

# Image-Guided Quantification of Cardioplegia Delivery during Cardiac Surgery

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## ABSTRACT

**Background.** Homogenous distribution of cardioplegia delivered to the myocardium has been identified as an important predictor of post-cardiopulmonary bypass ventricular recovery and function. Presently, a method to determine adequate distribution of cardioplegia in patients during cardiac surgery does not exist. The goal of this study was to evaluate the feasibility of quantifying cardioplegia delivery using a novel, noninvasive optical method. Such a system would permit instantaneous imaging of jeopardized myocardium and allow immediate, intraoperative corrective measures.

**Methods.** We have previously developed a portable, intraoperative near-infrared (NIR) fluorescence imaging system for use in large animal cardiac surgery that simultaneously displays color video and NIR fluorescent images of the surgical field. By introducing exogenous, NIR fluorophores, specific cardiac functions can be visualized in real-time.

**Results.** In a porcine cardiopulmonary bypass model, we demonstrate that the FDA-approved intravascular fluorophore indocyanine green (ICG) permits real-time assessment of cardioplegia delivery. ICG was injected into an aortic root and/or transatrial coronary sinus catheter during delivery of crystalloid cardioplegia solution. Segmental distribution was immediately noted at the time of injection. In a subset of animals, simulated coronary occlusions resulted in imaging defects consistent with poor cardioplegia delivery and jeopardized myocardium. Videodensitometric analysis was performed on-line to quantify distribution to the right ventricle and left ventricle.

**Conclusions.** We report the development of a novel, noninvasive, intraoperative technique that can easily and safely provide a visual assessment of cardioplegia delivery (antegrade and/or retrograde) and that offers the potential to quantify the relative segmental distribution during cardiac surgical procedures.

Received April 27, 2007; accepted June 11, 2007.

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## INTRODUCTION

Conventional cardiac surgery utilizes cardiopulmonary bypass for circulatory support while the aorta is occluded and the heart is arrested in order to create a bloodless, motionless operative field. Aortic occlusion, however, results in a period of warm ischemia and subjects the heart to a time-dependent hazard for myocardial injury. Typically, the heart is protected during this phase by injecting cardioplegia solution [Takaba 2000].

The adequacy of myocardial protection during this period of ischemia is dependent upon uniform distribution of cardioplegia to the myocardium [Zaroff 1994]. Antegrade administration of cardioplegia via the aortic root is the most common delivery method. However, significant coronary stenoses and poor collateral supply may limit its distribution to compromised areas of myocardium. Retrograde delivery of cardioplegia through the coronary sinus has a theoretical advantage in patients with high-grade coronary lesions since it might supply regions inaccessible by the antegrade route [Menasche 1991]. Retrograde cardioplegia, though, suffers from poor preservation of the right ventricle (RV) [Winkelmann 1995], regional heterogeneity, and a significant delay before diastolic arrest [Partington 1989]. Often, a combination of antegrade and retrograde delivery techniques is used to optimize myocardial protection. The adequacy of cardioplegia distribution, though, is difficult to ascertain and quantify. At present, surgeons rely on the generation of an asystolic and motionless heart together with the delivery of an optimal volume [Takahashi 1988] of cardioplegia solution as a guide to the adequacy of cardioplegia distribution. These measures, however, are all surrogates for real-time visualization of cardioplegia delivery. Contrast echocardiography utilizing sonicated renografin-76 microbubbles can provide an indirect assessment of injected cardioplegia, yet this method is operator-dependent and lacks resolution [Aronson 1991]. The optimal method for assessing the adequacy of cardioplegia distribution would direct intraoperative visualization of cardioplegia flow and would allow the cardiac surgeon to identify territories of poor delivery prior to ischemic damage, to direct the sequence of grafting based on territories at risk, and to determine the need for retrograde cardioplegia supplementation. Additionally, the direct visualization of

retrograde cardioplegia flow would permit early identification of a malpositioned coronary sinus catheter and allow immediate correction.

Our goal was to provide the cardiac surgeon with highly sensitive, real-time intraoperative imaging of cardioplegia distribution and regional cardiac ischemia using noninvasive methods. We recently developed a near-infrared (NIR) fluorescence optical imaging system that permits real-time, intraoperative imaging using the FDA-approved NIR fluorescent agent indocyanine green (ICG) [Nakayama 2002; De Grand 2003]. NIR light, otherwise invisible to the human eye, provides extremely high signal to background ratios without changing the look of the surgical field. In this present study, we investigated the feasibility of using ICG for intraoperative visualization and quantification of cardioplegia distribution in a large animal model of cardiac surgery.

## MATERIALS AND METHODS

### NIR Imaging System

The large animal intraoperative NIR fluorescence imaging system used in this study has been described in detail previously [De Grand 2003]. Briefly, it is composed of two wavelength-isolated excitation sources, one generating 1 mW/cm<sup>2</sup> of 400 to 700 nm "white" light, and the other simultaneously generating 5 mW/cm<sup>2</sup> of 725 to 775 nm light over a 15-cm diameter field of view. Photon collection is achieved with custom-designed optics that maintain separation of the white light and NIR fluorescence (>795 nm) channels. The system has variable zoom capability, achieving a spatial resolution of 625  $\mu$ m at a field-of-view of 20  $\times$  15 cm, and 125  $\mu$ m at a field-of-view of 4  $\times$  3 cm. After acquisition, anatomic (white light) and functional (NIR fluorescent light) images can be displayed separately and merged. Images acquired with the 12-bit Orca-AG (Hamamatsu, Bridgewater, NJ, USA) NIR camera were within its linear range. All screen images are refreshed 15 times per second. The entire apparatus consists of a portable console with an articulating arm that suspends the camera over the operative field, at a distance of 18". Data were acquired and quantified on a Dell computer using LabVIEW 6.0 (National Instruments, Austin, TX, USA).

### NIR Fluorophores and Cardioplegia

ICG was purchased from Akorn (IC-Green; Decatur, IL, USA). A 2.5 mg/mL stock solution in saline was prepared fresh for each surgical procedure and stored at room temperature. ICG is FDA-approved for indicator dilution studies in humans and remains intravascular after injection, with a half-life of 30 to 60 seconds. It is also, however, a NIR fluorophore, with peak excitation at 779 nm and a peak emission at 806 nm in aqueous buffer. Since its approval in 1958, ICG has had a remarkable safety record with minimal adverse reactions [Hope-Ross 1994].

Standard cold (4°C), hyperkalemic crystalloid cardioplegia was used in this study and consisted of 154 mmol sodium, 154 mmol of chloride, 4 mEq of MgSO<sub>4</sub>, and 40 mEq of KCl per liter. 100  $\mu$ g of ICG was added to 150 mL of

cardioplegia solution resulting in an 860 nM final injection concentration.

### Surgical Preparation

Adult Yorkshire pigs (n = 10; mean weight, 35 kg) of either sex were used in this study. Animals were purchased from EM Parsons and Sons (Hadley, MA, USA). All animals received humane care in compliance with approved institutional protocols. General anesthesia was induced with 4.4 mg/kg of intramuscular Telazol (Fort Dodge Labs, Fort Dodge, IA, USA) and 2.2 mg/kg xylazine. Once sedated, the animals received oxygen and 5% isoflurane to effect. Animals were intubated and anesthesia was maintained with 2% isoflurane. Continuous oxygen saturation and 3-lead electrocardiographic tracing were monitored. After median sternotomy and systemic heparinization (3 mg/kg), a 14 F arterial cannula was placed in the left femoral artery and a two-stage, single-venous cannula was placed through the right atrial appendage into the right atrium. These were connected in the standard fashion, and cardiopulmonary bypass was initiated at 36°C.

A retrograde cardioplegia catheter (auto-inflating balloon catheter, 15 F, Medtronic, Minneapolis, MN, USA) for retrograde cardioplegia administration was advanced transatrially into the proximal coronary sinus and sutured in place. The left anterior descending coronary artery (LAD) was identified and isolated just proximal to its first diagonal branch. The ascending aorta was occluded, and a 14-gauge cannula was inserted into the proximal aorta for antegrade cardioplegia administration.

Images of the surgical field were obtained prior to the administration of cardioplegia in order to document background autofluorescence. Cardioplegia containing ICG was then administered via the aortic root and/or coronary sinus catheters according to protocols detailed below. Cardioplegia was injected at a rate of 100 mL/min. Continuous real-time NIR fluorescence imaging was obtained during cardioplegia injection and for 5 minutes thereafter. In 4 animals, hearts were explanted, sectioned along their short axes, and then re-imaged. In the remaining animals, hearts were allowed to wean from cardiopulmonary bypass. All images were archived for videodensitometric analysis.

Cardioplegia was infused according to the following protocols:

- (1) Antegrade cardioplegia delivery (n = 4);
- (2) Retrograde cardioplegia delivery (n = 2);
- (3) Antegrade cardioplegia delivery with temporary ligation of the proximal LAD followed by reinjection of cardioplegia after ligation removal (n = 2);
- (4) Antegrade cardioplegia delivery with temporary ligation of the proximal LAD (n = 2).

### Videodensitometric Analysis

Distribution of cardioplegia delivery was analyzed by review of the recorded NIR fluorescent imaging sequences. NIR fluorescent density was determined in 4 reproducible regions of the heart: mid-anterior right ventricular free wall, mid-anterior left ventricular free wall, lateral left ventricular free wall, and posterior left ventricular free wall. Background-subtracted pixel

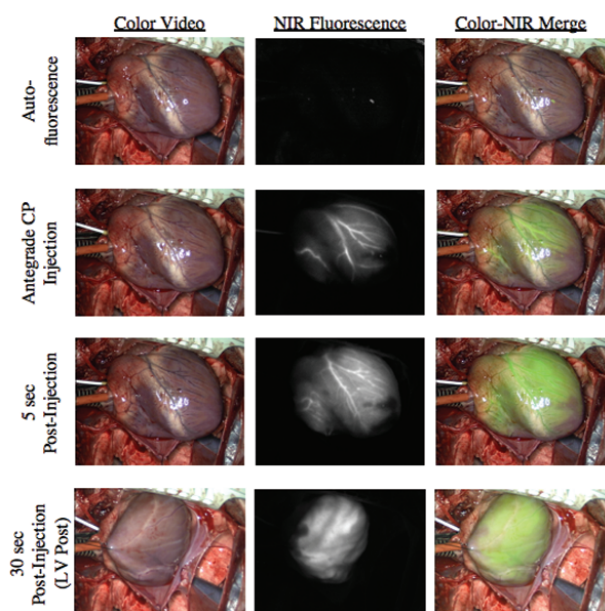


Figure 1. Kinetics of antegrade cardioplegia delivery to the porcine heart during cardiopulmonary bypass. The autofluorescence of the heart is minimal (top row). Antegrade cardioplegia delivery can be visualized in real-time, with 1 second (second row), 5 seconds (third row), and 30 seconds (posterior) images displayed. Shown are color video images (left), NIR fluorescence images (middle), and a merge of the two with near-infrared fluorescence pseudo-colored in lime green (right). All near-infrared fluorescence images have identical exposure times (67 milliseconds) and normalizations.

intensity was normalized for each imaging sequence by dividing each background-subtracted pixel intensity by the maximum pixel intensity for that imaging sequence. Similar videodensitometric measurements were made of the short-axis cross sections at the epicardial, myocardial, and endocardial levels. A Student *t* test was used to compare regional NIR fluorescent cardioplegia density between control and ligation animals.

## RESULTS

### Real-Time NIR Fluorescence Imaging System

The NIR imaging system was able to unobtrusively provide real-time images to the surgeon during the entire procedure. Despite cardiac motion, real-time images of cardioplegia flow were easily obtained at high resolution. While operating, the surgeon can view color video, NIR fluorescent, and pseudo-colored merged images of the operative field in real-time. This latter image permits visualization of cardioplegia flow against a background of normal regional cardiac and coronary anatomy. By using a nonanatomic color such as lime green (ie, a pseudo-color) for this overlay, cardioplegia flow and any regions of inadequate myocardial protection can be clearly delineated. The imaging system's variable field of

view allows zooming capability, and the invisible nature of the light does not disturb the operative field. Finally, the entire imaging system is portable and easily maneuverable.

### Quantification of Antegrade Cardioplegia

Tissue autofluorescence of the heart was negligible (Figure 1). Upon injection of 150 mL of cardioplegia solution in an antegrade fashion via the aortic root, immediate fluorescence of the coronary vessels was visible in real-time (Figure 1). Myocardial distribution of cardioplegia was evident within 5 seconds after injection, and by 8 seconds homogenous fluorescence of all surfaces of the heart was easily appreciated. Visual assessment alone confirmed homogenous cardioplegia distribution to the right and left ventricles (LV).

Background-subtracted videodensitometric analysis demonstrates relatively homogenous distribution of cardioplegia throughout regions of the LV (Figure 2A). Compared

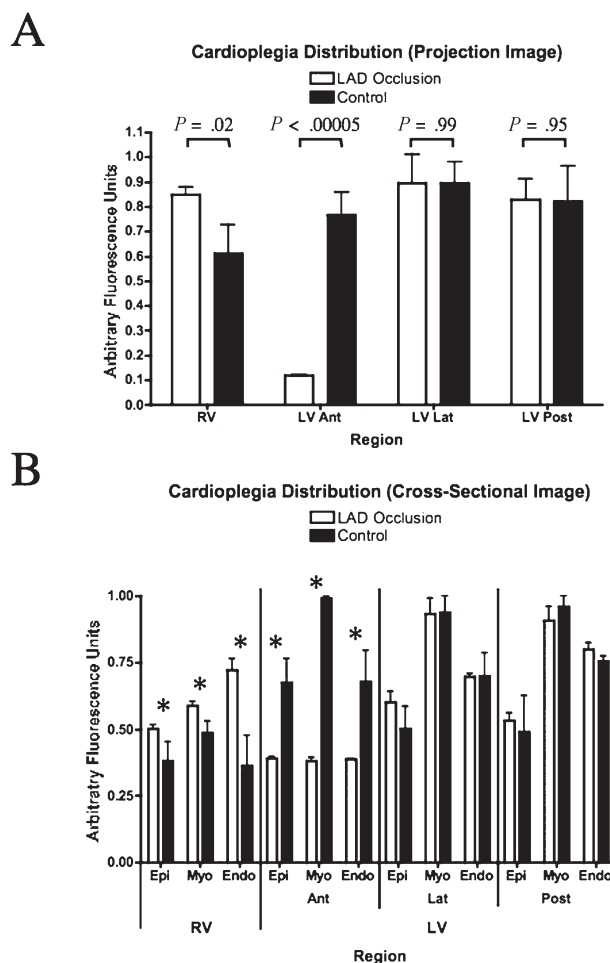


Figure 2. Quantification of cardioplegia delivery by surface and cross-sectional imaging. Near-infrared fluorescence signals were quantified from reflected surface images (A) and cross-sectional imaging (B) of the same heart. RV indicates right ventricle; LV Ant, anterior left ventricle; LV Lat, lateral left ventricle; LV Post, posterior left ventricle; Epi, epicardial; Myo, myocardial; Endo, endocardial. \* $P < .05$ .

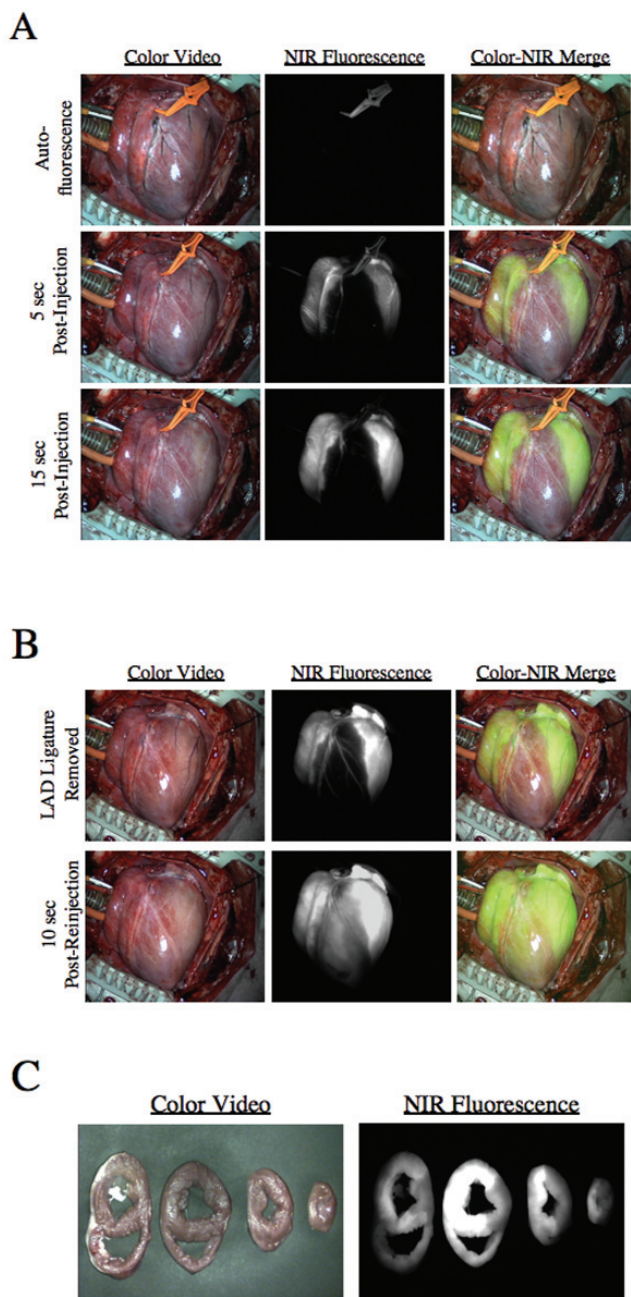


Figure 3. Inadequate cardioplegia delivery to the porcine heart during cardiopulmonary bypass and corrective action. A, Antegrade cardioplegia delivery after clamping of the left anterior descending artery instantly reveals a large wedge-shaped defect. B, Correction of the defect in (A) can also be visualized in real-time. Shown are color video images (left), near-infrared (NIR) fluorescence images (middle), and a merge of the two with NIR fluorescence pseudocolored in lime green (right). C, Cross-sectional analysis from base (left) to apex (right) of the heart from (B). All NIR fluorescence images have identical exposure times (67 milliseconds) and normalizations.

to the RV, only the lateral region of the LV demonstrates proportionately more fluorescence, suggesting more cardioplegia distribution to this portion of the heart. Quantitative analysis of ventricular cross sections shows that distribution of cardioplegia to the myocardium predominated distribution to the epicardium and endocardium (Figure 2B).

#### Quantification of Retrograde Cardioplegia

As in the previous animals, tissue autofluorescence of the heart was negligible. Following aortic cross-clamping, 300 mL of cardioplegia was infused via the transatrial coronary sinus catheter. Preliminary experiments demonstrated that a larger volume of cardioplegia was necessary to adequately visualize retrograde distribution. Fluorescence of the coronary veins followed by coronary arteries was immediately visible. By 15 seconds after injection, myocardial uptake was visible. Unlike the homogenous fluorescence seen with antegrade cardioplegia delivery, retrograde delivery resulted in a patchy heterogeneous fluorescence pattern indicating less efficient cardioplegia delivery (data not shown).

#### Acute Coronary Occlusion Imaging

Injection of 150 mL of cardioplegia solution in an antegrade fashion via the aortic root following temporary proximal ligation of the LAD resulted in an immediate flow defect throughout the LAD territory (Figure 3A). On-line background-subtracted videodensitometric analysis confirmed significantly less fluorescence in the LAD territory as compared with other regions of the heart (Figure 2A). Additionally, fluorescence in the LAD territory was significantly less in occluded animals than in control animals. During LAD occlusion, the RV received relatively more cardioplegia flow as evidenced by increased fluorescence in this region (Figure 2A). When the temporary ligature was removed and 150 mL of cardioplegia was reinjected, NIR fluorescence imaging confirmed patency of the previously ligated vessel (Figure 3B). Regional myocardial fluorescence in the LAD territory demonstrated adequate delivery of cardioplegia to this previously unprotected area. Immediately explanted cross sections of the hearts show homogenous reperfusion of the LAD territory (Figure 3C). Since myocardial tissue fluorescence is cumulative and complete wash-out of ICG would require either injection of cardioplegia devoid of ICG contrast or cardiac reperfusion, the LAD territory is less fluorescent than other territories since it effectively received half the ICG concentration.

In a subgroup of animals, hearts with LAD ligations were immediately explanted following cardioplegia injection in order to determine whether surface imaging defects correlated with cross-sectional defects. Cross-sectional analysis of these hearts demonstrated significantly less fluorescence in the LAD territory compared to control hearts (Figure 2B). Importantly, epicardial fluorescence in the occluded LAD territory was similar to myocardial and endocardial fluorescence. Thus, surface imaging of cardioplegia delivery correlated strongly with cross-sectional imaging.

## DISCUSSION

Despite significant advances in cardioplegia solutions and techniques, inadequate myocardial protection during cardiac surgery continues to be a potential source of intraoperative injury. Intraoperative myocardial protection has been identified as an important predictor of post-cardiopulmonary bypass ventricular recovery and function [Kumbhani 2004]. A growing number of patients with advanced coronary artery disease are experiencing increasing rates of delayed postoperative ventricular recovery partially attributable to inadequate intraoperative myocardial protection.

Presently, there is no reliable method for intraoperatively determining the distribution of cardioplegia infusion during cardiac surgery. The presence of asystole is an unreliable surrogate marker for global arrest and can exist despite large territories of poorly protected myocardium. Septal temperature measurements have also been used as markers for the adequacy of cardioplegia delivery, yet these measurements are regional and might not reflect a more distant area of poor myocardial protection [Dearani 2001]. Myocardial tissue pH probes can identify regions of myocardial acidosis, a correlate of regional myocardial ischemia [Khuri 1983]. Although the presence of regional myocardial acidosis correlates with postoperative outcomes [Kumbhani 2004], the probe technology can be obtrusive to the surgeon and only allows for measurement of two regions of the heart. Finally, contrast echocardiography utilizing sonicated microbubbles is highly operator dependent and lacks resolution.

In this study, we report a novel technique for real-time intraoperative visualization of cardioplegia distribution. Our system takes advantage of the unique properties of NIR fluorescence imaging and provides the cardiac surgeon with precise visualization of cardioplegia distribution, and as such, overcomes many of the limitations of current techniques. Even more important, the system is not operator dependent or invasive; the entire imaging system is portable and does not obstruct the operative field. The NIR fluorescent contrast agent, ICG, is inexpensive, already FDA-approved for other indications, and has an excellent safety profile. This system allows rapid assessment of the presence or absence of cardioplegia perfusion and provides for quantitative estimates of flow.

In this study, NIR fluorescence imaging of control animals rapidly confirmed homogenous distribution of cardioplegia to the RV and LV with antegrade delivery. Quantitative analysis demonstrated more fluorescence in regions of the LV compared to the RV, suggesting better cardioplegia distribution to the LV. This finding has been corroborated in many other studies examining cardioplegia distribution in normal hearts [Aldea 1994]. When a temporary ligature was placed on the LAD, NIR fluorescence imaging detected an immediate flow defect in the LAD territory, suggesting a lack of cardioplegia distribution to this region. Images of ventricular cross sections in a subgroup of these animals confirmed a transmural flow defect. As expected during proximal LAD ligation, right ventricular distribution of cardioplegia flow actually increased compared to baseline. Imaging of retrograde cardioplegia

demonstrated less uniform distribution of cardioplegia as compared to antegrade cardioplegia delivery. Malposition of the coronary sinus catheter and inadequate pressure of retrograde cardioplegia in our studies may have contributed to less than ideal visualization.

ICG is a nontoxic dye used for more than 40 years in ophthalmologic angiography, liver function testing, and cardiac output measurement. It is a partially water-soluble dye excreted unchanged by the liver into bile. As such, it poses no risk of renal toxicity. Adverse reactions are rare; Garski et al reported only 4 adverse reactions in 24,000 administered doses [Garski 1978]. Our imaging system, combined with the biodistribution and pharmacokinetics of ICG, allows for repeated injections and imaging. Within 15 seconds following ICG injection, the vascular fluorescence signal rapidly declines to near background while the myocardial signal remains for approximately 10 minutes. Since the myocardial signal during this time is far less than the vascular signal peak, computerized background subtraction allows for repeated injections during this obligate period of myocardial signal wash-out.

A major limitation of the simple reflectance imaging system used in this study is its depth penetration and surface weighting. Although it can detect fluorescent lymph nodes through up to 1 cm of solid tissue [Kim 2004] and 5 cm of lung tissue [Soltesz 2005], the epicardium and outermost myocardium will contribute almost all of the measured signal after intravascular ICG injection. Clinically, this might lead to visualization of adequate epicardial cardioplegia distribution in the presence of subendocardial or septal ischemia, regions that presently cannot be visualized with this technology. Recent advances in optical tomography suggest that depth penetration up to 4 cm may be possible in the future [Ntziachristos 2003]. A second limitation of this method is its inability to measure the functional metabolic response to cardioplegia delivery; in essence, adequate flow of cardioplegia does not always correlate with protection from myocardial ischemia. Nevertheless, without the technology we describe in this study, there is no simple way to even assess cardioplegia distribution prior to cardiac arrest. Although our system does not directly assess functional myocardial protection, protection always begins with adequate flow. As our data show, if a myocardial region does not exhibit epicardial evidence of cardioplegia delivery, there is likely poor protection in this region that must be surgically addressed.

In addition to visualizing cardioplegia distribution, our NIR imaging system is capable of providing intraoperative high-definition coronary angiography. Additionally, our imaging system can provide intraoperative graft patency confirmation similar to the SPY imaging system (Novadaq Technologies, Concord, ON, Canada) [Vogt 2003]. In a series of 100 patients, Balacumaraswami et al used intraoperative cardiac fluorescence imaging with ICG to evaluate graft patency and found 8 graft failures in 241 total grafts [Balacumaraswami 2005]. Such immediate intraoperative quality control is becoming increasingly important as coronary operations become more complex.

In summary, this study demonstrates the development of a novel, noninvasive, intraoperative technique using NIR fluorescence imaging that can easily and safely delineate and

quantify relative regional cardioplegia distribution during cardiac surgery. This system can also provide optical coronary angiography and post-bypass graft patency evaluation without the attendant hazards of ionizing radiation. Such a system should allow surgeons to more readily identify regions of poor myocardial protection and guide interventions to ameliorate intraoperative myocardial injury in the hopes of improving patient outcomes.

## ACKNOWLEDGMENTS

This work was funded by NIH grants R01-CA-115296, R01-EB-005805, and R21-CA-110185 to J.V.F. We thank Barbara L. Clough for editing and Grisel Vazquez for administrative assistance.

## REFERENCES

- Aldea GS, Hou D, Fonger JD, Shemin RJ. 1994. Inhomogeneous and complementary antegrade and retrograde delivery of cardioplegic solution in the absence of coronary artery obstruction. *J Thorac Cardiovasc Surg* 107:499-504.
- Aronson S, Lee BK, Liddicoat JR, et al. 1991. Assessment of retrograde cardioplegia distribution using contrast echocardiography. *Ann Thorac Surg* 52:810-4.
- Balacumaraswami L, Abu-Omar Y, Choudhary B, et al. 2005. A comparison of transit-time flowmetry and intraoperative fluorescence imaging for assessing coronary artery bypass graft patency. *J Thorac Cardiovasc Surg* 130:315-20.
- De Grand AM, Frangioni JV. 2003. An operational near-infrared fluorescence imaging system prototype for large animal surgery. *Technol Cancer Res Treat* 2:553-62.
- Dearani JA, Axford TC, Patel MA, et al. 2001. Role of myocardial temperature measurement in monitoring the adequacy of myocardial protection during cardiac surgery. *Ann Thorac Surg* 72:S2235-43; discussion S2243-4, S2267-2270.
- Garski TR, Staller BJ, Hepner G, et al. 1978. Adverse reactions after administration of indocyanine green. *JAMA* 240:635.
- Hope-Ross M, Yannuzzi LA, Gragoudas ES, et al. 1994. Adverse reactions due to indocyanine green. *Ophthalmology* 101:529-33.
- Khuri SF, Josa M, Marston W, et al. 1983. First report of intramyocardial pH in man. II. Assessment of adequacy of myocardial preservation. *J Thorac Cardiovasc Surg* 86:667-78.
- Kim S, Lim YT, Soltesz EG, et al. 2004. Near-infrared fluorescent type II quantum dots for sentinel lymph node mapping. *Nat Biotechnol* 22:93-7.
- Kumbhani DJ, Healey NA, Birjiniuk V, et al. 2004. Intraoperative regional myocardial acidosis predicts the need for inotropic support in cardiac surgery. *Am J Surg* 188:474-80.
- Menasche P, Subayi JB, Veyssie L, et al. 1991. Efficacy of coronary sinus cardioplegia in patients with complete coronary artery occlusions. *Ann Thorac Surg* 151:418-23.
- Nakayama A, del Monte F, Hajjar RJ, Frangioni JV. 2002. Functional near-infrared fluorescence imaging for cardiac surgery and targeted gene therapy. *Mol Imaging* 1:365-77.
- Ntziachristos V, Bremer C, Weissleder R. 2003. Fluorescence imaging with near-infrared light: new technological advances that enable in vivo molecular imaging. *Eur Radiol* 13:195-208.
- Partington MT, Acar C, Buckberg GD, Julia PL. 1989. Studies of retrograde cardioplegia. II. Advantages of antegrade/retrograde cardioplegia to optimize distribution in jeopardized myocardium. *J Thorac Cardiovasc Surg* 97:613-22.
- Soltesz EG, Kim S, Laurence RG, et al. 2005. Intraoperative sentinel lymph node mapping of the lung using near-infrared fluorescent quantum dots. *Ann Thorac Surg* 79:269-77; discussion 269-77.
- Takaba T, Inoue K. 2000. Past and present in myocardial protection. *Ann Thorac Cardiovasc Surg* 6:3-8.
- Takahashi A, Chambers DJ, Braimbridge MV, Hearse DJ. 1988. Optimal myocardial protection during crystalloid cardioplegia. Interrelationship between volume and duration of infusion. *J Thorac Cardiovasc Surg* 96:730-40.
- Vogt PR, Bauer EP, Graves K. 2003. Novadaq Spy Intraoperative Imaging System--current status. *Thorac Cardiovasc Surg* 51:49-51.
- Winkelmann J, Aronson S, Young CJ, et al. 1995. Retrograde-delivered cardioplegia is not distributed equally to the right ventricular free wall and septum. *J Cardiothorac Vasc Anesth* 9:135-9.
- Zaroff J, Aronson S, Lee BK, et al. 1994. The relationship between immediate outcome after cardiac surgery, homogeneous cardioplegia delivery, and ejection fraction. *Chest* 106:38-45.