Functional optical coherence tomography: spatially resolved measurements of optical properties
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In CHAPTER 1, we argued that the clinical value of OCT can be greatly enhanced by quantitative measurement of the optical properties of tissue. Two applications were investigated in this thesis: measurement of the attenuation coefficient which may be used as a marker to distinguish between different tissues; and measurement of local absorption spectra to determine oxygen saturation. In this chapter the results will be further discussed, next to future clinical implications.
8.1 concluding remarks

To date, OCT imaging is routinely used in ophthalmology and has great potential as an 'optical biopsy' tool in other fields of medicine. Contrary to other optical techniques, in OCT, the path length of the detected light can be controlled. Thus OCT can perform quantitative, 'point-like' local measurements of reflectivity, flow/perfusion, index of refraction, birefringence, absorption and scattering.

In this thesis, we explored two applications of quantitative measurement of local optical properties with OCT. The attenuation coefficient differs between tissues and may therefore be used to as a marker in an OCT image. Measurement of local tissue oxygen saturation may be helpful in understanding the basic mechanisms of oxygen transport and consumption in tissues, and can be of great diagnostic value. This chapter is organized as follows: in section 8-2 and 8-3, additional discussion of multiple scattering and cooperative scattering is given. In section 8-4 we discuss clinical implications of attenuation coefficient measurements and oxygen saturation measurements.

ATTENUATION COEFFICIENT MEASUREMENTS (CHAPTERS 3 AND 4)

To determine optical properties, a mathematical model of the OCT signal is fitted to data from a region of interest in the OCT image. Consequently, it is important to establish the range of validity of this model. We investigated the use of a new description of the point spread function (PSF) of a single mode fiber-based OCT system, in combination with the single (back) scattering model to determine $\mu_s$. We have applied this model to accurately extract $\mu_s$ of weakly scattering media in the clinically relevant fixed-focus measurement geometry (e.g. such as found in imaging probes and catheters). Nevertheless, due to differences between theory and experiment, the influence of multiple scattering on the OCT signal, and consequently the range of validity of the single backscattering model remains subject of discussion. The multiple scattering contribution to the OCT signal depends on both the scattering properties of the sample and on the optical components of the setup. Section 8-2 provides an additional analysis of multiple scattering to discuss the range of applicability of the single backscattering model.

OXYGEN SATURATION MEASUREMENTS (CHAPTER 5 - 7)

The combination of OCT with spectroscopic measurements is straightforward, given the large optical bandwidths required for OCT imaging. With Spectroscopic OCT (SOCT), localized absorption spectra of native or foreign chromophores in the tissue are measured. Specifically, given the overlap of characteristic features of the (oxygenated) hemoglobin absorption spectrum with the Ti:Sapphire laser spectrum, localized oxygenation measurements may be feasible. For quantitative measurements, the influence of scattering on the SOCT signal has to be accounted for. Light scattering by blood is not a trivial problem. First, given the high scattering coefficient and highly forward directed scattering, it is likely that the contribution of multiple scattering to the OCT signal is far from negligible. Second, given the high volume concentration of the scatterers (i.e. red blood cells), the scattering properties do not scale linearly with concentration. Expanding on the discussion of multiple scattering in section 8-2, cooperative scattering is discussed more detail in section 8-3.

Finally, section 8-4 discusses clinical implications of these two applications.
8.2 multiple scattering

The detection of multiple scattered light hampers both OCT imaging and the quantitative measurement of optical properties from the OCT data, and thus the identification of different (pathologic) tissues. The contribution of multiple scattering to the OCT data consequently is the subject of many investigations [1-6]. It depends on the optical properties of the tissue as well as on the parameters of the OCT system. As has been argued in CHAPTER 4, the use of the single backscattering model is beneficial, because of its simplicity. Consequently, we need to establish the range of validity of this model.

We will limit the discussion of multiple scattering to multiple forward-directed scattering (i.e. light that has been backscattered more than once is not considered). The single and multiple scattering contributions to the OCT signal are given by

\[ i_{\text{single}}(z) \propto \sqrt{T_{\text{single}}(z)\exp(-2\mu z)}; \quad i_{\text{mult}}(z) \propto \sqrt{T_{\text{mult}}(z)[1 - \exp(-2\mu z)]} \] (8-1)

respectively. Here \( T_{\text{single}} \) and \( T_{\text{mult}} \) represent the point spread function (PSF) for the single and multiple scattered beam, respectively. For single mode fiber-based OCT systems, the PSFs depend on mismatches in mode field diameter and waist position of the reflected beam and of the fundamental mode of the receiving fiber (equation 2-23).

The PSF for single backscattering was extensively discussed in CHAPTERS 3 AND 4. The PSF can be completely parameterized by the Rayleigh length \( Z_0 \) of the fundamental mode of the receiving fiber, and is a function of distance between the focus location and the probe location (i.e. equivalent to the reference mirror position) in the sample. For dynamic focusing, these are co-localized and consequently \( T_{\text{single}}(z) = 1 \). Due the scattering, the multiple scattered beam is progressively broadened when propagating in a medium, increasing the mode field diameter mismatch with the fundamental mode of the receiving fiber. From equation 2-23, this results in a decreased coupling efficiency of the multiple scattered beam. Thus, for dynamic focusing, \( T_{\text{mult}} \) decreases with depth, counteracting to the increase of \([1 - \exp(-2\mu z)]\) with depth.

There are other mechanisms reducing the contribution of multiple scattered light. First, the polarization of the multiple scattered light is increasingly randomized with the number of scattering events, which reduces the amplitude of the detected interference pattern. Possibly the phase is also slowly randomized, further reducing the multiple scattering contribution.

Presently, a single suitable model for describing multiple scattering in OCT is available. This model [5], see section 2.3, is only valid in the paraxial regime and does not account for the theoretically and experimentally observed differences between specular and diffuse reflection discussed in CHAPTER 3. Nevertheless, it provides some insight into the contribution of single and multiple scattering to the OCT signal. From equation 2-40, the multiple scattering contribution to the OCT signal is calculated as:

\[ i_{\text{mult}}(z) = i(z) - \frac{\exp(-\mu z)}{W(z)} \] (8-2)

Here \( i(z) \) is the total OCT signal as calculated by equation 2-40. In this model \( T_{\text{single}}(z) \propto 1/W(z) \). For dynamic focusing, \( W(z) \) and consequently \( T_{\text{single}}(z) \) is constant.
We can (arbitrarily) define this range by the number of mean free paths \( \text{mfp}_c = \mu_s z_e \) at which the contributions of single and multiple scattering to the total OCT signal are equal (\( z_e \) is the corresponding depth). Figure 8-1A and B show \( \text{mfp}_c \) (as defined above) vs. NA and scattering anisotropy, respectively, for scattering coefficients of 2 mm\(^{-1}\) and 20 mm\(^{-1}\), for dynamic focusing.

From figure 8-1A, \( \text{mfp}_c \) increases with increasing NA (i.e. extending the range of validity of the single backscattering model to a larger depth at fixed scattering properties of the sample). In other words, high NA optics are required to measure single backscattered light at large probe depths – a familiar result from confocal microscopy in turbid media [1]. From figure 8-1B, \( \text{mfp}_c \) decreases with \( g \). Large angle scattering is predominant for low \( g \), which means that the multiple scattered beam profile will deviate faster from its undistorted form compared to high \( g \). Consequently, for lower \( g \), the depth at which the single and multiple scattering contributions are equal is increased and so is \( \text{mfp}_c \). From both graphs, \( \text{mfp}_c \) decreases with increasing \( \mu_s \). If the PSF for the multiple scattered beam \( T_{\text{mul}}(z) \) were independent of depth, \( \text{mfp}_c \) itself would not change when \( \mu_s \) is increased, but the physical depth corresponding to \( \text{mfp}_c \) would be decreased. For decreasing depth however, \( T_{\text{mul}}(z) \) increases, and the relative contribution of multiple scattering to the OCT signal is actually increased. Consequently, the \( \text{mfp}_c \) (at which both contributions are equal) is decreased when \( \mu_s \) is increased.

For the dynamic focusing condition, the transition between single and multiple scattering regimes in low coherence interferometry was investigated experimentally in [4,6]. Brownian motion in the sample causes Doppler shifts in the sample arm light, which are reflected in the power spectrum of the detector current. This power spectrum was measured at different depths in the medium. It has a Lorentzian shape, and the scattering order can be characterized by its width, \( \Omega \). In the single backscattering regime \( \Omega \) is constant; in the multiple scattering regime \( \Omega \approx \text{mfp}(1-g) \), where \( \text{mfp} = \mu_s z \). It was found that the transition from the single to multiple scattering regime occurs at shorter \( \text{mfp} \) with increasing \( g \), consistent with the calculations of figure 8-2B. However, for \( g > 0.75 \), as in most tissues, the transition was almost independent on NA. The scattering coefficient itself was not a parameter in these experiments. It was found that for scattering suspensions with \( g = 0.75 \) using dynamic focusing with NA = 0.12 optics, the single backscattering regime extends to approximately 4–5 \( \text{mfp} \). This is in reasonable agreement with our results (figure 4-3C, squares) from which we concluded that the combination of confocal and coherence gating to a large extent suppresses the multiple scattered part of the diffuse reflected beam at least up to 3.5 \( \text{mfp} \) (dynamic focusing,
NA = 0.08, g = 0.75). Pan et al [3] found for NA = 0.1 and g = 0.8 that the ‘effective penetration depth’ was approximately 6 mfp. At this depth, a specularly reflecting object imbedded in a scattering medium could still be resolved in an OCT image. These findings are in agreement with our own measurements of a mirror imbedded in intralipid (fig. 4-3C).

For the specific samples used in CHAPTER 4, the OCT signal can be calculated using equations 2-40 and 8-2, and split into contributions due to single and multiple scattering. Figure 8-2A shows the measured average A-scan of sample A1 (μ = 2.35 mm⁻¹, g = 0.75) and the best fit to the data using the single backscattering model. The corresponding calculations (eqs. 8-2 and 2-40) shown in figure 8-2B indicate that the use of the single backscattering model is indeed valid because the multiple scattering contribution to the total signal is less than 5% over the total depth scan. (Note that the single backscattering contribution and the total OCT signal coincide).

Likewise, panels C and D show the average A-scan plus best fit, and corresponding calculations for epoxy sample E1 (μ = 6 mm⁻¹, g = 0.75). The single backscattering model still provides a good description of the data for this sample, even though the total signal starts to deviate from the single backscattering contribution around 0.5 mm inside the sample. However, this is about the depth at which the OCT signal reaches the noise floor. These calculations substantiate the conclusions in CHAPTER 4, i.e. the single backscattering model is appropriate for describing the dynamic focusing OCT signal with depth, for μ < 6 mm⁻¹ and our measurement setup. Also note in panel D that the contribution due to multiple scattering first increases with depth and then decreases, illustrating the opposing effects of Tₘₐᵢₜ and [1 - exp(-2μz)] with depth.

The situation for the fixed-focus geometry is more complicated. This is illustrated in figure 8-3, which shows the calculated OCT signal (using equation 2-39 and 8-2) for three different positions of the focus in epoxy sample E1.
Note the obvious suppression of multiple scattered light at the focus position (indicated by the arrows). The total OCT signal closely matches the single backscattering contributions over a large part of the depth scan. In practice, data from larger depths have reduced weight in the curve fitting. Consequently, it is not surprising that $\mu_t$ can be fitted with reasonable accuracy using the single backscattering model as shown in CHAPTER 4.

In conclusion, a more thorough theoretical and experimental analysis is required to fully elucidate the range of validity of the single backscattering model. Experimentally, this may be achieved by combining the measurement procedure of Bizheva et al and that of CHAPTER 4. For a given sample and setup, a 2D dataset can be recorded where, instead of the OCT signal, each element of the dataset holds the width $\Omega$ of the frequency spectrum at a certain position of confocal and coherence gates. The range of validity of the single backscattering model depends on the optical properties of the samples and on the OCT setup. For dynamic focusing, as a rule of thumb, this range is increased for decreased scattering coefficient and anisotropy, and for increased NA of the detection optics. For the fixed focus geometry, the position of the focus is important. Further research can reveal its optimal position, including effects of $\mu_s$, $g$ and NA. The calculations in this chapter substantiate the use of the single backscattering model in CHAPTERS 3 AND 4.
8.3 cooperative scattering

It is usually assumed that both the absorption and scattering coefficient increase linearly with concentration of the absorbing/scattering particles. This is in general true for the absorption coefficient. For high concentrations of scattering particles, their individual locations are correlated, and the scattering coefficient $\mu_s$ no longer scales linearly with concentration. For example, shielding of one particle by another would reduce its scattering cross section. This effect is called cooperative, or dependent scattering.

From Van der Hulst, as a rule of thumb, when the particles are separated by more than three times the particle radius, independent scattering occurs. For the samples used in CHAPTER 3 AND 4, independent scattering is expected. However, because the red blood cell concentration (hematocrit, Hct) is around 50% in whole blood, the samples used in CHAPTER 7 fail the requirement for independent scattering. Cooperative scattering effects are usually addressed by introducing packing factors $W(Hct)$ such that $\mu_s = W(Hct) \cdot Hct \cdot \sigma_s / V$. Next to Twersky’s well known formula [8] $W_T = 1 - Hct$, packing factors for hard spheres, $W_S = (1 - Hct)^2 (1 + 2Hct)^2$ and for cylinders, $W_C = (1 - Hct)^2 / (1 + Hct)$ have been utilized in ultrasound measurements of whole blood.

In earlier experiments we determined the attenuation coefficient as a function of hematocrit of whole blood samples (figure 8-4).

![Figure 8.4: Attenuation coefficient of whole blood samples (subjected to simple shear 300 s^-1) vs. hematocrit. Also shown are the best linear fit for low hematocrit and calculated curves using different packing factors.](image)

In these experiments, the blood was flowing (shear rate was $\gamma = 300$ s^-1) in order to prevent rouleaux formation [9]. Clearly, the linear relation between attenuation coefficient and concentration only holds for low hematocrit. When the data is fitted using the different packing factors (rather than calculated), only $W_T$ yields reasonable values for the scattering cross section. In conclusion, appropriate packing factors for blood have to be established to account for the contribution of scattering to e.g. the SOCT signal. Both multiple and cooperative scattering effects must be accounted for to enable quantitative oxygen saturation measurements.
Two applications of quantitative measurement of local optical properties with OCT were explored in this thesis, i.e. attenuation coefficient measurements and spectroscopic OCT. In this section, the clinical implications of the results will be discussed.

IDENTIFICATION OF TISSUE STRUCTURES
Conventionally, the differentiation between tissue structures in an OCT image is based on their reflectivity (gray scale value in the image) in combination with the (relative) position with respect to other layers and structures. The different structures can then be identified through comparison with histology. Sometimes specific anatomical landmarks appear which eases this approach. Figure 8-5 shows a histology section (left) and corresponding OCT image [10] of normal esophageal wall tissue. The appearance of an elliptical structure, identified as a lymphoid follicle, improved accurate determination of the different tissue layers.

However, these structures may not always be present, the demarcation between different layers may not always be as clear and the gray level of a certain tissue region may be influenced by its position relative to the focus of the imaging probe. Optical properties such as the attenuation coefficient $\mu$, are inherently different for different tissues and may therefore be used as markers in an OCT image.

The measured signal is influenced by the optical components of the OCT system itself. To quantitatively measure the attenuation coefficient, the effect of the confocal point spread function (PSF) of the used optics has to be taken into account. In chapter 3 we have derived a novel description for the PSF of single mode fiber based OCT systems. This PSF consequently applies to a large range of clinically used OCT probes and catheters. The PSF is characterized by one parameter only, the Rayleigh length (half the depth of focus) which can be determined using a single calibration measurement which facilitates fast clinical implementation. The Rayleigh length for diffuse reflection is 2 times that of specular reflection. This is of importance because it is diffuse reflection that actually occurs in tissues, and this effect should be taken into account when extracting the optical properties from OCT data.

Use of this PSF in combination with the single backscatter model allowed determination of the attenuation coefficient of a dilute suspension of calibrated scattering particles. In chapter 4
we showed that the range of validity of the single backscattering model and the PSF extends to weakly scattering media ($n_s < 6 \text{ mm}^{-1}$) using our low NA (0.08) setup. Furthermore, the methods outlined in CHAPTER 4 provide a template for validating the single backscattering model for other ranges of the optical properties of tissues and properties of the OCT setup.

OCT has shown to be valuable in the imaging of unstable atherosclerotic plaques because it is the only technique that allows for intravascular determination of plaque thickness. Unfortunately, differentiation between lipid rich and calcified lesions can currently only be made based on qualitative interpretation of the images. We proceeded to determine the attenuation coefficient of human atherosclerotic arterial segments obtained at autopsy [11] using the setup in fixed focus geometry, and the same data analysis methods as in CHAPTER 4. After imaging, the fitted regions of interest were classified using histology (20 lesions in 13 arterial segments). The results are shown in figure 8-6.

The attenuation coefficients of diffuse intimal thickened tissue ($5.5 \pm 1.2 \text{ mm}^{-1}$) and lipid-rich regions ($3.2 \pm 1.1 \text{ mm}^{-1}$) differed significantly from medial tissue ($9.9 \pm 1.8 \text{ mm}^{-1}$), calcifications ($11.3 \pm 4.9 \text{ mm}^{-1}$) and thrombi ($11.2 \pm 2.3 \text{ mm}^{-1}$), ($p<0.01$). Even in this limited dataset the clinically interesting lipid-rich regions are distinguishable from calcifications, which is not possible based on grey levels alone. Figure 8-7 presents a possible clinical implementation of these results.

Panels A and B show OCT images of a calcified lesion (c in A) and a lipid rich lesion (l in B) respectively. Note that both the calcified and the lipid rich lesion appear as dark area in the OCT image. The average A-scans of the regions of interest encompassed by the dotted rectangles in A and B are depicted in figs. C and D, respectively, by the grey thin lines. The thick lines in these panels depict the individual fits using our model. Note the differences in $\mu_e$ (presented in $\text{mm}^{-1} \pm 95\% \text{ CI}$) for the different tissue types. A moving region of interest (~50 $\mu\text{m}$ by 50 $\mu\text{m}$) was used to determine the local $\mu_e$. In figs. E and F, gray scale overlays are superimposed on the original OCT image presented in A and B, respectively. The scale indicates the local attenuation coefficient ranging from 0 to 15 $\text{mm}^{-1}$. In E, the calcified lesions of panel 1 are accentuated by thresholding the attenuation coefficients below 12 $\text{mm}^{-1}$, in F, the lipid rich lesion of B is
accentuated thresholding \( \mu_t \) above 4 mm\(^{-1}\). This data is of course better presented using color overlays (see leaflet).

![Image of OCT images showing intima and lipid-rich regions](image)

**Figure 8-7:** OCT images of a calcified lesion (c in A) and a lipid-rich lesion (l in B). C and D show average A-scans from the regions of interest in A and B respectively. Thick lines correspond to individual fits. E and F show false color overlays of \( \mu_t \) on the image of panels 1 and 2. The color bar indicates the local attenuation coefficient ranging from 0 to 15 mm\(^{-1}\). L: lumen, l: lipid-rich lesion, c: calcified lesion, i: diffuse intimal thickening.

Figure 8-8 further demonstrates the value \( \mu_t \) measurements using the same overlay procedure. Adding the \( \mu_t \) data in full color to the OCT image will facilitate the identification of calcification (figure 8-8A) or lipid-rich regions (figure 8-8B) at a glance.

![Image of OCT images with false color overlays](image)

**Figure 8-8:** examples of OCT images combined with a false color overlay of the attenuation coefficient \( \mu_t \). To accentuate calcified (A) lesions, areas with \( \mu_t \) larger than 12 mm\(^{-1}\) are plotted, to accentuate lipid lesions (B) areas with \( \mu_t \) smaller than 4 mm\(^{-1}\) are plotted. Bars indicate 0.5 mm.

Schmitt et al. were among the first to measure \( \mu_t \) of rat aorta by OCT at 830 nm [12]. The larger reported \( \mu_t = 14.9 \pm 2.3 \text{ mm}^{-1} \) can be attributed to the high content of elastin in their segments compared to our human arterial samples and differences in measurement procedure. Recently, Levitz et al. used the model of equation 2-39 to determine the scattering coefficient \( \mu_s \) at 1300 nm of arterial tissue in a similar analysis [13]. A range of \( \mu_s \) values was reported which exceeded \( \mu_t \) values from figure 8-6 for all tissues. For approximately 95% of the normal arterial samples, \( \mu_s \) was between 15 and 39 mm\(^{-1}\), while \( \mu_t \) was lower than 15 mm\(^{-1}\) in 60% of
l lipid-rich and fibrocalcific plaques. Fibrous lesions showed very considerable variation in $\mu_s$. The differences with our results are most likely due to differences in the experimental procedures. We snap froze our tissue prior to imaging which is known to preserve optical properties well [14], and in our measurements care was taken to keep the samples at 37 °C because especially the $\mu_s$ of fatty tissue depends on the temperature. The difference between their and our results may also be due to the different model used: when the single backscattering model is used in the multiple scattering regime, lower $\mu_s$ is observed. Conversely, when using a multiple scattering model in the single backscattering regime, the multiple scattering terms simply account for the leveling off of the OCT signal due to noise, leading to higher observed $\mu_s$. Finally, for correct application of the model of Levitz et al., only data from the top, homogeneous layer can be extracted.

TOWARDS LOCALIZED OXYGEN SATURATION MEASUREMENTS

Interrogation of tissue with light offers the potential for non-invasive chemical measurements. Specific features in the absorption spectra of clinically relevant compounds, such as oxygenated and deoxygenated hemoglobin, enable safe and convenient measurement of their concentration. This is the basis for clinically used near-infrared spectroscopy methods, e.g. pulse oxymetry. The data analysis in these methods is complicated by the fact that the exact optical path length of the detected light is unknown. This drawback can be overcome by spectroscopic OCT, which consequently enables highly localized assessment of tissue oxygenation. Many areas of medicine would benefit from a technique that allows determination of spatially resolved tissue oxygenation.

In the intensive care patient, maintenance of adequate tissue oxygen transport is a primary objective. Hypoxia is a major factor contributing to organ failure. Lack of knowledge of basic mechanisms controlling oxygen transport and utilization in the microcirculation is one of the reasons for the uncertainty surrounding potential benefits of various therapeutic strategies in different types of shock [15].

Hypoxic regions are typical of virtually all solid tumors and exhibit significant variability within and between tumors. Tumor oxygen status is associated with tumor growth, progression and resistance to radiotherapy, photodynamic therapy and chemotherapy. Hypoxia is also a driving force behind angiogenesis [16]. Oxygen saturation measurement (on a scale comparable to the oxygen diffusion distances) can help understand how tumors become hypoxic [17].

In neonatology, premature babies are at increased risk of medical and developmental problems. One of the biggest problems faced by premature infants is underdeveloped lungs. In addition, other vital metabolic systems, e.g. those that produce glucose, have to develop until a level of maturity whereby bodily chemical balance has evolved. Therefore, optimal management of a newborn neonate requires accurate monitoring of multiple functional parameters, e.g. blood oxygenation, bilirubin and glucose levels. Currently, monitoring of these and other functional parameters is performed offline, and involves frequent lancing of the heel ('heel prick'), an invasive, painful and stressful procedure, to obtain a small volume of blood for laboratory evaluation. Furthermore, the low sampling frequency inevitably prolongs the time between onset and detection of a problem, which is unfavorable for optimal management. The need for non-invasive continuous monitoring devices of functional parameters is paramount.
CHAPTERS 5-7 of this thesis describe necessary, intermediate steps towards quantitative, localized oxygen saturation measurement using spectroscopic OCT.

In CHAPTER 5 quantitative measurements of the absorption coefficient of phantoms and of hemoglobin and oxygenated hemoglobin solutions with spectroscopic optical coherence tomography (SOCT) are presented. We showed that SOCT has the required sensitivity to distinguish between both oxygenation states of hemoglobin. It was later shown [18] that SOCT is able to extract $\mu_a(\lambda)$ as small as 0.5 mm$^{-1}$ from 450 μm thick, weakly scattering phantoms with a precision of ~2% in the central part and ~8% at the edges of the spectrum. To date, no SOCT measurement on highly scattering media are reported in the literature.

Blood is a highly (forward) scattering medium. From the discussion of sections 8-2 and 8-3, modeling the contribution of scattered light to the SOCT signal is not trivial and should therefore be investigated. Moreover, the oxygen saturation dependence of the scattering properties has so far largely been ignored in literature, even though it is predicted by the causality relations governing the complex refractive index of (oxy)hemoglobin. CHAPTER 6 reports on the scattering properties of oxygenated and de-oxygenated whole blood in the range 250-1000 nm. The complex refractive index of oxygenated and de-oxygenated hemoglobin is determined using Kramers Kronig analysis and OCT measurements. Combining these data with Mie theory, the oxygen saturation dependent scattering properties are calculated. Furthermore, the presented method provides a template for retrieving the optical properties of dense, highly (forward) scattering media (such as blood) where direct measurement is virtually impossible.

Current optical techniques to assess oxygen saturation (e.g. pulse oxymetry) do not take into account oxygen saturation dependence of the scattering coefficient, but rather account for scattering losses by using calibration factors. It depends on the actual contribution of scattering to the measured signal of such techniques whether or not this omission is justified. It can be expected that techniques that have very localized probe volumes, e.g. SOCT, should take oxygenation dependent scattering effects into account in their data analysis.

A significant drawback however, is the fact that there is currently no suitable theory for describing the contribution of multiple, cooperative scattering by blood on the SOCT signal. Consequently, in CHAPTER 7 we have fitted a single exponential decay to the SOCT signal, simply because it was found to describe the data well. Good correlation between the measured differential attenuation coefficient and oxygen saturation of whole blood samples was found. However, to enable quantitative, localized oxygen saturation measurements, significantly more theoretical and experimental work has to be performed.
REFERENCES AND LINKS


7. In this paper, mfp is defined as the number of mean free paths traveled, whereas we define it as the location of the reflector. To avoid confusion, the values reported by Bizheva et al are halved to comply with our definition.


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