

# Intraoperative Imaging Techniques to Assess Coronary Artery Bypass Graft Patency

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Graft patency verification is increasingly recognized as an important component of coronary artery bypass grafting. Intuitively, eliminating intraoperative graft failure should reduce cardiac mortality and morbidity in the short term and improve clinical outcome in the long term. Although conventional angiography remains the gold standard technique for assessing graft patency, it is rarely available in the operating room and consequently several other less invasive approaches have been advocated. This article reviews the two currently most commonly used modalities for graft patency assessment, intraoperative

fluorescence imaging and transit-time flowmetry, and discusses their value and limitations. Both techniques can reliably detect otherwise unsuspected occluded grafts and this is crucial for internal thoracic arteries because of their prognostic significance. Although neither technology can consistently identify more minor, non-occlusive abnormalities, the intraoperative fluorescence imaging technique seems to be more sensitive and less susceptible to “false positive” images.

(Ann Thorac Surg 2007;83:2251–7)

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Verification of graft patency should be a key aspect of coronary artery bypass grafting (CABG) as immediate intraoperative graft failure occurs in up to 4% of grafts (8% of patients) during CABG [1]. Furthermore, intraoperative technical errors almost certainly contribute to the graft failure, which is detectable in 5% to 20% of patients at discharge [2], and in up to 30% of graft failures by 1 year. Six recent studies of postoperative angiographic graft patency in 1,814 patients, including 4,735 grafts, up to 1 year after surgery reported an average failure rate of 20% (Table 1) [3–8]. Early graft failure is an important cause of perioperative myocardial infarction, which is detectable in up to 9% of CABG patients [9], and it is not only a major cause of immediate cardiac surgical morbidity and mortality but also results in an unfavorable long-term outcome [10].

Recently the 30% failure rate in more than two thousand vein grafts at 1 year in the PREVENT IV trial has emphasized the potential advantages of arterial grafts [8]. However, although arterial grafting and off-pump CABG have been respectively promoted to improve long-term outcome [11, 12] and reduce the complications of cardiopulmonary bypass [13], both techniques are technically more demanding. Furthermore, a recent meta-analysis of randomized trials by Parolari and colleagues [14] has suggested that there may be a reduced graft patency rate with off-pump CABG [14]. However in the absence of intraoperative graft patency assessment, it is not known what proportion of these grafts failed and could have been corrected during surgery.

## Techniques for Intraoperative Assessment of Graft Patency

Conventional coronary angiography is still the “gold standard” assessment for graft patency, but its requirements for additional equipment and personnel along with the need for arterial puncture, the use of potentially nephrotoxic contrast agents, and increased operating time usually precludes it from the operating room. Using fixed angiographic equipment in a specially designed operating room, Hol and colleagues [15] recently reported that angiography took 30 minutes and detected a 4% graft failure rate after chest closure. Despite refinements in equipment, such as pulsed fluoroscopic systems with dynamic acquisition, and refinements in technique, such as radial artery catheterization or dye injection into the distal end of the free radial artery graft [16, 17], the additional resource and personnel implications mean that conventional angiography is unlikely to become freely available in the operating room.

Consequently several other techniques [17–23] summarized in Table 2 have been used to assess intraoperative graft patency. Doppler velocity measurements use the principle of changes in frequency relative to the position of the transducer (Doppler shift); continuous wave systems are easy to use but their range resolution does not permit precise graft flow evaluation while the pulsed wave technique provides flow velocities that vary with the angle of insonation [21]. Elbeery and colleagues [16] found that in 8% of 50 patients, Doppler flow measurements failed to detect occluded grafts when compared with intraoperative angiography and concluded

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Dr Taggart discloses that he has a financial relationship with Novadaq Technologies, Inc.

Table 1. Recent Studies of Postoperative Graft Patency Using Conventional Angiography

Study	Year	Patients Enrolled	Patients Undergoing Angiography	Time to Angiography (Mo)	Grafts (n)	Graft Failure				
						No. of OP CABG	No. of ON CABG	Total No.	% Grafts (Total)	% Patients (Total)
Nathoe and colleagues (3)	2003	281	70	12	158	6	6	12	7.6	N/A
Widimsky and colleagues (4)	2004	400	255	12	639	86	92	178	27.8	N/A
Lingaas and colleagues (5)	2004	120	115	3	303	16	10	26	8.6	N/A
Khan and colleagues (6)	2004	104	82	3	260	16	3	19	7.3	N/A
Puskas and colleagues (7)	2004	200	184	3	622	3	7	10	1.6	N/A
Puskas and colleagues (7)	2004	200	153	12	511	16	11	27	5.3	17.6
PREVENT IV Trial (8)	2005	1,506 (placebo group)	955	12	2242	N/A	N/A	671	30	46
Total			1,814		4735			943	19.9	N/A

N/A = not available; ON CABG = on-pump coronary artery bypass grafting; OP CABG = off-pump coronary artery bypass grafting.

that it was unreliable for graft patency assessment. Similarly, although electromagnetic flowmetry accurately quantifies blood flow in experimental conditions with laminar flow, this does not apply in the clinical setting [18]. Consequently, as electromagnetic flowmetry flow values vary with movement, hematocrit, and other interference, it is no longer used in clinical practice. High frequency epicardial ultrasound scanning can provide acceptable images of coronary stenoses and graft anastomoses, but it does not offer real-time angiographic images [22]. Thermal coronary angiography uses infrared light to detect temperature differences generated between the myocardium and coronary arteries by the infusion of cold or warm saline or cardioplegic solutions, but image resolution is often unsatisfactory [19].

Consequently the two most commonly used techniques in current clinical practice are intraoperative fluorescence imaging (IFI) [23] and transit-time flowmetry (TTFM) [19]. We have described the clinical application of IFI and TTFM techniques in a previous review article [24], and this article provides current data regarding IFI as well as a review of two prospective comparative trials of both techniques.

### Intraoperative Fluorescence Imaging

#### Principle

Intraoperative fluorescence imaging is a novel imaging technique (SPY; Novadaq Technologies Inc, Toronto,

Table 2. Different Techniques for Intraoperative Graft Patency Assessment

Technique	Year	Reference Article	Patients (n)	Strengths	Limitations	Current Use
Conventional angiography	1998	Elbeery and colleagues (16)	50	Precise definition of graft patency	Invasive, requires contrast, rarely available in operating room	-
Electromagnetic flowmetry	1994	Louagie and colleagues (18)	262	Ease of use, Noninvasive	Motion artifacts, Interference	-
Transit-time flowmetry	1994	Canver and Dame (19)	63	Accurate graft flow value	Inability to define degree of stenosis	+
Thermal angiography	1995	Falk and colleagues (20)	370	No contrast or radiation	No clarity with increasing depth	-
Doppler velocity measurements	2000	Lin and colleagues (21)	35	Ease of use, noninvasive	Flow values affected by angle of insonation	-
Epicardial color doppler scanning	2002	Haaverstad and colleagues (22)	23	Noninvasive	Imprecise definition of all coronary territories	-
Intraoperative fluorescence imaging	2003	Taggart and colleagues (23)	84	Real-time "angiographic" images	Semiquantitative	+

Table 3. Review of Studies With Intraoperative Fluorescence Imaging

Site	Year	Reference	No. of Patients	No. of Grafts	Revised Grafts		
					No.	% of Grafts	% of Patients
Canada	2002	Rubens and colleagues (27)	20	N/A	1	N/A	5
Oxford, UK	2003	Taggart and colleagues (23)	84	213	4	1.9	5
Switzerland	2004	Reuthebuch and colleagues (28)	38	107	4	3.7	N/A
Oxford, UK	2004	Balacumaraswami and colleagues (29)	200	533	8	1.5	4
Japan	2004	Takahashi and colleagues (30)	72	290	4	1.4	N/A
Canada	2005	Desai and colleagues (31)	120	348	5	1.4	4.2
Summary of studies with graft details			514	1491	26	1.7	5.1

N/A = not available.

Canada) that has both CE marking for Europe and recently acquired Food and Drug Administration approval for the United States. It is currently used in Canadian, European, North American, and Japanese centers.

Intraoperative fluorescence imaging is based on the fluorescent properties of indocyanine green (ICG) dye. After intravenous injection ICG binds immediately to plasma proteins and when illuminated with a monochromatic light source at 806 nm (near infrared) it emits light with a wavelength at 830 nm. This fluorescence is captured on a charged couple device video camera.

The IFI system raises two potential safety issues regarding the laser light source and ICG dye. The total output of the laser is 2.7 watts, it operates at a distance of 30 cm above the heart, and is spread over an area of 7.5 cm × 7.5 cm. The laser light is of low intensity with a depth of tissue penetration of about 1 mm to avoid myocardial thermal damage. The laser has an excellent safety profile for both the patient and operating room staff, and no protective eyewear or clothing is required. Indocyanine green itself has an excellent safety profile and has been in clinical use for more than 4 decades. The incidence of allergic reaction to ICG is strongly dose-dependent, being greatest with doses in excess of

0.5 mg/kg, and is reported to be approximately 1:40000, especially in patients allergic to iodine [25].

*Procedure*

The camera imaging head is covered with a sterile polyethylene drape and positioned 30 cm above the heart. A green diode on its range detector gauge guides the positioning of the imaging head directly over the operative field. Indocyanine green is made up of a concentration of 2.5 mg/mL, and on completion of the distal coronary anastomosis in off-pump CABG, a bolus of 1 mL of ICG dye is injected into the central venous catheter, which is rapidly flushed with 10 mL of normal saline. Alternatively the dye can be injected into the ascending aorta [26]. For on-pump CABG the dye is injected directly into the oxygenator. Immediately after intravenous dye injection (or after a 5-second delay if the dye is injected into the oxygenator), the laser power is activated and captured images are recorded on the computer hard drive. The appearance of fluorescent ICG dye passing antegradely through the bypass grafts confirms graft patency. The visualization of dye fluorescence is better with skeletonized internal thoracic artery and radial artery conduits compared with pedicled conduits.

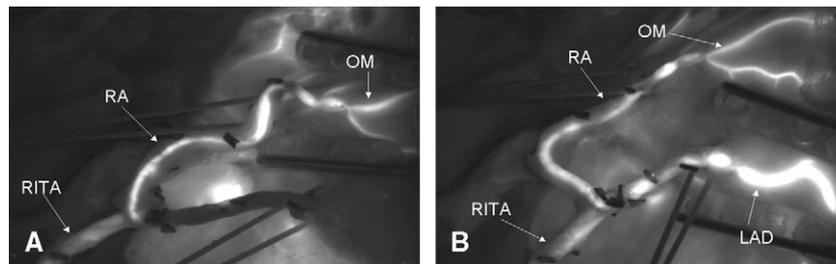


Fig 1. (A) SPY (Novadaq Technologies, Inc, Toronto, Canada) image showing the right internal thoracic artery (RITA) graft to the left anterior descending coronary artery (LAD). A composite radial artery (RA) graft was placed from the RITA to the obtuse marginal (OM) coronary artery. Note that no fluorescence was seen in the RITA distal to the radial artery anastomosis, which was therefore reconstructed (see Fig 1B). (B) SPY image taken after revision of radial artery (RITA anastomosis seen in Fig 1A). Note fluorescence seen in the distal portion of the RITA graft and in the LAD. (Reprinted from Ann Thorac Surg, 75, Taggart DP, et al, Preliminary experience with a novel intraoperative fluorescence imaging technique to evaluate the patency of bypass grafts in total arterial revascularization, 870-3, Copyright (2003), with permission from The Society of Thoracic Surgeons.)

REVIEW

The procedure takes approximately 3 minutes per graft, and ICG injections can be administered repeatedly.

### Current Experience and Results

As summarized in Table 3 [27-31], several centers have now reported their experience with IFI to detect graft failure in the operating room. A summary of these six independent studies using IFI in 1,491 grafts in 514 patients demonstrates an overall graft revision rate of 1.7% in approximately 5% of patients, being remarkably consistent among different centers (Table 3).

In our initial experience using IFI in 213 grafts performed in 84 patients we reported graft failure in 1.9% of grafts (5% of patients) [23]. More recently we imaged 533 bypass grafts in 200 patients undergoing off-pump CABG or on-pump CABG with a mean of 2.5 grafts per patient [29]. Graft revision was necessary in eight grafts (1.5%) in 8 patients (4%), in two on-pump CABG patients (4%) and 6 off-pump CABG patients (4%). Most importantly, graft occlusion would otherwise have remained "silent," as no patient showed any associated hemodynamic or electrocardiographic changes. After revision of occluded grafts, re-imaging with IFI confirmed patency in all, and an example is presented in Figure 1. Vitality the use of the ICG dye seemed safe with no adverse consequences.

Recently, Desai and colleagues [31] reported their experience with IFI imaging in 348 grafts in 120 patients and confirmed the value of IFI in the clinical setting. They found an interobserver agreement of 100% for graft occlusion between two surgeons, one experienced and another inexperienced with the interpretation of IFI images, and 100% sensitivity and 100% specificity when compared with postoperative angiography to detect graft occlusion or a graft narrowing greater than 50%.

### Limitations

Although detection of occluded grafts is relatively straightforward, IFI does not produce precise measurements of flow in patent grafts but rather a semi-quantitative assessment of graft patency as "excellent," "satisfactory," or "poor."

As the transit time for ICG dye in the circulation is dependent on several factors such as the systemic arterial pressure, hematocrit, conduit diameter, resistance of the distal coronary vascular bed, and especially, competitive native coronary flow (related to the severity of the proximal coronary stenosis), the reason for poor flow in a graft may not be immediately obvious. If competitive flow is suspected to be the cause of poor graft flow, then a Silastic sling (Quest Medical Inc, Allen, TX) used to snare the proximal target coronary vessel minimizes competitive flow [1].

Another limitation is that because of limited tissue penetration and the imaging of anastomoses from directly above, IFI can not provide precise details of anastomotic quality. For the same reason there is a concern that a bend in the graft away from the laser light source may seem to lose clarity and be potentially perceived as graft stenosis on a still image capture. This concern can be allayed by visualizing a movie video clip that would

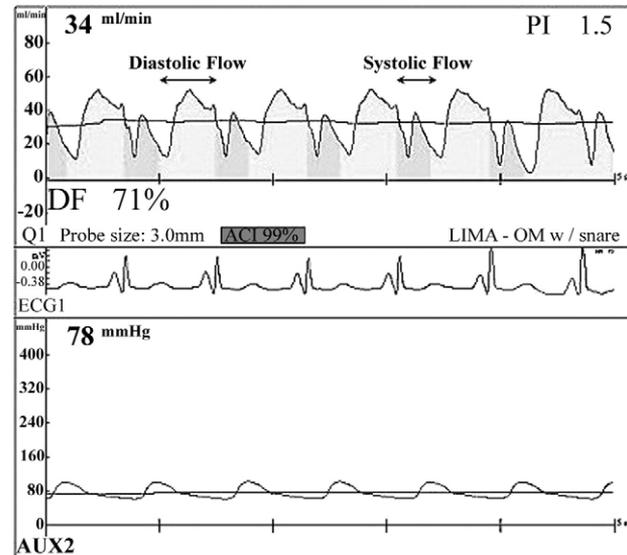


Fig 2. Transit-time flowmetry (TTFM) display (Medistim AS, Oslo, Norway) showing the flow waveform in a left internal mammary artery (LIMA) graft to obtuse marginal (OM) branch of circumflex artery with a mean graft flow of 34 mL/min, pulsatility index (PI) of 1.5, and diastolic flow (DF) of 71%. The acoustic coupling index (ACI), which indicates the degree of contact, is 99%. Simultaneous electrocardiogram (ECG) and mean arterial pressure (78 mm Hg) are displayed on the auxiliary option (AUX 2).

confirm antegrade flow in a proximal segment of the same graft.

Finally, as for TTFM, IFI may not allow complete visualization of the whole length of a graft to the circumflex or posterior descending coronary artery, although this is not necessary to simply confirm graft patency.

## Transit-Time Flowmetry

### Principle

Transit-time flowmetry is based on the principle of transit-time ultrasound technology. It uses a flow probe, which holds the graft perpendicular to two ultrasonic transducers and a fixed acoustic reflector housed within the probe. The ultrasound pulse signals transmitted from the transducers propagate both upstream and downstream of the direction of blood flow through the reflector. The integrated transit time that measures the difference between the duration taken for signal travel between the two transducers is used to provide a precise measure of flow volume.

### Technique

An ultrasound couplant (gel) is applied to the lumen of the flow probe to ensure that the graft occupies at least 75% of the probe. As illustrated in Figure 2, an integrated chart recorder provides a simultaneous flow waveform and various calculated derivatives including:

- Mean graft flow (MGF) expressed as mL/min: this value is dependent on several factors such as the

Table 4. Review of Studies With More Than 100 Patients Using Transit-Time Flowmetry

Center	Year	Reference	No. of Patients	No. of Grafts	Revised Grafts		
					No. of Grafts	% of Grafts	% of Patients
Denmark	1999	Jakobsen and Kjaergard (33)	280	N/A	5	N/A	1.8
New York	2000	D'Ancona and colleagues (1)	409	1,145	37	3.2	7.6
Japan	2001	Hirotnani and colleagues (34)	171	481		N/A	N/A
Germany	2003	Schmitz and colleagues (35)	896	2,247	N/A	N/A	N/A
Denmark	2004	Kjaergard and colleagues (36)	217	N/A	N/A	N/A	N/A
Germany	2005	Hassanein and colleagues (37)	445	845	N/A	N/A	N/A
Oxford, UK	2005	Balacumaraswami and colleagues (38)	100	266	8	3	8
Summary of studies with graft revision details			509	1,411	45	3.2	8.8

N/A = not available.

quality of the graft and coronary vessel, mean arterial pressure, and distal vascular bed.

- Diastolic flow index: the percentage of total flow occurring in diastole and should exceed 50% of the MGF. The proportion of measured diastolic flow is variable within an individual graft and increases as the flow probe is placed further distally on the graft (mirroring the pattern of native coronary flow). Although there is a predominantly diastolic flow pattern in all grafts, this is more marked in the left coronary system because of a comparatively greater systolic flow component in grafts to the right coronary system due to a lower right ventricular transmural pressure gradient.
- Pulsatility index: an estimate of the resistance to graft flow expressed as an absolute number derived by the difference between maximum and minimum flow divided by the mean flow. The pulsatility index is influenced by any factor that increases the resistance to distal flow, including graft stenosis or occlusion, distal native coronary artery stenosis, and poor "run-off" in the distal microvasculature. Generally a pulsatility index value of more than 5 is considered to indicate unsatisfactory graft flow.

The flow waveform and all the derived values should be considered in the interpretation of graft patency [32].

#### Current Experience and Results

Several groups have reported the clinical value of TTFM to assess graft patency as summarized in Table 4 [1, 33-38]. Overall 3.2% of 1,411 grafts in 8.8% of 509 patients were revised based on TTFM findings (Table 4).

D'Ancona and co-authors reported the need to revise 37 out of 1145 grafts (3%) in 33 out of 409 (8%) off-pump CABG patients. They stressed the particular importance of TTFM flow pattern interpretation as reliance on derived values alone is variable and may lead to wrong conclusions [1]. Jakobsen and Kjaergard [33] reported a 1.8% graft revision rate in a series of 280 CABG patients

and emphasized that in only one of the five cases was the graft impairment reflected in abnormal ECG findings.

Transit-time flowmetry has been used in the assessment of graft patency with a greater degree of accuracy compared with other flow measurement modalities. Canver and colleagues [39] used both TTFM and electromagnetic flowmetry techniques in 226 grafts in 66 patients and concluded that TTFM was more precise as flow values obtained with electromagnetic flowmetry were higher and more variable depending on the probe size and placement [39].

However, TTFM alone does not reliably predict either graft or anastomotic stenosis as reported by several groups. Hirotnani and colleagues [34] compared intraoperative TTFM measurements in 291 internal thoracic artery grafts and 190 saphenous vein grafts in 171 patients with postoperative coronary angiography performed prior to hospital discharge. Although they found strong correlations between the MGF, the diameter of the grafted coronary arteries, and their respective perfusion territory, they also reported that MGF did not predict stenosed or partially occluded grafts. Hol and colleagues [40] compared the use of TTFM and angiography in 124 grafts in 72 CABG patients and reported that TTFM did not detect significant angiographic abnormalities in arterial and venous grafts including an occluded internal mammary artery graft and concluded that TTFM alone may underestimate graft failure. In contrast, in our own experience with TTFM in 266 grafts in 100 patients, we found it to be useful in confirming graft patency in most patients with good MGF values, but as discussed below, in comparison with IFI we found that it unnecessarily indicated the need for graft revision in a small proportion of patients [38].

#### Limitations

Transit-time flowmetry reliably confirms graft patency in the majority of grafts with good flow. However, in low flow conditions, interpretation of derived values is arbitrary and there may be considerable uncertainty regarding graft patency. As for IFI, the MGF is dependent on

several factors such as the systemic arterial pressure, hematocrit, conduit diameter, resistance of the distal coronary vascular bed, and especially, competitive native coronary flow (related to the severity of the proximal coronary stenosis), and the reason for poor flow in a graft may not be immediately obvious.

### Prospective Comparison of IFI and TTFM

In an attempt to assess the accuracy of IFI to detect graft failure, we performed a prospective observational study comparing the simultaneous use of IFI and TTFM to assess graft patency [38]. Both techniques confirmed good flow in 241 grafts (91%) in 75 patients (75%). Transient poor flow that subsequently improved with time, hence not requiring revision was seen in 7 grafts (2.6%) in 7 patients (7%). Persistently poor flow was seen in 8 grafts (3.6%) in 8 patients requiring graft revision. Thus in the majority of patients both IFI and TTFM are useful to confirm graft patency. However in 3.8% of grafts (10% of patients), TTFM indicated persistently poor flow when IFI demonstrated satisfactory flow. In these cases the use of TTFM alone would probably have prompted unnecessary graft revision demonstrating the value of real-time images using IFI.

One randomized trial compared intraoperative IFI and TTFM followed by postoperative angiography in 46 patients receiving 139 grafts and reported 83% sensitivity and 100% specificity for IFI and 25% sensitivity and 95% specificity for TTFM to detect graft failure (defined as 50% stenosis or occlusion). The difference in sensitivity between IFI and TTFM in detecting graft failure was significant ( $p = 0.023$ ), with a confidence interval of 30% to 86%, and the authors concluded that IFI provided better diagnostic accuracy for detection of graft failure [41].

### Comment

Intraoperative graft occlusion is a consistent finding affecting up to 5% of grafts and almost certainly contributes to adverse outcomes in the short and long term. Detection of internal thoracic artery occlusion is of particular relevance because of its adverse prognostic implications, and it reinforces the need for intraoperative assessment of graft patency to permit immediate revision when necessary.

Among the available techniques for assessing graft patency, the currently most commonly used systems are IFI and TTFM. Both systems will reliably detect occluded grafts but cannot consistently detect more minor, nonocclusive abnormalities. The advantages of the IFI system are that it is a safe, simple, and repeatable technique, but its limitations are that it only provides a semi-quantitative estimate of graft flow and does not show precise anastomotic quality. In contrast, TTFM provides more objective measurements of graft flow but is more likely to both underestimate and overestimate the need for graft revision, and in comparison with postoperative angiography TTFM has been reported to be less sensitive than IFI for the intraoperative detection of graft failure.

Lognathen Balacumaraswami was supported in part by the Oxford University Medical Research Fund. Novadaq Technologies, Inc, Toronto, Canada, and Medistim AS, Oslo, Norway, provided financial support for equipment and disposables.

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