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Intraoperative Laser Speckle Contrast Imaging to Assess Vessel Flow in Neurosurgery: A Pilot Study

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BACKGROUND AND OBJECTIVES: Laser speckle contrast imaging (LSCI) has emerged as a promising tool for assessment of vessel flow during neurosurgery. We aimed to investigate the feasibility of visualizing vessel flow in the macrocirculation with a new fully microscope-integrated LSCI system and assess the validity and objectivity of findings compared with fluorescence angiography (FA).

METHODS: This is a single-center prospective observational study enrolling adult patients requiring microsurgical treatment for brain vascular pathologies or brain tumors. Three independent raters, blinded toward findings of FA, reviewed regions of interest (ROIs) placed in exposed vessels and target structures. The primary end point was the validity of LSCI for assessment of vessel flow as measured by the agreement with FA. The secondary end point was objectivity, measured as the inter-rater agreement of LSCI findings.

RESULTS: During 18 surgical procedures, 23 observations using FA and LSCI were captured simultaneously. Using LSCI, vessel flow was assessable in 62 (86.1%) and not assessable in 10 (13.9%) ROIs. The agreement between LSCI and FA was 86.1%, with an agreement coefficient of 0.85 (95% CI: 0.75-0.94). Disagreement between LSCI and FA was observed in the 10 ROIs that were not assessable. The agreement between ROIs that were assessable using LSCI and FA was 100%. The inter-rater agreement of LSCI findings was 87.9%, with an agreement coefficient of 0.86 (95% CI: 0.79-0.94).

CONCLUSION: Fully microscope-integrated LSCI is feasible and has a high potential for clinical utility. Because of its characteristics, LSCI can be viewed as a full-field visual micro-Doppler that can be used as a complementary method to FA for assessing vessel flow during neurosurgery. Despite technical limitations related to the early development phase of the fully microscope-integrated system, we demonstrated reasonable validity and objectivity of findings compared with FA. Further research and refinement of the system may enhance its value in neurosurgical applications.

KEY WORDS: Cerebral blood flow, Cerebrovascular neurosurgery, Laser speckle contrast imaging, Indocyanine green angiography

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ABBREVIATIONS: AChA, anterior choroidal artery; ACOM, anterior communicating artery; dAVF, dural arteriovenous fistula; FA, fluorescence angiography; ICG, indocyanine green; ICGA, indocyanine green angiography; LSCI, laser speckle contrast imaging; PMA, pulsatile motion artifact.

Laser speckle contrast imaging (LSCI) has emerged as a promising tool for continuous assessment of vessel flow during neurosurgery that requires simple hardware: a laser source and a camera. LSCI is an optical technique based on the principle that laser light illuminating the operative field is

scattered differently by moving particles, namely, red blood cells, than static tissue, which leads to local spatial variations in the interference pattern imaged by a camera. LSCI provides high-resolution imaging of vessel flow without needing a contrast agent or tissue contact.^{1,2} Clinical neurosurgical studies have demonstrated the potential of LSCI for visualizing cortical microcirculation during revascularization surgeries and awake craniotomies and in stroke patients.³⁻¹¹ In most previously conducted studies, LSCI was performed with external devices that were positioned over the craniotomy, interrupting the surgery for several minutes and therefore lacking the ability to provide real-time information.^{4,6-8,10}

Recently, we demonstrated a novel LSCI instrumentation setup that is fully integrated into the operative microscope, enabling continuous and real-time LSCI acquisition without interrupting surgical workflow.^{2,12} The most common intraoperative vessel flow assessment technique is fluorescence angiography (FA) with indocyanine green (ICG) or sodium fluorescein.^{13,14} Despite FA's utility for assessing vessel flow, it is limited by restricted repeatability and the need to inject dyes. LSCI can be repeated without restriction, requires no injection of dyes, and has the potential of an immediate switch-on solution in a fully microscope-integrated setup. Studies systematically investigating LSCI for assessment of vessel flow in the macrocirculation are missing. To close this data gap, this pilot study aimed to assess the validity and objectivity of LSCI compared with FA in a fully microscope-integrated system.

METHODS

Study Design

We conducted a single-center prospective observational cohort study including consecutive adult patients, requiring microsurgical treatment for brain vascular pathologies or brain tumors (ie, aneurysms, arteriovenous malformations, dural arteriovenous fistulas, gliomas, meningiomas, metastases, schwannomas) during the study period of 3 weeks. There were no exclusion criteria except for the inability to provide written informed consent. The study was approved by the local ethics committee in Bern, Switzerland (Project-ID: 2021-D0043), registered (NCT05028400), and conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.¹⁵

Outcome Measures

The primary end point was the validity of LSCI for assessment of intraoperative vessel flow, measured by the agreement of LSCI findings with FA. The secondary end point was objectivity, measured as the inter-rater agreement of LSCI findings.

LSCI Instrumentation

A commercially available operating microscope (OPMI Pentero 900, Carl Zeiss) was equipped with instrumentation required to perform LSCI. The LSCI instrumentation followed previous similar designs by our group.^{2,12} The instrumentation included a $\lambda = 785$ nm laser diode, a

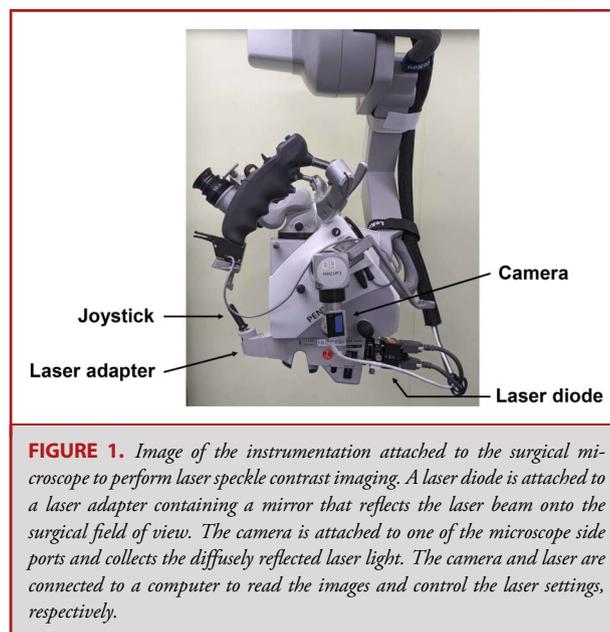


FIGURE 1. Image of the instrumentation attached to the surgical microscope to perform laser speckle contrast imaging. A laser diode is attached to a laser adapter containing a mirror that reflects the laser beam onto the surgical field of view. The camera is attached to one of the microscope side ports and collects the diffusely reflected laser light. The camera and laser are connected to a computer to read the images and control the laser settings, respectively.

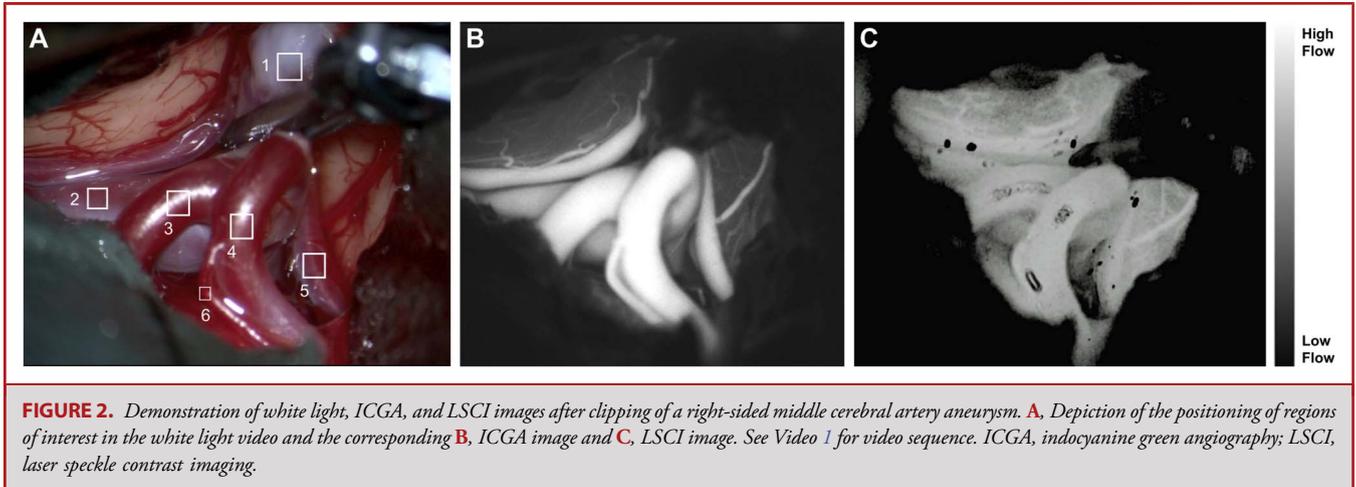
lens, and a steering mirror to center the illumination light, housed in a laser adapter (MM6 Micromanipulator, Carl Zeiss Meditec Inc) and mounted to the bottom of the microscope. The maximum laser irradiance was 0.10 W/cm^2 , which is below the American National Standards Institute¹⁶ limit of 0.3 W/cm^2 for skin at 785 nm. Light that diffusely reflected from the cortical surface was collected through the microscope's optics onto a near-infrared enhanced camera (Basler AG) mounted on the observer port. A band-pass filter was positioned in front of the camera to block ambient light. This enabled acquisition of quality LSCI images throughout the procedure and simultaneous acquisition of LSCI and FA. The LSCI instrumentation was covered below the sterile draping without limiting the microscope's range of motion. Two identical setups were used throughout the study (Figure 1).

LSCI Visualization Software

SpeckleView, a custom software package developed by Dynamic Light Inc, was used during each case to continuously record and process LSCI images in real time and display them to the operating surgeons on monitors within the operating room. The SpeckleView software controlled (1) collecting the raw camera image at a user-specified camera exposure time, (2) processing the raw camera image into a spatial speckle contrast image by calculating the speckle contrast value at each pixel, (3) co-registering the LSCI image with FA images by applying an affine transformation, (4) applying a color map to the LSCI image, and (5) displaying the processed LSCI images on monitors. SpeckleView software performed steps 1 to 5 in real time on a laptop computer.

Fluorescence Angiography

FA was conducted using microscopes (OPMI Pentero 900, Carl Zeiss) with built-in fluorescent light sources ($\lambda = 460\text{-}500$ and $700\text{-}780$ nm) for ICG and sodium fluorescein visualization, along with wavelength-sensitive cameras. Room lighting was reduced, and 0.25 mg/kg ICG



(Diagnostic Green GmbH) dissolved in 5 mL of distilled water or 250 mg of sodium fluorescein (Curatis AG) was injected via a central venous catheter, followed by saline.

TABLE 1. Patient Characteristics	
No. of patients	18 (100%)
Female	9 (50%)
Mean age (y, SD)	51.7 (\pm 11.3)
Range (y)	30-72
Indication for surgery	18 (100%)
Unruptured intracranial aneurysm	9 (50%)
MCA	7 (38.8%)
ACOM	1 (5.6%)
AChA	1 (5.6%)
AVM	2 (11.1%)
dAVF	1 (5.6%)
Brain tumor	6 (33.3%)
Metastasis	2 (11.1%)
Glioma	2 (11.1%)
Meningioma	1 (5.6%)
Vestibular schwannoma	1 (5.6%)
Fluorescent dye	23 (100%)
Indocyanine green	19 (82.6%)
Sodium fluorescein	4 (17.4%)

AChA, anterior choroidal artery; ACOM, anterior communicating artery; AVM, arteriovenous malformation; dAVF, dural arteriovenous fistula; MCA, middle cerebral artery.

Data Collection

Vessel flow was assessed using LSCI and FA. LSCI was performed before, during (simultaneously), and after FA measurements, whenever indicated during neurovascular procedures (eg, after clipping) and after durotomy in brain tumor cases. Video recordings of white light, LSCI, and FA were displayed during procedures and stored and reviewed postoperatively (Figure 2, Video 1, and Video 2). Regions of interest (ROIs) were defined based on white light videos. For neurovascular procedures, ROIs were placed in vessels proximal and distal to the target pathology, eg, harboring and branching arteries, and the aneurysm sac in aneurysm surgery. In brain tumor procedures, ROIs were placed in cortical vessels that were visible under white light.

Assessment of vessel flow using FA was performed by two independent raters who were not involved in the rating process of LSCI videos. Three neurovascular surgeons at Bern University Hospital independently assessed vessel flow in LSCI videos. Raters were blinded toward the results of FA and were provided with a static white light image with annotated ROIs (Figure 2A), along with synchronized white light and LSCI videos for the rating process. Raters categorized vessel flow as flow, no flow, not assessable because of poor image quality, or not assessable because of pulsatile motion artifact (PMA). PMA can occur with LSCI because LSCI is sensitive to motion from both blood flow and the mechanical pulsation of the brain during each heartbeat. For most situations, blood flow is the significant contributor to the LSCI signal; however, when the laser intensity reaching the camera is low, often because of a lack of illumination light reaching the imaging region, it becomes more challenging to distinguish blood flow from the pulsatile motion of the brain. Insufficient illumination can lead to poor image quality and resolution of LSCI, making assessments more challenging. This issue is particularly pronounced in deep surgical fields with high magnification and simultaneous acquisition of FA because it can impede the LSCI camera's ability to collect adequate light for optimal imaging.

Statistical Analysis

Statistical analysis was performed using Stata Version 16.1 (StataCorp LLC). Descriptive statistics were performed to illustrate frequencies and percentages. Agreement was analyzed by calculating Gwet's agreement coefficients (\pm standard error) with the "kappaetc" command.^{17,18} To investigate validity, the agreement between a combined rating result and

TABLE 2. ROI and Agreement With FA

ROI type	ROI type, n (%)	Agreement between LSCI and FA findings, n (% of ROI type)		Reasons for disagreement, n (% of disagreement)	
		Agreement	Disagreement	PMA	Poor image quality
Total, n (%)	72 (100%)	62 (86.1%)	10 (13.9%)	4 (40%)	6 (60%)
Aneurysm	9 (12.5%)	6 (66.7%)	3 (33.3%)	3 (100%)	—
Harboring artery	5 (6.9%)	4 (80%)	1 (20%)	—	1 (100%)
Branching artery	28 (38.9)	24 (85.7%)	4 (14.3%)	—	4 (100%)
Cortical artery	15 (20.8%)	15 (100%)	—	—	—
Perforator	7 (9.7%)	7 (100%)	—	—	—
Nidus	1 (1.4%)	1 (100%)	—	—	—
Feeder	3 (4.2%)	3 (100%)	—	—	—
Arterialized vein	1 (1.4%)	1 (100%)	—	—	—
Vein	3 (4.2%)	1 (33.3%)	2 (66.7%)	1 (50%)	1 (50%)

ROI background type	ROI background, n (%)	Agreement between LSCI and FA findings, n (% of ROI background)		Reasons for disagreement, n (% of disagreement)	
		Agreement	Disagreement	PMA	Poor image quality
Total, n (%)	72 (100%)	62 (86.1%)	10 (13.9%)	4 (40%)	6 (60%)
CSF	5 (6.9%)	5 (100%)	—	—	—
Brain	44 (61.1%)	38 (86.4%)	6 (13.6%)	1 (16.7%)	5 (83.3%)
Clip	3 (4.2%)	2 (66.7%)	1 (33.3%)	1 (100%)	—
Vessel	20 (27.8%)	17 (85%)	3 (15%)	2 (66.7%)	1 (33.3%)

CSF, cerebrospinal fluid; FA, fluorescence angiography; LSCI, laser speckle contrast imaging; PMA, pulsatile motion artifact; ROI, region of interest.

FA was measured. Combined rating was obtained by choosing the most frequently selected rating for each ROI (at least two identical answers with three reviewers). There were no situations with three different ratings. To assess objectivity, the agreement between all three independent raters was measured.

RESULTS

Patient Characteristics

Between February 21 and March 11, 2022, 18 consecutive patients were enrolled in the study. Nine (50%) patients were female, and nine were male (50%). Nine patients (50%) were treated with clipping of an unruptured intracranial aneurysm, two (11.1%) with resections of an arteriovenous malformation, one (5.6%) with disconnection of a cranial dural arteriovenous fistula, and six (33.3%) with resections of a brain tumor. Baseline characteristics are displayed in Table 1. During the 18 surgical procedures, 23 observations with FAs and corresponding LSCI videos were captured. Nineteen (82.6%) FAs were performed

using ICG angiography, and four (17.4%) using sodium fluorescein. For all 23 observations, a total of 72 ROIs were defined, classified, and included in the rating process (Table 2).

Validity of LSCI Findings: Comparison With FA

With LSCI, vessel flow was assessable in 62 (86.1%) ROIs. Of those, flow was observed in 56 (77.8%) and no flow was observed in six (8.3%) ROIs. Vessel flow was not assessable in 10 (13.9%) ROIs. Of those, PMA was present in four (5.6%) and poor image quality was present in six (8.3%) ROIs. In FA, vessel flow was assessable in all 72 (100%) ROIs. Flow was present in 63 (87.5%), and no flow was observed in nine (12.5%) ROIs. The overall agreement between the combined LSCI ratings and FA ratings was 86.1% with an agreement coefficient of 0.85 (95% CI: 0.75-0.94). Disagreement between LSCI and FA was only observed in the 10 ROIs that were not assessable by LSCI because of PMA or poor image quality (n = 10, 13.9%). The agreement between ROIs that were assessable by LSCI and FA was 100% (Figure 3, Table 2).

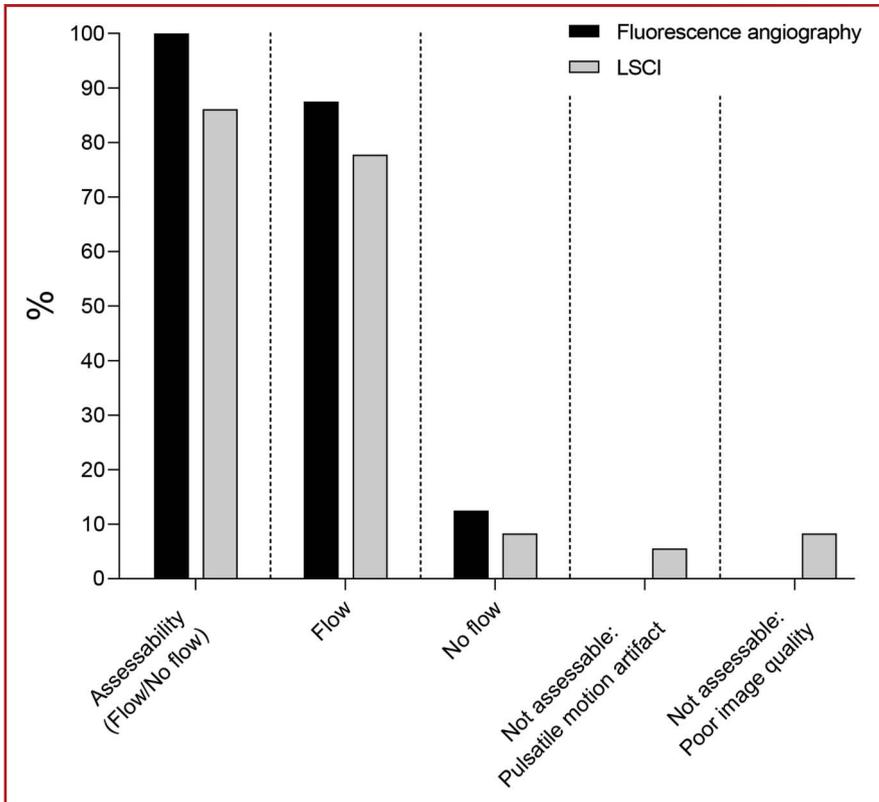


FIGURE 3. Validity of LSCI findings in comparison with fluorescence angiography. LSCI, laser speckle contrast imaging.

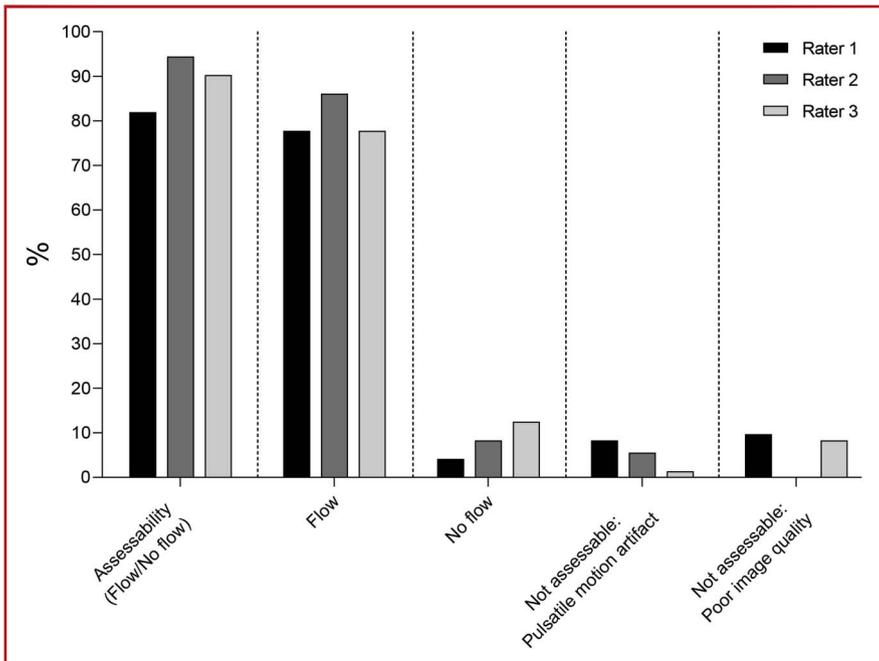


FIGURE 4. Objectivity of laser speckle contrast imaging findings indicated with the inter-rater agreement (raters 1-3).

Objectivity of LSCI Findings: Inter-Rater Agreement

The rating results of three independent reviewers for each ROI were as follows: Rater (1): flow = 56 (77.8%), no flow = 3 (4.2%), not assessable because of PMA = 6 (8.3%), or not assessable because of poor image quality = 7 (9.7%); rater (2): flow = 62 (86.1%), no flow = 6 (8.3%), not assessable because of PMA = 4 (5.6%), and not assessable because of poor image quality = 0 (0.0%); rater (3): flow = 56 (77.8%), no flow = 9 (12.5%), not assessable because of PMA = 1 (1.4%), and not assessable because of poor image quality = 6 (8.3%). The overall inter-rater agreement was 87.9%, with an agreement coefficient of 0.86 (95% CI: 0.79-0.94) (Figure 4).

To illustrate the rating process and present LSCI images, Figures 5 and 6 show exemplary pairs of white light and LSCI images containing the ROIs that were rated. Video 2 shows clipping of a right-sided middle cerebral artery (MCA) aneurysm comparing LSCI and white light. Video 3 shows the situation after clipping of a left-sided MCA aneurysm.

During the study, two primary limitations of LSCI were encountered: (1) inability to visualize slow flow, such as in the case of incomplete clipping of a MCA aneurysm, where a small opening is left at the neck with consequent slow inflow of fluorescent dye in a later phase (see Figure 7A-7C) and (2) difficulty in assessing flow in deep locations because of a limited amount of available light, as observed during the evaluation of flow in the anterior choroidal artery after clipping of an anterior choroidal artery aneurysm (see Figure 7D-7F).

DISCUSSION

This pilot study shows that assessing vessel flow using LSCI in a fully microscope-integrated system is feasible and provides results with reasonable validity and objectivity compared with FA despite the current technical limitations of the instrumentation setup. We generally observed high agreement between LSCI and FA (86.1%, agreement coefficient 0.85). Nevertheless, higher accuracy is necessary to justify the implementation of LSCI in routine clinical use. Notably, disagreement between LSCI and FA occurred in scenarios where the assessment of vessel flow using LSCI was not feasible because of technical limitations (13.9%, poor image quality, or PMA) and not because of a misjudgment of vessel flow itself, emphasizing that overcoming existing technical limitations could achieve the necessary accuracy for implementing LSCI in routine clinical use.

Strengths and Potential of Fully Microscope-Integrated LSCI

Previous LSCI instrumentations relied on portable, external devices such that the surgery was paused while LSCI recordings were obtained.^{3,5-7,10} We view full microscope integration as the crucial step for LSCI to be a useful adjunct during neurosurgery

because (1) it aligns the surgeon's angle of view with the angle of the LSCI system and therefore allows convenient assessment of deeper vessels despite narrow surgical corridors during microneurosurgery and (2) it eliminates interruption of surgical workflow and (3) the ability to provide real-time data on vessel flow while the surgeon is operating.

LSCI does not require fluorescent dye administration and can be repeated as often as desired during surgery and used for continuous measurement. With these properties, LSCI represents a tool available immediately at the push of a button for rapid assessment of vessel flow.

A further advantage of LSCI is the rich data it captures, allowing for extensive postprocessing with significant potential, particularly considering the ongoing advancement of imaging and data processing capabilities in modern operative microscopes. We envision that LSCI could be used for automatic vessel and diameter detection to provide real-time quantitative measurements of cerebral blood flow. Furthermore, LSCI could run continuously in the background and alert the surgeon when vessel flow or perfusion declines. To fully realize the potential of LSCI, close collaboration with microscope manufacturers is crucial.

Limitations of Fully Microscope-Integrated LSCI

There are technical limitations of LSCI related to the instrumentation setup that can be mitigated with further technical development. PMA and poor image quality were the most relevant technical limitations that became evident during this study. PMAs were most often visible in aneurysm clipping cases, with disagreement between FA and LSCI for judging the occlusion of clipped aneurysms occurring 3 out of 9 times. These artifacts occurred because of the movement of the closed aneurysms with each pulse. When PMAs were present in the LSCI video, this posed a challenge for raters when determining the assessability of a specific ROI. This was because the LSCI videos frequently lacked the clarity needed to definitively discern the presence or absence of flow in such situations with reasonable certainty. Consequently, raters would label these regions as not assessable because of a certain ambiguity caused by PMAs. Postprocessing of LSCI data could be used to minimize such artifacts because they can easily be linked to the patient's electrocardiography and display a different LSCI pattern than typical vessel flow.¹

Poor image quality was mainly caused by the simultaneous acquisition of FA and LSCI, which hampered the light collection of the LSCI camera. The amount of near-infrared light that was ultimately available to the LSCI camera in these scenarios was approximately 13% or less, which reduced the image quality of the LSCI recordings (see Figure 7F) and additionally amplified the effects of PMAs. Furthermore, the signal-to-noise ratio of the LSCI signal diminishes with reduced collected light, which potentially impedes the precise assessment of blood flow and the identification of vessel borders, particularly when situated in proximity to a well-perfused cortex. If present, this decrease in

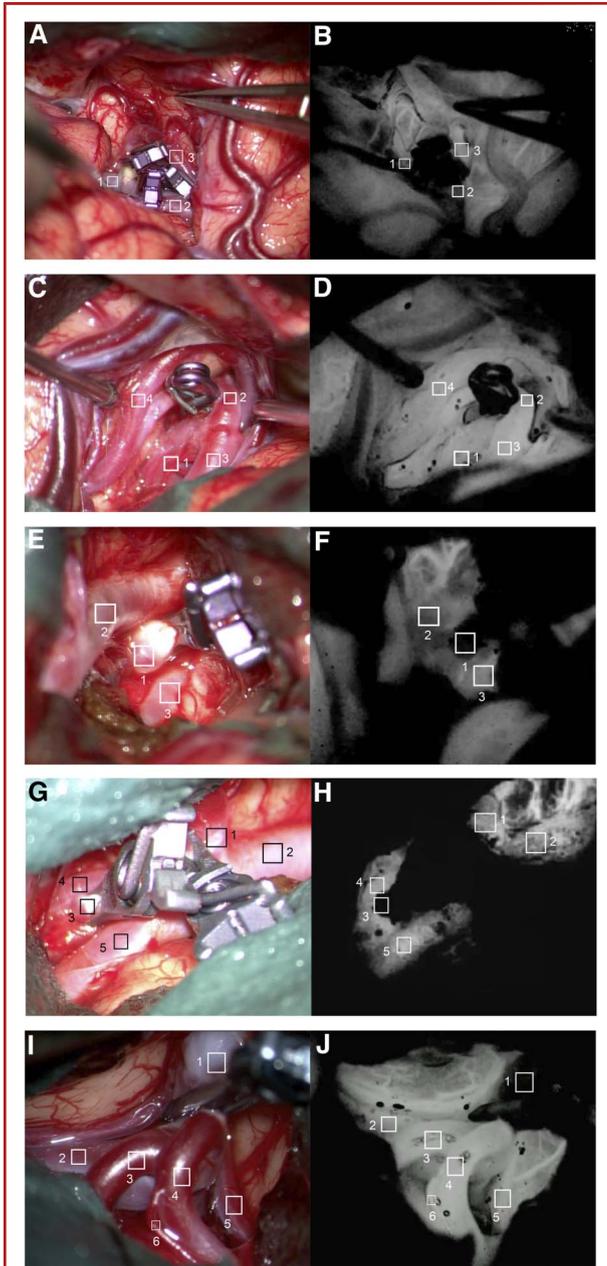


FIGURE 5. Demonstration of pairs of white light and laser speckle contrast imaging images with corresponding regions of interest: **A, B, I, and J**, After clipping of right MCA aneurysm, **C, D, E, and F**, after clipping of left MCA aneurysm, and **G and H**, after clipping of two left MCA aneurysms. Image 5I used with permission of Elsevier Science & Technology Journal, from *Intraoperative Laser Speckle Contrast Imaging To Assess Vessel Flow In Neurosurgery*. Goldberg J, et al, *Brain and Spine* 2023; permission conveyed through Copyright Clearance Center, Inc. MCA, middle cerebral artery.

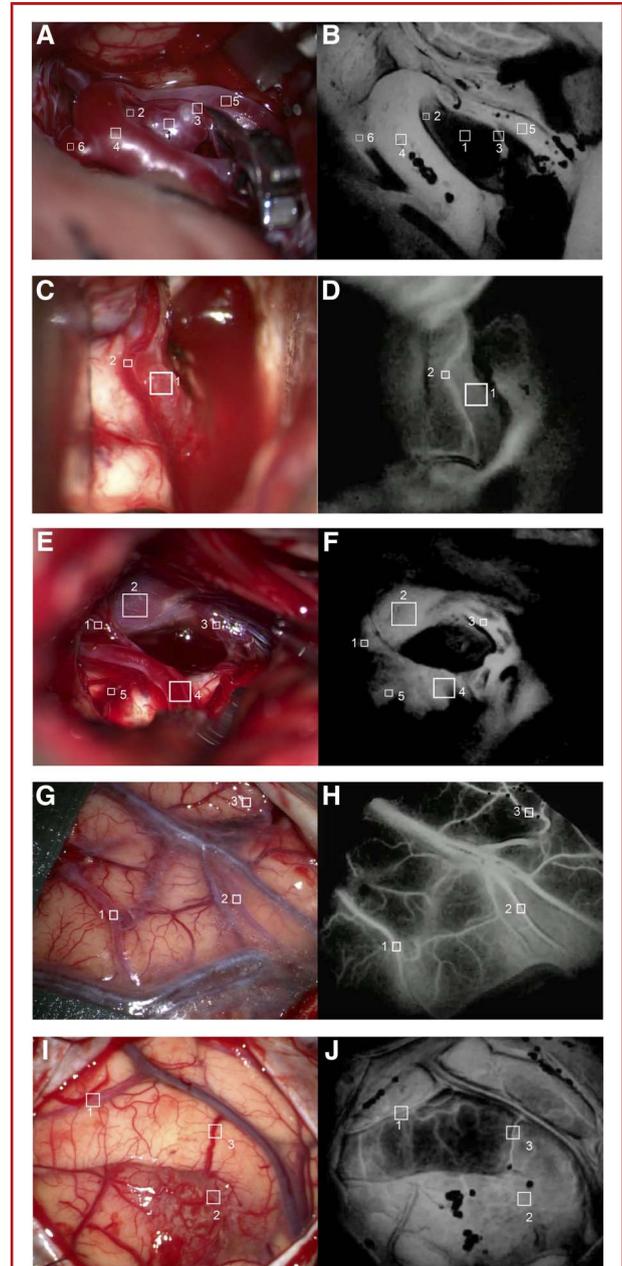


FIGURE 6. Demonstration of pairs of white light and LSCI images with corresponding ROIs: **A and B**, After clipping of right middle cerebral artery aneurysm, **C and D**, after disconnection of a ethmoidal dural arteriovenous fistula, **E and F**, view into the right cerebellopontine angle after resection of a vestibular schwannoma, **G and H**, after durotomy for left temporal high-grade glioma, and **I and J**, after durotomy for right parietal high-grade glioma. LSCI, laser speckle contrast imaging; ROIs, regions of interest.

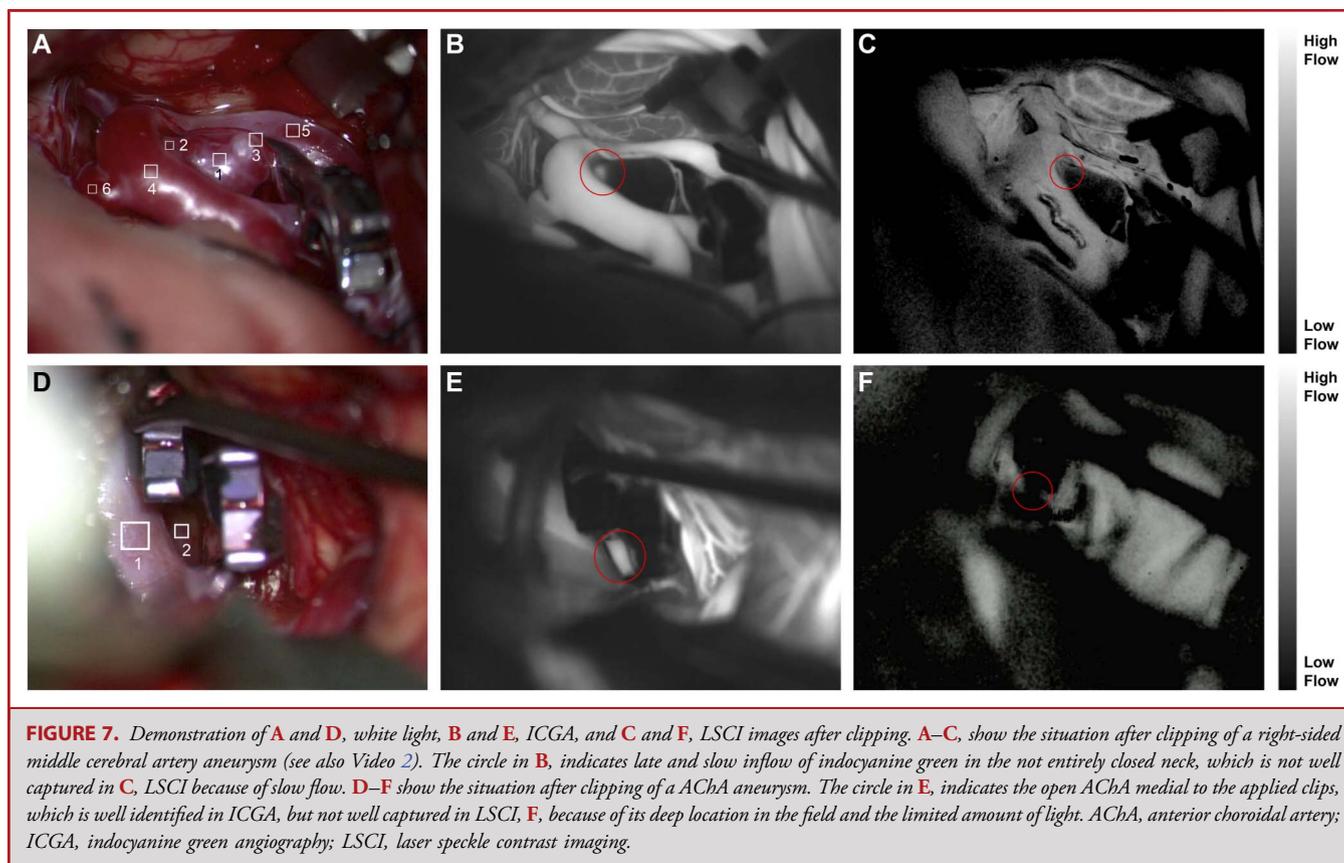


image quality resulted in raters classifying the region as not assessable because of poor image quality and their inability to discern vessel flow with the necessary clarity. Future advances of the instrumentation setup could potentially increase the light collection efficiency by 300%, significantly reducing or eliminating PMAs and increasing image quality, particularly in deeper regions where light illumination can be limited.

While LSCI's lack of reliance on dyes is advantageous, it also introduces limitations. Dye wash-in during FA allows flow direction assessment, which is not feasible with LSCI. Single-exposure LSCI struggles with slow flow, as observed during late dye accumulation in not entirely clipped aneurysms (see Figure 7B and 7C). Multiexposure speckle imaging could overcome this.² LSCI's image contrast is lower than that in FA because LSCI senses perfusion in all areas of the field of view, whereas the FA signal is restricted to the dye in vessels only. Thus, FA is more sensitive to deeper-located regions with low light.

Implications and Future Directions

Given the above-described advantages and disadvantages, we believe that fully microscope-integrated LSCI has the potential to become an adjunct to FA in the neurosurgeon's armamentarium for the assessment of vessel flow during neurosurgical procedures. Because

LSCI has different and incomparable properties to FA, we think that the technology should be understood as complementary to FA and not as a replacement for FA. FA provides high-resolution visualization of vessel patency, flow direction, and temporal resolution of flow, whereas LSCI can provide real-time and continuous assessment.

Unlimited repeatability and immediate availability of information on vessel flow is the key advantage of LSCI. Because of these characteristics, LSCI occupies a similar niche as micro-Doppler ultrasound. We view LSCI as a full-field visual micro-Doppler that offers relevant advantages compared with the classical micro-Doppler: (1) LSCI can image flow in vessels that are too small for measurement with a micro-Doppler probe, such as perforators (Video 2); (2) LSCI is able to show vessel flow simultaneously in all visible vessels of the entire operative field and is not limited to one point; and (3) LSCI does not require interruption of surgical workflow as it is the case for positioning of a micro-Doppler probe.

Strengths and Limitations

The strengths of our study include its prospective design and blinding of raters toward the results of FA to reduce bias. Furthermore, this is the first study reporting on the use and technique of a fully microscope-integrated LSCI system to assess vessel flow in the macrocirculation systematically.

The main limitation of this study, especially given the strong agreement observed in cases without technical limitations (PMA or poor image quality), lies in the limited number of patients and observations. This results in a reduced frequency of less common findings, such as persistent perfusion of an aneurysm after a clipping attempt or flow disruption in a branching vessel. These specific cases are essential for studying the specificity and sensitivity of LSCI compared with FA.

As a result, the nature of this study remains descriptive. Larger studies, with a more advanced prototype, will be necessary to evaluate these properties of LSCI. Furthermore, the subjectivity of the rating process is a limitation because different raters may interpret findings with some variability.

CONCLUSION

Fully microscope-integrated LSCI is feasible and has a high potential for clinical utility. Because of its characteristics, LSCI can be viewed as a full-field visual micro-Doppler that can be used as a complementary method to FA for assessing vessel flow during neurosurgery. Despite technical limitations related to the early development phase of the fully microscope-integrated system, we demonstrated reasonable validity and objectivity of findings compared with FA. To unlock the full potential of LSCI, development of a more advanced prototype is needed to overcome technical limitations and further validate LSCI in larger clinical studies.

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Disclosures

David R. Miller and Andrew K. Dunn hold stock in, serve on the board of directors, and consult for Dynamic Light. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

- Richards LM, Towle EL, Fox DJ Jr, Dunn AK. Intraoperative laser speckle contrast imaging with retrospective motion correction for quantitative assessment of cerebral blood flow. *Neurophotonics*. 2014;1(1):015006.
- Richards LM, Kazmi SS, Olin KE, Waldron JS, Fox DJ Jr, Dunn AK. Intraoperative multi-exposure speckle imaging of cerebral blood flow. *J Cereb Blood Flow Metab*. 2017;37(9):3097-3109.
- Hecht N, Müller MM, Sandow N, Pinczolits A, Vajkoczy P, Woitzik J. Infarct prediction by intraoperative laser speckle imaging in patients with malignant hemispheric stroke. *J Cereb Blood Flow Metab*. 2016;36(6):1022-1032.
- Hecht N, Schrammel M, Neumann K, et al. Perfusion-dependent cerebral autoregulation impairment in hemispheric stroke. *Ann Neurol*. 2021;89(2):358-368.
- Hecht N, Woitzik J, Dreier JP, Vajkoczy P. Intraoperative monitoring of cerebral blood flow by laser speckle contrast analysis. *Neurosurg Focus*. 2009;27(4):E11.
- Hecht N, Woitzik J, König S, Horn P, Vajkoczy P. Laser speckle imaging allows real-time intraoperative blood flow assessment during neurosurgical procedures. *J Cereb Blood Flow Metab*. 2013;33(7):1000-1007.
- Klijn E, Hulscher HC, Balvers RK, et al. Laser speckle imaging identification of increases in cortical microcirculatory blood flow induced by motor activity during awake craniotomy. *J Neurosurg*. 2013;118(2):280-286.
- Nomura S, Inoue T, Ishihara H, et al. Reliability of laser speckle flow imaging for intraoperative monitoring of cerebral blood flow during cerebrovascular surgery: comparison with cerebral blood flow measurement by single photon emission computed tomography. *World Neurosurg*. 2014;82(6):e753-e757.
- Parthasarathy AB, Weber EL, Richards LM, Fox DJ, Dunn AK. Laser speckle contrast imaging of cerebral blood flow in humans during neurosurgery: a pilot clinical study. *J Biomed Opt*. 2010;15(6):066030.
- Woitzik J, Hecht N, Pinczolits A, et al. Propagation of cortical spreading depolarization in the human cortex after malignant stroke. *Neurology*. 2013;80(12):1095-1102.
- Woitzik J, Pinczolits A, Hecht N, et al. Excitotoxicity and metabolic changes in association with infarct progression. *Stroke*. 2014;45(4):1183-1185.
- Miller DR, Ashour R, Sullender CT, Dunn AK. Continuous blood flow visualization with laser speckle contrast imaging during neurovascular surgery. *Neurophotonics*. 2022;9(2):021908.
- Raabe A, Nakaji P, Beck J, et al. Prospective evaluation of surgical microscope-integrated intraoperative near-infrared indocyanine green videoangiography during aneurysm surgery. *J Neurosurg*. 2005;103(6):982-989.
- Zhao X, Belykh E, Cavallo C, et al. Application of fluorescein fluorescence in vascular neurosurgery. *Front Surg*. 2019;6:52.
- von Elm E, Altman DG, Egger M, et al. Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ*. 2007;335(7624):806-808.
- Institute ANS. *American National Standard for Safe Use of Lasers*. Laser Institute of America; 2007.
- Gwet KL. Testing the difference of correlated agreement coefficients for statistical significance. *Educ Psychol Meas*. 2016;76(4):609-637.
- Klein D. Implementing a general framework for assessing interrater agreement in Stata. *Stata J*. 2018;18(4):871-901.

VIDEO 1. LSCI in comparison with FA and white light after clipping of a right-sided middle cerebral artery aneurysm. *Images used with permission of Elsevier Science & Technology Journal, from Intraoperative Laser Speckle Contrast Imaging To Assess Vessel Flow In Neurosurgery, Goldberg J, et al, Brain and Spine 2023; permission conveyed through Copyright Clearance Center, Inc.*

VIDEO 2. Clipping of a right-sided middle cerebral artery aneurysm comparing LSCI and white light; the video is shown first at normal speed, then at 0.5× speed, and then at 0.5× speed. Note how the flow in the aneurysm changes after the clip has been applied and the aneurysm turns black. Yellow arrows indicate flow in a perforator running on top of the aneurysm dome.

VIDEO 3. LSCI in comparison with FA and white light after clipping of a left-sided middle cerebral artery aneurysm.

COMMENTS

The authors present an interesting study investigating laser speckled contact imaging (lsci) for use in cranial neurosurgical applications. This technology has been reported before, but the authors report that their study is the first report of integration of this technology when using the operative microscope. This paper clearly has utility in describing new, practical, technology for cranial neurosurgical applications.

However, there are clearly methodological limitations such as in the cases in which the operator and the LSCI did not agree they state that there was poor lighting. If all the cases that did not agree were due to technical errors, then it begs the question of should they even have included these cases in their analysis. Additionally, nearly 15% of their observations were excluded.

Despite these limitations, this article allows real-time repeated measurements of flow using the intraoperative microscope without the injection of dye, which makes the concept appealing. One must always use caution when using the concept of flow on ICG or other modalities such as “lsci” as a positive result on imaging may not indicate “adequate” flow, which currently can only be determined when using ultrasonic intraoperative flow probe measurements.

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This paper compares the assessment of microvascular vessel patency using fluorescence angiography (FA) with a novel laser speckle contrast imaging (LSCI) technique using a prototype laser system integrated into an operative microscope. The latter method has the theoretical advantage of allowing real-time and repeated measurement of flow without the need for injection of dye. The concept is very appealing despite the current limitations. There were no observed technical issues with FA, but nearly 15% of LSCI observations were excluded due to inadequate visualization. The cause was typically motion-related signal degradation. It appears that under ideal circumstances, the two modalities agree nicely. One shortcoming of fluorescence angiography is that it does not always correlate with sufficient flow to support perfusion. Interpretation of flow is based on the subjective impression of the observer. It is possible to have a stenotic segment that still allows opacification of the distal vessel segment albeit, with inadequate flow. LSCI may offer an ability to quantitate blood flow, especially when used in conjunction with FA.

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