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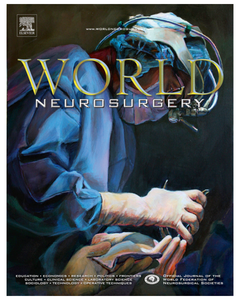

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Key words: DIVA; indocyanine-green videoangiography; aneurysm; AVM; patency; intraoperative

Running head: DIVA in vascular microneurosurgery

Abstract

Objective. Indocyanine-green videoangiography (ICG-VA) is a precious tool to assess vessels and aneurysm patency during neurovascular surgical procedures. However, ICG-VA highlights vascular structures, which appear white over a black background. Therefore, anatomical relations are sometimes not easy to understand at first glance. The recently developed dual-image videoangiography (DIVA) enables the simultaneous visualization of both light and near-infrared (NIR) fluorescence images of ICG-VA.

Methods. The DIVA system was mounted on OPMI Pentero Flow 800 intraoperative microscope (Carl Zeiss Meditec, Jena, Germany). DIVA was used during microsurgical procedures on 5 patients, who were operated for aneurysm clipping and STA-MCA bypass.

Results. DIVA provides real time simultaneous visualization of both aneurysm and vessels and surrounding structures, as brain, nerves, and surgical clips. Although visual contrast between vessels and background is higher with the standard black-and-white imaging, DIVA makes it easier to understand anatomical relations between intracranial structures. Moreover, it gives a better vision of the depth of field.

Conclusions. DIVA has the potentials to become a widely used intraoperative tool to check the patency of intracranial vessels. It should be considered an adjunct to standard ICG-VA for a better understanding of vascular anatomy in relation to surrounding structures, and can have an impact in decision-making during surgery.

Introduction

The monitoring techniques for blood flow and vessel patency during vascular neurosurgery have quickly developed in the recent years.[1-4] Besides flowmetry and Doppler ultrasonography, the use of endoscope and indocyanine-green video-angiography (ICG-VA) have significantly improved the surgeon's ability to assess aneurysm exclusion and patency of parent vessels and perforating arteries.[5-18]. Since Raabe et al introduced it in the clinical practice in 2003, showing its usefulness during neurovascular surgery, ICG-VA has proven to be particularly user-friendly, as it can provide a clear and real-time picture of vasculature during microsurgical operations.[12] However, this technique has some limitations, like its qualitative-only nature, and the impossibility to observe surrounding structures as nerves, brain, and surgical clips, because the very clear fluorescent vessels appear white over a black background.

The recently developed dual-image videoangiography (DIVA) enables the simultaneous visualization of both light and near-infrared (NIR) fluorescence images of ICG-VA.[19] We used DIVA during surgery on 5 patients with cerebral aneurysm or MCA arteritis, and we evaluated its potentials as an adjunct to conventional ICG-VA.

Materials and methods

Microscope and DIVA system

The OPMI PENTERO Flow 800 intraoperative microscope (Carl Zeiss Meditec, Jena, Germany) was used for the operations. The near-infrared color camera MINIRC-2000K (Mizuho, Japan. 48mm x 48mm x 119mm; 0.3kg) was mounted on the PENTERO microscope in order to visualize DIVA during surgery. DIVA requires the same conventional ICG injection, without any need for additional injections. A bolus of 12.5 mg intravenous ICG was injected each time visualization of DIVA images was required.

The objective lens of the microscope should be positioned 285 mm above the operative field. As described by Sato et al, the halogen lamp of the microscope illuminates the operative field with white light (wavelength 380-750 nm), and a xenon lamp connected to the microscope provides NIR fluorescence excitation light (wavelength 720-780 nm). In the camera unit, a special sensor unit with an optical filter processes visible light (400-700 nm) and NIR fluorescence emission light (800-900 nm). A color imaging process and an NIR imaging process detect visible light and NIR fluorescence emission light, respectively. A control system regulates visible light and NIR fluorescence images, which are subsequently overlaid and displayed on a high-definition monitor. As the visible light image is displayed with a resolution of 1920 x 1080 pixels and the high-resolution NIR fluorescence image data are available with a resolution of 1280 x 720 pixels, the NIR image is overlaid in the center of the visible light image. The control system can change gray-scale NIR images to a designated color, selected from a palette of more than 256 visible colors. Green was selected because it is a non-biological color.

Patients

DIVA was used during operation on 5 patients, who underwent surgery for unruptured aneurysm and MCA arteritis (Table 1). We performed a qualitative comparison between conventional ICG-VA and DIVA using both of them in each procedure.

Results

In patients 1 and 2 two clips were necessary for a complete exclusion of the aneurysm. In these cases, compared to ICG-VA, DIVA allowed us to better recognize the vascular anatomy despite the visual obstacle due to multiple clipping (Figures 1 and 2). In patients 1 and 3 (bypass surgery), the long depth of field was clearer using DIVA than ICG-VA (Figures 1 and 3). In patient 4 we found a VA aneurysm with a very thick wall. Both ICG-VA and DIVA failed highlighting the aneurysm, although with DIVA the relations between the thick aneurysm dome and the surrounding structures were more evident (Figure 4). In patient 3, both ICG-VA and DIVA were effective showing the backflow through MCA after proximal clipping (Figure 3). Both ICG-VA and DIVA showed good images of the thin-walled paraclinoid aneurysm (Figure 5). In particular, DIVA is useful in such cases because it shows vascular perfusion and the position of vascular structures in relation to the clinoid.

Discussion

The continuous effort to improve effectiveness and safety during neurovascular microsurgical procedures has led to the development of Doppler ultrasound, flowmetry, and ICG-VA. These tools have been progressively refined, and are nowadays currently adopted in the majority of Neurovascular Surgery departments in developed countries. Particularly ICG-VA has proven to be very helpful not only to confirm aneurysm obliteration, but also to visualize parent vessels, perforating arteries, and veins, enabling a comparison between pre-clipping and post-clipping vasculature patency.[5,6,8,12-14,16,18,20] Despite its great value in the routine surgical practice and its user-friendliness, ICG-VA has the limitation that NIR fluorescent vessels are seen on a black background. Therefore it is not possible to immediately appreciate the relationship between the fluorescent vessels and other structures, as brain, nerves, surgical clips, or even particularly tiny vessels, which have been inadvertently obliterated.

In order to find a solution to this problem, Martirosyan and colleagues realized a fluorescence angiography with augmented microscopy enhancement (FAAME), and published it in 2015.[21] This system allows green-fluorescent NIR images to be superimposed to white light anatomical field. After applying FAAME during *ex vivo* and *in vivo* animal studies, the authors noted that this technique helped to identify small vessels covered with a thin connective tissue. This is potentially useful in many situations, as the dissection of the superficial temporal artery for bypass procedures.

In a recent publication, Sato and colleagues described a similar intraoperative imaging system to simultaneously visualize both light and near-infrared fluorescence images of ICG-VA.[19] They called this system DIVA (dual-image videoangiography), and they applied it on 17 Japanese white rabbits, and later on 15 patients who underwent neurovascular surgery. Green was selected as the color for NIR fluorescence, as it is usually not evident in living tissues and it provides a clear contrast with the background brain. In this study, the authors claimed that DIVA offered a better understanding of vessels and flow compared to conventional ICG-VA. Only 15 patients have been operated with the aid of this new technology so far, and certainly more data need to be collected from different Institutions.

Our short experience showed that DIVA is actually effective to highlight vessels preserving the vision of the surrounding structures. This implies the great advantage for the surgeon to be able to immediately recognize the relations between vessels, aneurysm, brain, and nerves at the first glance. Moreover, surgical clips hamper the vision of ICG-highlighted vessels that stay behind them. Although this is true for both ICG-VA and DIVA, DIVA allows a more clear vision of the clips position, which is particularly helpful especially in the case of multiple clipping. We also noticed that while ICG-VA flattens all structures on a single layer, DIVA preserves the field depth, and its resolution is high even in deep fields thanks to the high-resolution video system. Conversely, ICG-VA has been shown to have a suboptimal quality because increased magnification in narrow and deep fields decreases spatial resolution and light intensity.[5,17,18,20,22] This is particularly useful when the surgical field is narrow and deep, or in areas where many vascular structures are present at different depths, as in our patient 1. Sato et al claim that DIVA is valuable in the detection of obstructed flow through very small vessels, which could be overlooked without the reference of normal anatomy.[19] We agree on that. However, in our opinion ICG-VA has better image contrast, which is also precious to detect tiny vessels. This feature enables ICG-VA to better emphasize, at least in those aneurysms with a very thin wall, the blood flow inside the aneurysm dome.

The need for a better detection of vessels patency at deep operative corridors prompted surgeons to investigate new intraoperative imaging techniques. Sodium fluorescein video-angiography has also been proposed to this purpose.[23] However, despite its improved resolution and the possibility to overlap light and fluorescein-enhanced images, it requires the administration of a second drug after ICG, as it has been shown to be complementary to ICG-VA.

Overall, we think that the first clinical results using DIVA are very promising, since it makes often easier to quickly recognize the vascular anatomy and the anatomical relations between structures, also when they are located at different depths. However, DIVA should not replace standard ICG-VA at this stage. It is rather a precious adjunct. The simultaneous use of both systems can be a valuable tool for surgeons during microvascular operations.

Conclusions

Although image contrast between vascular structures and background is higher with standard ICG-VA, DIVA not only excellently highlights vessels, but also provides simultaneous visualization of the surrounding structures. Therefore the anatomical and functional picture is immediately clear at first glance, without any need to switch camera. Moreover, the depth of field is more evident with DIVA than with standard ICG-VA. This technique, which should be an adjunct and not a replacement of standard ICG-VA, can improve intraoperative decision-making during neurovascular surgical procedures.

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References

1) Akdemir H, Oktem IS, Tucer B, Menkü A, Başaslan K, Günaldi O. Intraoperative microvascular Doppler sonography in aneurysm surgery. *Minim Invasive Neurosurg.* 2006;49:312–316.

2) Klopfenstein JD, Spetzler RF, Kim LJ, Feiz-Erfan I, Han PP, Zabramski JM, et al. Comparison of routine and selective use of intraoperative angiography during aneurysm surgery: a prospective assessment. *J Neurosurg.* 2004;100:230–235.

3) Tang G, Cawley CM, Dion JE, Barrow DL. Intraoperative angiography during aneurysm surgery: a prospective evaluation of efficacy. *J Neurosurg.* 2002;96:993–999.

4) Vitaz TW, Gaskill-Shipley M, Tomsick T, Tew JM Jr. Utility, safety, and accuracy of intraoperative angiography in the surgical treatment of aneurysms and arteriovenous malformations. *AJNR Am J Neuroradiol.* 1999;20:1457–1461.

5) Dashti R, Laakso A, Niemelä M, Porras M, Hernesniemi J. Microscope-integrated near-infrared indocyanine green videoangiography during surgery of intracranial aneurysms: the Helsinki experience. *Surg Neurol.* 2009;71:543–550.

6) de Oliveira JG, Beck J, Seifert V, Teixeira MJ, Raabe A. Assessment of flow in perforating arteries during intracranial aneurysm surgery using intraoperative near-infrared indocyanine green videoangiography. *Neurosurgery* 2008;61(3 suppl):1300–1310.

7) Ichikawa T, Suzuki K, Watanabe Y. Intra-arterial fluorescence angiography with injection of fluorescein sodium from the superficial temporal artery during aneurysm surgery: technical notes. *Neurol Med Chir (Tokyo)* 2014;54:490–496.

8) Killory BD, Nakaji P, Gonzales LF, Ponce FA, Wait SD, Spetzler RF. Prospective evaluation of surgical microscope-integrated intraoperative near-infrared indocyanine green angiography during cerebral arteriovenous malformation surgery. *Neurosurgery* 2009;65:456–462.

9) Kinouchi H, Yanagisawa T, Suzuki A, Ohta T, Hirano Y, Sugawara T, et al. Simultaneous microscopic and endoscopic monitoring during surgery for internal carotid artery aneurysms. *J Neurosurg.* 2004;101:989–995.

10) Kono K, Uka A, Mori M, Haga S, Hamada Y, Nagata S. Intra-arterial injection of indocyanine green in cerebral arteriovenous malformation surgery. *Turk Neurosurg.* 2013;23:676–679.

11) Kuroda K, Kinouchi H, Kanemaru K, Nishiyama Y, Ogiwara M, Yoshioka H, et al. Intra-arterial injection fluorescein videoangiography in aneurysm surgery. *Neurosurgery* 2013;72(2 Suppl Operative):141–150.

12) Raabe A, Beck J, Gerlach R, Zimmermann M, Seifert V. Near-infrared indocyanine green video angiography: a new method for intraoperative assessment of vascular flow. *Neurosurgery* 2003;52:132–139.

13) Raabe A, Nakaji P, Beck J, Kim LJ, Hsu FPK, Kamerman JD, et al. Prospective evaluation of surgical microscope-integrated intraoperative near-infrared indocyanine green videoangiography during aneurysm surgery. *J Neurosurg.* 2005;103:982–989.

14) Roessler K, Krawagna M, Dörfler A, Buchfelder M, Ganslandt O. Essentials in intraoperative indocyanine green videoangiography assessment for intracranial aneurysm surgery: conclusions from 295 consecutively clipped aneurysms and review of the literature. *Neurosurg Focus* 2014;36:E7.

15) Suzuki K, Kodama N, Sasaki T, Matsumoto M, Ichikawa T, Munakata R, et al. Confirmation of blood flow in perforating arteries using fluorescein cerebral angiography during aneurysm surgery. *J Neurosurg.* 2007;107:68–73.

16) Takagi Y, Sawamura K, Hashimoto N, Miyamoto S. Evaluation of serial intraoperative surgical microscope-integrated intraoperative near-infrared indocyanine green videoangiography in patients with cerebral arteriovenous malformations. *Neurosurgery* 2012;70(1 Suppl Operative):34–43.

17) Washington CW, Zipfel GJ, Chicoine MR, Derdeyn CP, Rich KM, Moran CJ, et al. Comparing indocyanine green videoangiography to the gold standard of intraoperative digital subtraction angiography used in aneurysm surgery. *J Neurosurg.* 2013;118:420–427.

18) Zaidi HA, Abla AA, Nakaji P, Chowdhry SA, Albuquerque FC, Spetzler RF. Indocyanine green angiography in the surgical management of cerebral arteriovenous malformations: lessons learned in 130 consecutive cases. *Neurosurgery* 2014;10 Suppl 2:246-251.

19) Sato T, Suzuki K, Sakuma J, Takatsu N, Kojima Y, Sugano T, et al. Development of a new high-resolution intraoperative imaging system (dual-image videoangiography, DIVA) to simultaneously visualize light and near-infrared fluorescence images of indocyanine green angiography. *Acta Neurochir. (Wien)* 2015;157(8):1295-1301.

20) Dashti R, Laakso A, Niemelä M, Porras M, Hernesniemi J. Microscope integrated indocyanine green video-angiography in cerebrovascular surgery. *Acta Neurochir Suppl.* 2011;109:247–250.

21) Martirosyan NL, Skoch J, Watson JR, Lemole GM Jr, Romanowski M, Anton R. Integration of indocyanine green videoangiography with operative microscope: augmented reality for interactive assessment of vascular structures and blood flow. *Neurosurgery* 2015;11 Suppl 2:252-257.

22) Gruber A, Dorfer C, Standhardt H, Bavinzski G, Knosp E. Prospective comparison of intraoperative vascular monitoring technologies during cerebral aneurysm surgery. *Neurosurgery* 2011;68:657–673.

23) Lane B, Bohnstedt BN, Cohen-Gadol AA. A prospective comparative study of microscope-integrated intraoperative fluorescein and indocyanine videoangiography for clip ligation of complex cerebral aneurysms. *J Neurosurg.* 2015;122(3):618-626.

Figure legends

Figure 1. Patient 1. A), B), and C) show the isolated aneurysm with light, ICG-VA, and DIVA images, respectively. D), E), and F) show the anatomy after positioning the first clip with light, ICG-VA, and DIVA images, respectively. G), H), and I) show the final picture after second clip positioning, with light, ICG-VA, and DIVA images, respectively.

Figure 2. Patient 2, affected by left ICA aneurysm as shown with light (A), ICG-VA (B), and DIVA (C) images. First clip positioning with light (D), ICG-VA (E), and DIVA (F) images, respectively. A second clip is required to secure the aneurysm, as shown by light (G), ICG-VA (H), and DIVA (I) images, respectively.

Figure 3. Patient 3 with right MCA arteritis. A) cortical anatomy; B), and C) cortical perfusion with ICG-VA and DIVA images, respectively. D) isolated MCA and its perfusion with ICG-VA (E) and DIVA (F). G) Proximal MCA clipping. Backflow is visible with both ICG-VA (H) and DIVA (I). J) STA-MCA bypass with good perfusion as shown by ICG-VA (K) and DIVA (L).

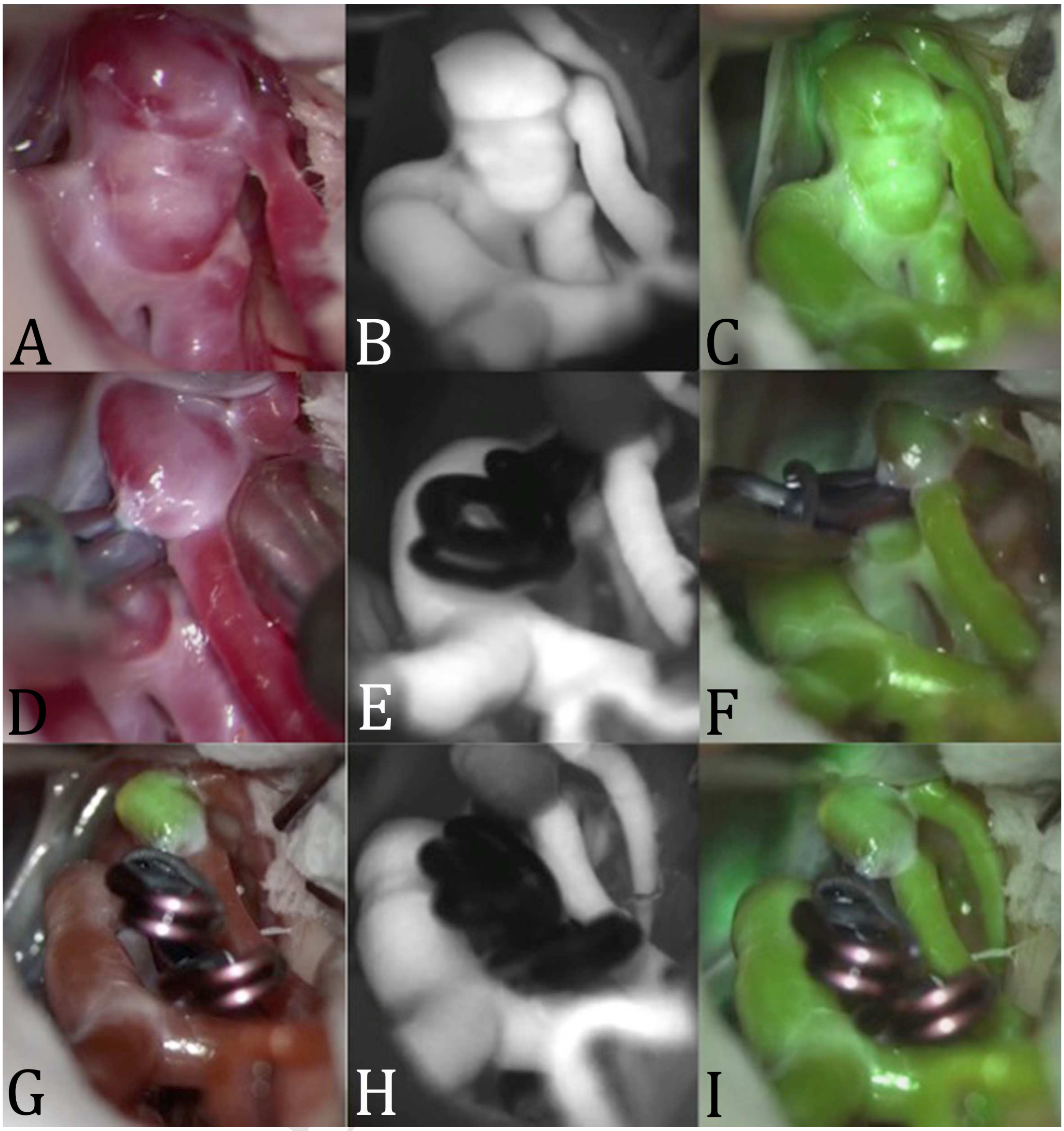
Figure 4. A) 3D CT reconstruction of right VA aneurysm. B) Intraoperative view reveals a thick, whitish wall. C) ICG-VA is not able to visualize the aneurysm because of the thick wall. D) Also DIVA is not visible through the aneurysm wall, but it provides perfusion data preserving the vision of all anatomical structures. E) Wrapping of the aneurysm.

Figure 5. Right ICA paraclinoid aneurysm before (A) and after clipping (B). C) and D) ICG-VA images before and after clipping, respectively. E) and F) DIVA images before and after clipping, respectively.

Table 1. Patients demographics and vascular diseases

Patient	Sex, age	Vascular disease	Symptoms	Surgery
1	F, 70	Unruptured Rt MCA aneurysm	None	Clipping
2	M, 62	Unruptured Lt ICA aneurysm	None	Clipping
3	F, 48	Rt MCA arteritis	TIA last year (lt paresthesia and facial paralysis)	STA-MCA bypass
4	M, 58	Unruptured Rt VA aneurysm	None	Wrapping
5	M, 33	Unruptured Rt ICA paraclinoid aneurysm	None	Clipping

F: female; M: male; Rt: right; Lt: left; MCA: middle cerebral artery; ICA: internal carotid artery; VA: vertebral artery; STA: superficial temporal artery; TIA: transient ischemic attack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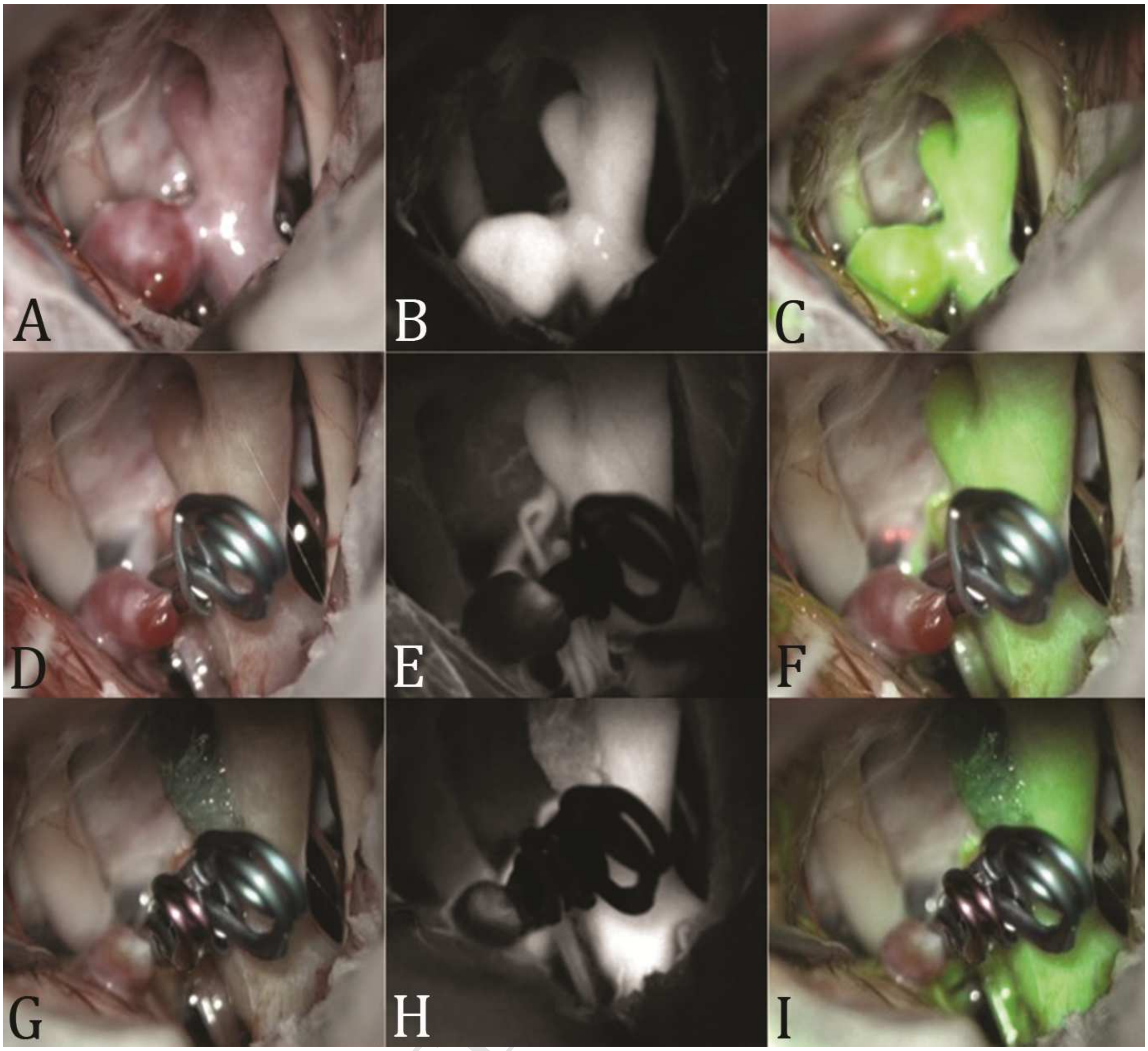
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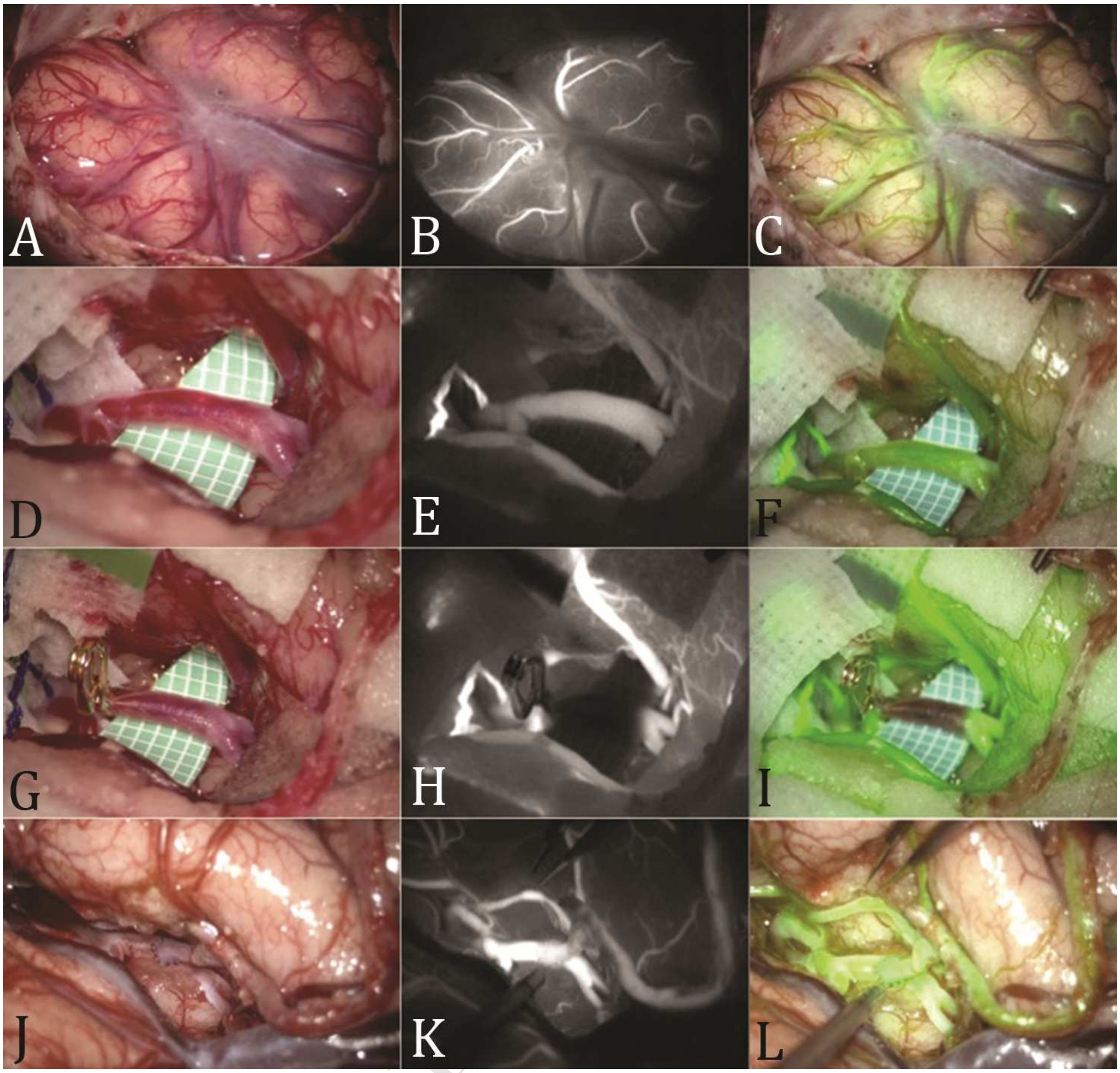
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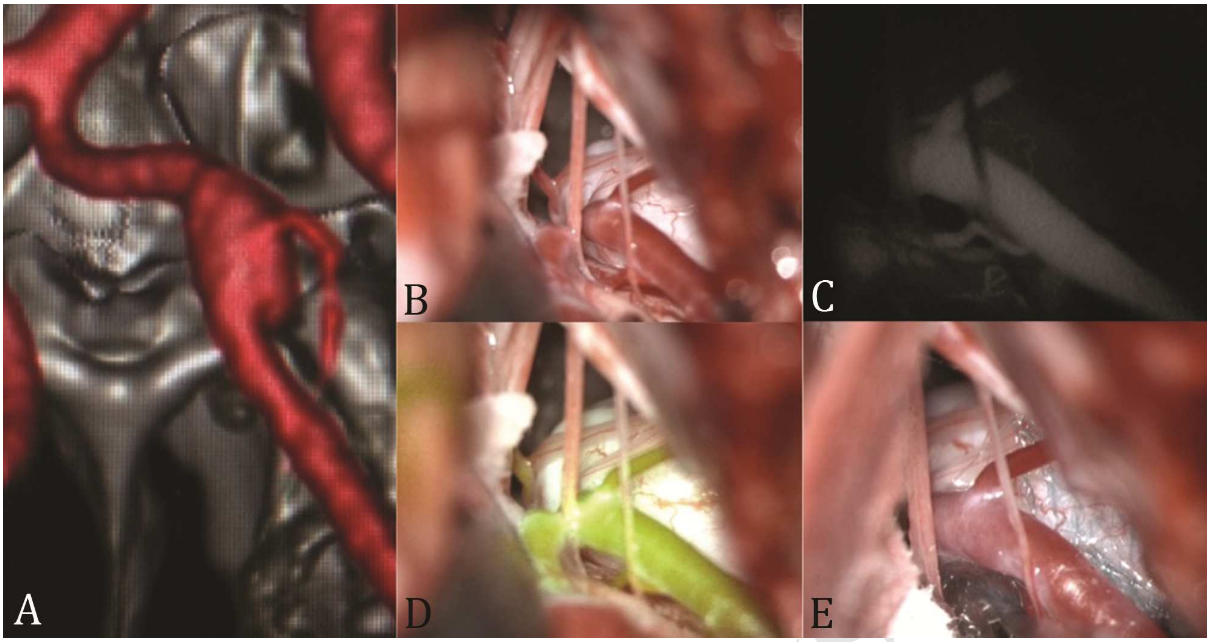
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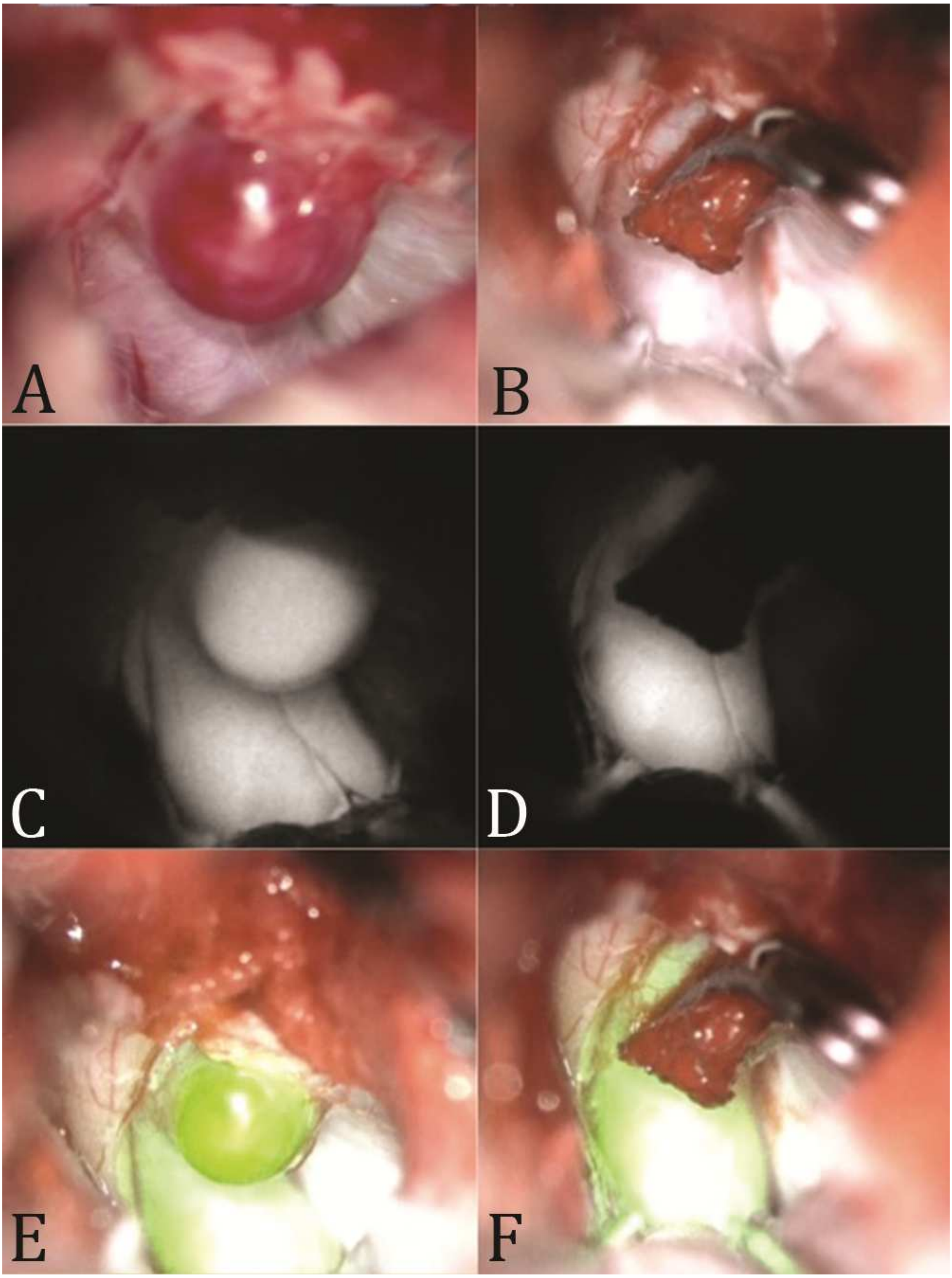
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Highlights

1) Dual-image videoangiography enables simultaneous visualization of both light and near-infrared images

2) Anatomical relations between vessels and other structures are clearer with dual-image videoangiography

3) Dual-image videoangiography provides a better vision of the depth of field compared to indocyanine-green videoangiography

Abbreviation list

DIVA	dual-image videoangiography
FAAME	fuorescence angiography with augmented microscopy enhancement
ICG-VA	indocyanine-green videoangiography
MCA	middle cerebral artery
NIR	near-infrared
STA	superficial temporal artery