Contributed paper

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Application of transillumination quotient for monitoring of the instantaneous width of the subarachnoid space

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The authors describe the application of the newly designed method of near-infrared transillumination-back scattering in monitoring of the instantaneous width of the subarachnoid space. Description is provided with the method of elimination of influence of blood circulation in the scalp on the signals recorded from individual sensors. This influence has been eliminated through application of two sensors located at different distances from the source of radiation. The quotient of the intensities of radiation received by the sensors – distal over proximal – referred to as the transillumination quotient, contains information on propagation of infrared radiation within the subarachnoid space. Mathematical background of this solution has been given. The method of near-infrared transillumination-back scattering allows for continuous non-invasive assessment of cerebrovascular pulsation through its direct effect – pulsatile changes in the width of the subarachnoid space. The authors present examples of recordings obtained in healthy volunteers.

Keywords: subarachnoid space, transillumination, quotient, cerebrovascular, pulsation.

1. Introduction

The subarachnoid space (SAS) is a 1–4 mm wide space between the pia-covered surface of the brain and the dura/arachnoid lined inner surface of the skull bones. Under normal conditions, this space is filled with translucent cerebrospinal fluid (CSF). At such conditions its width is not constant but exhibits long- and short-period fluctuations and oscillations around the average value. The average value is a result of interrelations between the volumes of the brain and the volumes of blood in the intracranial vascular bed and of the CSF, all three contained in the rigid box of the skull and filling it entirely. The interrelations between these volumes and the capacity of the skull are well expressed in the Monro-Kelly principle: ICV = BV + IBV + CSF, and ICV = const. where ICV denotes the total of the intracranial volume, BV is the brain volume, IBV is the intracranial blood volume, and CSF is the cerebrospinal fluid volume. The average or hypothetical "static" width of the SAS is different in different individuals and depends on the amount of CSF filling the space, inversely proportional to brain volume.

In physiological conditions the width of the SAS does not remain constant, but shows fluctuations synchronous with and resulting from such phenomena as the respiratory action, changes in the position of the head, and most importantly – oscillations resulting from the rhythmic pulsation of the brain and its deep and superficial arteries. These oscillations are fully synchronous with the heart rate (HR) and their magnitude is directly proportional to the amplitude of the cerebrovascular pulsation, i.e., degree of distension of the intracranial arteries in the cardiac cycle. In conditions of pathology, the SAS width decreases in the initial phase of the cerebral oedema, until the point of zero-SAS-width is reached with displacement of all the CSF from the cranial compartment to the more compliant spinal compartment of the cranio-spinal system. Then, with no CSF present in the cranial SAS, the width of that space is zero, and no fluctuations or oscillations in the SAS-width-dependent signal are detectable. This is one of the reasons why non-invasive monitoring of the changes in the width of the SAS is of great practical importance for clinical management of patients with the life-threatening condition of cerebral oedema or with cranio-cerebral conditions predisposing to the development of this important hazard.

In the past, a method of detection or crude qualitative assessment of the relative magnitude of hydrocephalus was designed, based on the dependence of white light conductivity within the head on the width of the CSF layer in the SAS. This technique was called transillumination of the head [1–5]. Due to technical limitations of the method, its career has not been very successful. Only child's skull proved sufficiently transparent to white light to allow for the assessment, while the skull of an adult person is too serious an obstacle to the white light. As in our new technique of near-infrared transillumination-back scattering

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(NIRT-BS) the radiation penetrates the tissue layers of the scalp and skull, enters the head and brain, travels within the SAS and escapes back out, we decided to make reference in the name of the technique to that old method of transillumination. However, the name of the technique must also reflect the complex nature of the process of the propagation of the near-infrared radiation (NIR) within the tissues of the head. Therefore, contained in the name of the technique is also the back-scattering part.

Near-infrared radiation has been successfully employed in the techniques of non-invasive assessment of the changes in the oxygenation of tissues, including the brain, known as near-infrared spectroscopy (NIRS) and pulse oximetry. These techniques consist in non-invasive assessment of changes in the saturation with oxygen of the haemoglobin of the circulating blood. Foundations for NIRS were laid in Jöbsis works made in 1977 [6], and developed later by many other investigators [7–17]. Over the years, much knowledge has been accumulated about the propagation of near-infrared radiation in tissues, and NIRS has become an important tool for non-invasive incidental and continuous assessment of tissue oxygenation. Attempts are also made to employ the NIRS in measurements of cerebrovascular reactivity [18,19], detection of intracranial haematomas [20], and defining thresholds for critical cerebral ischemia [21]. The question of penetration of NIR through the skull bones, absolutely essential to our new technique, has been addressed in a number of those earlier studies.

The attempts to employ NIR for the assessment of changes in cerebrovascular pulsation had not been successful until the concept of NIRT-BS was created by our team, primarily due to the powerful modulation of the received signals by the pulse-generated changes in the filling with blood of the vessels of the skin in the frontal region. These pulsatile alterations, very prominent in absolute values, overshadowed the much weaker modulation of the signal by the deeper fluctuations of the signal resulting from synchronous also pulse-dependent changes in the width of the propagation duct formed by the SAS. It has been only the new method of near infrared transillumination-back scattering NIRT-BS [22] that allowed for elimination of that strong influence of the circulation in the skin of the head on the recorded signals, and enabled monitoring of the changes in the width of the SAS. This became possible with the application of the NIR sensor module of a special design as well as of a dedicated signal processing algorithm, based on the on-line calculation of the transillumination quotient, i.e., the quotient of the intensities of the signals received by the distal and proximal sensors, DS and PS, respectively.

In the method of NIRT-BS the information-bearing medium is NIR, emitted from the source or emitter (E) which is an electroluminescent diode (LED). NIR penetrates the scalp and the skull bone, and reaches as deep as to the brain. Multiple photo-optic phenomena are involved in the propagation of the NIR within the tissue layers of the head, including scattering and partial reflection from the surface of the brain. Part of the NIR manages to escape the head. These photons come into interaction with two infrared photo-sensors-receiving photodiodes, located at different distances from the source (Fig. 1).

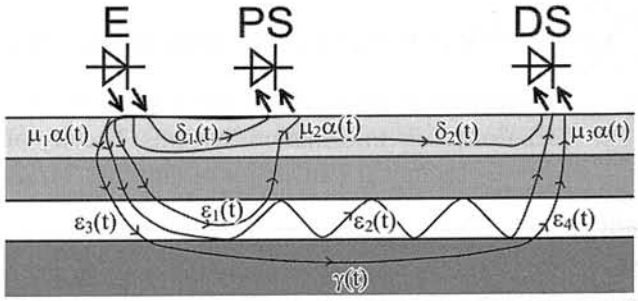

Fig. 1. A simplified graphic representation of the propagation of the NIR within the head, from the source (E) to the proximal (PS) and distal (DS) sensors. The Greek characters denote transfer coefficients at the locations marked with arrows. The layers correspond to those at horizontal section of the head at the frontal tubers. Subsequent layers, top-to-bottom: skin, skull bone, subarachnoid space, brain.

The optimum distances between the photo-elements of the NIR sensor module were determined on the basis of the results of mathematical-statistical modelling of propagation of the NIR in the tissues of the human head [23,24]. On-line division of the instantaneous values of the signal from DS over that from PS yields the, so-called, transillumination quotient which is time-dependent, TQ(t). The characteristic feature of the TQ(t) is that it does not depend on proportional factors influencing each of the individual signals from DS and PS. The factors affecting the currents from both of the receiving sensors are cancelled in the operation of division. The proportional modulation of the amplitude of the DS and PS signals, which is eliminated through division, results from a double pass of the radiation through the scalp. Therefore, TQ(t) is a signal carrying information mainly on the instantaneous width of the propagation duct, i.e., the SAS. However, indirectly, from the TQ(t) we can derive information on the factors affecting the instantaneous width of the SAS, e.g., cerebrovascular pulsation and long-period fluctuations. The details of the NIRT-BS method were described in other papers by our team [22].

For further application of the method in clinical practice it is particularly important to describe the dynamics of the changes in the width of the SAS, i.e., creation of a formal model of behaviour of the width of the SAS and its verification. Such an attempt is made in this paper.

2. Instantaneous width of the SAS

The term of instantaneous width of the SAS is used for a non-negative continuous function of time (time waveform) $s(t) \geq 0$, where $s(t)$ is the instantaneous value of the width of SAS, and the real variable t stands for time. It is consid-

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ered normal that $s(t) \geq 0$. The situation when, however shortly, $s(t) = 0$ is considered pathological, because this means that there is no CSF between the brain surface and the skull bones and the brain is pressed against the inner surface of the skull. The behaviour of the width of the SAS largely depends on both pressure in the intracranial arteries and movements of the body and the head itself. Some influence on the instantaneous width of the SAS is also exerted by peristaltic movements of the intestines and mechanical activity of the lungs and heart.

Physiological background of the influence of various internal and external factors on the value of $s(t)$ is presented in other papers by our team, which are being prepared for print. In this paper, however, we would like to focus on mathematical-statistical properties which can be noted during long-term observations of the SAS status and of the well-defined and experimentally verified transillumination quotient TQ(t), reflecting changes in the SAS status, mainly the instantaneous width of the SAS.

The changes in the width of the SAS have the nature of continuous fluctuations. The normal behaviour of the tracing of the instantaneous width of the SAS can be treated as a non-stationary or more precisely evolutionary stochastic process with limited bandwidth of power density spectrum. Within this process, relatively long time intervals can be found, when the properties of the process remain invariant. Such periods will be referred to as quasi-stationary realisations of the process. Examples of such quasi-stationary segments in the width of the SAS are encountered in resting conditions, when both heart rate and respiratory rate are regular. Under such conditions the width of the SAS is a superposition of two different processes: slow – with spectrum frequencies equal or lower than respiratory rate, and fast – consisting of the periodic, pulsatile process generated by the beating heart.

The power spectrum of each such quasi-stationary, relatively long implementation of the tracing of the width of the SAS has a polimodal or formant character. The maxima of these modes or formants occur at the following frequencies: zero (frequency of the maxima for the spectrum of the slow-variable component), f_c, $2f_c$, $3f_c$,...(mean heart rate and a few of its harmonics).

The hypothetical typical shape of the power density spectrum for a quasi-stationary observation of the width of the SAS is presented in Fig. 2.

Clearly seen in the lower bandwidth, is the slower sub-cardiac component comprising the respiratory sub-component, while in the upper part of the periodogram the principal and its two harmonics are observed of frequencies equal to f_c, $2f_c$ i $3f_c$, respectively.

On the basis of the frequencies for the maxima for particular modes, two additive components can be distinguished in the behaviour of the width of the SAS. Proceeding from the higher frequencies downwards, we observe:

- cardiac component with bandwidth between the frequencies: $(1/2)f_c$ – lower limit and $(k + 1/2)\, f_c$ – upper limit, where k =1, 2, 3,... is the number of the highest harmonic still considered within the cardiac component.

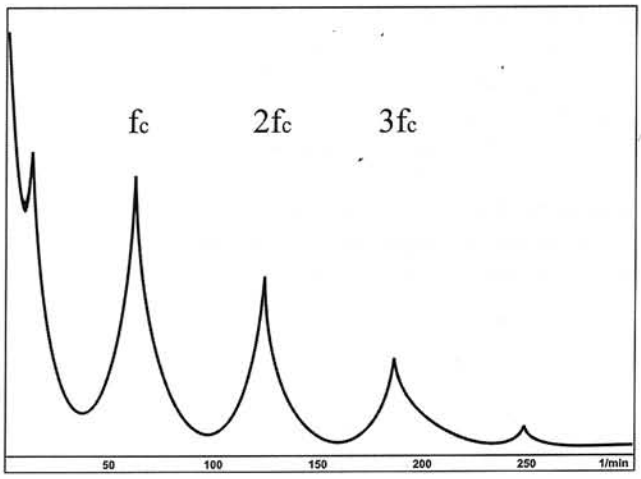

Fig. 2. The hypothetical power density spectrum estimate (periodogram) of a quasi-stationary realisation of the instantaneous width of the SAS.

Due to high elasticity of the superficial cerebral arterial vessels, the cardiac component well reflects the variable component of the pulsating instantaneous pressure in these vessels. The waveform of the cardiac component will be further referred to as $s_c(t)$,

- sub-cardiac component of the base bandwidth concentrated below the frequency $(1/2)f_c$. The sub-cardiac component is treated as a superposition of the movements of the brain against the skull caused by respiratory action, dynamic moves of the head and trunk, peristaltic activity of the bowels, etc., conveyed both mechanically and via the circulatory system. Many observations indicate that the spectrum of such a superposition concentrates mainly well below the frequency $(1/2)f_c$. Under normal conditions, when the width of the SAS is non-zero, the function $s_s(t)$ assumes positive values. What is more, $s_s(t) > s_c(t)$. The distinction of the two additive components in the behaviour of the width of the SAS can be formally expressed as the sum:

$$s(t) = s_c(t) + s_s(t). \tag{1}$$

In the spectrum of typical realisation of the process s(t), there occurs a characteristic depression (anti-formant) close to the frequency $(1/2)f_c$. This facilitates spectral separation of the two components. According to the aforementioned proposal, the sub-cardiac component $s_s(t)$ can be referred to also as slow or slow-variable component, while the cardiac component $s_c(t)$ can well be named fast or fast-variable one.

Clearly enough, these names reflect the differences in the statistical properties of these components only, without reference to their origin and background. Such two-component model of the process of the instantaneous width of the SAS is verified in practice, when average respiratory rate is distinctly, several-fold lower than the heart rate, and other phenomena affecting the instantaneous width of the SAS exhibit yet lower frequencies than respiration. It is

particularly important, that no mechanical vibrations or moves of the head at a frequency higher than respiratory rate should occur.

In physiological conditions the respiratory rate – about 16/min, is much lower than the heart rate – about 75/min. In some cases of pathology, respiratory rate may rise to a value very close to the heart rate, yet still lower than HR. The influence of respiration on the width of the SAS is rather complex, as it is not limited to respiration's contribution to the slow sub-cardiac component, but it also affects the other component through the well-known influence of respiration on the heart rate and arterial blood pressure. Therefore, we intend to devote a whole separate study to the issue of influence of respiration on the width of the SAS, as monitored by the TQ. In the present publication we wish to focus more on the cardiac component, while the sub-cardiac component will be further regarded as indivisible and significantly slower than the cardiac component.

A hypothetical tracing of changes in the width of the SAS with typical realisation of the process according to Eq. (1) is presented in Fig. 3.

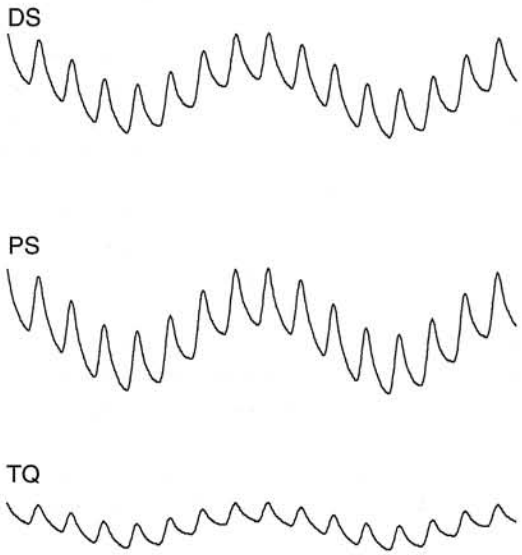

Fig. 3. Typical plots recorded from the distal (DS) and proximal (PS) sensors, and their quotient TQ(t).

Just as suggested by the power density spectrum in Fig. 2, we shall now interpret the cardiac component as the sum of k of modulated harmonics

$$s_c(t) = \sum_{m=1}^{k} a_{cm}(t)\cos\varphi_{cm}(t), \tag{2}$$

where the natural number k is the number of harmonics taken into account in the model of the cardiac component.

In the formula above, the positive waveforms $a_{c1}(t)$, $a_{c2}(t)$,...., $a_{ck}(t) > 0$ are the instantaneous amplitudes (envelopes) of the particular harmonics of the cardiac component, while the real waveforms $\varphi_{c1}(t)$, $\varphi_{c2}(t)$,..., $\varphi_{ck}(t)$ are the instantaneous phases of these harmonics. Derivatives of these phases are the waveforms of the instantaneous frequencies of these harmonics, different from the spectral frequencies, e.g., from the abscissa of the periodogram in Fig. 2:

$$f_{cm}(t) = \varphi'_{\chi\mu}(t)/(2\pi), \quad m = 1,2,\ldots, k. \tag{3}$$

In the formula, the prim sign " ' " denotes time derivative, and the coefficient $1/(2\pi)$ assures conversion of the frequency unit from (rad/s) to (Hz). The average values of the waveforms of the instantaneous frequency of Eq. (3) are equal to spectral frequencies corresponding to the maxima for particular modes of the spectrum in Fig. 1

$$\overline{fc1(t)} = f_c, \ \overline{fc2(t)} = 2f_c,\ldots, \ \overline{fc3(t)} = kf_c. \tag{4}$$

The bar over the symbol of a waveform denotes here its arithmetic mean value of the realisation used for the estimation of the spectrum from Fig. 1. With the additional assumption on the domination of the principal (first) harmonic over the others, which holds true practically in every case and can be expressed as

$$a_{c1}(1) > \sum_{m=2}^{k} a_{cm}(t), \tag{5}$$

we arrive at the equity of mean frequencies, well-known from the theory of signals

$$\overline{fsc(t)} = \overline{fc1(t)}, \tag{6}$$

where

$$f_{sc}(t) = \varphi'_{sc}(t)/(2\pi), \tag{7}$$

is the instantaneous frequency of the global cardiac component $s_c(t)$, treated as the result of simultaneous amplitude (AM) and frequency (FM) modulation

$$s_{sc}(t) = a_{sc}(t)\cos\varphi_{sc}(t). \tag{8}$$

Here the positive waveform $a_{sc}(t) > 0$ and the real waveform $\varphi_{sc}(t)$ are the instantaneous amplitude (envelope) and the instantaneous phase of the cardiac component, respectively. The mathematical model of the behaviour of the cardiac component of the width of the SAS in time accepted above Eq. (2), takes into account both the modulation of the amplitude or magnitude (AM) and the modulation of the frequency or rate of oscillations (FM) of all the harmonics of the component. Such AM/FM model, Eq. (2), is particularly adequate for describing the behaviour of the cardiac component of the width of the SAS, for two main reasons:

- this model is sufficiently universal and naturally encompasses the influence of the cerebrovascular pulsation on the width of the SAS, and

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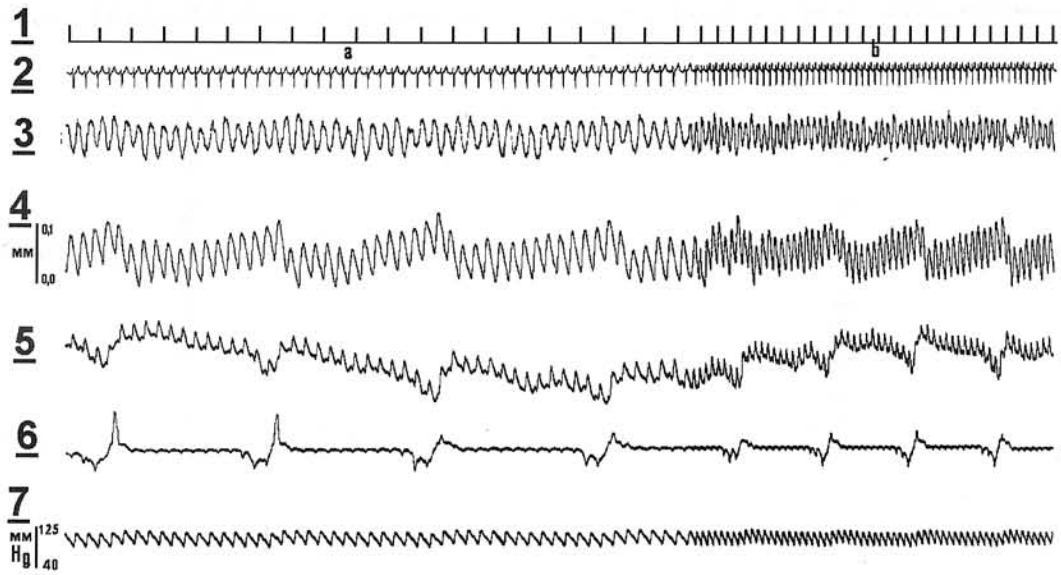

Fig. 4. Synchronous NIRT-BS and tensometric recordings in resting conditions in cat. Pressure transducer fixed firmly directly to the skull bone, foot of the tensometric probe resting on the dura. 1 – time base (1 sec.), 2 – ECG, 3 – auricular pulse, 4 – instantaneous values of the power of the reflected stream of NIR in the NIRT-BS technique, 5 – tensometric recording (ICP), 6 – respiration, 7 – systemic arterial pressure. The phase inversion of the tensometric recording resulted from the electrical connections applied.

- the second element of the sum (1), i.e., sub-cardiac component, represents the local mean value of the width of the SAS, around which oscillates the almost periodic cardiac component.

Direct recording of the instantaneous width of the SAS has until now been possible only with the application of a highly invasive method employing trepanation of the skull and insertion of a special probe through the foramen into the SAS. In a laboratory animal we performed such an experiment, in which the foot of the tensometric probe was positioned on the dura. The recording obtained from a cat is presented in Fig. 4. Simultaneous recordings with the NIRT-BS method were taken from the opposite hemisphere.

All the pressures were recorded from direct line access, using Statham P23 ID pressure transducers.

Clearly seen in the synchronous recordings is prominent correlation between the non-invasive recording of cerebrovascular pulsation with NIRT-BS and the invasive recording of the changes in the intracranial pressure with the tensometer.

4. The indirect method of recording of the instantaneous width of the SAS

Recordings of signals from both sensors, their quotient TQ and the quotient's spectrum with well separated 2nd and 3rd harmonics of the cardiac component, are presented below in Fig. 5.

The recordings change greatly, if they are taken at resting conditions with regular, normal heart rate, but with vol-

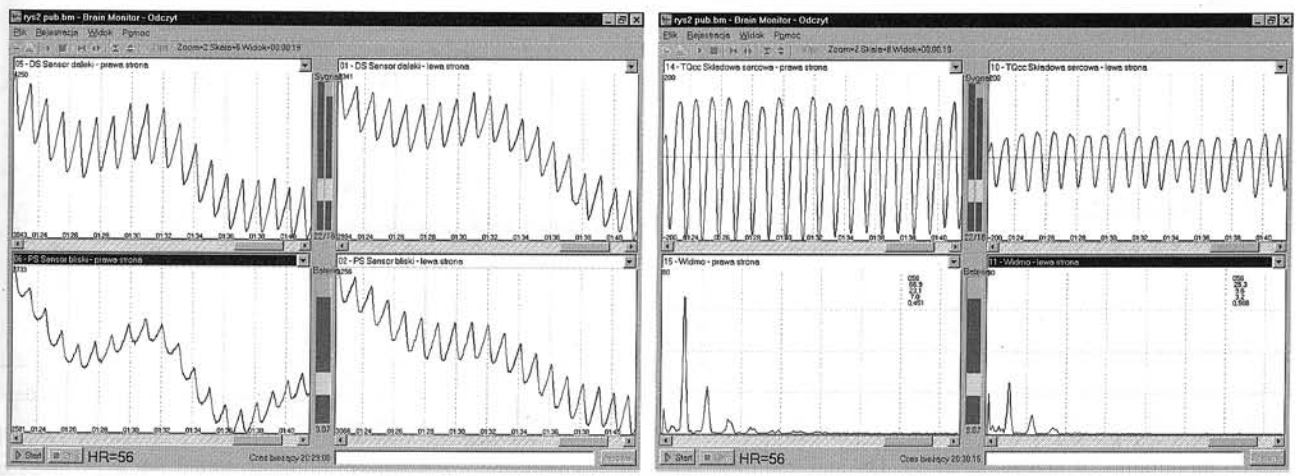

Fig. 5. Recordings of signals from the DS and PS, their quotients TQ, and the quotient's spectrum at resting conditions. Recordings were taken from above both hemispheres.

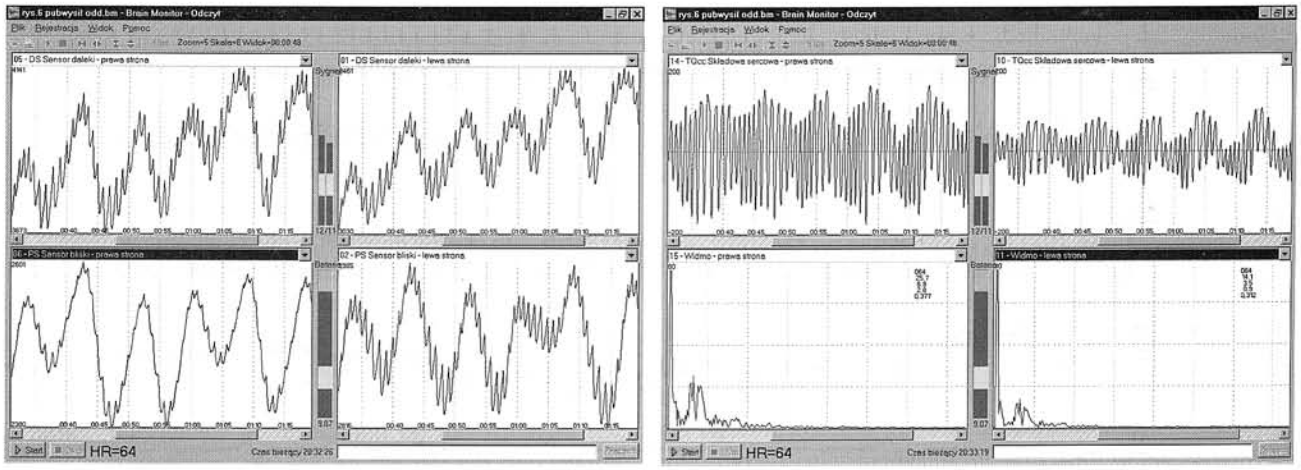

Fig. 6. Recordings of signals from the DS and PS, their quotients TQ, and the quotient's spectrum at resting conditions with voluntarily hyperventilation. Recordings were taken from above both hemispheres.

untarily increased amplitude and frequency of respiration. At such conditions the sub-cardiac component becomes artificially increased. An example of such a recording is given in Fig. 6.

Clearly seen in the recording are periodic changes of the width of the SAS related to respiration, on which the changes resulting from the cardiovascular action are superimposed. The split observed in the cardiac component of the power spectrum of the TQ results from changes in heart rate accompanying hyperventilation.

Other experiments, performed in humans with elimination of the blood flow in the superficial arteries of the scalp, provided information which explains processes occurring at particular sensors. In these experiments 2-mm hard rubber strips were mounted around each of the sensors, DS and PS. The elastic ribbon containing the NIR sensing modules for each hemisphere was placed on the head of the examined individual. Wrapped around the head, over the ribbon, was the cuff of a blood pressure monitor. The cuff was then inflated up to the pressure of 70-mm Hg, which caused the hard rubber separating strips around the sensors to press firmly against the skin of the head and ceased blood flow in the vessels of the skin. Application of the cuff allowed for repeated recordings in standardised conditions of pressure exerted on the scalp. Recordings from the experiment are presented in Fig. 7.

Inflation of the cuff and increasing pressure exerted on the scalp resulted in pronounced and steep rise in the value of the sub-cardiac component and cessation of pulsation of the signals from individual sensors. The phase of constant scalp compression shows further, but slower exponential (asymptotic) rise in the non-pulsatile constant component of the currents from each sensor, until a certain level of saturation is reached. Noteworthy, when the DS and PS tracings are zoomed, low but clear pulsation of the signal from the DS is observed at the end of the pressure rise and throughout the whole period of constant scalp compression, when there is no flow in the blood vessels of the scalp. As this pulsation reveals in the tracing from the DS only, the origin of this pulsation can be no-where else but in the

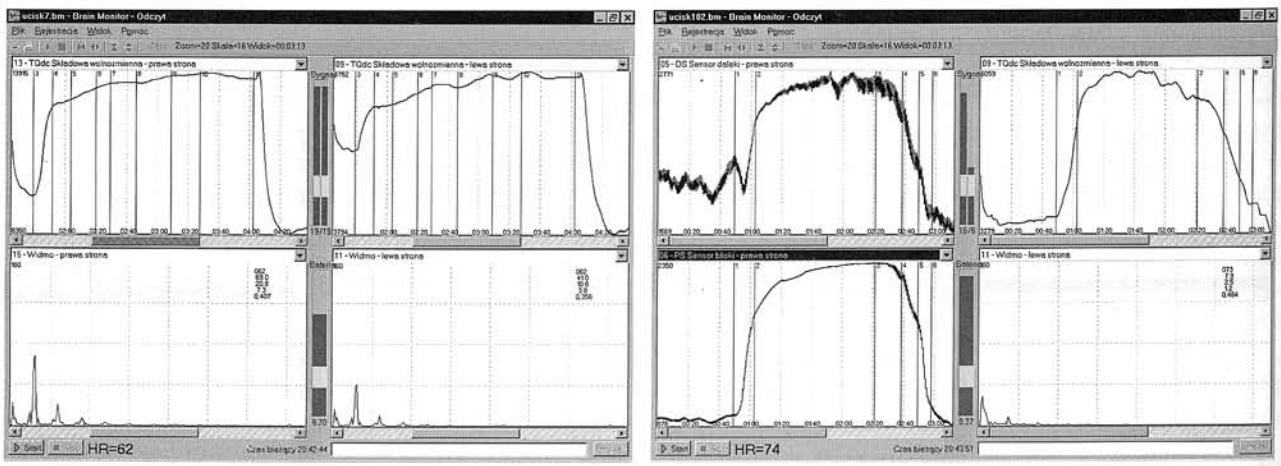

Fig. 7. Recordings of signals from the DS and PS, their sub-cardiac components and power spectrum during the experiment of no-scalp-flow due to scalp compression. Vertical lines denote: 1 – cuff inflation begins, 2 – cuff pressure of 40 mm Hg reached (uphill), 3 – slow cuff release begins, 4 – cuff pressure of 40 mm Hg reached (downhill), 5 – end of cuff inflation and scalp compression.

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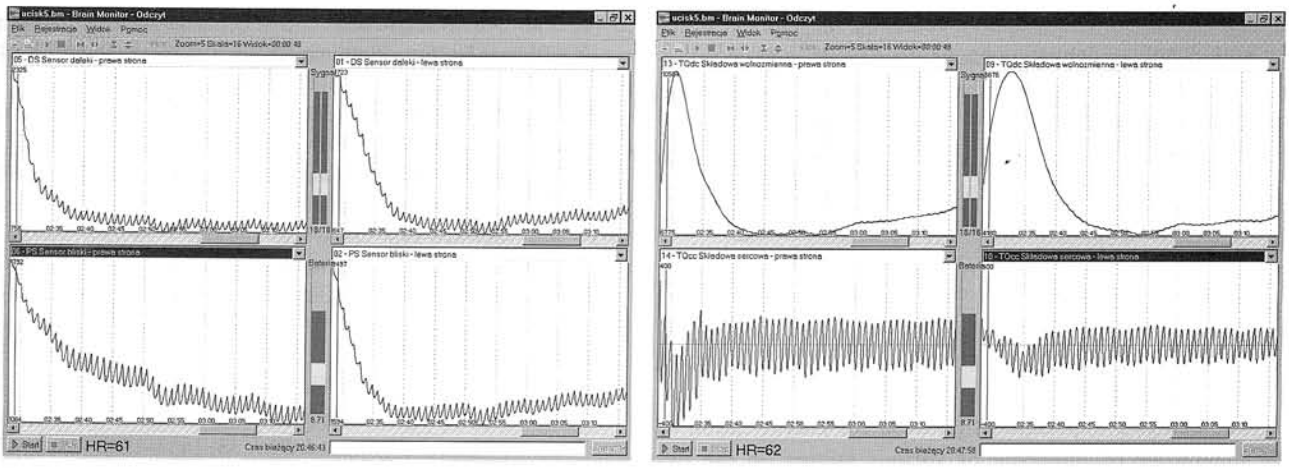

Fig. 8. Zoom of the segment of the plot when blood flow and pulsation in the scalp are reassumed during cuff release.

SAS, whose width undergoes oscillatory changes synchronous and caused by cerebrovascular pulsation. Clear pulsation was also revealed in the analysis of the TQ. The segment of the plot, when the cuff is released and blood flow and pulsation in the scalp are reassumed, containing synchronous recording of the cardiac component, TQ, and sub-cardiac component is presented in Fig. 8.

The results of yet another experiment confirming the recording from the SAS only, are presented in Fig. 9. In the examined individual, scalp compression was performed in the manner described above. During the compression, external factor affecting the width of the SAS was added, namely rhythmic forward tilt of the head.

It can be noticed that the pulsation is present in the signal from the DS and in the cardiac component of the TQ only. The pulsation of the signal from the DS originates in the SAS. Importantly, also the movements of the head are well reflected in the DS tracing only. There is no pulsation observed in the signal from the PS.

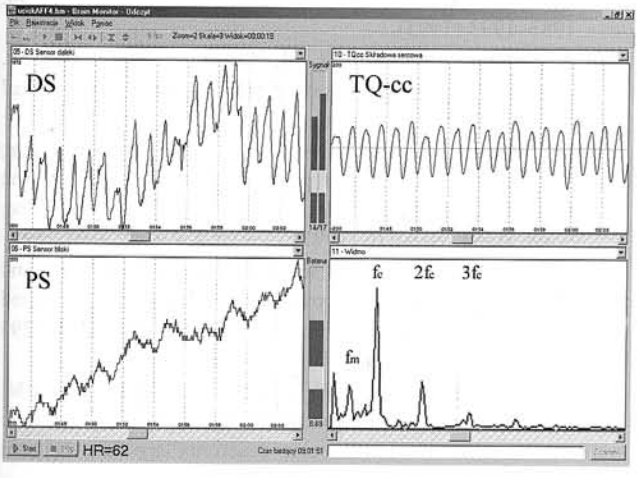

Fig. 9. Recordings of signals from the DS and PS, cardiac component of the TQ (cc-TQ) and the power spectrum, recorded during scalp compression with concomitant rhythmic forward tilt moves of the head.

6. Discussion and conclusions

Theoretical considerations on the influence of different physiological conditions and factors on the instantaneous width of the SAS have led to creation of a theoretical description of these changes. Practical experiments with analysis of the TQ provided arguments confirming the accuracy of the theoretical considerations. In practice, it is just the instantaneous width of the SAS that is recorded and used to derive information which can be valuable in detection and monitoring of life-threatening cranio-cerebral conditions.

Here, we would like to comment some more on the experiments with scalp compression. The abrupt rise in the constant component of the signals can be explained with an increase in the optical permeability of the scalp, resulting from steady pressing of the blood away from the compressed area of the skin under the ribbon. The second phase of the compression, i.e., the steady phase of constant compression is characterised with further, but much slower rise in the constant component. During the phase of no-scalp-flow, the saturation with oxygen of the blood contained in the scalp vessels decreases. This leads to an increase in the optical permeability of the scalp to NIR in our technique, because with a decrease in haemoglobin saturation with oxygen, the absorption of the 860 nm NIR decreases.

This positively verifies our theoretical approach with the proportional factors, not only with regard to the constant components (DS) but also with regard to the variable components. The theory on further modulation in the SAS of what has been initially deeply modulated in the scalp layer is not suitable for explanation of this experiment, because in the compressed scalp there is no modulation possible. It is apparent that we rather have to accept two "parallel" modulations by the SAS:

- modulation of the radiation received by the PS via time-dependent transmittance $\varepsilon_1(t)$ because $\delta_1(t) \approx 0$, and $\mu_1\alpha(t)$ and $\mu_2\alpha(t)$ should be constant, as well as

- modulation of the radiation reaching the DS via time- and SAS width-dependent transmittance $\varepsilon_2(t) + \gamma(t)\varepsilon_3(t)\varepsilon_4(t)$, in which the latter element should be close to zero – see Fig. 1. If our theory of "secondary modulation and proportional factors" is correct, the depth of modulation of the radiation reaching the DS should be greater than that of radiation reaching the PS. This has been confirmed in our last experiment with scalp compression and concomitant rhythmic forward-tilt movements of the head. In this experiment, the movements of the head are reflected in the DS tracing only.

The last two experiments allowed for classification of the magnitude of influence of various factors on the dynamics of the propagation of the radiation received by the sensors. First rank factor would be the influence exerted by the volume of blood in the scalp; when blood is pressed away from the compression area beneath the sensor module in the experiment with scalp compression with the cuff, there was a dramatic change observed in the constant component of the signals from DS and PS. The inflow and outflow of blood to and from the scalp during the rhythmic movements of the head can be used for explaining the modulation being deeper than the one caused by the pulse--related changes in the content of blood in the scalp. The second rank factor would be the effect of "oxygen saturation or de-saturation" of the haemoglobin on the constant component of the DS and PS signals, as observed in the experiment with scalp compression with scalp circulation totally blocked. It is only the third rank that we would attribute to the very subtle influence of the SAS-width modulation of the signals, resulting from changes in the position of the head, alterations in cardiac or cerebrovascular function, respiratory activity, or other phenomena. This is why any movements of the head or frowning of the skin in the sensor area and the like, may have so great impact on the technical quality of the recordings.

The quality of the recorded signals may be greatly improved if noise-elimination algorithms are applied. As the data obtained in the NIRT-BS technique are of great importance, further research is conducted, aimed at extraction and underpinning of these most subtle changes in signal modulation. The results of that research will be presented in subsequent papers.

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