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Abstract. Localized spectroscopic measurements of optical properties are invaluable for diagnostic applications that involve layered tissue structures, but conventional spectroscopic techniques lack exact control over the size and depth of the probed tissue volume. We show that low-coherence spectroscopy (LCS) overcomes these limitations by measuring local attenuation and absorption coefficient spectra in layered phantoms. In addition, we demonstrate the first in vivo LCS measurements of the human epidermis and dermis only, from the measured absorption in two distinct regions of the dermal microcirculation, we determine total hemoglobin concentration (3.0 ± 0.5 g/l and 7.8 ± 1.2 g/l) and oxygen saturation.

Keywords: spectroscopy; low-coherence; absorption; attenuation; hemoglobin; human skin.

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The derivation of physiological parameters from the spectroscopic determination of tissue optical properties can offer a fast and painless alternative to invasive diagnostic procedures such as tissue biopsies and drawing of blood. For instance, the absorption coefficient of the dermal microcirculation is directly related to the tissue hemoglobin concentration, which provides information on oxygen saturation, blood volume, and potentially the wavelength of the dermal microcirculation is directly related to the tissue biopsies and drawing of blood. For instance, the absorption coefficient of the dermal microcirculation is directly related to the tissue hemoglobin concentration, which provides information on oxygen saturation, blood volume, and potentially the concentration of deoxygenized hemoglobin (Hb) and oxygenated hemoglobin (HbO2) for the in vivo skin measurements.9 The μa of the dye was obtained from a background corrected S(λ) versus μa of deoxygenized hemoglobin absorption

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we acquired lateral averaging and the μ-estimates (μ-t to μ-fits (dotted lines) are minimally affected by the covering medium. Also, the fits on μ-t are unaffected by the optical density of the layer covering the medium. Therefore, we are primarily interested in the total hemoglobin concentration ([tHb] = gHbO2 + gHb) and the oxygen saturation (SO2 = gHbO2/[tHb]) with their uncertainty estimates (± 95% c.i.) for the in vivo measurements, we directly fit the [Hb] and the SO2 by substituting gHbO2 = SO2 · [Hb] and gHb = (1–SO2) · [Hb] in the fitting algorithm.

The volume from which we obtain μ-t is controllable in both size and position inside the medium, by choosing the region for lateral averaging and the μ-μ-fits for whole blood.9 The fitted SO2 of 81 ± 3% in Region 2 and 7.8 ± 2% in Region 3 indicate the presence of blood and can be related to normal dermal blood volume fractions of 2% and 5%, respectively, when assuming a fixed hemoglobin concentration of 150 g/l for whole blood.1 The fitted SO2 of 81 ± 3% in Region 2 and 100 ± 31% in Region 3 are also within physiological range.

Presumably, Region 3 encloses a flexure line and Region 2 encloses surrounding skin, since relative differences in hemoglobin absorption up to 63% were found between these two palmar skin regions during stretching,7 which is consistent with our [Hb] results. This also explains the difference in scattering between the two regions, because tissue homogeneity and organization of collagen fiber content, the major contributor to dermal scattering, differ significantly between these skin regions.3 The value of the μ-t-contributions to the measured μ-t fall within the physiological range1 of 1 to 100 mm−1, but the actual dermal μ-t may be underestimated due to the contribution of multiple scattering to the LCS signal.6 Nevertheless, since absorption takes place along the controlled photon path,5 this contribution does not influence the determination of μ-t.

These in vivo measurements show that LCS can be used to measure hemoglobin concentration and oxygenation in the microcirculation. Although no gold standard exists to confirm our in vivo [Hb] and SO2 determinations, their values are convincing biologically and the optical properties from which they were derived are within the range of optical properties that were validated in our phantom study. The accuracies at which we determined [Hb] (~15%) and SO2 (~30%) are influenced by the homogeneity of their distribution within the investigated region, and by the accuracy of the determination of μ-t. The latter is affected by the size of the investigated region (i.e., the number of spatial averages and the length of the μ-μ-fits for the exponential decay model) and the OD of the medium covering this region, which limits the maximum probing depth of LCS to ~0.5 to 1 mm in vivo. The limiting accuracy of the in vivo determination of [Hb] can be expected to be 8%, as found for the dye concentration in the phantoms. Since the epidermal OD (~0.8) is comparable to the OD’s of the layers in our phantom study, the extra inaccuracy of the [Hb] and SO2 determination can be ascribed to the skin’s heterogeneity.1 Although the size of the investigated region improves accuracy, it negatively affects measurement speed. Faster acquisition can be achieved by optimizing this trade-off, and by investigating the possibility for Fourier domain acquisition. In contrast to time domain

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acquisition, the latter will require correction for unwanted signal attenuation due to out-of-focus detection and sensitivity roll-off in depth.8,12

Potentially, the dermal [tHb] can be related to the hemoglobin concentration in whole blood, if the blood volume within the investigated region can be assessed. A possible method that deserves further investigation for this purpose is obtaining the blood volume from the OCT image by assessing the vessel density using advanced signal analysis, for instance as described in Ref. 11. When measuring other tissue types, the contribution of additional chromophores (e.g., bilirubin, melanin) to the measured $\mu_t$ may need to be incorporated in our analysis. Also, a correction for Doppler broadening or shifting of the measured $\mu_t$ spectra may be needed for tissues that exhibit blood flow. We did not observe any of those influences on the measured $\mu_t$ spectra in Fig. 2(b), which can be explained by a temporary decrease of blood flow due to applied pressure on the skin.

In conclusion, we have shown that we can use LCS to locally obtain absorption coefficient spectra within confined volumes of optically inhomogeneous media. This enabled us to perform the first in vivo LCS measurements of hemoglobin concentration and oxygen saturation inside the dermal microcirculation. By confining the measurement volume to specific tissue structures, LCS overcomes the limitations of conventional spectroscopic techniques. LCS therefore offers a potential alternative to invasive drawing of blood for the determination of whole blood hemoglobin concentration and oxygen saturation.

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