ISSN 1062-8738, Bulletin of the Russian Academy of Sciences: Physics, 2022, Vol. 86, Suppl. 1, pp. S85–S91. © Allerton Press, Inc., 2022.

Imaging Photoplethysmography as a Reliable Tool for Monitoring Tissue Perfusion during Open Brain and Abdominal Surgeries

A. A. Kamshilin[a, b, c, *] (ORCID: 0000-0003-2506-9736)

[a] *Institute of Automation and Control Processes, Far Eastern Branch, Russian Academy of Sciences, Vladivostok, 690041 Russia*

[b] *Sokolov North-Western District Scientific and Clinical Center, Federal Medical and Biological Agency, St. Petersburg, 194291 Russia*

[c] *Almazov National Medical Research Centre, St. Petersburg, 197341 Russia*

**e-mail: alexei.kamshilin@yandex.ru*

Received September 20, 2022; revised October 14, 2022; accepted October 20, 2022

Abstract—Assessment of microcirculation and tissue perfusion parameters is extremely important during surgical interventions, especially during operations on the brain and abdominal organs. Such a system must be handy, non-invasive, and directly integrated into the surgical workflow. To date, there is no standard procedure for assessing blood circulation in routine clinical practice. All the technical proposals are in the stage of research and development. This paper is discussing features of imaging photoplethysmography (IPPG) application to intraoperative visualization and quantitative assessment of tissue perfusion. Measurement of perfusion using photoplethysmography has been known since the 30s of the last century. Nevertheless, discussions of the physiological model underlying this method are still ongoing. An alternative model of light modulation in interaction with blood vessels in vivo was proposed in our group in 2015. Based on this model, we developed a system of intraoperative visualization of blood flow, which uses only video recording of a tissue under study followed by appropriate data processing. Distinguishing feature of the system is synchronous recording of video frames and electrocardiogram. The developed system allows for contactless monitoring of blood flow in cortex and abdominal organs in real time with high spatial resolution. This report is an overview of recent pilot studies on monitoring blood flow parameters during open brain and abdominal surgeries using the IPPG system. It was demonstrated that the quantitative assessment of blood perfusion by IPPG is in good agreement with that obtained by ICG-fluorescence angiography. IPPG can become an objective quantitative monitoring system for tissue perfusion in the operating room due to its simplicity, low cost and no need for any agent injections.

Keywords: optical technology, imaging photoplethysmography, intraoperative perfusion assessment, cerebral, abdominal

DOI: 10.3103/S1062873822700447

INTRODUCTION

Intraoperative monitoring of tissue perfusion is of great importance for optimizing surgery and reducing postoperative complications. However, there is no standard procedure for assessing blood circulation in routine clinical practice. The requirements for the measurement/visualization system are very tough: It should be easy to handle, contactless, and provide quantitative visualization of blood flow in a wide field of view in real time. Optical techniques are widely considered as very promising for contactless measurements of blood-flow parameters. Different methods such as indocyanine green fluorescence angiography (ICG-FA), laser speckle contrast imaging (LSCI), laser Doppler flowmetry, near infrared spectroscopy, hyperspectral imaging (HSI), sidestream darkfield microscopy (SDF), infrared thermographic imaging, and optical coherence tomography (OCT) have been researched as candidates for contactless intraoperative measurement of tissue perfusion [1]. There are two methods from this list (ICG-FA and LSCI) that use a conventional video camera to visualize perfusion, thereby providing the necessary conditions for implementation into clinical practice. Recent comparative study of four imaging modalities (LSCI, OCT, SDF, and ICG-FA) on performing an intraoperative quantitative perfusion assessment during oesophagectomy showed that the ICG-FA technique is the most promising for applications in real clinical conditions [2]. Both commercial and custom ICG-FA systems are available for intraoperative use; however, only feasibility studies have been performed [3]. ICG-FA has predominantly been performed using visual assessment of the fluorescence angiography, where the surgeon subjectively evaluates the fluorescence signal. However, the main disadvantage of ICG-FA evaluation is that

the assessment requires a fluorescence agent ICG to be injected locally or systemically before measurements. In addition, there are problems with perfusion monitoring in the prolonged time scale: repeated ICG injections in the presence of preexisting background fluorescence make it difficult to assess tissue perfusion [4].

It is worth noting that all of the above listed techniques for assessing blood flow were proposed much later than photoplethysmography (PPG), which was the first optical method for measuring blood perfusion in-vivo. Perfusion measurements using PPG has been known since the 30s of the last century [5]. Nevertheless, despite the long and high activity of research in this area, the widespread use of the PPG method in clinical practice began in the 80s after the invention of pulse oximetry [6]. However, pulse oximeters are contact-type sensors that assess blood flow parameters at a single point of the tissue. A significant step in the PPG development was made in the end of the 20th century, when it was proposed to obtain information about blood circulation using a video recording of biological tissue with a conventional camera [7]. This approach is called imaging photoplethysmography (IPPG); it is completely contactless and allows visualization with quantitative assessment of blood flow simultaneously in a large number of points. Significant advantage of the IPPG system is the ability to measure not only spatially resolved local perfusion strength [8, 9] but also the relative phase of the pulse wave arrival in various areas of the biological tissue [10, 11]. Moreover, it is a simple, noninvasive, inexpensive, and easy-to-use tool. Nevertheless, intraoperative applications of IPPG are currently also at the research and development stage. One of the reasons for the difficulties with the clinical implementation of this method is that the physiological model of PPG waveform formation remains a subject of continuing debate in spite of intensive investigations over a long time.

The conventional model of the PPG waveform generation assumes that the main reason of the light-intensity modulation registered by the photodetector is variations of the blood volume in the tissue [5, 12]. However, this model fails to explain why the greatest modulation of light intensity at the heart rate is observed at the green wavelength [13, 14], the light of which does not interact with pulsating vessels (arteries and arterioles), whereas the capillaries efficiently absorbing this light do not pulsate [15]. To resolve this contradiction, an alternative model of light interaction with blood vessels in vivo was proposed in 2015 that considers modulation of the blood volume in the capillary bed due to mechanical compression/decompression of the density of capillaries by adjacent arteries [16]. Based on this theoretical model, our group developed an IPPG system for intraoperative quantitative assessment of blood flow parameters in organs.

This minireview focuses on discussion of features and prospects of IPPG system for intraoperative quantitative assessment of tissue perfusion. Special attention is paid to description of recent pilot studies carried out during brain and abdominal surgeries.

MEASURING SYSTEM AND DATA PROCESSING

Instrumental implementation of an IPPG system can be quite straightforward: only a video camera with illumination of the tissue is required. Description of the custom-made IPPG system in details can be found elsewhere [10, 17]. Briefly, it consists of a monochrome camera and several light-emitting diodes (LEDs) mounted around the camera lens, which illuminate a tissue region by green light (the wavelength of 530 ± 30 nm). Incoherent light from LEDs was linearly polarized by thin-film polarizer, whereas the light returned from the tissue was filtered by another polarizer (with orthogonal orientation) attached to the camera lens (see Fig. 1). Such polarization filtration reduces both the skin specular reflections and influence of motion artefacts on the detected PPG waveform [18]. Choice of the system parameters (incoherent green light, monochrome camera, and polarization filtration) was determined by the need to achieve the highest signal-to-noise ratio (SNR) of PPG signal, which is the key parameter in any measuring system [19]. The most important distinguishing feature of our IPPG system is recording of video frames synchronously with an electrocardiogram. Synchronization accuracy between the electrocardiograph and the camera was better than 1 ms that allows us to use correlation analysis aimed at increasing sensitivity when detecting tiny light modulations associated with cardiac activity against a highly variable background.

Recorded video frames were processed jointly with ECG by using an algorithm described in details in [4, 10]. It includes five stages: (a) image stabilization, (b) calculation of the PPG waveform in each pixel within a floating window of 12–15 cardiac cycles, (c) evaluating the PPG pulse shape averaged over the selected cycles, (d) assessing the amplitude of blood pulsations in each pixel, and (e) mapping the perfusion index. The processing pipeline of the algorithm used for visualization and quantitative assessment of blood-flow parameters using IPPG is shown in Fig. 2 on the example of intraoperative assessment of colon perfusion.

INTRAOPERATIVE MONITORING OF CEREBRAL BLOOD FLOW

We recently conducted pilot studies to assess feasibility of cerebral-microcirculation monitoring during open brain surgery using multimodal IPPG–ECG system [20]. Cortical blood flow was monitored in five patients with different diagnoses. Two cases (tumor

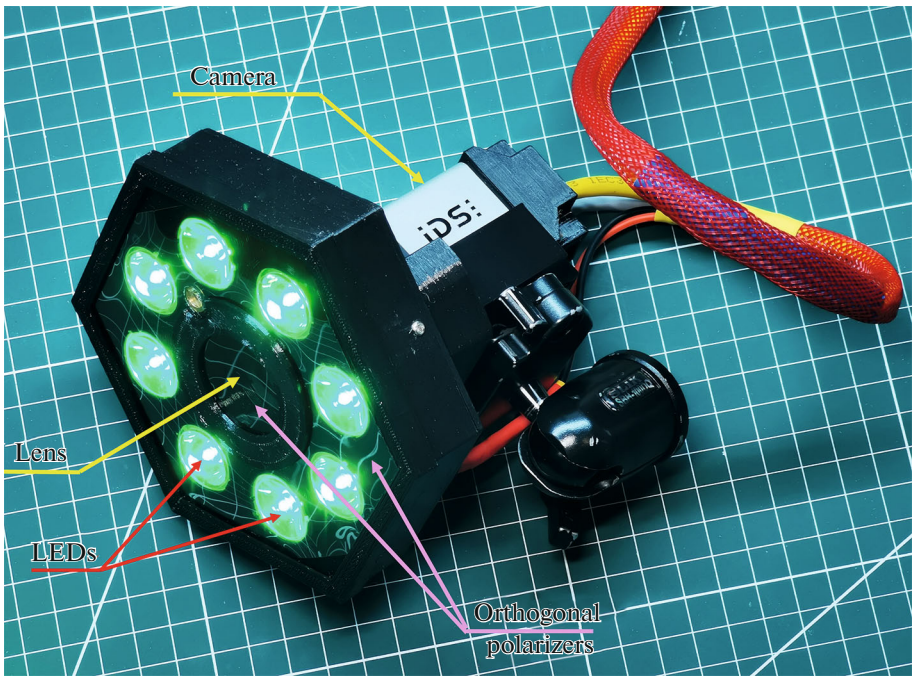

Fig. 1. Photograph of the custom-made IPPG module consisting of a digital camera, green LEDs, and mutually orthogonal polarizing films.

resection and extra-intracranial bypass grafting) were presented in detail. Good quality and highly resolved spatial distributions of hemodynamic parameters perfusion index (AC/DC) and pulse arrival time (PAT) were obtained in all studied cases. An example of assessing the microcirculation parameters during surgical intervention of a patient with atherosclerotic occlusion of the internal carotid artery after ischemic stroke is shown in Fig. 3. Maps of the blood-flow parameters measured before and after applying anastomosis overlaid with photographs of the open brain are shown in the left and right columns of Fig. 3, respectively. Perfusion maps are shown in Figs. 3a and 3c, and PAT maps are shown in Figs. 3b and 3d. Comparing the maps of AC/DC before and after surgery (Figs. 3a and 3c), one can see not only significant diminishing of the perfusion index after anastomosis (note the big difference in the color scale of these maps) but also strong change in the perfusion index pattern. The mean perfusion index in the whole cortex were 2.13 ± 0.50 and 0.80 ± 0.07 before and after the anastomosis, respectively. We hypothesize that the observed decrease in perfusion after anastomosis is caused by an increase in the volumetric blood-flow velocity, which, through the autoregulation mechanism, increases the vascular tone, ensuring the constancy of cerebral perfusion. A similar decrease in perfusion of the cerebral cortex of animals was recently observed in response to an increase in systemic arterial pressure [17].

Even more flashy changes can be seen comparing PAT maps before and after anastomosis. Before anastomosis, PAT had extremely heterogeneous distribution (Fig. 3b), whereas the travel time of the pulse wave turned out to be uniformly distributed after (Fig. 3d). The prolonged arrival time of the pulse wave before anastomosis was caused by the brain's supply via the collateral artery. The mean PATs in the whole cortex were 407 ± 137 and 147 ± 117 ms before and after the surgery, respectively. The difference in hemodynamics due to anastomosis becomes even more evident when analyzing the stability of the PPG pulse shape. The graphs to the left of the perfusion/PAT maps in Fig. 3 show the variability of the PPG waveform in three representative points before surgery, while similar graphs to the right show the shape variability in the same points after anastomosis. It is clearly seen that the PPG-pulse shape is extremely unstable before surgery (graphs to the left in Fig. 3) whereas revascularization results in considerable stabilization of the pulse waveform (graphs to the right) and recovery of typical PAT-value despite a significant decrease in the amplitude of pulsations. We hypothesize that atherosclerotic occlusion is the main reason for the observed instability of the blood-pressure wave reaching the cortex, enforcing blood flow to be additionally supplied via various circumferential routes. The observed stabilization of the pulse shape after anastomosis is a consequence of recovery of the direct pathway of blood supply to the cerebral cortex [20].

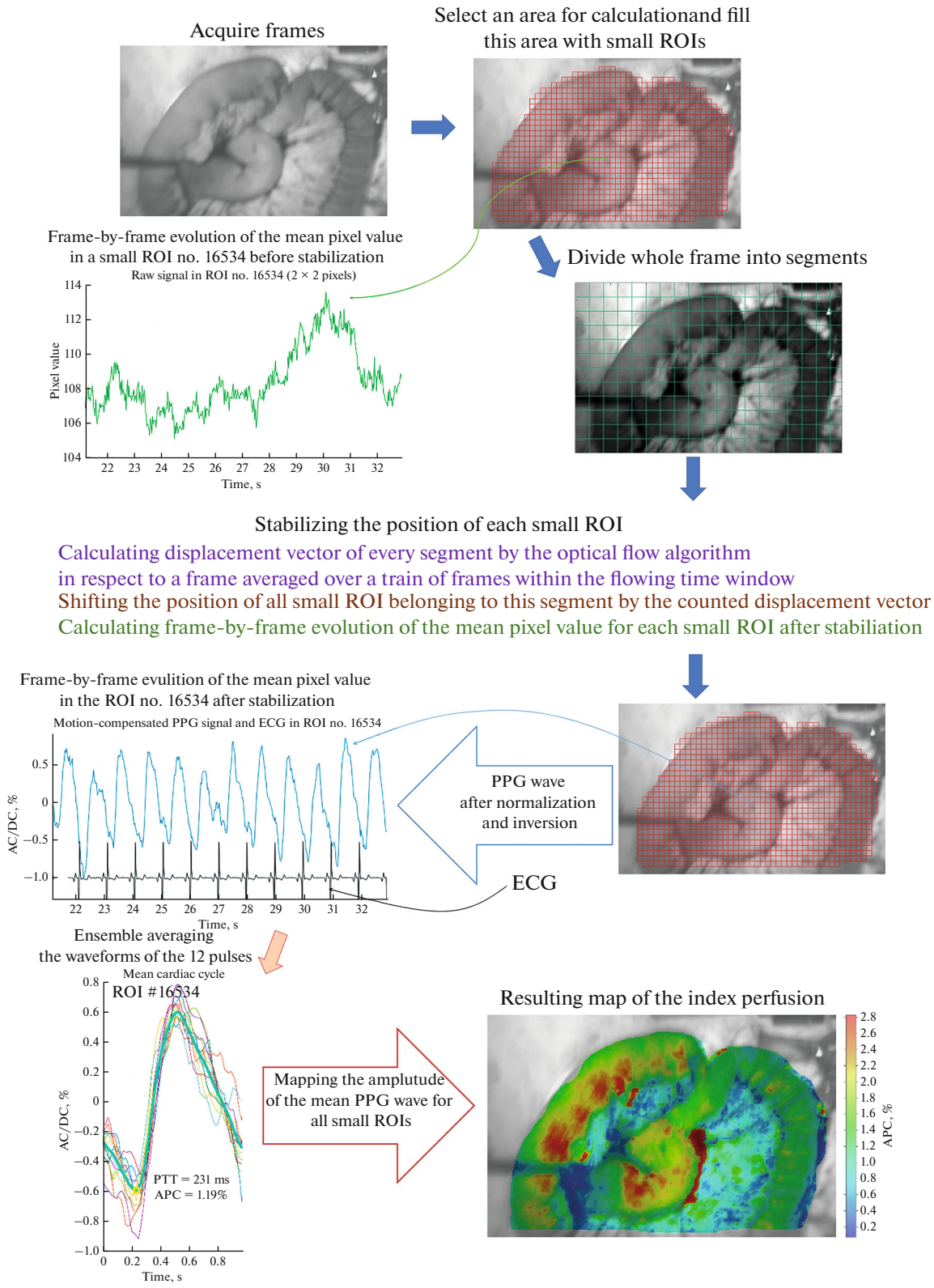

Fig. 2. Processing pipeline of the algorithm for perfusion index assessment in the multimodal IPPG–ECG system.

The experimental data indicates that the multimodal IPPG-ECG system operating at green illumination offers a new approach to objective quantitative assessment of the blood-flow changes in cerebral microvessels caused by surgical interventions.

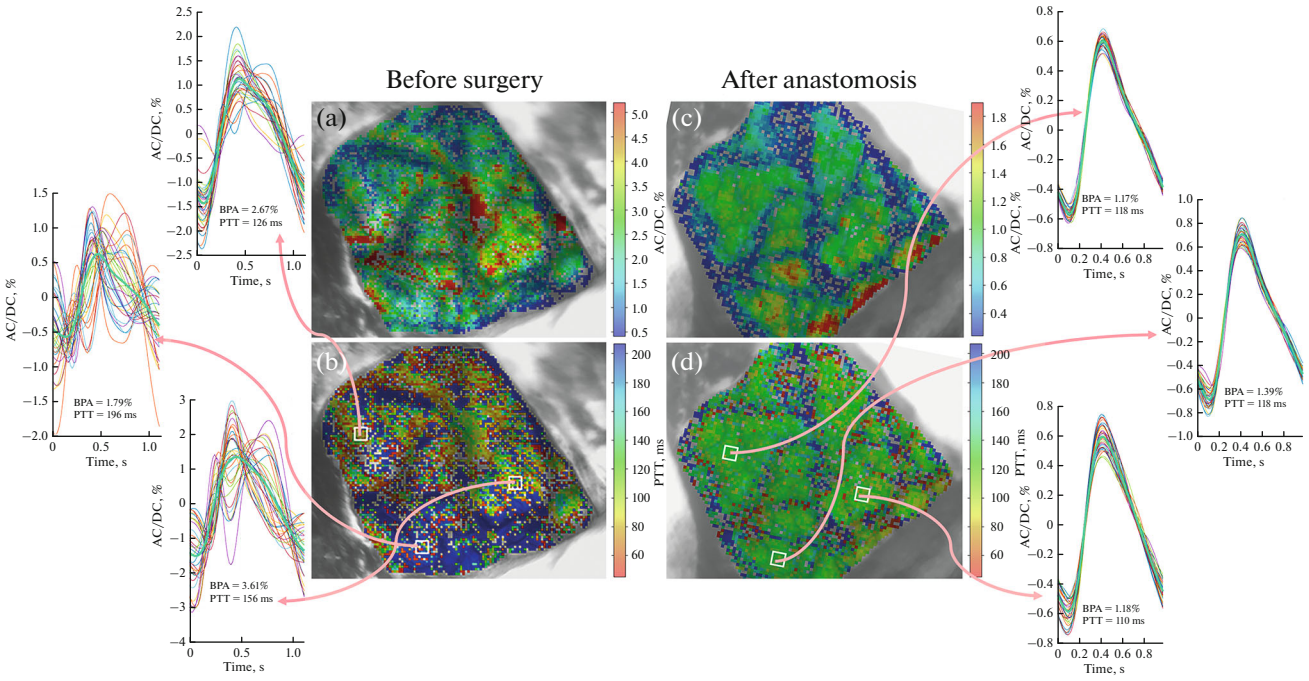

Fig. 3. Parameters of pulsatile blood flow in an open brain cortex before (left column) and after (right column) anastomosis application: The maps of the perusion index are shown in panels (a) and (c), whereas maps of the pulse arrival time (PAT) are shown in panels (b) and (d). The graphs to the left of the images show the variability of the PPG waveform in three representative points before surgery. The thin color lines in these graphs show PPG pulses of 15 consecutive cardiac cycles calculated in the selected points. The thick green lines in these graphs are PPG pulses averaged over these 15 cardiac cycles. The graphs to the right of the images show the variability of the PPG waveform in the same points after surgery.

BLOOD PERFUSION MONITORING DURING ABDOMINAL SURGERY

The use of IPPG in the abdominal space is a challenging task due to significant variations in the morphology of the studied organs caused by respiration and peristalsis. These variations lead to motion artifacts that are many times higher than the changes in the returned light intensity due to blood pulsations. As is known, the main problem of IPPG systems is their weak resistance to motion artifacts [21, 22], which becomes even more serious in the case of variable geometry of the tissue under study. However, the multimodal approach (synchronous recording of IPPG at green light and ECG) allowed us to solve these problems. Recently we demonstrated feasibility of this technology to visualizing and quantifying the perfusion in organs during abdominal surgery [23]. In our study, we followed 14 different surgical cases (four stomach and ten colorectal cancers) requiring reconstruction of various organs with anastomosis. Blood perfusion was successfully visualized and quantified in all 14 patients. This was the first demonstration of perfusion monitoring using the IPPG–ECG system performed in real clinical conditions. A month later, another group from the Netherlands also demonstrated feasibility of using the IPPG technique for tissue perfusion assessment during intestinal surgery [24].

Most recently, we compared our multimodal IPPG-ECG and a commercial ICG-fluorescence system for intraoperative assessment of tissue perfusion during eight different gastrointestinal surgeries [4]. It was shown that the intraoperative tissue-perfusion distribution quantified with the multimodal IPPG–ECG system matches well the distributions obtained with ICG-FA. An example of such comparison is shown in Fig. 4. The correlation between measured distributions of tissue perfusion was observed in all eight cases without exclusion. As it was shown during the comparative study in a clinical operating room [4], the Pearson correlation coefficients between the spatial distributions of the perfusion index obtained using both visualization methods turned out to be very high: $0.85 \le r \le 0.96$; $P < 0.01$. The observed matching of the perfusion distributions obtained by the two methods once again confirms that the alternative model of the light interaction with blood vessels [16] is more correct than the classical one. Indeed, ICG-FA uses infrared light that penetrates much deeper into the tissue [25] than the green light used in our IPPG. It is assumed that the intensity of fluorescence corresponds to the blood volume because the concentration of fluorophore is fairly uniformly distributed in the blood vessels [26]. In contrast, the green light interacts only with superficial blood vessels due to its very small penetration depth, less than 0.5 mm [27]. Nonetheless,

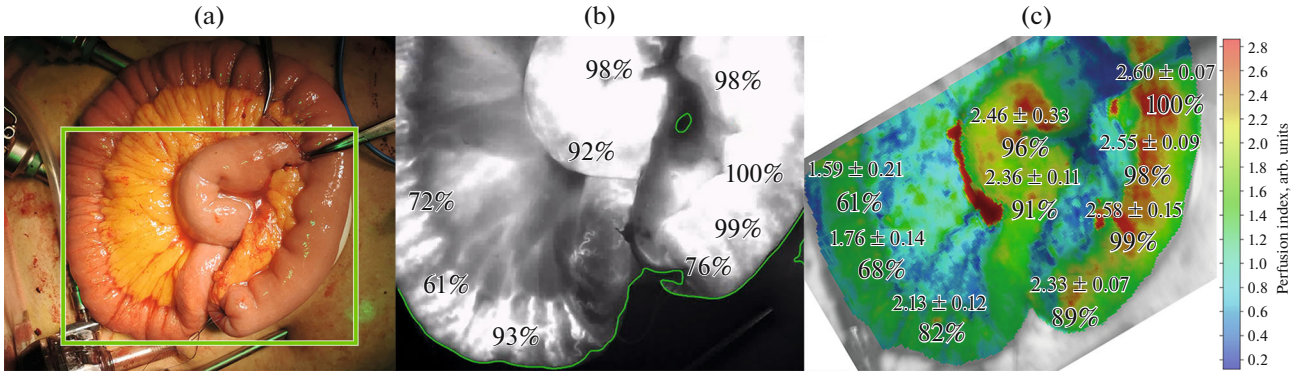

Fig. 4. Comparison of the perfusion distribution at the second step of reconstruction (after anastomosis) in the case distal laparoscopic gastrectomy with D2 lymphadenectomy for cancer of the antrum. (a), Photograph of the prepared alimentary and biliopancreatic loops, (b), perfusion visualization by ICG-fluorescence imaging, and (c), by the multimodal IPPG–ECG system. The green rectangle in the panel (a) indicates the location of organs in the frame for assessing perfusion.

the network of the superficial vessels acts as a distributed sensor of the pulsating transmural pressure in larger arteries located much deeper, but near the measuring point. Due to the tissue compression by transmural pressure at the locality of the measurement, both absorption and scattering coefficients of the light are increasing that lead to corresponding changes in the reflected light intensity. Therefore, a change in the amplitude of PPG waveform is associated with a change in arterial tone [17, 28, 29], which determines the blood supply to the tissue.

CONCLUSIONS

Synchronous recording of video and ECG allowed us to obtain highly resolved spatial distributions of three parameters of the blood flow in cerebral microvessels (APC, PAT, and shape of PPG pulses) that provides useful information for maximizing positive surgical outcome and minimizing risk. The multimodal IPPG–ECG system enables a new technique of tissue perfusion visualization and quantization with following advantages: no needs of any substance injection, possibility of continuous perfusion monitoring, simplicity and low cost of the equipment. These features should benefit both surgeons and patients by reducing probability of postoperative complications. The low cost of the components of the multimodal IPPG system, the high information content and noncontact nature of the method, as well as its ease of use determine great prospects for its wide application in clinical practice. Further development of imaging photoplethysmography and deeper understanding of its physiological basis will help clarify the prognostic factors of a threatening decrease in perfusion, and the introduction of pharmacological tests will open up the possibility of drug correction of circulatory disorders.

FUNDING

This research was financially supported by the Russian Science Foundation (Grant no. 21-15-00265).

CONFLICT OF INTEREST

The author declares that he has no conflicts of interest.

REFERENCES

1. Jansen, S.M., de Bruin, D.M., van Berge Henegouwen, M.I., Strackee, S.D., Veelo, D.P., van Leeuwen, T.G., and Gisbertz, S.S., *Dis. Esophagus* 2018, vol. 31, dox161. https://doi.org/10.1093/dote/dox161
2. Slooter, M.D., Jansen, S.M.A., Bloemen, P.R., van den Elzen, R.M., Wilk, L.S., van Leeuwen, T.G., van Berge Henegouwen, M.I., de Bruin, D.M., and Gisbertz, S.S., *Appl. Sci.*, 2020, vol. 10, p. 5522. https://doi.org/10.3390/app10165522
3. Lütken, C.D., Achiam, M.P., Osterkamp, J., Svendsen, M.B., and Nerup, N., *Langenbeck's Arch. Surg.*, 2021, vol. 406, p. 251. https://doi.org/10.1007/s00423-020-01966-0
4. Kashchenko, V.A., Zaytsev, V.V., Ratnikov, V.A., and Kamshilin, A.A., *Biomed. Opt. Express*, 2022, vol. 13, p. 3954. https://doi.org/10.1364/BOE.462694
5. Hertzman, A.B., *Am. J. Physiol.*, 1938, vol. 124, p. 328. https://doi.org/10.1152/ajplegacy.1938.124.2.328
6. J. W. Severinghaus and Honda, Y., *J. Clin. Monit. Comput.*, 1987, vol. 3, p. 135. https://doi.org/10.1007/BF00858362
7. Wu, T., Blazek, V., and Schmitt, H.J., *Proc. SPIE*, 2000, vol. 4163, p. 62.
8. Kamshilin, A.A., Miridonov, S., Teplov, V., Saarenheimo, R., and Nippolainen, E., *Biomed. Opt. Express*, 2011, vol. 2, p. 996. https://doi.org/10.1364/BOE.2.000996

9. Trumpp, A., Schell, J., Malberg, H., and Zaunseder, S., *Curr. Dir. Biomed. Eng.*, 2016, vol. 2, p. 199. https://doi.org/10.1515/cdbme-2016-0045
10. Kamshilin, A.A., Krasnikova, T.V., Volynsky, M.A., Miridonov, S.V., and Mamontov, O.V., *Sci. Rep.*, 2018, vol. 8, p. 13663. https://doi.org/10.1038/s41598-018-32036-7
11. Fleischhauer, V., Ruprecht, N., and Zaunseder, S., *Curr. Dir. Biomed. Eng.*, 2019, vol. 5, p. 105. https://doi.org/10.1515/cdbme-2019-0027
12. Reisner, A., Shaltis, P.A., McCombie, D., and Asada, H.H., *Anesthesiology*, 2008, vol. 108, p. 950. https://doi.org/10.1097/ALN.0b013e31816c89e1
13. Cui, W., Ostrander, L.E., and Lee, B.Y., *IEEE Trans. Biomed. Eng.*, 1990, vol. 37, p. 632. https://doi.org/10.1109/10.55667
14. Maeda, Y., Sekine, M., and Tamura, T., *J. Med. Syst.*, 2011, vol. 35, p. 829. https://doi.org/10.1007/s10916-010-9506-z
15. Fung, Y.C., Zweifach, B.W., and Intaglietta, M., *Circ. Res.*, 1966, vol. 19, p. 441. https://doi.org/10.1161/01.RES.19.2.441
16. Kamshilin, A.A., Nippolainen, E., Sidorov, I.S., Vasilev, P.V., Erofeev, N.P., Podolian, N.P., and Romashko, R.V., *Sci. Rep.*, 2015, vol. 5, p. 10494. https://doi.org/10.1038/srep10494
17. Lyubashina, O.A., Mamontov, O.V., Volynsky, M.A., Zaytsev, V.V., and Kamshilin, A.A., *Front. Neurosci.*, 2019, vol. 13, p. 1235. https://doi.org/10.3389/fnins.2019.01235
18. Sidorov, I.S., Volynsky, M.A., and Kamshilin, A.A., *Biomed. Opt. Express*, 2016, vol. 7, p. 2469. https://doi.org/10.1364/BOE.7.002469
19. Zaunseder, S., Vehkaoja, A., Fleischhauer, V., and Hoog Antink, C., *Biomed. Signal Process. Control*, 2022, vol. 74, 103538. https://doi.org/10.1016/j.bspc.2022.103538
20. Mamontov, O.V., Shcherbinin, A.V., Romashko, R.V., and Kamshilin, A.A., *Appl. Sci.*, 2020, vol. 10, p. 6192. https://doi.org/10.3390/app10186192
21. de Haan, G. and van Leest, A., *Physiol. Meas.*, 2014, vol. 35, p. 2878. https://doi.org/10.1088/0967-3334/35/9/1913
22. Sun, Y., Hu, S., Azorin-Peres, V., Greenwald, S.E., Chambers, J., and Zhu, Y., *J. Biomed. Opt.*, 2011, vol. 16, p. 77010. https://doi.org/10.1117/1.3602852
23. Kamshilin, A.A., Zaytsev, V.V., Lodygin, A.A., and Kashchenko, V.A., *Sci. Rep.*, 2022, vol. 12, p. 1143. https://doi.org/10.1038/s41598-022-05080-7
24. Lai, M., van der Stel, S.D., Groen, H.C., van Gastel, M., Kuhlmann, K.F.D., Ruers, T.J.M., and Hendriks, B.H.W., *J. Imaging*, 2022, vol. 8, 94. https://doi.org/10.3390/jimaging8040094
25. van Manen, L., Handgraaf, H.J.M., Diana, M., Dijkstra, J., Ishizawa, T., Vahrmeijer, A.L., and Mieog, J.S.D., *J. Surg. Oncol.*, 2018, vol. 118, p. 283. https://doi.org/10.1002/jso.25105
26. Son, G.M., Kwon, M.S., Kim, Y., Kim, J., Kim, S.H., and Lee, J.W., *Surg. Endosc.*, 2019, vol. 33, p. 1640. https://doi.org/10.1007/s00464-018-6439-y
27. Anderson, R.R. and Parrish, J.A., *J. Invest. Dermatol.*, 1981, vol. 77, p. 13. https://doi.org/10.1111/1523-1747.ep12479191
28. Rasche, S., Huhle, R., Junghans, E., de Abreu, M.G., Ling, Y., Trumpp, A., and Zaunseder, S., *Sci. Rep.*, 2020, vol. 10, p. 16464. https://doi.org/10.1038/s41598-020-73531-0
29. Volynsky, M.A., Mamontov, O.V., Osipchuk, A.V., Zaytsev, V.V., Sokolov, A.Y., and Kamshilin, A.A., *Biomed. Opt. Express*, 2022, vol. 13, p. 184. https://doi.org/10.1364/BOE.443477