Path length resolved optical Doppler flowmetry

Babu Varghese, Vinayakrishnan Rajan and Ton G Van Leeuwen*, Wiendelt Steenbergen

Biomedical Technology Institute, Biophysical Engineering Group, University of Twente,
P.O Box 217, NL-7500 AE Enschede, The Netherlands.
*Also Academic Medical Center, Laser Center, Meibergdreef 9, 1105 AZ, Amsterdam,
The Netherlands
Email: W.Steenbergen@utwente.nl

ABSTRACT

The readings in laser Doppler perfusion monitoring are affected by the optical properties of the tissue in which the microvasculature is embedded, through their effect on the optical path lengths. Thus for a constant perfusion, the LDF output signal is affected by the variance in individual photon path lengths due to the changes in tissue optical properties and probe geometry. We will present efforts to render blood flow measurements independent of the tissue optical properties by using low coherence interferometry. We will give evidence of the improvement in quantification of our approach. In particular we show that low coherence interferometry can measure dynamic properties of particles in Brownian motion, independent of optical properties of the surrounding tissue matrices. Furthermore, demonstration is given of the applicability of the method *in vivo*.

Keywords : Light scattering, Low coherence, Interferometry, Laser Doppler perfusion monitoring

1. INTRODUCTION

Laser Doppler flowmetry (LDF) is a non-invasive technique for monitoring blood microcirculation in biological tissues [1]. In this technique, the coherent light delivered to the tissue through an optical fiber, interacts with static as well as moving scatterers, e.g. red blood cells. The light scattered by moving red blood cells receives a slight frequency shift due to the Doppler effect. The Doppler shifted and non-shifted light scattered from the tissue is guided by a second optical fiber, spatially separated from the first fiber to a photodetector where it is mixed, resulting in a speckle pattern. LDF characterizes the time-varying signal arising from the temporal variations in the speckle pattern to estimate the perfusion in biological tissues.

In laser Doppler blood flowmetry, perfusion values averaged over different and basically unknown path lengths are recorded. The average optical path lengths will be different for different tissue types due to the variation in tissue optical properties in terms of absorption and scattering. Also, the variance in individual photon path lengths (e.g., length and depth) increases with the average photon path length. A longer path length will increase the probability of Doppler scattering events, thus yielding a relative overestimation of the blood perfusion, compared to the short path length situation. Hence inter-and intra-individual variations in the LDPM readings will occur for the same perfusion values, introduced by the variance in average optical path length resulting from the changes in tissue optical properties. To overcome this limitation and to obtain more-quantitative and more-qualitative perfusion information, several successful approaches were made [2-8].

Path length resolved temporal fluctuations of photons intensity can be measured using time resolved measurements [2], or by amplitude modulation of the light intensity [3]. However, for a spatial resolution of 50 micrometers, these techniques require either a temporal resolution of 150 fs or electronics working in the GHz range. Coherence gated interferometric systems have been applied as an alternative approach to make path-length-resolved measurements of particle Brownian motion within highly scattering media [4-8]. Unlike most coherence gated interferometric geometries used in path length resolved measurements, utilizing a Michelson interferometer with on axis back reflection [4-6], we use fiber-optic Mach–Zehnder interferometer with separate fibers for illumination and detection, mutually separated by a distance of at least ten times the scattering mean free path [7-8]. This scheme offers

Biomedical Applications of Light Scattering III, edited by Adam Wax, Vadim Backman
Proc. of SPIE Vol. 7187, 71870A · © 2009 SPIE · CCC code: 1605-7422/09/$18 · doi: 10.1117/12.807951

flexibility, since the distance between the illumination and the detection fiber can be chosen freely, giving some control on the overall physiological information of the deeper layers of the tissue, when extended to path length sensitive tissue perfusion measurements.

While these path length measurements depend upon the photons that are Doppler shifted only, the light that has been scattered statically will be added to the interference signal by modulating the phase of the reference beam. By this phase modulation, light that has been scattered by static structures only will also contribute to the interferometric signal. Furthermore, phase modulation will enhance the signal-to-noise ratio since the signal component generated by phase modulation can be shifted to higher frequencies than the signal component caused by mutual interference of Doppler shifted light, which occupies the low frequency range of the spectrum [9].

In this study, we will demonstrate that using phase-modulated interferometry, dynamic properties of turbid media can be measured independent of optical absorption, when absorption levels are in the range for biological tissues. We will give evidence of the improvement in quantitation of our approach. In particular we show that low coherence interferometry can measure dynamic properties of particles in Brownian motion within an almost static tissue matrix. We also report first *in-vivo* measurements by measuring optical path lengths of Doppler shifted and unshifted light and path-length-dependent Doppler broadening of multiply scattered light from human skin. Furthermore we demonstrate the applicability of this method for real time perfusion monitoring and we compare the results with the results obtained with a conventional laser Doppler perfusion monitor.

2. MATERIALS AND METHODS

We use a fiber-optic Mach–Zehnder interferometer (Fig. 1) with a superluminescent diode (Inject LM2-850, λ =832nm, $\Delta\lambda_{FWHM}$ =17 nm, coherence length L_C =18 μm) that yields 2 mW of power from the single-mode pigtail fiber as the light source. Single mode fibers (mode field diameter=5.3 μm, NA=0.14) are used for illumination, while multimode graded-index fibers (core diameter =100 μm, NA=0.29) are used for detection, providing a large detection window and a small modal dispersion. The fibers are spatially separated by a centre to centre distance of 300 μm and are embedded in a black epoxy resin surrounded by a metal tube of internal diameter 6 mm. The reference beam is polarized using a linear polarizer and the phase is sinusoidally modulated at 6 kHz using an electro optic broadband phase modulator (New Focus Model 4002) with a peak optical phase shift of 2.04 radians applied to the modulator. The AC photocurrent is measured with a 12 bit analogue to digital converter (National Instruments), sampling at 40 kHz, averaged over 1000 spectra and was measured in steps of 200 microns in air. The setup has been described in more detail elsewhere [9-14].

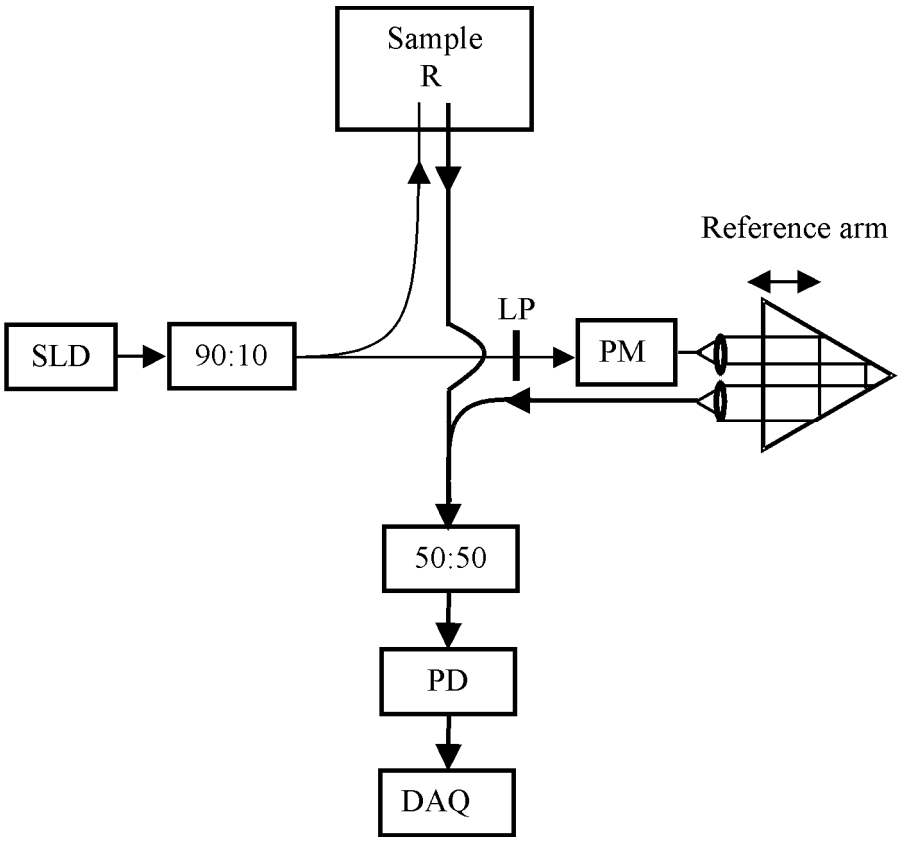

Fig. 1. Schematic of the fiber optic Mach–Zehnder interferometer. Single-mode and gradient index multimode fibers are shown by thin and thick lines, respectively. SLD denotes superluminescent diode, PD is the photodetector, LP is a linear polarizer, PM is the electrooptic phase modulator, 90:10 and 50:50 are single-mode and multimode fiber couplers, respectively (Figure reprinted from Fig. 2 in Ref. [9] Copyright (2008) with permission from SPIE).

The fundamental output quantity of a laser Doppler perfusion monitor is the first moment of the power spectrum $P(\omega)$ of the detector signal; in general, the ith moment is being defined as

$$M_i = \int_a^b P(\omega)\omega^i d\omega \qquad (1)$$

Here a and b are device dependent low and high cut-off frequencies. With i=0, a quantity is obtained which is proportional to the concentration of moving red blood cells, while i=1 describes red blood cell flux, which is the product of concentration and the root mean square of the red cell velocity, at least for low blood concentrations [15].

In our instrument, for large phase modulation angles ($\Delta\phi$ =2.04 radians) the power spectra contain interference peaks at both the phase modulation frequency and higher harmonics (Fig.2). When path length resolved information from these high-order harmonics is utilized, the signal to noise ratio is increased by almost one order or magnitude, as compared to a situation where the peak phase modulation angle is kept lower to avoid higher harmonic peaks ($\Delta\phi$ =0.51). Optical path length distributions are obtained by adding the areas of all interference peaks (after subtraction of the background noise, and within a bandwidth of $\pm$ 2 kHz around all center frequencies) in the power spectrum [11,14]. The FWHM of the interference signal is about 50 Hz in a statically scattering medium whereas in the case of dynamic media more and more power is set to frequencies around the phase modulation frequency, resulting in Doppler broadening [14]. Thus, the area of the Doppler broadened peak, excluding the statically scattered light contribution at the

interference peaks, forms an estimation of the amount of Doppler shifted light at that specific optical path length. The average Doppler shift corresponding to the Doppler shifted light is calculated from the weighted first moments (M_1/M_0) of the heterodyne peak at the modulation frequency, after correction for the sample signal and for the reference arm noise (in a bandwidth of 50 Hz-2 kHz close to the phase modulation frequency and its higher harmonics, indicated by *a* and *b* in Eq.2)

$$M_i = \sum_{j=1}^{3} \int_{j\omega_m+a}^{j\omega_m+b} P(\omega)(\omega - j\omega_m)^i \, d\omega \qquad (2)$$

To study the effect of absorption on Doppler shift, measurements were performed on three samples with identical scattering properties but increasing absorption levels. The media were an aqueous suspension of 25% of Intralipid 20% [16] and the same suspensions with absorption coefficients of 0.50 mm^{-1} and 0.85 mm^{-1}. For absorption, a black dye (Royal Talens black Ecoline™ Black) was used. The transmission spectrum of a water solution of the black ink in the wavelength range 600-900 nm was measured by a spectrophotometer (Shimadzu UV-2101- PC).

Mixed static-dynamic scattering phantoms were prepared with aqueous suspensions of polystyrene microspheres of ∅4.7 μm and ∅0.20 μm respectively. Although particles of both sizes will be in Brownian motion, particles with ∅4.7 μm will move sufficiently slow to consider them as effectively static. Three scattering phantoms with the same concentration of particles ∅0.20 μm (g=0.18, μ_s'=0.55 mm^{-1}, μ_a=0.001 mm^{-1}) were prepared and two scattering levels of the static medium were realized (μ_s'=1.4, 0.8, 0.4 mm^{-1}).

The Doppler shift measured from the weighted first moments averaged over all optical path lengths will lead to an overestimation for long path lengths. To avoid this overestimation in the perfusion signal and to measure flux in absolute units, the Doppler shift for a given optical path length is weighted with the corresponding optical path length distribution of Doppler shifted photons. The flux (M_1) is defined as the product of Doppler fraction of photons in the perfusion signal and the weighted average Doppler shift.

The conventional laser Doppler perfusion monitor used in our measurements is a PF5000 monitor (Perimed AB, Sweden) with a laser diode (780 nm) as the light source. The PF5000 has a bandwidth of 20 Hz -13 kHz (*a* and *b* in Eq.1) and a time constant of 0.2 s was used for monitoring. The fiber-optic probe (Probe 408, standard probe) consists of two spatially separated fibers (core diameter =125 μm, NA=0.37) with a center-to-center separation of 250 μm. The calibration of the PF5000 was done with motility standard (water suspension of polystyrene microspheres with a diameter of 320 nm). After the calibration, PF5000 displayed a standard reading of 250 perfusion units when measuring in the motility standard.

Measurements were performed on the skin of the dorsal side of the right forearm of a healthy human volunteer (Skin type- Type II) in the sitting position. A probe holder (PH 08) was attached to the skin with a double-sided adhesive tape. The subject rested approximately 10 minutes prior to the measurements. The fiber optic probe of the PF5000 was inserted into the probe holder and the perfusion was measured for comparison with the succeeding measurements with our developed probe. Skin sites were avoided with visible large superficial blood vessels, hair and pigment variations.

For monitoring the perfusion changes in real time, measurements were performed on the dorsal side of the forearm with the length of the reference arm tuned such that the optical path length in the tissue was 1.7 mm in the sample arm. The signal was sampled at 40 kHz for 2.6 seconds to get an average of 100 spectra. Simultaneous measurement of perfusion was performed with the PF5000 at a position approximately 3 cm distant with respect to the probe of the low coherence interferometer. The perfusion was recorded for 30 seconds before occlusion, 90 seconds during occlusion, 105 seconds between occlusions, second occlusion for another 90 seconds and final measurements for 30 seconds.

3. RESULTS AND DISCUSSION

Figure 2 shows power spectra measured for the water suspension of polystyrene microspheres for $\Delta\phi$ =0.51 and 2.04 radians. For the lowest modulation angle, the power spectrum is composed of an interference peak at the phase

modulation frequency, and a low frequency component. For large phase modulation angles, the amplitudes of the interference signals at the modulation frequency and higher harmonics are increased.

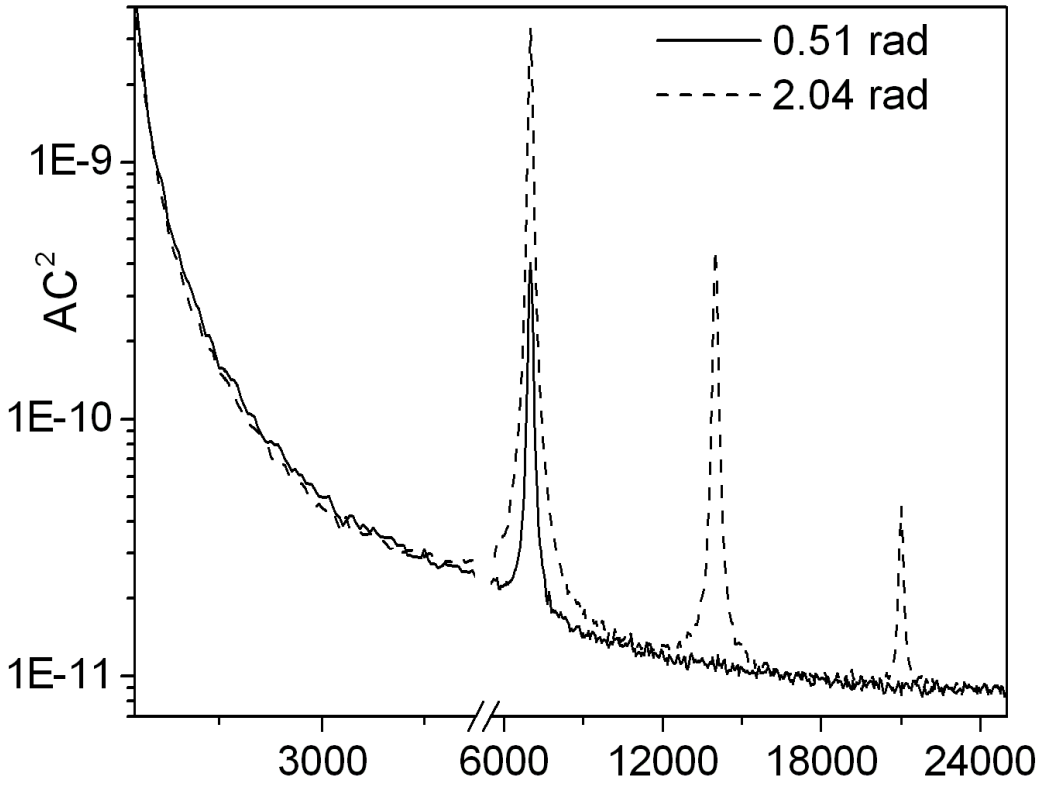

Fig. 2. Power spectra measured for water suspension of Polystyrene microspheres for two different peak optical phase shifts (0.51 and 2.04 radians), with the position of the retroreflector corresponding to an optical path length difference of 1.3 mm. (Figure reprinted from Fig. 1 in Ref. [13] Copyright (2008) with permission from Elsevier B.V.).

The optical path length distribution is obtained by adding the areas of all interference peaks (after subtraction of the background noise, and within a bandwidth of 2 kHz around all centre frequencies). Typical optical path length distributions measured for a scattering medium (g=0.85,μ'_s=2.0 mm^{-1}, μ_a = 0.001 mm^{-1}) for a peak optical phase shift of 2.04 radians is shown in figure.3. The distribution is normalized with respect to the maximum value.

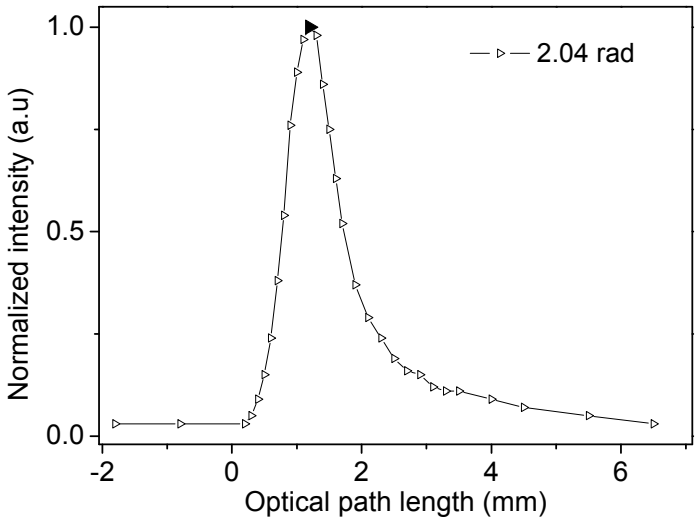

Fig. 3. Optical path length distributions measured for a scattering medium (g=0.85, μ'_s=2.0 mm^{-1}, μ_a = 0.001 mm^{-1}) from the areas of interference peaks with a peak optical phase shifts 2.04 radians applied to the modulator. (Figure reprinted from Fig. 2 in Ref. [13] Copyright (2008) with permission from Elsevier B.V.).

The average Doppler shift, measured from the width of Doppler broadened phase modulation interference peaks is represented in fig.4 as a function of the optical path length. The average Doppler shift increases with the optical path length, which can be expected from the increase in the number of scattering events with the optical path length. Further, for a given optical path length the Doppler broadening of the modulation peak is equal for the media with zero absorption and the lowest nonzero absorption coefficient (μ_a = 0.50 mm^{-1}). But in the case of the highest absorption level (μ_a = 0.80 mm^{-1}), the Doppler broadening is equal to those of the other absorption levels for optical path lengths up to 1.1 mm, while for large optical path lengths, the Doppler broadening is found to be decreased, in particular in the optical path length interval between 1.1 and 2 mm.

The observed line width broadening results from the detection of multiply scattered photons and as the number of scattering events increases the width of the peak increases with optical path length. For a given medium with a constant scattering coefficient but absorption coefficients μ_a = 0.001 and 0.50 mm^{-1} the Doppler broadening of path length resolved heterodyne spectra is shown to be independent of the absorption level, for a given optical path length. But in the case of a higher absorption coefficient (μ_a = 0.85 mm^{-1}), for optical path lengths between 1.3 and 2 mm, the Doppler broadening deviates from those obtained for the lower absorption levels. This absorption level would correspond to an unrealistically high relative blood volume of 45%. The nonzero absorption levels used in this study are larger than the values found on average in normally perfused tissue. Therefore, our results indicate that for absorption levels realistic for tissue, our method enables Doppler measurements independent of the absorption level of the medium in which the moving particles are embedded.

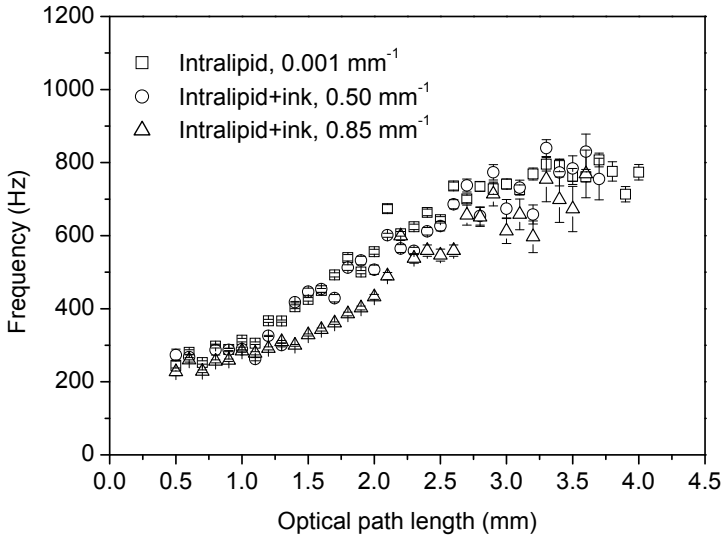

Fig.4. The average Doppler shift extracted from the phase modulation peak, as a function of the optical path length for an aqueous Intralipid suspension (μ_a=0.001mm^{-1}) and for identical suspensions with two different absorption coefficients (0.50 mm^{-1} and 0.85 mm^{-1}). (Figure reprinted from Fig. 5 in Ref. [9] Copyright (2008) with permission from SPIE).

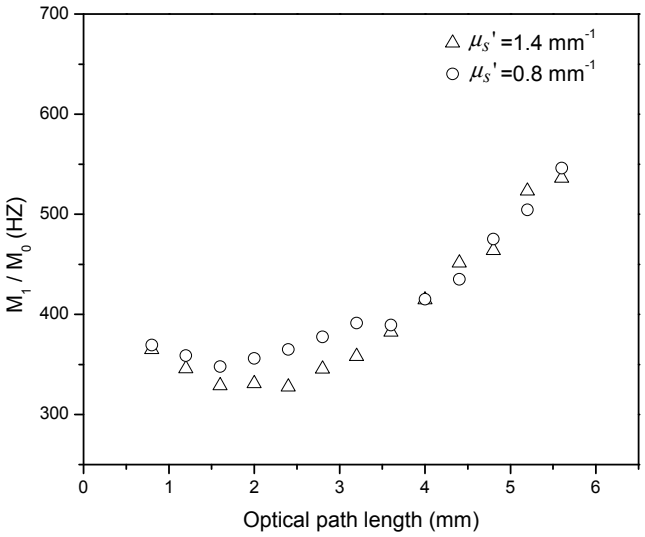

Fig. 5. The weighted Doppler shift measured as a function of optical path length in the medium.

Figure 5 shows the weighted first moment M_1/M_0 of the Doppler shifted light, which represents the average Doppler shift generated by the moving particles. Also this quantity shows a different behaviour for optical path lengths smaller and larger than 2 mm, while the overal dependence on the static matrix optical properties is small. For larger optical path lengths, the average Doppler shift increases with the optical path length, as expected. For smaller optical path lengths, the average Doppler shift decreases with the path length. There is not a simple explanation for this

behaviour. In this regime of single scattering, the Doppler shift depends on the scattering angle and the diffusion coefficient of particles in Brownian motion.The overall dependence on the static matrix optical properties is small. In the case of a higher scattering coefficient (μ_s'= 1.44 mm^{-1}), for optical path lengths between 2.5 and 3.5 mm, the Doppler broadening is lower in comparison with those obtained for the lower scattering levels.

The intensity of Doppler shifted and nonshifted photons measured in skin as a function of optical path length are shown in Fig. 6. The fraction of Doppler shifted photons and nonshifted photons averaged over the entire optical path length measured from the respective areas of the optical path lengths are 22 and 78%, respectively. As shown in Fig. 6, the weighted first moment M_1 /M_0 of the Doppler shifted light, which represents the average Doppler shift, increased with the optical path length due to the greater probability of interaction of photons with moving scatterers for large optical path lengths.

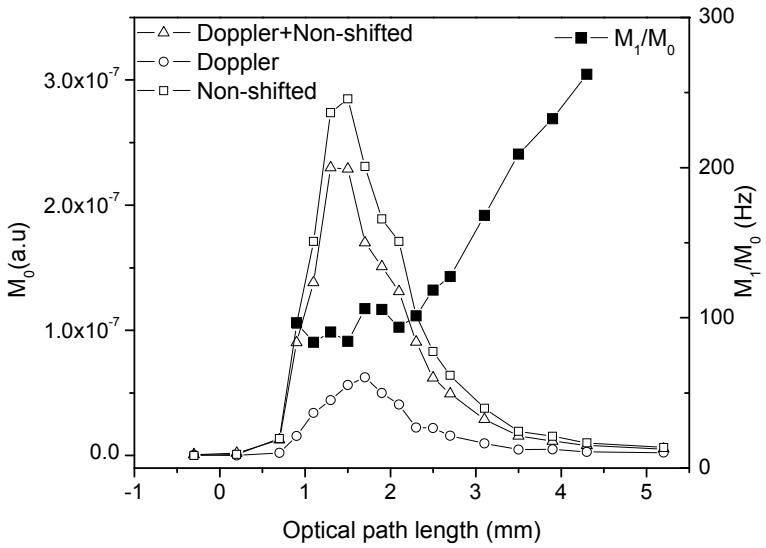

Fig. 6: Intensity of Doppler-shifted, nonshifted photons and the average Doppler shift as a function of optical path length measured in skin (Figure reprinted from Fig. 1 in Ref. [14] Copyright (2008) with permission from SPIE).

Figure 7 shows the perfusion signal measured in skin in real time for an optical path length difference of 1.7 mm in air. The occlusion results in the suppression of mean flow velocity of red blood cells to nearly zero values (biological zero). The flux of red blood cells (Fig. 7, left, bottom) and the Doppler-shifted fraction of photons are reduced due to occlusion (Fig. 7, left, top). Since the realization of occlusion takes some time, the perfusion decreases gradually and finally drops to biological zero values. After the occlusion is released, the perfusion signal increases above the normal value, an effect called postocclusive reactive hyperemia (PORH). PF5000 traces recorded with a time constant of 0.2 s are averaged for the same measurement time used in our measurements (2.6 s). Real-time measurements performed with our setup show similar trends as the perfusion readings measured with the PF5000. However, smoother perfusion signals are shown from the PF5000 compared to the fluctuating perfusion signal obtained with our LCI set up. Although the mean depth is of the order of 1 mm, in PF5000, perfusion values averaged over all optical path lengths are measured, which often spans a range of zero to 5 mm. In our setup, the coherence length of the light source acts as a bandpass filter in selecting the photons that have traveled a specific optical path length, for instance, 1.7 mm in the skin with a tolerance of ±50 μm, as defined by the path length resolution of the setup. Hence, in a LDPM, due to the large coherence length of the light source, more photons are involved in the interference process, leading to a large signal-to-noise ratio of the raw signal, and a more stable estimation of its spectral moments. The lowest value recorded with PF5000 is relatively lower during occlusion, and the PORH peak with LDPM is shorter in time than with LCI. These variations could result from the fact that both techniques probe different positions with a spatial separation of 3 cm and

our probe measures physiological perfusion in the superficial layers with an optical path length of 1.7 mm compared to the perfusion averaged over all path lengths and depths. Also, we only have heterodyne detection, while in

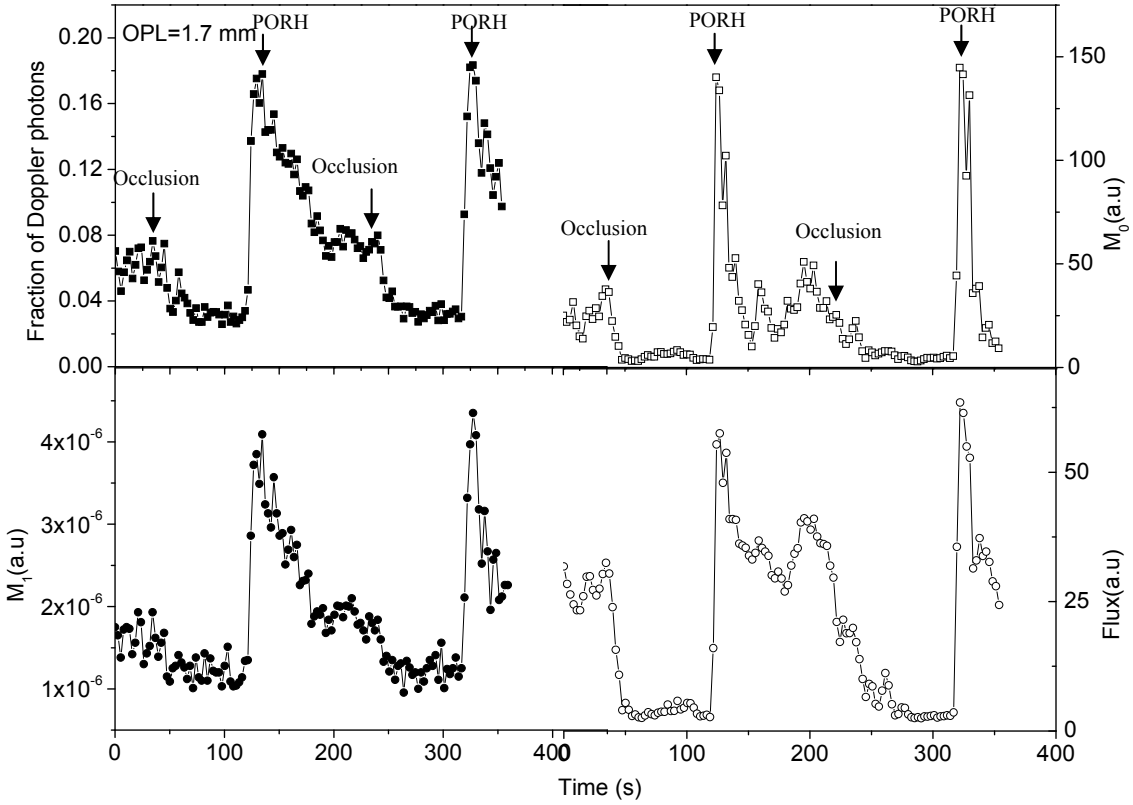

Fig. 7: Real time monitoring of the Doppler-shifted fraction of photons and the weighted first moments measured with our setup (Left) for an optical path length of 1.7 mm. Simultaneous perfusion measurements recorded with PF5000 at an adjacent position (Right) (Figure reprinted from Fig. 2 in Ref. [14] Copyright (2008) with permission from SPIE).

LDPM the signal power spectrum is composed of mutual interference of the Doppler-shifted and nonshifted light detected from the tissue. Temporal resolution of 2.6 s makes it difficult to follow all physiologic changes, such as cardiac cycle and reactive hyperaemia responses. During occlusion, the observed discrepancy between the calibrated zero of the instrument PF5000 and the "biological zero" level is attributed to the fact that though the blood perfusion is arrested by the inflated cuff, minor Doppler components are recorded by the instrument due to the no-flow laser Doppler signal from vasomotion, Brownian motion from within the vascular compartment and of macromolecules in the inter- and intracellular fluids, and the effects of cuff compression.[16] The zero on the vertical scale(Fig. 7, left) represents the calibrated instrumental zero of our instrument. The offset between the perfusion readings during occlusion and the calibrated zero of LCI represents the perfusion signal corresponding to the biological zero for an optical path length difference of 1.7 mm. The lowest value recorded with LCI during occlusion is relatively higher compared to PF5000. With an optical path length difference of 1.7 mm, perfusion from superficial layers is only measured. Due to the smaller and more shallow measurement volume in LCI for an OPL of 1.7 mm, the maximum perfusion within the probed volume is smaller, since fewer vessels are probed. Hence, the maximum perfusion value is relatively lower, which makes the minimum perfusion value during occlusion relatively larger.

4. CONCLUSIONS

We have developed an improved method to determine path length distributions of multiple scattered light in static and dynamic turbid media using phase modulated coherence gated interferometry. We have shown that path length-resolved dynamic light scattering can measure the dynamic properties of a medium independent of its optical absorption properties, at least when absorption levels are applied in the range found for biological tissues. Furthermore, we show that our method enables optical Doppler or dynamic light scattering measurements of dynamic media embedded in a static medium, with suppressed dependence of the effect of the scattering coefficient of the static matrix in which the moving particles are embedded. We show the first results on path-length resolved laser Doppler perfusion measurements in skin. Optical path length distributions of multiply scattered Doppler shifted and unshifted light, spanning a range of 0 to 5 mm, have been measured. For a given optical path length of 1.7 mm, perfusion was measured in real time before, during, and after an occlusion of the upper arm and the results showed correlation with the perfusion signal measured using a conventional LDPM.

In general, the path-length-resolved perfusion measurements presented here will overcome the influence of photon path lengths on the measured perfusion signal, and make it possible to perform depth-resolved perfusion measurements. Also, our method allows us to discriminate between the Doppler-shifted and nonshifted fraction of photons in the detected photodetector signal. This ability of our technique is an important condition for absolute perfusion measurements. The differences in the perfusion signal when different tissue types are compared must partly be explained from the difference in tissue optical properties rather than real perfusion differences. Path length resolved optical Doppler perfusion monitoring, of which the basic technique is presented in this work, may overcome this limitation and enable to measure blood perfusion in tissue with suppression of the confounding influence of optical properties in the tissue matrix.

ACKNOWLEDGEMENTS

This work was sponsored by the Netherlands Technology Foundation STW (Grant TTF 5840) and the Institute for Biomedical Technology of the University of Twente. Perimed AB, Stockholm, Sweden is acknowledged for providing instrumentation.

REFERENCES

[1] A. P. Shepherd and P. Å. Öberg, *Laser-Doppler Blood Flowmetry* (Kluwer Academic, Boston, 1990).

[2] B.Chance, J.S.Leigh, H.Miyake, D.S.Smith, S.Nioka, R.Greenfeld, M.Finander, K.Kaufmann, W.Levy, M.Young, P.Cohen, H.Yoshioka, and R.Boretsky, "Comparison of Time-Resolved and -Unresolved Measurements of Deoxyhemoglobin in Brain", Proc.Natl. Acad.Sci., 85, 4971-4975(1988).

[3] E.Gratton and M.Limkerman, "A continuously variable frequency cross-correlation phase fluorometer with picosecond resolution", Biophys. J, 44, 315-324 (1983).

[4] A.Wax, C.Yang, R.R. Dasari, and M.S. Feld, "Path-length-resolved dynamic light scattering: modeling the transition from single to diffusive scattering", Applied Optics, 40, 4222-4227 (2001).

[5] G. Popescu, A. Dogariu, "Optical path-length spectroscopy of wave propagation in random media", Opt. Lett. 24(1999).

[6] K.K. Bizheva, A.M. Siegel, and David A. Boas, "Path-length-resolved dynamic light scattering in highly scattering random media: The transition to diffusing wave spectroscopy", Physical Review E, 58(1998).

[7] A.L.Petoukhova, W.Steenbergen, and F.F.M.de Mul, "Path-length distribution and path-length resolved Doppler measurements of multiply scattered photons by use of low-coherence interferometer", Opt.Lett.26, 1492-1494(2001).

[8] A.L.Petoukhova, W. Steenbergen, T.G. van Leeuwen and F. F. M. de Mul, "Effects of absorption on coherence domain path length resolved dynamic light scattering in the diffuse regime", Applied Physics Letters 81, 595-597(2002).

[9] B. Varghese, V. Rajan, T. G. van Leeuwen and W. Steenbergen, "Path length resolved measurements of multiple scattered photons in static and dynamic turbid media using phase modulated low coherence Interferometry," Journal of Biomedical Optics, 12 (2), 024020 (2007).
[10] B. Varghese, V. Rajan, T. G. van Leeuwen and W. Steenbergen, "Quantification of Optical Doppler broadening and optical path lengths of multiply scattered light with phase modulated low coherence interferometry," Optics Express, 15 (15), 9157-9165 (2007).
[11] B. Varghese, V. Rajan, T. G. van Leeuwen and W. Steenbergen, "Discrimination between Doppler-shifted and non-shifted light in coherence domain path length resolved measurements of multiply scattered light," Optics Express, 15 (20), 13340-13350 (2007).
[12] B. Varghese, V. Rajan, T. G. van Leeuwen and W. Steenbergen, "Evaluation of a multimode fiber optic low coherence interferometer for path length resolved Doppler measurements of diffuse light," Review of Scientific Instruments, 78(12):126103 (2007).
[13] B. Varghese, V. Rajan, T. G. van Leeuwen and W. Steenbergen, "High angle phase modulated low coherence interferometry for path length resolved Doppler measurements of multiply scattered light," Optics Communications, 281(3),494-498 (2008).
[14] B. Varghese, V. Rajan, T. G. van Leeuwen and W. Steenbergen, "Path length resolved optical Doppler perfusion monitoring," Journal of Biomedical Optics Letters, 12(6):060508 (2007).
[15] G.E.Nilsson, "Signal processor for laser Doppler tissue flowmeters, Med. Biol.Eng. comput, 22, 343-348(1984).
[16] S. T. Flock, S. L. Jacques, B. C. Wilson, W. M. Star, and M. J. C. van Gemert, "Optical properties of intralipid: a phantom medium for light propagation studies," Lasers Surgery Med. 12, 510-519 (1992).