

Intra-Arterial Fluorescence Angiography with Injection of Fluorescein Sodium from the Superficial Temporal Artery during Aneurysm Surgery: Technical Notes

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Abstract

Intra-arterial fluorescence angiography from a catheter inserted into the external carotid artery (ECA) via the superficial temporal artery (STA) allowed us to satisfactorily evaluate cerebral arterial and venous blood flow. We report this novel method that allowed for repeated angiography within minutes with a low risk of complications due to catheter placement from the STA. The STA was secured at the edge of the standard skin incision during cerebral aneurysm surgery. A 3 Fr catheter was inserted approximately 5 cm to 10 cm into the STA. After manual injection of 5 ml of 20 times diluted 10% fluorescein sodium (fluorescein), fluorescein reached the intracranial internal carotid artery (ICA) through the common carotid artery or anastomoses between the ECA and ICA. Fluorescence emission from the cerebral arteries, capillaries, and veins was clearly observed through the microscope and results were recorded. Quick dye clearance makes it possible to reexamine within 1 minute. In addition, we made a graph of the fluorescence emission intensity in the arteries, capillaries, and veins using fluorescence analysis software. With intravenous fluorescence angiography, dye remains in the vessels for a long time. When repeated examinations are necessary, intervals of approximately 10 minutes are required. There were some cases we could not correctly evaluate with intravenous injection due to weak fluorescence emission. Fluorescence angiography with intra-arterial injection from a catheter inserted into the carotid artery or another major vessel, like conventional angiography, has a risk of procedure-related complications. We report our new method since it solved these problems and is useful.

Key words: aneurysm surgery, fluorescence angiography, fluorescein sodium, superficial temporal artery

Introduction

Although multimodality monitoring such as Doppler ultrasonography,¹⁾ conventional cerebral angiography,²⁾ and electrophysiological monitoring^{3–6)} have been used in intracranial aneurysm surgery to avoid blood flow insufficiency, cases of unexpected postoperative blood flow insufficiency have been reported.^{7,8)} Recent studies have reported the usefulness of fluorescence angiography using indocyanine green (ICG) or fluorescein for preventing insufficient blood flow in the parent and perforating arteries.^{9–12)} Although intravenous dye injection is commonly used for fluorescence angiography at present, dye remains in vessels for a long time and fluorescence emission does not decrease quickly due to the rela-

tively large amount of dye in each bolus injection. It takes at least 5 minutes to wash out either fluorescein or ICG during intravenous injection fluorescence angiography. In situations when insufficient image contrast necessitates repeated examination, the results are difficult to evaluate and may cause problems. To solve these problems, intra-arterial fluorescence angiography, which allows for repeated examinations in a short period of time and images with good contrast for the analysis of blood flow, has been attempted.^{9,13)} However, intra-arterial fluorescence angiography from a catheter situated in the carotid artery or another major vessel has a risk of complication due to procedures. Here we describe intra-arterial fluorescence angiography from a catheter inserted into the external carotid artery (ECA) via the STA that we found useful for evaluating cerebral blood flow with fewer complications related to catheter insertion.

Materials and Methods

OPMI Pentero 900 (Carl Zeiss, Oberkochen, Germany) was the microscope system used. After the standard skin incision, the STA was secured at the edge of skin incision. A 3 Fr. peripherally inserted central catheter (PICC) (Argyle™, Covidien) was inserted approximately 5 cm to 10 cm into the STA. A tip of the catheter achieved near the zygomatic arch. The catheter was filled with heparin to avoid thrombus formation. After these procedures, clipping was done. When examination of blood flow was necessary before or after clipping, the microscope system was set to fluorescence angiography mode and the lights of the operating room was turned off. Then a 5 ml of 20 times diluted 10% fluorescein sodium (Fluorescite®, Alcon) was manually injected through the PICC. Injected fluorescein reached the intracranial arteries via anastomoses between the ECA and the internal carotid artery (ICA) or retrograde flow from ECA to the common carotid artery (Fig. 1). Flow of fluorescence was observed through the microscope directly and recorded as a video. Region of interests (ROIs) were determined at the major artery, brain surface, and vein on the video, then changes in fluorescence intensity at each ROI were plotted by the ROI software (Hamamatsu Photonics K.K., Tokyo) to evaluate blood flow.

In order to clarify the advantage of intra-arterial injection from the STA, both intra-arterial and intravenous fluorescein angiography were performed in two cases and changes in fluorescence intensity at various ROIs (at the artery, brain surface, and vein) were evaluated.

A pilot study was performed in three patients undergoing aneurysm surgery to estimate the optimal dose of intra-arterial fluorescein. During the pilot

study, 5 ml of various concentrations (80, 40, 20, and 10 times diluted) of fluorescein was injected into the ECA through the PICC, and the contrast of fluorescence images and duration of wash out were evaluated.

The local ethics committee approved this study, and all patients provided written informed consent giving us permission to perform intraoperative fluorescence angiography with fluorescein sodium dye.

Results

In the pilot study to identify the optimal dose of fluorescein, a 5 ml bolus injection of fluorescein diluted more than 40 times showed less fluorescence emission. A bolus injection of 20 and 10 times diluted fluorescein yielded good contrast (Fig. 2). The duration of fluorescence with 20 times diluted fluorescein was less than 1 minute, but the 10 times diluted concentration resulted in fluorescence detectable in the veins after 1 minute. Based on these data, we selected a 5 ml bolus injection of 20 times diluted fluorescein as the optimal dose for obtaining images with good contrast that also allows for repeated angiography in a short period of time.

Based on the data from the pilot study, we performed intra-arterial fluorescence angiography with injections into the STA using a 5 ml bolus injection of 20 times diluted fluorescein in 10 patients undergoing aneurysm surgery. In all 10 patients clear fluorescence flow were observed during the arterial, capillary, and venous phases (Fig. 3). Since fluorescence clearance was rapid, we could perform repeated examinations within 1 minute.

In comparison between intra-arterial and intravenous injection angiography, blood flow could be

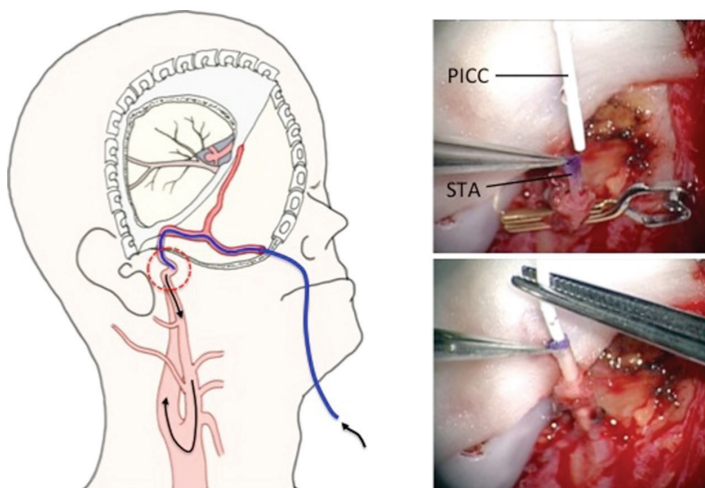


Fig. 1 Illustration of intra-arterial fluorescence angiography from the STA. A catheter was inserted approximately 5 to 10 cm into the STA from the edge of skin incision. A tip of the catheter achieved near the zygomatic arch (*dotted circle*). Fluorescein injected from the STA reaches the intracranial arteries via anastomoses between the ECA and the internal carotid artery or retrograde flow from ECA to the common carotid artery. Flow of fluorescence in the cerebral vessels is observed through the microscope. ECA: external carotid artery, PICC: peripherally inserted central catheter, STA: superficial temporal artery.

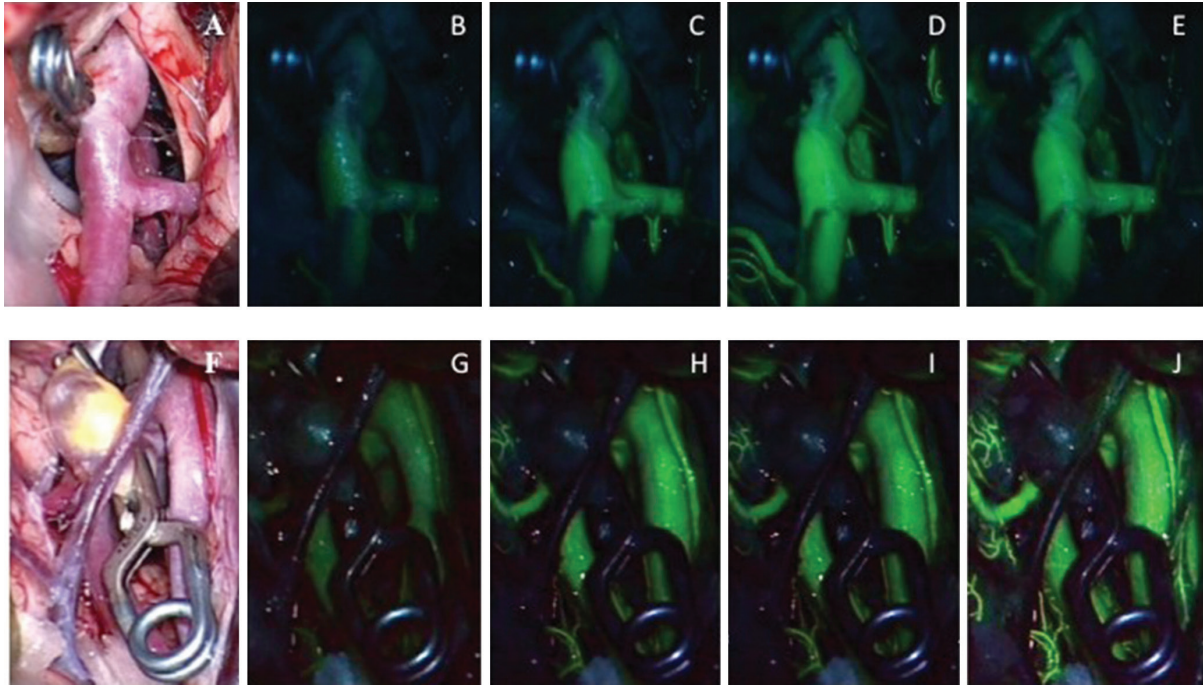


Fig. 2 Intraoperative regular microscopic and fluorescence angiographic photographs in patients with a left internal carotid artery–posterior communicating artery aneurysm (A–E) and right middle cerebral artery aneurysm (F–J). Regular microscopic views (A, F) and fluorescence angiograms after a 5 ml injection of 80 times- (B, G), 40 times- (C, H), 20 times- (D, I), and 10 times- (E, J) diluted fluorescein. More than 40 times diluted fluorescein showed less fluorescence emission. A bolus injection of 20 and 10 times diluted fluorescein showed good contrast.

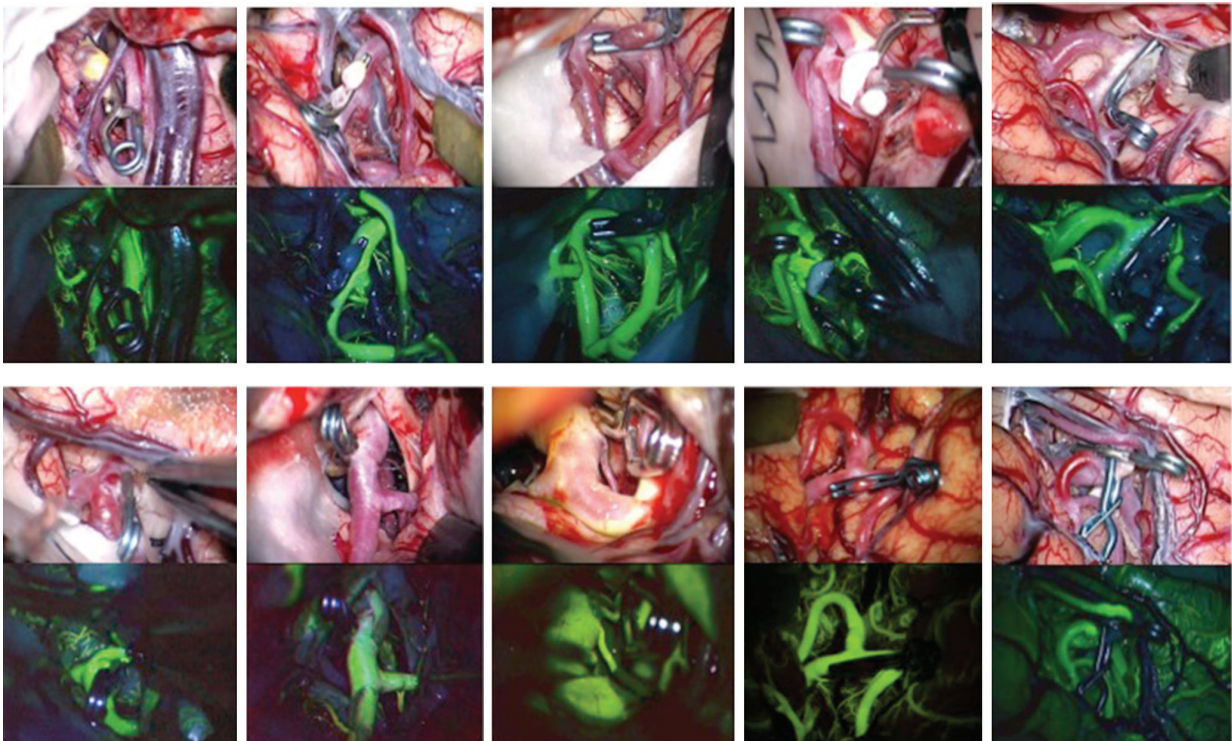


Fig. 3 Intraoperative photographs and fluorescence angiograms of 10 cases. Regular microscopic view (*upper columns*) and arterial phase of fluorescence angiograms (*lower columns*) of each case. Fluorescence emission from the cerebral arteries was clearly observed through the microscope.

independently evaluated during the arterial, capillary, and venous phase by intra-arterial injection as same as conventional angiography. Intra-arterial injection could detect delay of blood flow and clearance of fluorescence. It was thought to be difficult to evaluate clearance of fluorescence, which means congestion of blood flow, by intra-venous injection (Fig. 4). A graph of fluorescence intensity changes by intra-arterial injection showed a sharp peak first in the artery, followed by independent peaks at the brain surface and in the vein. Fluorescence intensity decreased at base line before administration in a minute by intra-arterial injection and more than 5 minutes by intra-venous injection respectively (Fig. 5).

Additional time to perform fluorescence angiography from preparation to catheter insertion at the edge of skin incision was less than 10 minutes.

Illustrative Case

A 56-year-old female underwent neck clipping of an unruptured right middle cerebral artery (MCA) aneurysm via a standard frontotemporal craniotomy. To confirm the blood flow of the superior trunk of the left MCA, intra-arterial fluorescence angiography from the STA was performed. The timing and intensity of fluorescence emission in the M1 and

M2 segments were the same. There were no differences in fluorescence emission between the frontal and temporal lobes. Fluorescence was washed out from the arteries and capillaries without delay, and during the venous phase fluorescence had already disappeared from the arteries and capillaries (Fig. 4). When the ROIs were set at M1 and M2, the fluorescence intensity graph showed M2 had almost the same peak as M1 (Fig. 5). Based on these findings, we concluded that clipping did not cause stenosis of the parent arteries. A postoperative CT showed no ischemic lesions and the patient was discharged without neurological deficits.

Discussion

To detect blood flow insufficiency of parent arteries and perforators during aneurysm surgery, Doppler ultrasonography,¹⁾ conventional cerebral angiography,²⁾ endoscopic observation,¹⁴⁾ and electrophysiological monitoring³⁻⁶⁾ have been used and modified. Even with these multiple modalities, unexpected ischemic complications might occur.^{7,8)} To avoid these complications, fluorescence angiography has been used.

Fluorescence angiography was first used in neurosurgery in 1967 when Feindel et al.^{15,16)} injected fluorescein

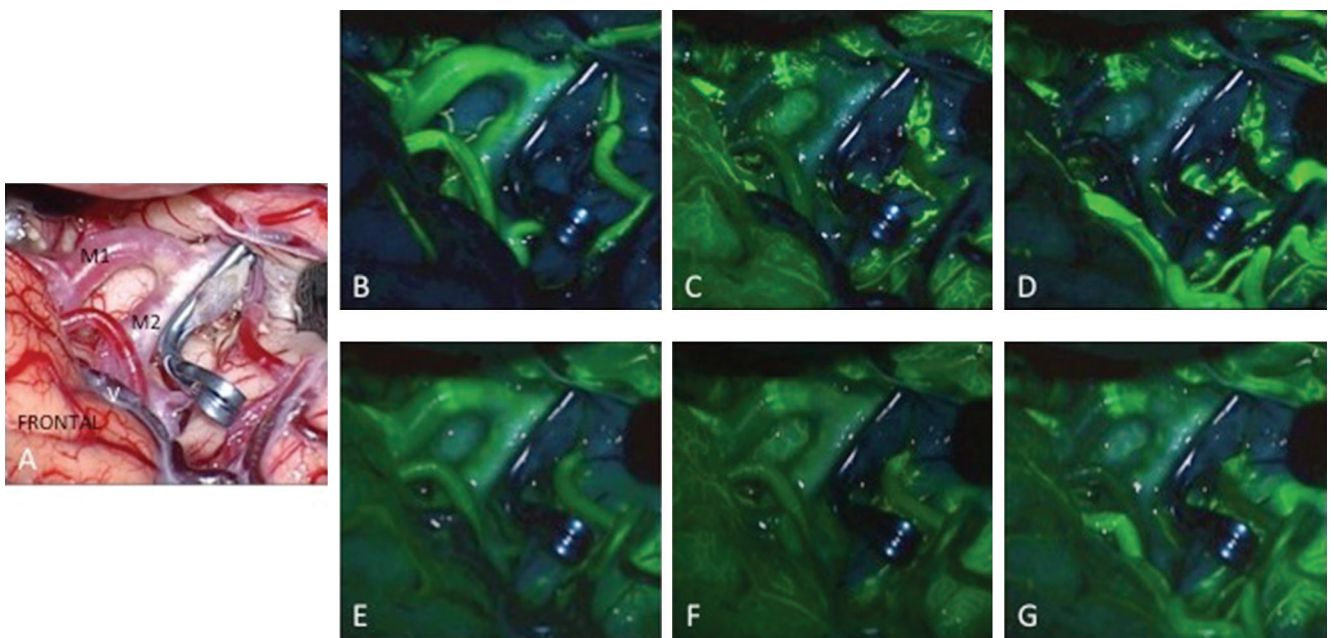


Fig. 4 Intraoperative photographs and fluorescence angiograms of the illustrative case. Regular microscopic view (A), intra-arterial angiography via the superficial temporal artery at arterial phase (B), capillary phase (C), and venous phase (D) and intra-venous angiography at arterial phase (E), capillary phase (F), and venous phase (G) are shown. Bright fluorescence emission with quick clearance was observed in intra-arterial angiography.

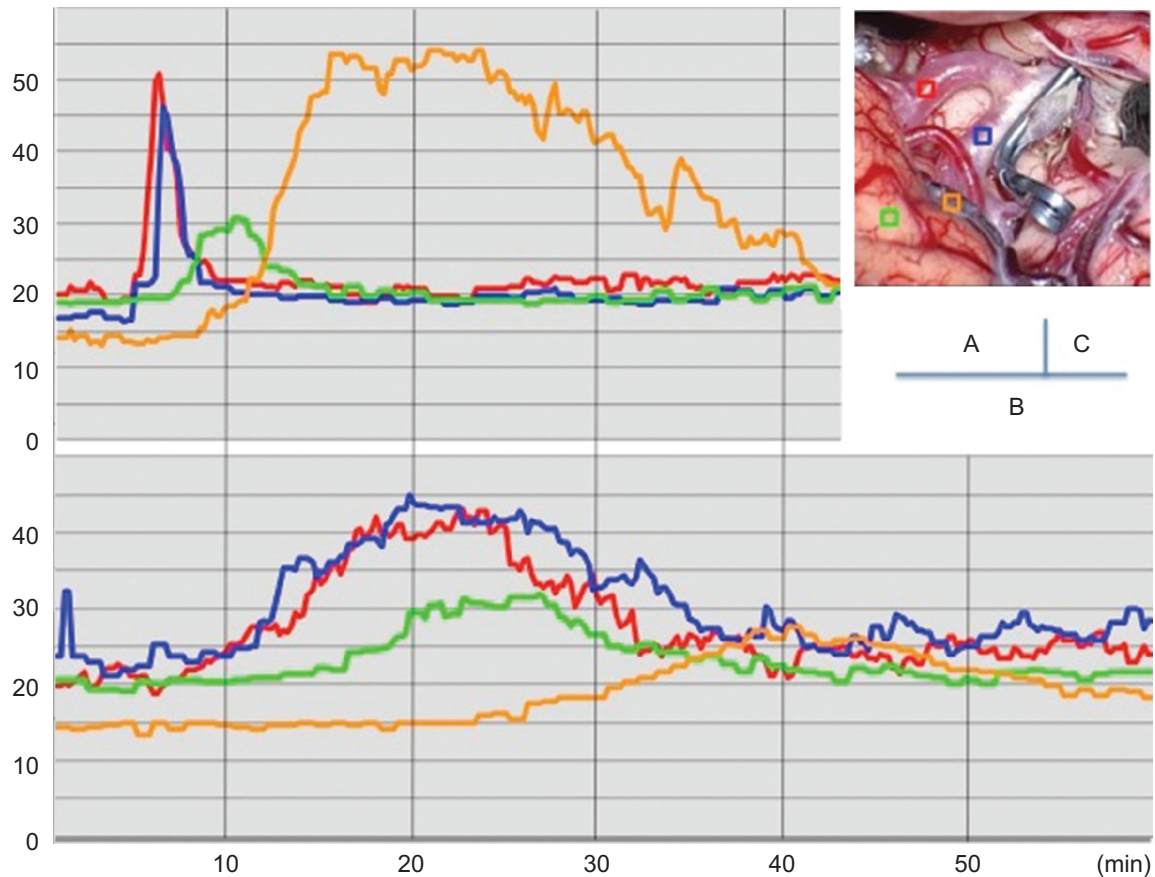


Fig. 5 Changes in fluorescence intensity at various ROIs by intra-arterial injection via the superficial temporal artery (A) and intra-venous injection (B) and regular microscopic view (C) in the illustrative case. ROIs were set at the M1 segment of the middle cerebral artery (*red open square*), the M2 segment (*blue open square*), the frontal lobe (*green open square*), and the vein (*orange open square*), and changes in fluorescence intensity at each ROI were plotted. Blood flow could be independently evaluated during the arterial, capillary, and venous phase because of the quick clearance of fluorescence by intra-arterial injection (A). It took only a minute and more than 5 minutes to decrease fluorescence intensity at the base line before administration in intra-arterial angiography and intra-venous fluorescence angiography, respectively (A, B). ROI: region of interest.

sodium into the carotid artery and observed the blood flow in the cortical vessels. In 1994 Wrobel et al.¹⁷⁾ injected fluorescein intravenously and observed the blood flow of the parent artery during aneurysm surgery but it was difficult to procure images due to weak illumination and poor imaging technology at that time. In 2003 Raabe et al.¹⁰⁾ injected ICG intravenously and confirmed the patency of the parent artery with an infrared camera after the aneurysm was clipped. In 2005, a microscope system with an integrated high-power light unit allowed the observation of blood flow through perforators deep in the surgical field.¹¹⁾ In 2007 Suzuki et al. reported that fluorescence angiography with fluorescein could detect insufficient blood flow through perforators deep in the surgical field.¹²⁾ At present, there are commercially available microscope systems such

as the OPMI Pentero 900 by Carl Zeiss that can support fluorescence angiography with both ICG and fluorescein.

Although there are many recently published reports on fluorescence angiography, most of them involve intravenously injected dyes. Intravenous fluorescence angiography is useful to evaluate blood flow intraoperatively, but some challenges remain.

First, dye remains in the vessels and emit fluorescence 5 minutes to 6 minutes after examination because intravenous fluorescence angiography requires a larger amount of fluorescent dye, and approximately 10 minutes are required until the examination can be repeated.⁹⁾ When cerebral vascular insufficiency occurs, repeated examinations in a short period of time are required because rapid reperfusion is necessary to avoid irreversible ischemic changes

occur in the brain.

Second, there is a low concentration of fluorescent dye in the cerebral vessels because intravenously injected dye dilutes in the cardio-pulmonary circulation before it reaches the cerebral vessels, resulting in weak fluorescence. Sometimes it might be difficult to confirm blood flow through deep-seated perforators and arteries with thick walls. In a study of aneurysm clipping with intravenous ICG fluorescence angiography, Dashti et al. described the risk of unexpected branch occlusion when fluorescence angiographic images are inadequate.¹⁸⁾

Intra-arterial fluorescence angiography has been attempted to overcome these problems with intravenous fluorescence angiography.^{9,13)} Intra-arterial fluorescence angiography can provide clear images of blood flow and allows for repeated examinations within 1 minute due to the low dye dose involved and rapid clearance. Previously reported methods of intra-arterial fluorescence angiography, however, require catheter placement as with conventional digital subtraction angiography. The risk of complications associated with catheter placement should be considered. In order to perform intra-arterial fluorescence angiography more safely, injection from a catheter inserted into the ECA from the STA was evaluated. Conventional angiography via the STA was already reported.^{19–21)} In these reports, intraoperative angiography could detect blood flow insufficiency of the parent artery or unexpected residual aneurysms during aneurysmal surgeries. To our knowledge, intra-arterial fluorescence angiography via the STA has not yet reported. This method allowed us to evaluate more fine cerebral vessels and does not require a large imaging device compared to conventional angiography.

The fluorescence intensity of fluorescein is not dose-dependent but peaks at the optimal dose. It was necessary to estimate the optimal dose of fluorescein in the STA. Therefore a pilot study was performed, where we determined that a 5 ml bolus injection of 20 times diluted fluorescein is the optimal dose for the clearest fluorescence imaging in the cerebral vessels while also allowing for repeated angiography within 1 minute. The operator can directly observe blood flow stagnation, delay, or direction with fluorescence angiography.^{7,22,23)} Furthermore, for ICG fluorescence angiography, blood flow analysis software integrated with the microscope system (Flow 800, Carl Zeiss) is commercially available. Although blood flow analysis software for fluorescein fluorescence angiography is not available, we used common intensity analysis software. Intra-arterial fluorescence angiography with our method provided very clear images of blood flow

at arterial, capillary, and venous phase respectively. Due to quick clearance of fluorescence, blood flow congestion could be detected as a delay of clearance of fluorescence. It took more than 5 minutes to decrease fluorescence intensity at the base line before administration in intra-venous fluorescence angiography, whereas only a minute in intra-arterial angiography. Based on these findings, we conclude that only a minute of interval is required until the next repeated examinations.

Technological advances in image quality, safety, and objective analysis have improved fluorescence angiography. However, we cannot determine whether blood flow confirmed by fluorescence angiography is adequate for avoiding cerebral infarction. Quantitative blood flow evaluation methods should be developed in the future.

Conclusion

Intra-arterial fluorescence angiography through a catheter inserted into the STA and secured at the standard skin incision site is easy and safe. Intra-arterial fluorescence angiography with our method can provide very clear images of blood flow and allows for repeated examinations to be performed within minutes due to the small dye bolus and quick clearance of fluorescence. Making a graph of fluorescence intensity allows for objective evaluation of blood flow.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices in the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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