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A NEW METHOD OF INTRAOPERATIVE ASSESSMENT OF THE DYNAMICS OF CORTICAL BLOOD FLOW USING IMAGING PHOTOPLETHYSMOGRAPHY

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Background. Intraoperative assessment of changes in cerebral blood flow is an important component of objective quality control of surgical treatment of cerebral artery aneurysms. Various techniques have been tried to solve this task, but they all have their drawbacks, which forces us to look for new ways of blood flow monitoring. We propose to use the technology of imaging photoplethysmography (IPPG) – a technically simple, contactless, safe and cheap optical method for assessing the perfusion of biological tissues.

Aim. To demonstrate the possibility of using IPPG to assess the dynamics of cerebral blood flow parameters during aneurysm clipping surgery, as well as to identify early changes in blood supply to the cerebral cortex.

Materials and methods. The study was carried out during six surgeries of clipping aneurysms of the anterior part of the Willis's circle, both in the acute stage of rupture ($n = 1$) and in a planned manner ($n = 5$). The IPPG system, which is an LED illuminator in a single unit with a digital video camera, was located on a tripod 25 cm from the intervention zone. During each operation, two one-minute recordings of the illuminated surface of the cerebral cortex were performed: after dissection of the dura mater and before its suturing at the end of the main stage of the intervention. To improve the measurement accuracy, video frames of the studied area were recorded synchronously with the registration of an electrocardiogram. After recording, two IPPG parameters were calculated and compared: the amplitude of the pulsatile component and the pulse wave transit time. Thereafter, the obtained data were compared with the results of computed tomography. Statistical analysis was performed using pairwise comparison tests in the GraphPad Prism software package.

Results. Clipping of cerebral vessel aneurysms are accompanied by significant changes in the parameters of cerebral blood flow. Analysis of the data for all patients revealed significant differences in IPPG parameters before and after surgery, namely, statistically significant increase in amplitude of the pulsatile component ($n = 3$) and decrease in pulse wave transit time ($n = 5$). The absence of significant changes in both parameters was found only in one patient who had mechanical damage in the cortex in the region of video recording.

Conclusion. The IPPG system is capable to quantify changes in blood supply to the cortex during surgical treatment of cerebral artery aneurysms and to identify areas with either increased or decreased blood supply. In-depth studies are required to obtain additional markers of the postoperative state of cerebral blood flow.

Keywords: imaging photoplethysmography, aneurysm, microsurgical clipping, cerebral blood flow, cerebral vessels, neurosurgery

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BACKGROUND

Modern neurosurgery in combination with neurosurgical anesthesia has enormous technical potential allowing to perform surgeries of almost any complexity. The

main unsolved problem is determination of physiological permissibility of certain brain manipulations. Current methods of intraoperative evaluation of changes in regional cerebral blood supply have several limitations. For example,

Doppler ultrasound allows to follow blood flow in individual vessels but does not show blood filling of the brain matter; cerebral oximetry allows to evaluate changes in regional blood flow only in small superficial areas of the brain and cannot be used working in an open wound. The most adequate techniques to evaluate realignment of cerebral blood supply are computed tomography (CT) – assisted perfusion analysis methods but they are almost impossible to perform intraoperatively and are not widespread due to the high cost of equipment. Optical methods such as indocyanine green fluorescence angiography [1, 2], laser speckle contrast imaging [3], and hyperspectral imaging are attractive to researchers because they allow to visualize cerebral blood flow in the whole operative wound without direct contact. However, each method has its advantages and disadvantages, and none of them has achieved routine use in clinical settings. Therefore, the search continues for new methods allowing to increase safety of neurosurgical operations and to identify possible unfavorable blood flow alterations as early as possible for their correction.

One of such methods is imaging photoplethysmography (IPPG), and principal possibility of its use for intraoperative evaluation of changes in the cortical blood flow during open neurosurgical operations was demonstrated by our research group in 2020 [5]. Moreover, in a series of experiments involving laboratory animals, we have demonstrated the utility of using IPPG for evaluation of changes in intracranial hemodynamics in response to various interventions such as CO₂ inhalation [6], dura meter electrostimulation [7], administration of various pharmaceuticals [8, 9], and somatovisceral nociceptive stimulus [10]. Despite positive and reproducible results of these pilot studies, their interpretation is not always sufficiently substantiated due to continued discussions on the physical and physiological model of IPPG signal origin.

Photoplethysmography (PPG) is an optical technique of blood flow evaluation based on measurement of intensity of light stream reflected or passed through biological tissues containing blood vessels using a photosensitive element. Translated from Greek, “photo” means light, “plethysmos”

means becoming full, and “grapho” mean writing. PPG has been known since 1937 [11] and is the first optical method of blood flow examination *in vivo*. It was determined that after light interacts with live tissue supplied with blood, its intensity acquires time modulation with frequency of the heartbeat [11, 12].

According to the accepted PPG model, the main cause of light intensity modulation is changes in tissue blood volume [12–15]. This mechanism is easy to understand in the PPG system for near infrared light transmission: increased blood filling in the systole phase causes absorption of a larger number of photons, and light intensity measured by the photosensor decreases; and vice versa in diastole phase, decreased blood volume causes increased light intensity. This PPG model is known as the classic model. In classic PPG, light source and photosensor are both in contact with the studied organ [12].

It should be noted that according to reports from various research groups, the maximal relative amplitude of modulation associated with cardiac contractions is observed for green light with wavelength of about 0.53 μm [16–19]. The classic PPG model cannot explain this observation as usually green light penetrates tissues at depth below 0.5 mm [20, 21] where pulsing vessels are absent and capillaries do not pulse. To explain abnormally high green light intensity modulation in its interaction with live tissue, an alternative PPG theory was proposed [22]. Essentially, pulsating oscillations of arterial walls transmurally compress and release the capillary network at the surface of the tissue: this reversibly changes the distance between capillaries which actively absorb green light and, therefore, leads to modulation of interacting light. Thus, the capillary network serves as a distributed transformer of blood pressure pulse wave into light intensity change (Fig. 1).

In all PPG systems, the studied biological tissue is illuminated with a incoherent light source, and luminous flux passed through a tissue with blood vessels or reflected from it is measured by a photosensor. The only difference between IPPG and classic PPG is that in IPPG a video

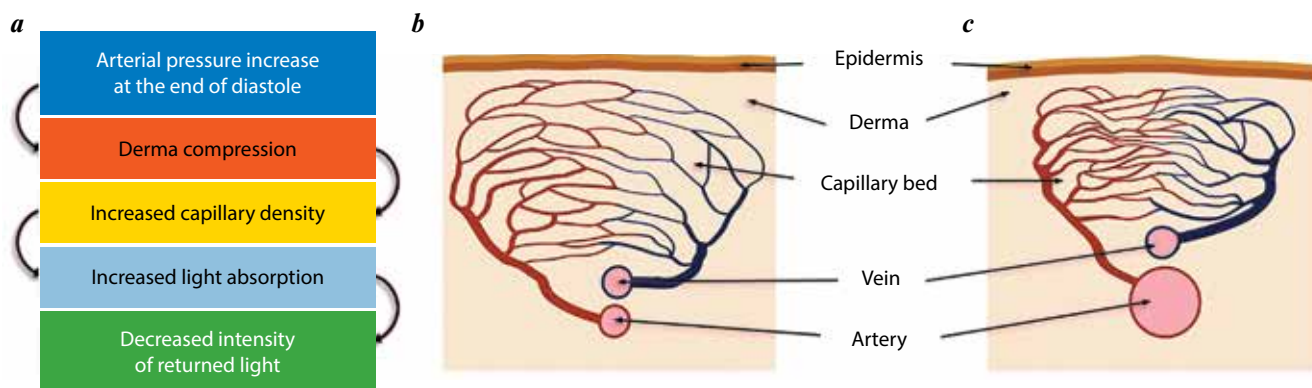


Fig. 1. Alternative model of the photoplethysmography waveform formation: *a* – the basic doctrine of the alternative model; *b* – during diastole, the density of capillaries interacting with light decreases; *c* – during systole, the density of capillaries interacting with green light increases

camera is used as a photosensor and the system works in reflection mode. The use of a camera transforms measuring PPG scheme from contact to contactless. The positive effect of this transformation is more realistic measurements of blood flow parameter ratios during microcirculation monitoring using contactless technology. However, very small light intensity modulations during cardiac contractions are hard to detect against the backdrop of motion artifacts using contactless technology. The latest achievements in computed image processing attributed to synchronous recording of an electrocardiogram (ECG) and video signal [23] significantly expanded the capabilities of IPPG which allows to obtain reliable information even with significant movement of the illuminated area during examination [24].

Microsurgical clipping of cerebral artery aneurysms is associated with high risk of postoperative ischemic complications, and their intraoperative prevention remains a priority for microsurgeons.

Aim. to demonstrate the possibility of using IPPG to quantitatively assess the dynamics of cerebral blood flow parameters during aneurysm clipping surgery, as well as to identify early changes in blood supply to the cerebral cortex.

MATERIALS AND METHODS

Patients. The pilot study was performed at the L.G. Sokolov North-Western District Scientific and Clinical Center of the Federal Medical and Biological Agency during 6 cerebral aneurysm clipping surgeries. The patient group included 3 men and 3 women (mean age 54.7 ± 12.6 years) who underwent standard microsurgical clipping of aneurysm of the anterior circle of Willis using pterional and lateral supraorbital approaches. The localization of the clipped aneurysms was the following: 2 aneurysms of the anterior

communicating artery (ACoA), 1 of the M1–M2 segment of the middle cerebral artery (MCA), 1 of the communicating segment of the internal carotid artery, 1 of the bifurcation of the internal carotid artery and 1 of the M3 segment of the MCA.

One female patient with aneurysm of the ACoA underwent surgery at the acute stage of aneurysm rupture, other patients underwent planned surgeries. All surgical procedures were performed in full compliance with the approved standards for interventions of this kind using adequate anesthesiology with constant monitoring of the key physiological parameters and full control of the vital functions which ensured high safety of the treatment.

Prior to surgery, all patients underwent CT, CT angiography, and cerebral angiography of the cerebral vessels. In the first hours after surgery completion, all patients underwent CT and CT angiography, and CT was repeated after 24 hours and at discharge. According to postoperative CT angiography data, in all cases aneurysms were radically excluded from the blood flow. No signs of stenosis of the parent artery or its branches were observed. Evaluation of the results of postoperative CT of the brain showed ischemia areas in 5 cases: in 3 cases, locally in the places of spatula installation for brain traction; in 1 case, distally in the system of the MCA of interest; in 1 case, in the temporal lobe in the projection of the trephination window.

The female patient with aneurysm rupture died of progressive cerebral vasospasm and meningitis on day 8 after surgery; the rest of the patients were discharged in satisfactory condition. Short information on the patients, interventions and outcomes is presented in Table 1.

IPPG system. Instrumental support for IPPG is very simple as it requires only a camera and a light source. to increase the accuracy of blood pulsation measurement

Table 1. General information about patients who underwent microsurgical clipping of cerebral aneurysms

Patient	Sex	Age, years	Localization of aneurysm	Rupture presence	Duration and location of temporary clipping	Presence and region of ischemia according postoperative CT	Outcome
1	Male	51	M3 MCA	No	10 min M3 MCA	Ischemia of the temporo-occipital region outside the projection of trepanation	Discharge
2	Female	36	ACoA	Yes	5 min A1 ACA from 2 sides	Ischemia of the basal surface of the frontal lobe from traction	Death
3	Male	55	ACoA	No	2 times for 5 min A1 ACA from 2 sides	Ischemia of the basal surface of the frontal lobe from traction	Discharge
4	Male	66	ICA	No	5 min ICA and A1 ACA	Ischemia of the basal surface of the frontal lobe from traction	Discharge
5	Female	49	M1–M2 MCA	No	2 times for 5 min M1 MCA	Ischemia of the temporal lobe in the trepanation zone	Discharge
6	Female	71	Branching of ICA	No	5 min ICA and A1 ACA	No ischemic zones	Discharge

Note. M1–M2 MCA – M1–M2 segments of the middle cerebral artery; M3 MCA – M3 segment of the middle cerebral artery; ICA – internal carotid artery; ACoA – anterior communicating artery; A1 ACA – A1 segment of the anterior cerebral artery; CT – computed tomography.

and suppress motion artefacts, videorecording of the studied patient's organs is performed simultaneously with ECG recording which serves as a time guide for cardiac function.

To monitor cortical blood flow, we used a laboratory prototype of a multimodal system developed and manufactured by our group and consisting of:

- monochrome digital camera IDS GigE Smartek Vision GC1391MP with KOWA LM5NCL lens and focal distance 18 cm;
- light source of 8 type BL-HP20APGCL-5W STAR LEDs located around the lens and emitting light with wavelength 525 ± 30 nm;
- electrocardiograph KAP-01 "Kardiotekhnika-ECG" which allows to record 3 standard ECG leads from patient's limbs with sampling frequency 1 kHz.

The system is presented in Fig. 2. Video camera allowed to record images of the cerebral cortex with spatial resolution 752×480 pixels and time resolution of 39 frames per second. The LEDs and lens were covered by polarization films with mutually orthogonal orientation of transmission vectors to suppress bright glares reflected from the studied tissues which allowed to significantly increase the signal/noise ratio of incoming PPG signal [25].

Digital camera was connected to a personal computer through a LAN port. Images were saved on the computer using software in C++ language developed by our group using software library supplied by the camera manufacturer. Monochromatic images of the cerebral cortex were recorded in uncompressed (lossless) PNG format with 8-bit resolution. To synchronize ECG and videorecording, the

camera generated a signal of flash synchronization at the moment of electronic shutter operation which was registered in the 4th ECG lead. For more convenient data monitoring during examination, ECG signal was shown on an additional display connected to the computer which received both video and ECG data.

Signal processing. Detailed description of the data processing algorithm during ECG-synchronized PPG recording for evaluation of study object perfusion can be found in other articles by our group [5, 23, 26]. Here we will list the main stages of processing of the obtained videorecording of illuminated area of live tissue.

1. After IPGG recording, the studied area is automatically divided into small regions of interest (ROI) with size of 2×2 pixels corresponding to about $40 \times 40 \mu\text{m}$ on the cerebral cortex. To minimize the effect of motion artifacts, at the 1st stage digital image stabilization using the optical flow algorithm is used [27] with variable temporal window equal to the duration of cardiac cycle. The location of each ROI is shifted by the calculated displacement vector of image sectors to maintain stability relative to the details of the measured area.
2. Unfiltered and unaveraged signal recorded in each ROI has 2 modulations: rapidly changing component with frequency of cardiac contractions (AC) and slowly changing component (DC). Both components are proportional to the illuminating light intensity [18] which allows to compensate illumination heterogeneity by calculating AC/DC ratio using their absolute values. After AC/DC signal calculation, it is linearly

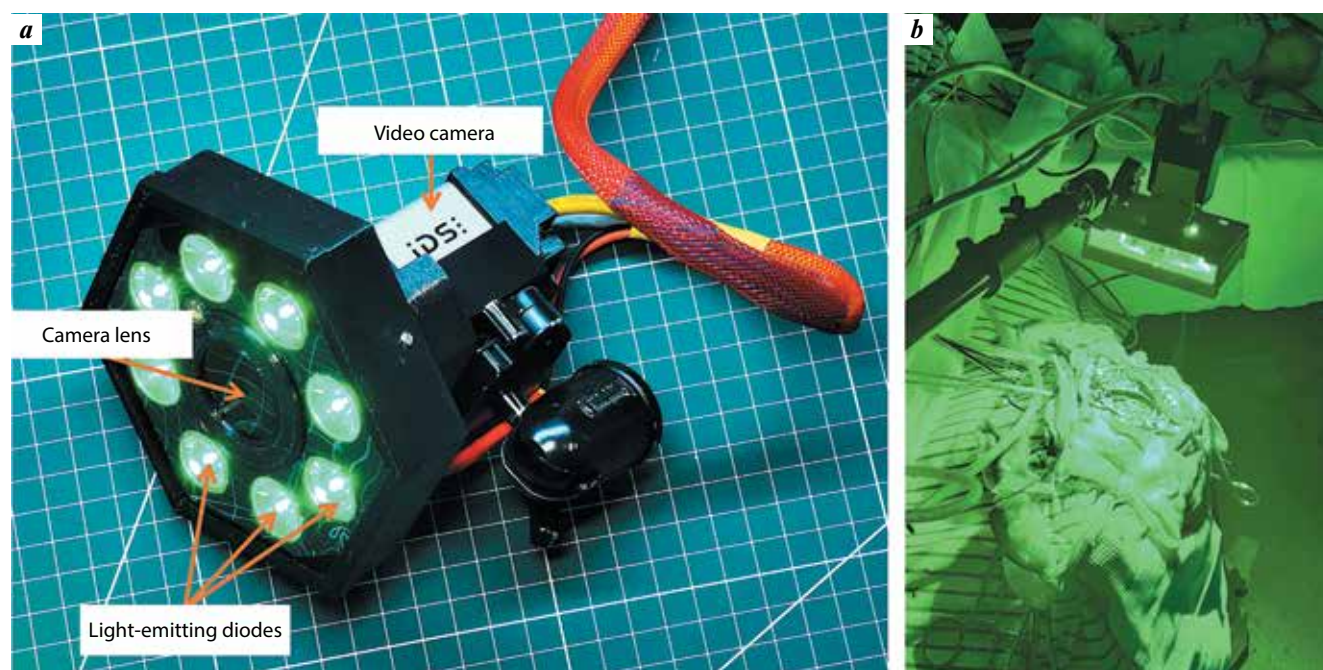


Fig. 2. Laboratory mock-up of a multimodal blood flow visualization and assessment system: a — a photograph of the imaging photoplethysmography unit consisting of 8 green LEDs fixed around the video camera; b — a general view of the intraoperative location of the illuminator with a camera over the operating wound during recording

transformed into bipolar value by subtraction of one and inversion so the changes in signal shape positively correlate with changes in arterial pressure [22, 28]. The obtained signal is called PGG signal, an example for one ROI is presented in Fig. 3. to demonstrate the effectiveness of stabilization algorithm, on Fig. 3, *a* the initial modulation of the size of mean pixel is shown; on Fig. 3, *b*, PGG signal calculated in the same ROI is shown. In the initial signal (see Fig. 3, *a*), periodic modulation is impossible to discern but after image stabilization pronounced modulation with heartbeat frequency correlating with ECG signal synchronously recorded with the video is apparent.

3. To evaluate the shape and value of mean PGG pulse in each ROI, we selected 15 subsequent cardiac cycles (see Fig. 3, *b*) and divided the calculated PGG signal into 15 parts so every next ECG R peak served as the start of temporal scale of each pulse. Mean PGG pulse shown on Fig. 3, *c* as a bold green line was calculated through averaging individual PGG pulses of 13 cardiac

cycles excluding the first and the last pulses as the most affected by artifacts. The difference between mean PGG pulse maximum and minimum, or amplitude of pulsatile component (APC) (see Fig. 3, *c*), is called perfusion index and reflects tone of the vessels supplying the studied tissue area [10, 12, 29, 30].

4. Mean PGG pulse is calculated for each ROI and is used to evaluate and plot spatial distribution of 2 blood flow parameters: perfusion index and time to pulse wave. The first parameter is described above, the second is the pulse transit time (PTT) from the heart to the measurement point or time of pulse pressure propagation which is defined as time delay between R peak and minimal mean PGG pulse corresponding to diastole duration. For greater clarity, spatial distributions of the cortical blood flow parameters are presented on the display coded through pseudo colors, and their distribution is layered atop the image of the studied area in the first selected frame for evaluation of mean PGG pulse. Examples of such distributions are presented in the *Discussion* section.

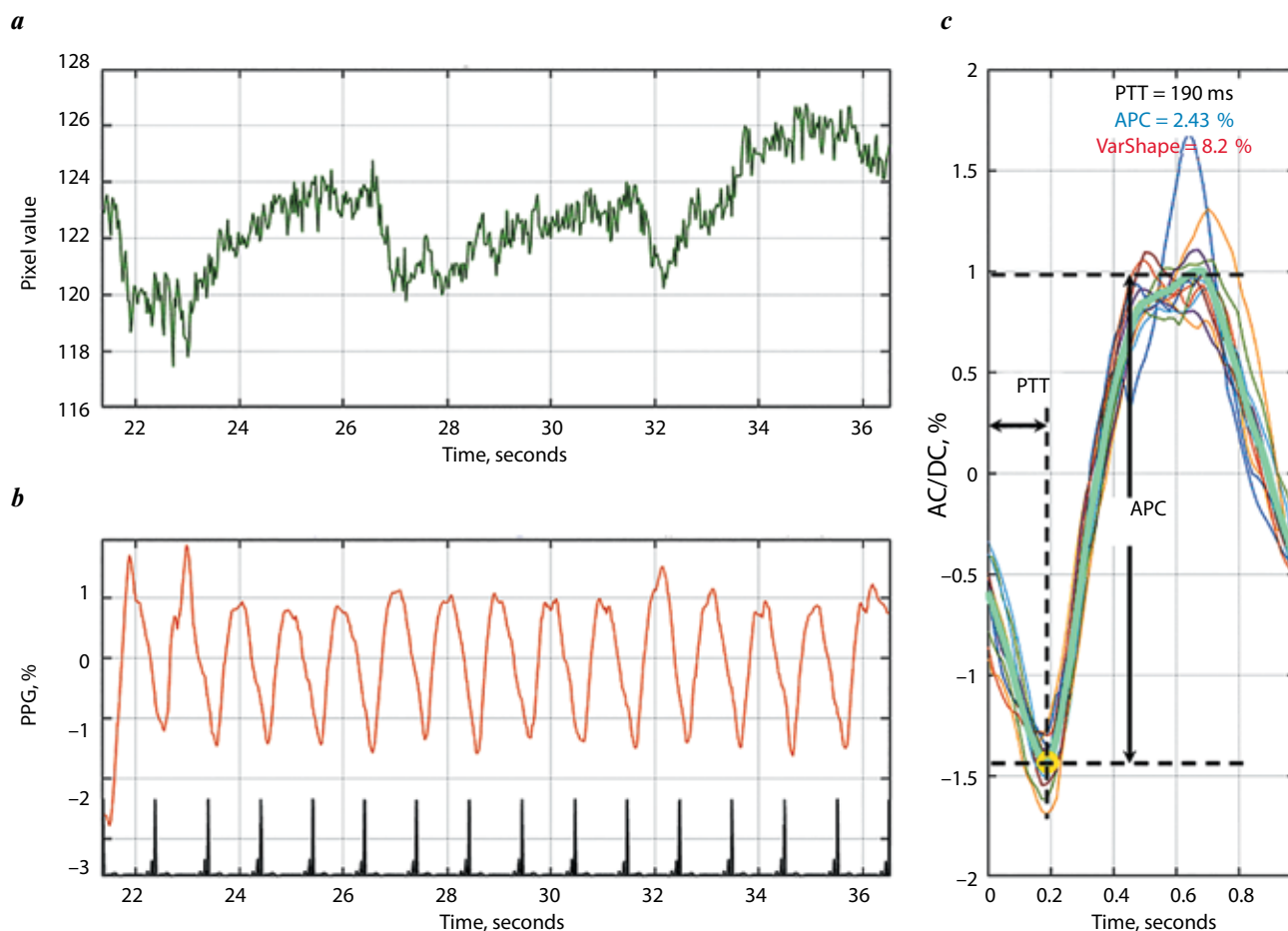


Fig. 3. An example of calculating the photoplethysmography (PPG) waveform in one of the regions of interest sizing 2×2 pixels: *a* – frame-by-frame evolution of the average pixel value before stabilization in 15 consecutive cardiac cycles; *b* – PPG signal after stabilization, normalization and inversion. Vertical lines on the time axis indicate synchronously recorded R-peaks of the electrocardiograms signal; *c* – thin colored lines show the PPG waveforms in 13 cardiac cycles superimposed on each other so that the beginning of each cycle is determined by the corresponding R-peak. The signal averaged over these 13 cycles is shown by a bold green line. Here and on Fig. 5, 6, 8: APC – amplitude of the pulsatile component; PTT – pulse wave transit time

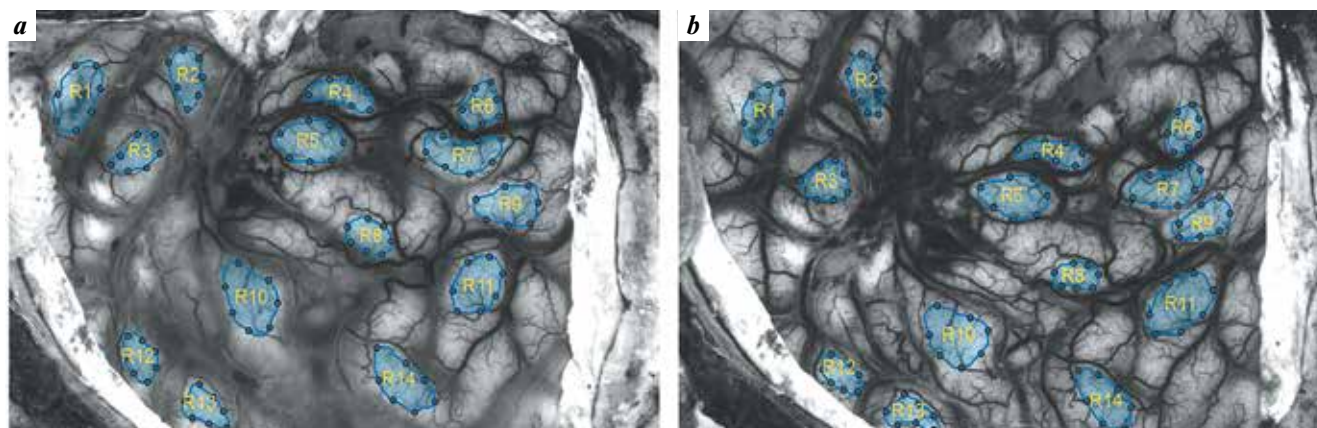


Fig. 4. An example of selecting large regions of interest before (a) and after (b) the main stage of the operation

Quantitative comparison of PGG distributions. During each surgery, 2 recordings of the illuminated surface of the cerebral cortex were performed: the 1st one immediately after dissection of the dura mater, the 2nd one after completion of the main surgery stage prior to dura mater suturing. Duration of each recording was 60 s. After that, for ~5 min calculation of spatial distributions of the APC and PTT parameters was performed. It should be noted that due to surgery the shape and position of cerebral lobes changes significantly which complicates quantitative comparison of the measured blood flow parameters before and after the main surgery stage. To solve this problem, the operator manually selected 14 or 15 large ROI (each consisting of 150 to 250 small 2×2 pixel ROI) in the most recognizable and comparable areas of the cortex not containing easily observable large vessels (Fig. 4). Additionally, the location of large ROI was chosen in a way so before and after surgery areas with the same numbers were located in anatomically comparable areas of the cortex. Then, APC and PTT parameters were averaged by all small ROI of the large ROI, and the parameters were compared to each other. Depending on the obtained measurements, preliminary conclusions on increase or decrease of blood supply to the same parts of the brain or its whole surface recorded by the IPGG camera could be made. After surgery, the obtained data were compared to CT results.

By themselves, calculated parameters of the PGG signal (APC and PTT) do not have any significance that can be cross-referenced with the traditional characteristics of tissue perfusion: linear or volumetric blood flow velocity or blood volume per 100 g of matter. PGG perfusion parameters can significantly differ between biological tissues and test subjects. However, comparison of these parameters at the same points in the beginning and at the end of a manipulation allows to make conclusions on the character of regional blood flow alteration. Clearly, decreased tone of arterial vessels leads to an increase in blood volume passing through the vessel. Moreover, amplitude of modulation of the neighboring capillaries inevitably leads to APC parameter increase. Therefore, increased APC is a sign

of increased blood flow through arterial vessels supplying the measured area.

PTT parameter reflects changes in blood supply to a biological tissue differently. If we assume that as a result of some pathology the studied area is supplied through possible collaterals, and after resolution of the problem blood starts to flow to this area through a natural and shorter pathways, then pulse wave propagation time should become shorter which is reflected in PTT parameter decrease. Therefore, we have defined the expected changes in the perfusion parameters measured by IPGG in response to improved or worsened blood supply of the studied area.

Statistical analysis. Statistical processing and graphing were performed using the GraphPad Prism v. 9 (GraphPad Software Inc., USA) software. From each value of APC (in %) and PTT (in ms) calculated for each ROI (from 9 to 15 ROI in the illuminated study area) of each patient before and after aneurysm clipping (more precisely, before traction of cerebral lobes to gain access to the affected vessels and after completion of the main stages prior to trepanation window closure) digital arrays were formed and compared pairwise. If according to the Shapiro–Wilk and Kolmogorov–Smirnov tests the data were distributed normally, t-test for matched samples was used to determine significance of differences between the “before” and “after” values. In cases of non-normal distribution, non-parametric Wilcoxon signed-rank test was used. If the distribution normalcy tests gave different results, non-parametric test was used due to relatively small ROI sample in each studied area. Significance level was defined as $\alpha = 0.05$. In the tables and plots, data are shown as mean value \pm standard deviation ($M \pm SD$) or as median with interquartile range ($Me [Q_1 - Q_3]$).

RESULTS

Cortical blood flow before and after aneurysm clipping.

It was established that cerebral aneurysm clipping causes major changes in parameters of cortical blood flow evaluated using the IPGG system. Typical blood flow changes are shown on Fig. 5 through distribution of the

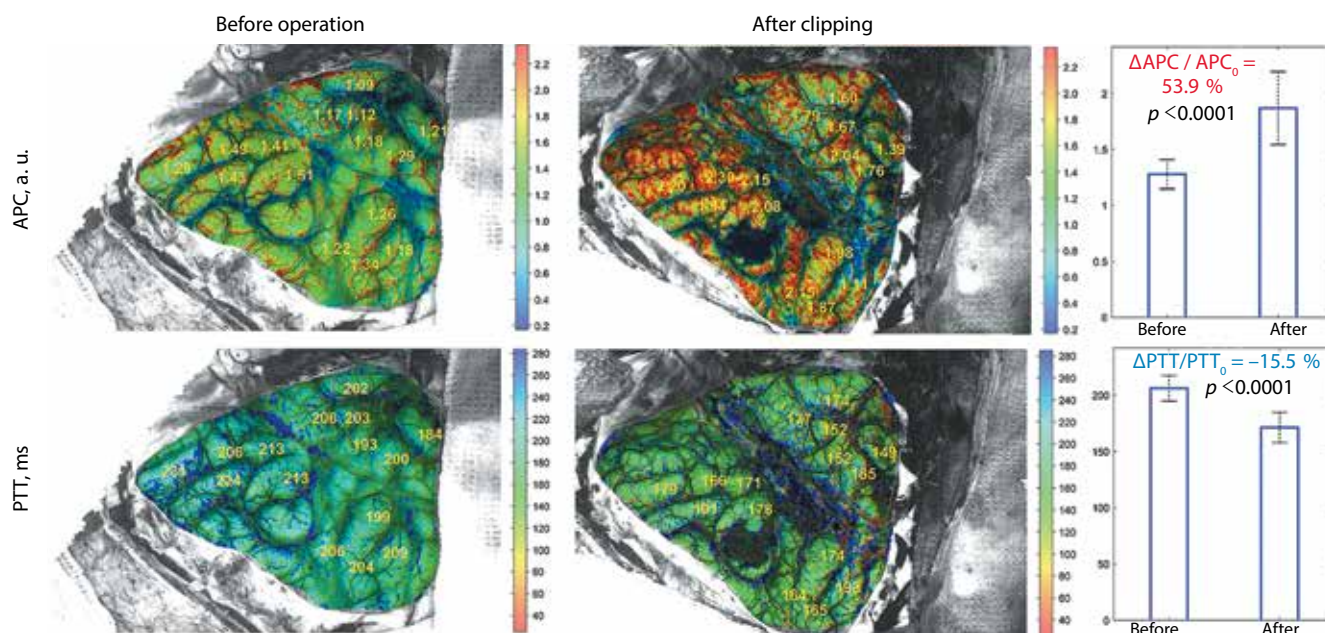


Fig. 5. Comparison of spatial distributions of cortical blood flow parameters before and after clipping of M3-segment of the middle cerebral artery aneurysm for patient 1. The left column shows the maps of blood flow parameters before surgery, and the central one — after. The right column shows the statistics of changes in each parameter calculated by the t-test

Table 2. Changes in the parameters of cortical blood flow during microsurgical clipping of cerebral artery aneurysms

Patient	Amplitude of the pulsatile component, %			Pulse transit time, ms		
	before clipping	after clipping	<i>p</i>	before clipping	after clipping	<i>p</i>
1	1.27 ± 0.13	1.90 ± 0.37	<0.0001	200 ± 15	171 ± 12	<0.0001
2	0.68 ± 0.22	1.24 ± 0.20	<0.0001	245 ± 33	191 ± 7	<0.0001
3	1.52 ± 0.17	1.63 ± 0.25	0.25	197 ± 11	163 ± 11	0.001
4	1.34 ± 0.47	2.14 ± 0.58	<0.0001	308 ± 34	241 ± 15	<0.0001
5	1.23 ± 0.43	1.15 ± 0.51	0.20	156 ± 19	159 ± 35	0.56
6	1.73 ± 0.39	1.62 ± 0.31	0.14	134 ± 14	104 ± 20	0.0002
All patients	1.28 ± 0.46	1.61 ± 0.53	<0.0001	193 [156–257]	171 [148–195]	<0.0001

2 measured perfusion parameters, APC and PTT, on the cerebral cortex. Yellow numbers on the spatial distribution maps on Fig. 5 correspond to the values of the parameters in the selected large ROI. Plots on the right reflect statistical comparison between APC and PTT before and after surgery performed between groups of large ROI using the t-test.

As seen on Fig. 5, in this case statistically significant differences in both parameters of cortical blood flow after aneurysm clipping are observed. Notably, while perfusion index increased after surgery, pulse wave propagation time decreased. Statistically significant APC increase was observed in 3 of the 6 studied cases of aneurysm clipping, statistically significant PTT decrease in 5 of 6. Changes in parameters of blood filling in the selected comparison areas before and after surgery are summarized in Table 2.

There were no significant changes in both parameters in patient 5. In cases of patients 3 and 6, as seen in Table 2,

APC parameter did not change significantly while PTT significantly decreased. Summation of data from all 6 patients showed significant differences between IPGG parameters before and after surgery, namely increase in APC and decrease in PTT.

Changes in cortical blood flow during brain traction. to identify possible hyperperfusion blood flow changes in response to prolonged displacement of a brain part during aneurysm access, IPGG study before and after frontal lobe traction for transwillis approach to a tumor of the insular area in 1 patient not included in the main cohort was performed. APC and PTT parameter distributions during the study are presented on Fig. 6. The changes in the studied parameters of cortical blood flow in the frontal and temporal lobes did not achieve statistical significance. Before traction perfusion index APC was 1.71 ± 0.31 %, after traction it was 1.65 ± 0.33 % ($p = 0.56$). Moreover,

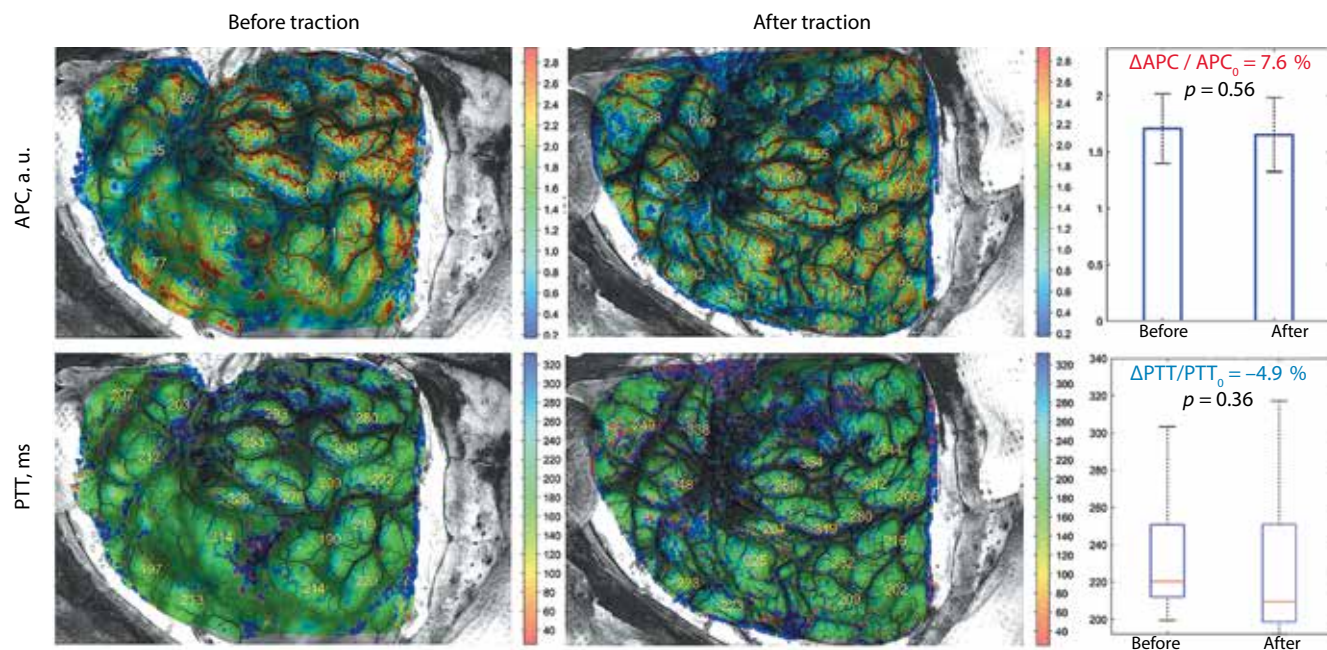


Fig. 6. Comparison of spatial distributions of cortical blood flow parameters before and after frontal lobe traction

changes in PTT were also insignificant: 220 [211–259] ms before traction and 209 [198–253] ms after traction ($p = 0.36$). Therefore, the hypothesis that cerebral perfusion parameters during aneurysm clipping change in response to frontal and temporal lobe traction was not confirmed.

DISCUSSION

As seen in Table 2, cerebral aneurysm clipping surgery causes changes in cerebral perfusion parameters. In 3 cases, APC increased; in 5 cases, PTT decreased which broadly characterizes increased blood filling of the studied area. In patient 5, no significant changes in these parameters were observed. The values of the parameters were calculated based on their mean values obtained in the same areas before and after surgical manipulation on the whole surface of the brain accessible for visualization after craniotomy.

The registered improvements in cerebral blood filling were likely caused by the manipulation on vessels during the main surgical stage. It is hard to imagine that aneurysm exclusion from the blood flow can in itself cause these changes but this possibility cannot be completely dismissed. And if lower blood supply can be explained by simple decrease in blood flow due to vessel stenting or its transient spasm in response to intervention, increased blood filling is supposedly associated with compensatory hyperperfusion after transient cerebral ischemia due to transient clamping of the large vessels. This interpretation can be used to explain IPGG parameters changes in patients 2 and 3, in which transient clamping of the A1 segment of the anterior cerebral artery on both sides was performed to separate the neck of aneurysm of the ACoA. This could cause formation of transient ischemia of the frontal lobes and compensatory hyperperfusion after blood flow restoration registered using IPGG through changes in APC and/or PTT. According

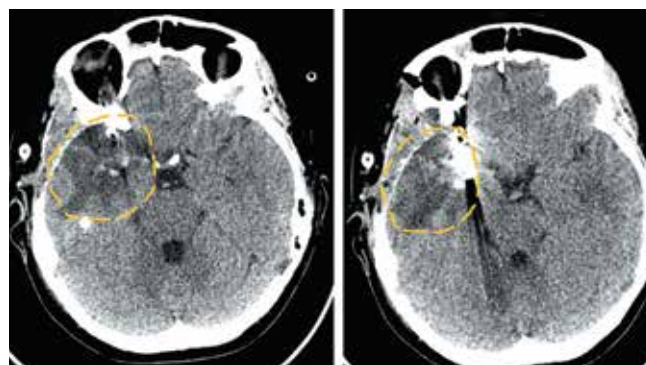


Fig. 7. Computed tomography of the brain of patient 5 after clipping of the M1–M2 segments aneurysm of the right middle cerebral artery. The zone of ischemia of the anterior parts of the right temporal lobe is marked with an orange dashed line

to CT performed immediately after surgery and on day 6, no ischemia foci formed except for the changes in the basal frontal lobes.

In patient 5 (aneurysm of the M1–M2 MCA segments), postoperative CT showed an area of ischemia in the anterior temporal lobe (Fig. 7). However, IPGG (Fig. 8) of the whole examination area did not show changes in perfusion parameters for this patient. It should be noted that PGG parameter evaluation separately in the temporal and frontal lobes showed significant decrease in PTT only in the frontal lobe while ARC for separate lobes did not significantly change.

In this case, the aneurysm was located on the MCA bifurcation. For its separation and clipping, transient clamping of the M1 MCA segment was performed. This segment is responsible for blood supply to the lower parts of the frontal lobe where significant PTT decrease was

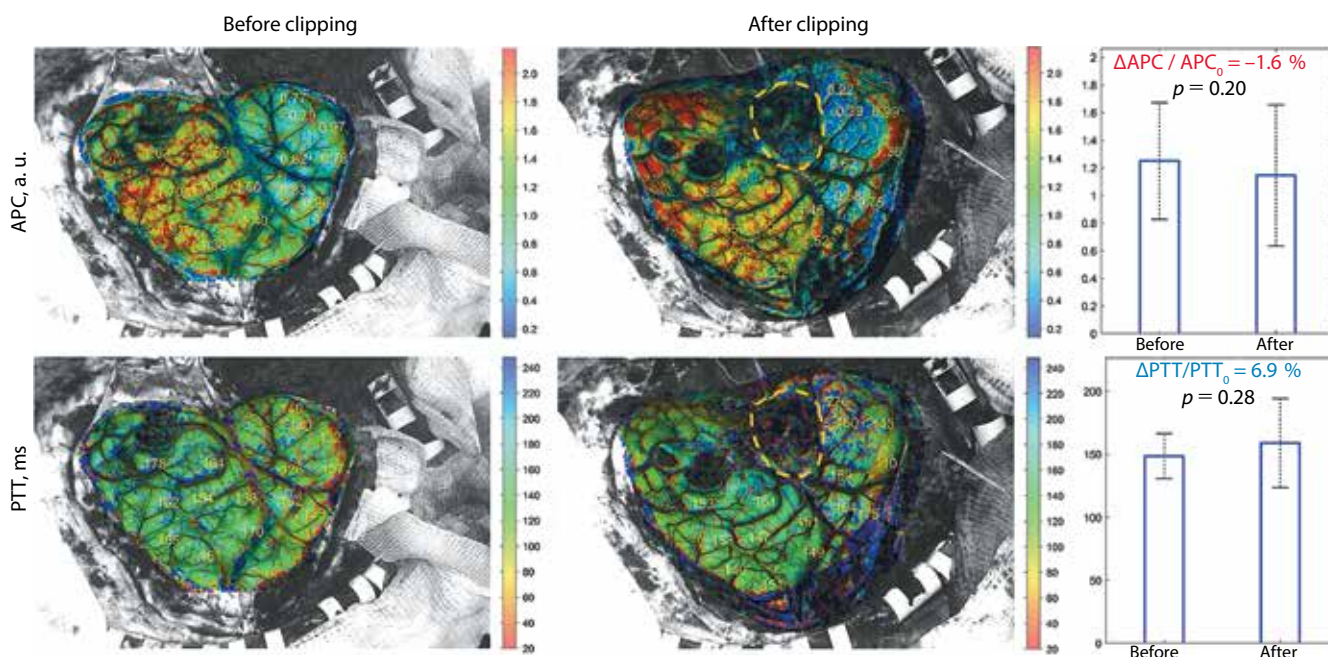


Fig. 8. Comparison of spatial distributions of cortical blood flow parameters before and after clipping of the M1–M2 segments aneurysm of the right middle cerebral artery in patient 5. Damaged region of the temporal lobe, in which measurements using imaging photoplethysmography are difficult, is marked with an orange dashed line

observed. During aneurysmal dome resection, anterior temporal lobe where CT showed ischemia was mechanically injured which made perfusion measurement using IPGG impossible (see Fig. 7, 8).

Explaining IPGG-measured perfusion parameters changes in cases of patients 1, 4 and 6 from the point of view of transient artery clipping is more difficult. Due to the absence of spatial and anatomical relations between the blood supply pool of the clamped artery and studied areas, there are no definite connection between the areas with increased blood flow and locations of temporary clamps. However, in all of these cases postoperative CT images did not show any ischemia areas in the studied parts of the brain.

Notably, in patient 1 IPGG measurement area included anterior and medial temporal lobe and partially frontal lobe. During surgery, it was necessary to temporarily clamp hypertrophic M3 MCA segment containing a large fusiform aneurysm requiring formation of a neck for clipping. Blood supply of the main part of the temporal lobe did not suffer and there were no CT signs of ischemic abnormalities after the surgery (Fig. 9, *a*). In this case, IPGG-measured perfusion parameters showed increased blood filling of the studied area. However, the delayed result of prolonged clamping of the M3 segment was formation of ischemia zone in the temporooccipital area located outside the trepanation window on day 3 after surgery (Fig. 9, *b*).

Interpretation of blood flow parameters registered with IPGG is very ambiguous and is based on the method of obtaining the values of PGG signal. APC is calculated from the difference in light absorption (maximal and

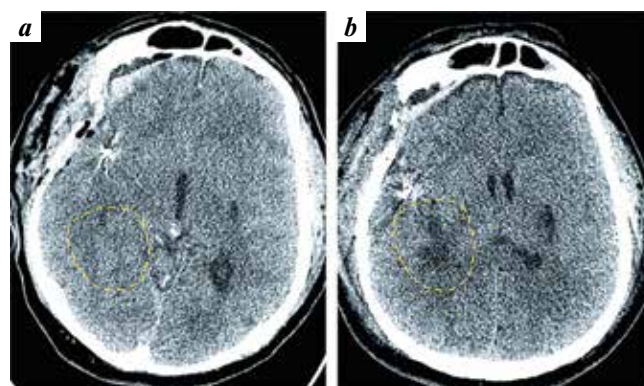


Fig. 9. Computed tomography of the brain of patient 1: *a* – immediately after the operation of clipping the M3 segment aneurysm of the right middle cerebral artery: no data for ischemic changes were found; *b* – three days after operation: the formation of an ischemic zone (marked with a yellow dashed line) of the deep sections of the right temporal lobe outside the trepanation window is visible

minimal) during one pulse wave. It is accepted that the larger it is the bigger are the oscillations of the artery wall which can be caused by lower tone and therefore larger diameter of the vessel increasing the volume of blood passing through it. Accordingly, APC index increase can serve as an indirect sign of vasodilation and increased blood flow.

The PTT parameter reflecting the velocity of pulse oscillation propagation in a vascular wall serves as an integral value depending both on heart function and condition of the main arteries and/or local microcirculatory network. Our data allows to suggest that PTT is an even

more sensitive marker of ischemic and reperfusion changes in the analyzed part of the brain than APC. If APC increase is mechanistically considered to be an indirect sign of vasodilation and increased tissue blood filling then decreased PTT can indicate acceleration or “levelling and vectorization” of blood flow due to, at least, reorganization of local hemodynamics, for example, bypass closure or changes in collateral blood supply.

Therefore, increased APC and/or decreased PTT correspond to classical increase in blood filling in the studied area in cases of the absence of initial deficit in inflowing blood supply.

CONCLUSIONS

- IPPG allows to intraoperatively evaluate changes in blood filling in the cerebral cortex during surgical treatment of cerebral arteries.

- Comparison of spatial distribution maps of the studied perfusion parameters before and after surgery allows to identify areas with increased or decreased blood flow.
- Accuracy of IPGG index measurement depends on the level of displacement of the cortex before and after the main surgical stage and its curvature: flat surfaces provide more accurate results.
- Brain traction does not cause statistically significant changes in blood flow parameters measured by IPGG.
- For successful blood flow monitoring through IPGG, intact capillary network on the surface of the studied area is necessary.
- Standard changes in IPGG signals characteristic of improved blood supply to the studied area of the brain are increased APC and decreased PTT; presumably, this is accurate only in cases of deficit-free blood filling and intact autoregulation of vascular tone.

REFERENCES

1. Fredrickson V.L., Russin J.J., Strickland B.A. et al. Intraoperative imaging for vascular lesions. *Neurosurg Clin N Am* 2017;28(4):603–13. DOI: 10.1016/j.nec.2017.05.011
2. Kakucs C., Florian I.A., Ungureanu G., Florian I.S. Fluorescein angiography in intracranial aneurysm surgery: a helpful method to evaluate the security of clipping and observe blood flow. *World Neurosurg* 2017;105:406–11. DOI: 10.1016/j.wneu.2017.05.172
3. Kazmi S.M.S., Richards L.M., Schrandt C.J. et al. Expanding applications, accuracy, and interpretation of laser speckle contrast imaging of cerebral blood flow. *J Cereb Blood Flow Metab* 2015;35:1076–84. DOI: 10.1038/jcbfm.2015.84
4. Shapey J., Xie Y., Nabavi E. et al. Intraoperative multispectral and hyperspectral label-free imaging: a systematic review of *in vivo* clinical studies. *J Biophotonics* 2019;12(9):e201800455. DOI: 10.1002/jbio.201800455
5. Mamontov O.V., Shcherbinin A.V., Romashko R.V., Kamshilin A.A. Intraoperative imaging of cortical blood flow by camera-based photoplethysmography at green light. *Appl Sci* 2020;10(18):6192. DOI: 10.3390/app10186192
6. Volynsky M.A., Mamontov O.V., Osipchuk A.V. et al. Study of cerebrovascular reactivity to hypercapnia by imaging photoplethysmography to develop a method for intraoperative assessment of the brain functional reserve. *Biomed Opt Express* 2022;13(1):184–96. DOI: 10.1364/BOE.443477
7. Sokolov A.Y., Volynsky M.A., Zaytsev V.V. et al. Advantages of imaging photoplethysmography for migraine modeling: new optical markers of trigemino-vascular activation in rats. *J Headache Pain* 2021;22(1):18. DOI: 10.1186/s10194-021-01226-6
8. Mamontov O.V., Sokolov A.Y., Volynsky M.A. et al. Animal model of assessing cerebrovascular functional reserve by imaging photoplethysmography. *Sci Rep* 2020;10(1):19008. DOI: 10.1038/s41598-020-75824-w
9. Sokolov A.Y., Volynsky M.A., Potapenko A.V. et al. Duality in response of intracranial vessels to nitroglycerin revealed in rats by imaging photoplethysmography. *Sci Rep* 2023;13:11928. DOI: 10.1038/s41598-023-39171-w
10. Lyubashina O.A., Mamontov O.V., Volynsky M.A. et al. Contactless assessment of cerebral autoregulation by photoplethysmographic imaging at green illumination. *Front Neurosci* 2019;13:1235. DOI: 10.3389/fnins.2019.01235
11. Hertzman A.B., Sealman C.R. Observations on the finger volume pulse recorded photoelectrically. *Am J Physiol* 1937;119:334–5. DOI: 10.1152/ajplegacy.1937.119.2.257
12. Reisner A., Shaltis P.A., McCombie D., Asada H.H. Utility of the photoplethysmogram in circulatory monitoring. *Anesthesiology* 2008;108(5):950–8. DOI: 10.1097/ALN.0b013e31816c89e1
13. Hertzman A.B. The blood supply of various skin areas as estimated by the photoelectric plethysmograph. *Am J Physiol* 1938;124:328–40. DOI: 10.1152/ajplegacy.1938.124.2.328
14. Nieveen J., Reichert W.J., van der Slikke L.B. Photoelectric plethysmography using reflected light. *Cardiologia (Basel)* 1956;29(3):160–73. DOI: 10.1159/000165601
15. Roberts V.C. Photoplethysmography-fundamental aspects of the optical properties of blood in motion. *Trans Inst Meas Control* 1982;4:101–6. DOI: 10.1177/014233128200400205
16. Verkruysse W., Svaasand L.O., Nelson J.S. Remote plethysmographic imaging using ambient light. *Opt Express* 2008;16(26):21434–45. DOI: 10.1364/OE.16.021434
17. Maeda Y., Sekine M., Tamura T. The advantages of wearable green reflected photoplethysmography. *J Med Syst* 2011;35(5):829–50. DOI: 10.1007/s10916-010-9506-z
18. Kamshilin A.A., Miridonov S., Teplov V. et al. Photoplethysmographic imaging of high spatial resolution. *Biomed Opt Express* 2011;2(4):996–1006. DOI: 10.1364/BOE.2.000996
19. Fallow B.A., Tarumi T., Tanaka H. Influence of skin type and wavelength on light wave reflectance. *J Clin Monit Comput* 2013;27:313–7. DOI: 10.1007/s10877-013-9436-7
20. Anderson R.R., Parrish J.A. The optics of human skin. *J Invest Dermatol* 1981;77(1):13–9. DOI: 10.1111/1523-1747.ep12479191
21. Bashkatov A.N., Genina E.A., Kochubey V.I., Tuchin V.V. Optical properties of human skin, subcutaneous and mucous tissues in the wavelength range from 400 to 2000 nm. *J Phys D Appl Phys* 2005;38(15):2543–55. DOI: 10.1088/0022-3727/38/15/004
22. Kamshilin A.A., Nippolainen E., Sidorov I.S. et al. A new look at the essence of the imaging photoplethysmography. *Sci Rep* 2015;5:10494. DOI: 10.1038/srep10494
23. Kamshilin A.A., Krasnikova T.V., Volynsky M.A. et al. Alterations of blood pulsations parameters in carotid basin due to body position change. *Sci Rep* 2018;8(1):13663. DOI: 10.1038/s41598-018-32036-7

24. Kamshilin A.A., Mamontov O.V. Imaging photoplethysmography and its applications. In: Photoplethysmography. Technology, signal analysis and applications. Ed. by J. Allen, P.A. Kyriacou. Academic Press, 2022. Pp. 439–468.
DOI: 10.1016/B978-0-12-823374-0.00014-1
25. Sidorov I.S., Volynsky M.A., Kamshilin A.A. Influence of polarization filtration on the information readout from pulsating blood vessels. Biomed Opt Express 2016;7(7):2469–74.
DOI: 10.1364/BOE.7.002469
26. Kashchenko V.A., Zaytsev V.V., Ratnikov V.A., Kamshilin A.A. Intraoperative visualization and quantitative assessment of tissue perfusion by imaging photoplethysmography: comparison with ICG fluorescence angiography. Biomed Opt Express 2022;13(7):3954–66.
DOI: 10.1364/BOE.462694
27. Kearney J.K., Thompson W.B., Boley D.L. Optical flow estimation: an error analysis of gradient-based methods with local optimization. IEEE Trans Pattern Anal Mach Intell 1987;9(2):229–44.
DOI: 10.1109/TPAMI.1987.4767897
28. Allen J. Photoplethysmography and its application in clinical physiological measurement. Physiol Meas 2007;28:R1–R39.
DOI: 10.1088/0967-3334/28/3/R01
29. Lima A.P., Beelen P., Bakker J. Use of a peripheral perfusion index derived from the pulse oximetry signal as a noninvasive indicator of perfusion. Crit Care Med 2002;30:1210–3.
DOI: 10.1097/00003246-200206000-00006
30. Zaramella P., Freato F., Quaresima V. et al. Foot pulse oximeter perfusion index correlates with calf muscle perfusion measured by near-infrared spectroscopy in healthy neonates. J Perinatol 2005;25:417–22. DOI: 10.1038/sj.jp.7211328

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Compliance with patient rights and principles of bioethics. The work was carried out in accordance with the ethical standards presented in the Helsinki Declaration of 2013. Permission to conduct the study was obtained through the Ethics Committee of the North-Western District Scientific and Clinical Center, decision No. 4 of 27.03.2023. All patients and/or their legal representatives provided voluntary informed consent in writing to participate in the study.