



# Coronary Angiography

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Tohru Asai

## Summary

- Indocyanine green fluorescence angiography has been applied as an ideal method for intraoperative graft evaluation in coronary artery bypass grafting.
- A small amount of ICG is administered intravenously, and a clear angiogram can be obtained instantaneously by a CCD video camera.
- Graft failure can be detected with higher sensitivity than the conventional Doppler-based test (TTFM).
- Indocyanine green fluorescence angiography is attracting attention as a method enabling functional evaluation of bypass grafting as well as an assessment of graft patency.

In CABG, the diameter of the anastomotic site is 1.0–2.0 mm. If a subtle intraoperative problem causes stenosis and/or occlusion at the anastomosis, the value of bypass surgery itself can disappear. In fact, previous reports have indicated that 4% of bypass grafts (8% of cases) are occluded intraoperatively [1], and 5–20% of grafts are occluded before hospital discharge [2]. These results suggest that intraoperative detection of invisible problems enables re-anastomosis, leading to the improvement of graft patency after surgery, as performed in current coronary artery bypass surgery. In Japan, we can claim medical expenses for intraoperative graft evaluation, which has played an important role in the quality control of coronary artery bypass surgery.

## 1 Introduction

Coronary artery bypass grafting (CABG) not only relieves anginal pain in severe ischemic heart disease but also prevents possible future myocardial infarction and ischemic heart failure and prolongs life expectancy. There are two methods of coronary artery bypass surgery: “on-pump CABG,” in which a bypass anastomosis is constructed under cardiac arrest with a cardioplegic solution under the heart-lung machine, and “off-pump CABG,” in which the position of the heart is controlled and the anastomosis is performed with a local stabilizer while the heart is beating without circulatory support. In Japan, 50–60% of CABG are currently performed as off-pump CABG. The graft vessels used for bypass include arterial grafts (the internal thoracic artery, ITA; right gastroepiploic artery, GEA; and radial artery, RA) and the great saphenous vein. Types of grafts and surgical procedures are determined by surgeons and surgical teams according to the conditions of each patient.

## 2 Conventional Graft Evaluation Methods and Problems

The most common method for intraoperative graft evaluation is transit time flow measurement (TTFM), which uses the Doppler principle to measure graft blood flow, because of its simplicity and repeatability. Limitations of TTFM lie in the fact that it does not visualize the actual graft vessel and some of the measurements require understanding and interpretation by surgeons. Recently, the morphology of the graft anastomosis can be confirmed by using TTFM with high-frequency ultrasound images of the cardiac surface. However, this technique requires a surgeon’s skills, and it is still difficult to understand the gross and spatial status of blood perfusion like radiographic coronary angiography. A conventional coronary angiography following injection of radiographic contrast materials provides information on the coronary artery and graft patency with the highest resolution. Radiographic angiography can be performed intraoperatively in some medical centers with a hybrid operating room. In daily clinical practice, however, it is rarely performed because of the lack of equipment and the increasing number of patients with renal dysfunction.

T. Asai (✉)  
Department of Cardiovascular Surgery, Juntendo University,  
Bunkyo-ku, Tokyo, Japan  
e-mail: [t.asai.jj@juntendo.ac.jp](mailto:t.asai.jj@juntendo.ac.jp)

In contrast, intraoperative fluorescence imaging allows the visualization of the bypass graft only with a small amount of intravenous indocyanine green (ICG), enabling real-time and on-site evaluation of the blood supply. It also has the advantage of preventing renal dysfunction due to angiography. In addition, unlike radiographic coronary angiography following bolus injection of contrast materials, ICG fluorescence imaging can reflect the balance of blood flows between the coronary artery and the bypass with information on collateral vessels under the natural cardiac circulation. In this chapter, we will describe methods and outcomes of ICG fluorescence imaging in CABG mainly with a SPY system.

### 3 Development History of Indocyanine Green Fluorescence Imaging in Cardiac Surgery

The application of intraoperative contrast-enhanced fluorescence imaging for CABG was developed by Novadaq Technology in Toronto, Canada, in 2000 as the “SPY Intraoperative Imaging System.” Detter et al. [3] reported that ICG fluorescence angiography was useful for clear angiographic images in a porcine coronary artery bypass model. The first clinical use in humans was reported in 2002 by Rubens et al. [4] in 20 bypass operations, resulting in graft re-anastomosis in one patient. In 2005, Balacumaraswami et al. [5] compared TTFM with the SPY system and found that TTFM alone may lead to unnecessary graft re-anastomosis. In 2005, the US FDA approved the use of the SPY system for perfusion assessment in coronary artery surgery. In addition, in 2006, Desai et al. [6] conducted a randomized trial on the usefulness of the TTFM and SPY systems and reported that the SPY system detected intraoperative graft failure with greater accuracy than the TTFM. In Japan, the SPY system was introduced in 2002, and the number of facilities using the system has been gradually increasing since then; as of 2018, approximately 50 SPY systems nationwide have become widely available for intraoperative evaluation of coronary artery bypass surgery.

#### Point

- Indocyanine green fluorescence angiography has been used as an ideal method for the detection of graft failure in CABG.

### 4 Methods of Fluorescence Imaging

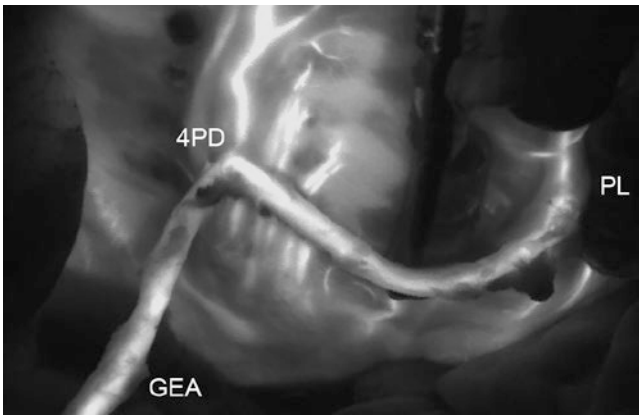
Recently in Japan, the majority of patients undergo CABG as off-pump surgery. Off-pump CABG has advantages over on-pump CABG in terms of operation time and duration of car-

diac arrest required for revisions of bypass when insufficient blood flow is detected by cardiac angiography. Intraoperative fluorescence angiography using the SPY system is particularly useful in off-pump CABG.

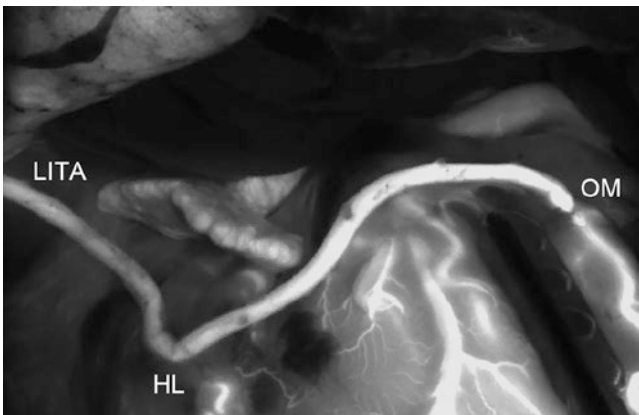
Following the bypass grafting, the camera arm of the SPY system is introduced from the opposite side of the operating surgeon. The camera head is covered with sterilized plastic and set just above the operation field. The surgical lights should be turned off. Then, ICG is administered through a central vein to assess the graft patency and tissue perfusion. The advantage of ICG fluorescence imaging lies in the fact that surgeons can understand the outcomes of fluorescence angiography clearly and easily within 2–3 minutes. Although the graft anastomosis can be located on the side, back, or bottom of the heart, we can obtain fluorescence images just after the anastomosis because the heart has already been mobilized sufficiently. Even if there are five or six coronary anastomoses, all evaluations can be performed in two or three imaging sessions. When fluorescence imaging is used repeatedly, it is necessary to wait at least 3 minutes per acquisition for the ICG to disappear from the bloodstream. The images (movies) of fluorescence angiography can be played back immediately, enabling surgeons to review graft perfusion whenever necessary. In addition, ICG fluorescence angiography has potential advantages over conventional radiographic angiography in that it enables assessment of graft perfusion under normal circulation (without bolus infusion of contrast materials) with fewer people, without catheter insertion or a risk of radiation exposure and renal disorder.

The SPY system can be used easily at any point during surgery. In our off-pump CABG, we have used ICG fluorescence angiography when all anastomoses are completed, because it enables us to redo the problematic bypass anastomosis under a beating heart immediately, although the incidence is very low.

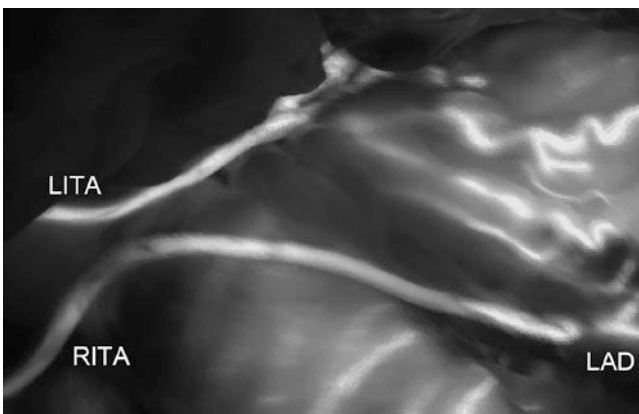
In Figs. 8.1, 8.2, and 8.3, specific examples of intraoperative fluorescence angiography are demonstrated. The RITA was anastomosed to the left anterior descending artery (LAD) of the left coronary artery. The GEA was sequentially anastomosed through the posterior descending artery (4PD) of the right coronary artery to the posterior lateral branch (PL). As soon as the last anastomosis was constructed, the camera arm of the SPY system was covered with a sterile cover and fluorescence angiography was performed. The examination was recorded as a clear movie in three shots. This movie could be played back repeatedly after imaging. In both the internal thoracic artery graft and the gastric major artery graft, the skeletonized arterial graft allows us to clearly follow the movement of blood flow through the vessel wall as in the venous graft. Examples of problematic cases are shown in Fig. 8.4. In this case, the RITA graft to the LAD



**Fig. 8.1** Sequential anastomosis with the right gastroduodenal artery (GEA-PDA-PL). Indocyanine green fluorescence angiography of a five-vessel beating coronary artery bypass using only an in situ arterial graft; this imaging was performed with intact cardiac deployment and stabilization after the last anastomosis



**Fig. 8.2** Sequential anastomosis with the left internal thoracic artery (LITA-HL-OM). Indocyanine green fluorescence angiography of five-vessel beating coronary artery bypass with in situ arterial graft alone



**Fig. 8.3** Single anastomosis of the right internal thoracic artery to the left anterior descending branch (RITA-LAD). Indocyanine green fluorescence angiography of five-vessel beating coronary artery bypass with in situ arterial graft alone

was not visualized at all, so the anastomosis was revised. As shown in Fig. 8.4b, the graft blood flow after re-anastomosis was well depicted.

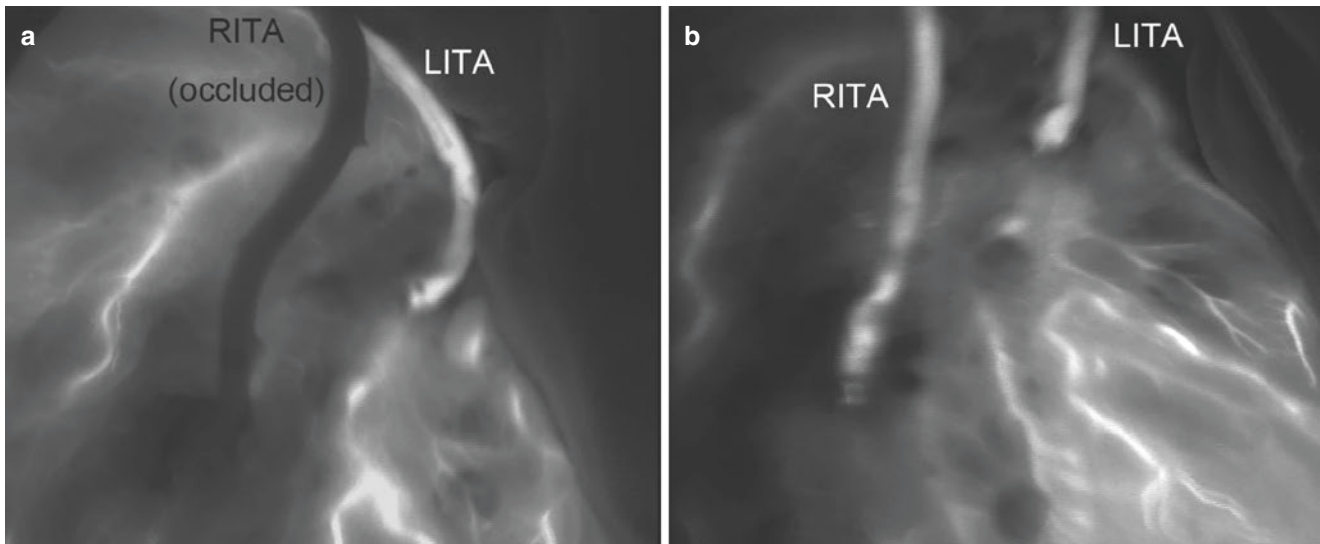
Although the incidence is low, graft occlusion can develop during CABG because of technical errors in the anastomosis, vessel dissection, lumen occlusion due to hematoma, wandering of surrounding tissue into the anastomotic vessel, and thrombus formation. The SPY system allows visualization of the actual blood flow inside an apparently normal bypass anastomosis and is a valuable tool for resolving problems before the end of surgery.

Our initial experiences with intraoperative fluorescence angiography were as follows [7, 8]: From April 2009 to November 2011, we performed intraoperative fluorescence angiography using the SPY system in 159 patients. In this series, fluorescence imaging was used after the completion of all anastomoses based on conventional techniques (TTFM and redo, if necessary). Although the TTFM detected abnormal values in 12/142 RITA, 13/155 LITA, 20/88 GEA, and 10/50 SVG, ICG fluorescence angiography visualized sufficient blood flow in all anastomoses; but all intraoperative fluorescence images (IFI) showed contrast enhancement. Confirmatory angiography (CT angiography in 128 patients and direct angiography in 31 patients) at about 1 week after surgery showed that all arterial grafts were open and only two venous grafts were occluded.

Some authors have also reported the detection rate of intraoperative graft failure by the SPY system: Taggart et al. [9] reported 4 of 213 grafts (1.9%), Reuthebuch et al. [10] reported 4 of 107 grafts (3.7%), Desai et al. [11] reported 5 of 348 grafts (1.4%), Balacumaraswami et al. [5] reported 8 of 533 grafts (1.5%), Takahashi et al. [12, 13] reported 4 of 290 grafts (1.9%), and Kishimoto et al. [14] reported 4 of 533 grafts (1.9%). Since some of these abnormal findings might have been undetected by conventional techniques, ICG fluorescence angiography is expected to contribute greatly to the improvement of surgical outcomes of CABG.

#### Point

- Intraoperative fluorescence angiography using the SPY system provides clear images of the coronary artery and anastomosis only with a small amount of ICG through a central vein.
- ICG fluorescence angiography detects abnormal blood flows sensitively at any time during surgery, enabling surgeons to revise the anastomosis immediately.



**Fig. 8.4** A graft problem detected by intraoperative fluorescence angiography. (a) The left internal thoracic artery was well delineated, but the blood flow from the right internal thoracic artery was not contrasted. (b) The anastomosis was immediately revised, the right internal tho-

racic artery was slightly shortened, and the anastomosis was reconstructed. Fluorescence angiography identified sufficient blood flows through the anastomosis

## 5 Expected Roles of Indocyanine Green Fluorescence Angiography in Coronary Artery Bypass Grafting

### 5.1 Evaluation of Blood Flow in Bypass Grafts

The real-time images on the monitor clearly demonstrate the blood flow from the bypass vessel into the coronary artery, which can easily be interpreted and shared by surgeons. If there is no contrast effect at all, this may indicate a problem due to blood clots, dissection, kinking, or bending of the anastomosis or graft. In such a case, the coronary anastomosis can be redone immediately, followed by repeated fluorescence angiography. A possible limitation of the SPY system is that when bypass vessels are harvested with surrounding connective tissues, blood flow can be invisible because of the limited tissue permeability of near-infrared light. In addition, blood flow from the anastomosis to the peripheral coronary artery itself cannot be visualized by fluorescence imaging because the fluorescence signals are blocked by fatty tissues on the cardiac surface. These points are considered to be the limitations of the current imaging system.

### 5.2 Assessment of the Competing Blood Flows Between the Graft and Host Coronary Artery

When the arterial graft is used for mild stenosis of the coronary artery, the blood flow through the graft may compete with the native blood flow, causing the bypass vessel to become thin and lose blood supply in some cases. Unlike

conventional catheter angiography, in which contrast materials are forcefully injected from the target vessel, ICG fluorescence angiography can delineate the real status of blood flows under natural circulation, including the competing blood flows. Therefore, intraoperative fluorescence angiography may become an important method for future research on the proper use of arterial grafts and the long-term postoperative effects of the competing blood flows.

## 6 Technical Notes

When ICG fluorescence angiography is used for visualization of the internal thoracic artery and the right gastroduodenal artery, fluorescence signals can be identified slowly because they are far from the origin of the coronary artery. This should not be misunderstood as insufficient blood supply. In addition, there can be a time lapse in the visualization of the host coronary artery, the vein graft from the ascending aorta, and the arterial grafts, which may affect the incidence of the competing blood flows. It is unclear what the clinical significance of these phenomena is, how they affect subsequent bypass function, or whether they are at all problematic, but assessments of blood flow status by ICG fluorescence imaging may provide clues to the clinical significance of these phenomena.

The most important issue in this technique would be the quantitative assessment of blood flows. A semi-quantitative assessment of graft vessels and corresponding myocardial regions before and after bypass grafting may be useful to propose new criteria for the intraoperative evaluation of the graft patency, as suggested by Ferguson et al. [14].

One of the limitations of intraoperative fluorescence angiography lies in its tissue permeability especially due to connective tissues attached to the graft and cardiac muscles. Further improvement of signal detectability by fluorescence imaging and combination with other diagnostic modalities such as TTFM and fractional flow reserve (FFR) [15] would clarify unknown functions and long-term changes of the graft vessels.

## 7 Conclusions

Although the mainstream of intraoperative graft evaluation in Japan remains TTFM, applications of ICG fluorescence angiography in CABG will be expanded as a safe, easy, and reliable diagnostic tool, with the improvement of imaging systems.

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