Improving the clinical applicability of laser Doppler perfusion monitoring

Morales, Fernando

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2005

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Laser Doppler perfusion monitoring (LDPM) is a well known optical technique that can be used for assessing the microvascular function of the skin in a continuous and non-invasive way. Because several vascular diseases cause impairment of microcirculation, LDPM has become an interesting tool in vascular research. After two decades, however, LDPM still exhibits some technical shortcomings that limit its use in daily clinical practice.

This thesis presents results of a study that was performed within the framework of a European project (SMT4-CT97-2148) aiming at the standardisation of laser Doppler flowmetry instrumentation and improving the clinical applicability of the LDPM technique. Within the European consortium, various LDPM studies were designed to evaluate the influence of different LDPM probes and devices in a clinical setting. Furthermore, a novel method to analyse the LDPM signal was developed that can be helpful for clinical evaluation of patients.

In Chapter 2, we aimed to investigate the influence of fibre separation on clinical LDPM measurements. For this, a dual-channel LDPM system was used in combination with a probe that consists of two sets of detection fibres, at 0.2 mm and 1.0 mm from the illuminating fibre. Measurements were performed at the big toe of 8 healthy subjects and 11 subjects who had vascular disorders. In most cases, fluxes detected at both fibre distances showed very similar fluctuations. For each fibre separation, flux values of healthy and patients subjects were not significantly different. Furthermore, skin temperature (22-34 °C) influenced the toe’s pulp microcirculation markedly, increasing similarly at both probe separations, with higher flux at 1.0 mm than at 0.2 mm separation. The fibre flux ratio signal, obtained by dividing the flux at 0.2 mm by the flux at 1.0 mm, was significantly different between the two groups (p < 0.05). In conclusion, the flux detected in vivo by means of LDPM, is influenced by the distance between the optical fibres. Use of the flux ratio with a multiseparation probe deserves attention as it is a possible marker to discriminate normal tissue perfusion from pathological skin tissue perfusion, independently from tissue temperature.

The standardisation of manoeuvres to perform clinically discriminative microvascular flow-reserve tests is still poorly developed, as well as the response analysis. In Chapter 3 we aimed to establish a reproducible analysis method for the post-occlusive reactive hyperaemia (PORH) test measured using laser Doppler perfusion monitoring (LDPM). LDPM data were measured from the PORH response of 24 Fontaine class II-III peripheral atherosclerotic/arterial obstructive disease (PAOD) patients and 30 healthy subjects. The PORH response was recorded from the dorsum of the foot after 3 minutes of arterial occlusion at the thigh. The resulting tracings were
analysed by describing their morphology through five defined parameters: resting flux (RF), time to RF level (t_{RF}), maximum flux (MF) during reactive hyperaemia, time to maximum flux (t_{MF}), and time to half recovery (t_{HR}). While the time parameters were discriminative between patients and controls, flux parameters were not. The time to resting flux (t_{RF}) led to the most discriminative model that correctly predicted 88.5% of the cases. Hence, we concluded that obtaining t_{RF} with the presented procedures is a promising approach for evaluating patients’ microvascular function by using the PORH test.

Another current limitation of the LDPM technique is the different signal output between monitors. Hence, in Chapter 4 we evaluated the flux signals of two different commercial laser Doppler perfusion monitors in a clinical application. The flux signals and response times from a post-occlusive reactive hyperaemia manoeuvre were studied from two foot locations of subjects representing a broad range of perfusion conditions. Two multi-channel perfusion monitors were used simultaneously to assess the skin blood perfusion at the dorsum of the foot and at the pulp of the hallux by means of two multifibre probes. Measurements were performed on thirty subjects from three groups: ten patients with peripheral arterial obstructive disease, ten patients with diabetes mellitus and ten healthy controls. Resting and maximum fluxes were studied as well as three characteristic time parameters from the hyperaemic response. In both foot locations, the two monitors assessed the same perfusion variations, but delivered different flux values for the various fibre distances. Moreover, no differences in flux values were found between the patient and control groups. The time parameters at each foot location were practically the same for both instruments at each of the fibres. For each monitor, the time to resting flux after detection of reflux after occlusion release, t_{RF}, when obtained at the dorsum of the foot, was significantly different between the controls and PAOD patients. Of all investigated variables, the response times to the reactive hyperaemia had the largest discriminating value between PAOD patients and controls, and were similar for both laser Doppler perfusion monitors. In addition, relative flux values had similar values in many cases. Other flux results from different monitors or fibre separations needed correction to allow comparison.

To facilitate the quantitative analysis of Post Occlusive Reactive Hyperae-mia (PORH), measured with Laser Doppler Perfusion Monitoring (LDPM) on extremities, we presented in Chapter 5 a flow model for the dynamics of the perfusion of the tissue during PORH, based on three parameters: two time constants ($\tau_1$ and $\tau_2$) and the ratio of the maximum flux and the resting flux. With these three constants, a quantitative comparison between experiments is possible, and we propose to standardise this procedure for
the PORH test accordingly. For this reason, we also developed a computer program that determines the constants after performing a fit of the model to the measured data.

Laser Doppler flux signals show temporal fluctuations caused by physiological phenomena like heartbeat, respiration, and local tissue flow motion. In Chapter 6, we investigated in the PORH signal whether the laser Doppler fluctuations caused by the heartbeat contain clinically useful information. The dependence of these fluctuations on monitor type, fibre arrangement and probe location was also addressed. By using two perfusion monitors and two probes at the skin with different fibre arrangement, the flux signals during an occlusion test were analysed in subjects suffering from Fontaine class II-III peripheral arterial obstructive disease (PAOD) and patients with diabetes mellitus, and compared with those of healthy subjects. The flux signals were filtered with a band-pass filter between 0.5 and 3 Hz followed by root mean square processing and averaging over 4 seconds. The processed flux signals resembled the original tracing. The ratio between these signals, referred to as pulsatility, was shown to be significantly smaller in patients with PAOD (p < 0.05) on all channels at the dorsum of the foot, and for one of the fibre distances at the toe. For each probe, the pulsatility almost had the same value for the results for all detection fibres and instruments. Pulsatility during the hyperaemia peak showed a maximum value of ~0.3. From this study it is concluded that the laser Doppler fluctuations caused by the heartbeat contain clinically useful information.

This thesis focussed on the standardisation of LDPM in a clinical setting using the post occlusive reactive hyperaemia test. In our studies, we mainly investigated healthy subjects and patients with low to mild symptoms of peripheral arterial obstructive disease using various LDPM monitors and multi-fibre probes simultaneously. Clinical discrimination was achieved with the time parameters, flux ratio, and the pulsatility. It is concluded that our studies may contributed to improve the clinical applicability of LDPM.