INFRARED 800 Video Angiography
A practical guide for the surgeon

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1 Introduction

The goals of surgical treatment of intracranial vascular malformations are to occlude or to excise the lesion and to maintain blood flow in parent, branching, and perforating vessels. These goals, however, are not always achieved. There are numerous publications showing that postoperative imaging often demonstrates unexpected and incomplete treatment as well as compromise of normal vessels, neither of which is diagnosed by visual inspection during the surgery.

The logical consequence was therefore to develop or adopt techniques that assist the surgeon during intraoperative decision making such as intraoperative angiography or microdoppler sonography. These techniques have undoubtedly improved the quality of surgery in many cases, however, they also have inherent limitations that significantly restrict their value to specific clinical applications.

With the introduction of INFRARED 800 angiography, a technology is now available that provides complementary information and increases the number of patients who may benefit from intraoperative fluorescence in vascular neurosurgery.

We do believe that, with the development of intraoperative fluorescence methods and a better understanding of neurovascular disease processes, the bar has been raised for the management of patients with intracranial vascular malformations such as aneurysms, arteriovenous malformations, dural fistulas or bypass procedures. As emphasized by others, all neurosurgeons caring for patients with these lesions should use, to the best of their ability, the technological advances in neurosurgery, interventional neuroradiology, and neurological critical care to lower the morbidity and mortality rates associated with the management of these patients (1).

Fig. 1: Intraoperative anatomical (A) and INFRARED 800 (B) photograph showing a clipped aneurysm of the posterior inferior cerebellar artery (PICA), which appears as a black dot on the INFRARED 800 angiography image. All visible vessels are patent.
2 Technical principles of INFRARED 800 angiography

The intraoperative fluorescence technology is fully integrated into the surgical microscope. The operative field is illuminated by a light source from the microscope with a wavelength that covers part of the indocyanine green (ICG) dye absorption band (700-850 nm, maximum 805 nm). A specially designed dielectric filter transmits an excitation light to generate fluorescence and simultaneously provides UV and thermal protection from the light source. Light passing through this filter in the near-infrared wavelength fits exactly to the absorption band of the injected ICG. In the observation path of the surgical microscope a beam splitter directs the ICG fluorescence light, which is invisible to the human eye, towards an infrared-sensitive camera providing a black and white image. The fluorescence light (780 nm to 950 nm, maximum 835 nm) is recorded by a non-intensified infrared video camera, with optical filtering to block the ambient and excitation light for collection of only ICG-dye induced fluorescence. Thus arterial, capillary and venous angiography can be observed on the screen in real-time.

3 Fluorescence dye for INFRARED 800 angiography

ICG (C43H47N2NaO6S2) is a near-infrared fluorescent tricarbocyanine dye approved by the United States Food and Drug Administration (FDA) in 1956 to evaluate cardio-circulatory and liver function. Supplemental FDA approval for ophthalmic angiography was granted in 1975. The absorption and emission peaks of ICG (805 and 835 nm, respectively, Fig. 2) lie within the “optical window” of tissue where absorption attributable to endogenous chromophores is low.

3.1 Pharmacokinetics
Within 1 to 2 seconds of intravenous injection, ICG is bound mainly to globulins (alpha-1 lipoproteins). It remains intravascular with normal vascular permeability. ICG is not metabolized in the body and is excreted exclusively by the liver. It has a plasma half-life of 3 to 4 min. It is not reabsorbed by the intestine and does not enter the enterohepatic circulation. The dose of ICG for video angiography is 0.2 to 0.5 mg/kg. The maximum daily dose should not exceed 5 mg/kg. We recommend using a standard dose of 25 mg/injection for all patients.

3.2 Side-effects
Indocyanine green can cause adverse reactions due to sodium iodine (drug contains 5%) or the molecule itself. The dye has been used widely in medical imaging, and it has been proven to be a relatively safe drug (3). Adverse reactions, however, can occur, ranging from mild to severe, including rare cases of death. Mild reactions such as temporary nausea, vomiting, extravasation, sneezing and pruritus were reported in the literature to occur in about 0.15% of all cases. Moderate transient adverse reaction (urticaria, other skin eruptions, syncope and local tissue necrosis) were found in 0.2%. Prolonged adverse reactions that required intense treatment were regarded as severe adverse events. These neurological, cardiac or respiratory system reactions such as bronchio-spasms, laryngospasm, anaphylaxis, circulatory shock, myocardial infarction, arrest and tonic clonic seizures occurred in 0.05% of cases. There are reports in the literature about deaths after ICG administration, however, these mostly occurred in critically ill intensive care patients. A literature review performed in 1994 identified 16 cases of severe adverse events or deaths in the world wide literature after more than 30 years of use in medical practice (3). Regardless of the high safety profile, patients should give their informed consent comparable to other types of administration of intravenous contrast media. Patients who have a history of adverse reactions to contrast media or iodine allergy must not be administered the dye. The specific drug information must be read and considered before using.
4 Implementation of INFRARED 800 angiography during surgery

The INFRARED 800 technique is designed to perform infrared angiography without interruption to the surgical procedure. This technique involves full microscope integration (Fig. 3A) enabling clear visualization of the surgical situs during the angiography. The surgeon maintains his microscope view and can move structures out of sight with the use of suction or any surgical instrument to focus on the structure of interest. Thus, the setup permits easy-to-use angiography procedure without interference with the surgical workflow. The time between the decision of the surgeon to perform the INFRARED 800 angiography and the judgement based on the INFRARED 800 video reviews usually does not exceed a few minutes (Fig. 3B).

4.1 Preoperative preparation

Patients scheduled for an INFRARED 800 procedure during aneurysm clipping, removal of arteriovenous malformations or dural fistula disconnections need to provide their informed consent. A history of adverse reactions to contrast media and an iodine allergy must be excluded. The dye should be available in the operating room and the anesthesiologist must be thoroughly familiar with the procedure. The specific drug information must be considered before using the dye.

4.2 Microscope preparation and workflow

Set up the microscope for INFRARED 800 use before surgery (Fig. 4). The user should be familiar with the set-up menu of the microscope which can be found under the configuration menu in the fluorescence option.

It is important to decide where on the configurable handgrip the INFRARED 800 mode will be activated (Fig. 5). Other parameters such as length of short and long review loops and number of repetitions, Picture-in-Picture mode or signal for external monitors are already predefined, but can also be adjusted according to the surgeon’s preference.

Fig. 3: INFRARED 800 is fully integrated in the OPMI® Pentero® surgical microscope (A), allowing efficient surgical workflow (B).

Fig. 4: Select INFRARED 800
An initial press of a button on the handgrip sets up the system automatically. User guidance ensures optimum settings for zoom and focus. Pressing the button again activates the synchronous video recording of white light and the infrared view. The brightness of the infrared image is automatically adjusted to the respective application. After recording, the automatic repeat function for the first seconds of the flow phase is activated. During playback, INFRARED 800 recognizes the start of the inflow on the video and jumps directly to this sequence, skipping over the blank recording. The Picture-in-Picture function enables a direct optical comparison of the white light and infrared recordings. The INFRARED 800 video and image data can easily be transferred to a DVD or USB media device.

For detailed menu settings for Setup, Record and Playback, see chapter 9.

4.3 Patient preparation

There is no special preparation necessary, except for the exclusion criteria of a history of adverse reaction to contrast media or iodine. For dye injection, a venous access such as a central venous catheter or a peripheral line is needed.

4.4 Dye preparation and administration

The surgeon usually announces the need for INFRARED 800 a few minutes ahead of time, enabling the anesthesiologist to prepare the fluorescence dye (25 mg per injection). The final command to inject the dye is given by the surgeon after he has started INFRARED 800 (Fig. 5), adjusted the zoom and focus (Fig. 6A and 6B), activated recording and has ensured that the monitor is in the INFRARED 800 mode by seeing the black INFRARED 800 screen.

The anesthesiologist must ensure that the dye arrives as a bolus and is not blocked, distributed or retained in the peripheral line. The fluorescence image appears on the screen in 10 to 30 seconds after ICG administration depending on cardiac and circulatory parameters. During this time, the surgeon should ensure that the structures of interest are visible and the field of view is dry. The automatic INFRARED 800 playback mode of OPMI Pentero will allow to review and analyze the INFRARED 800 angiography thereafter. It is more important to ensure that the image quality is perfect than to view and interpret the original dye inflow. The dye may interfere with peripheral oxygen saturation measurements and may falsely show lower values during the first pass of the dye. The surgeon ends recording of INFRARED 800 after 30 seconds or at his discretion.
4.6 Repeated ICG administrations

Dye administration and INFRARED 800 angiography can be repeated several times if necessary. Classical situations are complex aneurysms with a thickened and calcified base and branching vessels originating from the base of the aneurysm. In these cases, it may be helpful to perform INFRARED 800 angiography before clipping to ascertain the time pattern of filling of the branching arteries and to compare flow properties with INFRARED 800 after clipping. If stenosis or occlusion of a branch is visible, the clip can be corrected and INFRARED 800 angiography can be repeated.

The ICG dye is excreted by the liver with a plasma half-life of 3 to 4 minutes. After 20 minutes, INFRARED 800 can be repeated without much interference from residual fluorescence of the previous dye injection.

4.5 Optimizing fluorescence image quality intraoperatively

Optimum image quality depends on several factors such as light intensity, zoom, focus, iris, cardiocirculatory factors, depth and width of the surgical field and avoidance of bleeding or cerebrospinal fluid (CSF) accumulation around the structures of interest.

Many factors can be influenced and the surgical microscope OPMI Pentero supports the user by providing an intelligent AutoGain function for optimum brightness as well as fluorescence detection and automatic iris adjustment.

Image contrast is increased with a shorter focus distance and less magnification*. We recommend starting with a focus distance of less than 300 mm and magnification of less than 5x. Contrary to the anatomical image seen in white light, a higher zoom does not necessarily provide better details of the fluorescence, and in fact, flow in perforators are better detected with increased contrast in a lower zoom setting.

When the INFRARED 800 mode is activated, the actual focus and zoom settings are checked and, if they exceed the setting made in the configuration menu by the user, a warning is displayed (Figs 6A and 6B). The user can then decide to proceed or to adjust zoom and focus for better image quality.

The user can also switch to manual adjustment of light intensity and/or gain by pushing the “light” button on the handgrip (Fig. 5, buttons D and E) during INFRARED 800 recording, however, except in rare cases, automatic adjustment provides the best image quality.

* The terms “zoom” and “magnification” are used equally in the OPMI Pentero user interface.
INFRARED 800 angiography provides a real-time video of dye inflow in brain vessels consisting of an arterial, a capillary and a combined arteriovenous phase. This mixed arteriovenous image is generated by the recirculating dye. The most important phases are:

1) The first inflow (early arterial phase) for identifying delay or cessation of flow in branching vessels or perforators suggesting vessel stenosis or occlusion,
2) Intermediate phase after 2-5 seconds to judge whether there is still early venous filling in arteriovenous or dural fistulous malformations and
3) A view delayed by 10-20 seconds to judge whether there is complete occlusion or still residual filling of the aneurysm sack.

5.1 Normal findings
Arterial vessels fill almost simultaneously. There are only differences between arterial branches when they are at different distances from the proximal bifurcation. For instance, A1 fills slightly earlier than M2 because the former is closer to the point where the blood flow bifurcates. Or, when comparing flow in the frontal and temporal M2-branches, a branch that runs at a loop around the aneurysm and then runs parallel to the other more direct running branch will show a slight delay in filling compared to the latter because the vessel where flow is observed is more distant to the compared direct-running vessel. Normally, these differences are very difficult to detect, but they may occur physiologically. Therefore, it may be advisable to consider baseline INFRARED 800 administration before clipping when the visible vessels of interest are at different distances from the previous bifurcation.

Venous vessels fill more slowly because flow and pressure are less. Flow in veins may also be easily obstructed by a brain retractor. In patients where the aneurysm was clipped, the sack remains black without any visible fluorescence (Fig. 10), except in those cases where a previous INFRARED 800 angiography was performed and the aneurysm was clipped when there was still dye in the circulation. This dye is then trapped in the aneurysm by the clip and residual fluorescence may be seen. However, when INFRARED 800 is repeated, there should be no change in the signal of the aneurysm sack.

5.2 Pathological findings
When an aneurysm was clipped or a spastic vessel is judged for flow compromise, it is of the utmost importance to compare the appearance of fluorescence with other vessels in the surgical field. Any delay in filling should be considered pathological unless it is comparable to the delay visible during the baseline INFRARED 800 angiography. The signal of the aneurysm sack should not increase with time, otherwise it is not completely clipped (Fig. 11).
In case of a branch occlusion, the diagnosis is confirmed by the missing inflow, judged during the first 1-2 seconds. Yet after a few seconds, the occluded vessel will often fill distally by collateral circulation and this may be mistaken for a normal flow. Often, a pulsating level is seen and should be suspicious of an occlusion (Fig. 12).

Reviewing the time and dynamics of dye inflow by using the loop function helps to better identify the occlusion. In surgery of arteriovenous or dural fistulous malformations, an early venous filling is obvious. Feeding arteries in arteriovenous malformations fill very quickly and in a shorter time than other non-feeding arteries. Arterial filling in dural fistulas does not necessarily occur faster compared to other arteries in the surgical field, but the hallmark is the early venous filling.

5.3 Limitations of INFRARED 800 angiography

Near-infrared angiography is based on light at approximately 800 nm. Essentially, INFRARED 800 video angiography is comparable to visible light. Therefore, only those vessels visible in the surgical field can be assessed by this technology. There is no possibility of judging flow in segments of a vessel or an aneurysm covered by a clip, brain tissue or cotton pads.

The diagnosis of minor to moderate stenosis and flow delay is often difficult with INFRARED 800 angiography. This is attributable to the limited exposure of the vessel of interest. Often, only a few millimeters of an A-2 artery or the posterior communicans artery can be seen which hinders the diagnosis of a delay in contrast inflow rendering. In this case the procedure is not possible or left only to those surgeons with significant experience in image interpretation. In other locations, the vessel can be exposed sufficiently and this difficulty is unlikely to occur.

5.4 OPMI Pentero tools for image interpretation

Keeping the surgical field dry and the vessels of interest exposed as well as judging all aspects of INFRARED 800 angiography in real time is not always possible. Here, dedicated review functions of OPMI Pentero are helpful to go in re-evaluating the flow dynamics in branching vessels, perforators and the aneurysm. This loop function is complemented by a built-in algorithm that recognizes the inflow so that only the effective time of angiography is repeated. This loop can be adjusted in terms of numbers of repetitions and length of time. It should be noticed that the loop function is designed to review the first seconds of inflow. It should therefore be adjusted to a length of 8-10 seconds. The long-review is activated after finishing the loop function to review a longer period of time. Again, numbers of repeated review cycles and length of review can be adjusted in the menu (see chapter 9.3).

6 Clinical studies

6.1 Aneurysm surgery

A recent study (6) prospectively compared INFRARED 800 with intraoperative or postoperative digital subtraction (DS) angiography. The technique was performed during 187 surgical procedures in which 124 aneurysms in 114 patients were clipped. The patency of parent, branching, and perforating arteries and documentation of clip occlusion of the aneurysm as shown by INFRARED 800 were compared with intraoperative or postoperative findings on DS angiography. The results of INFRARED 800 corresponded with intra- or postoperative DS angiography in 90% of cases. The INFRARED 800 technique missed mild but hemodynamically irrelevant stenosis evident on DS angiography in 7.3% of cases. The INFRARED 800 technique missed angiographically relevant findings in three cases (one hemodynamically relevant stenosis and two residual aneurysm necks [2.7% of cases]). In two cases, the missed findings were clinically and surgically inconsequential; in the third case, a 4-mm residual neck may require a second procedure.

However, INFRARED 800 provided significant information for the surgeon in 9% of cases, most of which led to clip correction. This study found that the INFRARED 800 technique may be useful during routine aneurysm surgery as an independent form of angiography or as an adjunct to intra- or postoperative DS angiography.
6.2 Bypass surgery

Woitzik et al. (7) investigated whether the INFRARED 800 technique is also suitable for the intraoperative confirmation of extracranial-intracranial bypass patency. They included forty patients undergoing cerebral revascularization for hemodynamic cerebral ischemia (11 patients), moyamoya disease (18 patients), or complex intracranial aneurysms (11 patients) in their study. Superficial temporal artery (STA)-middle cerebral artery (MCA) bypass surgery was performed 32 times in 30 patients (five patients with moyamoya disease underwent bilateral procedures), STA-posterior cerebral artery bypass surgery in two patients, and saphenous vein (SV) high-flow bypass surgery in eight patients. In each patient, following the completion of the anastomosis, ICG (0.3 mg/kg body weight) was given systemically via an intravenous bolus injection. The findings of ICG videoangiography were compared with those of postoperative digital subtraction (DS) or computerized tomography (CT) angiography. In all cases, excellent visualization of cerebral arteries, the bypass graft, and brain perfusion were noted. ICG videoangiography was used to identify four nonfunctioning STA-MCA bypasses which were revised successfully in all cases. In two cases, of SV high-flow bypasses, ICG videoangiography revealed stenosis at the proximal anastomotic site, which was also revised successfully. In all cases, the final findings of ICG videoangiography could be positively validated during the postoperative course by performing DS or CT angiography.

6.3 Other INFRARED 800 studies

- First intracranial use of ICG angiography (4)
- Microscope integration of INFRARED 800 technology (5)
- INFRARED 800 angiography and intraoperative perforating artery imaging during aneurysm surgery (2)

7 Checklist

7.1 Before surgery

- Iodine or contrast media allergies excluded.
- Written informed consent for intraoperative angiography.
- OPMI Pentero microscope set-up for INFRARED 800 complete.
- Parameters such as loop length and number of repetitions are set as outlined previously.
- Handgrip bar is configured for INFRARED 800 mode.
- External monitors (if required) are connected and setup in the INFRARED 800 menu.

7.2 During surgery

- Surgeon informs the anesthesiologist of planned INFRARED 800 procedure within the next minutes.
- Anesthesiologist prepares the 25 mg syringe (5 ml).
- Surgeon asks for confirmation that ICG dye is ready for injection (syringe connected).
- Surgeon activates INFRARED 800 by pressing the configured button on the handgrip.
- The system performs a focus and zoom check for optimum image quality.
- If the settings are out of the range for best image quality, adjust or confirm to proceed. Surgeon starts INFRARED 800 angiography by pressing the configured button again.
- Monitor turns black.
- Surgeon asks the anesthesiologist to administer the ICG dye as a bolus in 1 second. Surgeon pays attention to the surgical field and ensures a free line of sight to the vessels of interest.
- Surgical assistant informs the surgeon when fluorescence is seen.
- Recording should continue for 20-30 seconds. Surgeons finishes recording by again pressing the configured button.
- Surgeon reviews the automatic replay of the video.
- Short replay loops are stopped by pressing the configured button.
- Long replay loops are stopped by pressing the configured button.
- Monitor switches back to visible light.

8 Reference list
9 Appendix

9.1 IR 800

Setup menu

The Setup menu (Fig. 13) is used to configure the setup procedure in order to achieve optimum quality of the video image. Any deviation from the preconfigured parameters (items 1, 3 and 4) may lead to a loss in video image quality.

1 Auto zoom

– On: the total magnification is changed automatically to the preconfigured value (item 3) without-pop-up message.
– Off: a setting dialog is displayed (see Fig. 6A) for changing the total magnification beyond the preconfigured range (item 3).

Factory setting: Off

1 MultiVision

– On: The content of the touchscreen monitor is also displayed in the data injection system during the PLAYBACK mode. Please switch to the full screen mode for better visualization.
– Off: No display in the data injection system.

Factory setting: Off

If the current total magnification is within the configurable limit value (blue range is our recommendation), the zoom is not changed during the setup phase.

If the magnification value is outside the preset limit, the following happens:

– With Auto Zoom on: the zoom factor setting is automatically changed to the preconfigured value (item 3).
– With Auto Zoom off: a pop-up box with a setting bar appears (see Fig. 6A). The setting bar automatically disappears after correction of the value within the setting range. To retain the current settings, press “Ignore” on the touchscreen or the center button of the joystick on the right handgrip.

Adjustment range: 2x - 13x

Factory setting: 5x

4 Focus threshold (working distance)

If the current focus value is within the limit configured with the maximum focus slider (item 4), no message is displayed to the user during the setup phase. If the focus value exceeds the set limit, the user is prompted in a pop-up window to reduce the focus value accordingly (see Fig. 6B).

Adjustment range: 200 mm-500 mm

Factory setting: 300 mm

Fig. 13: Setup menu screen
9.2 IR 800

Record menu

The Record menu (Fig. 14) permits you to make the following settings for the recording phase:

1 External monitor
   – Standard: output of the white light camera signal on the external monitor.
   – IR800: output of the INFRARED 800 camera signal on the external monitor. No text displays or time data are displayed on the external monitor.
   Factory setting: IR800

2 IR camera gain
   – Auto: the camera gain is automatically adjusted to the current conditions. Manual Gain Setting slider (item 3) is disabled.
   – Manual: you can set the camera gain to a fixed value. Use Manual Gain Setting slider (item 3) to select this value.
   Factory setting: Auto

3 Manual gain setting
   Slider for manual adjustment of the camera gain (item 2).
   Adjustment range: 1% - 100%
   Factory setting: 70%

4 Auto IR detection
   – On: The video signal is analyzed for fluorescence flow in the RECORD mode. If fluorescence flow is detected, the black leader is not displayed in the playback mode.
   – Off: No automatic fluorescence detection, the complete recorded video is played in the playback mode.
   Factory setting: On

Note:
When Auto Camera Gain is deactivated (end Auto Gain or select manual setting), you can manually adjust the gain value on the touchscreen or using the yellow light button on the right handgrip. In both cases, Gain button (item 5) is displayed on the bottom right of the video image for activation of the slider (item 6).

Fig. 14: Record menu screen
9.3 IR 800 Playback menu

The Playback menu (Fig. 15) is used to configure video playback.

1 External monitor

– Standard: The white light camera signal is output on the external monitor during the PLAYBACK mode instead of the white light video recorded synchronously with the INFRARED 800 video.
– IR 800: The INFRARED 800 video is output on the external monitor during the PLAYBACK mode.

Factory setting: IR 800

2 MultiVision

– On: The content of the touchscreen monitor is also displayed in the data injection system during the PLAYBACK mode. Please switch to the full screen mode for better visualization.
– Off: No display in the data injection system.

Factory setting: Off

3 PiP in Replay (playback mode only)

– On: When Picture in Picture (PiP) has been activated, the simultaneously recorded white light video is displayed in a small window at the top right of the touchscreen.
– Off: No PiP display.

Factory setting: On

Note:
A video clip is recorded and saved in the white light mode at the same time as the fluorescence video clip. Videos started with REC START are recorded irrespective of this process. If IR 800 is selected for the external monitor (item 1), this video is briefly interrupted by the displayed replay screens. *)

4 Short replay

– On: Only the initial phase of the recorded INFRARED 800 video is displayed at the beginning of the PLAYBACK mode. You can adjust the length of the sequence using the Short Replay Duration slider (item 5). The replays can only be stopped by pressing the fluorescence button. They will be stopped automatically after 25 replays. If fluorescence detection has been activated, the video starts after detection of the fluorescence flow. The preceding black leader will not be displayed.

*) Digital video recording option is required.
– Off: No replay function available. The Short Replay Duration slider is disabled.

Factory setting: On

5 Short replay duration

This slider permits you to select the length of the video clip to be played when Short Replay has been activated:

Adjustment range: 3s - 30s
Factory setting: 6s

6 Long replay

– On: The complete recorded fluorescence video is played repeatedly. You can select the number of playbacks using the Number of Long Replays slider. If fluorescence detection has been activated, the video sequence starts after detection of the fluorescence flow. The preceding black leader will not be displayed.
– Off: No long replay function available. The Number of Replays slider is disabled.

Factory setting: On

7 Number of long replays

After the end of recording, the complete recorded fluorescence video clip can be automatically replayed up to 10 times (as an endless loop). The process can be stopped at any time by pressing the fluorescence button on the handgrip or foot control unit.

Adjustment range: 1-10
Factory setting: 5

Note:
During playback of an INFRARED 800 video, you can use the joystick on the right handgrip to stop, fast forward or rewind the video, or to extract images from it.