

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedures overview of intraoperative fluorescence angiography for the evaluation of coronary artery bypass graft patency

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared by NICE in October 2003 (updated August 2004).

Procedure name

Intraoperative fluorescence angiography.
Fluorescent cardiac imaging.

Specialty society

- British Society of Interventional Cardiology.
- British Society of Cardiothoracic Surgeons

Description

Indications

Coronary artery bypass grafting is one of the most common cardiac surgical interventions. It is a procedure carried out to reroute, or “bypass,” blood around clogged arteries in order to improve the flow of blood and oxygen to the heart. Vessels from another part of the body are grafted in front of and beyond the blocked arteries so that the blood flows through the new graft around the blockage.

Other forms of coronary artery bypass grafting (CABG) include off-pump coronary artery bypass grafting (OPCABG) and minimally invasive direct coronary artery bypass grafting (MICABG). However there are concerns, particularly with OPCABG, about poor graft quality or incomplete revascularization¹.

Early graft failure due to poor graft function may be a significant cause of morbidity and mortality in patients who have undergone coronary artery bypass grafting. Complications of cardiopulmonary bypass include arrhythmia, refractory angina and myocardial infarction.

Current treatments and alternatives

Several techniques are used to intraoperatively assess graft patency. These include electromagnetic flow measurement, Doppler US studies, and conventional and thermal coronary angiography techniques.

A limitation with many of these techniques is that they provide poor-resolution and definition of the grafts, and indirect measurement of bypass graft flow.

What the procedure involves

Intraoperative fluorescence angiography allows confirmation of the location of the coronary arteries and assessment of bypass graft functionality during coronary artery bypass procedures.

The intraoperative fluorescence imaging system consists of a laser diode emitting monochromatic light at 806 nm and a video camera head.

The camera head guided by a range-detector diode is positioned safe distance above the heart. A small amount of indocyanine green (ICG) dye is then administered as a central venous injection. This dye fluoresces when illuminated using laser energy and the images are recorded digitally.

Currently the technique is only semiquantitative, in that it permits assessment of graft flow as 'excellent', 'satisfactory' or 'poor' – it cannot provide an exact measure of graft flow (2). The laser beam penetrating depth is also only around 1 mm, limiting the use of this technique in certain grafts.

Indocyanine green (ICG) dye has been used for fluorescence imaging since the 1980s in indications such as ophthalmology. This procedure is an extension of its application to the assessment of coronary bypass grafts.

Efficacy

The evidence on efficacy is based upon four case series studies, with three studies reporting on clinically relevant results. In one study, intraoperative graft patency was assessed in 200 patients: graft patency was confirmed in 192 patients (96%) and the additional information provided by the procedure resulted in graft revision of these eight patients. Similar results were reported in two other studies with 1.4 % (4/290) – 3.7% (4/107) of grafts revised following the procedure. No other outcomes were reported.

Safety

Complications associated this procedure appear to be uncommon. There were no reports of adverse events associated with the use of the indocyanine green dye in evaluating the patency of coronary bypass grafts. Six additional papers were identified that described complications following the administration of indocyanine green dye for indications other than coronary graft patency. Most of these were reports of patients developing anaphylactoid reactions, with an incidence ranging from 0.02–0.3%.

One Specialist Advisor stated that anaphylactic/allergic reactions may occur very rarely as a result of this procedure and one Specialist Advisor stated that graft damage was a potential adverse effect.

Literature reviews

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to intraoperative fluorescence angiography for the evaluation of bypass graft patency. Searches were conducted using the following databases: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and Science Citation Index, and covered the period from their commencement to September 2003. Trial registries and the Internet were also searched. No language restriction was applied to the searches.

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies included. Emphasis was placed on identifying good-quality comparative studies. Abstracts were excluded where no clinical outcomes were reported, or the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients who have undergone coronary artery bypass grafting
Intervention/test	Intraoperative fluorescence angiography
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on four full text studies ^{2,3,15,16,17}.

Three abstracts detailing this technique have also been included in the summary tables.

Excluded studies

As noted above, animal studies were excluded from the overview ^{4,5}.

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Table 2 Summary of the key safety and efficacy findings

Abbreviations used: OPCABG - off pump coronary artery bypass grafting; CABG - coronary artery bypass grafting

Study details	Key efficacy findings	Key safety findings	Comments
Balacumaraswami et al (2004) ¹⁷ Taggart et al (2003) ² November 2001 – June 2003 200 patients, 533 distal coronary anastomoses Mean age: 63 years. 155 patients underwent off pump coronary artery bypass grafting (OPCABG), the remaining cases (45 patients) underwent on-pump coronary artery bypass grafting (CABG).	Visual yield Eight (1.5%) grafts in 8 (4%) patients demonstrated no fluorescence within the conduits. – all eight were revised There was no difference in number of grafts revised between the OPCABG and CABG groups. Therapeutic impact: Authors note that eight patients had change in management as a result of the procedure (graft revision). No other outcomes reported.	Authors note that there were no mortalities and no adverse consequences associated the use of the ICG dye.	No comparison made with standard imaging technique (conventional angiography) – authors note that this is invasive. Primary outcomes: rate of graft revision influence by the additional information. All procedures performed by a single surgeon.
Rubens et al (2002) ³ January–June 2001. 2 sites were involved. 20 patients undergoing non-emergent surgery 18 patients underwent standard CABG and 2 underwent minimally invasive direct coronary artery bypass (MIDCAB)	Visual yield 110 images were acquired. 50 were considered good quality images. No other outcomes reported.	• 1 patient experienced atrial fibrillation • 1 patient was re-explored for chest wall bleeding • 1 patient had an episode of postoperative delirium • 1 patient developed temporary renal insufficiency However authors report that there were no ICG- or imaging device related complications.	Termed a feasibility study. Limited information.
Reuthebuch, O (2003) ⁶ April 2002 – August 2002. 37 consecutive patients with 107 grafts (45 arteries/62 veins)	Therapeutic impact: 4/107 grafts had to be revised (3 anastomotic constrictions, 1 graft dissection). No other outcomes reported.	No side-effects were observed.	Abstract only. Limited information.

Abbreviations used: OPCABG - off pump coronary artery bypass grafting; CABG - coronary artery bypass grafting

Study details	Key efficacy findings	Key safety findings	Comments
Desai, ND et al (2003) ⁷ 48 patients No other information given.	Authors reported that one patient (2.1%) was found to have a twisted vein graft that was revised successfully.	No side-effects were observed	Abstract only. Some information to suggest that there is a learning curve involved. Limited information.
Takahashi, M (2003) ⁸ Unclear	Visual yield 'Vivid and fantastic images' could be obtained in all 136 grafts and 34 OPCAB cases. No other outcomes reported.	Authors note that side-effect rate of ICG (0.17%) is lower than iodine contrast media (1.6-4.0%).	Abstract only. Limited information.
Reuthebuch et al (2004) ¹⁵ Switzerland March – September 2002 38 consecutive patients undergoing coronary artery bypass grafting (124 grafts/107 grafts) - 36 patients were grafted via median sternotomy - 2 patients were operated by MIDCAB Mean age was 64.6 years	Visual yield 97/107 grafts were acquired using 1.25mg of ICG 10 grafts needed 2.5 mg of ICG. Therapeutic impact: 4/107 grafts had to be revised (3.7%) (3 anastomotic constrictions, 1 graft dissection).	No acute or long-term side effects of ICG were observed.	This study was identified during consultation in June 2004. Full text paper of earlier abstract ⁶ Seventeen grafts were not able to visualised (unevaluable)
Takahashi et al (2004) ¹⁶ 72 consecutive patients (290 distal anastomoses) - 64 patients OPCAB - 8 patients MIDCAB 21 patients underwent emergency operation for acute coronary syndrome. Mean age: 68.5 years	Vivid yield Excellent images could be obtained for all 290 distal anastomoses Therapeutic impact: 4/290 grafts had to be revised (1.4%)	Authors note that no adverse drug reactions were observed and no major complications occurred post-operatively.	This study was identified during consultation in June 2004.

Additional safety information

Safety of Indocyanine green

Six additional papers were identified that described complications following the administration of ICG for indications other than coronary graft patency⁹⁻¹⁴. Most of these papers were reports of patients developing anaphylactoid reactions following administration of ICG^{14,10,9}. The cited incidence of anaphylactoid reactions varied from 0.02–0.3%¹¹.

In one study, a review of 3774 ophthalmology cases of ICG injection there were 13 cases of adverse reactions (0.34%), ten of which were mild reactions including nausea, exanthema and itchiness. There was also one case of pain along the injected vein, which required treatment, and two cases of hypotension¹¹.

Safety of the laser diode

Only one of the publications³ reported on the safety of the laser diode used in the procedure. The authors of this paper state that the light of the wavelength (806 nm) used in the present study is not transmitted through the tissues and presents no known hazard to the patient.

Validity and generalisability of the studies

- There is currently limited information available on the use of this procedure to evaluate the patency of bypass grafts.
- As such, limited information is available on outcomes.
- Some of the studies simply reported on image quality and whether grafts could be visualised, rather than on revision rate/therapeutic impact. None of the studies compared this procedure with other forms of imaging or conventional angiography.

Specialist Advisor's opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

- A minor variation on an existing procedure that is unlikely to alter the procedure's safety and efficacy.
- The procedure is primarily of interest to those surgeons who undertaken coronary artery bypass grafting using the off pump technique and who wish to verify the patency of the graft.

Issues for consideration by IPAC

ICG has been used for fluorescence imaging since the 1980s in indications such as ophthalmology. This procedure is an extension of its application in coronary bypass graft patency assessment.

According to the manufacturer's website, the company is in the process of obtaining regulatory approval for the imaging system from the FDA and has completed a preliminary plan for Phase II and III clinical trials. (website access 1/10/2003).

A co-author of one of the studies ² has also had some additional data accepted for publication. It is anticipated that this data will become available mid 2004.

References

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- 2 Taggart DP, Choudhary B, Anastasiadis K, Abu-Omar Y, Balacumaraswami L, Pigott DW. Preliminary experience with a novel intraoperative fluorescence imaging technique to evaluate the patency of bypass grafts in total arterial revascularization. *Ann Thorac Surg* 2003; 75(3):870-873.
- 3 Rubens FD, Ruel M, Fremes SE. A new and simplified method for coronary and graft imaging during CABG. *Heart Surg Forum* 2002; 5(2):141-144.
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- 5 Russ D, Detter C, Iffland A, Wipper S, Schurr MO, Sailer R et al. Imaging of perfusion with indocyanine green fluorescence - A promising approach. *Medical Laser Application* 2002; 17(1):31-36.
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- 7 Desair ND, Pelletier MP, Cohen G, Mallidi HR, Christakis GT, Goldman BS et al. Indocyanine green - laser coronary angiography: a novel method of intraoperative patency assessment. *Canadian Cardiac Conference* October 2003. 2003.
Ref Type: Abstract
- 8 Takahashi M. The first asian experiences using innovative spy intra-operative imaging system. *Heart Surg Forum* 2003; 6 Supp 1:S30-S31.
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- 13 Aume M, Kotake H, Kosaka T, Hoshio A, Yamasaki J, Hasegawa J et al. Two cases of coronary artery spasm induced by indocyanine green. *Japanese Heart Journal* 1988; 29(6):877-881.
- 14 Garski TR, Staller BJ, Hepner G, Banka VS, Finney RA, Jr. Adverse reactions after administration of indocyanine green. *JAMA* 1978; 240(7):635.

- 15 Reuthebuch O, Haussler A, Genoni M, Tavakoli R, Odavic D, Kadner A et al. Novadaq SPY: Intraoperative Quality Assessment in Off-Pump Coronary Artery Bypass Grafting. *Chest* Vol 125(2)(pp 418-424), 2004 2004;(2):418-424.
- 16 Takahashi M, Ishikawa T, Higashidani K, Katoh H. SPY: an innovative intra-operative imagine system to evaluate graft patency during off-pump coronary artery bypass grafting. *Interactive Cardiovascular and Thoracic Surgery* 2004; (in press).
- 17 Balacumaraswami L, Abu-Omar Y, Anastasiadis K, Choudhary B, Pigott DW, Yeong, S-K. Taggart DP. Does off-pump totoal arterial grafting increase the incidence of intraoperative graft failure? *Cardiopulmonary Support and Physiology* 2004; 128:238-44.

Appendix A: Literature search for intraoperative fluorescence angiography

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in EMBASE, Current Contents, PredMedline and all EMB databases.

For all other databases a simple search strategy using the key words in the title was employed.

#	Search History
1	coronary artery bypass.mp. or exp Coronary Artery Bypass/
2	indocyanine green.mp. or exp Indocyanine Green/
3	ICG.tw.
4	2 or 3
5	1 and 4
6	intraoperative fluorescence.mp.
7	(graft adj4 imaging).mp. [mp=title, abstract, cas registry/ec number word, mesh subject heading]
8	coronary angiography.mp. or exp Coronary Angiography/
9	(fluorescence adj4 coronary).mp. [mp=title, abstract, cas registry/ec number word, mesh subject heading]
10	or/7-9
11	10 and 4
12	exp SPECTROMETRY, FLUORESCENCE/ or FLUORESCENCE/
13	12 and 1
14	12 and 10
15	5 or 6 or 11 or 13 or 14