The Application of FLOW 800 ICG Videoangiography Color Maps for Neurovascular Surgery and Intraoperative Decision Making

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■ BACKGROUND: **Indocyanine green (ICG) videoangiography can assess cerebral blood flow, but results are primarily qualitative. FLOW 800 software measures fluorescence dynamics and creates a semiquantitative color delay map for assessment of relative sequence of blood flow within the vasculature.**

■ METHODS: **We retrospectively reviewed 23 consecutive patients for whom FLOW 800 ICG videoangiography was used. They harbored aneurysms, arteriovenous malformations (AVMs), dural arteriovenous fistula (dAVF), or hemangioblastoma. Patients' characteristics, FLOW 800 data, and clinical findings were recorded. Color map data were readily available intraoperatively and guided surgery.**

■ RESULTS: **The cohort included 10 patients with AVMs, 11 with aneurysms, 1 with dAVF, and 1 with hemangioblastoma. Approximately two thirds of patients underwent intraoperative angiography. FLOW 800 data provided semiquantitative data regarding localization, flow status in major feeding arteries, and dominance of the arterialized draining veins for AVMs, more than data from ICG videoangiography alone. For complex aneurysms, color maps confirmed relative adequate flow in parent and branching vessels. For the foramen magnum dAVF, the location of the dominant transdural connection was appreciated only via flow analysis. Flow analysis created the blood flow map of a large complex solid brainstem hemangioblastoma and guided devascularization. All FLOW 800 findings agreed with intraoperative and postoperative angiography.**

■ CONCLUSIONS: **ICG videoangiography with FLOW 800 analysis can provide semiquantitative and relative flow magnitude data that are efficient and noninvasive. This process helps identify early arterialized veins and their flow status during AVM and dAVF surgery and can confirm adequate relative flow within branching vessels during aneurysm surgery when clip-induced stenosis is suspected.**

INTRODUCTION

Indocyanine green (ICG) was first used in surgery in ophthalmology to study retinal blood flow.[1] It was not until 2003 that Raabe et al.[2] introduced ICG in neurosurgery. ICG videoangiography is a useful qualitative instrument to detect blood flow during microsurgery of aneurysms. It allows the surgeon to assess the filling of vessels and the timing of the arterial and venous phases of interest. However, it does not replace a cerebral angiogram, the gold standard for vasculature assessment, because it can assess only the vasculature directly within the field of view of the microscope and lacks quantitative interpretation.

FLOW 800 (Zeiss Meditec, Oberkochen, Germany) is a relatively new software program that allows ICG data to be analyzed in a semiquantitative manner through a color delay map, which identifies the direction and sequence of blood flow relative to the surrounding vasculature via fluorescence dynamics.[3] Stummer et al.[4] previously provided a detailed analysis of the fluorescence curves for this technology for measuring cortical blood flow. In

Key words
- Brain arteriovenous malformations
- Cerebral aneurysm
- Dural arteriovenous fistula
- FLOW 800
- Indocyanine green
- Ligation
- Videoangiography

Abbreviations and Acronyms
AVF: Arteriovenous fistula
AVM: Arteriovenous malformation
dAVF: Dural arteriovenous fistula
DSA: Digital subtraction angiography
ICG: Indocyanine green
MCA: Middle cerebral artery

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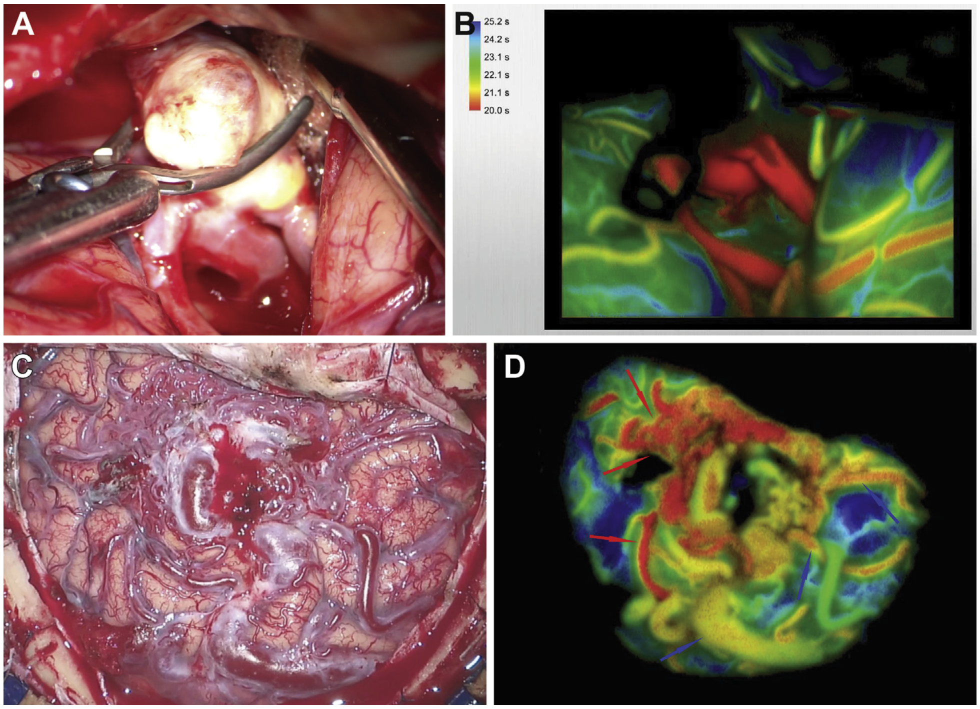

Figure 1. An atherosclerotic middle cerebral artery (MCA) aneurysm was clip ligated. Clip stenosis of the M2 branches was likely because the atherosclerosis extended from the neck into the origin of the M2 branches (**A**). After application of the clip, the FLOW 800 color map confirmed balanced flow within the M1 and M2 branches (**B**). The application of this technology for arteriovenous malformation (AVM) surgery is shown in (**C**) and (**D**). A giant right parietotemporal AVM was exposed (**C**). The FLOW 800 map showed the angioarchitecture of the AVM and localized the predominant cortical feeding vessels (*red*) that were disconnected at the first phase of resection strategy *(red arrows*). The locations and dominance of the draining veins were also clarified (*blue arrows*). (Used with permission from *The Neurosurgical Atlas* by Aaron Cohen-Gadol, MD.)

this article, we describe our experience using FLOW 800 analysis for various vascular lesions including arteriovenous malformations (AVMs), aneurysms, a dural arteriovenous fistula (dAVF), and a hemangioblastoma. More specifically, we used the color map data that are readily available during surgery and can provide actionable information. We hope that this experience can further identify the advantages and disadvantages of this technology for handling vascular lesions. To our knowledge, this is the largest study to date that has used the FLOW 800 color maps alone in guiding immediate intraoperative decisions.

METHODS

Twenty-three consecutive patients who underwent evaluation of their vascular lesions intraoperatively via FLOW 800 analysis were retrospectively reviewed for this study. Patients who underwent clip ligation of aneurysms ($n = 11$), disconnection of dAVFs ($n = 1$), resection of AVMs (10), or resection of hemangioblastomas ($n = 1$) were included in this cohort. Patients who harbored vascular lesions treated via endovascular methods alone, patients who were allergic to ICG, pediatric patients, or patients who had surgical treatment in which FLOW 800 technology was not used were excluded from the study.

The age, gender, disease, location, size, presenting characteristics, modified Rankin Scale score, number of ICG injections, intraoperative findings, FLOW 800 results, postoperative imaging, and complications were recorded on every case. This information was obtained after our institutional review board approved the study.

For each ICG injection, 25 mg of ICG was administered intravenously, although a smaller dose may be used. All motion during the imaging process was strictly avoided to capture the most optimal color map.

FLOW 800 Software

FLOW 800 provides a user-friendly interface that allows manipulation and visualization of fluorescence video data captured by the INFRARED 800 fluorescence option. It compiles INFRARED 800 video data in color-coded summary maps, outlining the sequence of fluorescence appearance (Delay) in an accessible way.

The Delay Map ("map") outlines time attributes of the fluorescence signal in a single image. For visual assessment of the blood flow situation, an intuitive color-coding is automatically

Table 1. Patient Demographics

Patient Demographic	Value
Age (years), mean	52.4
Gender, male/female	9/14 (39/61)
Type of lesion	
AVM	10 (44)
Aneurysm	11 (48)
Dural arteriovenous fistula	1 (4)
Tumor	1 (4)
AVM location (superficial/deep)	7/3 (70/30)
Spetzler-Martin AVM grade	
1	2 (20)
2	5 (50)
3	3 (30)
4	1 (10)
5	0 (0)
Number of aneurysms	13
Aneurysm size (mm), mean	8
Aneurysm location	
Anterior circulation	12 (92)
Posterior circulation	1 (8)
Presentation	
Hemorrhage	11 (48)
Seizure	1 (4)
Incidental	9 (39)
Other	2 (9)
Modified Rankin Scale score	
0	8 (35)
1	7 (30)
2	3 (13)
3	1 (4)
4	1 (4)
5	0 (0)
6	1 (4)
Unknown	2 (9)
Indocyanine green injections (n)	
1	16 (70)
2	4 (17)
3	3 (13)
Intraoperative angiogram (yes/no)	15/8 (65/35)

Values are number (%) except where indicated otherwise.
AVM, arteriovenous malformations.

applied to the maps. The time delay is displayed as a false-color image. The time when a fluorescence signal appears is recorded for each image point and visualized in a color-encoded map. This process provides an overview on the sequence when fluorescence appears in part of the video image. An intuitive scale marks early appearance of fluorescence in red and late appearance in blue. The displayed intensity values and seconds (SI units) are rounded values. They are provided only for clearer indication, not for absolute measurement. To receive in-depth interpretation of a specific vessel or area within the video image, the user can select up to 8 regions of interest.

To provide optimized FLOW 800 visualization maps, the INFRARED 800 video images are processed. The vignetting of the corners of the field of view, because of reduced illumination in the illumination beam path and the vignetting in the video camera beam path, are corrected. Furthermore, the movement correction is calculated to compensate for small movements of the microscope during recording of the INFRARED 800 video. Once the movement correction has been determined, the two-dimensional summary maps are calculated and stored.

In our study, fluorescence angiography was performed as clinically indicated. The fluorescence curves that have been the subject of the previous studies were not analyzed because these analyses require more extensive time that is often not available during surgery. Although the time intensity curves of the regions of interest allow hemodynamic analysis of the vessels, we did not use this information during our operative sessions and relied solely on the color map data that are efficiently producible for guiding intraoperative maneuvers.

On the color delay map, red represents the initial blood inflow and the other color gradients show the subsequent sequences of flow. Therefore, the relative rate of flow is easily inferred and the identity of the feeding arteries, en passage vessels, and draining veins, as well as normal cortical arteries and veins, is quickly disclosed. In addition, differential flow within branching arteries at the neck of the aneurysm can be detected to assess clip-associated stenosis (**Figure 1**).

RESULTS

Twenty-three consecutive patients were included in this study. The ages at the time of operation ranged from 20 to 67 years (mean, 52 years). Among this cohort, 10 patients harbored AVMs, 11 had aneurysms, 1 patient had a complex dAVF, and 1 patient had a solid brainstem vascular tumor (hemangioblastoma). Demographic and clinical information is shown in **Table 1**.

All patients underwent FLOW 800 analysis at least once, with 4 patients requiring 2 injections and 3 patients requiring 3 separate injections. All vascular structures within the field of view were visualized with adequate spatial resolution. All cases resulted in flow-related information that was helpful in guiding the subsequent microsurgical intraoperative planning. Moreover, 15 of 23 patients underwent an intraoperative angiogram, which confirmed the findings of the FLOW 800 analysis in each patient.

The following sections describe our algorithm and results for the use of FLOW 800 technology.

AVMs

For AVMs, fluorescence angiography was performed before resection to assess the angioarchitecture of the malformation as well as identification of the dominant superficial feeding arteries, en passage vessels and questionable draining veins (5 cases). In 2 cases, as in the cases of lateral pontine and petrosal AVMs, the surgeon was able to clearly differentiate the identity of an arterialized vein from a conjoint normal branch of the superior petrosal vein and therefore selectively preserve the normal vein despite disconnection of the pathologic arterialized vein. Moreover, for medial interhemispheric AVMs, the FLOW 800 color delay map allowed comparative flow assessment among the parasagittal arterialized draining veins so that the less dominant vein(s) can be sacrificed after the more superficial section of the malformation had been disconnected (1 case). This maneuver was necessary for lateral mobilization of the hemisphere, exposure of the medial aspect of the malformation, and its subsequent extraction.

In 2 vermian AVMs, the early recognition of the draining vein over the cerebellar hemisphere altered the dissection strategy over the nidus (cases 1 and 11, Table 2).

A reliable understanding of the angioarchitecture of the AVM allowed early disconnection of the feeding arteries and preservation of the draining veins.

Overall, 1 fluorescence angiogram was completed at the time of preresection, additional injections were performed as necessary to identify the flow status of the remaining feeding arteries and draining veins as the AVM disconnection progressed, and a final injection confirmed absence of the flow within the AVM and the remaining draining veins before the malformation was excised. The details of the findings for individual cases are summarized in Table 2.

Aneurysms

The FLOW 800 technology was used for comparative semiquantitative flow within the branching arteries after the aneurysm was clip ligated. We used this technology only if we believed that the complex morphology of the aneurysm and the presence of atherosclerosis may have led the clip to cause intraluminal stenosis of branching arteries that may have not been appreciated via extraluminal inspection (10 cases). Also, in 1 case, retrograde flow within the posterior communicating artery was confirmed after the clip had unavoidably sacrificed this artery during clip ligation of a large and complex posterior communicating artery aneurysm. Additional information for these cases is included in Table 2.

dAVFs

The FLOW 800 technology was used to assess the direction of flow within the tangle of tortuous intradural veins so that the surgeon could reliably identify the exact location of the most proximal part of the pathologic vein as it entered the dura.

Vascular Tumors (Hemangioblastoma)

For a large solid brainstem hemangioblastoma, the map of blood flow within the tumor allowed identification of the tumor vascular pedicle to facilitate its early devascularization.

As mentioned earlier, only the color delay maps were used for immediate and efficient intraoperative decision making, and the fluorescence curves and their associated ICG-specific perfusion parameters were not analyzed.

Illustrative Cases

Case 1. A 43-year-old man presented with acute paresthesias in all 4 extremities and was found to have subarachnoid hemorrhage near the left posterior brainstem. A cerebral angiogram showed a Cognard type IV dAVF of the left foramen magnum, predominantly supplied by the external carotid artery branches (Figure 2). The patient was taken to the operating room for a lateral suboccipital craniotomy and multiple tortuous dilated veins were identified on the left side of the posterior brainstem. However, the surgeon was unable to find the exact location of the most proximal portion of the arterialized vein where it originated at the level of the dura.

FLOW 800 analysis showed the sequence of flow within the tortuous veins and localized the most proximal part of the arterialized vein at the level of the dura of the foramen magnum. The vein at its exact intradural entry point was clip ligated (Figure 2F and G). Repeat FLOW 800 data showed disconnection of the fistula (Figure 2H) (Video 1). The patient had an uneventful postoperative course and his neurologic examination result returned to normal.

Video

Video available at www.sciencedirect.com

Case 2. A 35-year-old woman who presented with a sudden-onset left facial droop and left hemiparesis was found to have hemorrhage within the pons. She underwent further imaging including a cerebral angiogram, which showed a high-flow right anterior pontine AVM supplied directly by the perforating branches of the basilar artery and draining into the deep vasculature via a posteriorly draining vein into a prepontine and premedullary vein that drained into the vein of Galen and bilateral basal veins (Figure 3). The patient underwent a retrosigmoid craniotomy and the malformation was exposed anterior to the trigeminal nerve and the facial/vestibular nerve complex.

The first 2 ICG injections identified the pathologic venous outflow and the uninvolved normal venous outflow superior and inferior to the AVM, respectively (Figure 3C–F). This information was important because the limited visualization of the vasculature along the anterior brainstem did not allow easy identification of the true identity (normal vs. arterialized draining veins) of the vessels. Epipial disconnection of the malformation was completed using the FLOW 800 color map data; all the feeding arteries were disconnected and then the draining vein was coagulated without resecting the portion of the AVM within the brainstem (Video 2). The intraoperative and postoperative angiograms showed disconnection of the AVM. The patient returned to her preoperative neurologic status after a period of rehabilitation.

Case 3. A 56-year-old man was diagnosed with a 7-mm incidental left middle cerebral artery (MCA) aneurysm during diagnostic tests for vertigo (Figure 4). During surgery, a broad-based and partially fusiform MCA bifurcation aneurysm was identified that required multiple clips for its effective exclusion (Figure 4C). Because of the complex clip construct and potential intraluminal narrowing of

Table 2. Description of FLOW 800 Findings for All 22 Patients with Associated Disease

Case Number	Disease	FLOW 800 Findings and Their Effect on Intraoperative Strategy
1	Vermian AVM	Numerous tentorial bridging veins were present. Identification of a large draining arterialized bridging vein altered the surgical dissection strategy
2	Highly complex PICA atherosclerotic aneurysm	Highly complex atherosclerotic aneurysm with questionable clip-induced stenosis at the PICA origin. FLOW 800 confirmed adequate flow in the PICA
3	Complex ACoA aneurysm	Complex ACoA aneurysm with a blister at the origin of A2, requiring complex clip reconstruction. Questionable clip-induced stenosis at A1-A2 junction. Flow through the ACoA complex was confirmed semiquantitatively relative to the adjacent vessels
4	Giant right temporoparietal AVM	First FLOW 800 analysis identified the location of the dominant MCA feeding vessels reliably and prioritized the dominance of the draining veins; this later affected the operative strategy in terms of which vein to sacrifice first to expose the depth of the malformation. The second FLOW 800 run showed complete exclusion of the malformation and adequate flow in the en passage vessels
5	Petrosal AVM	An obstructive vein, crossing the cerebellopontine angle, to this petrosal AVM was confirmed to be an arterialized branch of the superior petrosal vein via FLOW 800 analysis. This vein was preserved and instead one of its non-arterialized branches was disconnected to allow mobilization of the cerebellum and exposure of the AVM. Second injection confirmed continued arterialization of the vein; this guided the surgeon to identify the previously overlooked superior cerebellar artery feeding vessels at the shoulder of the vein. On disconnection of these last feeders, the third injection confirmed very low flow within the draining vein; therefore, the surgeon disconnected the vein to remove the entire AVM nidus
6	Anterior pontine AVM and superior petrosal sinus dAVF	First injection allowed a better understanding of the angioarchitecture of the malformation on the anterior brainstem and near the root entry zone of the trigeminal nerve. After in situ devascularization of the nidus, the second injection showed continued arterialization of the draining vein along the anterior pons and localized the petrosal dAVF. After disconnection of the dAVF, other feeding vessels at the axilla of the trigeminal nerve were disconnected. The last injection showed no additional arterialized veins
7	Lateral pontine AVM	First injection identified the arterialized branch of the superior petrosal vein. Please see the strategy for patient 5
8	Large atherosclerotic PCoA aneurysm	Massive intraoperative rupture before proximal control was secured. Clip application seemed to compromise the origin of the PCoA. FLOW 800 evaluation showed retrograde filling of the PCoA. The clip was not repositioned
9	Atherosclerotic aneurysm	Anterior temporal artery aneurysm with heavy atherosclerosis at the neck. FLOW 800 confirmed adequate flow through the distal branches after clip application
10	Atherosclerotic MCA bifurcation aneurysm	Highly atherosclerotic aneurysm with atherosclerotic plaque extending into the temporal trunk. FLOW 800 confirmed adequate flow into the temporal trunk after clip deployment
11	Vermian AVM	Two noncontiguous AVMs. FLOW 800 identified a large arterialized vein that was not clearly apparent during the initial inspection. This vein was preserved via altering the surgical dissection strategy
12	Broad-base aneurysm with adjacent perforator	Broad-base MCA bifurcation aneurysm with a large lateral lenticulostriate artery incorporated onto the neck of the aneurysm. Adequate clipping of the neck seemed to have placed the perforating artery at risk. FLOW 800 analysis confirmed adequate flow within the perforator, obviating clip adjustment
13	Broad-base MCA aneurysm	Very broad-base MCA bifurcation aneurysm. Adequate clipping of the aneurysm placed the origin of M2 at risk. FLOW 800 results confirmed equal flow within the M1 and M2 branches
14	Complex broad-base MCA aneurysm	Complex broad-based MCA bifurcation aneurysm requiring multiple clips for its occlusion. FLOW 800 data identified adequate comparative flow within the M2 branches
15	Highly atherosclerotic MCA aneurysm	The aneurysm incorporated the origin of the temporal branch at the neck of the aneurysm. After application of the clips, FLOW 800 analysis confirmed equal flow within both M2 trunks
16	Foramen magnum dAVF	Complex fistula, the operator was unable to find the intradural entry point of the vein. FLOW 800 adequately localized the fistulous point. Postclipping FLOW 800 data confirmed complete disconnection of the fistula
17	Anterior pontomedullary AVM	First FLOW 800 injection differentiated arterialized draining veins versus normal pontine veins cranial to the malformation. The second injection explored the veins caudal to the malformation. In situ disconnection of the nidus was performed. The final injection confirmed a lack of arterialization of the draining veins on the anterior pons
18	Large parietal AVM	FLOW 800 data assisted with identification of the nidus, dominant arterial feeders versus en passage arteries. It also studied the angioarchitecture of the malformation

Continues

Table 2. Continued

Case Number	Disease	FLOW 800 Findings and Their Effect on Intraoperative Strategy
19	Large ruptured parietal AVM	The AVM was mainly subcortical. The identity of the feeding and draining vessels was not clear. FLOW 800 results allowed identification of the dominant feeding arteries versus draining veins. This information affected the dissection strategy
20	Atherosclerotic MCA aneurysm	Atherosclerosis extended into the origin of the temporal trunk. After the clip was applied, FLOW 800 ensured adequate flow into the M2 vessels
21	Large parasagittal frontal AVM	Based on FLOW 800 data, select nondominant obstructive parasagittal arterialized veins were sacrificed for malformation exposure
22	Partially fusiform, atherosclerotic MCA bifurcation aneurysm	Clip-induced stenosis of the temporal trunk was suspected. FLOW 800 analysis determined equal flow in the M2 trunks
23	Large recurrent solid brainstem hemangioblastoma	The FLOW 800 color map allowed identification of the vascular pedicle of the tumor as the petrous dura

All the intraoperative FLOW 800 data were consistent with the postoperative angiogram results.
AVM, arteriovenous malformations; PICA, posterior inferior cerebellar artery; ACoA, anterior communicating artery; MCA, middle cerebral artery; dAVF, dural arteriovenous fistula; PCoA, posterior communicating artery.

the temporal M2 trunk, a FLOW 800 analysis was obtained. This analysis showed adequate relative flow; the flow within the M1, temporal, and frontal trunks was compared (Figure 4D) (Video 3). This finding was corroborated with those of intraoperative angiography. The patient made a full recovery and returned to his previous work after surgery.

DISCUSSION

ICG videoangiography can be used to identify vasculature in an array of diseases including AVMs, aneurysms, dAVFs, and highly vascular tumors. This tool is used by many neurosurgeons because of its ease and feasibility with the integrated camera on the operating room microscope. One of the criticisms of this technology assessment is that the data are qualitative and not quantitative and do not reliably assess the direction of the blood flow.

FLOW 800 is a software program available on the OPMI Pentero and Kinevo 900 microscopes (Zeiss Meditec, Oberkochen, Germany) that allows semiquantitative evaluation of flow rate by allowing comparative assessment of blood flow within adjacent vessels. Once an unaffected artery or normal vein within the field of view is identified, the flow within the potentially pathologic vessels of interest can be comparatively evaluated. It exercises an algorithm using near-infrared light (λ = 800 nm). Arbitrary intensity units are used to measure fluorescence intensity. Time to half-maximal fluorescence ($T^{1/2}$ peak) and delay times are shown as a two-dimensional color map. This information shows the relative flow rate through the area of interest.[4]

AVM Surgery

ICG videoangiography has been commonly used in AVM surgery. Zaidi et al. reported their experience with 130 consecutive patients with AVM, 56 of whom received ICG and 74 of whom did not. There was no statistical difference in the presence of residual AVM or final outcomes in these 2 groups.[5] However, the same study showed that FLOW 800 analysis allowed the surgeons to better visualize subtle differences in flow patterns within the AVM more effectively. In addition, other studies[6] have shown how AVMs can alter cortical blood flow throughout AVM resection. These studies[6] concluded that ICG and FLOW 800 analysis did not change outcomes in AVM surgery and that digital subtraction angiography (DSA) remains the gold standard to assess the true extent of resection.

Fukuda et al.[7] reviewed 7 cases of AVM resections in which multiple ICG injections were used (average, 4.75 injections per case) and showed delayed flow within the vein after arterial feeder clipping.[7] These investigators found that ICG videoangiography was statistically significantly quicker than DSA and visualized the nidus and draining veins well, but deeper arterial feeders were not always observed by others using this method.[8]

In Beijing, Ye et al.[9] reported their prospectively collected data using ICG and FLOW 800 in cerebrovascular surgery. There was a significant difference in $T^{1/2}$ peak between AVM arterial feeders and normal cortical arteries. These investigators also reported improvement of cortical flow after AVM resection in 17 patients.[9]

Kono et al.[10] injected ICG intra-arterially by placing a catheter in the common carotid and vertebral arteries. The carotid artery ICG injection differentiated AVM feeder versus normal cortical artery. The vertebral injection was not useful because the vasculature ran deep and could not be visualized under the operating microscope. In our opinion, the usefulness of intra-arterial injection of ICG is diminished as a result of the invasiveness of catheter placement. If an intra-arterial catheter were to be placed, true angiography would be likely to provide superior visualization and more actionable information to the surgeon.[10]

The limitations of ICG videoangiography in AVM surgery are related to the field of view of the microscope: the superficial nidus and superficial arterial feeders and draining veins can be seen well. However, deep feeders and deep drainage cannot be visualized unless dissection is performed around that vasculature. Therefore, atherosclerotic plaque, blood pressure and heart rate, ICG dye injection speed variations, and microscope position can all affect FLOW 800 results.[9]

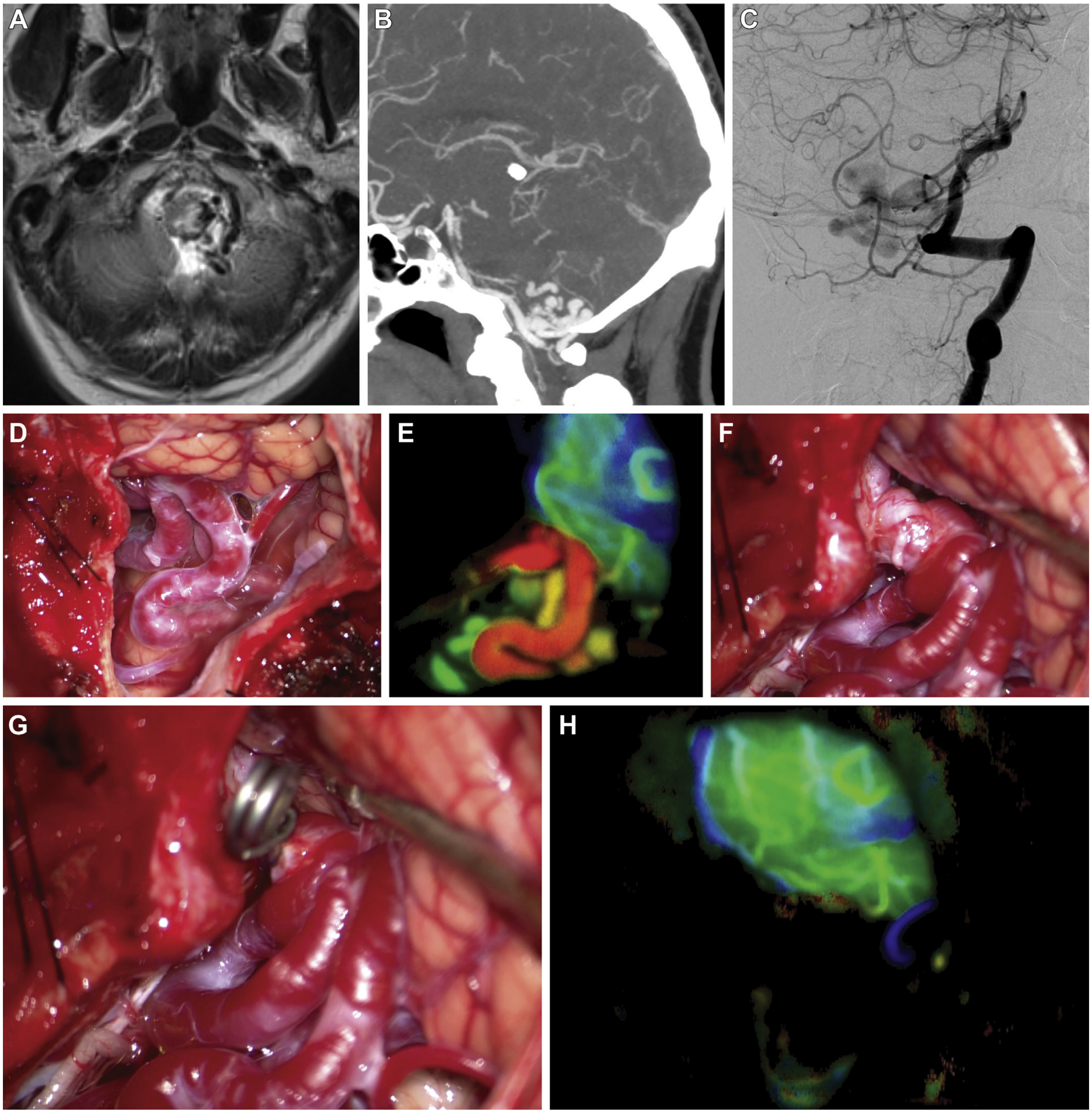

Figure 2. Axial T2-weighted magnetic resonance and sagittal computed tomography angiogram images show a vascular complex around the lower brainstem (**A, B**). A lateral vertebral angiogram confirms the diagnosis of dural arteriovenous fistula at the level of the foramen magnum (**C**). Initial inspection of the wandering tortuous pathologic vessels, exposed via a lateral suboccipital craniotomy, did not show the transdural entry point for the fistula (**D**). FLOW 800 analysis identified the direction and relative rate of flow within different segments of the pathologic vasculature, leading the surgeon to find the proximal part of the intradural portion of the fistula (**E, F**). A permanent clip disconnected the fistula (**G**); this finding was confirmed on the postdisconnection FLOW 800 color map (**H**). (Used with permission from *The Neurosurgical Atlas* by Aaron Cohen-Gadol, MD.)

We agree with the conclusion of the previous studies that the usefulness of ICG angiography along with FLOW 800 analysis does not rely on the assessment of extent of AVM resection. In our experience, the FLOW 800 data have the potential to provide information regarding the superficial hemodynamic flow differences in the cortical vessels. We used the flow data in the case of large superficial AVMs, in which additional information about the dominance of the feeding vessels and draining veins can be

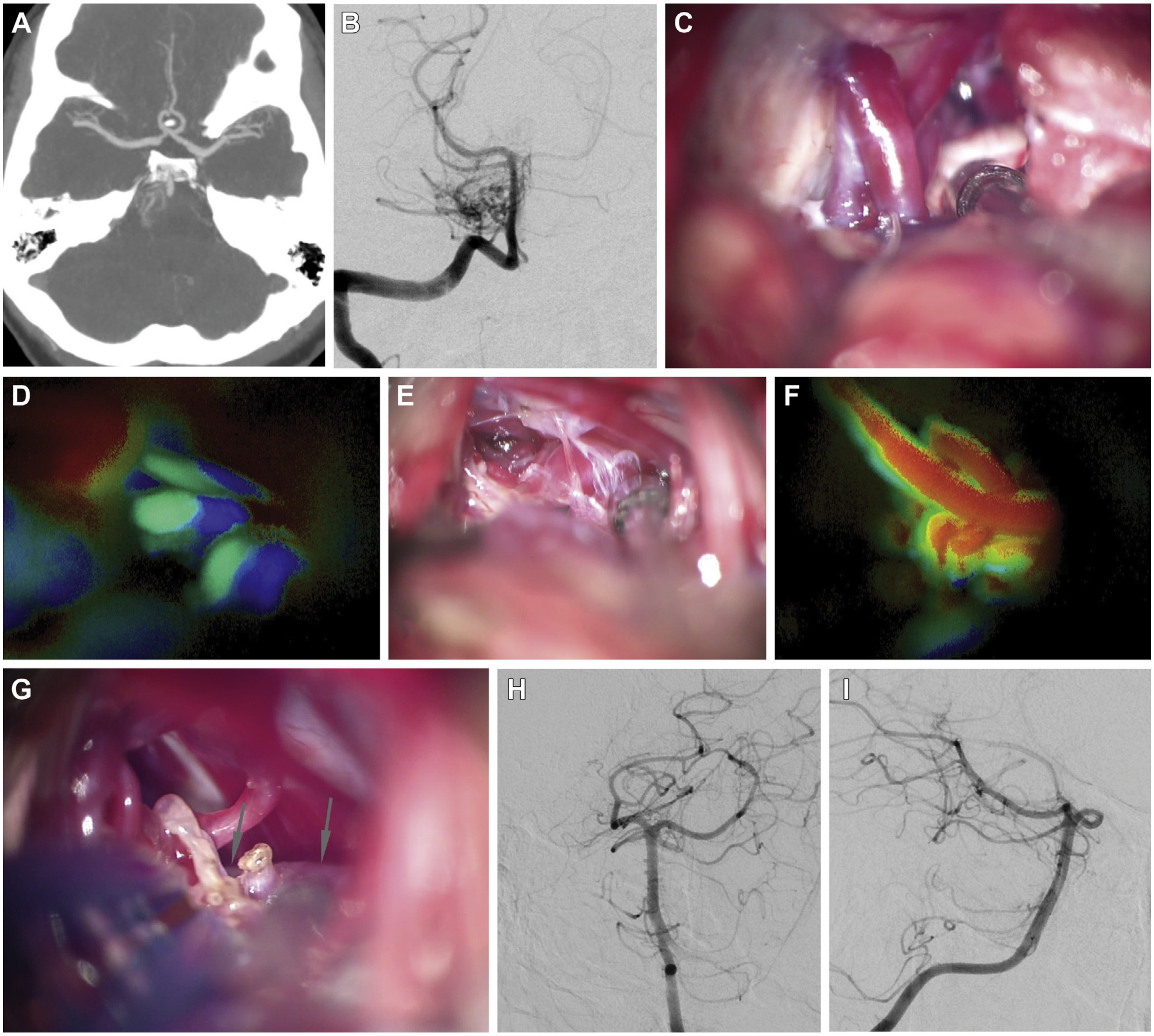

Figure 3. An axial computed tomography angiogram and an anteroposterior arteriogram show a high-flow right anterior pontine arteriovenous malformation (AVM) supplied directly by the perforating branches of the basilar artery and draining into the deep vasculature (**A, B**). A retrosigmoid craniotomy exposed the malformation anterior to and between the trigeminal nerve and the facial/vestibular nerve complex. The first 2 ICG injections identified the pathologic venous outflow and the uninvolved normal venous outflow superior and inferior to the AVM, respectively (**C**–**F**). Epipial disconnection of the malformation was completed using the FLOW 800 color map data and the basilar artery (**G**, *arrows*) was skeletonized in this region; the draining vein was coagulated. The intraoperative and postoperative angiograms showed disconnection of the AVM (anteroposterior and lateral vertebral artery injections [**H, I**]). (Used with permission from *The Neurosurgical Atlas* by Aaron Cohen-Gadol, MD.)

helpful in guiding the disconnection strategy. This information is especially important when the thick arachnoid bands that often encase the surface of the AVMs complicate reliable identification of AVM angioarchitecture.

As shown in Table 2, we also used FLOW 800 analysis for posterior fossa and brainstem AVMs in which the limited and narrow operative corridor did not permit adequate inspection of the AVM associated vessels. FLOW 800 is a reasonable method for obtaining additional information in these cases to protect the vital normal vasculature. In addition, cerebellopontine angle and parasagittal AVMs often require early sacrifice of one of the nondominant draining veins for adequate exposure of the nidal depth. Flow analysis can provide useful information about the flow within the nondominant veins before any of them are disconnected.

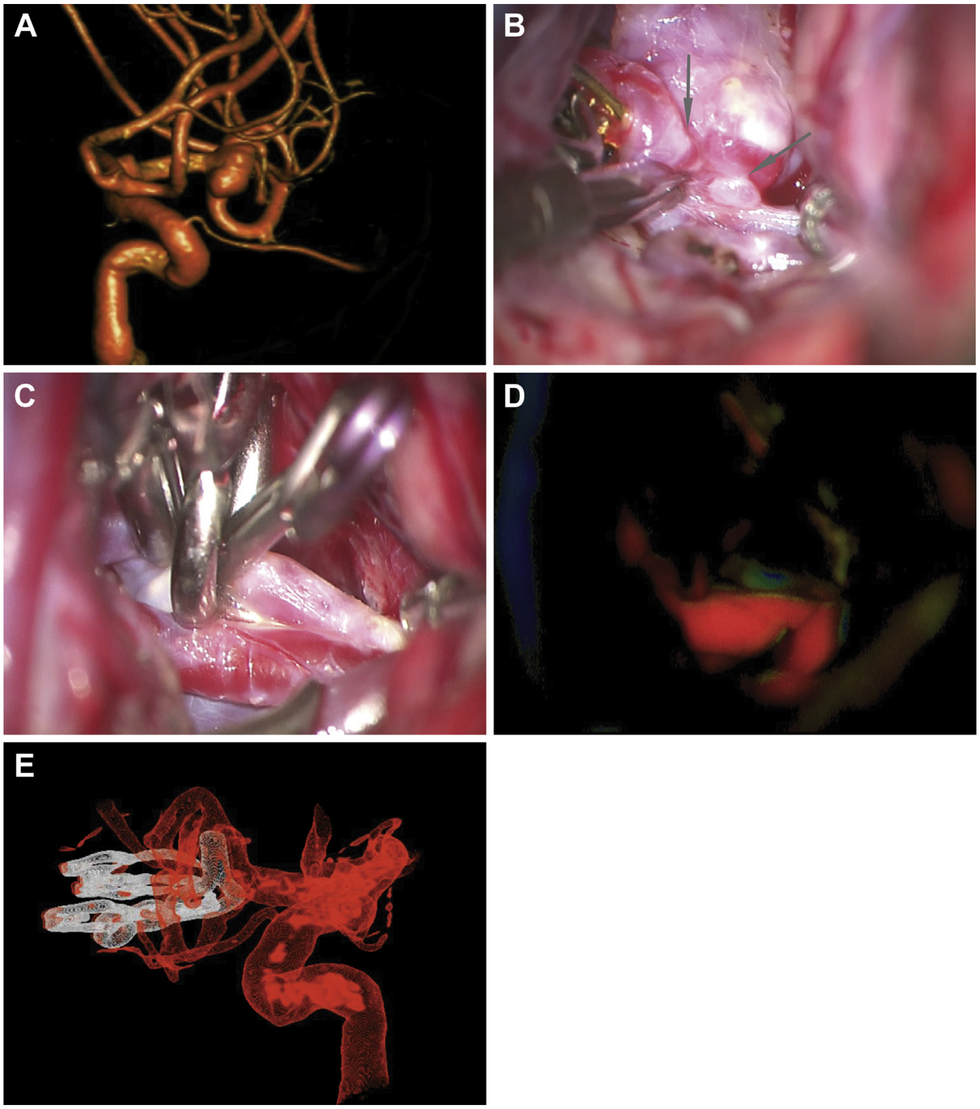

Figure 4. A broad-based and partially fusiform 7-mm middle cerebral artery bifurcation aneurysm was diagnosed during a workup for vertigo (**A**). During surgery, the M2 branches were found to originate from the midsection of the aneurysm sac (**B**, *arrows*). Multiple clips were required for effective aneurysmal occlusion (**C**). Because of the complex clip construct and potential intraluminal narrowing of the temporal M2 trunk, a FLOW 800 analysis was obtained, which showed adequate relative flow through all the adjacent branches (**D**). A postoperative three-dimensional reconstruction arteriogram image confirmed adequate aneurysmal occlusion and patent branching vessels (**E**). (Used with permission from *The Neurosurgical Atlas* by Aaron Cohen-Gadol, MD.)

Aneurysm Surgery

Many investigators have written about their successful experience using ICG videoangiography without FLOW 800 analysis during aneurysm clipping.[11-14] They describe the usefulness of the tool but also mention its limitations. ICG angiography may be able to replace DSA in select cases.[15] One of the drawbacks of ICG videoangiography has been the lack of any measurable quantitative value.

As mentioned earlier, FLOW 800 technology does not measure the absolute rate of flow but rather provides reliable comparable flow among the vasculature within the field of view. Therefore, we applied the color maps for comparing flow within the arteries or veins of interest with those vessels that were unaffected by surgical intervention and expected to have intact flow. Our primary goal of using FLOW 800 was to confirm relatively adequate flow within the arteries that may have had clip-induced stenosis on extraluminal inspection.

Table 3. Review of the Literature

Reference	Disease	Patients	Findings
Acerbi et al., 2018[27]	Tumors	71	FLOW 800 data were helpful to identify patency of sinuses and veins as well as preresection identification of pathologic vascularization
Feng et al., 2017[28]	AVM	16	FLOW 800 assessments were carried out an average of 3.6 times per case and helped the surgeons identify the flow patterns during resection of AVMs
Ferroli et al., 2011[20]	Various	8	Postprocessing FLOW 800 data allowed for semiquantitative comparison between various flow patterns in the venous phase
Fukuda et al., 2015[7]	AVM	7	FLOW 800 data showed delayed venous draining after arterial clipping of the AVMs
Holling et al., 2013[16]	Arteriovenous fistula	5	Transit time through the fistulous vein increased significantly after occlusion of the fistula. Parenchymal perfusion also improved after occlusion of the fistula
Kamp et al., 2012[4]	Various	30	FLOW 800 data were useful intraoperatively to determine arterial patency and regional cerebral blood flow/perfusion
Kato et al., 2011[29]	AVM	3	FLOW 800 analysis helped identify arterial feeders and draining veins; the role of FLOW 800 was limited in deep-seated AVMs unless they were well dissected and exposed
Ng et al., 2013[30]	AVM	8	FLOW 800 analysis allowed for semiquantitative assessment of AVM perfusion
Okawa et al., 2014[26]	Carotid stenosis	20	FLOW 800 evaluation showed greatly increased flow after carotid endarterectomy
Prinz et al., 2014[24]	Hemodynamic compromise, giant aneurysm	30	Superficial temporal artery to middle cerebral artery bypass and intermediate-flow to high-flow bypass constructs were analyzed and bypass patency was confirmed. Hemodynamic changes within the microcirculation and macrocirculation were shown
Shi et al., 2015[31]	Dural arteriovenous fistula	9	Identification and treatment of the disease with significantly altered transit times before and after obliteration of the fistula
Takagi et al., 2012[8]	AVM	11	Indocyanine green and FLOW 800 analyses were efficient in providing additional information, specifically with identification of the nidus and superficial draining veins. Digital subtraction angiography was superior when identifying the deep arterial feeders
Uchino et al., 2013[25]	Occlusive carotid artery disease	7	FLOW analysis before and after superficial temporal artery to middle cerebral artery bypass showed patency of the bypass and hyperperfusion in 5 of 7 patients
Ye et al., 2013[9]	Various	87	FLOW 800 data identified feeding arteries and draining veins and their relation to normal cortex. After AVM resection, increased perfusion in the surrounding brain was documented

AVM, arteriovenous malformation.

Clip ligation continues to remain a viable strategy for MCA aneurysms; these aneurysms are often broad-based and atherosclerotic and therefore require complex clip constructs. FLOW 800 provides an opportunity to compare flow within the M2 trunks with each other and with the M1. Differential clip stenosis of 1 trunk should be detectable and lead to clip adjustment. Based on the findings for aneurysms summarized in Table 2, all the FLOW 800 intraoperative results corresponded to those on postoperative DSA without any discordance between these imaging modalities.

dAVF Surgery

ICG is also a valuable tool for dAVF surgery. Holling et al.[16] reported their results of 5 patients with dAVF or pial AVF. These investigators concluded that real-time parenchymal perfusion in the perilesional neural tissue improved after occluding the feeding artery. Multiple investigators have detailed their experience with AVF and ICG.[17-19]

Although we used FLOW 800 technology only in 1 case, this technology proved invaluable because the surgeon was initially unable to identify the proximal and distal parts of the tortuous fistulous vein on dural opening (see case 1 described earlier). Because of the uncertainty regarding the angioarchitecture of the fistula, we believed that the ICG flow analysis would be especially helpful. The direction of flow within the arterialized vein provided much needed information for localizing the most proximal fistulous point as the dura of the foramen magnum.

Other Vascular Lesions

Although ICG has traditionally been used for vascular diseases because of its rapid clearance from vessels, occasional highly vascular tumors such as hemangioblastomas can be highlighted via the use of this fluorescence contrast agent. Kamp et al.[4] were able to use ICG and FLOW 800 analysis on tumor cases to show that quantitative data could be obtained in these applications. The usefulness of this technology during meningioma surgery has also been shown to help identify arterial feeders and venous architecture.[20,21]

Spinal cord tumor surgery has also used ICG and FLOW 800, specifically with vascular-rich tumors such as hemangioblastomas.[22,23]

We used FLOW 800 analysis in 1 case of recurrent solid brainstem hemangioblastoma to evaluate the tumor vascularity in different compartments of the tumor. In this case, the FLOW 800 color map guided us toward the vascular pedicle of the tumor at the petrous dura so that early devascularization could be attempted.

Other Potential Vascular Applications

The possibilities of ICG videoangiography and FLOW 800 technology are potentially numerous. In any modality in which vascular flow information is valuable, ICG data could play a role. Extracranial to intracranial bypass has benefited from ICG analysis. Prinz et al.[24] performed 30 bypass procedures and used FLOW analysis before and after the bypass. They concluded that it was valuable to determine flow across the bypass but did not correlate their findings to Doppler or perfusion assessment. Uchino et al.[25] prospectively performed FLOW 800 analysis before and after superficial temporal artery to MCA bypass. Their data determined patency across the bypass as well as hyperperfusion in 5 of 7 patients. These patients' blood pressure was closely monitored postoperatively and no neurologic sequela occurred.[25] In addition, improved flow to the local cortex was reported in 12 of 13 patients in another series.[9]

Carotid endarterectomy surgery has also involved ICG and FLOW 800 analysis. Okawa et al.[26] visualized the proximal and distal ends of the plaque. They also confirmed significantly increased flow after carotid endarterectomy through the internal carotid artery. It remains to be seen if such information is useful for translation to actionable operative maneuvers.

Table 3 summarizes the major case series that have reported the application of FLOW 800 technology and its potential value to date. Almost all these studies relied on perfusion data using the post hoc analysis of the fluorescence intensity curves.

Limitations

Our study and those of other investigators have numerous limitations. Most importantly, these studies are retrospective, observational, and significantly affected by selection bias. There is no randomized trial to reliably assess the effect of this new technology, and multi-institutional projects are needed to achieve this goal. Moreover, surgeons' experiences and their expertise affect their subjective evaluation of this technology.

For example, all the patients with aneurysms who underwent FLOW 800 analysis in our study showed reasonable comparative flow within the parent and branching arteries. These findings were collaborated with postoperative angiographic evaluations. Therefore, it is difficult to assess the efficacy of such a technology in cases in which clip-induced stenosis is detected and clip readjustment is accomplished. Despite these obvious deficiencies, we believe that FLOW 800 technology has a role in cases of giant and brainstem AVMs. Its role in cases of aneurysms and other vascular diseases requires further attention.

CONCLUSIONS

FLOW 800 data allow the surgeon to visualize the direction and relative magnitude of flow to and from vascular lesions. This information can alter the strategy for intraoperative maneuvers. Similar to other fluorescence technologies, it has limitations, including inability to visualize deep vasculature and absolute flow rates that are most likely affected by ICG injection rate variations. Its safety warrants its use in select vascular cases in which additional flow information can provide the surgeon with added information as part of the overall intraoperative decision-making process.

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