Acta Neurochir (2010) 152:1519–1525
DOI 10.1007/s00701-010-0723-5

CLINICAL ARTICLE

Near-infrared indocyanine green videoangiography versus microvascular Doppler sonography in aneurysm surgery

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Received: 20 April 2010 / Accepted: 17 June 2010 / Published online: 11 July 2010
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Abstract
Introduction The quality of surgical treatment of intracranial aneurysms is determined by complete aneurysm occlusion and restoration of flow in the parent, branching and perforating vessels. In postoperative digital subtraction angiography (DSA), unexpected aneurysm residuals and vessel occlusions are frequently detected. Here, the value of two nearly noninvasive and cost-effective techniques for intraoperative flow evaluation (near-infrared indocyanine green video angiography (ICG-VA) and microvascular Doppler sonography (mDs)) is investigated in a prospective study.
Patients and methods Over a period of 10 months, the authors surgically clipped 50 aneurysms under intraoperative pre- and post-clipping evaluation of flow in the parent, branching and perforating vessels and the aneurysm sack by the two techniques. Intraoperative applicability of each technique was compared to each other and to postoperative digital subtraction angiography as standard evaluation technique.
Results Forty-five aneurysms were totally occluded without vessel compromise (90%). Intraoperatively, ICG-VA was considered useful in 43 cases (86%) and mDs in 44 cases (88%), respectively. Both techniques could compensate each other's weak points to a certain degree; but two branch occlusions (4%) and three neck remnants (6%) were revealed by postoperative DSA.
Conclusion Both techniques have specific drawbacks that could be compensated by each other, to a certain extent. Intraoperatively, ICG-VA and mDs should not be considered competitive, but complementary. This study implicates that the combination of both applications on a routine basis assures the quality of aneurysm surgery by nearly noninvasive and cost-effective techniques. However, DSA remains the gold standard for evaluation of aneurysm occlusion.

Keywords Microvascular Doppler sonography · Near infrared indocyanine green videoangiography · Aneurysm clipping · Digital substraction angiography

This manuscript has not been previously published in whole or in part, or submitted elsewhere for review. The work presented in this manuscript was not supported. The authors have nothing to disclose.

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Introduction

Surgical clipping remains the most definitive treatment for intracranial aneurysms. It aims at complete occlusion of the aneurysm while preserving the patency of parent, branching and perforating vessels. Incomplete occlusion or neck remnants may lead to re-growth and re-rupture [8, 13, 14]. Unexpected vessel obstruction is associated with a higher morbidity [21]. The standard technique to assess anatomic results and confirm aneurysm obliteration is postoperative digital subtraction angiography (DSA). In these, the incidence of unexpected neck residuals ranges from 4% to 19% [1, 11, 21, 23, 27, 28] and the incidence of unexpected vessel occlusions from 0.3% to 12% [1, 11, 21, 23, 27]. Numerous authors have recommended the application of intraoperative DSA to readjust an imperfect clipping immediately [3, 5, 10, 18–20, 29]. However, the routine use of intraoperative angiography is not available at most centers. Instead, many surgeons advocate the use of microscope-integrated near-infrared indocyanine green videoangiography (ICG-VA) and/or microvascular Doppler sonography (mDs) for intraoperative assessment [2, 4, 7, 9, 12, 15, 22, 24–26, 30]. The objective of this study was the comparison of ICG-VA and mDs with respect to aneurysm occlusion and vessel patency.

Material and methods

Patient population

Between October 2008 and August 2009, 50 aneurysms were surgically treated by the authors in 43 operations at the Department of Neurosurgery, Johannes Gutenberg-University, Mainz, Germany. The patient population consists of 17 males and 23 females. The patients' age ranged from 34 to 78 years (mean 57.0 years). Twenty-three procedures followed an acute subarachnoid hemorrhage (SAH); 20 operations were performed on patients with incidentally found aneurysms.

Surgical procedure

Every aneurysm case, regardless if it is acute or incidental, was individually discussed with the endovascular surgeons for the safest and least traumatic treatment option. Sixty percent of all cases were treated surgically, 40%, endovascularly. In acute cases, the aneurysm was secured as soon as possible to minimize the risk of re-bleeding. For aneurysm clipping, a subfrontal, transfissural, interhemispheric, or retromastoidal approach was performed depending on site and size of the aneurysm. Patients classified H&H°5 were also considered for surgery in the early stage if no signs of brain herniation were present, and if endovascular treatment was not suitable.

Application of ICG-VA and mDs

Intraoperative ICG-VA was realized using a commercially available surgical microscope (OPMI® Pentero™ , Carl Zeiss, Oberkochen, Germany). The principles of this technique are described in detail elsewhere [24–26]. It has become a well-accepted technique for intraoperative vessel and aneurysm evaluation. In this series, ICG-VA, with a standard intravenous bolus of 0.5 mg/kg ICG, was performed before and after clipping of every aneurysm.

Microvascular Doppler sonography was accomplished using a 1-mm microprobe (DWL Electronic Systems Inc., Santa Clara, CA). Blood flow in the involved vessels and in the aneurysm sac was assessed by listening, rather than watching the amplitude response. Intraoperative applicability and quality of evaluation of each technique was recorded by the operating neurosurgeon for every aneurysm. Particular respect was given to: patency of parent artery, patency of branching arteries, patency of perforating arteries, and degree of aneurysm occlusion. In each case, the value of the evaluation technique was separately addressed, considering a technique "valuable" if all aspects could be evaluated accurately. If one or more aspects remained insecure, the technique was considered as a "failure". During the hospital stay, postoperative DSA was performed as standard evaluation technique, and intraoperative evaluation results were compared with this gold standard.

Results

Fifty aneurysms were clipped by the three authors in 43 sessions (Table 1). ICG-VA, as well as mDs, was applied before and after clipping of every single aneurysm without technical problems. The subfrontal approach was used 30 times mainly via a supraorbital skin incision (20 times) to occlude fifteen anterior communicating artery (ACoA), three internal carotid artery (ICA), twelve middle cerebral artery (MCA), two posterior communicating artery (PCoA) and four anterior cerebral artery aneurysms. The classic pterional approach was used nine times on four MCA, two ICA, two PCoA and two basilar tip aneurysms. The unilateral interhemispheric approach was employed to treat one A3 aneurysm. The retromastoidal approach was reserved for one anterior inferior cerebellar artery (AICA) and two posterior inferior cerebellar artery (PICA) aneurysms. Postoperative DSA showed 45 aneurysms with fully occluded aneurysm sack, no neck remnant, and without vessel compromise (90%), two cases of branch occlusion (4%), and three neck remnants (6%). Two of the latter were small 1-mm remnants disposed for follow-up observation. The other case was opted for endovascular occlusion. Intraoperative findings of ICG-VA and mDs in relation to postoperative DSA are listed in Table 2.

ICG-VA

ICG-VA was technically possible in all cases. No technique-related complications were observed.

Table 1 Patient collective

	Patients	Aneurysms	Operations
Numbers	40 (23 female, 17 male)	50 (36 single aneurysms, 4 multiple aneurysms)	43 (23 SAH, 20 elective; 37 single craniotomy, 3 two craniotomies)

Table 2 Cases with noticeable findings

No	Gender	Age	Aneurysm location[a]	Approach[b]	ICG-VA	mDs	Postoperative DSA	Comment
1	W	73	BA	pter	Failure	Failure	Ok	Restricted lighting conditions in the dephth of the field
2	M	44	PICA	RM	Useful	Useful	Neck remnant	
3	W	52	AComA	SF	Useful	Useful	Neck remnant	
4	W	58	MCA	SF	Failure	Failure	Branch occlusion	Clip reconstruction with eight clips
5	W	45	PerA	IH	Failure	Useful	Neck remnant	Microbleedings, dye extravasation
6	W	40	MCA	pter	Failure	Useful	Ok	Vessel wall calcification
7	W	58	PICA	RM	Failure	Useful	Ok	
8	M	65	MCA	SO	Failure	Useful	Ok	Achnoidal scarring
9	M	65	MCA	SO	Failure	Useful	Ok	Restricted lighting conditions, small craniotomy
10	M	48	PComA	SO	Failure	Useful	Ok	Restricted lighting conditions, small craniotomy
11	W	39	MCA	SO	Useful	Failure	Ok	
12	W	45	MCA	SO	Useful	Failure	Ok	Branch behind aneurysm sack
13	W	54	AICA	RM	Failure	Useful	Branch occlusion	

The columns ICG-VA and mDS represent the intraoperative impression of the applicability of the respective method

AComA anterior communicating artery, *PICA* posterior inferior cerebellar artery, *BA* basilar artery, *MCA* middle cerebral artery, *PComA* posterior communicating artery, *PerA* pericallosal artery, *AICA* anterior inferior cerebellar artery*pter* pterional approach, *RM* retromastoidal approach, *SF* subfrontal approach, *IH* interhemispheric approach, *SO* supraorbital approach

A total of 65 evaluations of parent vessels (including 15 assessments of both A1 vessels in AComA aneurysms) were done. In 65 investigations, the vessel could be evaluated accurately in 60 cases (92.3%). In one patient with hemostasis dysfunction after acetyl salicylic acid therapy for expected myocardial infarction, diffuse micro-bleeding in the surgical field occurred. Dye extravasation made an assessment of the vasculature by ICG-VA impossible (case 5, Fig. 1). In a case of a ruptured giant MCA aneurysm, the view was restricted after application of eight clips to reconstruct the MCA bifurcation (case 4). In the three other cases, the quality of ICG-VA was restricted by reduced lighting conditions in the depth of the field (case 1, basilar artery (BA) aneurysm; case 9, MCA aneurysm approached by supraorbital key hole craniotomy; case 10, posterior communicating artery (PCom) aneurysm). Nevertheless, no parent artery occlusion occurred.

Out of 89 branching vessels, 78 were accurately assessed (87.6%). Again, dye extravasation in the patient with hemostasis dysfunction (case 1, Fig. 1) made an assessment of the two branches impossible. In the case with the multi-clip reconstruction of a ruptured MCA aneurysm (case 4), evaluation of flow in the two branching vessels was also not possible. In this case, a branch occlusion occurred and was not detected. In all three patients where poor lightning conditions restricted the evaluation of the parent vessels, the five branching vessels could not be evaluated as well (case 1, BA aneurysm, two branches; case 9, MCA aneurysm, two branches; case 10, PCom aneurysm, one branch). In one case of a ruptured PICA aneurysm, no flow was visible in ICG-VA after clip application in one of the branches as a false negative result (case 7). A false positive result was achieved in one patient with an unruptured AICA aneurysm. After clip application, ICG-VA showed good dye contrast in the branching vessel. DSA later on revealed a branch occlusion with retrograde filling of the occluded segment via distal anastomotic branches (case 13, Fig. 2).

Small perforators were present in 46 of 50 aneurysms. Those were correctly investigated in 41 of the 46 cases (89.1%). The assessment of perforators was not possible in one case with hemostasis dysfunction and dye extravasation (case 5, Fig. 1), in the three cases with restricted lighting conditions (case 1, 9, 10) and in one case with extensive arachnoidal scarring (case 8, MCA aneurysm).

Out of the 50 aneurysms, 45 aneurysms appeared to be occluded in the ICG-VA (90%; Table 2). Evaluation of aneurysm sack occlusion was not possible in the case of dye extravasation caused by hemostasis dysfunction (case 5), in the case of multi-clip reconstruction of the ruptured complex MCA aneurysm (case 4), and in the three cases of restricted lighting conditions (cases 1, 9, 10).

The detection of neck remnants was not possible in the five mentioned cases (cases 1, 4, 5, 9, 10), as well as in one case of arachnoidal scarring (case 8, MCA aneurysm) and in one case of vessel wall calcification (case 6, MCA aneurysm). In two cases (case 2, PICA aneurysm; case 3, ACoA aneurysm), ICG-VA revealed false negative results when postoperative DSA showed neck remnants that were not detected intraoperatively.

Overall, evaluation of parent, branching and perforating vessels, and aneurysm morphology was considered valuable

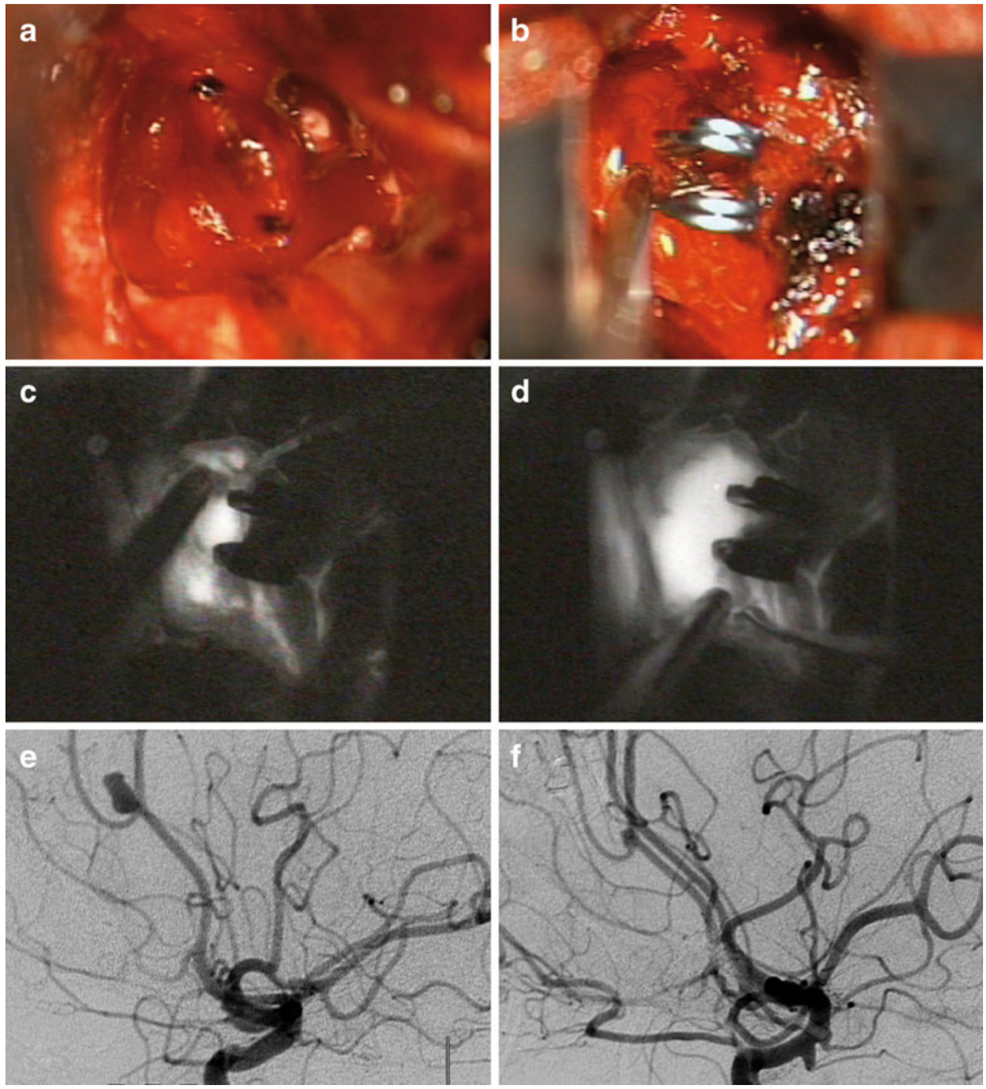

Fig. 1 Aneurysm of the right APerA (case1) exposed and clipped via a unilateral interhemispheric approach. **a**, **b** Coagulation dysfunction with microbleeding caused a constant dye extravasation during ICG-VA. **c**, **d** Preoperative and postoperative DSA showing the aneurysm (**e**) and the 1-mm neck remnant (**f**)

(meaning that the parent, branching and perforating vessels, as well as the aneurysm, could be well evaluated) in 42 aneurysms (84%).

mDs

There were no technique-related complications with micro Doppler sonography.

Parent arteries were accurately investigated in 63 of 65 cases (96.7%). In a case of a ruptured giant MCA aneurysm, the maneuverability was restricted after application of eight clips to reconstruct the MCA bifurcation (case 4). In a case of a basilar artery tip aneurysm, the interpeduncular space after clip application was too narrow to bring the Doppler probe to the basilar trunk (case 1).

Branching vessels were securely evaluated in 85 cases (95.5%). Assessment via mDs failed in the two mentioned cases with the multi-clip reconstruction of the MCA bifurcation after rupture of a giant MCA aneurysm (case 4) and the narrow situation within the interpeduncular space after clipping a BA aneurysm (case1). In one case of an MCA aneurysm, a major branch aroused rectangular-shaped image behind the aneurysm which was not caught with the Doppler probe (case 12). In another case of an MCA aneurysm, mDs revealed a false negative result (case 11). Although no flow was detected in one of the branching vessels, postoperative DSA showed no branch occlusion.

Small perforators were present in 46 of 50 aneurysms. Those were correctly investigated in 38 of the 46 cases (82.6%). In case 1, it was impossible to bring the Doppler probe into the interpedunclar cistern after clip application on a BA aneurysm. In the other seven cases, technical problems were experienced in catching tiny perforating vessels with the 1-mm probe.

Aneurysm sac occlusion was confirmed by mDs in 48 of 50 cases (96.0%). Again in case 1, the Doppler probe could not be brought into the interpeduncular space after clipping of a BA aneurysm and the assessment of mDs

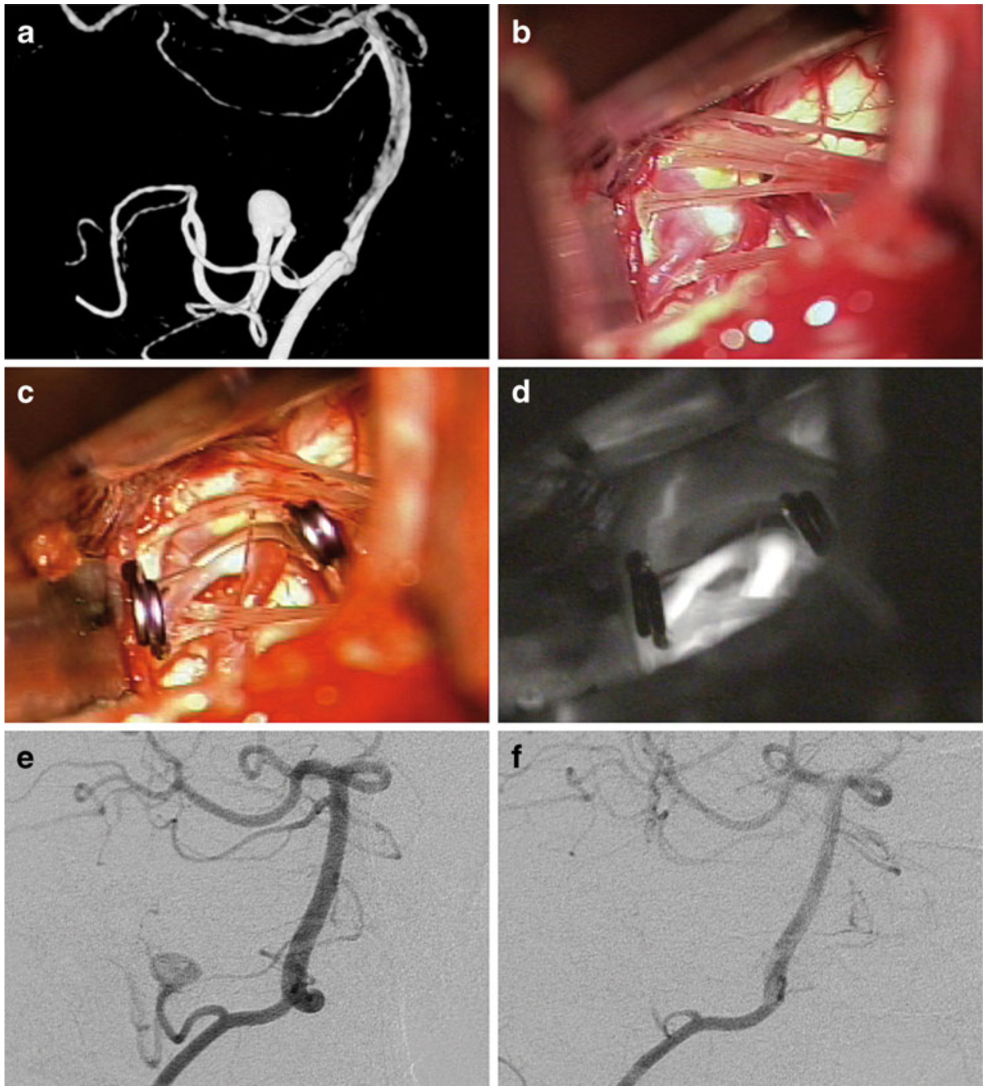

Fig. 2 Aneurysm at the angular point of an AICA loop (case13, **a**). Exposure and clip reconstruction of the vessel course (**b**, **c**). Although mDs detected no flow in the major branch, ICG-VA showed substantial dye contrast (**d**). DSA revealed a branch occlusion and a retrograde filling of the distal vessel segment by anastomotic branches (**e**, **f**)

was restricted in the case of multi-clip reconstruction of the MCA bifurcation after rupture of a giant MCA aneurysm (case 4).

The ability to detect aneurysm neck remnants by mDs is literally not given. A secure assessment of this aspect was not possible.

The overall evaluation of the flow in the aneurysm and the involved vessels was found useful in 45 cases (90%).

Discussion

The principle of microsurgical clipping of an intracranial aneurysm is to completely occlude the aneurysm while preserving blood flow in the involved parent, branching and perforating vessels. However, unexpected branch occlusions or hemodynamically relevant constrictions, as well as insufficient aneurysm obliteration, can be detected in postoperative angiograms even in the most experienced centers. The rate of postoperative aneurysm remnants is reported to range from 4% to 19% [1, 11, 21, 23, 27, 28] and of unexpected vessel occlusion to range from 0.3% to 12% [1, 11, 21, 23, 27]. Postoperative detection of unexpected findings might necessitate reoperation and readjustment of clip position. The results of such revision procedures are questionable [21]. In cases of unexpected vessel obstruction, it is frequently too late to avoid permanent deficits. Accordingly, the quality of surgical treatment could be enhanced by intraoperative vascular imaging and monitoring. Intraoperative DSA was considered to be the ideal evaluation technique by many authors [3, 5, 6, 18, 20, 29], but has failed to become a routine during aneurysm surgery for several reasons [16, 17, 20]. In most centers, its application is limited to complex, giant, basilar artery and paraclinoidal aneurysms since it is an expensive, technically demanding, personnel-intensive and invasive procedure. In this study, two alternative intraoperative vascular imaging or monitoring techniques were assessed on all subsequent aneurysm cases of the authors.

ICG-VA is a technique to visualize blood flow in the cerebral vasculature after intravenous injection of ICG dye. Microvascular Doppler sonography is used to compare flow in the parent and branching vessels, as well as in the aneurysm sack, before and after clipping. It is a safe and easy to use procedure with low costs and low rate of morbidity. It is quickly accessible and can be used repeatedly even over the recommended daily dose of 5 mg/kg. Microvascular Doppler is a quick, noninvasive and valuable tool to provide information about parent or branching vessel occlusion or stenosis, as well as residual filling of the aneurysm.

The goal of the present study was to evaluate the potential advantages and pitfalls of these two intraoperative evaluation techniques in comparison with each other, but also in comparison with the "gold standard" postoperative DSA. The study demonstrated that 90% of all aneurysms could be correctly evaluated when both techniques were simultaneously used. If only one technique was applied, the percentage of correct evaluation was sometimes reduced down to almost 80%.

In detail, ICG-VA provided good evaluation of complete aneurysm occlusion, neck remnants, and flow in the parent and branching vessels (Table 3). The percentage of correct evaluations reached from 89.1% to 92.3%, depending on the quality assessed. ICG-VA showed peculiar advantages in the evaluation of perforating vessels. While frequently the small Doppler probe was not or only under difficulties suitable for blood flow assessment in small perforators, ICG-VA gave a direct reliable display of the perfusion of even smallest perforators. Additionally, and in contrast to mDs, ICG-VA allows not only an investigation of physiological qualities, but also enhances the visualization of the anatomy. Thus, ICG-VA supports the evaluation of aneurysm neck remnants which cannot be done with mDs. However, in comparison with microvascular Doppler testing, some peculiar drawbacks have also to be discussed. Most important to the authors, the illumination deep in the surgical field was found to be too weak for the polarization filter to irradiate through rather small craniotomies (cases 1, 9, 10). Presence of blood clots, intramural thrombi, or calcifications further limited the intraoperative evaluation with ICG-VA (case 7). In acute cases with coagulation disorders and constant microbleeding, dye effusion makes an evaluation of the vessels of interest impossible (case 5).

One of the biggest advantages of mDs is its easy availability. No particular microscope equipped with polarization filter is required. No contrast dye has to be prepared. In the present study, mDs gave immediate valuable results. Its peculiar advantage in comparison with ICG-VA lies in its high accuracy. Even deep in the surgical field, mDs evaluation was possible. Also, it was not much influenced by other problems with visualization such as microbleedings. Thus, for most of the evaluated qualities, mDs was the preferred method of evaluation by the authors. However, the assessment of perforator arteries is less accurate than with ICG-VA. Additionally, mDs does not enhance the display of anatomy like ICG-VA does, which might be particularly valuable in neck remnant evaluation.

Thus, both techniques, ICG-VA and mDs, have their particular advantages and drawbacks. Overall, eleven cases were considered as failure by either one or both methods. Since mDs could deliver correct findings in six cases of ICG-VA failure and ICG-VA could compensate for mDs problems in another two cases, the combination of both methods can compensate each other's weak points to a certain extent that only five unexpected objectionable findings were detected by postoperative DSA. Thus, the authors rather prefer to apply both techniques supplementary and cannot find a preference for one of the evaluation techniques described.

Nevertheless, five findings were only detected by postoperative DSA, although this did not cause any neurological deficit. Thus, despite the combination of both techniques compensating each other weak's points, postoperative DSA will remain the gold standard. Whether intraoperative DSA is absolutely necessary or not will remain a continuous debate. At least, the present small series does not support the absolute necessity to apply DSA intraoperatively since no neurological deficits due to unexpected findings occurred and only one postoperative intervention for occlusion of a neck remnant was required. However, based on the study results, only by the implementation of more hybrid neurovascular suites in dedicated neurovascular centers, a further improvement of neurovascular surgery results can be expected.

Table 3 Compilation of the presumable assets and limitations of each method in detecting flow in the vessel sections

	Completeness of aneurysm occlusion (*n*=50)	Aneurysm neck remnant exclusion (*n*=50)	Flow parent vessel (*n*=65)	Flow branching vessel (*n*=89)	Flow perforator vessels (*n*=46)
ICG-VA	45 (90.0%)	41 (82.0%)	60 (92.3%)	78 (87.6%)	41 (89.1%)
mDs	48 (96.0%)	0	63 (96.7%)	85 (95.5%)	38 (82.6%)

Acknowledgement The authors gratefully acknowledge Mr. S. Kindel's expert support in the preparation of the figures.

Disclosure J Oertel is a consultant of Karl Storz company but there is no relation to this study.

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