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**NOTE**

# Monitoring cerebral perfusion using near-infrared spectroscopy and laser Doppler flowmetry

**J H G M Klaessens[1], R G M Kolkman[3], J C W Hopman[1], E Hondebrink[3], K D Liem[2], W Steenbergen[3], F F M de Mul[3] and J M Thijssen[1]**

[1] Clinical Physics Laboratory, University Children's Hospital Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands
[2] Department of Neonatology, University Children's Hospital Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands
[3] Biophysical Techniques Group, University of Twente, Faculty of Science and Technology, PO Box 217, 7500 AE Enschede, The Netherlands

E-mail: j.klaessens@cukz.umcn.nl

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**Abstract**

This paper describes the simultaneous use of two, noninvasive, near-infrared techniques near-infrared spectroscopy (NIRS) and a continuous wave NIR laser Doppler flow system (LDF) to measure changes in the blood oxygenation, blood concentration and blood flow velocity in the brain. A piglet was used as animal model. A controlled change in the arterial $CO_2$ pressure ($PaCO_2$) was applied for achieving changes in the listed cerebrovascular parameters. The time courses of blood concentration parameters (NIRS) and RMS blood flow velocity (LDF) were found to correspond closely with those of carotid blood flow and arterial carbon dioxide pressure ($PaCO_2$). This result shows the additional value of LDF when combined with NIRS, preferably in one instrument. Development of pulsed LDF for regional blood flow measurement is indicated.

Keywords: cerebral perfusion, hypercapnia, laser Doppler, near infrared spectroscopy, NIRS, pig

## 1. Introduction

Many children are born prematurely, i.e. after a pregnancy of 37 weeks or shorter. Those who survive have a high risk of developing a handicap, varying from a severe psychomotor disturbance (e.g. cerebral palsy) to educational and behavioural problems during adolescence.

  

This is most likely caused by cerebral damage due to hemorrhage or to hypoxic-ischemic injury related to perturbation of cerebral hemodynamics and/or oxygenation in the perinatal period (from birth at about 22 weeks of pregnancy until the first 28 days after delivery).

Local monitoring of cerebral perfusion, oxygenation and blood volume may provide important information for preventive treatment of those children. The same holds for the detection of non-optimally perfused brain tissue in full-term or near-term neonates at risk (e.g. those born asphyxiated).

Monitoring of *changes* in oxygenation and total blood concentration is possible using near-infrared spectroscopy (NIRS) (Jobsis 1977). Information about rms velocity of red blood cells and blood concentration can be obtained using laser Doppler flowmetry (LDF) (Stern 1975).

In this paper the possibility of combining the results of NIRS and LDF measurements while measuring changes in cerebral perfusion is examined. NIRS has proven to be a useful clinical tool for noninvasive, continuous, bed-side monitoring of brain oxygenation and hemodynamics (Liem *et al* 1997, Meek *et al* 1999, Wyatt 1993). LDF has proven to be a useful clinical tool for noninvasive monitoring of microcirculation in tissue (Sheperd and Öberg 1990).

Cerebrovascular reactivity caused by carbon dioxide changes in the inspired air was investigated with NIRS in several piglet studies (Benni *et al* 1998, Liem *et al* 1995), in lamb (Shadid *et al* 1999), and in clinical cerebral perfusion studies (Wyatt *et al* 1991). Increase in $CO_2$ will give vasodilatation which causes increase in the blood flow. In these studies NIRS has proven to be an adequate tool to qualify the effects of hypercapnia on cerebral oxygenation and hemodynamics.

## 2. Materials and methods

The measurements were carried out on the brain of a piglet. The Ethical Committee on Animal Research of the University of Nijmegen approved the experiments described in this work.

The preparation of the piglet was started with light anesthesia (intra-muscular midazolam, 1.5 mg $kg^{-1}$; intra-muscular ketamine, 20 mg $kg^{-1}$ and intra-venous atropine, 0.05 mg $kg^{-1}$). After orotracheal intubation, the animal was ventilated with a mixture of 30% oxygen, 67% nitrous oxide and 3% isoflurane (ventilator: Modulus II plus, Datex-Ohmeda BV, Hoevelaken, The Netherlands) The time courses of the $O_2$ and $CO_2$ levels in the respiration gasses (i.e. $O_2$ and $CO_2$ wave) were obtained from a standard monitor (Datex-Capnomac Ultima, Datex-Ohmeda BV, Hoevelaken, The Netherlands) by collecting samples from the respiratory tubing.

A major vein of the left ear was cannulated for the administration of glucose 5% at a rate of 1.0 ml $kg^{-1}$ $h^{-1}$ and of medication (Pancuronium 0.15 mg $kg^{-1}$ $h^{-1}$).

A polyvinyl catheter (diam. 2.1 mm) was placed in the abdominal aorta through the left femoral artery for measuring the arterial blood pressure (disposable transducers: Edwards Life Science BV, Los Angeles, CA, USA) and for arterial blood gas sampling.

A second polyvinyl catheter (diam. 2.1 mm) was introduced in the left femoral vein and the tip was placed in the inferior caval vein for measuring the venous blood pressure (disposable transducers: Edwards Life Science BV, Los Angeles, CA, USA).

After exposing the left carotid artery, an appropriately sized perivascular transit-time ultrasonic blood flow transducer (Transonic System Inc., Ithaka, NY, USA) was fitted around this vessel for measuring the carotid arterial blood flow ($Q_{car}$).

For monitoring the condition of the animal physiological data (ECG, arterial and venous blood pressure, arterial oxygen saturation ($SaO_2$); respiratory $O_2$-wave and $CO_2$-wave)

were measured and continuously recorded with a computer system and stored for further analysis.

The NIRS instrument used in the experiments was developed and built at the Instrumentation Department of the University Medical Centre, Nijmegen, The Netherlands (Klaessens *et al* 2003, van der Sluijs *et al* 1997). The equipment contains three laser diodes (767, 850, 905 nm) operated in pulsed mode (100 ns) at 1 kHz per wavelength and the receiving signals are averaged over 100 pulses resulting in an effective 10 Hz sampling. The light is coupled into an optical fiber and is transmitted through the skull and is received by a photodiode. When using the modified Lambert Beer law,the absolute change in hemoglobin concentrations: $\Delta cO_2Hb$, $\Delta cHHb$, $\Delta ctHb$ can be calculated from the optical density data (Delpy *et al* 1988). In this paper the modified 'Keele' matrix (Wickramasinghe and Rolf 1993) was used. The custom-built LDF instrument contains a continuous wave single-mode laser-diode at $\lambda = 783$ nm (DL-8032–001, Sanyo Inc.). The light of the laser-diode was coupled into an optical fiber (step index NA $= 0.23$, core diameter 400 $\mu$m). Scattered light was probed using the same type of fiber. Light transmitted through this detection fiber was detected by a photodiode (HFD3022–002, Honeywell). The output of this photodiode was sampled for 0.96 s with a frequency of 50 kHz. During this time 48 000 samples were acquired. This time trace was then divided into 32 time windows of 1500 samples each. From all these 32 time windows the power spectra were calculated, which then were averaged. These power spectra ranged from 0 to 25 kHz, with a frequency-resolution of 33.3 Hz.

The weighted first moment of the power spectrum was calculated using a high pass cut-off frequency of 66.6 Hz, excluding the influence of low speed tissue motion (e.g. due to breathing). The low pass filter was set at 25 kHz. The moment was normalized by the square of the signal off-set in the time domain ($DC^2$) to automatically correct for fluctuations in laser power. According to the literature (Bonner and Nossal 1981), the weighted first moment is proportional to the root-mean-square (rms) red blood cell velocity.

By alternately switching the laser in the NIRS and the LDF instrument on and off for 1 s, cross talk between the instruments was avoided. The LDF instrument acted as master during the experiment, generating an enable/disable square wave with a frequency of 0.5 Hz.

The distance between source and detector fibers of the NIRS instrument was about 4 cm, resulting in a penetration depth of the light of about 1.5 cm (Klaessens *et al* 2003). The separation of the LDF fibers was 4 mm. For this separation the penetration depth was assumed to be a few mm.

The LDF fibers were directly placed on the dura to avoid any influence of absorption in the skull. This is done to mimic the clinical situation of newborns with a fontanel. It was achieved by drilling holes in the skull, through which the fibers could be inserted. The fibers were glued to the skull to ensure a firm fixation during the measurements. The NIRS fibers were glued on the skin, thus measuring through the skin and the skull (Liem *et al* 1992). The hypercapnia was induced by increasing the $CO_2$ fraction in the inspired respiration air. The end-tidal $CO_2$ percentage was in normocapnic state 5%, in mild hypercapnia 8–9% and in severe hypercapnia 12%.

## 3. Results

The changes in the physiological variables due to hypercapnia were:

- During hypercapnia the heart rate (HR) increased: in severe hypercapnic state the HR increased up to 50%. But after returning to normocapnia the HR returned to the normal level.

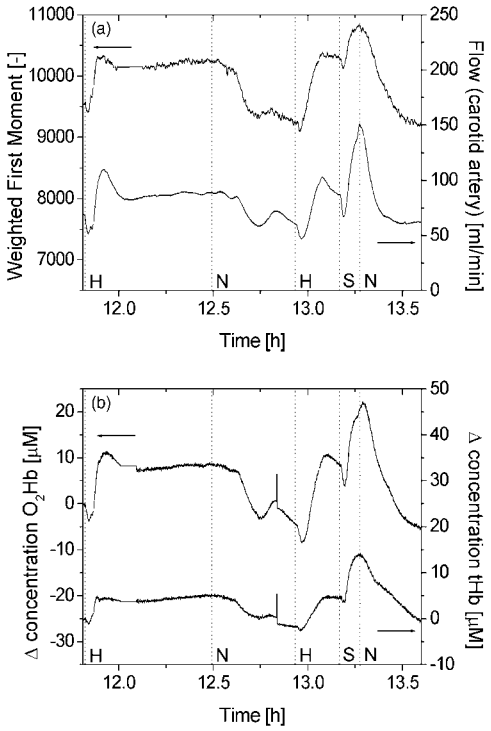


**Figure 1.** Time traces of the LDF (a) and NIRS (b) measurements, while monitoring changes in cerebral perfusion. H, S and N indicate the starting of a mild hypercapnia, severe hypercapnia and the return to normocapnia respectively. The weighted first moment was derived from the LDF data and indicates the rms velocity of the red blood cells. The flow in the carotid artery (ml $min^{-1}$) was measured using an ultrasound flow probe. Changes in oxy-hemoglobin ($O_2Hb$) and total hemoglobin (tHb) concentration were estimated using NIRS. The tHb curve was shifted over 25 $\mu$M for clarity.

- The mean arterial blood pressure (MABP) rose from 60 to 70 mmHg. After returning from severe hypercapnia to normocapnia the MABP sometimes went up transiently to higher values (90 mmHg) before returning to normal state.
- The $SaO_2$ remained constant (98 $\pm$ 1%) during the whole experiment.

An example of time traces obtained with NIRS, LDF $Q_{car}$ is shown in figure 1. The weighted first moment, measured with LDF (figure 1(a)), shows an increase during hypercapnia, indicating an increase in rms velocity of the red blood cells. NIRS (figure 1(b)) shows an increase in oxy- and total hemoglobin concentrations ($O_2Hb$ and tHb) during hypercapnia. These observations both agree with the measured increase of flow through the carotid artery ($Q_{car}$), as measured with the ultrasound flow probe, and they reflect the cerebral hyper-perfusion.

As the LDF weighted first-order moment of the power spectral density is proportional to the rms of the red blood cell velocity, a linear relationship with $Q_{car}$ might be expected. It can be observed in figure 2 that this linearity was found when plotting the relative change of RMS blood flow velocity vs carotid flow (range 60–90 ml $min^{-1}$). At higher carotid flows the RMS velocity becomes saturated. This observation is consistent with figure 1 where the increase of $Q_{car}$ going from normocapnia (N) to mild hypercapnia (H) practically equals that from H

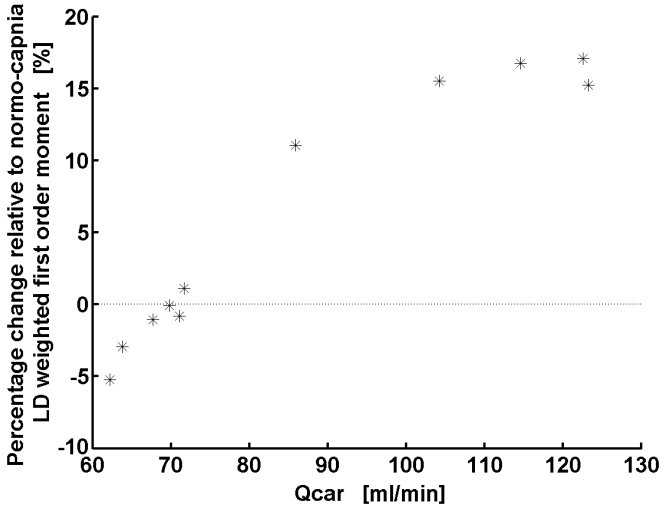


**Figure 2.** Percentage change in LDF weighted first moment (rms red blood cell velocity) as a function of the carotid flow ($Q_{\mathrm{car}}$).

to severe hypercapnia (S), whereas this equality of steps does not hold for the weighted first moment. In the latter case, the second step is much smaller than the first one.

## 4. Conclusions and discussion

The NIR techniques used in this paper, i.e. spectroscopy and laser Doppler flowmetry, are measuring complementary physiological features, i.e. blood oxygenation and concentration (NIRS) and blood flow velocity (LDF). The effective measurement volume can be approximated by a 'banana' shaped volume between the positions of the optodes, for both techniques. A possible explanation for the apparent 'saturation' effect of the RMS blood flow velocity (figure 2) might be the superficial measured volume of LDF. LDF measures flow in the arterioles and microvasculature; the velocity in these small vessels may vary over a limited range. Above that range, further increase in flow will be reached by recruitment of more arterioles. This option will yield a limited potential for an increase in velocity and we might expect to see at high flows a lag in velocity which becomes visible as a saturation in figure 2. When the LDF could be improved towards larger fiber separations by using pulsed wave techniques (Kolkman *et al* 2001) allowing for a larger penetration depth, integration of the techniques into a single instrument would become feasible. The effect of the larger fiber separations on laser Doppler flow measurements has been studied by Watanabe and Okada (2003) in Monte Carlo simulations. These authors concluded, among other things, that the influence of the depth of perfusion on the Doppler spectrum is different for large optode separations as compared to small separations. So further, preferably experimental, studies are indicated for optimizing the design of a pulsed laser Doppler flow meter system.

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