Cortical Perfusion Measurement by Indocyanine-Green Videoangiography in Patients Undergoing Hemicraniectomy for Malignant Stroke

Johannes Woitzik, MD; Pablo G. Peña-Tapia, MD; Ulf C. Schneider, MD; Peter Vajkoczy, MD; Claudius Thomé, MD

Background and Purpose—Assessment of cerebral perfusion during neurosurgical procedures would be beneficial to identify areas at risk and to guide placement of monitoring probes. Therefore, we have adapted near-infrared indocyanine-green (ICG) videoangiography to assess cortical perfusion intraoperatively.

Methods—ICG videoangiography was performed intraoperatively in 6 patients after decompressive hemicraniectomy for middle cerebral artery stroke. Flow maps of cortical perfusion were generated with IC-CALC 1.1 software by calculating the ratio of difference in fluorescence intensity and rise time.

Results—Excellent visualization of cerebral arteries, cortical perfusion and collateral circulation via leptomeningeal anastomoses could be demonstrated in all cases. Flow maps revealed high spatial resolution and showed heterogeneous maple-leaf-shaped hypoperfusion. 26.5±13.7% and 29.0±9.1% of the exposed cortical surface (141±18 cm²) demonstrated core and penumbral flow, respectively.

Conclusions—ICG videoangiography appears to be a valuable tool to precisely detect relative cortical tissue perfusion. Thus, it may provide useful research data on the pathophysiology of human stroke, help surgeons to maintain adequate brain perfusion intraoperatively, and simplify adequate placement of tissue probes to monitor critically hypoperfused brain tissue. (Stroke. 2006;37:000-000.)

Key Words: angiography ■ cerebrovascular circulation ■ indocyanine green ■ stroke

Data on the spatial distribution and the pathophysiology of cerebral perfusion in human stroke is scarce. Advanced monitoring strategies using locally implanted probes are used to further characterize the hypoperfused tissue in patients with malignant stroke. The critically hypoperfused tissue, ie, the penumbra, has been suggested as a potential probe target to maximize the clinical benefit of monitoring.1,2 Currently, however, no method is available for intraoperative determination of the cerebral areas at highest risk.

Fluorescence angiography has been applied to assess capillary blood flow in various experimental set-ups.3 During neurosurgical procedures commercially available indocyanine-green (ICG) videoangiography has been used.4,5 The following study was performed to adapt high resolution capillary blood flow measurements by ICG videoangiography to patients with malignant middle cerebral artery (MCA) infarction undergoing decompressive hemicraniectomy.

Materials and Methods

Intraoperative ICG videoangiography was performed in 6 patients after decompressive craniectomy for malignant MCA infarction described previously.6 In brief, the surgical field was illuminated using a commercially available laser-fluorescence imaging device (IC-View; Pulsion Medical Systems). The fluorescence signal after intravenous bolus injection of ICG (0.3 mg/kg body weight; ICG-Pulsion; Pulsion Medical Systems) was recorded (25 images/second) with a digital camcorder. Pictures were generated with Windows Movie Maker 5.1 and Adobe Photoshop 5.0. Using IC-CALC 1.1 Software (Pulsion Medical Systems) a cerebral blood flow index (BFI) was calculated according to Kuebler et al.6 The BFI was defined as ratio of difference in fluorescence intensity and rise time, which is the time interval between 20% and 80% of maximum fluorescence intensity. For standardization purposes and to allow interindividual comparisons, the BFI was expressed in relation to an area of suspected undisturbed perfusion. Flow maps were then generated by calculating the BFI in 1 mm² squares, and flow areas of ischemic core (<20%), penumbra (20% to 40%) and oligemia (40% to 80%) were determined by volumetric analysis.

Postoperative computed tomography (CT) was used to volumetrically determine the volume of infarction, the degree of hemispheric swelling7 and the craniectomy size. Outcome was evaluated after 6 months using modified Rankin Scale and National Institutes of Health Stroke Scale (NIHSS). Statistical analysis for correlations between infarct size and hypoperfused tissue was performed using Pearson χ² test. Significance was defined as P<0.05.
Results

The pial arteries, the superficial brain tissue and the pial veins were visualized by ICG filling (Figure 1). Image quality and spatial resolution were high. Retrograde filling of pial arteries via leptomeningeal anastomoses could be observed in the MCA territory. Relative blood flow could be measured for all visible brain regions (Figure 2). The signal-to-noise ratio amounted to ≈50 in 10 mm² squares, 20 in 1 mm² squares and 10 in 0.1 mm² squares.

The infarct volume amounted to 255±100 mL, which corresponded to 38.9±11.4% of the hemisphere and caused hemispheric swelling of 18.6±4.4% (Table). 26.5±13.7% and 29.0±9.1% of the exposed cortical surface (141±18 cm²) demonstrated core and penumbral flow, respectively, whereas...
oligemia could be observed in 37.3±9.8%. The ischemic core resembled a maple-leaf centered around the Sylvian fissure. There was a significant correlation between the area of BFI <40% and the infarct volume (P<0.05).

**Discussion**

Fluorescent dyes are used experimentally and clinically to measure cerebral perfusion. ICG is one of the most widely used dyes proven to be safe and is largely restricted to the intravascular compartment.1–5 Its passage through the cerebral vasculature can be assessed by an optical filter-equipped video camera after near-infrared illumination. Repeated measurements are possible after hepatic elimination of ICG in 15-minute intervals.

In the present study, the technical feasibility of cortical perfusion measurements using ICG videoangiography was assessed in patients after decompressive hemicraniectomy for malignant stroke. The method allows to study the superficial vascular anatomy and the filling of leptomeningeal anastomoses. Furthermore, the significant increase in fluorescence caused by ICG injection leads to an excellent signal-to-noise ratio, so that relative blood flow can be measured accurately with high spatial resolution. Previous studies have demonstrated a good agreement of these measurements with perfusion-weighted MRI or radioactive microspheres.6–9

Interestingly, cortical perfusion demonstrated a maple-leaf–shaped ischemic core, which corresponds well to the heterogeneity of flow described with other imaging techniques.10,11 Possibly, reversal of this pattern may indicate reperfusion. Stratification of cortical perfusion in ischemic core, penumbra and oligemia revealed a significant amount of tissue with penumbra flow pattern in all patients.

ICG videoangiography may offer potential applications for studying the pathophysiology of ischemic stroke. The method, however, is restricted to the superficially visualized cerebral cortex and to patients with open craniotomy. It may help to control perfusion during cerebrovascular surgery and to determine cerebral areas at highest risk during these interventions. Furthermore, it may guide surgeons in placing monitoring probes, when areas at risk, like the penumbra in stroke patients, are intended to be studied.

**Summary**

ICG videoangiography has been applied to measure relative cerebral perfusion in patients undergoing decompressive hemicraniectomy for malignant stroke. Heterogeneous hypoperfusion could be demonstrated with excellent spatial resolution.

**References**


**Summary of Demographic and Treatment-Related Data in 6 Patients Who Underwent Hemicraniectomy for Malignant Stroke**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (y), Sex</th>
<th>Cause of Stroke</th>
<th>Surgery</th>
<th>Anesthesia</th>
<th>Side</th>
<th>Time After Ictus (h)</th>
<th>Infarct Volume (% of Hemisphere)</th>
<th>Swelling (%)</th>
<th>Cranectomy Size (cm²)</th>
<th>Oligemic Flow (%†)</th>
<th>Penumbral Flow (%†)</th>
<th>Core Flow (%†)</th>
<th>Modified Rankin Scale</th>
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<td>no prop/fen/bre</td>
<td>Left</td>
<td>34</td>
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<td>18.1</td>
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<tr>
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<td>2</td>
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</tbody>
</table>

*No proven source of stroke, presumably embolic origin; †% of craniectomy size.

bre indicates brevimytal, fen, fentanyl, mida, midazolam, prop, propofol; NA, not available (patient lost to follow-up after return to his home country).
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