Development of functional near-infrared optical coherence tomography
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Wavelength-dependent NIR light penetration depth in Intralipid and biological tissues
Chapter 2

The light penetration depth in biological tissues depends on the wavelength. We propose a method for the estimation of the light penetration depth in different biological tissues in the spectral range 1000-2000 nm. The scattering power parameter and the water content are used to characterize the optical properties of tissues. In particular, a comparison of the light penetration depth at 1300 nm and 1600 nm is performed. Light transmission measurements with different concentrations of Intralipid demonstrate good agreement with theoretical predictions. Calculations based on the published values of the optical properties of sclera, enamel, and dentin show that significant improvement in the light penetration depth can be achieved in enamel, moderate – in sclera, and no improvement is expected in dentin.
INTRODUCTION

Optical coherence tomography (OCT) has proven to be an important imaging modality in biomedical optics [1, 2]. OCT imaging performance is determined by the technical characteristics of the system (axial and lateral resolutions, sensitivity, imaging rate) and by the optical properties of the biological tissue under investigation (scattering and absorption coefficients, and scattering anisotropy).

One of the limitations of current OCT systems is the shallow imaging depth, which is in the range of 1-2 mm in scattering tissues. An increase of the imaging depth can improve the diagnostic potential of OCT. Since the optical properties of the tissue vary with wavelength [3], the imaging performance of OCT systems depends on the center wavelength of the light source that is used. Considering an OCT system with equivalent performance for different wavelengths (such as in Chapter 3), an optimal wavelength can be chosen to achieve the highest imaging depth for a particular tissue.

According to Mie theory, the general trend for the scattering coefficient is to decrease with increasing wavelength. As a result, the light penetration depth potentially can be increased by using longer wavelengths. Historically, after the introduction of OCT with 800 nm central wavelength, OCT at longer wavelengths was demonstrated and improvements in the imaging depth was shown [4, 5]. Current commercially available OCT systems operate in the spectral range of 800-1300 nm. Interest in using wavelengths longer than 1300 nm is growing, but the higher light absorption by water at these wavelengths raises questions about the feasibility of imaging depth improvements.

Knowledge of optical properties of different biological tissues does not cover all wavelengths, and especially for the NIR range not all optical properties are known. To compare the light penetration depth at different wavelengths, it is necessary to predict the optical properties for an extended spectral range. In this work, we propose a method that allows for a comparison of the light penetration depth in different biological tissues without direct measurements at these wavelengths. In particular, we compare the light penetration depth at 1300 nm and 1600 nm. The first wavelength is widely used in current OCT systems [6, 7], whereas the second wavelength is recognized as a potential wavelength for OCT imaging depth improvement [8].

THEORY

Light propagation inside turbid media is described by scattering and absorption. The probability of light to interact with the tissue per unit path length equals the attenuation coefficient $\mu_t$, which is the sum of scattering and absorption coefficients: $\mu_t = \mu_s + \mu_a$. The reciprocal of $\mu_t$ is the mean free path length (e.g. the expectation value of the path length light travels without interaction). The light penetration depth can (arbitrarily) be defined as equal to the mean free path: $D = 1 / \mu_t$. 
Chapter 2

If multiple scattering effects are avoided, i.e. all light that is scattered is removed from the light beam and does not contribute to the measured transmitted intensity, then the light inside a turbid media is attenuated exponentially with depth. The intensity $I$ of light at a certain depth $d$ can be described by Lambert-Beer’s law:

$$ I = I_0 \exp(-\mu d) $$  \hspace{1cm} (2-1)

where $I_0$ is the intensity of the incident light.

The main biological tissue chromophores responsible for the light absorption are melanin, hemoglobin, oxyhemoglobin, bilirubin and water. In the NIR spectral range (for wavelengths longer than 1000 nm) light absorption is dominated by the presence of water. The water content varies in biological tissues, but for most of them it is in the range of 70-80%. Therefore, the volume fraction of water in tissue $C$ is the parameter determining the absorption of NIR light and the absorption coefficient of biological tissues can be described as $\mu_a = C\mu_a\text{water}$.

The scattering coefficient is wavelength dependent and in general tends to decrease for longer wavelengths. The wavelength dependency of the scattering coefficient $\mu_s$ can be approximated empirically in the form of a power law:

$$ \mu_s \sim A\lambda^{-SP} $$  \hspace{1cm} (2-2)

where $A$ and $SP$ are the model parameters for scattering amplitude and scattering power, respectively [9-11]. Parameter $A$ is associated with the scattering strength: tissues with high scattering coefficient $\mu_s$ have high $A$ parameter and vice versa. The value of $SP$ is related to the average size of the scatterers: for particles with diameter $d$ much smaller than the wavelength of light ($d<<\lambda$) the $SP$ parameter is 4 (Rayleigh scattering regime, see Equation 1-10). With increasing particles size, the $SP$ decreases (Mie scattering). The $SP$ parameter determines how strong the scattering changes with wavelength, and thus if the $SP$ parameter is high, then the variation in scattering with wavelength is stronger, and the possible gain in penetration depth is larger. Thus, the wavelength dependent light penetration depth $D_{\lambda}$ in biological tissues is $D_{\lambda} = 1/(C\mu_a\text{water} + \mu_s)$. To quantify the enhancement or decrease of light penetration depth with wavelength, we calculate the ratio $R$ of the light penetration depths at wavelengths $\lambda_1$ and $\lambda_2$ ($\lambda_1<\lambda_2$). Based on the empirical scattering power law with $SP$ parameter, the scattering coefficient at $\lambda_2$ is described in terms of the scattering coefficient at $\lambda_1$, i.e. $(\mu_s)_{\lambda_2} = (\lambda_1/\lambda_2)^{SP}(\mu_s)_{\lambda_1}$. Then, the ratio $R$ of the light penetration depths $D$ at $\lambda_2$ and $\lambda_1$ can be calculated:

$$ R = \frac{D_{\lambda_2}}{D_{\lambda_1}} = \frac{(\mu_s)_{\lambda_2}}{(\mu_s)_{\lambda_1}} = \frac{(\mu_s)_{\lambda_1} + C(\mu_a)_{\lambda_1}}{(\lambda_1/\lambda_2)^{SP}(\mu_s)_{\lambda_1} + C(\mu_a)_{\lambda_2}} $$  \hspace{1cm} (2-3)
Wavelength-dependent NIR light penetration depth

For $R > 1$ the use of $\lambda_2$ light results in a larger penetration depth. A quantitative analysis of both the absorption and scattering characteristics in terms of $SP$ and $\mu_a$ shows how much we can gain or lose in light penetration depth using different wavelengths.

EXPERIMENTAL SETUP

To measure the optical properties of optical phantoms we perform light transmission measurements using the experimental setup depicted in Figure 2-1. Fiber coupled light from a supercontinuum light source (Fianium SC 450-4) is collimated (Fiber collimating package F230SMA-C, focal length 4.64 mm, Thorlabs) and directed to a 1 mm diameter diaphragm. A glass cuvette (1 mm optical pathlength) with scattering medium is placed directly behind diaphragm. The transmitted light is coupled to a monochromator (Oriel, Cornerstone 130 1/8 m, 0.12 mm slit size, 2 nm spectral resolution) for spectral measurements in the wavelength range of 1250 – 1650 nm. The distance between cuvette and input slit of the monochromator is 250 mm long to reduce the detection of multiple scattered light. A long-pass filter (Thorlabs, FEL0950) with a cut-on wavelength of 950 nm is implemented in front of the monochromator input slit to block the visible light. Light at the exit of the monochromator is detected by a photodetector (New Focus, model 2011) and the obtained signal is captured by a data acquisition card (National Instrument, USB-6009) and stored in a personal computer.

Figure 2-1. Layout of the experimental setup for light transmission measurements: L - collimator; D - diaphragm; S - cuvette with scattering sample; MF - multimode fiber; F - long-pass filter.
MEASUREMENTS WITH INTRALIPID

Measurements are conducted with Intralipid (Fresenius-Kabi) as a scattering medium. Intralipid is widely available fat emulsion, of which the scattering coefficient can be easily adjusted by water dilution. Intralipid is often used as a tissue simulating phantom in optical measurements [11].

By dilution of 22.7 vol.% stock solution with deionized water the following concentrations are prepared: 0.7, 1.4, 2.8, 5.7, 11.4 and 17 vol.%. The value of $I_0$ is measured on a cuvette filled with heavy water (which has negligible absorption in the spectral range of interest [12]), and $I$ on the cuvette filled with Intralipid solution. Then, using Equation 2-1, the attenuation coefficient for each concentration is calculated using the thickness of the cuvette. Figure 2-2(a) shows the obtained attenuation coefficients. As can be seen, the attenuation coefficient decreases up to approximately 1360 nm, then starts to increase to a maximum at approximately 1460 nm, and, after the water peak, again decreases for longer wavelengths. To obtain the scattering coefficient $\mu_s$, the absorption coefficient of water $\mu_a$ is subtracted from the total attenuation coefficient (Figure 2-2(b)) using the water volume fraction $C$ obtained from the dilution and the known absorption coefficient of water [13]. The thus obtained scattering coefficient decreases monotonically with increasing wavelength. This clearly demonstrates that the peak in the attenuation in 1400-1500 nm spectral range is solely due to light absorption by water.

Figure 2-2. Experimentally determined attenuation (a) and scattering (b) coefficients as a function of wavelength for solutions with varying volume percentage of Intralipid (indicated).
Wavelength-dependent NIR light penetration depth

Figure 2-3 depicts, as a function of Intralipid concentration, the scattering coefficient of Intralipid at different wavelengths. As can be seen, up to 5.7 vol.% Intralipid the increase of $\mu_s$ is linear, which is expected for the independent and single scattering regime. However, for higher concentrations, the measured value of the scattering coefficient is lower than expected, with the same trend at different wavelengths. This saturation effect can be explained by the increased influence of multiple and dependent scattering effects on the measurements. To estimate the contribution of multiple scattering to our signal, we modeled our measurement geometry by calculating the total transmission of a slab of thickness $d$ (corresponding to our cuvette thickness of 1 mm) using diffusion theory according to Star [14]. The calculation yields ballistic ($T_{bal}$) and diffuse ($T_{diff}$) contributions, the latter is integrated over the acceptance angle of the setup. We then estimate the measurement error as:

$$
\varepsilon = \frac{\mu_{t, measured} - \mu_t}{\mu_t} = \frac{1}{d} \ln \left( \frac{T_{bal} + T_{diff} \frac{\theta_d^2}{4}}{\mu_t} \right)
$$

(2-4)

where $\theta_d$ is the setup acceptance angle of detection. $T_{diff}$ is a function of the optical properties and cuvette thickness $d$. For values of $\mu_s = 15$ mm$^{-1}$, $\mu_a = 0.1$ mm$^{-1}$, $g = 0.34$, $d = 1$ mm, $\theta_d = 0.5/250$, the error in the $\mu_t$ estimation is $\approx 1\%$ due to detection of multiply scattered light. This suggests that the observed deviation from the expected linear
increase of the scattering coefficient with Intralipid concentration is mainly due to dependent scattering, which will be discussed in Chapter 7.

The scattering power parameter $SP$ can be obtained by fitting the wavelength dependent changes of the scattering coefficient (Equation 2-2). Fitting of the data presented in Figure 2-2(b) resulted in $SP$ values as shown in Figure 2-4. As can be seen, the $SP$ is almost constant. The average value is $SP = 3.0 \pm 0.3$ (which is higher than $SP = 2.4$ as reported by van Staveren [9]).

![Figure 2-4. Experimental results of the $SP$ parameter for varying Intralipid concentration (obtained from Fig. 2-3). The horizontal line indicates the average $SP$ value.](image)

Measurements of the attenuation coefficient (Figure 2-2(a)) shows that for wavelengths longer than 1500 nm the light attenuation decreases, which suggests that improvement in light penetration depth can be achieved for this wavelength range. To quantify this, we calculate the ratio $R$ of light penetration depths at wavelengths 1300 nm and 1600 nm for each Intralipid concentration based on our experimental results. Then, to compare experimental results with theoretical calculations, the ratio of the light penetration depths $R$ at 1600 nm to 1300 nm is calculated using Equation 2-3 with a scattering power parameter $SP$ of 3.0 and the known optical absorption of water (light absorption coefficient of water is 0.11 mm$^{-1}$ at 1300 nm and 0.67 mm$^{-1}$ at 1600 nm). Figure 2-5 shows the obtained results and, as can be seen, the experimental results closely correspond to the theoretical calculations.
APPLICATION TO BIOLOGICAL TISSUES

Our measurements with Intralipid demonstrate that the calculations based on the scattering power parameter $SP$ and known water content $C$ give a good approximation for the comparison of the light penetration depths at different NIR wavelengths. This method can be extended to biological tissues using the published values of their optical properties. An advantage of our method is that comparisons can be performed for biological tissues at wavelengths where the optical properties are not reported, i.e. without direct measurements at these wavelengths.

We performed light penetration calculations for rabbit eye sclera, human enamel and dentin (Table 2-1) as these tissues represent key application areas for OCT and are tissues with very different optical properties in terms of absorption and scattering. Sclera is a tissue with a high scattering coefficient, high $SP$ and water content of 70%; enamel has a low scattering coefficient, high $SP$ and almost no water; dentin is a tissue with a high scattering coefficient, low $SP$ and low water content.
Table 2-1. Optical properties of biological tissues analyzed in this article. Grey cells are calculated values.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Volume fraction of water</th>
<th>λ, nm</th>
<th>$\mu_s$ at λ, mm$^{-1}$</th>
<th>SP</th>
<th>R</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit eye sclera</td>
<td>0.70</td>
<td>500</td>
<td>86.0 ± 29.0</td>
<td>2.3 ± 0.2</td>
<td>1.5 ± 0.1</td>
<td>[15]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>550</td>
<td>75.5 ± 25.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>700</td>
<td>50.4 ± 15.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>850</td>
<td>29.8 ± 7.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1050</td>
<td>16.3 ± 3.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enamel</td>
<td>0.01</td>
<td>543</td>
<td>10.5 ± 3</td>
<td>2.9 ± 0.2</td>
<td>1.8 ± 0.1</td>
<td>[16]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>632</td>
<td>6.0 ± 1.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1053</td>
<td>1.5 ± 0.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dentin</td>
<td>0.15</td>
<td>543</td>
<td>28.0 ± 8.4</td>
<td>0.12 ± 0.03</td>
<td>1.02 ± 0.01</td>
<td>[16]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>632</td>
<td>28.0 ± 8.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1053</td>
<td>26.0 ± 7.8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

First, the $SP$ parameter is calculated based on the reported values of the scattering coefficient. The value of $\mu_s$ is fitted using Equation 2-2 with $SP$ and $A$ as a fitting parameter. Then, using Equation 2-3, we calculated the wavelength dependent changes in the light penetration depth ratio $R$ for enamel, dentin and sclera in the spectral range 1050 – 2000 nm, with the ratios calculated relative to the light penetration depth at 1050 nm (i.e. at 1050 nm $R$=1 for all tissues). Figure 2-6 shows that there is no significant change in the light penetration depth for dentin, which can be explained by the low $SP$ parameter and low water content. Scattering changes slowly with increasing wavelength and the influence of the absorption by water is insignificant. In the case of the sclera, the light penetration depth is increasing up to 1850 nm, and then starts to decrease due to increasing optical absorption by water. It is interesting to note, that the increase is almost monotonic, and, despite of the high water content, the influence of the absorption by water at 1400-1500 nm is low. This monotonic behavior can be explained by the fact that sclera has a high scattering coefficient and high scattering power parameter $SP$, which means that the scattering is the dominating process determining the light attenuation in the sclera. Finally, for enamel the light penetration depth is monotonically increasing for longer wavelengths, which is the result of a high $SP$ parameter and very low water content.
Figure 2-6. Theoretical calculations of changes in the light penetration depth for enamel, dentin and sclera, based on the water contents and scattering powers given in table 2-1.

To compare the differences in light penetration depths at 1300 nm and at 1600 nm, the ratio \( R = \frac{D_{1600}}{D_{1300}} \) is calculated (Equation 2-3). For dentin \( R \) is 1, for rabbit eye sclera \( R \) is 1.5, and for enamel it is highest: \( R \) is 1.8. These results demonstrate that the light penetration depth \( D \) with 1600 nm light can be higher in sclera and enamel, but not for dentin. If we compare the \( R \) values, we can note that the increase in \( R \) mainly corresponds to the increase in \( SP \), i.e. for higher \( SP \) the value of \( R \) is also higher. As an example, for enamel with low scattering coefficient and no water content, but high \( SP = 2.9 \), the \( R \) is highest. In contrast, for dentin with low \( SP = 0.12 \) and low water content, the \( R \) is 1.

It is important to note that for real OCT systems with broadband light sources the weighted attenuation coefficient for the spectrum of the light source should be used. Furthermore, the wavelength dependent backscattering properties of the scatterers should be taken into account, which is the topic of Chapter 3.

CONCLUSIONS

In conclusion, we demonstrated a method for predicting of the wavelength dependent changes in the light penetration depth in biological tissues. Using this method, we compared the light penetration depth at 1300 nm and at 1600 nm in Intralipid (based on the light transmission measurements) and in some biological tissue (based on the published optical properties). Our results show that the improved light penetration depth at 1600 nm can be achieved for the biological tissues with high \( SP \) parameter, high scattering coefficient, and low water content. This information is important for predicting the imaging depth for OCT systems operating at different wavelengths and imaging different tissue types.
REFERENCES