data beyond 1000 nm wavelength is difficult to find in the literature. Beyond 1000 nm water absorption (Fig. 4) might begin to dominate over hemoglobin absorption.

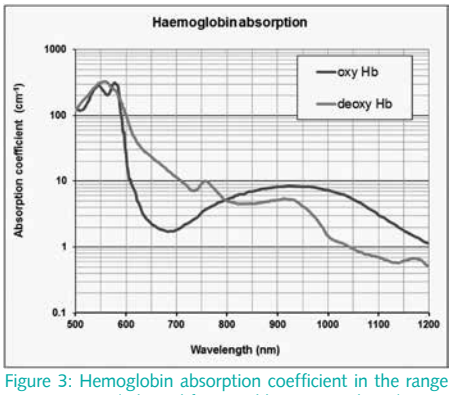

Figure 3: Hemoglobin absorption coefficient in the range 500-1200 nm (adapted from Prahl 2012, cited in 5).

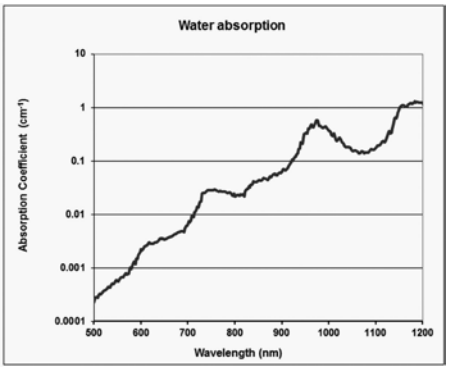

Figure 4: Water absorption coefficient in the range 500-1200 nm (adapted from 4 and 5).

Water

Although water is nearly transparent in the range of visible light, it becomes absorbing over the near-infrared region. Water is a critical component since its concentration is high in human tissue. The absorption spectrum of water in the range 500-1200 nm is shown in Fig. 4 [3,4,5 and bibliography therein]. Although absorption is rather low in this spectral range, it still contributes to the overall tissue attenuation.

Melanin

Melanin is the chromophore of the human skin epidermal layer responsible for protection from harmful UV radiation. When melanocytes are stimulated by solar radiation, melanin is produced. Melanin is one of the major light absorbers 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. The molar

extinction coefficient spectra corresponding to both types are shown in Fig. 5.

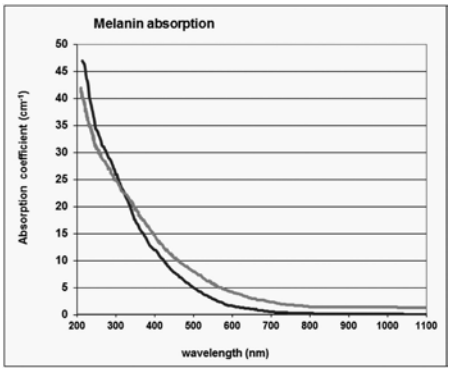

Figure 5: Absorption coefficient for Eumelanin (orange curve) and Pheomelanin (blue curve) – adapted from 5.

Yellow pigments: Bilirubin and Caroten

The yellow pigments, bilirubin and β -caroten, are sometimes present to a small degree in the absorption spectra of tissues. Bilirubin absorption in the skin is routinely used to detect hyper-bilirubinemia in neonates. β -carotene can also give a yellow hue to tissues. The extinction coefficients spectra (data not shown) for bilirubin and β -caroten in vivo are in the violet-blu range of the visible light, adding their contribution to the main absorption band of other pigments like haemoglobins and melanins.

2. Physical properties and structure of the investigated tissues

Following our analysis of the main tissue chromophores, let us now consider the most important tissues involved in a therapeutical approach with light: skin, muscle and the mucous membrane. In the following we will briefly present literature data about tissue optical properties. It has to be considered that the complexity and variability of the tissue structure may lead to different results, as for example corrections for water content (i.e. water absorption/scattering) may have been applied.

2.1 Skin

The skin presents a complex heterogeneous medium, where the blood and pigment content is spatially distributed with depth variations. The skin consists of three main visible layers from the surface: stratum corneum (~20μm thick), epidermis (100μm thick, the blood free layer), dermis (1–4mm thick, vascularized layer). We remember that the optical properties of the layers are characterized by the absorption and scattering coefficient, which equals the average number of absorption and scattering events per unit path length of photon travel in the tissue, and by the anisotropy factor, which represents the average cosine of the scattering angles.

2.1.1 Epidermis

The epidermis can be subdivided into the two sublayers: corneous tissue and living epidermis. The stratum corneum (about 10-40 μm thick) consists of only dead squamous cells, which are highly keratinized with a high lipid and protein content, and has a relatively low (~20%) water content. Living epidermis (~100μm thick) contains most of the skin pigmentation, mainly melanin, which is produced in the melanocytes occurring in the stratum basale. There are two types of this pigment: the red/yellow phaeomelanin and a brown/back eumelanin. The relative percentage of these two pigments varies from person to person also depending from the race.

2.1.2 Dermis

Dermis is a vascularized layer and the main absorbers in the visible spectral range are the blood hemoglobin, β-carotene and bilirubin. In the NIR spectral range, absorption properties of skin dermis are defined by absorption of water. The scattering properties of the dermis are mainly defined by the fibrous structure of the tissue, where collagen fibrils are packed in collagen bundles and have lamellae structure. This layer is highly backscattering. The blood volume fraction in the skin varies from 0.2% to 4%. The volume fraction of water in the dermis is estimated ranging from 65 % to 76%. Fig. 6 shows the penetration depth calculated by these parameters. Because of its thickness, dermis is the skin layer contributing the most to skin optical properties.

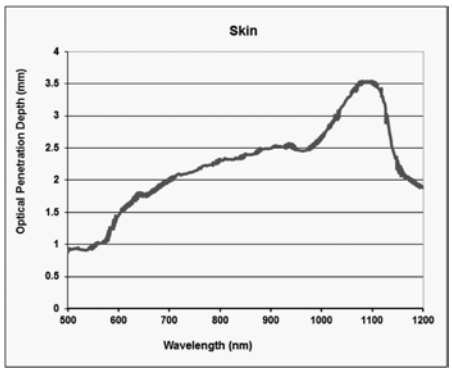

Figure 6: Skin optical penetration depth in the range 500-1200nm, (adapted from 3)

2.1.3 Subcutaneous adipose tissue

The subcutaneous adipose tissue (1-6mm thick depending from the body site) is formed by aggregation of fat cells (adipocytes) containing stored fat (lipids) in the form of a number of small droplets for normal (not obese) humans. In the spaces between the cells, there are blood capillaries (arterial and venous plexus), nerves, and reticular fibrils connecting each cell and providing metabolic activity of fat tissue . [6] Absorption of the human adipose tissue is defined by absorption of hemoglobin, lipids, and water (about 11%) [7] (Figure 7).

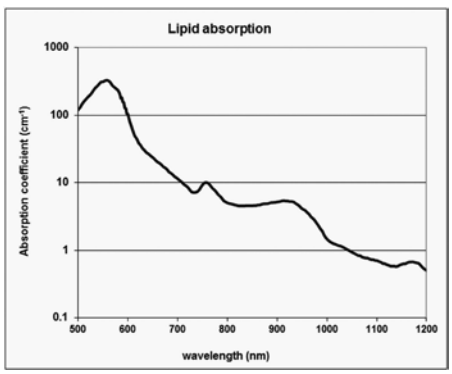

Figure 7: Lipid absorption coefficient in the range 500-1200nm (adapted from 4)

To sum up, the average scattering properties of the skin are defined by the scattering properties of the reticular dermis because of the relatively large thickness of the layer (up to 4mm) and of the comparable scattering coefficients of the epidermis and the reticular dermis. Absorption of hemoglobin (both oxy- and deoxy- forms) and water of the skin dermis and lipids of the skin epidermis define absorption properties of the whole skin.

2.2 Muscle

Muscle is one of the most abundant tissues in the human body. It is well understood that muscle is made up of individual components known as muscle fibers. These fibers are made from myofibrils, which are long cylinders of few μm diameter.
Absorption of the muscle tissue is defined by the absorption of hemoglobin and of water, ranging from 52 % to 73 % according to the specific muscle type and conditions (data from the literature) (52% from [7] or 73% from [8] and [9]).

2.3 Mucous membrane

The proper layer of the mucous membrane is similar in structure to connective tissue, consisting of collagen and elastin fibrils. The interstitial fluid of the mucous membrane contains proteins and polysaccharides and is similar in composition to the interstitial fluid of most of the connective tissues. Figure 8 shows the optical penetration depth in human mucous membrane.

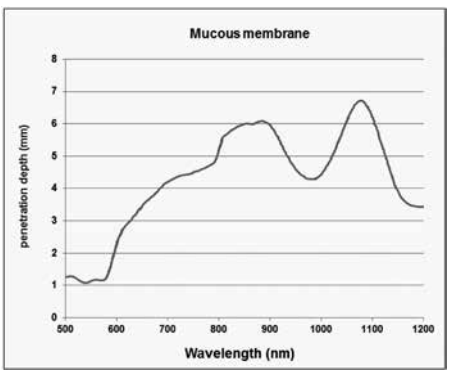

Figure 8: Penetration depth of 500-1200nm light in human mucosa (adapted from 3)

CONCLUSIONS

In this article we have presented a brief review of the physical principles at the basis of the light-tissue interaction, together with experimental data on tissue and tissue chromophore scattering and absorption.
The concepts of absorption and scattering are fundamental and relatively simple, but stem for much complex studies of laser interaction with human tissues. After the introduction of the optical coefficients μ_a, μ_s and g, we have analyzed the main tissue chromophores and, then, tissue optical properties. Most light therapies are concentrated in few but fundamental organs like skin, muscles and the mucous membrane. Even if most literature in this field is based on experimental data, nevertheless the understanding of the basic physical principles remains a fundamental step to understand and plan future applications.

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