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A laser Doppler system for monitoring of intracerebral microcirculation

Peter Rejmstad, Gustav Åkesson, Jan Hillman, and Karin Wårdell

***Abstract* - A two-channel standard laser Doppler perfusion monitor has been adapted for intracerebral measurements. Software developed in Labview makes it possible to present the microvascular perfusion, total light intensity (TLI), heart rate and trend curves in real-time during surgery. A custom-made optical probe was designed in order to enable easy fixation during brain surgery. The constructed brain probe was evaluated and compared to a standard probe. Both probes presented similar feasibility when used for the skin recordings. In addition, evaluation was done in one patient in relation to tumor resection. Stable perfusion and TLI signals were immediately recorded when the probe was positioned in cerebral tissue. Movement artifacts were clearly seen when the probe was moved to a new site. Recordings in cortex and tumor border showed higher perfusion and lower TLI compared to measurements in subcortical white matter. The calculated heart rate estimate agreed well with the noted value from the electrocardiographic patient monitoring system.**

I. Introduction

Laser Doppler perfusion imaging (LDPI) and monitoring (LDPM) are optical methods for microvascular studies [1]. Since the 1980s, the laser Doppler technique has been used in a wide range of applications including assessment of skin reactions [2], [3], intra-operative monitoring of myocardial blood perfusion in relation to bypass surgery [4], and recently also for intra-operative measurements of microcirculation in relation to aneurismal subarachnoid haemorrhage [5] and deep brain stimulation (DBS) implantation [6]. During the last decades the interest for optical brain monitoring and imaging has increased [7]. A majority of the scientific investigations are, however, related to animal studies. Very few of the new optical techniques have been adapted for clinical use i.e. during neurosurgery and neurointensive care. This paper presents an LDPM system modified for measurements in cerebral tissue.

Cerebral blood flow (CBF) is a parameter of the outmost importance in the neurointensive care setting. CT scanners with inert xenon gas inhalation (Xe-CT) as a blood flow tracer [8] is the first blood flow method available for bedside use in critically ill, unstable patients that cannot be transported out of the intensive care unit environment.

However, the method only provides repetitive, "snap-shot"-like CBF information. Reliable online bedside monitoring of cerebral blood flow is still not available although this problem has been addressed using thermodilution probes in the jugular bulb to estimate global cerebral blood flow [9]. In clinical routine more robust and stable methods must be sought for continuous assessment of CBF. A possible solution for this monitoring problem would be to use optical methods. In this setting LDPM may be a suitable technique, however, still not adapted to this task. In this study, the first step towards such a system is presented. The aim of this paper is to adapt and evaluate a LDPM system suitable for bedside monitoring and to evaluate the principle feature both experimentally, on skin tissue, and clinically during open brain surgery.

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P. Rejmstad and K. Wårdell at the Department of Biomedical Engineering, Linköping University, Sweden, (phone: +46-10-103-7704; e-mail: peter.rejmstad@liu.se).

G. Åkesson and J. Hillman at the Department of Neurosurgery, Linköping University Hospital, Sweden.

II. Methodology

A. Laser Doppler system for intracerebral measurements

The system for intracerebral measurement of microvascular perfusion comprises a two channel laser Doppler perfusion monitor (Periflux 5000, Perimed AB, Sweden), a specially designed optical probe and a personal computer (Dell Latitude EP5420) with a data acquisition card (DAQ Card 6024E, National Instruments) and software (Labview 2010, National Instruments Inc., USA). A schematic overview of the system is presented in Fig. 1a-b.

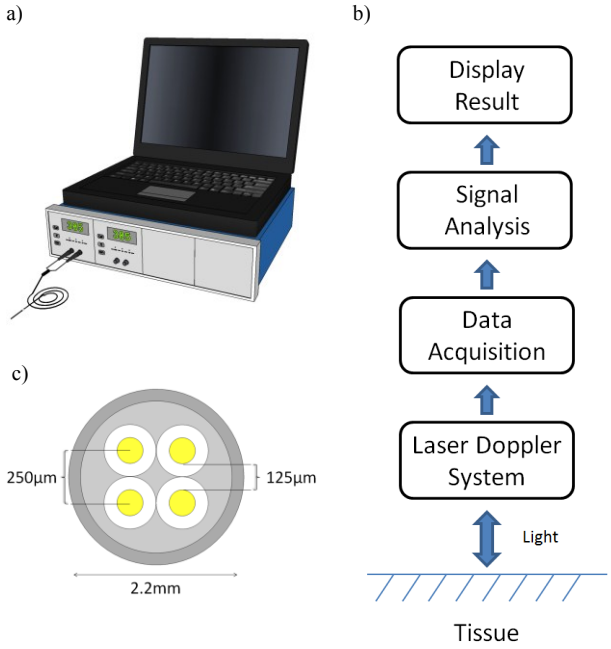

Figure 1. a) Model of the measurement system, b) Overview of the process steps, c) Schematic of the probe tip with dimensions and fiber separation.

The measurement probe (Fig. 1c) is designed in order to be flexible during insertion in the area of study. Four optical fibers ($\varnothing_{core}$ = 125 μm, $\varnothing_{core+cladding}$ = 140 μm, $\varnothing_{total}$ = 250 μm, numerical aperture = 0.37) are aligned along the interior side of the probe ($\varnothing$ = 2.2 mm) towards the tip. Two of the fibers are used for laser Doppler recordings and the two additional fibers can be used for e.g. reflectance spectroscopy registration. In order to minimize tissue trauma during probe insertion but still keep the optical fibers intact, the probe tip is smoothly rounded and the fiber tips carefully polished. To keep the measurement equipment on a safe distance from the operation area, an optical cable length of at least 4 m is used. With the used construction the probe and cable were possible to sterilize according to the STERRAD® [10] protocol.

With the described probe design one of the fibers delivers laser light (1mW, λ = 780 nm) towards the tissue and after interaction with the moving red blood cells and static tissue, a fraction of the light is backscattered to a receiving fiber connected to the detector unit in the Periflux. Two signals are extracted: the TLI corresponding to the DC-part of the signal and the stochastic fluctuating photo detector signal which is further processed to the perfusion signal. For details regarding signal processing see Nilsson et al. [1]. During intracerebral measurements, the TLI signal represents the tissue's reflectivity which is related to tissue type whereas the perfusion is related to relative changes in the tissue's microcirculation. For all measurements, the sampling frequency (f_s) was set to 100 Hz and the time constant on the Periflux system (τ) to 0.03 s.

B. Software

The software, developed in Labview 2010 makes it possible to sample, store and present two channels of both perfusion and TLI signals in real-time as well as to perform online-processing and analysis of captured signals. The total range of the perfusion and TLI signals are presented as 0 - 999 arbitrary units (a.u.) and 0 – 10.0 a.u. The software is designed with three modes consisting of; View, Record and Analyze. These modes cover features such as presentation of TLI and perfusion, trend curves with signal averages of 10, 20, 30 or 60 s intervals and online heart rate (HR) estimation. Two different functions are used to estimate the heart rate by either; peak finding or spectral component analysis of low frequencies. Prior to heart rate estimation the signals are low-pass filtered to get rid of high frequency noise and in the spectral analysis case the signal is run through a Hanning window to reduce leakage.

C. Evaluation

The system performance was evaluated in two ways: during experimental skin measurements and intra-operatively on a patient prepared for tumor resection. Before the measurements, the system was calibrated with the brain probe in Motility Standard (Perimed AB, Sweden) and thus the perfusion values set to 250 a.u. This resulted in a TLI of 0.96 and 0.83 a.u. for channel one and two respectively. The corresponding values for the standard probe (PF408) used as reference during the measurements were 1.80 and 1.58 a.u.

1) Skin measurements

Recordings were performed on finger tips and forearm while the following was investigated; sensitivity to movement artifacts and hemodynamic response by performing two experiments with occlusion and skin provocation. During the occlusion study, the brain probe was connected to channel one and positioned on the left hands index-fingertip. The standard probe was connected to the second channel and positioned on the middle finger. Simultaneous recordings were done before, during and after occlusion of the brachial artery with a blood pressure cuff. The occlusion lasted for at least 90 s. Secondly a provocation measurement was done on the ventral forearm. During this measurement session the skin in the vicinity to the probe was mechanically provoked with a blunt instrument in order to induce an axon reflex [2] and thus increase the perfusion.

2) Intraoperative cerebral measurements

The clinical measurements were approved by the local ethics committee (M182-04, 2010/359-32) and written consent was received from the patient. During surgery, in relation to preparation for tumor resection, the probe was inserted in the cortex and manually moved to positions in the vicinity of the tumor before it was fixated by a suture in subcortical white matter. The TLI and perfusion signals were recorded 30-70 s at four positions before a 15 min. long recording was done in subcortical white matter. Notes were taken of the heart rate as recorded with the patient monitoring system for each new measurement position.

III. RESULTS

Skin measurements

The skin measurements showed that the probe had similar characteristics as the standard probe. Occlusion curves from the two probes are presented in Fig. 2. During normal blood flow, the curves followed each other. However, during the reactive hyperemia the waveform amplitude differed between the probes due to the spatial variability in the underlying vessel structure [11]. The mechanical provocation resulted in temporary elevated perfusion, which leveled out to baseline after approximately 3 minutes as seen in Fig. 3. However the prominent increase in perfusion seen as a peak during the provocation (values between the green and red vertical lines) in Fig. 3 is a result of movement artifacts occurring when the mechanical skin provocation is taking place and should thereby be discarded when looking for physiological hemodynamic changes in the perfusion signal.

The skin measurements were somewhat affected by movement artifacts during the experiments due to arm movements and small amount of shaking during handheld probe measuring.

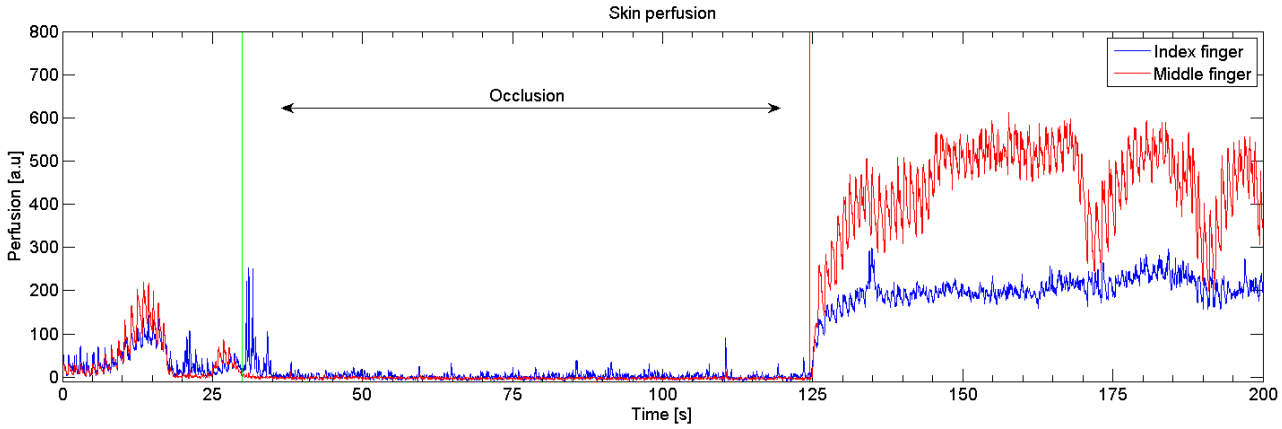

Figure 2. Occlusion experiment with two-channel recording on fingertips using two different probes. Blue line: index finger (brain probe, channel one), Red line: middle finger (standard probe, channel two).

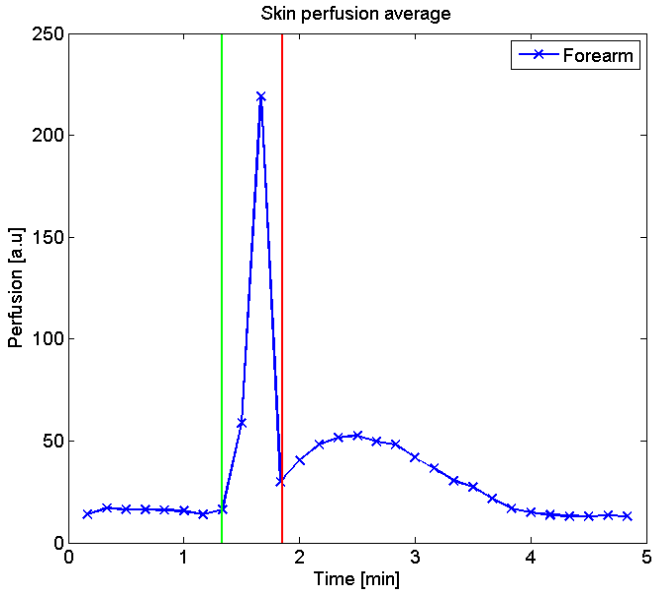

Figure 3. Skin provocation response where each discrete value corresponds to the perfusion average over 10 s. Provocation (between green and red vertical lines) with a blunt instrument followed by a physiological increase of microvascular blood flow.

Intraoperative cerebral measurements

Stable perfusion and TLI signals were immediately recorded when the probe was positioned at a cerebral tissue site. Movement artifacts were seen in the perfusion signal when the probe was moved from one site to another. Fig. 4 presents examples of recorded perfusion and TLI signals at different sites. The TLI was lower and the perfusion higher in cortical and suspected tumor tissue compared to subcortical white matter. When the probe was positioned and fixated in white matter, the 15 min. recording presented a stable signal. The calculated heart rate estimate agreed well with the monitored electrocardiographic signal.

IV. Discussion and Conclusions

A laser Doppler system adapted for intracerebral measurements has been presented. It is configured around a two-channel standard laser Doppler perfusion monitor. Software developed in Labview makes it possible to present both the perfusion and TLI signals in real-time during surgery and as trend curves. The constructed brain probe was evaluated and compared to a standard probe. Both probes presented the same feasibility when used for the skin recordings. It was, however, easier to fixate the brain probe in the cerebral tissue, which was manifested in a stable signal as long as the tissue was not interfered by movement artifacts introduced by the surgeons preparation. When considering monitoring during hours or even days, as in the neurointensive care, the microvascular perfusion and TLI trends would be of more interest. For such presentations it is important to take movement artifacts into consideration by e.g. automatic detection and removal before trend curve calculations are done. These trend curves may become a useful new tool in the neurointensive care unit in order to detect physiological processes such as vasospasm related to secondary insults at an early stage.

It must be noted that as this was a re-operation, there may be scarred tissue and thus not clear distinctions between tissue types at the various sites. Nevertheless, the measurements at the different sites showed clear variation in TLI-signal when moving from assumed cortical to subcortical white matter. This is in agreement with previous studies where diffuse reflectance spectroscopy [12], [13] and LDPM [6] has been used for measurements along the precalculated trajectory in relation to DBS implantation. Similarly the microvascular perfusion was higher in assumed cortical and tumor tissue compared to white matter. Further evaluation is, however, necessary before the technique can be applied for monitoring in the neurointensive care. Such evaluation could for instance include two point/channel measurements over longer time

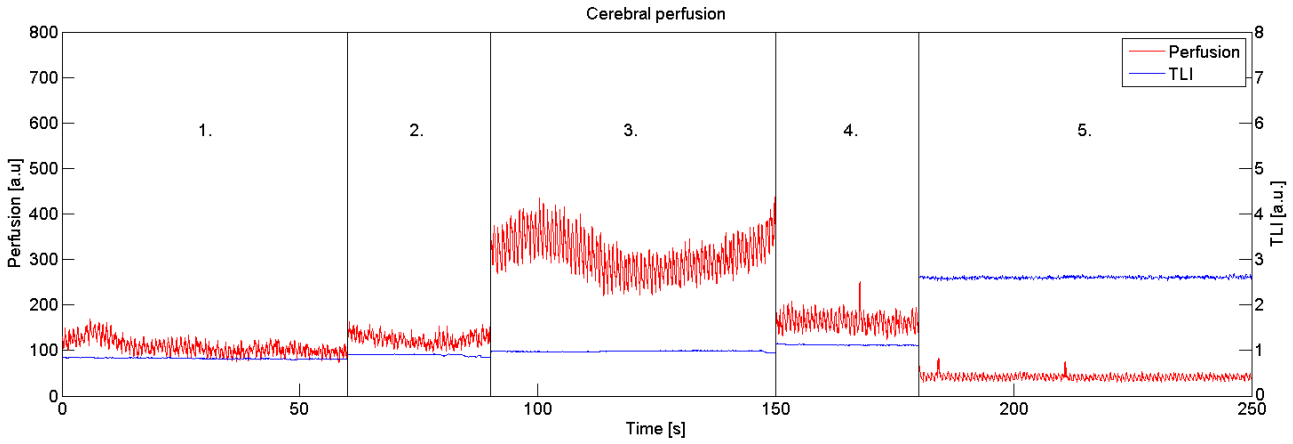

Figure 4. Cerebral perfusion and TLI signals during tumor resection at different sites, 1: gray suspected tumor scar tissue (60 s, HR=69), 2: gray suspected tumor tissue (30 s, HR=74), 3: gray superficial tumor suspected tissue (60 s, HR=70), 4: gray visually tumor-free tissue (30 s, HR=72), 5: white tumor-free tissue (70 s, HR=71).

periods in various tissue sites, and response to controlled change of ventilation settings.

In conclusion: a laser Doppler system was adapted for cerebral perfusion monitoring. Feasibility tests on skin tissue confirmed functionality of the system and probe prior to surgical measurement. Evaluation during surgery showed promising results with stable signals. Future studies will focus on further development of the software and user interface as well as clinical measurements and implementation in neurointensive care.

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