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New Insights in the Phenomenon of Distributed Dermal Perfusion Rhythmicity using Computer Aided Optoelectronic Sensor Measuring Strategies

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BIOGRAPHICAL NOTES

prof. Dr.-Ing. Vladimir Blazek, Dr.h.c. was born Czechoslovakia in 1945. He received his first degree in Electrical Engineering, with a specialization in Biomedical Engineering in 1969 from Technical University in Brno. Since 1971 he is with the RWTH Aachen University, Germany, and has conducted Biomedical Optics & Optical communication in teaching, research & development at the Institute of High Frequency Technology. In 1979 he received Dr.-Ing. degree in Aachen and in 1993 venia legendi at the Czech Technical University in Prague; since May 1995 he has been professor for measurements and biomedical engineering and works from this time in both partner universities in Aachen and Prague. Prof. Blazek's research interests include optoelectronics in medicine, biomedical sensors, functional optical imaging techniques and tissue optics. He is author respective co-author of more than 300 publications in books, scientific journals and conference proceedings and of 49 patents and patent registrations.

KEY WORDS

Skin perfusion, blood volume changes, optoelectronical sensors, Photoplethysmography, contactless Photoplethysmography-Imaging method, space resolved perfusion signal calculation, visualization of dermal perfusion patterns

ABSTRACT

In recent years optoelectronic sensor concepts have gained an important role in medical diagnosis because of their non-invasive nature. They are generally accepted by the patients since they don't cause pain and are devoid of harmful radiation or ionising phenomena. One method which is nowadays an accepted and widely used diagnosis technique for assessment of skin perfusion is Photoplethysmography (PPG). It assesses the optical attenuation of the skin, which is modulated by the time varying blood contents. This non-invasive technique allows acquiring functional data from the arterial and/or venous system. However the classical PPG sensors, which consist of a LED as light source and a photodiode as detector, need skin contact for the measurements and can only assess a single spot of a few square millimetres. Advancement to classical PPG is camera based Photoplethysmography-Imaging Method (PPGI), which is not only non-invasive but can assess dermal perfusion completely without skin contact and also delivers spatially resolved measurements.

INTRODUCTION

The phenomena of rhythm fluctuation of arterial blood pressure were discovered

in the 18th cen-tury. Since the first continuous recording of blood pressure, a series of investigations have been de-veloped, which deal with the problem of acquisi-tion of the rhythm fluctuation of the circulation. However, the formation of such rhythms hasn't be explained till now. A practical, noninvasive acquisition of the perfusion rhythms of skin can be realized by optoelectronic method with the help of quantitative Photoplethysmography (PPG).

A multi sensor system is introduced, which is capable of identification of rhythms from several sensors together with the acquisition of the respiration and ECG signal. The measured data can be analyzed using a high time resolution and can also be displayed in time and frequency domain.

Recently, the optoelectronics, using new camera based sensors and signal processing strategies, al-low the contactless measurement of cutaneous perfusion with spatial resolution (PPGI method). The possibilities of this concept will be explained in some examples and perfusion protocols. Actual research concentrates especially on the perfusion frequency range of about 0.1 Hz, however the assessment and interpretation of these perfusion rhythms are especially hindered by the fact that these patterns have very strong spatial variability and are highly transient.

Together with the necessary mathematical analysis tools like the Wavelet Transform, artifact reduction algorithms, advanced signal processing and visualization of virtual perfusion 2D skin im-ages a sound basis for assessment and evaluation of rhythm fluctuations in human hemodynamics is provided. Using the presented framework new, spatial resolved phenomena of high distributed blood volume movements in dermal perfusion in vivo observed by PPGI were discovered at RWTH Aachen University in the last time.

PHOTOPLETHYSMOGRAPHY: HISTORICAL NOTES AND BIOPHYSICAL FUNDAMENTALS

Apart from Doppler ultrasonography, photoplethysmography is the most popular noninvasive method for monitoring peripheral vascular hemodynamics. The history of PPG goes back to over 60 years. After ground works by Cartwright, Haxthausen, Mathes and Molitor et al., Hertzman [1] found a relationship between the intensity of backscattered polychromatic light and blood volume in the skin in 1938. His instruments consisted of three essential components still found in modern systems: a light source, a light detector and a registration unit. He called the device Photoelectric Plethysmograph and wrote about his findings ([1], p. 336): "The volume pulse of the skin as an indicator of the state of the skin circulation at rest" and "Amplitude of volume pulse as a measure of the blood supply of the skin".

The basic principle behind the measurement of blood volume changes in the skin by means of PPG is the fact that hemoglobin in the blood absorbs infrared light many times more strongly than the remaining skin tissues [2] (Fig. 1). For example as blood pressure in the skin vessels decreases, the surface area of the vessels is reduced. This increases the average reflection in the measuring window under the sensor (Fig. 2), so it will be recorded as an increase in PPG signal.

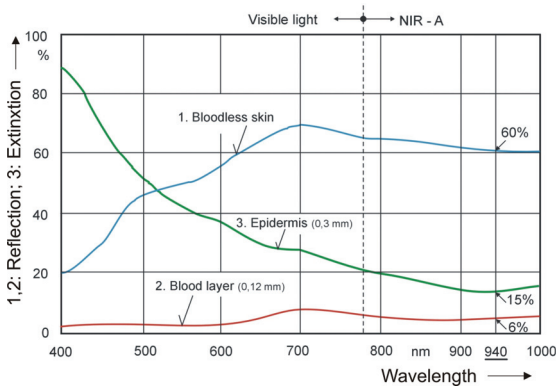

Fig. 1 *Optical properties of human skin and blood in the visible and near infrared area of the spectrum.. Typical reflection spectra of anemic skin and of a 0.12 mm thick blood layer on glassare are shown as well as an extinction spectrum of a 0.3 mm epidermal layer. The difference in reflectivity between the skin tissue and the blood is evident and results in a high optical contrast between skin and dermal vessel plexus. The optical attenuation of epidermis is very high in the ultraviolet and blue regions and lowest at IR wavelengths of about 950 nm.*

Following this principle, the optoelectronic PPG sensor signal reflects the blood volume changes in the cutaneous and partially also the subcutaneous vessel plexus and consists of a high constant part which is independent from the perfusion (light scattering in tissue), a smaller quasi static vein signal and a very small, periodical modulated arterial signal (Fig. 3). It must not be forgotten that this indirect

kind of blood volume measurement is also associated with some fundamental disadvantages:

- ***dependency on the optical attenuation of the skin due to individual texture and pigmentation of the skin,***
- ***dependency on the initial blood volume in the measurement zone below the sensor and thus on the actual perfusion status of the skin and the temperature.***

In the quantitative photoplethysmography discussed here, these disadvantages were reduced by the introduction of a patented control concept which provides an automatic calibration of the PPG signal [2, 3]. The skin is not illuminated with constant light intensity: instead, the integrated microprocessor adjusts the amount of light in a control loop until a defined skin illumination is achieved beneath the PPG sensor. Its signal can be recorded with common terminal equipment, a connection to external PC and means of data storage is also part of today's standard.

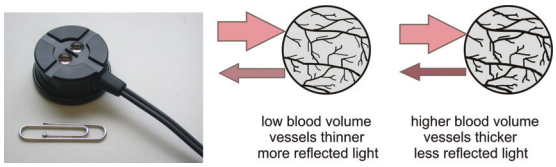

Fig. 2 *Typical PPG sensor, working in reflection mode. The sensor consists of a light source (LED) and a light detector (Si photodiode), both optoelectronic components are placed at a distance of 6 mm inside the sensor case and are equipped with optical lenses (left). Schematic illustration of a transilluminated skin vessel plexus under the sensor to explain the correlation between blood volume and PPG signal (right).*

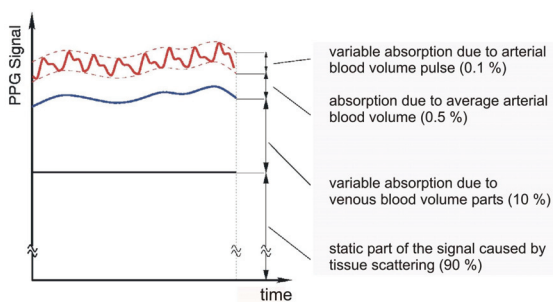

Fig. 3 *Composition of the photoplethysmographic signal. The intensity of the backscattered light depends on the blood volume in arterial and venous vessels in the measuring zone. A separation of the venous and arterial parts of the detected signal is possible by electronic filtering of the signal.*

A sensitivity profile in relation to skin depth can be calculated when the light intensity I(x,y,z) at different locations are regarded. The contribution of any skin depth dz to the whole detector signal can be specified as

$$dI(z) = \frac{\iint I(x,y,z)\,dxdy}{dz} \qquad (1)$$

Figure 4 shows typical sensor sensitivity profiles, calculated by Monte Carlo method for different wavelengths. A strong influence of wavelength on penetration depths can be observed. The "green" sensor, which only measures the upper skin layers up to a depth of about 0.3 mm will provide measurements solely of the skin microcirculation. While sensors utilising red or infrared light will additionally collect information of deeper and larger vessels in the skin and thus gather information of the macrocirculation.

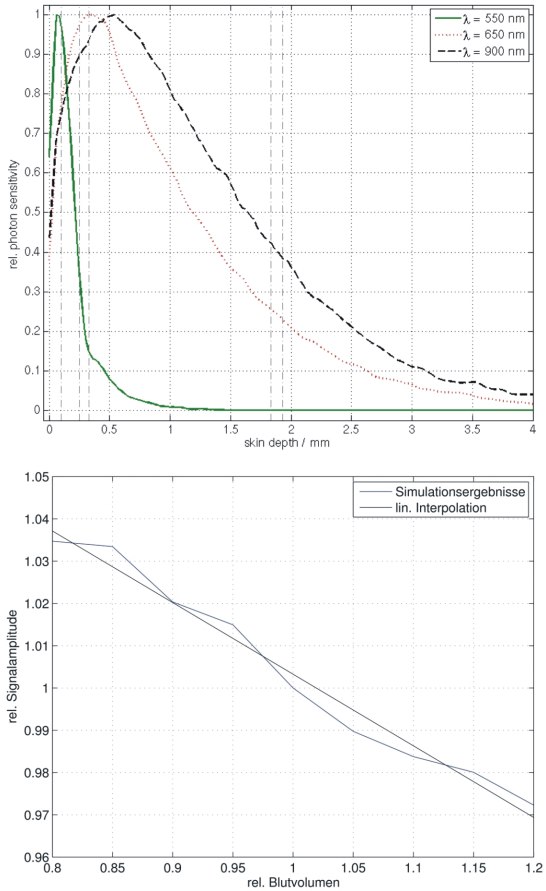

Fig. 4 *Sensor sensitivity dI in relation to skin depths for different wavelengths (top) and expected signal intensity changes on rela-*

tion to blood contents on the skin (below). The blood volume in the capillary layer has been changed by 20 %, a linear relation between blood contents and sensor intensity could be found [4, 13].

FIRST EXPERIMENTAL SETUP

The design of our multi-chanel PPG measuring system with microprocessor control for noninvasive monitoring of neurological induced skin perfusion dynamics is shown in Fig. 5.

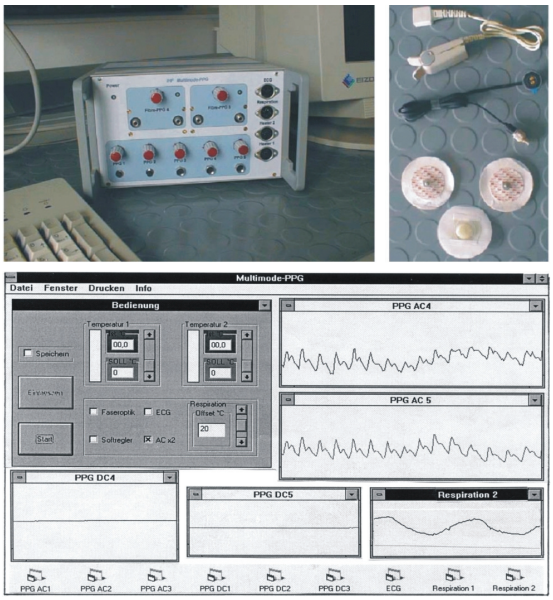

Fig. 5 *Multi sensor measuring system for non-invasive monitoring of skin perfusion dynamics, capable of simultaneously reading multiple PPG channels, ECG, temperature and respiratory signal (left) and used ECG electrodes & PPG sensors for detection of blood volume changes in reflection and transmission mode (right); selected windows in the screenshot allow the control and visualization of the detected signals (below) [5].*

Five PPG channels will be provided allowing instantaneous measurements on different locations of the human body. Two of these channels are equipped with interfaces for both standard electrical and special fibre optical sensors which are free of any metallic parts. Possible applications of such sensors are for example comparative studies and dynamic control during NMR imaging. Two other PPG channels are prepared for the use of recently developed optical sensors with heating facilities that can be adapted to the skin surface temperature or which can even locally warm up the tissue to increase the blood volume in the skin and to paralyze local vasomotion of dermal vascular plexus. The processing of the PPG signals includes filters to distinguish between major frequency components as well as an automatic calibration process and a compensation network for the suppression of noise caused by surrounding light sources. In addition to the optical sensors, the system will provide two breath monitoring channels (for both nostrils) and an electrocardiograph. After A/D conversion all bio signals are transferred to a PC for the purpose of data visualization & storage. As a major advantage of our measuring concept, all functional settings and sensor control can be managed by the PC.

LOCAL SKIN PERFUSION DYNAMICS IN THE TIME AND FREQUENCY DOMAIN

First visualisation of pulsatile skin perfusion patterns in the time and frequency domain was published in 1985 [6]. Our "historical" results are shown in Fig. 6. These recording shows beside the heartbeat synchronous waveforms also other fluctuations in PPG signal with lower frequencies, which correspond to the respiration and other neurological (local or centrally induced) vasomotion activities. These rhythmical perfusion patterns can also be found in the FFT recording. The heartbeat as a "hemodynamical pump" is dominating here at the frequency of about 1.1 Hz (66 BPM). The respiratory rhythm of 0,2 Hz (12 per minute) is clearly seen as well. Apart from these cardiac and respiratory oscillations auto-nomous perfusion changes (vasomotion patterns) can also be observed at lower frequencies [7-10]. Our further experiments have shown that local perfusion vary greatly from place to place (Fig. 7), so that their spatial assessment and analysis appears to be necessary.

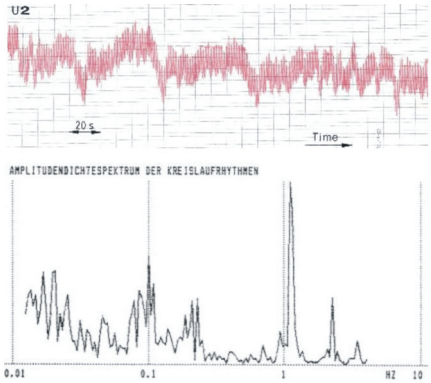

Fig. 6 *Skin perfusion behavior, recorded with a standard PPG sensor (reflection mode) on forehead of a resting subject in horizontal position.*

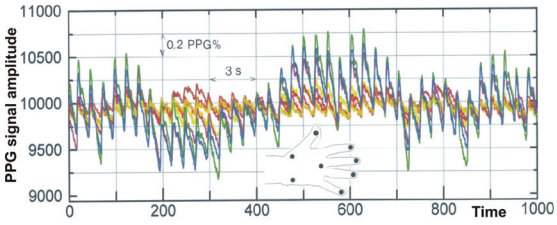

Fig. 7 *Distributed dermal rhythmicity, measured with five classical PPG sensors on the volar side on the left hand.*

EXPERIMENTAL PPGI SETUP

The PPG-Imager is a contactless and spatially resolving advancement of the classical and well established PPG [11-13]. A part of the skin surface is illuminated by illumination panels consisting of multiple LEDs and as optoelectronic sensor a high sensitivity CCD camera is used. To detect also the weak light modulation, which is caused by the hemodynamical perfusion changes in the skin, our setup utilizes the UltraPix FE 250 camera from Life Science Resources because of its high dynamic range of 84 dB and it's high readout speed of 5,5 MB/s. The imaging sensor is EEV 37-10, a silicon frame-transfer CCD with a pixel resolution 512x512, the spectral range is 400-1100 nm with a quantum efficiency of 40% at 800 nm. To reduce the readout noise, the camera is cooled down to -40° C.

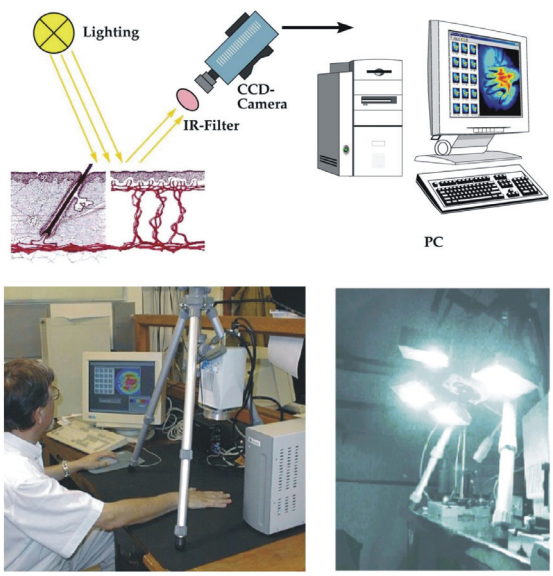

Fig. 8 *Photoplethysmography Imaging setup. The skin is illuminated by a custom LED floodlight and the backscattered light intensity dynamics is recorded by a high sensitivity CCD camera.*

Using the PPGI setup shown in Fig. 8 it is possible to measure arbitrary parts of the skin surface and to simultaneously assess the dermal perfusion in different skin regions. After recording of short video sequences of the skin surface the operator can chose different regions of interest (ROIs, "virtual PPG sensors") for which the backscattered light intensity is calculated. The resulting signals contain the same information as classical PPG signals.

The camera is connected to a high performance PC through a specially designed camera controller. The PPGI software was developed to control the camera settings, capture the image sequence, and perform the post processing and analysis. Currently, the PPGI software is capable of acquiring the video in on-line mode and saving it for off-line processing.

In the on-line mode, the live video can be dynamically displayed. By changing the sensitivity, readout speed and acquiring only subarray or through binning, the sample rate can be changed in a wide range according to different requirement. For the off-line processing, the video acquired will be calibrated first. The calibration includes equally intervaled resampling and motion compensation. The resampling is done by linear interpolation so that the time-varying PPG signal can be treated by Fast Fourier Transform (FFT). The motion compensation is intended to overcome the movement artifact of the patient during measurement to make the result more accurate [8]. Like in on-line mode, different ROIs can be chosen to investigate the spatial variation of dermal perfusion change. The software was written in Microsoft Visual C++ 6.0 under Windows 98. It utilizes the advantages of Windows programming environment like graphical user interface, large memory management and powerful painting function which are essential for imaging and image processing. The acquired video can be played back, displayed with different colormap scheme or zooming to increase the visual effects. The calculated PPG signals for ROIs give a description of the skin perfusion in time domain (Fig. 9).

ADVANCED SIGNAL PROCESSING

A typical recording with corresponding PPGI signals can be seen in Fig. 10, done on a left hand with a small fresh wound in the skin of the middle finger. As can be seen in the figure the perfusion patterns from healthy skin and the wound on the middle finger show significant differences. When looking only

at the heart beat it is slightly increased inside the wound, however the slow rhythms of about 0,1 Hz are strongly reduced inside the wound. Not only it is possible to discriminate the wound and the healthy skin when comparing the different three regions, it is also apparent, that the low perfusion patterns has strong local variation. Even the two ROIs on healthy skin in distance of some mm show evident differences in the 0,1 Hz band.

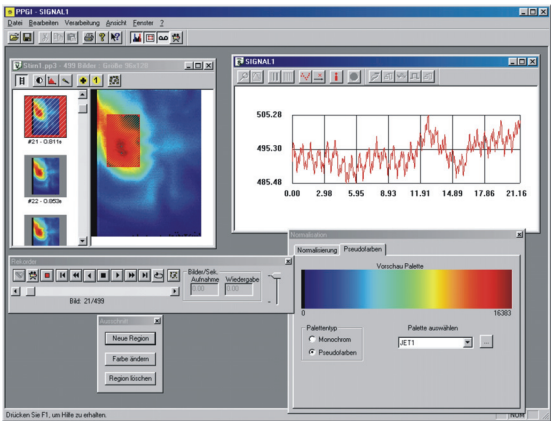

Fig. 9 *Typical program window of PPGI software*

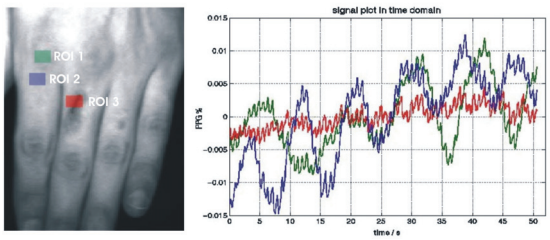

Fig. 10 *PPGI recordings of a hand with a wound on the middle finger. Calculated perfusion signals for three selected ROIs.*

When trying to further analyse the perfusion patterns with the classical Fourier Transform not much new information is revealed. It is possible to recognise differences at low frequencies; however the resolution is quite limited. The frequency spectrum can't reveal much advanced information, the reason is that the FFT is not well suited for analysis of transient signals.

Much more new insights into the distributed perfusion patterns allow the Wavelet Transform. This analysis leads to a 3dimensional time - fre-quency signal representation where the spectral evolution over time can be directly assessed [13]. It is in reality a family of transformations where a signal g(***t***) is transformed by an analysing function $\psi(t)$. The analysis function $\psi(t)$, which is called the "mother wavelet", is not fixed but can be chosen from a collection of functions. All of these have to meet certain restraints (see [10]), most notably are localisation in time as well as in frequency domain. To analyse the signal g(***t***), the mother wavelet is shifted across the time axis (by parameter b) and also scaled by different factors a. Thus a family of basis functions

$$\psi_{a,b}(t) = |a|^{\frac{1}{2}} \psi\left(\frac{t-b}{a}\right), \qquad (2)$$

is obtained.

The continuous Wavelet Transform is defined as:

$$\tilde{g}(a,b) = \int_{-\infty}^{\infty} g(t)\,\psi^{*}_{a,b}(t)\,dt. \qquad (3)$$

Utilising this transform a higher dimensional representation of the signal g(t) can be obtained where the dimension b is responsible for the time information and the other dimension a for the scaling information which is inversely proportional to the frequency.

The original function can be recovered from by the inverse transform

$$g(t) = C_{\psi}^{-1} \iint \tilde{g}(a,b)\,\psi_{a,b}(t)\,\frac{da\,db}{a^2}, \qquad (4)$$

where the normalising coefficient C_{ψ} is determined by the shape of the mother wavelet:

$$C_{\psi} = \int_{-\infty}^{\infty} |\hat{\psi}(\omega)|^2 |\omega|^{-1}\,d\omega, \qquad (5)$$

($\hat{\psi}$ designates the Fourier transform of ψ).

To fully describe the Wavelet Transform also the mother wavelet $\psi(t)$ has to be specified. An often applied function is the Morlet Wavelet, which is a wave modulated by a Gaussian of unit width (see Fig. 11):

$$\psi(t) = e^{\frac{1^2}{2}}(\cos(\omega_0 t) - i\,\sin(\omega_0 t)). \qquad (6)$$

The parameter ϖ determines the time versus frequency resolution, the relation between scaling and frequency becomes . When using the Morlet

wavelet the resemblance to the win-dowed Fourier Transform becomes apparent. The Gaussian can be interpreted as the windowing function. In distinction to the windowed Fourier Transform the width of the function is not fixed but is scaled together with the wave function. So for for every frequency the same number of oscil-lations is taken into account, i.e. if we search for slow rhythms of 0,1 Hz the window function will be ten times wider than if we would search for 1 Hz components. This makes the Wavelet Trans-form admissible to investigate a very broad fre-quency range of multiple decades.

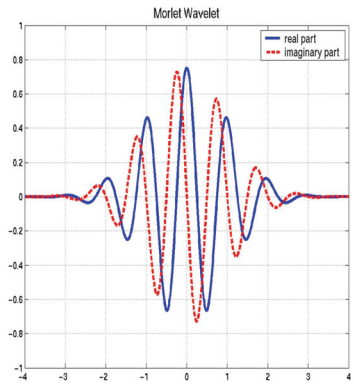

Fig. 11 *Morlet mother wavelet consisting of a complex wave modulated by a Gaussian*

The wavelet transform of the three PPGI signal plots from Fig. 10 is shown in Fig. 12. The resulting spectrum is a joint time-frequency representation of the signal, the evolution of different frequency components (vertical axis) can be directly recognised versus the time (horizontal axis). The classical FFT power spectrum can be interpreted as a projection of the Wavelet spectrum in horizontal direction and thus looses any time representation. The generated advanced signal visualisation reveals on first sight, that the slow rhythms of about 0.1 Hz are not stationary but fluctuate in amplitude and also slightly in frequency.

Besides the interactive inspection of perfusion patterns in selected skin regions also an automated spatial representation of the dermal perfusion status can be achieved. For this purpose a ROI is placed in one corner of the video sequence and from the related perfusion signal a characteristic parameter e.g. the amplitude of heart synchronous oscillations is calculated. According to the magnitude of the parameter the ROI is colourised by a specified colour-map. The ROI is then moved to an adjacent position and again colourised; this process is repeated until the whole image area is scanned. The resulting perfusion map does not depend on morphological informations anymore but only represents functional data of the perfusion status. The mentioned algorithms have been tested on different PPGI recordings. Figure 13 shows one example of locally applied vasocative liniment where the effect of the drug on the microcirculation can functionally be visualized. The treated skin region exhibits an increase in perfusion intensity of 250 %.

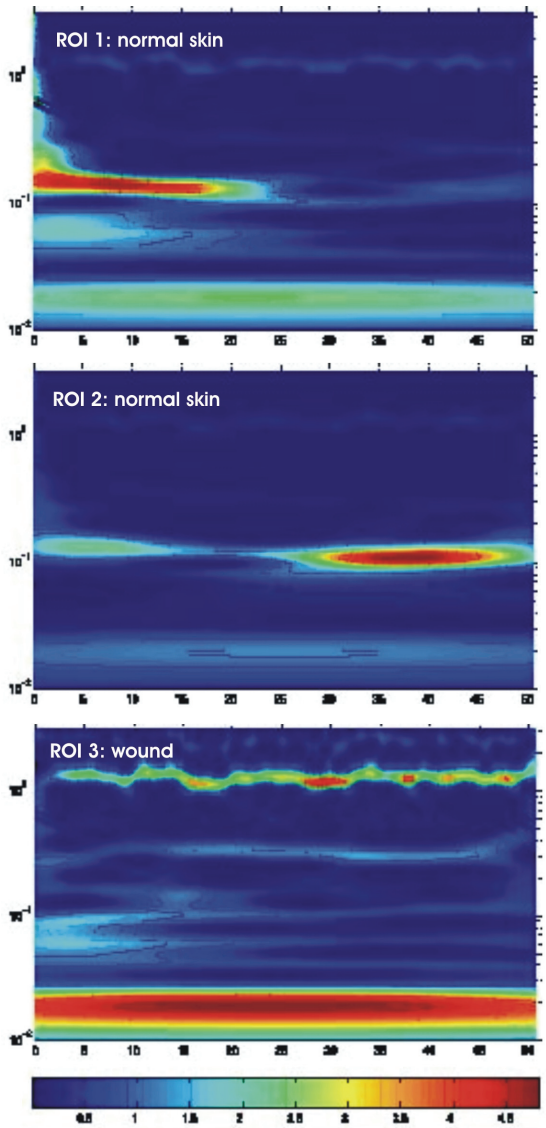

Fig. 12 *Example of the advanced analysis of transient perfusion patterns: Wavelet spectra of selected signals from Fig. 10.*

Apart from the strong temporal fluctuations in dermal perfusion also a new behaviour of distributed spatial rhythm fluctuations could be observed in our lab at IHF/RWTH Aachen University. This phenomenon which can only be observed in animated video representations of the PPGI recordings is "blood volume clouds" which move on the forehead in a coherent but complicated pattern [10].

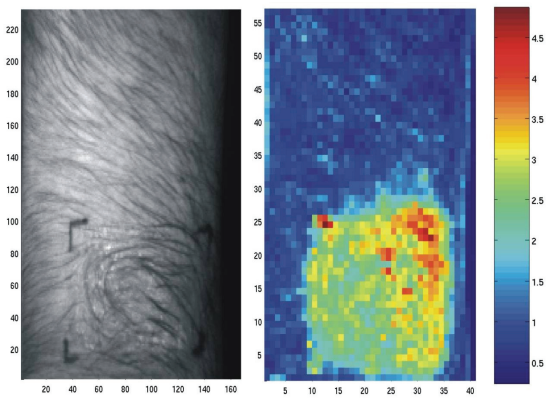

Fig. 13 *Functional mapping of a lower arm. Left: image from PPGI video sequence of a lower arm, the marked skin region is treated with a vasoactive liniment. Right: functional mapping of perfusion intensity, the colour displays the amplitude of the heart synchonous oscillations.*

CONCLUSIONS

The analysis of complex rhythmical changes in dermal perfusion requires sophisticated assessment strategies. Using selected multisensor concepts it is possible to acquire undistorted vital signals in a very broad frequency range, correlation of the different sensor signals reveals that besides the known central rhythms certain local oscillations especially around 0.1 Hz occur, which show endogenous influencability. The local variability of the perfusion patterns can further be assessed by novel imaging techniques. The presented Photoplethysmography Imaging is capable of assessing the skin perfusion of arbitrary skin surface regions in a completely contactless manner and at the same time provides results with high spatial resolution. This allows even perfusion studies in wounds or transplanted skin. Altered skin perfusion can already be detected in very small skin wounds. Together with advanced joint-time-frequency signal processing the local autonomy of slow rhythms even in adjacent skin regions can be visualised. The Wavelet Transform allows the analysis of a signal over a wide frequency range, while providing good resolution also at low frequencies. At the same time also the temporal evolution of different frequency components over time can be revealed.

A completely new, previously unreported phenomenon of distributed blood volume movements in dermal perfusion could first be observed using the PPGI technique. Latest results clearly document the existence of local oscillators which show high autonomy and local variability. The physiological cause and implications of this phenomenon are so far unknown. However it is expected that the low frequency "relaxation" rhythms around 0.1 Hz have a very important bearing on the human physiology and have potential therapeutic implications i.e. in psychosomatic medicine.

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