Flow-based evaluation of cerebral revascularization using near-infrared indocyanine green videoangiography

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Object. Indocyanine green (ICG) videoangiography has been established as a noninvasive technique to gauge the patency of a bypass graft; however, intraoperative graft patency may not always correlate with graft flow. Altered flow through the bypass graft may directly cause delayed graft occlusion. Here, the authors report on 3 types of flow that were observed through cerebral revascularization procedures.

Methods. Between February 2009 and September 2013, 48 bypass procedures were performed. Excluded from analysis were those cases in which ICG videoangiography was not performed during surgery (whether it was not available or there was a technical issue with the microscope or the quality of ICG angiography) and/or in which angiography or CT angiography was not done within 24–72 hours after surgery. After anastomosis, bypass patency was assessed first using a noninvasive technique and then with ICG videoangiography, and flow through the graft was characterized. Patients who received a vein or radial artery graft were also evaluated with intraoperative angiography.

Results. Thirty-three patients eligible for analysis were retrospectively analyzed. The patients had undergone extracranial-intracranial (EC-IC) or IC-IC bypass for ischemic stroke (13 patients), moyamoya disease (10 patients), and complex aneurysms (10 patients; 6 giant or large aneurysms, 2 carotid blister-like aneurysms, and 2 dissecting posterior inferior cerebellar artery [PICA] aneurysms). Thirty-six bypasses were performed including 26 superficial temporal artery (STA)–middle cerebral artery (MCA) bypasses (2 bilateral and 1 double-barrel), 6 EC-IC vein grafts, 1 EC-IC radial artery graft, 1 PICA-PICA bypass, 1 MCA–posterior cerebral artery bypass, and 1 occipital artery–PICA bypass. Robust anterograde flow (Type I) was noted in 31 grafts (86%). Delayed but patent graft enhancement and anterograde flow (Type II) was observed in 4 cases (11%); 1 of these cases with an EC-IC vein graft degraded gradually to very delayed flow with no continuity to the bypass site (Type III). Additionally, 1 STA-MCA bypass graft revealed no convincing flow (Type III).

The 5 patients with Type II or III grafts were evaluated with a flow probe and reexploration of the bypass site, and in all cases the reason the graft became occluded was believed to be recipient-vessel competitive flow. In no case was there evidence of stenosis or a technical issue at the site of the anastomosis. Three patients with Type II and the 1 patient with Type III flow (11% of procedures) did not have a patent bypass on postoperative imaging.

Conclusions. Indocyanine green videoangiography is reliable for evaluating flow through the EC-IC or IC-IC bypass. The type of flow observed through the graft has a direct relationship with postoperative imaging findings. Despite the possibility of competitive flow, Type III and some Type II flows through the graft indicate the need for graft evaluation and anastomosis exploration.

(key words • indocyanine green • extracranial-intracranial bypass • cerebral revascularization • bypass flow • ICG videoangiography)

Immediate postoperative patency of extracranial-intracranial (EC-IC) bypass has been reported to be between 89% and 96%.5,10 Graft patency can be influenced by many factors, including the diameter of the graft and donor vessel, atherosclerotic changes in the donor vessel, cerebral blood flow demand, and direction of flow in the bypass.11 It is, therefore, crucial to evaluate graft patency intraoperatively to prevent the potential consequences of early graft failure, such as ischemic neurological deficit, seizures, or a significant infarction that could result in death. Historically, intraoperative digital subtraction angiography (DSA) has been the gold standard in evaluating graft patency, but its invasive nature, high cost, and additional operative and anesthesia time, along with the use of ionizing radiation, make this technique less desirable.

Other noninvasive techniques previously described in literature include intraoperative ultrasonography and
thermal artery imaging; however, these techniques have not been adopted by vascular neurosurgeons because of unreliable findings that are difficult to interpret or poor spatial resolution. In 2003 Raabe et al. reintroduced a system in which fluorescence videoangiography could be performed using the fluorescent dye indocyanine green (ICG) to visualize blood flow through basal cerebral arteries, confirming successful aneurysm clipping.\(^3\) In 2005 Woitzik et al. used the same technique to evaluate EC–IC graft patency in real time and preemptively identify and correct the grafts that occluded intraoperatively, resulting in 100% short-term graft patency.\(^4\)

While it has been established that fluorescent ICG videoangiography is a useful, easy-to-use method for establishing EC–IC bypass graft patency with excellent spatial resolution, it is critical to evaluate the quality of flow through the graft as well. In this paper, we classify flow through the graft as follows: Type I, robust anterograde flow; Type II, delayed flow compared with that in other vascular structures but patent and anterograde; or Type III, anterograde flow but delayed with no continuity to the bypass site or no convincing flow.

**Methods**

**Patient Population**

Between February 2009 and September 2013, 1 surgeon performed 48 bypass procedures at 2 different institutions and collected data in a personal database. Reasons for bypass surgery were documented hemodynamic compromise in ischemic patients despite maximal medical therapy, symptomatic moyamoya disease, or a complex intracranial aneurysm not amenable to endovascular coiling or direct clipping procedures in which sacrifice of the vessel was considered to be at high risk for stroke. Excluded from analysis were those cases in which ICG videoangiography was not performed during surgery (whether it was not available or there was a technical issue with the microscope or the quality of ICG angiography) and/or in which imaging was not performed within 24–72 hours after surgery.

**Technique Used for ICG Videoangiography**

Intraoperative ICG videoangiography was performed using a Carl Zeiss OPMI Pentero 900 (Carl Zeiss Co.) surgical microscope with integrated, high-contrast near-infrared imaging. After systemic injection of ICG (standard 25 mg dissolved in 10 ml of water), the operative field was illuminated by a light source with a wavelength covering part of ICG absorption (700–850 nm). The fluorescence from ICG was recorded using a nonintensified video camera with an optical filter to block ambient light so that only ICG-induced fluorescence was recorded over a range of 780–950 nm. This allowed real-time visualization of arterial, capillary, and venous angiographic phases of flow with superb resolution.

**Study Protocol**

After the completion of anastomosis, bypass patency was first assessed using other noninvasive techniques such as intraoperative micro-Doppler ultrasonography and occasionally Doppler flow probe measurements. We then injected a bolus dose of ICG via a peripheral vein, switched off the operating room lights, and performed near-infrared imaging of dye fluorescence on the microscope monitor in real time. Video sequences were recorded on the microscope hard drive and later transferred to a personal computer for further review and analysis. One surgeon (A.R.D.) performed all bypasses, personally analyzed the videoangiograms, and characterized each category of flow.

Flow through the graft was characterized as Type I if it was robust and anterograde (early arterial phase), Type II flow correlated with patent anterograde flow that was delayed (usually corresponding to capillary or venous phase) as compared with that in other vascular structures or delayed compared with that in the recipient vessel. Type III flow was characterized as anterograde but delayed with no continuity to the bypass site or with no convincing flow at all. Type II and III flow grafts were reevaluated or explored, depending on the flow probe values if used and intraoperative judgment. Another ICG videoangiography study was performed after each reevaluation and revision. In cases in which a vein or artery graft was used, intraoperative angiography was usually performed to confirm bypass patency. Computed tomography angiography (CTA) or DSA was done within 24–72 hours of surgery to confirm bypass patency.

**Results**

Thirty-six EC-IC and IC-IC bypasses performed in 33 patients (15 males and 18 females) were selected for analysis, as these cases met our selection criteria. The mean patient age was 52.6 years (range 8–74 years). Bilateral operations were performed in 2 patients and a double-barrel bypass in 1 patient. Bypass surgery was performed in 13 patients with documented hemodynamic compromise, 10 patients with symptomatic moyamoya disease, and 10 patients with complex intracranial aneurysms not amenable to endovascular coiling or direct clipping procedures (6 giant or large aneurysms, 2 carotid blister-like aneurysms, and 2 dissecting posterior inferior cerebellar artery [PICA] aneurysms). Patients underwent standard superficial temporal artery (STA)–middle cerebral artery (MCA) bypass (26 procedures), saphenous vein EC-IC bypass (6 procedures), EC-IC radial artery bypass (1 procedure), PICA-PICA bypass (1 procedure), radial artery MCA–posterior cerebral artery (PCA) bypass (1 procedure), and occipital artery [OA]-PICA bypass (1 procedure; Table 1). Patients with moyamoya disease also underwent indirect encephaloduroarteriosynangiosis bypass.

All patients tolerated the intravenous injection of ICG without any side effects or allergic reactions. Fluorescence in arteries, capillaries, and veins was visualized within 5 seconds after injection. All images were high quality with good spatial resolution, which allowed real-time assessment of flow through the bypass.

Robust anterograde flow (Type I) was noted in 31 grafts (86%; Videos 1 and 2).

**Video 1.** Immediate robust Type I flow through the STA-MCA bypass. There is immediate contrast enhancement of the donor and recipient vessel. Area of anastomosis is slightly obscured by a small piece of Gelfoam used to control leak-
TABLE 1: Summary of characteristics and demographics in 33 patients who underwent bypass procedures and ICG videoangiography*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Ruptured Type of Bypass</th>
<th>Type of Bypass Flow</th>
<th>Intraop DSA</th>
<th>Intraop Doppler/Flow Probe</th>
<th>Postop CTA/DSA</th>
<th>Bypass Patency</th>
<th>Postop Stroke</th>
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</tbody>
</table>

ischemic stroke

1  63, M N/A STA-MCA I - +/- CTA + -
2  69, F N/A STA-MCA I - +/- CTA + -
3  47, M N/A STA-MCA (bila) I - +/- CTA + -
4  74, M N/A STA-MCA I - +/- CTA + -
5  54, F N/A STA-MCA I - +/- CTA + -
6  74, M N/A STA-MCA I - +/- CTA + -
7  57, F N/A STA-MCA II - +/- CTA - -
8  65, F N/A STA-MCA I - +/- CTA + -
9  62, F N/A STA-MCA I - +/- CTA + -
10 37, F N/A STA-MCA I - +/- CTA + -
11 57, M N/A STA-MCA I - +/- CTA + -
12 70, M N/A STA-MCA I - +/- CTA + -
13 64, F N/A STA-MCA I - +/- CTA + -

moyamoya disease

14 49, F N/A STA-MCA I - +/- CTA + -
15 34, F N/A STA-MCA I - +/- CTA + -
16 62, F N/A STA-MCA I - +/- DSA + -
17 8, M N/A STA-MCA I - +/- CTA + -
18 20, M N/A STA-MCA II - +/- CTA - -
19 65, F N/A STA-MCA I - +/- CTA + -
20 54, M N/A STA-MCA I - +/- CTA + -
21 17, F N/A STA-MCA (bila) I - +/- CTA + -
22 52, M N/A STA-MCA I - +/- CTA + DSA + -
23 24, M N/A STA-MCA I - +/- CTA + -

34 (Opt.) 42, F - EC-IC vein I + (patent graft) +/- CTA + DSA + minor embolic shower at 10 days postop
35 (Sup. Hypophys.) 64, F - EC-IC vein I + (patent graft) +/- CTA + DSA + -
36 (cavernous) 59, M - EC-IC vein I + (patent graft) +/- CTA + DSA + -
37 (MCA) 56, M - STA-MCA, STA-MCA radial I + (patent graft) +/- CTA + -
38 (PCoA) 52, M - EC-IC vein II +/+- CTA - -

(continued)
TABLE 1: Summary of characteristics and demographics in 33 patients who underwent bypass procedures and ICG videoangiography* (continued)

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Ruptured</th>
<th>Type of Bypass</th>
<th>Type of Bypass Flow</th>
<th>Intraop DSA</th>
<th>Intraop Doppler/FLOW Probe</th>
<th>Postop CTA/DSA</th>
<th>Bypass Patency</th>
<th>Postop Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 (BA)</td>
<td>56, F</td>
<td>−</td>
<td>MCA-PCA radial</td>
<td>II</td>
<td>−</td>
<td>+/- (signal dropped out but still patent)</td>
<td>DSA</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>30</td>
<td>58, F</td>
<td>+</td>
<td>EC-IC vein</td>
<td>I</td>
<td>+ (patent graft)</td>
<td>+/-</td>
<td>CTA</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>31</td>
<td>56, F</td>
<td>+</td>
<td>EC-IC vein</td>
<td>I</td>
<td>+ (patent graft)</td>
<td>+/-</td>
<td>CTA</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>32</td>
<td>50, F</td>
<td>+</td>
<td>PICA-PICA</td>
<td>I</td>
<td>−</td>
<td>+/-</td>
<td>DSA</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>33</td>
<td>66, M</td>
<td>+</td>
<td>OA-PICA</td>
<td>II</td>
<td>−</td>
<td>+/-</td>
<td>DSA</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

* BA = basilar artery; N/A = not applicable; Ophth. = Ophthalmic; PCoA = posterior communicating artery; Sup. Hypophys. = superior hypophyseal; + = positive finding; − = negative finding.
† One Type II flow degraded gradually until no continuity of flow was seen and became Type III on repeat ICG at the end of the surgery.

Fig. 1. Upper: Indocyanine green videoangiogram showing Type I flow (robust enhancement) in a STA-MCA bypass. Area of anastomosis is slightly obscured by a small piece of Gelfoam used to control leaking, however, very good flow is visualized between the donor and recipient vessels (see Video 1). Lower: Intraoperative microscopic image showing the bypass site.

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Flow evaluation by ICG videoangiography

Intraoperative DSA was performed for 6 of 8 high-flow bypasses (5 EC-IC vein grafts and 1 STA stump-MCA radial artery graft) to immediately assess the anastomosis site and the bypass flow with a known gold-standard technique. The DSA results were compared with the ICG videoangiography findings during the same operation. All high-flow bypass grafts assessed with DSA were patent and compared qualitatively with ICG videoangiography results (Fig. 2; Video 2). All grafts assessed with DSA correlated with Type I flow bypasses that were also open on postoperative imaging.

In the other 2 patients with high-flow bypasses, intraoperative DSA was not performed. In 1 patient, the graft was clearly open with a good flow value on flow probe measurement. Because this patient had difficult endovascular access, we decided not to perform intraoperative angiography. In the other patient, the graft became occluded as a result of competitive flow; therefore, we believed that intraoperative angiography would not be helpful.

Postoperative imaging revealed 4 occluded grafts (11%); all of them were Type II or III on ICG videoangiography. All Type I grafts and 1 Type II graft were patent on postoperative imaging. In all failed grafts, it was believed that occlusion was the result of competitive flow.

Fig. 2. Preoperative DS angiogram of a left giant partially coiled recurrent ophthalmic aneurysm (A) treated with high-flow EC-IC vein bypass and trapping of the diseased segment. Intraoperative ICG videoangiogram (B) showing Type I flow (see Video 2). Postoperative DS angiogram (C) confirming patency of the bypass and validating the ICG videoangiography finding.
on the recipient vessel and lack of demand for the bypass. No technical issue was identified or stenosis noted at the site of anastomosis or in the graft itself.

Postoperatively, there were 3 strokes. All occurred in cases of Type I bypass grafts (2 STA-MCA and 1 saphenous vein EC-IC graft). The patient with the vein graft underwent the bypass for a giant ophthalmic aneurysm with vessel segment trapping and demonstrated a minor embolic shower 10 days after surgery. The other 2 patients both had moyamoya disease and underwent STA-MCA bypass. One patient had a 3-day contralateral postoperative hemorrhage because of advanced disease; the bypass was occluded in the second patient 2 weeks after surgery because of dehydration. No patient with a Type II or III graft had a postoperative complication, further validating the theory of competitive flow.

**Discussion**

In this study we were able to show that ICG videoangiography can be used not only to assess the patency of the cerebrovascular bypass graft, but also to qualitatively analyze the type of flow through it. Based on our results, the type of flow through the bypass graft can be indicative of early postoperative occlusion, as confirmed on postoperative CTA or DSA. Some Type II and one Type III grafts were occluded on postoperative imaging. All Type I grafts remained open on postoperative imaging.

Intraoperative ICG videoangiography has already been shown to be a safe, practical, and relatively low-cost technique with high spatial resolution and excellent image quality with a minimum side-effect profile. Raabe et al. initially used this technique to evaluate occlusion of aneurysms and dural fistulas and suggested that it can also be used to document intraoperative vascular flow. Woitzik et al. then used this same technique to evaluate the flow in EC-IC bypass grafts and therefore to determine bypass patency intraoperatively. Woitzik and colleagues were able to visualize the occluded grafts in real time on the recipient vessel and lack of demand for the bypass.
Flow evaluation by ICG videoangiography

TABLE 2: Summary of ICG-based bypass flow and postoperative graft patency in 36 procedures

<table>
<thead>
<tr>
<th>Flow Type</th>
<th>Total Bypass Cases</th>
<th>Surgical Bypass Procedure</th>
<th>Total Cases of Each Bypass</th>
<th>Postop CTA/DSA w/in 24–72 hrs</th>
<th>Postop Patency</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>31</td>
<td>STA-MCA</td>
<td>24</td>
<td>CTA/angiogram</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC-IC vein</td>
<td>5</td>
<td>CTA</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC-IC radial</td>
<td>1</td>
<td>CTA</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PICA-PICA</td>
<td>1</td>
<td>angiogram</td>
<td>yes</td>
</tr>
<tr>
<td>II*</td>
<td>4</td>
<td>STA-MCA</td>
<td>1</td>
<td>CTA</td>
<td>no</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IC-IC radial (MCA-PCA)</td>
<td>1</td>
<td>angiogram</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OA-PICA</td>
<td>1</td>
<td>angiogram</td>
<td>no</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EC-IC vein†</td>
<td>1</td>
<td>CTA</td>
<td>no</td>
</tr>
<tr>
<td>III*</td>
<td>1</td>
<td>STA-MCA</td>
<td>1</td>
<td>CTA</td>
<td>no</td>
</tr>
</tbody>
</table>

* All grafts with delayed flow were evaluated/explored/revised intraoperatively, and 3 of 4 Type II grafts were patent at the end of surgery.
† This graft was originally found to be patent with Type II flow but slowly progressed to Type III.

time, diagnose the problem, and revise the problematic grafts without the need for intraoperative angiography. The success of, and ease in applying, this technique has sparked a rise in the reported cases in which ICG videoangiography has been used, such as for correct recipient-vessel identification.2,4,7,10

The qualitative value of this technique can also be quantified using specialized image analysis software. Awano et al.1 recently analyzed the ICG perfusion area at the point at which fluorescence intensity reached the maximum level. In a similar manner, the time course of ICG fluorescence intensity can also be analyzed at a specific region of interest to quantify graft flow in real time. Image analysis can be further extrapolated into flow characterization in which each type of flow can be given a numeric value range. In this way each type of flow reported in the present study could be objectified and used universally across all institutions without observer bias.

Intraoperative bypass patency may not be the best patency measure to follow since as many as 8% of patients (3 with Type II flow) with patent grafts during surgery had occluded grafts on CTA within 24–72 hours of surgery. It is important to characterize each bypass procedure based on the flow to avoid early graft occlusion that can lead to cerebral ischemia, which is responsible for most morbidity in cerebrovascular bypass procedures. Nevertheless, it is worth mentioning that none of the patients with either Type II or Type III graft flows in our study demonstrated any clinical or radiological manifestation of postoperative stroke. We believe that the reason for this is because the recipient vessel was in direct competition with the bypass for regional cerebral blood flow, with no demand for the bypass. It would be interesting to see if better selection of the recipient vessel could be achieved with the use of ICG videoangiography as described in other reports.4,7,10 Furthermore, it is worth reemphasizing that all patients with ischemia in our series underwent at least 2 preoperative perfusion and challenge studies (including CT perfusion, SPECT or MR perfusion with and without Diamox, and noninvasive optimal vessel analysis MR angiography), and the potential necessity of the bypass was confirmed. For patients with aneurysms, the bypass was indicated based on the test occlusion or on knowledge of the specific anatomy and collateral circulation.

Given our observations in this study, we would recommend reexploration of the anastomosis and the revision of most Type II flow grafts, as they may have delayed flow for reasons other than competitive flow and lack of demand for the bypass. In certain situations it may still be possible to achieve a working graft postoperatively (1 Type II flow in this series remained open). Type III flow is a more obvious indicator of bypass failure and could be related to technical problems at the anastomoses site, with graft quality, or to lack of demand for the bypass. In some situations the patient may have very well developed collateral circulation, and the bypass may have been unnecessary despite a preoperative evaluation and an assumed need for revascularization. However, we still recommend reexploration of the anastomosis to rule out technical or graft concerns as long as the primary indication for surgery was based on a thorough preoperative evaluation of the need for the bypass. The Doppler flow probe is an additional tool that, in combination with ICG videoangiography, can detect bypass flow-related problems. We did not systematically use the flow probe in all of our cases; therefore, a direct correlation between the type of flow observed on ICG videoangiography and the flow identified by the Doppler flow probe cannot be established. However, we did assess the majority of our high-flow bypass grafts with intraoperative DSA and confirmed that the quality of ICG videoangiography is very accurate and comparable with DSA. We believe that its clinical benefit can be translated to centers that currently use intraoperative DSA to confirm graft patency and flow.

Future directions should involve correlating the ICG-based bypass flow type and the Doppler flow probe values as well as evaluating patients’ long-term imaging findings and outcomes. More patients will be needed to establish whether there is any clinical correlation between the type of bypass flow and patient outcome, especially if the Type II or III flow is not related to competitive flow. Along the same lines, long-term patient follow-up is needed to see if
all Type I grafts remain open. The long-term evaluation of bypass patency was not among the objectives of our study.

Conclusions

Indocyanine green fluorescence videoangiography is a good, noninvasive method for not only evaluating EC-IC and IC-IC graft patency, but also establishing the type of flow through the bypass graft. Type I flow strongly correlates with early postoperative graft patency. Type II and Type III flows are both predictive of early graft failure. Characterization of flow through the EC-IC and IC-IC bypass can be used to predict early graft occlusion and perhaps to take steps to avoid postoperative complications. Alternatively, the possibility of competitive flow is retained if graft and anastomoses exploration is noncontributive. More patients and longer follow-ups are needed to establish the relationship among the type of flow, graft patency, and patient outcome.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Dehdashti. Acquisition of data: Dehdashti. Analysis and interpretation of data: Januszewski. Drafting the article: Januszewski. Critically revising the article: Januszewski, Dehdashti. Reviewed submitted version of manuscript: Beecher, Chalif, Dehdashti. Administrative/technical/material support: Beecher, Chalif, Dehdashti. Administrative/technical/material support: Beecher. Study supervision: Dehdashti.

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