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TECHNICAL NOTE

Enhanced analysis of intracerebral arterioveneous malformations by the intraoperative use of analytical indocyanine green videoangiography: technical note

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Abstract In cerebral arterioveneous malformations (AVMs) detailed intraoperative identification of feeding arteries, nidal vessels and draining veins is crucial for surgery. Intraoperative imaging techniques like indocyanine green videoangiography (ICG-VAG) provide information about vessel architecture and patency, but do not allow time-dependent analysis of intravascular blood flow. Here we report on our first experiences with analytical indocyanine green videoangiography (aICG-VAG) using FLOW 800 software as a useful tool for assessing the time-dependent intraoperative blood flow during surgical removal of cerebral AVMs. Microsope-integrated colour-encoded aICG-VAG was used for the surgical treatment of a 38-year-old woman diagnosed with an incidental AVM, Spetzler Martin grade I, of the left frontal lobe and of a 26-year-old man suffering from seizures caused by a symptomatic AVM, Spetzler Martin grade III, of the right temporal lobe. Analytical ICG-VAG visualization was intraoperatively correlated with in situ micro-Doppler investigation, as well as preoperative and postoperative digital subtraction angiography (DSA). Analytical ICG-VAG is fast, easy to handle and integrates intuitively into surgical procedures. It allows colour-encoded visualization of blood flow distribution with high temporal and spatial resolution. Superficial major and minor feeding arteries can be clearly separated from the nidus and draining veins. Effects of stepwise vessel obliteration on velocity and direction of AVM blood flow can be objectified. High quality of visualization, however, is limited to the site of surgery. Colour-encoded aICG-VAG with FLOW 800 enables intraoperative real-time analysis of arterial and venous vessel architecture and might, therefore, increase efficacy and safety of neurovascular surgery in a selected subset of superficial AVMs.

Keywords Arteriovenous malformation · FLOW 800 · Indocyanine green videoangiography · Intraoperative blood flow analysis · Surgery

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Introduction

Indocyanine green videoangiography (ICG-VAG) is a frequently used intraoperative technique to assess vessel patency. This method was initially established in ophthalmology and introduced in vascular neurosurgery in 2003 [10]. Later, ICG-VAG has been integrated into an operating microscope with a light source containing infra-red excitation light illuminating the operating field. In neurosurgery, intraoperative ICG-VAG is mainly used during microsurgery of intracranial aneurysms [11, 12, 15], spinal dural arteriovenous fistulas (AVFs) [5, 9], arteriovenous malformations (AVMs) [3, 6–8, 14] and central nervous system (CNS) tumors [2].

Conventional ICG-VAG visualizes vessel patency at the site of surgery but, unfortunately, does not allow quantitative, time-dependent and spatially precise analysis of intravascular

blood flow. However, this information must be considered crucial, e.g. during stepwise surgical obliteration of AVMs, in order to gain a better understanding of the complex vascular anatomy, as well as to avoid partial resections and any sequelae from uncontrolled bleeding. The microscope-integrated analytical ICG-VAG (aICG-VAG) FLOW 800 has been developed to overcome these technical limitations and provides a colour-encoded visualization to assess the real-time blood flow distribution by extracting data already contained in conventional ICG-VAG. Here we report on our first experiences with aICG-VAG for the intraoperative use in AVM surgery in two illustrative cases.

Patients and methods

Patients

Patient 1: A 38-year-old woman was admitted to our department with progressive headache, nausea and vomiting. Cranial MRI examination showed an AVM in the left superior frontal gyrus without any sign of haemorrhage. Digital subtraction angiography (DSA) confirmed an AVM, Spetzler Martin grade I, with feeders from the left callosomarginal and pericallosal arteries. The size of the nidus was about 2×2×2 cm with a venous drainage via enlarged bridging veins into the superior sagittal sinus. The draining veins were located anteriorly and posteriorly to the nidus (Fig. 1).

Patient 2: A 26-year-old male patient was transferred to our institution with a new onset of focal seizures. Cranial MRI examination revealed an AVM in the right inferior temporal gyrus with a plexiform nidus of 3.8×4×3 cm. DSA confirmed an AVM, Spetzler Martin grade III, with feeders from the right mid-cerebral and posterior communicating arteries. Only superficial large draining veins were detected, draining into the superior sagittal sinus and via the right vein of Labbe into the internal jugular vein (Fig. 2).

Application of aICG-VAG

The fluorescent dye ICG (indocyanin green, ICG-Pulsion; Pulsion Medical Systems, Munich) was administered intravenously (10 mg per dose) during surgery.

For imaging, a microscope-integrated infra-red sensitive monochrome video camera (OPMI Pentero with INFRARED 800) was used. The resulting video data were subsequently analysed by the FLOW 800 imaging software (Carl Zeiss Surgical, Oberkochen, Germany). Detailed visual assessment was achieved by extracting data contained in the conventional ICG-VAG (Fig. 3b). Time of appearance of ICG fluorescence was translated by the analysis tool into colours from red (early appearance) to blue (late appearance) and presented on an overview map (Fig. 4a). A specific software algorithm minimized possible artefacts caused by movements of the microscope during acquisition.

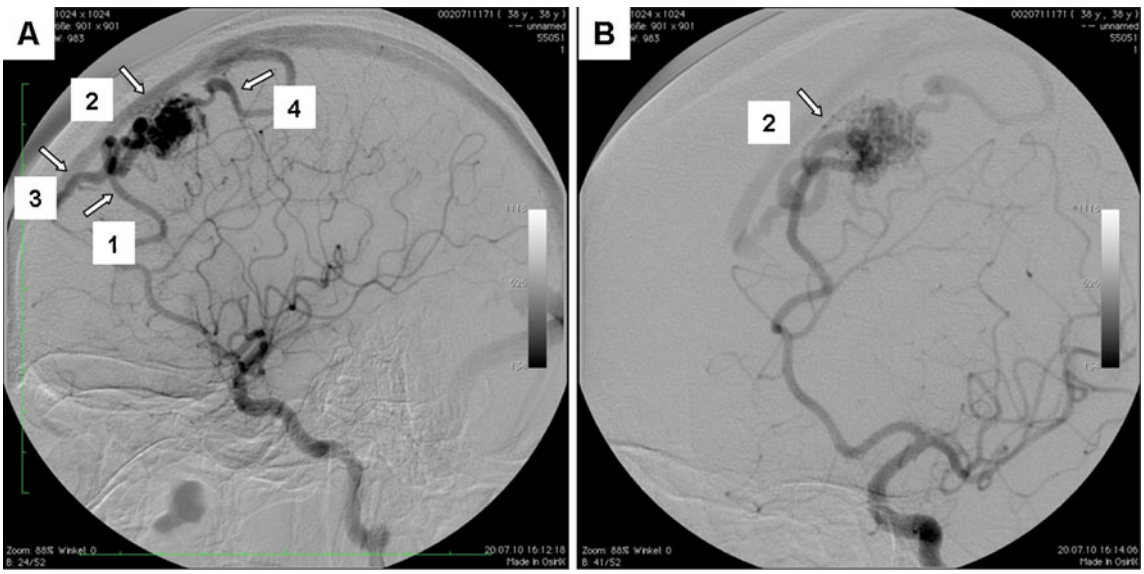

Fig. 1 Patient 1: preoperative DSA images of an AVM, Spetzler and Martin grade I, located in the left frontal lobe (**a** lateral view, **b** oblique view). The major arterial feeder (the callosomarginal artery) (*1*), a branch with small arterial feeders (*2*), the frontal draining vein (*3*) and dorsal draining vein (*4*) are labelled

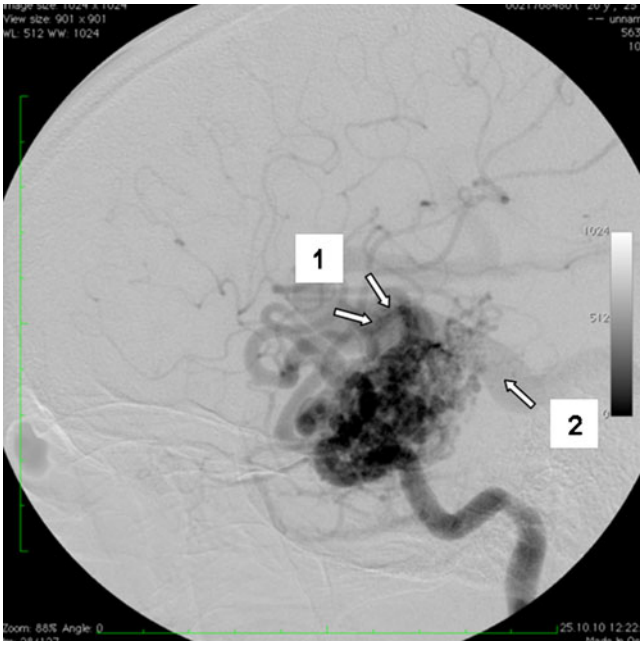

Fig. 2 Patient 2: preoperative DSA images of an AVM, Spetzler and Martin grade III, located in the right temporal lobe (lateral view). A major arterial feeder (from the right mid cerebral artery) with smaller arterial feeders (*1*) and a large superficial draining vein (*2*) are labelled

Intraoperative procedure

Both patients underwent AVM surgery assisted by microscope-integrated aICG-VAG FLOW 800. Visualization of time-dependent quantitative intravascular ICG fluorescence was achieved within a few minutes after data acquisition (mean, 3 min). Repetitive application (patient 1, n=3; patient 2, n=4) was used to address intraoperative changes of AVM blood flow distribution accompanying sequential obliteration of arterial and venous vessels. Finally, both AVMs were completely removed, which was verified by both intraoperative aICG-VAG and microscopical assessment.

Results

First experiences with intraoperative application of aICG-VAG

During the surgical procedure, aICG-VAG analysis guided the identification of feeding arteries and draining veins of the AVM and supplied information about the surrounding vascular anatomy. Moreover, a high (or low) blood flow velocity was confirmed by intraoperative micro-Doppler investigation of the feeding arteries (draining veins) identified by aICG-VAG.

In both cases total analysis time was shorter than 5 min per aICG-VAG. A high resolution and precise imaging quality was achieved with overall dosages of 30 and 40 mg of ICG, which is circa 10% of the upper dose limit (5 mg/kgKG) generally recommended for ICG administration. Accordingly, no side effects were observed.

In the first patient, aICG-VAG was repeatedly performed (three times) in order to identify major and minor feeding arteries and to assess the effects of stepwise vessel obliteration on AVM blood flow. After identification (Fig. 4a *arrow 1*) and obliteration of the major feeding artery, subsequent alterations in AVM blood flow velocity and distribution was assessed by repeated aICG-VAG (Fig. 4b). In line with the preoperative DSA, multiple smaller arterial feeders could be identified (Fig. 4b *arrow 2*). For selected areas, time intensity curves were calculated (Fig. 5), showing variations of blood flow over time by extracting grey values corresponding to the fluorescence signal. The aICG-VAG-guided identification of all feeding arteries resulted in complete obliteration of the nidus (Fig. 6a) and subsequent complete resection, confirmed by postoperative DSA (Fig. 6b).

In the second patient, intraoperative aICG-VAG was used to identify the main feeding arteries originating from

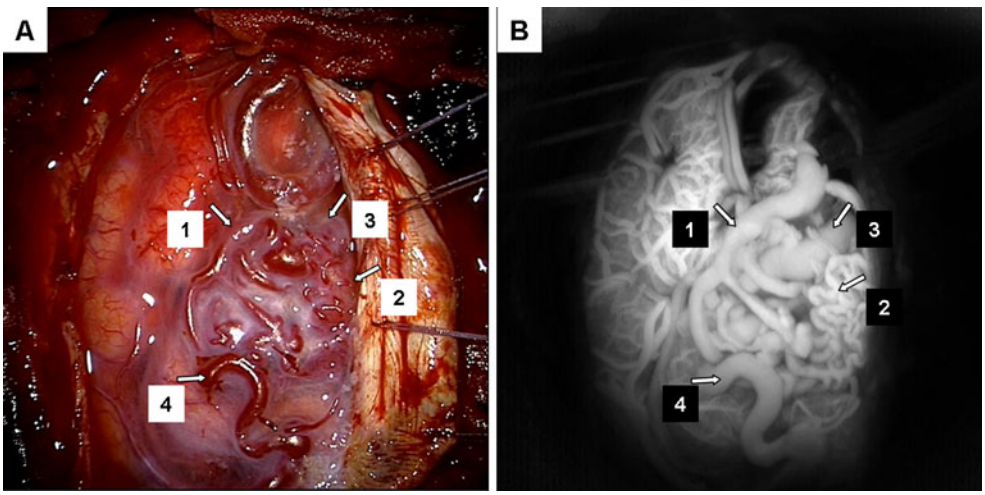

Fig. 3 Patient 1: intraoperative anatomic view (**a**) using a left frontal approach and the early phase of the initial ICG survey (**b**) obtained before surgical resection of the AVM. Corresponding to preoperative imaging, the major arterial feeder (1), smaller arterial feeders (2), frontal (3) and dorsal (4) draining veins are marked

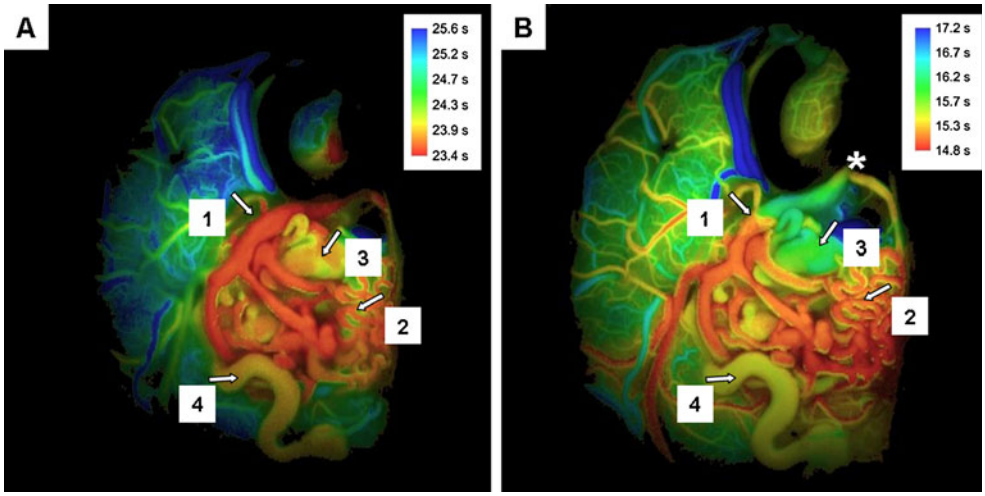

Fig. 4 Patient 1: aICG-VAG imaging before (**a**) and after (**b**) obliteration of the major arterial feeder. **a** The aICG-VAG-guided identification of distinction between major arterial feeder (*1*), the area of multiple arterial feeder branches (*2*) and the frontal (*3*) and dorsal (*4*) draining veins. **b** After obliteration of the major arterial feeder, aICG-VAG was repeated. A decreased perfusion in the major arterial feeder (*1*) and frontal draining vein (*3*) is visible, monitored by a slope of the fluorescence intensity increase. Moreover, the analysis accurately identified a persistent arterial blood supply of multiple smaller arterial feeders (*2*), corresponding to preoperative DSA imaging. *White asterisk* clip position

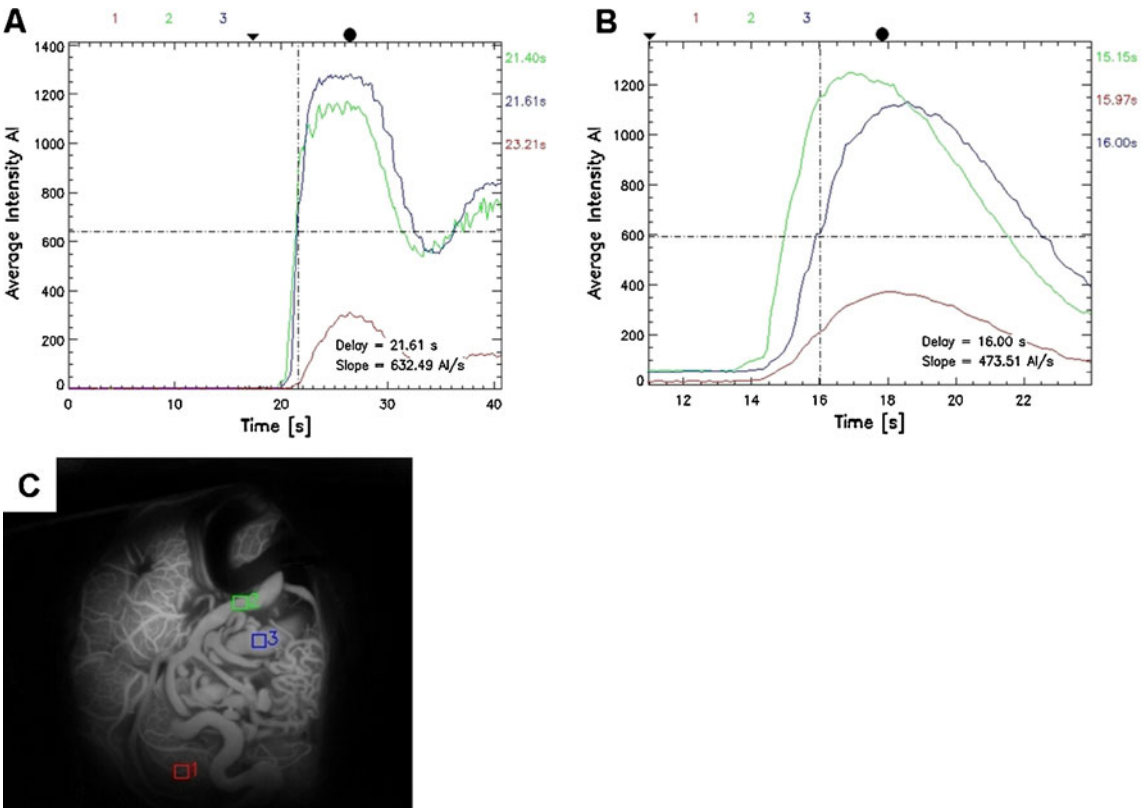

Fig. 5 Patient 1: time-intensity curves (after ICG injection) before (**a**) and after (**b**) obliteration of the major arterial feeder. Curves indicate time dependent averages of fluorescence intensity within the major arterial feeder (*green line*), frontal draining vein (*blue line*) and parenchyma (*red line*). Before obliteration of the major arterial feeder (**a**) no major difference between the time intensity curves of the major arterial feeder (*red line*) and the frontal draining vein (*green*) can be observed. Additionally, ICG fluorescence appears almost simultaneously in the arterial feeder and draining vein, indicating a very short arterio-venous transit time. After major arterial feeder occlusion (**b**) a delayed appearance of ICG fluorescence in the drainig vein compared with the arterial feeder becomes obvious, indicating a longer arterio-venous transit time. The parenchymal fluorescence intensity after major arterial feeder occlusion remained unaffected (*red*). Each graph colour corresponds to that indicated on the region of interest (ROI) (**c**)

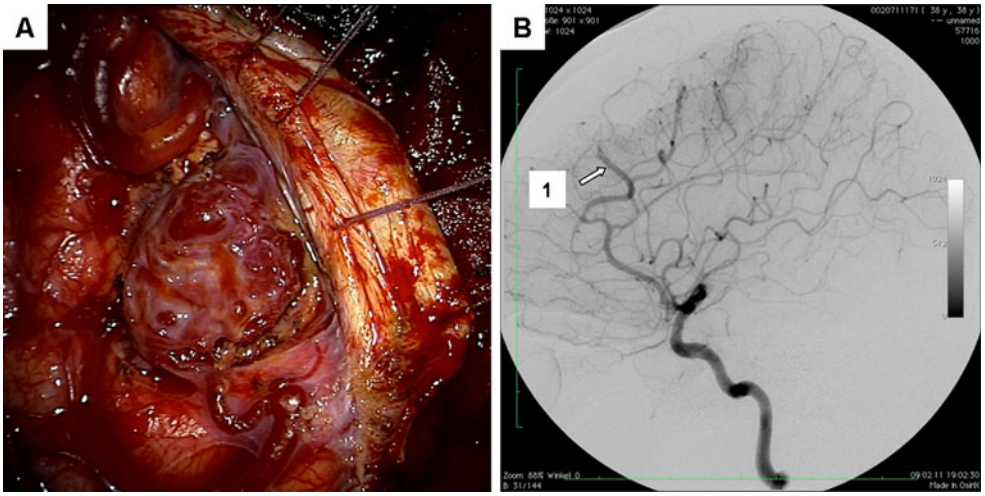

Fig. 6 Patient 1: operative view shortly before complete resection of the nidus (**a**). **b** Postoperative DSA confirmed the complete AVM resection

the middle cerebral artery (Fig. 7b, *arrow 1*). Transient vessel obliterations with repeated ICG administration and aICG-VAG analyses helped to separate this feeder from non-AVM-associated arteries of the sylvian fissure. Identification of the second micro-feeder arising from the posterior communicating artery (as suggested by preoperative DSA) was critically impaired by a large superficial vein (Fig. 7b, *arrow 2*) and therefore could not be sufficiently visualized within the depth of the sylvian fissure until partial removal of the AVM was achieved.

Discussion

Various intraoperative techniques have been introduced in order to increase both the efficacy and safety of AVM microsurgery. Intraoperative spectral Doppler sonography [1, 4] and colour-encoded duplex sonography [16, 17] have improved visualization of the AVM but must be considered less sensitive than intraoperative DSA in the estimation of the actual angioma size and detection of any residual AVM [17]. Intraoperative DSA or intraoperative computed tomographic angiography, however, is not always available, time consuming, costly and associated with radiation exposure [13]. Moreover, the three-dimensional imaging data cannot be routinely integrated into the surgeon's visual field under the microscope.

The use of intraoperative ICG-VAG has been introduced for vascular neurosurgery in 2003 and has been used increasingly ever since. The major advantages are: (1) the reliable visualization of vessel patency in situ, (2) the easy and time-efficient handling of the procedure, (3) lack of any side effects and (4), most importantly, excellent image quality and spatial resolution of real-time fluorescence angiography at the site of surgery. However, little data are available upon ICG-VAG in AVM microsurgery. In a recent single-institutional experience, 17 patients (15 AVMs, 2 AVFs) underwent a total of 46 intraoperative ICG analyses for surgical resection [6]. The initial survey ICG investigations were performed on superficial AVMs in order to obtain orientation with regard to the location of the nidus as well as the differentiation between terminal and en passant

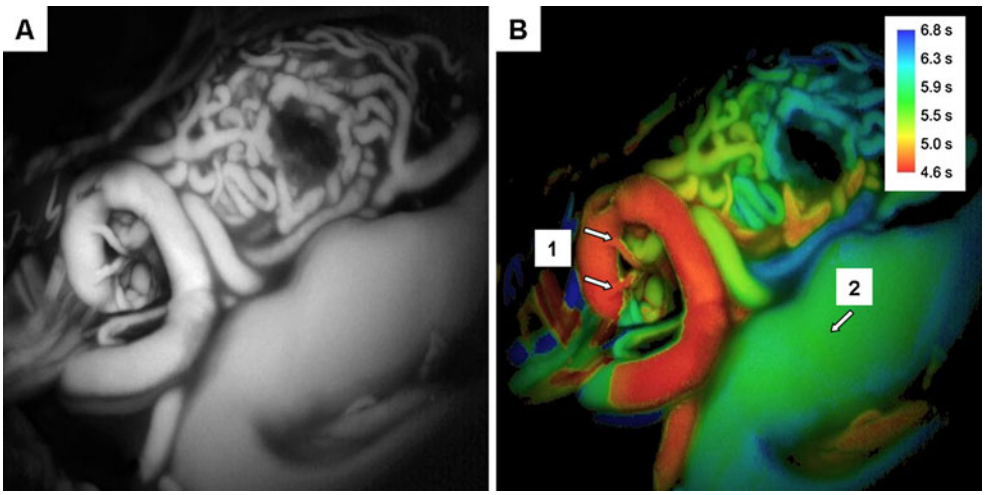

Fig. 7 Patient 2: intraoperative view at the initial ICG survey using a right temporal approach obtained before surgical resection of the AVM (**a**). Due to insufficient time-resolution of flow dynamics, a clear differentiation between major arterial feeders and draining veins was not possible in this high flow AVM with a large plexiform nidus. In contrast, the aICG-VAG imaging allows a reproducible distinction between major arterial feeders (**b**, *arrow 1*) and draining veins (**b**, *arrow 2*)

feeders. Intraoperative repetitive ICG investigations were used to sequentially assess AVM compartments and to identify adjacent arteries. Finally, ICG was used to determine the success of the operative procedures but does not allow time-dependent analyses of intravascular blood flow and transit time [6].

Objective assessment of blood flow, however, is especially important in AVM microsurgery, e.g. in order to determine surgery-related alterations of flow velocity and directions. In this context, the colour-encoded aICG-VAG FLOW 800 software tool has been developed. It supports an in-depth interpretation of ICG-VAG. Compared with the conventional method, aICG-VAG visualizes data that are contained in the ICG-VAG but were not accessible before.

Here we report about our surgical experiences with aICG-VAG in two patients with AVMs of Spetzler-Martin grades I and III. Patient selection was made because of (1) the superficial localization of the AVM, (2) the number of feeding arteries, (3) the compact three-dimensional angio-architecture of the nidus and (4) the superficial venous drainage making this case amenable for intraoperative visualization of all major AVM compartments at the site of surgery. Intraoperatively, aICG-VAG was repeatedly used to assess time-dependent blood flow and its alterations during stepwise surgical removal. Noteworthy, application of the ICG, visualization of fluorescence and data assembling did not differ from well-described ICG procedures. The aICG-VAG analysis was easy to perform, fast and integrated intuitively into the workflow. Most importantly, in the authors' impression colour-encoded blood flow visualization was found superior to conventional ICG visualization with respect to understanding of dynamic blood flow analysis within different AVM compartments and at different time points during surgery. However, sufficient analysis was limited to the site of surgery, while deeply located parts of the AVM within the complex three-dimensional anatomy were not accessible until partial removal was achieved. Consequently, only a selected subset of superficial AVMs would be amenable to this technique. Moreover, repeated administration of ICG during surgery increased background fluorescence within the surrounding tissues with some impairment of the colour-encoded overview maps.

Conclusion

The microscope-integrated aICG-VAG tool is feasible and quick, without interference to the surgical work flow, and increases our understanding of the anatomy of cerebral AVMs in situ and helps to objectify intraoperative blood flow processes accompanying stepwise resection with potential impact on the surgical strategy. Integration of aICG-VAG might, therefore, increase safety and facilitate surgical removal at least in case of superficial AVMs. However, prospective studies of a larger number of patients are necessary to determine critical limitations of this intraoperative imaging tool.

Conflicts of interest None.

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Comment

This is a well illustrated technical note on the application of the colour-encoded aICG-VAG FLOW 800 tool in AVM surgery.

Compared with conventional ICG-VAG, which has had a much larger number of patients, this paper reinforces the concept that microscope-integrated ICG angiography is a useful tool in cerebrovascular and oncological neurosurgery. The adjunct provided here is that colour-encoded visualization of blood flow distribution enhances temporal and spatial resolution, at least in a selected subset of AVMs, compared with routine ICG-VAG. The paucity in the published literature of this specific issue has made this contribution worthy of being published.

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