Laser Speckle Contrast Imaging in Neurosurgery: A Systematic Review

Anton Konovalov[1], Vadim Gadzhiagaev[1], Fyodor Grebenev[1], Dmitry Stavtsev[2,3], Gennadii Piavchenko[4], Alexander Gerasimenko[2,3], Dmitry Telyshev[2,3], Igor Meglinski[5,6], Shalva Eliava[1]

[1]Department of Cerebrovascular Surgery, Burdenko Neurosurgical Center, Moscow, Russian Federation;
[2]Institute for Bionic Technologies and Engineering, I.M. Sechenov First Moscow State Medical University;
[3]National Research University of Electronic Technology, Institute of Biomedical Systems;
[4]Department of Human Anatomy and Histology, I.M. Sechenov First Moscow State Medical University, Moscow, Russia;
[5]Opto-Electronics and Measurement Techniques, Faculty of Information and Electrical Engineering, University of Oulu, Oulu, Finland;
[6]College of Engineering and Physical Sciences, Aston University, Birmingham, UK

Correspondence: Anton N. Konovalov, Ph.D.
E-mail: ankonovalov@nsi.ru

Key words: Aneurysm, Cerebral blood flow, Cerebral perfusion, Laser speckle contrast imaging, LSCI, Neurosurgery

Abbreviations and acronyms: AVM: Arteriovenous malformation; CBF: Cerebral blood flow; ICGA: Indocyanine green angiography; LSCI: Laser speckle contrast imaging

ABSTRACT

BACKGROUND: Intraoperative study of blood flow in the brain vessels is among the most critical topics of modern neurosurgery. One of the promising methods for intraoperative monitoring of blood flow is laser speckle contrast imaging (LSCI). This systematic review aims to analyze the experience of using intraoperative LSCI in neurosurgical interventions.

METHODS: The literature search was carried out in the PubMed and Web of Science databases using the keywords “LasereSpeckle,” “Laser Speckle,” “Laser speckle contrast imaging,” and “LSCI.” We allowed the search to include the following criteria: 1) publication in the English language, 2) full access to the article, 3) information about the method of treatment, and 4) the results presented for at least one patient.

RESULTS: The initial search resulted in the detection of 508 publications, of which 476 were eliminated during the initial assessment of titles and abstracts. Two more articles were excluded due to the lack of data in the English language. Twenty articles were found to be focused on nonhuman studies and therefore were excluded. In three more studies treatment of non-neurosurgical patients was reported. The final analysis included 8 articles with 102 patients overall.

CONCLUSIONS: LSCI is a promising intraoperative method for intraoperative cerebral blood flow assessing. This method offers several advantages over other modalities. The experience of use is limited to a small number of case series. Further investigation of the method and its implementation in clinical practice is needed.

INTRODUCTION

Intraoperative study of blood flow in the brain vessels and identification of disturbances thereof are among the most critical challenges of modern neurosurgery. Many diseases of the central nervous system can cause functional and morphological changes in the vessels of the brain as a result of both the disease itself and intraoperative manipulations. Continuous monitoring of blood flow and prompt elimination of disturbances ensure the efficacy of neurosurgical interventions. It is generally accepted that the operating surgeon should evaluate blood flow using objective intraoperative techniques without relying only on visual control.[1] The use of objective methods, such as intraoperative Doppler sonography, fluorescein video angiography, flowmetry, intraoperative computerized tomography, magnetic resonance imaging, and digital subtraction angiography, has been proven to reduce the risk of complications in neurosurgical operations.[2,3] One of the promising methods for intraoperative monitoring of blood flow is laser speckle contrast imaging (LSCI). LSCI is a wide- field blood flow imaging technique based on the analysis of light speckle interference patterns, which is gaining popularity in the analysis of tissue perfusion with blood in various fields of medicine. This method is currently being implemented in neurosurgery at the level of preclinical and clinical trial experiments. Currently, there are no protocols and recommendations for using this technique.

This systematic review aims to analyze the experience of using intraoperative LSCI in neurosurgical interventions.

METHODS

The literature search was carried out in the PubMed and Web of Science databases using the keywords "LasereSpeckle," "Laser Speckle," "Laser speckle contrast imaging," and "LSCI." In accordance with the PubMed data- base search algorithms, we used the following search queries:

1. LasereSpeckle [All Fields] AND («Laser Speckle» [MeSH Terms] OR «Laser speckle contrast imaging» [All Fields] OR «LSCI» [All Fields]).
2. Brain [MeSH Terms] OR («Cerebral» [All Fields] AND «Neuro»[All Fields]) OR «Neurosurgery» [All Fields].

We allowed the search to include the following criteria: 1) publication in the English language, 2) full access to the article, 3) information about the method of treatment, and 4) the results presented for at least 1 patient. The exclusion criteria were as follows: 1) nonhuman LSCI studies, such as studies on animals or phantom models; 2) publications that duplicate information from other sources; 3) publications containing only summaries, abstracts of conferences, reviews, or reviews of articles or books; and 4) articles not available for full-text viewing.

The following data were collected from these studies: 1) use of LSCI in neurosurgical practice, 2) equipment used in the LSCI system, 3) technical specifications, 4) type of pathology and neurosurgical intervention, 5) safety, 6) effectiveness of the blood flow assessment by the LSCI method, and 7) limitations of the method.

RESULTS

Selection of Publications for Analysis

The initial search resulted in the detection of 508 publications, of which 476 were eliminated during the initial assessment of titles and abstracts because they did not correspond with the research topic. Two more articles were excluded due to the lack of data in the English language. When reviewing the full text of the articles, 20 were found to be focused on nonhuman studies and therefore were excluded. Three more studies were excluded due to the impossibility of evaluating the data since they were presented using non- neurosurgical patients. As a result, the final analysis[4-11] included 8 papers with a total of 102 patients. The flow chart in Figure 1 depicts the process of selecting publications for the study.

Publication Characteristics

Eight papers published between 2010 and 2022 were included in this study. All 8 are a series of observations (Table 1). Four studies used an LSCI setup built into an operating microscope. The other 4 used commercial external devices designed to study LSCI and process the findings without connection to a microscope.

LSCI in Neurosurgery

Three papers were devoted to using LSCI intraoperatively in patients with brain tumors,[4,8,9] 4 focused on using LSCI in patients with vascular pathology of the brain[5-7,11] and 1 was focused on studying the perfusion of sutures of the soft tissues of the scalp.[10]

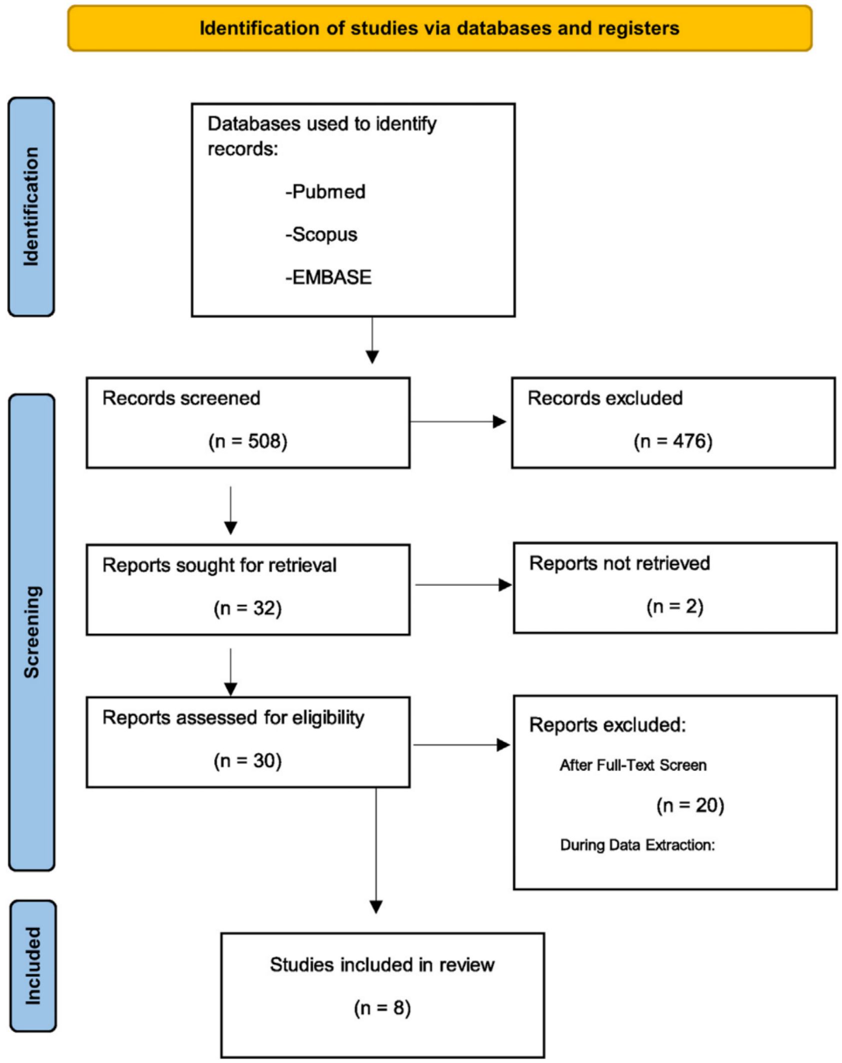

Figure 1. Flow chart showing the process of searching for suitable articles.

Table 1 shows the distribution of patients in the papers by type of neurosurgical pathology. A total of 102 patients were analyzed. LSCI was most commonly used when treating vascular pathologies (68 patients, 66.6%). Of these patients, 15 had aneurysms, 46 underwent a bypass procedure, 6 had arteriovenous malformations (AVMs), and 1 had a cavernoma. LSCI was used much less frequently for patients with tumors (23 patients, 22.5%). Of these patients, 22 had malignant gliomas and 1 had lymphoma. Additionally, in 1 article, soft tissue perfusion was assessed with LSCI before and after suturing in 8 neurosurgical patients,[10] and the use of LSCI was described in 3 patients with epilepsy.[6]

Table 1. Analysis of the Publications Included in the Study

Author	Year	N of Cases	Type of Pathology	Tools	Limitations
Parthasarathy et al.[4]	2010	3	Tumors - 3	Microscope-integrated camera and laser. Zeiss OPMI neurosurgical operating	One of the challenges in clinical measurement of CBF is the presence of artifacts due to the pulsatile motion of the brain.
Woitzik et al.[5]	2013	7	Malignant hemispheric stroke - 7	(MoorFLPI,Moor Instruments Ltd. Axminster, UK)	The system is not integrated into the surgical microscope.
N. Hecht et al.[6]	2013	38	ACVD - 14, MMD - 9 Aneurysms - 8, Tumors - 3	(MoorFLPI,Moor Instruments Ltd.	The system is not integrated into the surgical microscope.

			Epilepsy - 3, Cavernoma - 1	Axminster, UK)	
S. Nomura et al.[7]	2014	19	Aneurysms - 3, ACVD - 12, MMD - 4	Omegazone OZ-1 Omegawave Inc., Tokyo Japan	Not determined whethe preservation of CBF in LSC promised intact postoperative CBF, did not have a patien showing ischemic tolerance by ICA occlusion. The informatior on LSCI is only from the surface of the brain. The information or the CBF in the deep cortex and white matter could not be measured using LSCI.
L. Richards et al.8	2014	10	Tumors - 10	Microscope-integrated camera and laser. Zeiss OPMI Pentero, Carl Zeiss Meditec Inc., Oberkochen Germany	At rapid image acquisition, the camera more accurately captures the inheren physiological motion, which is why both cardiac and tissue motion correction significantly reduced CBF fluctuations in this study.
M. Ideguchi et al.9	2017	12	Tumors - 7, AVM - 5	Microscope-integrated camera and laser. OPMI Pentero; Carl Zeiss Meditec Omegazone OZ-1 Omegawave Inc., Tokyo Japan	If the resection area includes a nonfunctional area, the vasculature related to the lesion remains uncertain because the microcirculation and perfusion area of the lesion-related arteries cannot be visualized.
Carlson, et al.10	2021	8	Skin suturing - 8	Moor FLPI [full-field laser perfusion imager]: Moor Instruments, Ltd., UK	Due to the semiquantitative nature of the measurements, it is unknown if these relative reductions in blood flow reach truly ischemic levels.
D. Miller et al.11	2022	5	Aneurysms - 4, AVM - 1	Microscope-integrated camera and laser. Leica M530 OH6, Leica Microsystems GmbH Wetzlar, Germany	The integration of the hardware for this study is not optimal, and image quality could be improved with better hardware integration such as integrating both the laser and camera internally to the microscope. This would allow for optimization of ligh collection by reducing the number of optics that the collected light travels through before reaching the camera.
ACVD, arteriosclerotic cerebrovascular disease; MMD, Moyamoya disease; CBF, cerebral blood flow; LSCI, laser speckle contrast imaging.					

Thus, LSCI was found to be most frequently applied in neurosurgery in cerebrovascular diseases. In the majority of cases, the objective was to monitor the perfusion of the area of interest in the brain during revascularization (45%) (Figure 2). In one of the studies, the general applicability and sensitivity of LSCI were determined by testing the reactivity of cerebral vessels to hypercapnia. In oncological diseases and in AVMs, LSCI provided an opportunity to assess the area of blood supply to the examined artery during surgery and thus, to ascertain whether it needed to be preserved. For example, in the study conducted by Ideguchi et al.,[9] fluctuations in cerebral blood flow (CBF) made it possible to classify 3 types of arteries—feeding, "passing," and combined—based on a decrease in relative CBF in the internal resection zone. Thus, it was possible to avoid postoperative ischemic complications in most cases; only 1 patient had cerebral ischemia caused by damage to one of the arteries during tumor resection, which could not be seen with LSCI due to the deep location of the artery.

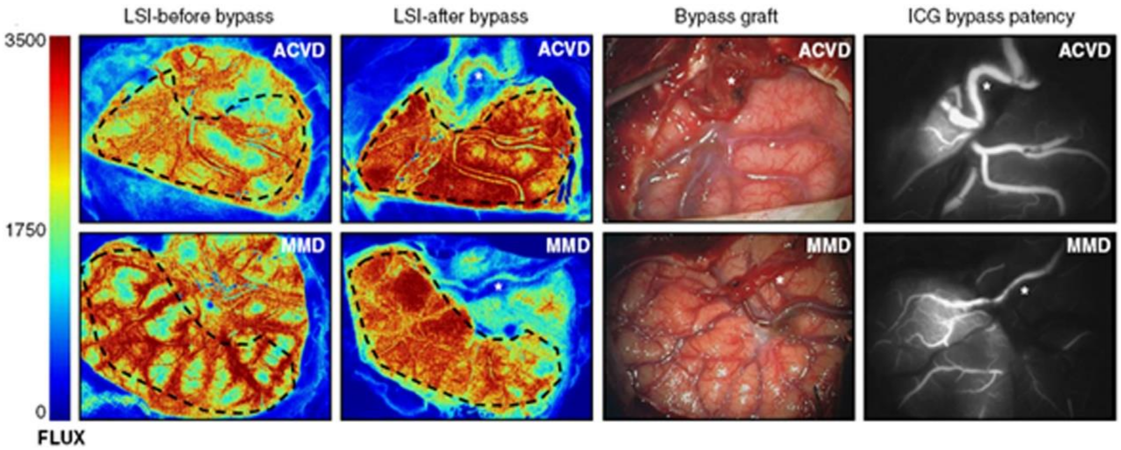

Figure 2. Adapted from «Laser speckle imaging allows real-time intraoperative blood flow assessment during neurosurgical procedures»,[6] https://doi.org/10.1038/jcbfm.2013.42, by courtesy of SAGE Publishing. (Pseudo) quantitative assessment of relative cerebral blood flow. Intraoperative laser speckle imaging screenshots of cortical baseline perfusion before and after superficial temporal artery to middle cerebral artery bypass grafting in patients with arteriosclerotic cerebrovascular disease (upper panels) or Moyamoya disease (lower panels). Perfusion is visualized as a two-dimensional color-coded map of blood flow in the arbitrary unit flux (red 1/4 high flow; blue 1/4 low flow). The dashed region of interest (ROI) shows the area where the mean cortical perfusion was calculated. The enhanced red-colored perfusion pattern after bypass completion (right panels, ICGA; the asterisk indicates the patent bypass) is an expression of a postoperative perfusion increase after STA-MCA bypass grafting.[6] rCBF, relative cerebral blood flow; STA-MCA, superficial temporal artery to middle cerebral artery; ACVD, arteriosclerotic cerebrovascular disease; MMD, Moyamoya disease; ICGA, Indocyanine green angiography

In the paper by D. Miller et al.,[11] published in 2022, the authors succeeded in creating a system with full integration into the operating microscope. The LSCI equipment was attached to the operating microscope and did not interfere with its normal operation. LSCI was performed during each operation with the microscope placed over the patient, which provided the surgeon with real-time visualization of blood flow changes before, during, and after aneurysm clipping (4 cases) or AVM resection (1 case). LSCI was also compared with indocyanine green angiography (ICGA) to assess CBF during aneurysm clipping and AVM surgery; the integrated LSCI equipment allowed LSCI and ICGA to be obtained simultaneously. The authors believe that LSCI can provide continuous real-time CBF imaging without interfering with the surgeon's workflow and without requiring the use of a contrast agent. The results also show that LSCI and ICGA provide different but complementary information on vascular perfusion.

Method Limitations

The main limitations of the method are low image resolution, the ability to assess only superficial areas of the brain, and the occurrence of "noise" during surgical procedures.[4-11] One of the studies also reported a low increase in perfusion recorded by LSCI after revascularization.[6] Coupled with the fact that oxygen demand was reduced under general anesthesia, this level of growth did not allow us to conclude that CBF was sufficient after surgery. Both the light spectrum of the microscope's lamp and noise from microscope movement can interfere with the accurate readings of the camera. The problem of obtaining data with the camera and simultaneously processing the image followed by its superimposition on the microscope view has not been completely solved.[11] Many authors consider it necessary to combine LSCI with other intraoperative methods for monitoring CBF and perfusion.[9]

Safety

No side effects of using LSCI, whether with a single use or repeated use, were reported in any of the studies examined herein.

Devices

In the publications studied, 2 options for the technical implementation of LSCI predominated; an external system[5-7,10] and a system integrated with the microscope.[4,8,9,11] An integrated system (Figure 3) provides several advantages, such as the possibility of using LSCI without interrupting the surgical procedures. When using an external system, its operation must be constantly monitored by an assistant, and the intervention time is significantly increased. Additionally, for further simplification, in one of the papers, LSCI images were recorded using the built-in white light camera of the microscope so that LSCI images were superimposed on white light images and continuously displayed to the neurosurgeon in real time.[11]

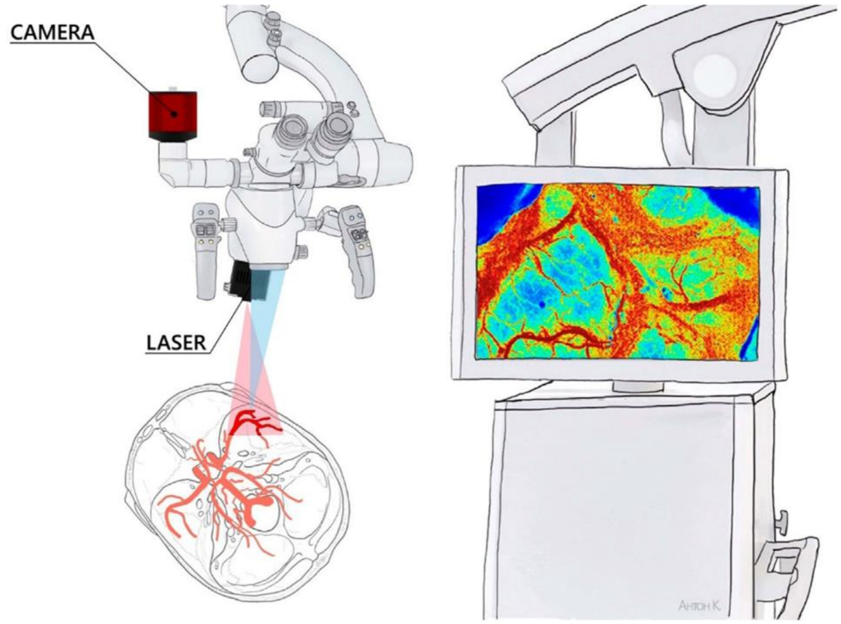

Figure 3. Schematic representation of the LSCI method and its integration into a microscope: camera, laser, and intraoperative visualization of the vessels of the human cerebral cortex. LSCI, Laser speckle contrast imaging.

DISCUSSION

LSCI is a wide-field blood flow imaging technique based on the analysis of light speckle interference patterns, which is gaining popularity in the analysis of tissue perfusion with blood in various fields of medicine. Speckle is a random interference pattern that occurs when coherent laser radiation is reflected from a rough surface. In this case, the maxima and minima of the interference appear as randomly arranged bright and dark spots observed on the object's surface. The process can only be described statistically. If the object itself is in motion, or if it contains moving scatterers, which is the case for biological objects, this leads to a change in the interference pattern and speckle oscillation. The flow rate of scatterers is considered to be inversely proportional to the decorrelation time sc. If such a speckle pattern is recorded with a finite exposure time, motions in the image area lead to blurring of the speckle pattern, i.e., a decrease in its contrast. The analysis of this effect underlies the method of LSCI. Traditionally, speckle contrast is defined as the ratio of the standard deviation of the intensity of neighboring pixels to the average intensity, usually determined in a 5 > 5 or 7 > 7 pixel window or in the same pixels in multiple adjacent frames. The first use of the speckle-based method of blood flow imaging was shown in the 1980s by Fercher and Biers.[12] Speckle contrast images of the retina were obtained. Unfortunately, using conventional photographic equipment required too much time for data processing, which significantly inhibited the research process and was the biggest obstacle to the continued development and implementation of this method. The introduction of digital photography in the 1990s made it possible to develop this method for obtaining images in quasi-real time.[13] The technical challenge in implementing the technology of LSCI is finding a solution to the main limitation of this technology: the relationship of the relativity of the speckle contrast parameter as such, which makes it impossible to quantify blood flow and limits the comparison of data collected in different time periods. There is also a problem of motion artifacts occurring during studies on living objects; the solution to this problem may increase the contrast of the resulting images and the signal-to-noise ratio.[14]

In recent years, LSCI technology has been gaining popularity in research in various fields of medicine; the first commercial samples of LSCI systems are already appearing. To a large extent, these systems are aimed at analyzing the perfusion of various tissues, such as skin, in patients with diabetes or other diseases.[15] Studies have been carried out on the use of LSCI for real-time analysis of CBF, most of which have been performed exclusively on laboratory animals, and imaging systems are at different stages of implementation.[16] In recent years, the method of speckle contrast imaging with multiple exposure times has become more widespread. Based on recording constant decorrelation, this approach reduces the speckle contrast parameter variability, increases the signal-to-noise ratio, and improves the visualization of small vessels. Decreasing the variability of the speckle contrast value and its dependence on the experimental conditions makes it possible to increase objectivity during long-term blood flow monitoring. The use of multiexposure speckle contrast has been shown in the case of sequential monitoring over several days of microvascular changes accompanying wound healing in laboratory mice.[17] LSCI may be a useful intraoperative option in neurosurgery based on the reviewed studies. Over the past 12 years, it has been used to treat various neurosurgery.

The possibility of effectively applying LSCI in neurosurgical interventions to monitor blood flow during clipping of aneurysms, removal of AVMs and brain tumors, and other neurosurgical pathologies has been confirmed by several studies.[4-11] According to the current review, the method is most widely used in vascular neurosurgery for chronic cerebral ischemia, moyamoya disease, complex aneurysms, and AVMs. Herewith, LSCI was used to control perfusion and blood flow before and after anastomoses when clipping complex aneurysms, visualizing the malformation feeder arteries, etc. Cases where LSCI was applied in the removal of tumors are found in the literature much less frequently.

A study by Miller et al. considered the use of speckle contrast imaging by integrating it into a microscope and continuously analyzing blood flow data.[11] The paper shows that the method of intraoperative LSCI has an advantage over fluorescein angiography and is easily integrated into the process of surgical intervention. The main advantage of the LSCI method is the possibility of evaluating the characteristics of pulsations in addition to the average characteristics, which can help assess the functional state of blood flow. The authors note that LSCI is a promising method, but further improvements to the system are required to solve several problems.

Thus, the experience of using LSCI systems in neurosurgery is limited to a small number of series of clinical observations thus far. LSCV remains experimental. According to most studies, this is a technically simple, inexpensive, easily reproducible technique that complements and, in some aspects, surpasses the existing methods for the intraoperative assessment of CBF. However, prospective comparative studies are needed to obtain more reliable data. Additionally, the possible limitations include the complexity of objectification, namely, quantitative assessment of blood flow, which is a major factor and is necessary for comparative analysis and systematization of data. Among other things, there are certain limitations associated with the technical and software support of the method, which does not yet allow it to be introduced into wide practice.

CONCLUSION

LSCI is a promising intraoperative method introduced into practice for assessing blood flow in cerebral vessels. This method offers several advantages over the existing methods for intraoperative blood flow monitoring. The experience of use is limited to a small number of series of clinical observations of intraoperative use in brain surgery. Further investigation into the characteristics of the method and its implementation in clinical practice is needed.

REFERENCES

1. Spetzler RF, Kalani Y, Nakaji P. Neurovascular Sur- gery, Thieme. Phoenix, AZ: Barrow Neurological Institute; 2015.
2. Stendel R, Pietilä T, Al Hassan AA, Schilling A, Brock M. Intraoperative microvascular Doppler ultrasonography in cerebral aneurysm surgery. J Neurol Neurosurg Psychiatry. 2000;68:29-35.
3. Roessler K, Krawagna M, Dörfler A, Buchfelder M, Ganslandt O. Essentials in intra- operative indocyanine green videoangiography assessment for intracranial aneurysm surgery: conclusions from 295 consecutively clipped an- eurysms and review of the literature. Neurosurg Focus. 2014;36:E7.
4. Parthasarathy AB, Weber EL, Richards LM, Fox DJ, Dunn AK. Laser speckle contrast imaging of cerebral blood flow in humans during neuro- surgery: a pilot clinical study. J Biomed Opt. 2010; 15:66030.
5. Woitzik J, Hecht N, Pinczolits A, et al. Propaga- tion of cortical spreading depolarization in the human cortex after malignant stroke. Neurology. 2013;80:1095-1102.
6. Hecht N, Woitzik J, König S, Horn P, Vajkoczy P. Laser speckle imaging allows real-time intra- operative blood flow assessment during neuro- surgical procedures. J Cereb Blood Flow Metab. 2013; 33:1000-1007.
7. Nomura S, Inoue T, Ishihara H, et al. Reliability of laser speckle flow imaging for intraoperative monitoring of cerebral blood flow during cere- brovascular surgery: comparison with cerebral blood flow measurement by single photon emis- sion computed tomography. World Neurosurg. 2014; 82:E753-E757.
8. Richards LM, Towle EL, Fox DJ, Dunn AK. Intraoperative laser speckle contrast imaging with retrospective motion correction for quantitative assessment of cerebral blood flow. Neurophotonics. 2014;1:015006.
9. Ideguchi M, Kajiwara K, Yoshikawa K, et al. Avoidance of ischemic complications after resec- tion of a brain lesion based on intraoperative real- time recognition of the vasculature using laser speckle flow imaging. J Neurosurg. 2017;126: 274-280.
10. Carlson AP, Denezpi T, Akbik OS, Mohammad LM. Laser speckle imaging to eval- uate scalp flap blood flow during closure in neurosurgical procedures. Surg Neurol Int. 2021;12: 1-7.
11. Miller DR, Ashour R, Sullender CT, Dunn AK. Continuous blood flow visualization with laser speckle contrast

imaging during neurovascular surgery. Neurophotonics. 2022;9:1-12.
12. Fercher AF, Briers JD. Flow visualization by means of single-exposure speckle photography. Opt Commun. 1981;37:326-330.
13. Briers JD, Webster S. Laser speckle contrast analysis (LASCA): a nonscanning, full-field tech- nique for monitoring capillary blood flow. J Biomed Opt. 1996;1:174-179.
14. Piavchenko G, Kozlov I, Dremin V, et al. Impair- ments of cerebral blood flow microcirculation in rats brought on by cardiac cessation and respira- tory arrest. J Biophotonics. 2021;14:e202100216.
15. Mennes OA, van Netten JJ, van Baal JG, Steenbergen W. Assessment of microcirculation in the diabetic foot with laser speckle contrast im- aging. Physiol Meas. 2019;40:65002.
16. Mangraviti A, Volpin F, Cha J, et al. Intraoperative laser speckle contrast imaging for real-time visu- alization of cerebral blood flow in cerebrovascular surgery: results from pre-clinical studies. Sci Rep. 2020;10:7614.
17. Rege A, Murari K, Seifert A, Pathak AP, Thakor NV. Multiexposure laser speckle contrast imaging of the angiogenic microenvironment. J Biomed Opt. 2011;16:56006.