

# Epicardial Ultrasound in Coronary Artery Bypass Surgery



Ricardo P.J. Budde

Epicardial Ultrasound in Coronary Artery Bypass Surgery  
Budde, Ricardo Peter Jurgen

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Doppler ultrasound image of cross-over anastomosis  
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**Epicardial Ultrasound in  
Coronary Artery Bypass Surgery**

**Epicardiale Echocardiografie  
in de Coronaire Bypass Chirurgie**

(met een samenvatting in het Nederlands)

Proefschrift

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Ricardo Peter Jurgen Budde  
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Promotor: Prof. dr. C. Borst

Co-promotores: Dr. P.F. Gründeman  
Dr. P.F.A. Bakker

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# INTRODUCTION



## **Coronary artery bypass grafting**

Coronary artery bypass grafting (CABG) is a routine procedure, traditionally performed via median sternotomy access on the arrested heart with use of cardiopulmonary bypass (CPB), that sets the clinical gold standard for myocardial revascularization [1-3]. Despite its routine nature, the procedure remains associated with significant morbidity [4-12], which can in part be attributed to the use of CPB with aortic cross-clamping [4,10,11] and the median sternotomy [8,12]. From the 1990's onwards, two complementary strategies have been (re)explored that aim to reduce morbidity. First, the elimination of CPB with aortic cross-clamping and its deleterious side-effects [13,14] by the use of tissue stabilizers that immobilize a section of the cardiac wall thereby allowing meticulous construction of the coronary anastomosis on the beating heart (so called off-pump CABG, OPCAB) [15-17]. Secondly, by operating through smaller incisions (limited access) without sternal splitting, reducing the associated chest wall trauma [18,19].

## **Totally endoscopic coronary artery bypass grafting**

The introduction of robotic systems with 3D vision, tremor elimination and instruments with 7 degrees of freedom (mimicking the human wrist) has enabled (off-pump) totally endoscopic CABG (TECAB) [20-26]. However, TECAB remains a technically very demanding procedure that is performed by only a selected number of surgeons worldwide. In order for TECAB to gain more acceptance and be adopted on a wider scale, first the key difficulties (target vessel presentation, exposure and identification, coronary stabilization and anastomosis suturing) need to be facilitated by enabling technology [20-26].

## **Intraoperative difficulties**

In all approaches to CABG surgery, the surgeon may encounter a number of intraoperative difficulties.

First, exposure, presentation and localization of the target coronary artery for bypass grafting. The artery is located by visual inspection of the epicardial surface. If, however, the artery is embedded in the epicardial fibrofatty tissue or runs intramyocardially, it is invisible to the eye. Time consuming and potentially harmful (i.e. accidental entering of the right ventricle) dissection of the epicardial and/or myocardial tissue is then needed to locate the artery. Retrograde vessel probing may be of help, but requires a visible distal part of the artery of adequate diameter that needs to be opened and



subsequently closed, which may stenose or occlude the artery [27,28]. In re-operations, fibrous tissue and previously constructed grafts provide additional difficulties [29].

Second, selection of the optimal site for anastomosis construction. Preoperative angiographic information on the coronary anatomy and the location and extent of diseased sections is intraoperatively related to anatomical landmarks to select the anastomotic site. Digital palpation of the vessel is the only means available to assess the vessel wall quality intraoperatively. However, angiography may underestimate the severity and extent of coronary pathology [30] and digital palpation is highly subjective and insensitive. In OPCAB, ideally, the isolated coronary segment (containing the anastomotic site) is also devoid of side branches from which backbleeding may occur through the arteriotomy, hampering visibility on the anastomotic site. Intraoperatively, side branches can be seen if they are not buried in fat. Septal perforators, however, can not be detected visually and often are not well delineated on the angiogram.

In minimally invasive CABG and TECAB locating and assessing the target coronary artery is more complicated because of limited overview, difficulty in interpreting anatomical landmarks and the inability to palpate the artery endoscopically [20,22,24]. Misidentification that resulted in subsequent grafting of the wrong artery (diagonal branch instead of left anterior descending coronary artery (LAD)) has been reported [31,32].

Third, coronary anastomosis suturing. The technique for vascular anastomosis suturing still strongly adheres to the basic principles set out more than 100 years ago by Alexis Carrel [33]. It requires multiple coordinated complex surgical maneuvers and is performed using surgical loupes (magnification 2.5-5.0x) to allow adequate suture placement in the small vessels (1.0-3.5 mm) encountered in CABG surgery.

CABG surgery on the arrested heart via median sternotomy provides the most optimal condition for anastomosis suturing. However, (minor) irregularities may be detected in up to 24% of anastomoses [34,35]. At short term (<2 weeks) angiographic follow up, the single most important graft (internal mammary artery (IMA) to LAD), is occluded in 1.2% and 7.8% has a 50-99% stenosis [36].

In OPCAB, backbleeding (see above) may severely hamper visibility on the arteriotomy which, combined with residual motion of the target area, makes correct suture placement more difficult, predisposing the occurrence of construction errors [37,38]. In TECAB, the lack of force feedback, limited working space and absence of an assistant to hold the graft add up and

make anastomosis suturing extremely demanding [21,23,24,26]. Several facilitated automated anastomotic techniques, aimed at creating a standardized reproducible vascular connection, are currently being evaluated [39-43]. Construction errors, however, may also occur during the application of anastomotic connectors [39,43].

### **Intraoperative anastomosis quality assessment**

Because anastomosis construction errors are not evident by external inspection, a diagnostic technique to intraoperatively check anastomosis quality is needed to allow revision of a suboptimal anastomosis before chest closure [44,45]. Several techniques have been described:

**Angiography**, is the gold standard for postoperative anastomosis quality assessment, but is only scarcely used intraoperatively [46-49]. It is invasive, time consuming, findings may be difficult to interpret [48,49] and it is not available in most operating rooms [48].

**Transit time flowmetry**, which measures the bloodflow through the graft, is fast and easy to use [50]. However, only severe stenoses (>75%) lead to abnormal flow values [51] and there is no clear cut-off point for adequate flow [50,51], which makes interpretation difficult [50-52]. Furthermore, in case of low or absent flow it does not provide information about the location or origin of the stenosis. It may be due to a severely narrowed distal coronary bed, a technical distal anastomosis suture error, graft spasm or kinking, or an inadequate proximal anastomosis. In addition, anastomoses with a severe narrowing of the outflow corner may give a normal flow reading when there is a large septal perforator at the level of the anastomosis or a large amount of retrograde flow.

**Thermal coronary imaging** is based on visualization of temperature differences between the myocardium and a (warm or cold) solution injected into the graft. [53,54]. It provides some anatomical information but it requires an expensive thermal camera, it does not visualize the anastomotic site in all cases and epicardial fat pads hinder visualization. [45,53].

**Fluorescence imaging**, is based on the injection of indocyanine green into the central venous line. The dye is caused to fluoresce by a laser light source [55-57]. A specially designed camera, captures the fluorescent light and the angiogram like image is subsequently displayed on a monitor. It is fast and easy to use but the imaging depth is limited which makes assessment of the

anastomotic orifice itself difficult [55,56]. Anastomoses on the posterior side of the heart may not be amenable to imaging [56].

**Epicardial high-frequency ultrasound** was described in the early 1980's for both assessment of the coronary artery [30] and anastomosis [58,59]. It is non-invasive, fast and provides anatomical information. However, image interpretation may be operator dependent [45]. The initial results were promising, but at the time the bulky ultrasound probes (which prohibited their use on the posterior side of the heart) and the limited resolution prevented widespread adoption of the technique [30,58,59].

### **Requirements**

Ideally, a technique to intraoperatively assess coronary anastomotic quality has the following characteristics:

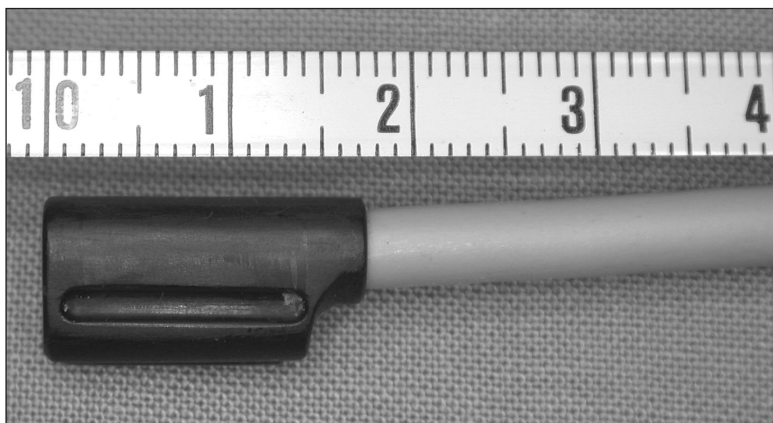
1. Non invasive
2. High sensitivity and specificity
3. Easy to use
4. Provides easy to interpret results
5. Reproducible / Operator independent
6. Applicable on all sides of the heart and all types of anastomoses
7. Fast
8. Provides both anatomical and functional information
9. Applicable in reduced access and totally endoscopic approaches
10. Inexpensive

## AIM OF THE THESIS

The aim of the thesis was to evaluate high-frequency epicardial ultrasound as a means to locate and assess coronary arteries and assess the quality of the distal coronary anastomosis in (totally endoscopic, off-pump) coronary artery bypass grafting. An epicardial ultrasound mini-transducer was evaluated on ex-vivo porcine and human hearts, in acute porcine experiments and in patients undergoing coronary artery bypass surgery.

For the studies described in this thesis, a commercially available 13 MHz epicardial ultrasound linear array mini-transducer (UST-5531, Aloka, Tokyo, Japan) was used (Figure 1).

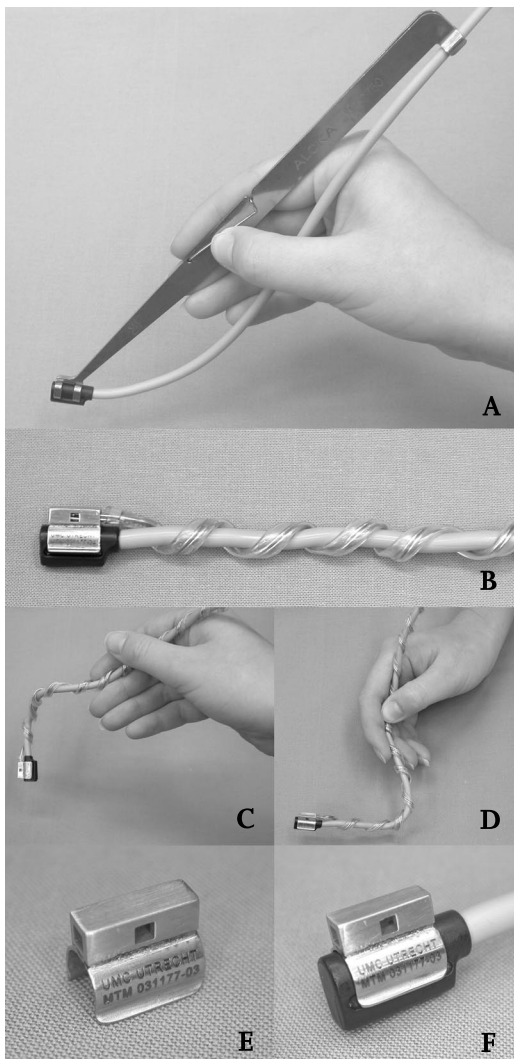
The mini-transducer measures 15 x 9 x 6 mm and has an imaging frequency of up to 13 MHz in B-mode and up to 7.5 MHz in color-Doppler imaging. The two point phantom resolution is <math><0.25\text{ mm}</math> (Figure 2) with a maximum imaging depth of approximately 4 cm. Several probe handling tools were used for easy manipulation in different approaches (Figure 3). The probe was placed in a gel filled cover (Ultracover, International Medical Products, Inc, Zutphen, the Netherlands) that acts as 1) a stand off sleeve for improved visualization in the near field and 2) a sterile and electric barrier (Figure 4). The probe itself can be sterilized but the ultrasound system used for imaging (SSD-5000, Aloka, Tokyo, Japan, Figure 5) does not have the required CF mark for direct use on the heart of the mini-transducer itself.



**Figure 1.** The 13 MHz epicardial ultrasound mini-transducer.



**Figure 2.** Image of an ultrasound phantom by the 13 MHz epicardial ultrasound mini-transducer. The smallest distance between the markers is 0.25 mm. The diameter of the markers is 0.1mm.

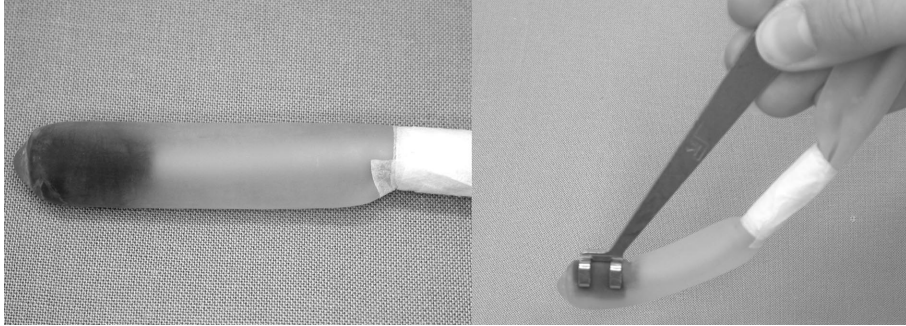


**Figure 3.**

Probe handling tools for the 13 MHz ultrasound transducer.

A commercially available pencil like handling tool (Aloka, Tokyo, Japan);

B,C,D custom made malleable handling tool that can be bended into any desired configuration; E,F custom made snap-on probe handling tool that can be easily handled by the end-effectors of the telemanipulation system during endoscopic use.



**Figure 4.** The 13 MHz epicardial ultrasound mini-transducer wrapped in a sterile gel-filled sleeve.



**Figure 5.** The SSD-5000 ultrasound system.

## OUTLINE OF THE THESIS

In chapter 2, three different surgical tools are described that enable totally endoscopic off-pump multivessel coronary bypass surgery in a porcine model of closed-chest CABG: a sternum lift, an endoscopic cardiac positioner and an endoscopic cardiac stabilizer.

In chapter 3, the endoscopic application of the ultrasound mini-transducer to locate and assess the major target arteries for bypass grafting is explored in the closed-chest porcine model described in chapter 2.

In chapter 4, the feasibility of visualizing and assessing the coronary anastomosis with epicardial ultrasound in both open- and closed-chest porcine beating heart coronary artery bypass grafting is evaluated.

In chapter 5, the quantitative impact of different technical construction errors on the coronary anastomosis geometry is evaluated by epicardial ultrasound on ex-vivo hearts.

In chapter 6, the sensitivity and specificity of epicardial ultrasound to detect 3 different technical construction errors in coronary anastomoses on ex-vivo porcine and human hearts is evaluated and compared to the gold standard angiography.

In chapter 7, the feasibility of matching target vessel to coronary bypass connector size and assessing proper deployment of a facilitated coronary anastomosis device by epicardial ultrasound is explored in porcine off-pump coronary artery bypass grafting.

In chapter 8, the initial findings during the application of the epicardial 13 MHz ultrasound mini-transducer for coronary artery and anastomosis assessment in patients undergoing coronary artery bypass grafting are described.

Chapter 9 contains the protocol for a study that will relate intraoperative evaluation of the coronary anastomosis by epicardial ultrasound to early postoperative evaluation by angiography and multislice CT in patients undergoing conventional coronary artery bypass grafting on cardiopulmonary bypass.

In chapter 10, the findings of the studies described in the preceding chapters are discussed and the role of epicardial ultrasound in coronary artery bypass grafting is reviewed.



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Endoscopic exposure and stabilization of posterior and inferior branches using the Endo-Starfish cardiac positioner and the Endo-Octopus stabilizer for closed-chest beating heart multivessel CABG: Hemodynamic changes in the pig



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P.F. Gründeman, R.P.J. Budde, H. Mansvelt Beck, W.J. van Boven<sup>1</sup>, C. Borst

Heart Lung Center Utrecht, University Medical Center Utrecht, Utrecht,

<sup>1</sup>St. Antonius Hospital, Nieuwegein, the Netherlands

## ABSTRACT

**Objective:** Closed-chest, off-pump, multivessel CABG requires modified instruments to expose and stabilize posterior and inferior coronary branches. Using three new prototype devices, we explored the feasibility of endoscopic bypass grafting on these branches and assessed cardiac function during cardiac displacement.

**Methods:** Eight pigs (75-85 kg) were instrumented for hemodynamics and paced at 80-100 beats/min. After closure of the sternotomy wound, the Da Vinci endoscope was inserted subxiphoidally. A sternal hook was used to hoist the sternum ventrally by 5 cm. The articulating EndoStarfish cardiac positioner was placed through a trocar (Ø12 mm). The positioner was fixed to the apex using -400 mmHg suction and the heart was displaced anteriorly to 90 degrees. In 12 other pigs (75-85 kg) both internal mammary arteries (IMA) were harvested and the sternal wound was closed. Five trocar ports were placed for instrumentation (Ø12 mm, 2 in left chest, 2 in right chest, one subxiphoidally). For coronary stabilization, a novel deployable EndoOctopus cardiac stabilizer was employed (suction -400 mmHg). The Da Vinci robot-telem manipulator system was used for endoscopic grafting of the left and right IMA on posterior and inferior branches (16 anastomoses).

**Results:** When circumflex arteries were fully exposed and accessible for coronary surgery, stroke volume decreased by  $18\% \pm 3$  vs baseline ( $p=0.02$ ) and mean arterial pressure by  $27\% \pm 6$  ( $p=0.001$ ). Additional 10 degrees Trendelenburg head-down positioning normalized stroke volume and arterial pressure. In the displaced heart, Obtuse Marginal branches (OM) and the Ramus Descending Posterior (RDP) of the right coronary artery became fully exposed with a mean arterial pressure  $>70$  mm Hg during grafting. No accidental detachment occurred. Coronary target motion was restrained to about 1x1 mm. In 2 test cases, 5 sham distal anastomoses were created (grafts sewn to epicardium, left IMA to OM2 jump to OM3, right IMA to RDP and composite graft from left IMA jump to diagonal branch). In 10 animals, 16 successfully completed anastomoses to RDP and OM branches of Ø1.75-2.5 mm required 25-60 minutes each to construct. At sacrifice, all anastomoses were patent.

**Conclusions:** In the closed-chest pig in Trendelenburg position and during lifting of the sternum, the EndoStarfish and EndoOctopus enabled IMA grafting of posterior and inferior branches on the beating heart without mean arterial pressure dropping below 70 mm Hg.

**Presented:**

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- 6th annual ISMICS meeting; San Francisco, CA, USA, 2003. Heart Surg Forum. 2003;6(Suppl I):I-24.



## INTRODUCTION

With the aid of computer-assisted telemanipulation, closed-chest, single-vessel coronary artery bypass surgery (TECAB) is feasible, but it remains a challenge [1]. To date, TECAB on the arrested heart [2,3,4] or the beating heart [1,5] has been limited mainly to the front of the heart.

In beating-heart multi-vessel TECAB, the heart needs to be dislocated and stabilized endoscopically. More working space than obtained by mild carbon dioxide insufflation [6] will be required to perform bypass grafting on e.g. the circumflex branches.

The primary objective of this study in the pig was to demonstrate the feasibility of beating-heart TECAB through mid-clavicular line and, for the endoscope, subxiphoidal access, with as target vessels the ramus descendens posterior (RDP) of the right coronary artery (RCA) and the second or third obtuse marginal branch (OM2/3) of the circumflex artery (CX). Both the left and the right internal mammary artery (LIMA and RIMA, respectively) served as grafts. To achieve endoscopic displacement and stabilization, Utrecht designed modifications were used of the Starfish cardiac positioner [7], EndoStarfish, and Octopus tissue stabilizer [8], EndoOctopus, respectively, as well as a novel, Utrecht designed sternum lift.

The secondary objective was to assess the hemodynamic consequences of closed-chest dislocation and stabilization of the beating heart.

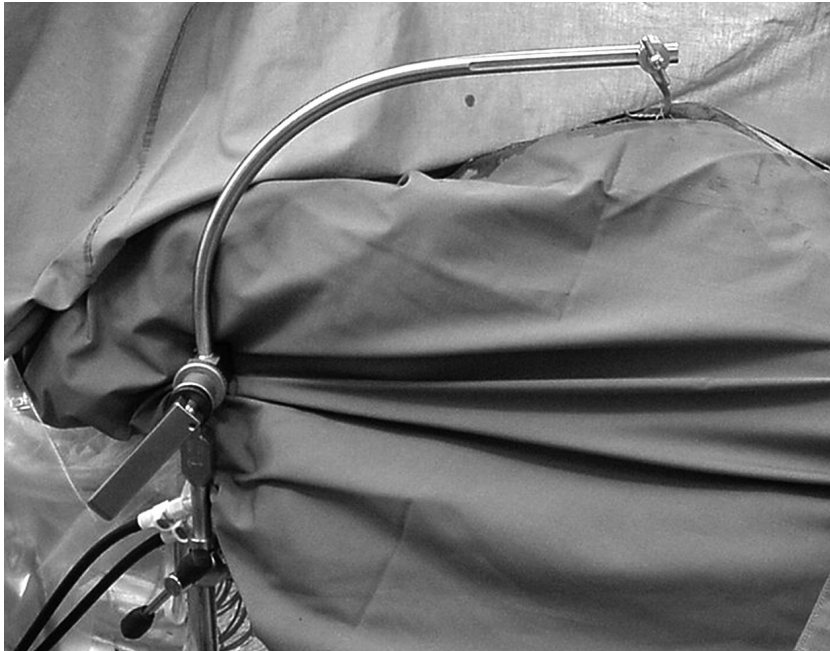


## MATERIAL AND METHODS

Twenty dutch land race pigs (75 - 85 kg) were used. All animals received humane care in compliance with the 'Guide for the Care and Use of Laboratory Animals' published by the National Institutes of Health (NIH publication 85-23, revised 1985). The study protocol was approved by the Animal Experimentation Committee of the Utrecht University.

### Anesthesia and instrumentation

The pig was premedicated and anesthetized as before [9]. First, midsternotomy was performed to allow easy instrumentation for hemodynamic measurements and time saving open-chest harvesting of the internal mammary arteries. After sternal closure, the amount of retrosternal working space was comparable with the space created after endoscopic dissection of mediastinal tissue and opening of the pleural spaces as performed in pilot studies. To create about 5 cm more space in the chest cavity ventrally, a novel design sternum lift was employed (Figure 1).

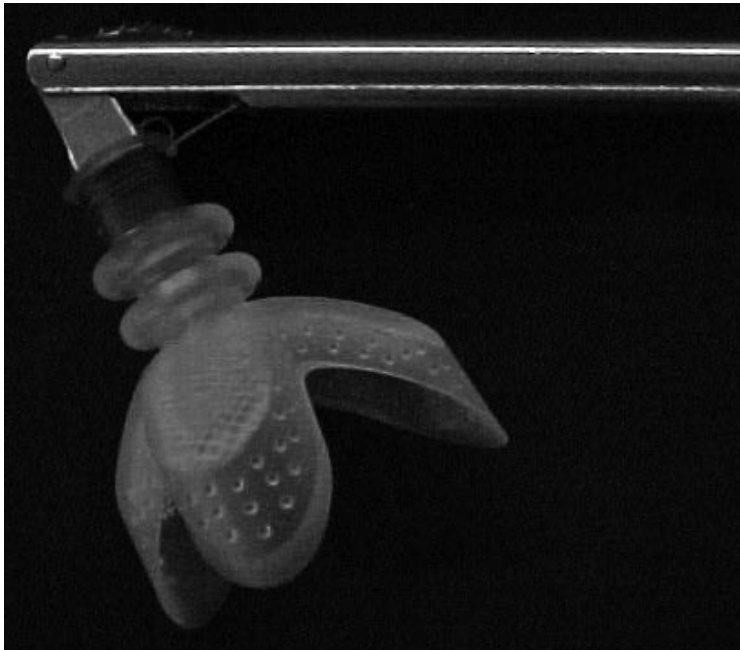


**Figure 1.** To create about 5 cm more space in the chest cavity ventrally, a novel design sternum lift was employed (Thorlift sky-hook)

### Hemodynamic measurements.

In eight pigs, catheter-tip manometers (pressure independent of body position, Millar Instruments, Houston, TX) were inserted as before [9,10,11]. After the administration of propranolol (range 15-25 mg) pacing at a fixed rate of 80-100 beats/min was started. An ultrasound transit time flow probe (Transonic Inc, Ithaca, N.Y., size 20 or 24 mm) was placed around the aorta for on-line measurement of the cardiac output (CO) as before [9]. SV was calculated by dividing CO by the heart rate.

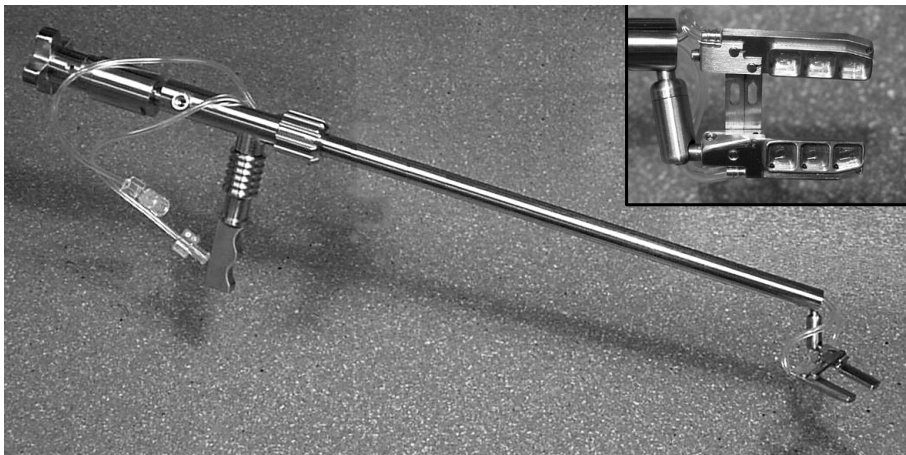
The Da Vinci robot-telemanipulator (Intuitive Surgical, Sunnyvale, CA) was used for both endoscopic visualization and manipulation. For the stereoscopic endoscope, subxiphoidal port access was used (port diameter, 13 mm). The EndoStarfish (Figure 2) that had been modified from a regular Starfish cardiac positioner (Medtronic Inc., Minneapolis, MN) was inserted through a trocar in the left chest (3rd i.c. space) and attached to the apex of the heart (-400 mm Hg). Guided by the on-line cardiac output reading, the heart was retracted anteriorly to 90 degrees by the EndoStarfish. After retraction, the device was bench-iced to the operating table rail. A personal computer based data acquisition system stored hemodynamic variables as before [9,10,11].



**Figure 2.** The porcine heart was retracted with the modified EndoStarfish cardiac positioner. Owing to its added articulation, only a few seconds were required to maneuver the device in position and attach it to the apex.

### Endoscopic coronary bypass grafting.

In 12 other pigs, both internal mammary arteries were harvested and the sternal wound was closed. Five trocar ports were placed ( $\text{\O}12$  mm, two in the left chest (3rd and 5th i.c. space), two in the right chest (3rd and 5th i.c. space), all in the midclavicular line, and one subxiphoidally). For displacement, the EndoStarfish (Figure 2) was fixed to the free apico-antero-lateral wall via the left upper access port, and fixed to the operating table rail. A novel, deployable EndoOctopus tissue stabilizer, also fixed to the operating table rail like the original Octopus [8] was introduced through the right upper trocar for local cardiac wall immobilization (Figure 3). The da Vinci end-effectors were introduced through the right and left lower trocar ports. In two animals, sham distal anastomoses were created to test graft length (distal IMA grafts sewn to epicardium without opening the coronary artery, i.e. LIMA with jump graft to OM2-3, RIMA to right posterior descending coronary artery (RDP), and composite graft from left IMA to jump diagonal 1 to LAD). In ten animals, a total of 16 anastomoses were constructed to RPD and to OM branches (1.75 - 2.5 mm diameter). The RIMA was grafted to the RPD (n=3) and to the OM3 (n=3). Both RPD and OM3 were grafted using RIMA and LIMA, respectively (n=2). The LIMA was jump-grafted to the OM2/3 (n=2). In the same animal, the RIMA was grafted to the RPD. The coronary stenosis was simulated by permanently occluding the proximal recipient coronary artery by a hemostatic clip. After making the arteriotomy, a microvascular bulldog clamp was used to eliminate backflow.



**Figure 3.** A novel, deployable Endo-Octopus tissue stabilizer, also fixed to the operating table rail like the original Octopus [8] was introduced through the right upper trocar for local cardiac wall immobilization. Insert: enlargement of endoscopic suction stabilizer pods viewed from below.

The beveled distal end of the graft was first tagged to the coronary arteriotomy rim, whereafter a running 7-0 monofilament continuous suture was used to complete the anastomosis.

### Experimental protocol

The experimental protocol to assess hemodynamic changes upon cardiac displacement was virtually identical to earlier open-chest studies [9,10,11]. In brief, baseline cardiovascular values were recorded after stabilization in the anatomic position after at least 15 minutes of pacing (phase 1, baseline anatomic position). Subsequently, values were taken three (phases 2-5) and fifteen minutes (phase 6) after stabilization following each intervention. In phase 2, the EndoStarfish was fixed to the apex while the heart remained in its anatomic position (FIX). In phase 3 (displacement to expose the last greater obtuse marginal branch of the circumflex coronary artery, DIS-Cx), the beating heart was hoisted by the cardiac positioner until 90 degrees extra-anatomic position relative to the spine was achieved (apex pointing ventrally). In phase 4, the EndoOctopus was attached to the epicardium adjacent to the proximal obtuse marginal coronary artery.

Subsequently, following stabilization of hemodynamics, the operating table was tilted 10° in the head-down position (Trendelenburg maneuver, TREN) without changing the position of the heart relative to the body (phases 5). After return from Trendelenburg, the heart was released from the cardiac positioner and fell back into the pericardial cradle (phase 6).

For endoscopic coronary bypass surgery, the EndoOctopus was attached to the epicardium adjacent to the proximal LAD, its first diagonal branch, the OM or the RDP.

### Statistical analysis

Data in Table I are presented as the mean value  $\pm$  standard deviation (SD, absolute values). Hemodynamic variables in the Results section and in Figure 4 are depicted as the mean value  $\pm$  standard error of the mean (SEM) of the percentage of protocol control values (the heart in anatomic position). Statistical analysis was performed using MANOVA to assess the influence of changing the apex position from anatomic position into 90 degrees extra-anatomic position relative to the spine. A paired Student t test was used to assess the modifying effect of Trendelenburg compared to control values (anatomic position, phase 1)

## RESULTS

All animals survived all procedures without the need to defibrillate or administer inotropic drugs. No inadvertent detachment of the heart from either one of the endoscopic suction devices occurred during the procedures. The hemodynamic consequences of closed-chest displacement and stabilization of the beating heart are summarized in Table 1 and Figure 4

### Attachment of the EndoStarfish to the apex (Phase 2)

Care was taken to avoid inclusion of the distal LAD in one of the suction cusps of the cardiac positioner. Owing to its added articulation, only a few seconds were required to maneuver the device in position and attach it to the apex. SV decreased to  $96\% \pm 3\%$  ( $P = 0.046$  and MAP decreased to  $91\% \pm 3\%$  ( $P = 0.012$ ).

### Endoscopic cardiac retraction (Phase 3)

Displacement of the heart by the apical suction device was performed by first pulling the apex in the axial direction of the left ventricle, whereafter

**Table 1.** Hemodynamic changes on closed-chest cardiac displacement and coronary stabilization

	Phase 1	Phase 2		Phase 3		Phase 4		Phase 5		Phase 6
	BASE	FIX	P-value	DIS Cx	P-value	OCT Cx	P-value	+ Trend	P-value	ANA
SV (mL)	44 ± 3	42 ± 3	.046	36 ± 3	.021	32 ± 3	.004	39 ± 3	.123	44 ± 4
MAP (mmHg)	109 ± 4	100 ± 6	.012	79 ± 6	.001	77 ± 5	.002	102 ± 5	.254	101 ± 8
Cardiac Output (L/min)	3.8 ± 3	3.7 ± .3	.049	3.2 ± .3	.017	2.8 ± 2	.006	3.4 ± 3	.148	3.8 ± .3
RVEDP (mmHg)	2 ± 1	2 ± 1	.016	4 ± 1	.020	5 ± 1	.005	9 ± 1	.002	2 ± 1
LVEDP (mmHg)	4 ± 1	4 ± 1	.882	6 ± 1	.076	8 ± 1	.042	13 ± 1	.006	5 ± 1

Values are expressed as mean ± standard deviation. BASE=anatomic position; FIX= EndoStarfish™ cardiac positioner fixed to the heart (-400 mmHg suction); DIS Cx=90 degrees vertical displacement; TREN=Trendelenburg maneuver (10° head-down body positioning). ANA=return to anatomic heart position. Data vs baseline, mean±SEM, at 3 min after maneuvers. Paired-Samples T Test

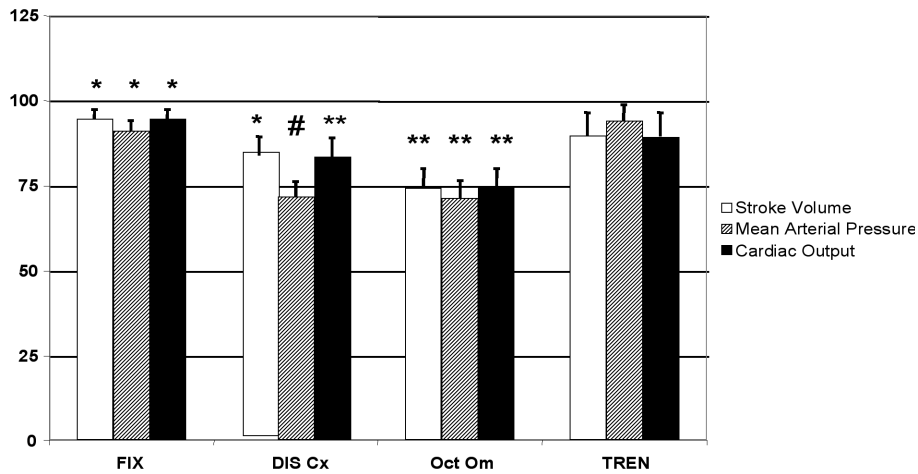
the suction device was moved ventrally and cranially at the same time. The maneuver resulted in a minor transient drop in MAP. The posterior aspect of the heart became fully exposed, which included excellent view on the circumflex artery and its branches, the distal RCA, the great cardiac vein, the coronary sinus, the inferior caval vein and the left lower pulmonary vein. In diastole, radial expansion of the left ventricle was observed. SV decreased to  $82\% \pm 3\%$  ( $P = 0.021$  vs. baseline) at the expense of increased right and left ventricular preloads. MAP decreased to  $73\% \pm 6\%$  ( $P = 0.001$  vs. baseline)

#### Endoscopic cardiac stabilization (Phase 4)

Additional attachment of the EndoOctopus and local wall stabilization marginally decreased SV and MAP (to  $74\% \pm 5\%$  ( $P = 0.004$ ) and  $72\% \pm 5\%$  ( $P = 0.002$ ), respectively. It took less than two minutes to maneuver and subsequently to fix the stabilizer to the coronary target site.

#### Whole-body head-down $10^\circ$ (Trendelenburg) (Phase 5).

SV and MAP normalized at the expense of further increased ventricular preloads. RVEDP increased to  $9 \pm 1$  mmHg ( $P = 0.002$ ) and LVEDP increased to  $13 \pm 1$  mmHg ( $P = 0.006$ ).



**Figure 4.** Comparison of hemodynamics upon vertical displacement of the beating porcine heart with the Endo-Starfish cardiac positioner. Mean percentage of baseline values  $\pm$  standard error of the mean. FIX=attachment EndoStarfish cardiac positioner, DIS Cx=exposure circumflex branch TREN=Trendelenburg maneuver ( $10^\circ$  head-down body positioning). Compared to base line: \*  $p < 0.05$ , \*\*  $p < 0.01$ , #  $p < 0.001$ .

Return of the table in the horizontal position, release of the Endo Octopus, replacement of the heart in the anatomical position and release from EndoStarfish (Phase 6)

SV, CO and MAP normalized quickly.

### **Endoscopic coronary bypass surgery**

In the displaced heart, the OM branches and the RDP became fully exposed. Provided that 10 degrees Trendelenburg body position was employed prior to displacement, mean arterial pressure was maintained >70 mm Hg during grafting. By hoisting the sternal bone, about 5 cm distance was gained between the anterior aspect of the heart and the sternal bone. This permitted unhindered manipulation of the heart with the suction positioner within the limits of the chest cage. For exposure of the circumflex branch, the heart was stowed maximally in the right pleural space.

Inside the chest, the deployable horse shoe of the EndoOctopus was easily placed on the heart by the robot end-effectors by grabbing heavy braided sutures attached to the EndoOctopus. Coronary artery motion was restrained to about 1x1 mm which allowed successful anastomosis suturing with the aid of the Da Vinci system. .

In the 2 test cases, LIMA and RIMA graft length was just sufficient to reach the target site for 5 sham distal anastomoses (grafts sutured to epicardium, LIMA jump graft to OM2-3, RIMA to RDP and composite graft from LIMA to diagonal and jump to LAD).

In ten animals, 16 successfully completed anastomoses to RPD and OM branches of 1.75 – 2.5 mm diameter (two jump grafts) required 25-60 minutes to construct. After sacrifice, inspection proved the anastomoses to be fully patent.

## DISCUSSION

The principal findings of the study were: (1) Hoisting the sternum created about 5 cm extra space, sufficient to allow maneuvering the EndoStarfish, EndoOctopus and Da Vinci end-effectors without the need for CO<sub>2</sub> insufflation of the chest cavity; (2) The EndoStarfish and EndoOctopus enabled closed-chest bypass grafting the OM branches and the RPD on the beating heart; (3) Both devices elicited hemodynamic changes similar to their open-chest counterparts [9, 10,11], but less pronounced.

### Work space expansion by ThoraLift

In the pig, mechanically lifting the sternum obviated the need for CO<sub>2</sub> insufflation that carries the risk of inadvertent displacement of the coronary target out of endoscopic view when the EndoOctopus detaches and intrathoracic CO<sub>2</sub> pressure drops abruptly [personal communication G. Wimmer-Greinecker M.D.].

### Closed-chest cardiac retraction and coronary stabilization

Placement of the EndoStarfish cardiac positioner was facilitated by the added angulation of the neck at the remote part of the device. The angulation enabled target approach at a lower than 90 degree angle (Figure 2). In practice, the positioner became attached just off-side the apex at the free anterior wall of the left ventricle. During cardiac repositioning, care was taken not to overstretch the heart in the long axis direction. All relevant coronary targets at the lateral, posterior and inferior of the heart became accessible for surgery. We observed no accidental release of the heart from the EndoStarfish, not even when the EndoOctopus was attached to the epicardium.

Guided by the on-line cardiac output readings with the ultrasound aortic probe, the optimal apical position was selected for each target vessel exposure. Occasionally, 1-2 cm change in apical position could improve cardiac output by some 10-15 %. Ninety degrees ventral cardiac dislocation resulted in excellent closed-chest exposure of the backside of the heart with a 18% decrease in stroke volume and 27% decrease in arterial pressure less than we observed earlier in during open-chest dislocation [9,10,11]. Similar to open-chest dislocation, right ventricular preload was markedly enhanced suggesting right heart dysfunction that we attribute to compression of the thin-walled right ventricle by surrounding tissue. Owing to its ability to adjust for different angles of approach, the novel Utrecht EndoOctopus was



versatile in immobilizing the LAD, it's first diagonal branch, the circumflex branches and the distal RCA using only one access port (the right lower trocar). By employing the original Octopus method [8], i.e. bench vicing the stabilizer to the operating table rail, cardiac motion was restrained sufficiently to perform grafting on coronary vessels down to 1.5 mm in diameter.

As shown before (9,10,11) in open-chest displacement of the beating heart, the Trendelenburg maneuver produced normalization of stroke volume, cardiac output and arterial pressure at the expense of further enhanced right and left ventricular preload pressure. Hemodynamics remained stable for more than one hour.

### **Closed-chest coronary surgery on the beating heart**

Thus, three major objectives that enable off-pump endoscopic coronary surgery were achieved: (1) adequate exposure of all target coronary segments; (2) hemodynamic stability during exposure of vessels located at the posterior and inferior side of the displaced heart and (3) endoscopic coronary stabilization. In 10 animals, it proved feasible to create off-pump 14 end-to-side and 2 side-to-side anastomoses with arterial grafts on posterior and inferior branches. However, owing to small vessel size, as well as extra time needed for endoscopic instrument changes and blood that obscured the arteriotomy, anastomosis construction required 25-60 minutes. We infer from these results that the use of automated coronary connectors may reduce endoscopic anastomosis construction time substantially and prove closed chest, off-pump, multivessel CABG to be feasible in a reasonable amount of time.

### **Limitations**

Possibly owing to experience in applying the Octopus since 1994 [8], we did not encounter inadvertent detachment of either EndoStarfish or EndoOctopus during these operations. There remains a risk, however, of losing grip of the heart and jeopardizing completion of the anastomosis.

The pig's chest cavity conformation is far more cartilaginous and 'carinad' shaped compared to the 'barrel' shaped human chest wall. The apex of the porcine heart is oriented somewhat right from the midline. Despite these anatomic differences, inferences on hemodynamic changes with open-chest cardiac displacement made from previous porcine studies [9,10,11] appeared to be largely applicable to coronary patients [12,13] It remains to be determined whether the current endoscopic observations may be extrapolated to coronary patients too.



## **CONCLUSION**

In the closed-chest pig in Trendelenburg position, sternal lift, EndoStarfish and EndoOctopus enabled IMA grafting of posterior and inferior branches on the beating heart. During the entire procedure, arterial pressure remained above 70 mm Hg without the use of inotropic agents.

## **Acknowledgements**

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# Endoscopic localization and assessment of coronary arteries by 13 MHz epicardial ultrasound



3

R.P.J. Budde, R. Meijer, P.F.A. Bakker, C. Borst, P.F. Gründeman

Heart Lung Center Utrecht, University Medical Center Utrecht, Utrecht,  
the Netherlands

Ann Thorac Surg. 2004;77:1586-92.

## ABSTRACT

**Objective:** In totally endoscopic coronary artery bypass grafting the target coronary artery is difficult to locate and assess. We explored the capacity of a high-frequency epicardial ultrasound mini-transducer to endoscopically locate and assess the left anterior descending (LAD), third obtuse marginal (OM3) and right posterior descending (RDP) coronary arteries.

**Methods:** In 8 pigs, the LAD, OM3 and RDP were endoscopically exposed. The mini-transducer was manipulated by the “da Vinci” telemanipulation system over the unstabilized and stabilized epicardium to identify the target artery, obtain a scout scan and both transverse and longitudinal images.

**Results:** In both unstabilized and stabilized condition, the LAD and RDP were identified within a median of 29 seconds. In stabilized condition, assessment was complete in 112 seconds (92-205) (median with range) for the LAD and 140 seconds (54-197) for the RDP. Stabilization of the OM3 was required for identification (16 (5-60)) and assessment (111 (82-225)). Overall, identification was correct in 23/24 arteries. The OM branches and RDP became fully exposed endoscopically with stroke volume (SV) and mean arterial pressure (MAP) remaining at  $67 \pm 11\%$  (mean  $\pm$  standard error of the mean) and  $70 \pm 5\%$  of baseline values, respectively. Scanning itself did not augment the decrease in SV and MAP significantly.

**Conclusions:** After proper endoscopic exposure and stabilization, robot-assisted epicardial ultrasound scanning enabled endoscopic identification and assessment of major coronary arteries within a median of 169 seconds per artery. Exposure, stabilization and scanning were accompanied by an acceptable drop in stroke volume and mean arterial pressure.

### Presented:

- 8th Utrecht Minimally Invasive CABG Workshop; Monte Carlo Monaco, 2002.
- 6th NewEra Cardiac Care Innovation and Technology Meeting; Dana Point, USA, 2003.
- Biannual Scientific Meeting of the Netherlands Association for Cardio-Thoracic Surgery; Utrecht, the Netherlands, 2003. Netherlands Heart Journal 2003;11:(5).

## INTRODUCTION

In totally endoscopic coronary artery bypass surgery (TECAB) several obstacles are encountered. The target coronary artery is often difficult to locate due to the epicardial fibrofatty layer, a tangential angle of view, difficult to interpret anatomical landmarks and bleeding during dissection of epicardial fat [1-3]. Failure to locate the left anterior descending artery (LAD) endoscopically has resulted in intra-operative conversion to an open-chest procedure in up to 9% of patients undergoing TECAB [3]. There is a risk of grafting the wrong vessel (diagonal branch instead of LAD).

Absence of tactile feedback on the telemanipulation systems used in TECAB prevents palpatory assessment of the target coronary artery in search of the optimal anastomotic site [1-3]. Intraoperative planning may be improved by knowledge of the internal luminal diameter, the presence and extent of plaque and the existence of nearby sidebranches which may hamper anastomosis suturing due to torrential backflow [1-3].

High-frequency epicardial ultrasound can accurately locate side branches and septal perforators as well as assess the dimensions and vessel wall quality of coronary arteries in open chest coronary artery bypass grafting (CABG) [4-8]. Experience with the endoscopic use of ultrasound to detect coronary arteries is anecdotic, partly due to the relatively bulky size of most transducers which prohibits their passage through a port [8,9]. Recently, a 13 MHz mini-transducer (Aloka, Tokyo, Japan) was developed that is small enough to pass an 11 mm trocar. It can be handled by telemanipulation systems. When used in combination with endoscopic cardiac positioning and stabilization devices [10], ultrasound assessment of coronary arteries on both the anterior, lateral and posterior side of the heart might prove feasible.

The aim of this study was to assess the feasibility of endoscopic exposure and subsequent localization and assessment by a 13 MHz mini-transducer of the LAD, third obtuse marginal branch (OM3) and right descending posterior artery (RDP) in the pig.

## MATERIAL AND METHODS

### Animals

Eight female Dutch landrace pigs (weight range 55-85 kg) were used. The animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press (revised 1996). The study was approved by the Animal Experimentation Committee of the Utrecht University.

### Anesthesia

Anesthesia was induced by ketamine (10 mg/kg), midazolam (0.2 mg/kg) and atropine (0.04 mg/kg) intramuscularly and thiopental sodium (4 mg/kg) intravenously. Loading doses of midazolam (0.5 mg/kg), sufentanilcitrate (6 µg/kg) and pancuronium bromide (0.1 mg/kg) were administered intravenously. Subsequently, the animal was connected to a positive pressure ventilator.

Anesthesia was maintained by a mixture of oxygen and air ( $FiO_2 = 0.5$ ) with added halothane (0-1.0 %), and a continuous intravenous infusion of midazolam (0.7 mg/kg/hour), sufentanilcitrate (2 µg/kg/hour) and pancuronium bromide (0.1 mg/kg/hour). To obtain a heart rate below 70 beats per minute and reduce cardiac irritability, propranolol was administered intravenously to a maximum of 25 mg. ECG, phasic and mean arterial blood pressure (MAP), end-tidal CO<sub>2</sub>, nasal temperature and cardiac output (CO) were monitored continuously. At the end of the procedure animals were sacrificed by pentobarbitalsodium (200 mg/kg) intravenously.

### Surgery

To obtain access to the aorta and right atrium, partial median sternotomy was performed and the pericardium was opened. A calibrated transit time flow probe (20-24S), connected to a calibrated flow meter (model T208, Transonic Systems, Inc, Ithaca, NY), was placed around the ascending aorta for continuous measurement of CO. After a bipolar pacing lead was sutured to the right atrial appendage, pacing was started at a fixed rate of 80 beats per minute. Stroke volume (SV) was calculated by dividing CO by heart rate (pacing rate of 80). A fluid manometer catheter was placed in the left femoral artery to measure phasic arterial blood pressure and MAP.

Trocars were placed as follows: one trocar (Ø12 mm) subxiphoidally for the stereoscope; two trocars (Ø 11 mm) for the "da Vinci" instruments [1]



approximately 5 cm lateral to the camera port at the left and right side; one trocar ( $\text{\O}15$  mm) for the endoscopic cardiac positioner [10] on the anterior axillary line in the left second intercostal space; one trocar ( $\text{\O}15$  mm) for the endoscopic cardiac stabilizer [11] and one trocar ( $\text{\O}15$  mm) for the ultrasound mini-transducer in the left and right fifth intercostal space, respectively, each on the mid-clavicular line.

The chest was closed and a hook, attached to a table rail mounted lifting device was inserted under the xiphoid process, hoisting the sternum ventrally approximately 5 cm [10].

The slave unit of the “da Vinci” computer enhanced telemanipulation system (Intuitive Surgical, Sunnyvale, Ca) was positioned at the head side of the operating table, and docked to the trocars [1].

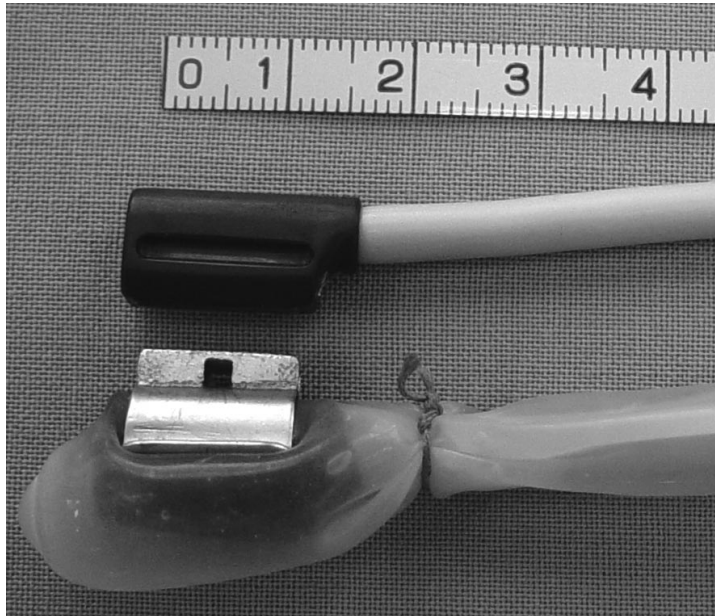
A modified, articulating version of the Starfish<sup>TM</sup> cardiac positioner (Medtronic, Minneapolis, MN), named the “EndoStarfish”, has been developed by us for endoscopic use [10]. The “EndoStarfish” enabled appropriate cardiac displacement to expose the OM branches and RDP. The EndoStarfish was fixed to the apex (-400 mm Hg) and by subsequently hoisting the apex ventrally, cranially and to the right, the OM branches of the circumflex coronary artery were exposed. To expose the RDP, the apex of the heart was hoisted ventrally, cranially and to the left.

A single Octopus-1 Tissue Stabilizer arm (Medtronic, Minneapolis, MN) was attached to the heart (-400 mm Hg) to stabilize the target area [11]. During displacement, CO and MAP were continuously monitored to determine the optimal position for presentation of the target vessel with the least decrease in SV and MAP. No Trendelenberg positioning was employed.

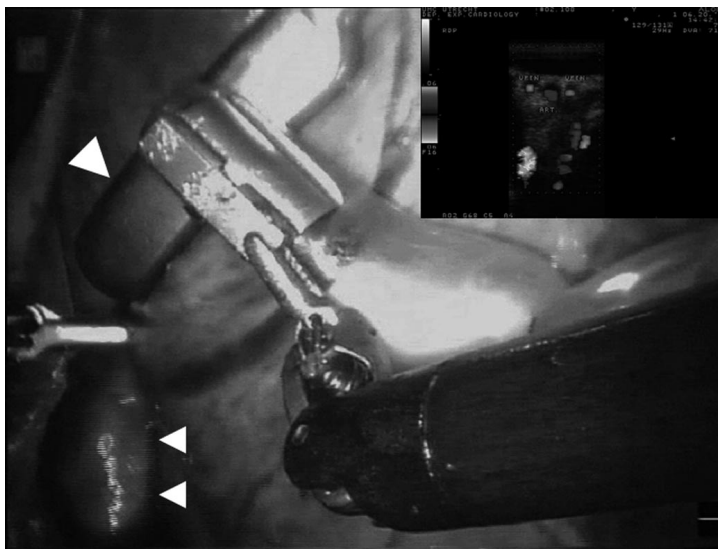
### Ultrasound equipment

A linear array mini-transducer (Aloka, Tokyo, Japan) with an imaging frequency of 13 MHz in B-mode and 7 MHz in color-Doppler was used. It measures 15 mm in length, 6 mm in width and 9 mm in height, has an image scanwidth of 10 mm and an image depth of approximately 4 cm. A custom made snap-on metal probe holder enabled manipulation of the transducer by the end-effectors of the “da Vinci” instruments. The transducer was placed in a gel filled protective cover (Ultracover, International Medical Products, Inc, Zutphen, the Netherlands), originally intended for use on a transesophageal echocardiography probe, which acted as a stand off sleeve to facilitate scanning and improve image quality by limiting near-field transducer artifacts (Figure 1).

The probe was connected to an SSD 5000 Prosound ultrasound system (Aloka, Tokyo, Japan) by a flexible cable. An experienced sonographer



**Figure 1.** The Aloka 13 MHz mini-transducer (top) and as it was used in this study, wrapped in sleeve with probe holder (bottom). The transducer can be passed through an 11 mm trocar. (Color image: page 164)



**Figure 2.** Surgeon's view on master console of the posterior side of the heart (apex pointing to right upper corner of image) during stabilized (single Octopus-1 arm, large arrowhead) scanning of a RDP. Note the picture-in-picture displayed ultrasound image, and inferior caval vein (small arrowheads). (Color image: page 164)

(RM) operated the ultrasound system. To enable retrospective analysis, selected images were stored on videotape and on a personal computer. The ultrasound image was displayed picture-in-picture on the master console of the “da Vinci” system, providing the operator with the real-time ultrasound image whilst scanning (Figure 2). All vessels were scanned by the same investigator (RPJB).

### **Ultrasound scanning and hemodynamic measurement protocol**

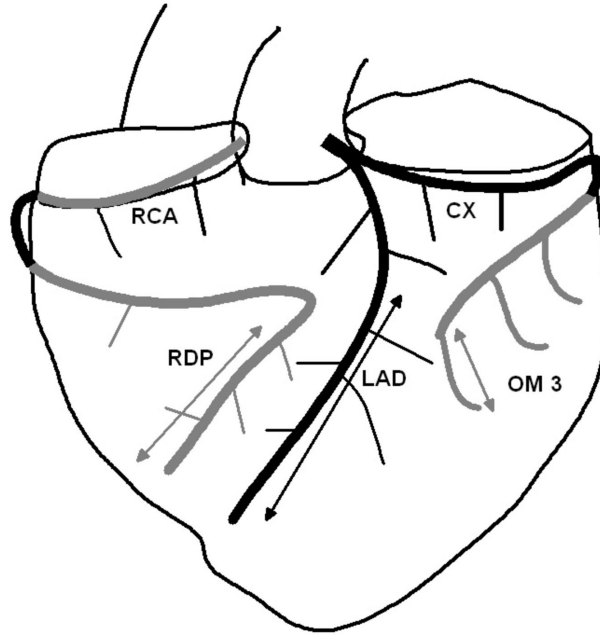
Cardiac output and MAP were recorded at baseline and during the scanning process. Baseline control values comprised 3 minutes of baseline measurements with the heart freely beating in its anatomical or displaced position depending on the target artery.

During the unstabilized scan, the target coronary artery was scanned with the mini-transducer. First, the exposed target area was visually inspected to locate the approximate position of the artery. Second, with the end-effectors of the “da Vinci” system instruments, the mini-transducer, orientated perpendicular to the expected vessel course, was manipulated over the epicardial surface utilizing the transducer's full image scanwidth of 10 mm to locate the artery. Third, to familiarize the operator with the course of the artery and spot side branches and septal perforators, a transverse scout scan was performed in the up- and down-stream direction of the vessel over a distance of about 6 cm (LAD), 3 cm (OM3) and 4 cm (RDP) (Figure 3). Fourth, a transverse image (vessel outline round, no signs of compression) and a longitudinal image were obtained (vessel visible over entire length of scan image) at the approximate mid part of the section scanned during the scout scan. In the transverse image, the internal coronary artery diameter was measured both top to bottom and side to side. In the longitudinal image, it was measured top to bottom. The time required to finish each scanning step was recorded.

During the stabilized scan, the previous scanning steps were repeated on the stabilized heart. The vessel location was marked by placing a microvascular clip on the epicardial surface.

### **Angiography**

After the animals were sacrificed, the heart was excised and X-ray markers were placed over the microvascular clips. The coronary arteries were visualized by selectively injecting the left main stem and right coronary artery with contrast medium (C-arm BV27, Philips, Eindhoven, the Netherlands). By comparing positions of the X-ray markers and the coronary angiogram, coronary artery identification was scored as correct or incorrect.



**Figure 3.** Schematic drawing of the porcine coronary anatomy. Arrows indicate the part of the target arteries scanned during the scout scan. Vessel diameter was measured in the mid portion of this section. CX = Circumflex Coronary Artery; OM3 =Third Obtuse Marginal Coronary Branch; LAD = Left Anterior Descending Coronary Artery; RCA = Right Coronary Artery; RDP = Right Posterior Descending Coronary Artery.

### Statistical analysis

Values are presented as median with range (scanning times) and mean  $\pm$  standard error of the mean (SEM, hemodynamic parameters).

A paired Student T-test was used to compare scanning times, to evaluate the effect of ultrasound scanning on SV and MAP compared to stabilized and unstabilized target artery exposure, and OM and RDP exposure alone compared to baseline. A post hoc Bonferroni correction was applied to adjust for multiple testing. Wilcoxon signed ranks test was used to evaluate the time needed to obtain longitudinal and transverse images. A p-value of  $p \leq 0.05$  was considered significant.

## RESULTS

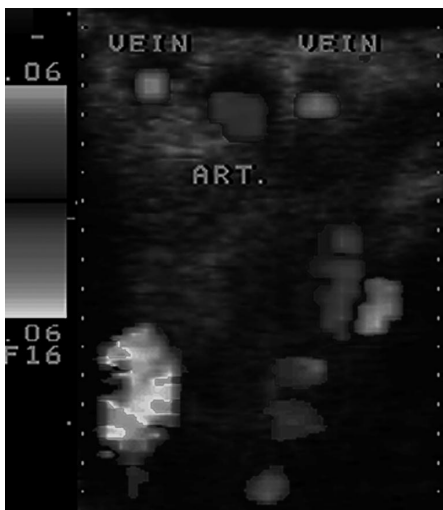
### Surgery

All animals survived the entire procedure without the need to defibrillate or administer inotropic drugs. Lifting the sternum increased the distance between the posterior side of the sternum and anterior wall of the heart by approximately 5 cm. Endoscopic displacement of the heart by the EndoStarfish enabled adequate exposure of the OM branches with SV remaining at  $69 \pm 8\%$  (mean  $\pm$  SEM,  $p=0.016$ ) and MAP at  $70 \pm 5\%$  ( $p=0.002$ ) of baseline values, and the RDP with SV remaining at  $67 \pm 11\%$  ( $p=0.022$ ) and MAP at  $85 \pm 7\%$  ( $p=0.154$ ) of baseline values. Full access for ultrasound scanning was obtained. Compared to target vessel exposure only, epicardial scanning by the mini-transducer did not result in significant hemodynamic consequences except for a 2 ml decrease in SV during unstabilized LAD scanning ( $p=0.011$ ). This decrease was of no clinical importance.

### Ultrasound scanning protocol

Endoscopic manipulation of the mini-transducer by the handling tool was easily achieved by the end-effectors of the “da Vinci” system instruments. It was not restricted by the transducer cable. Due to the gel filled sleeve, the near field of the ultrasound image was easy to interpret. The picture-in-picture displayed ultrasound image provided sufficient detail to adequately spot side branches and septal perforators from the robot master console.

During scanning, arteries and veins were easily discriminated by using color-Doppler imaging or on basis of the vessel outline, because veins collapse when mild pressure is applied with the transducer (Figure 4).



**Figure 4.** Transverse color-Doppler image of a RDP with two adjacent veins. Blue depicts arterial flow and yellow/red depicts venous flow.

(Color image: page 164)

Scanning times are listed in Table 1. Obtaining optimal longitudinal images was significantly more time consuming than optimal transverse images for the stabilized LAD ( $p=0.025$ ), OM3 ( $p=0.017$ ) and RDP ( $p=0.012$ ), but not for the unstabilized LAD ( $p=0.128$ ) and RDP ( $p=0.075$ ). Vessel diameter measured in longitudinal and transverse (mean of both measurements) images were  $1.9 \pm 0.4$  mm (mean  $\pm$  standard deviation) and  $2.1 \pm 0.5$  mm for the LAD,  $1.4 \pm 0.4$  mm and  $1.6 \pm 0.6$  mm for the OM3 and  $1.4 \pm 0.4$  mm and  $1.6 \pm 0.4$  mm for the RDP, respectively.

**Table 1** Time (seconds) required for scanning procedure subsets

	LAD		OM3		RDP	
	U	S	U	S	U	S
Identification	20 (12-25)	17 (13-30)	51 (5-102)	16 (5-60)	28 (12-70)	29 (11-84)
Scout Scan	70 (60-96)	60 (40-86)	71 (35-180)	52 (21-90)	51 (18-104)	40 (25-85)
Transverse Image	13 (6-50)	13 (5-40)	12, 20, 20	13 (3-60)	13 (10-80)	16 (3-38)
Longitudinal Image	40 (11-52)	35 (25-145)	9, 32, 80	57 (15-120)	60 (30-145)	60 (20-141)
Total Scan Time	130 (126-205)	132 (107-230)	156, 208	137 (89-267)	190 (110-255)	169 (74-281)

Values presented as median with range. S = Stabilized; U = Unstabilized. In 6 animals not all scanning steps could be completed during unstabilized scan of the OM3 due to excessive cardiac motion.

### Scanning of LAD

In both unstabilized and stabilized condition, the LAD was identified within 30 seconds in all animals. During the scout scan septal perforators and side branches were spotted easily. In stabilized condition the scan procedure was completed within a median of 132 seconds.

### Scanning of third OM branch

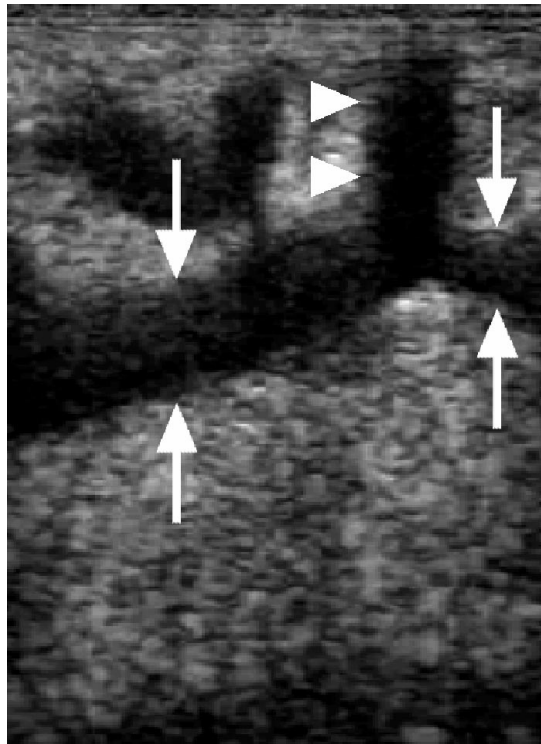
In 6 animals, completion of all scanning steps on the unstabilized heart was impossible due to excessive motion of the target area. After stabilization, local cardiac motion was sufficiently reduced to adequately visualize the third OM branch (identification within 60 seconds in all animals) and complete all scanning steps within a median of 137 seconds. During the stabilized scout scan, the third OM branch could be visualized up to its origin from the circumflex coronary artery (Figure 5).

### Scanning of RDP

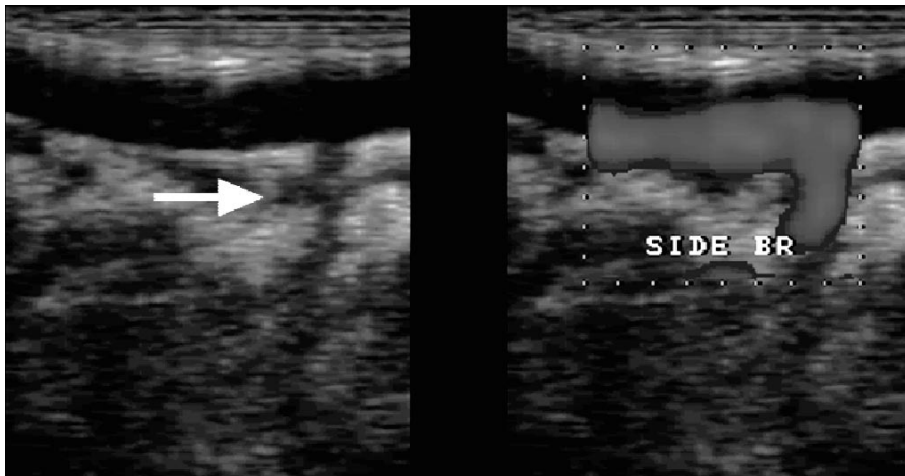
Cardiac motion of the RDP target area was less compared to the OM region, enabling completion of all scanning steps in both unstabilized and stabilized condition. In stabilized condition the RDP was identified within 84 seconds in all animals. The scan procedure was completed within a median of 169 seconds. Septal perforating branches were spotted easily (Figure 6).

### Angiography

Angiography confirmed that both the LAD and RDP were correctly identified in all eight animals. In one animal a diagonal branch was mistaken for the OM3.



**Figure 5.** B-mode image of circumflex artery (between arrows) with OM3 (arrowheads).



**Figure 6.** Split screen longitudinal B-mode and power Doppler flow image of a RDP with septal perforating branch. Note the sidebranches coming off the septal perforator running parallel to the RDP (arrow). (Color image: page 165)



## DISCUSSION

The principal results of this study are: (1) Epicardial 13 MHz ultrasound scanning enabled endoscopic identification and assessment of the LAD, OM3 and RDP in all eight animals within a maximum of 281 seconds; (2) Identification of the target vessel was correct in 23/24 arteries; (3) RDP and OM branches could be fully exposed endoscopically without too great a drop in SV and MAP; (4) Local stabilization was required to visualize the OM3 properly.

### Endoscopic epicardial ultrasound scanning

In open-chest CABG, epicardial ultrasound for visualization of the coronary artery [5,12] and quality assessment of the coronary anastomosis [13] has not gained wide acceptance in the 1980s and 1990s due to technical limitations. The relatively low frequency resulted in too low a resolution. The large size of the available transducers limited their use to the anterior side of the heart. The recent development of both (minimally invasive) off-pump CABG and small high-frequency transducers renewed interest in the technique, as epicardial ultrasound can aid in choosing the optimal anastomotic site with little or no coronary pathology or septal perforators (back-bleeding) [5-8]. The latter is particularly important in TECAB where bleeding from the anastomotic site is difficult to control and may be a reason for conversion [2].

Despite the small size of the current probes, visualization of arteries and anastomoses on the lateral and posterior side of the heart (especially parts of the left circumflex branch) is still difficult with most transducers [4,6]. To allow endoscopic use of a transducer, it must be small enough to pass through a port, have some kind of handling tool to allow it to be manipulated by endoscopic instruments and it should be connected to a very flexible cable that does not restrict positioning of the probe. To our knowledge, the mini-transducer employed in this study is the only transducer currently available that fits all these requirements. All major target sites for bypass surgery were visualized properly.

Endoscopic scanning of the LAD and RDP did not require stabilization of the target area as the transducers image scanwidth of 10 mm was sufficient to keep the target artery visualized in transverse imaging during each phase of the cardiac cycle. This facilitated subsequent first time correct placement of the stabilizer. For the OM3 stabilization was necessary to scan the artery. One artery identified as an OM3 during scanning proved to be a diagonal branch during the ex-vivo angiography. The coronary anatomy of this spe-

cific heart was unusual as the diagonal branches coming of the LAD were prominently extending to the left lateral side of the heart. Probably, knowledge of the coronary anatomy before scanning based on a pre-operative angiogram, as is routinely performed in the clinical setting, would have been helpful in this specific case.

Due to its small size and flexible cable, the mini-transducer was easily manipulated inside the chest. Inability to scan certain segments of the vessels was mainly due to limitations in endoscopic exposure achieved with the current endoscopic cardiac positioners and not related to the size and or maneuverability of the mini-transducer.

Complete scanning of the stabilized artery required from 74 to 281 seconds, with a median of 132, 137 and 169 seconds for LAD, OM3 and RDP, respectively. Endoscopic epicardial scanning did not significantly affect SV and MAP. Thus, it is a safe diagnostic technique.

#### **Hemodynamic effects of endoscopic exposure of OM branches and RDP**

Using the same tools as described before [10], the OM branches and RDP could be properly exposed endoscopically making them fully accessible for ultrasound scanning. In stabilized condition, MAP remained on average above 70 mm Hg without the use of inotropic drugs or Trendelenburg positioning.

#### **Limitations**

The coronary anatomy of the pig is somewhat different from that in the human, sometimes with less epicardial fat surrounding the coronary arteries, making them easier to spot. On the other hand, porcine epicardial tissue easily develops edema after opening of the pericardium making the coronary arteries more difficult to locate visually. Clinically, the smaller diameter of diseased coronary arteries might make them less easy to spot from the master console. With growing experience and use of color-Doppler, however this should not be a limiting factor. We successfully visualized the LAD and OM branches with plaques and calcifications using the mini-transducer in one patient undergoing on-pump CABG via sternotomy access.

Hemodynamic effects in patients with depressed left ventricular function may be clinically significant and require support with inotropic drugs and/or Trendelenburg position.

## **CONCLUSION**

After proper endoscopic exposure and stabilization, robot-assisted epicardial ultrasound scanning enabled endoscopic identification and assessment of major coronary branches within a median of 169 seconds per artery. Exposure, stabilization and scanning were accompanied by an acceptable drop in SV and MAP that did not require the Trendelenburg position or administration of inotropic drugs.

### **Acknowledgement**

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# Robot-assisted 13 MHz epicardial ultrasound for endoscopic quality assessment of coronary anastomoses



4

R.P.J. Budde, T.C. Dessing, R. Meijer, P.F.A. Bakker, C. Borst, P.F. Gründeman

Heart Lung Center Utrecht, University Medical Center Utrecht, Utrecht,  
the Netherlands

**ABSTRACT**

**Objective:** In totally endoscopic coronary artery bypass surgery, intraoperative assessment of anastomotic quality is needed. We evaluated the endoscopic application of epicardial ultrasound to visualize the coronary anastomosis and detect a construction error.

**Methods:** In 8 pigs (71-78 kg), 16 internal mammary artery to left anterior descending coronary artery anastomoses were constructed conventionally, either correctly (n=8) or incorrectly with a suture cross-over construction error (n=8). A 13 MHz mini-transducer (15x9x6 mm) was introduced through a port and manipulated by the “da Vinci” system. The chest was re-opened and scanning repeated manually. Postoperatively, macroscopic inspection served as reference and the intra-operative ultrasound images were scored as ‘correct’ or ‘construction error’ by two blinded observers.

**Results:** All anastomoses were scored accurately by both observers. One anastomosis constructed to be correct was scored as construction error, due to narrowing of the outflow corner and anastomotic orifice. Ultrasound images corresponded with macroscopic inspection. Closed-chest scan time was about 1.5 times longer than open-chest scan time, 176 s (88-464) (median, range) versus 125 s (75-314) (p=0.01), respectively.

**Conclusions:** Closed-chest epicardial 13 MHz ultrasound scanning required a median of 3 minutes and enabled discrimination between correctly and incorrectly constructed coronary anastomoses.

**Presented:**

- 6th annual ISMICS meeting; San Francisco, USA, 2003. Heart Surg Forum. 2003;6 (Suppl I):I-25.
- Scientific Sessions 2003, American Heart Association; Orlando, USA, 2003. Circulation. 2003;108(Suppl IV):IV-328.
- 7th annual EuroEcho meeting; Barcelona, Spain, 2003. Eur J Echocardiography. 2003;4(Suppl 1):S84.

## INTRODUCTION

In totally endoscopic coronary artery bypass surgery (TECAB), anastomosis suturing is technically more demanding compared to open-chest surgery [1,2]. Limited working space, lack of an assistant to present the graft, more difficult to control bleeding from the arteriotomy and lack of tactile feedback on the telemanipulation systems hamper anastomosis construction. As a result, the risk of a technical construction error like, for example, accidental interlocking of the suture on opposite sides of the anastomosis (suture cross-over) is likely to be increased. Therefore, a method to intraoperatively assess anastomotic quality is needed in TECAB [3].

Recently, we described a 13 MHz epicardial ultrasound mini-transducer (15 x 9 x 6 mm) for visualization of different construction errors [4] and endoscopic localization of coronary arteries [5]. We investigated in the pig the endoscopic application of this mini-transducer to visualize coronary anastomoses and detect a construction error.

## MATERIALS AND METHODS

### Animals

Eight female Dutch landrace pigs (71-78 kg) were used. The animals received humane care in compliance with the “Guide for the Care and Use of Laboratory Animals”. The study was approved by the Animal Experimentation Committee of the Utrecht University.

### Surgery

After anesthetizing the animals as described before [5], a partial median sternotomy was performed and the left and right internal mammary arteries (LIMA, RIMA) were harvested. Heparin was administered intravenously to obtain and maintain an activated clotting time (Hemotec, Inc., Englewood, CO, USA) of at least 200 seconds during anastomosis construction. The pericardium was opened and its edges suspended.

Using the Octopus-2 tissue stabilizer (Medtronic, Inc, Minneapolis, MN) [6], the distal anastomotic site on the left anterior descending coronary artery (LAD) was immobilized and dissected free. The pressurized LAD outer diameter and unpressurized IMA half circumference (diameter calculated with circle formula) was measured with a calliper. As described below, the distal RIMA-LAD anastomosis was constructed first followed by the proximal anastomosis (LIMA-LAD) at least one transducer length (15 mm) upstream. The pericardial suspension sutures were removed.

Trocars were placed as follows: one trocar ( $\varnothing$  12 mm) in the left 6th intercostal space (stereoscope); one trocar ( $\varnothing$  11 mm) subxiphoidally and one trocar ( $\varnothing$  11 mm) in the left 5th intercostal space (“da Vinci” instruments) [2]; two trocars ( $\varnothing$ 15 mm) in the left second and the right fifth intercostal space for the EndoOctopus endoscopic cardiac stabilizer [7] and the ultrasound mini-transducer.

The chest was closed and the sternum hoisted ventrally (5 cm) by a table rail mounted sternum lifting device [7]. The “da Vinci” computer enhanced telemanipulation system (Intuitive Surgical, Sunnyvale, CA) [2], was used for endoscopic manipulation of the mini-transducer. After the endoscopic scanning procedure, the chest was re-opened for open-chest manual scanning.

After sacrificing the animal, the anastomoses were excised and the posterior wall of the LAD was incised longitudinally to allow detailed macroscopic inspection of all areas of the anastomosis at 4,5x magnification and photography of the anastomosis.



### **Anastomotic procedure**

A single investigator (RPJB) constructed all anastomoses in a running suture fashion using a 7-0 prolene suture (Ethicon, Inc, Sommerville, NJ).

Anastomoses were constructed to be correct (n=8) or incorrect with a suture cross-over construction error (n=8) in which two suture bites on opposite sides of the arteriotomy were deliberately interlocked midway between heel and toe. In each animal, one correct and one incorrect anastomosis was constructed. Anastomosis types were distributed equally over the proximal and distal anastomotic sites.

The LAD was clipped (medium Atraumaclip; Piling, Inc, Fort Washington, PA) midway between the anastomoses and upstream of the proximal anastomosis.

### **Ultrasound equipment**

As before [4,5], a commercially available, high-frequency (up to 13 MHz in B-mode) linear array mini-transducer (15 x 9 x 6 mm) (Aloka, Tokyo, Japan) placed in a gel filled protective cover (Ultracover, International Medical Products, Inc, Zutphen, the Netherlands) was used.

For endoscopic handling of the mini-transducer by the “da Vinci” instruments, a custom made snap-on metal probe holder was used [5]. The ultrasound image was displayed picture-in-picture on the “da Vinci system” master console, providing the operator with the real-time scan image [5].

Open-chest manual handling was done using a commercially available handling tool (Aloka, Tokyo, Japan) [4].

Imaging was performed with an SSD 5000 Prosound ultrasound system (Aloka, Tokyo, Japan). Selected images were stored for retrospective analysis.

### **Ultrasound scanning protocol**

After immobilization by the EndoOctopus [7] or Octopus-2 stabilizer [6], all anastomoses were scanned by the same investigator (RPJB). First, the anastomosis was visualized in a longitudinal scan plane using power Doppler imaging. Second, in the same longitudinal scan plane, the anastomosis was visualized in B-mode. Third, by translating the transducer from the toe towards the heel of the anastomosis, a sweep of the anastomosis in the transverse scan plane was performed using power Doppler imaging. Fourth, a transverse power Doppler image was obtained at the level of the visually determined maximal anastomotic orifice. Fifth and sixth, the transverse sweep and image, respectively, were obtained in B-mode. The time required to finish each scanning step was recorded.



### **Off-line assessment by independent observers**

Two independent observers with prior experience in interpreting epicardial ultrasound images but without prior knowledge about number and type of anastomoses scanned, were separately presented sets of scan images in random order. Each set contained 4 images of one anastomosis (longitudinal and transverse image at level of visually determined maximum anastomotic orifice in both power Doppler and B-mode). The observers scored the anastomosis as correctly or incorrectly constructed.

### **Statistical analysis**

Scanning times are presented as median with range and were compared using Wilcoxon signed ranks test. A p-value of  $p < 0.05$  was considered statistically significant.

## RESULTS

### Surgery

Diameter of the IMA and LAD were  $2.3 \pm 0.4$  mm and  $3.2 \pm 0.6$  mm, respectively. Correct and incorrect anastomoses could not be discriminated by external examination.

### Ultrasound scanning

The picture-in-picture displayed ultrasound image provided sufficient detail for the operator to accurately position the transducer. Power Doppler imaging facilitated first time visualization and subsequent transducer manipulation to obtain images in the longitudinal axis. The transducer was easily manipulated endoscopically. By freezing the instruments and thus the transducer position, the operator was able to leave the master console of the “da Vinci” system and inspect the real-time image in detail on the monitor of the ultrasound machine.

Images of a correct anastomosis are shown in Figure 1. In the incorrect anastomosis, the overcrossing suture was easily spotted in longitudinal and transverse images as a strong echo reflection in the anastomotic orifice, (Figure 2). One anastomosis intended to be fully patent revealed a lateral ridge at the level of the anastomotic orifice and narrowing of the outflow corner (Figure 3). Endoscopically obtained image quality was comparable to manual scanning.

Scan times are presented in table 1. Endoscopic scanning was significantly more time consuming than manual scanning, 176 s (88-464) (median with range) versus 125 s (75-314), respectively ( $p=0.01$ ).



**Figure 1.** Longitudinal and transverse ultrasound images of a correct anastomosis with corresponding macroscopic view of the anastomotic orifice after incision of the posterior wall of the LAD. IMA: Internal Mammary Artery, LAD: Left Anterior Descending Coronary Artery.

(Color image: page 165)

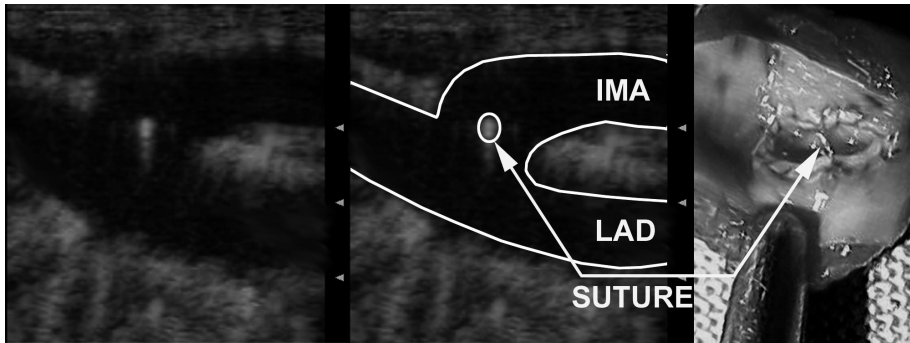
**Table 1.** - Time (s) required to finish scanning steps.

Anastomosis type	First longitudinal visualization	Longitudinal Power Doppler	Longitudinal B-Mode	Transverse sweep Doppler	Transverse Power Doppler	Transverse sweep image	Transverse B-Mode	Transverse image B-Mode	Total scan time	p-value
<b>Robot-assisted</b>	Correct	9 (6-47)	21 (5-62)	21 (7-189)	25 (9-43)	13 (8-48)	22 (13-28)	11 (4-45)	153 (88-363)	0.06
	Incorrect	12 (5-32)	57 (17-149)	81 (8-173)	38 (20-180)	20 (5-60)	30 (12-66)	28 (10-58)	305 (130-464)	
<b>Manual</b>	Correct	9 (4-13)	14 (9-37)	11 (8-23)	24 (6-56)	10 (8-13)	17 (10-96)	13 (4-42)	108 (75-221)	0.07
	Incorrect	7 (4-42)	31 (8-70)	28 (10-110)	28 (23-78)	17 (8-49)	22 (10-46)	21 (7-78)	178 (96-314)	

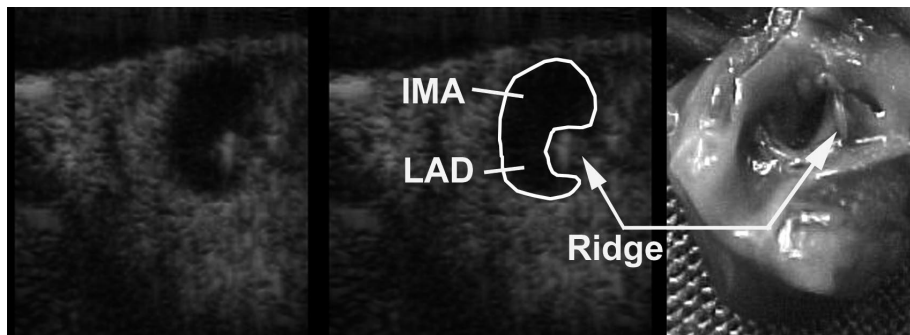
Values presented as median with range. Longitudinal: time to obtain a longitudinal image of the anastomosis using Power Doppler and B-mode imaging, respectively; Transverse sweep: time to obtain a sequence of transverse images of the anastomosis by translating the transducer from toe to heel using Power Doppler and B-mode imaging, respectively; Transverse image: time to obtain a transverse image of the anastomosis using Power Doppler and B-mode imaging, respectively.

### Inspection

The lateral ridge detected in one correct anastomosis during scanning, proved to be a small flap of the distal IMA end that was inverted between two suture bites (Figure 3). This anastomosis also showed outflow corner narrowing. In all incorrect anastomoses, a suture was seen transversing the middle of the anastomotic orifice (Figure 2). One incorrect anastomosis revealed an unintended second suture cross-over at the level of the heel.



**Figure 2.** Longitudinal ultrasound image of an incorrect anastomosis with suture cross-over with corresponding macroscopic view of the anastomotic orifice after incision of the posterior wall of the LAD. Arrow indicates overcrossing suture. IMA: Internal Mammary Artery, LAD: Left Anterior Descending Coronary Artery. (Color image: page 165)



**Figure 3.** Transverse ultrasound image of an anastomosis constructed with the intent to be correct which revealed a ridge (arrow) at the level of the anastomotic orifice. IMA: Internal Mammary Artery, LAD: Left Anterior Descending Coronary Artery. (Color image: page 165)



### **Off-line anastomosis assessment by independent observers**

A total of 30/32 image sets were scored. Two sets were unavailable due to failed data storage (manual scanning of 1 correct and 1 incorrect anastomosis). Of the remaining 15 correct anastomosis sets, 13 were scored as correct and 2 (endoscopic and manual image sets of the same anastomosis) as incorrect. The latter was the anastomosis that revealed irregularities at macroscopic inspection. Of the incorrect anastomosis sets, 15 out of 15 were scored as incorrect. Thus, all anastomosis image sets were scored accurately by both observers. Overall, scoring required less than one minute per anastomosis.

## DISCUSSION

The principal results of this study are: (1) Epicardial ultrasound enabled closed-chest visualization and assessment of the coronary artery anastomosis in a median of 3 minutes; (2) correct and incorrect anastomoses were identified properly during off-line assessment.

### Anastomotic quality control

In conventional coronary artery bypass grafting (CABG), several techniques have been described to intra-operatively assess anastomotic quality including: graft flow measurement [8], epicardial ultrasound imaging [4,9,10], and fluorescence imaging [11]. All these techniques have one or more features that limit or prohibit their use in TECAB. Angiography [12] is used in TECAB, and still considered the gold standard, but is invasive, time consuming and unavailable in most operating rooms. Flowmetry is fast and easy to use but may require removal of periadventitial tissue from the graft to ensure proper contact. This may damage the graft. Furthermore, only severe stenoses are detected (>75%) [8]. Fluorescence imaging uses a large camera to obtain images, preventing its use endoscopically [11]. In addition, the penetration depth of a fluorescence camera is limited, making visualization of vessels and anastomoses embedded in the epicardial fat and/or myocardium difficult. Epicardial ultrasound has shown promising results in open-chest CABG [4,9,10]. It is non-invasive, relatively inexpensive, fast, provides anatomical information and can also be used to select the optimal anastomotic site on the target artery [13]. The relatively large size of the transducer has limited its use mostly to the anterior side of the heart. With the recent development of smaller and higher frequency transducers they are under renewed interest [4,9,10,13].

In addition to the IMA-LAD anastomoses, we endoscopically scanned two IMA to obtuse marginal anastomoses in the pig model, indicating that the mini-transducer is small enough for visualization of anastomoses on the posterior side of the heart [unpublished observation].

### Suture cross-over anastomosis

We feel that the suture cross-over is a technical construction error that might occur during endoscopic anastomosis construction. It is conceivable that such an error would go unnoticed intra-operatively, possibly leading to anastomotic failure during longer follow up periods. Furthermore, it is difficult to detect by any other quality control method.



### **Validation by macroscopic inspection**

Macroscopic inspection at 4,5x magnification provides a true anatomical inspection and supplies more detailed information than the clinical gold standard angiography. We have made angiograms of suture cross-over anastomoses on ex-vivo hearts and found the suture cross-over error is very hard to detect angiographically (unpublished observation).

### **Epicardial ultrasound scanning**

Overall, endoscopic scanning time consumption was acceptable (maximum 464 s). Moreover, not all scanning steps as explored in this study need to be performed, as longitudinal still, transverse still and sweep B-Mode images provided most information. These were obtained by endoscopic scanning in 64 s (39-217) for correct and 133 s (58-242) for incorrect anastomosis.

### **Off-line assessment**

Even though epicardial ultrasound images are most easily interpreted on-line, all image sets were scored accurately off-line by both observers, including the unintended errors in one correct anastomosis (scored as incorrect). This illustrates the potential of epicardial ultrasound for anastomotic quality assessment. However, the anastomosis type was known to the person scanning the anastomosis. Potentially, this might have introduced a bias.



## **CONCLUSION**

In the pig, epicardial 13 MHz ultrasound was able to visualize correctly and incorrectly constructed coronary anastomoses in closed-chest beating heart CABG. During off-line assessment all anastomoses were accurately identified as correct or incorrect by two blinded observers. It therefore is a promising technology for intra-operative anastomotic quality control in totally endoscopic coronary artery bypass surgery.

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# Geometry assessment of coronary artery anastomoses with construction errors by epicardial ultrasound



5

T.C. Dessing, R.P.J. Budde, R. Meijer, P.F.A. Bakker, C. Borst, P.F. Gründeman

Heart Lung Center Utrecht, University Medical Center Utrecht, Utrecht,  
the Netherlands

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**ABSTRACT**

**Objective:** There is concern about the quality of the distal anastomosis in off-pump coronary artery bypass grafting. We investigated the impact of specific construction errors on anastomotic geometry using epicardial ultrasound.

**Methods:** Twelve ex-vivo pressure perfused porcine and 5 isolated post-mortem human hearts were used to construct 35 internal mammary artery (IMA) to coronary artery anastomoses, either without (n=7) or with a standardized construction error (oversutured toe, oversutured heel, cross-over or purse string (each error, n=7)). The anastomotic geometry was visualized and measured by a 13 MHz ultrasound mini-transducer. Impression cast material was used to validate anastomotic geometry.

**Results:** All 28 errors were visualized properly. Two unintended construction abnormalities were observed. In the porcine heart, the ratio of anastomotic orifice area and outflow corner area was  $1.3 \pm 0.2$  (mean  $\pm$  standard deviation) in the control group and reduced in the error groups: oversutured toe,  $0.6 \pm 0.2$  (p=0.001); oversutured heel,  $0.9 \pm 0.2$  (p=0.037); cross-over,  $0.4 \pm 0.2$  (p<0.001); purse string,  $0.3 \pm 0.2$  (p<0.001). None of the errors reduced the area of the inflow or outflow corner itself compared to the recipient coronary artery. In the human heart, all construction errors as well as wall plaque were visualized properly. In all anastomoses, ultrasound geometry corresponded to cast geometry.

**Conclusions:** Ex-vivo, epicardial 13 MHz ultrasound enabled accurate visualization and assessment of four different construction errors in the coronary anastomosis. All errors reduced the area of the anastomotic orifice, but not the inflow or outflow corner.

**Presented:**

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## INTRODUCTION

Concern has been raised about the quality of the distal anastomosis in off-pump and minimally invasive direct coronary artery bypass grafting (MID-CABG) [1]. Anastomotic suturing may be hampered by suboptimal conditions, such as limited access and working space, residual motion of the target area, poor angle of view and/or torrential back-flow. Due to these surgical limitations, there is the risk of technical construction errors, which is indicated by the detection of an immediate angiographic stenosis in up to 9% of patients undergoing MIDCABG operations [1]. However, little is known about the alteration of anastomotic geometry by specific construction errors [2,3].

In the 1980s, the potential value of epicardial ultrasound for the quantitative assessment of coronary artery luminal and wall dimensions has been demonstrated [4], as well as for coronary anastomosis visualization [5]. Recently, IVUS also showed to be a promising method to determine anastomosis dimensions [6]. With modern improvements in transducer size and technology [7,8], epicardial ultrasound may prove a helpful tool to assess the impact of construction errors on anastomotic geometry.

In pressure perfused porcine and human hearts, we investigated the epicardial ultrasound 2D presentation and geometry alteration of specific construction errors in coronary artery anastomoses. The constructed errors consisted of an oversutured toe, an oversutured heel, a cross-over and a purse string.

## MATERIAL AND METHODS

### Perfusion model-setup

On 12 ex-vivo porcine hearts 25 internal mammary artery (IMA) to left anterior descending coronary artery (LAD) anastomoses were constructed, and on 5 isolated post-mortem human hearts common target coronary arteries were used to construct 10 anastomoses. All conduits used for grafting were porcine IMA's.

After construction, the IMA was cannulated to pressure perfuse ( $95 \pm 9$  mm Hg) the anastomosis with saline using a Langendorff setup. The LAD proximal to the anastomosis was snared.

### Surgical procedure

All anastomoses were constructed end-to-side under an operating microscope (magnification x8, wild M680, Leica AG, Heerburg, Switzerland), using a running suture technique with a prolene 7-0 or 8-0 suture. The anastomoses were constructed with the intent either to be fully patent or to contain one of the following standardized construction errors; an oversutured toe, an oversutured heel, a cross-over or a purse string. In the porcine hearts, 5 of each anastomosis type were constructed, and in the post-mortem human hearts, 2 of each type were constructed.

The oversutured toe, oversutured heel and cross-over anastomoses were made by interlocking two suture bites on opposite sides of the arteriotomy in the toe area, the heel area or at the side, respectively. The purse string anastomosis was made by pulling heavily on the suture-ends before fashioning the suture.

### Ultrasound equipment

As before [7], a commercially available, high frequency (up to 13 MHz in B-Mode), linear array mini-transducer (UST-5531, Aloka, Tokyo, Japan) with an image width of 10 mm (transducer dimensions: 15 x 6 x 9 mm) was used. The transducer was placed in a gel filled probe cover (Ultracover, International Medical Products, Inc, Zutphen, the Netherlands), for clear visualization of the anterior wall of the vessels. Measurements accurate to 0.1 mm were performed using the electronic calipers of the ultrasound system. The 2-point phantom resolution of the transducer is  $<0.25$  mm (unpublished). Imaging was performed with an Aloka SSD 5000 Prosound ultrasound system (Aloka, Tokyo, Japan). Images were stored on a laptop to enable retrospective analysis.



### Scanning technique and measurements

Before anastomosis construction, the external diameter of the unpressurized coronary artery, the IMA and the length of the arteriotomy were measured (accurate to 0.1 mm) using a ruler. All anastomoses were scanned by the same investigator (TCD) who was aware of which type of anastomosis was scanned.

In the porcine heart, the anastomosis was first delineated in longitudinal and transverse planes using B-mode imaging. Subsequently, an optimal longitudinal image (defined as anastomotic orifice and in- and outflow corner captured in one image) and transverse images in B-mode were obtained. In frozen images of the anastomosis site, measurements were performed with the electronic calipers of the ultrasound system. In the anastomosis (figure 1), the size of the anastomotic orifice (1), internal diameters of the coronary artery at the toe site (3), heel site (5) and midways toe/heel site (7) were measured in both planes perpendicular to each other. The internal vessel area ( $A_1, A_3, A_5,$  and  $A_7$ ) at these sections was calculated using the ellipsoid area formula ( $\pi r_1 r_2$ ). The areas of the IMA ( $A_2$ ) and the coronary artery maximally 3 mm distal to the anastomosis ( $A_4$ ) and maximally 3 mm proximal to the anastomosis ( $A_6$ ) were calculated with the circle area formula ( $\pi r^2$ ) using the internal diameter measured in the longitudinal image (Figure 1). The area ratios  $A_1/A_2, A_1/A_3,$  and  $A_1/A_4$  were calculated to assess whether the specific construction error induced anastomotic orifice narrowing compared to IMA and target artery dimensions. The ratios  $A_3/A_4, A_5/A_6,$  and  $A_7/\text{mean } A_3;A_5$  were calculated to assess the impact on the outflow corner, inflow corner and the posterior wall of the coronary artery, respectively.

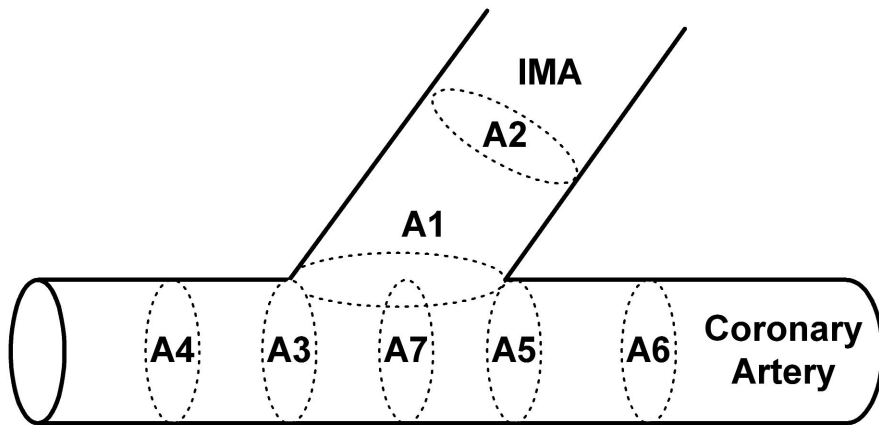
In the post-mortem human hearts, optimal images were obtained in both planes to visualize the geometry of the anastomosis.

### Statistical analysis

Statistical analysis was only done in the porcine group. Data are presented as mean  $\pm$  standard deviation (SD). One-way analysis of variance together with a post hoc comparison (Dunnett) was used to evaluate differences in the specific area ratios between the four construction error groups (oversutured toe, oversutured heel, cross-over and purse string) and the control group. Area  $A_1$  was normalized to the arteriotomy length, area  $A_2$  to the IMA diameter and areas  $A_3$  and  $A_4$  to the LAD diameter before statistical comparison of the area ratios  $A_1/A_2, A_1/A_3$  and  $A_1/A_4$  was made between the different error groups and the control group. A value of  $p < 0.0125$  was considered statistically significant.

### Validation

A polyvinylsiloxane impression material (Kerr Co, Romulus, MI, USA) was injected into the anastomosis and coronary artery through the IMA. After the hardening process, the impression material was removed from the vessels and the obtained 3D cast of the anastomosis was used to validate ultrasound anastomotic geometry qualitatively.



**Figure 1.** Schematic drawing of an anastomosis. ( $A_1$  = area anastomotic orifice,  $A_2$  = cross-sectional area IMA,  $A_3$  = area LAD at toe site,  $A_4$  = area LAD 3 mm distal to toe site,  $A_5$  = area LAD at heel site,  $A_6$  = area LAD 3 mm proximal to heel site,  $A_7$  = area LAD mid-way heel/toe site). IMA = internal mammary artery, LAD = left anterior descending coronary artery.

## RESULTS

### Porcine hearts

External vessel diameters are listed in table 1. All anastomoses were easily visualized in both longitudinal and transverse planes. The four different construction errors presented each with a characteristic alteration of anastomotic geometry. The oversutured toe and heel were seen longitudinally as ridges reducing the length of the anastomotic orifice by  $26\% \pm 7$  (mean  $\pm$  SD) and  $14\% \pm 10$ , respectively (Figure 2). The cross-over presented longitudinally as a bright echo from the suture in the middle of the anastomotic orifice resulting in two small orifices and a longitudinal diameter reduction of  $22\% \pm 12$  (figure 2). The purse string anastomosis showed a reduced anastomotic orifice in both scan planes (figure 2). In cross-section, all constructed errors showed a reduced width of the anastomotic orifice.

The area ratios  $A_3/A_4$ ,  $A_5/A_6$ , and  $A_7/\text{mean } A_3;A_5$  for the four different groups are presented in table 1. No statistically significant differences were observed between the ratios  $A_3/A_4$  and  $A_5/A_6$  of the different error groups and the control group. Thus, the specific construction errors had no effect on the in- or outflow corner of the anastomoses. After normalization of areas  $A_1$ ,  $A_2$ ,  $A_3$  and  $A_4$ , the area ratios  $A_1/A_3$  and  $A_1/A_4$  of all error groups, but for the oversutured heel, were significantly smaller than in the control group (table 2). In each of the four constructed errors the area of

**Table 1.** Measurements (mm) and area ratios for the control group and the four different construction errors in the porcine hearts.

	Control	Oversutured toe	Oversutured heel	Cross-over	Purse string
External LAD diameter	$3.4 \pm 0.6$	$2.7 \pm 0.5$	$2.7 \pm 0.6$	$2.4 \pm 0.5$	$2.5 \pm 0.6$
External IMA diameter	$3.4 \pm 0.5$	$3.9 \pm 0.7$	$3.2 \pm 0.2$	$3.5 \pm 0.4$	$2.8 \pm 0.4$
Arteriotomy length	$7.2 \pm 1.2$	$7.1 \pm 1.8$	$7.0 \pm 1.4$	$8.0 \pm 0.9$	$5.4 \pm 0.5$
$A_3/A_4$	$1.2 \pm 0.1$	$1.1 \pm 0.2$	$1.1 \pm 0.2$	$1.5 \pm 0.5$	$1.2 \pm 0.2$
$A_5/A_6$	$1.2 \pm 0.1$	$1.2 \pm 0.1$	$1.1 \pm 0.5$	$1.3 \pm 0.2$	$1.2 \pm 0.3$
$A_7/\text{mean } A_3;A_5$	$1.4 \pm 0.0$	$1.2 \pm 0.2$	$1.3 \pm 0.1$	$1.1 \pm 0.2$	$1.2 \pm 0.1$

Areas  $A_3$  to  $A_7$ , see figure 1. Values presented as mean  $\pm$  SD. No statistically significant difference was observed between  $A_3/A_4$  and  $A_5/A_6$  of the different error groups and the control group.  $A_3$  = LAD area at toe site,  $A_4$  = LAD area 3 mm distal to toe site,  $A_5$  = LAD area at heel site,  $A_6$  = LAD area 3 mm proximal to heel site,  $A_7$  = LAD area midway heel/toe site, IMA = internal mammary artery, LAD = left anterior descending coronary artery.

the anastomotic orifice was significantly reduced relative to the graft cross-sectional area (ratio  $A_1/A_2$ , table 2).

One control anastomosis showed a minor technical abnormality. A small ridge (0.7 mm) at the toe site was visible, due to an extra stitch placed at the toe area.

At the anastomotic site, small septal perforators with diameters ranging from 0.2-0.7 mm were easily spotted. In all anastomoses, ultrasound geometry corresponded qualitatively with cast geometry findings, including the location of septal perforators and side-branches.

**Table 2.** Area ratios after normalization of area  $A_1$  to arteriotomy length, area  $A_2$  to IMA diameter and areas  $A_3$  and  $A_4$  to LAD diameter.

Ratio	Control	Oversutured Toe	p-value	Oversutured Heel	p-value	Cross-over	p-value	Purse string	p-value
$A_1/A_2$	$1.1 \pm 0.2$	$0.5 \pm 0.3$	< 0.001	$0.6 \pm 0.1$	0.003	$0.3 \pm 0.1$	< 0.001	$0.3 \pm 0.2$	< 0.001
$A_1/A_3$	$1.3 \pm 0.2$	$0.6 \pm 0.2$	0.001	$0.9 \pm 0.2$	0.037	$0.4 \pm 0.2$	< 0.001	$0.3 \pm 0.2$	< 0.001
$A_1/A_4$	$1.5 \pm 0.4$	$0.7 \pm 0.3$	0.002	$1.0 \pm 0.2$	0.036	$0.5 \pm 0.3$	< 0.001	$0.3 \pm 0.2$	< 0.001

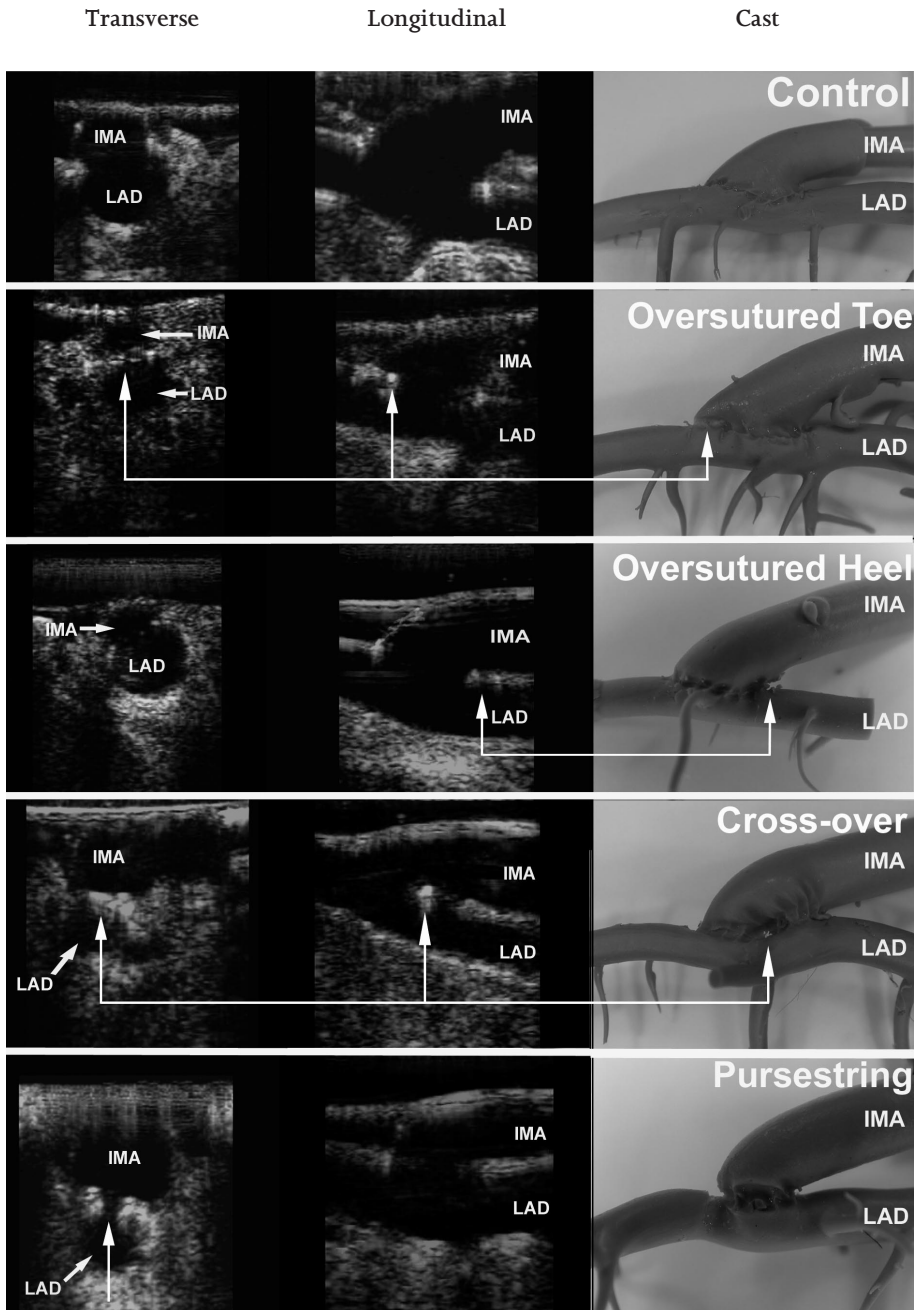
Areas  $A_1$  to  $A_4$ , see figure 1. Values presented as mean  $\pm$  SD.

$A_1$  = anastomotic orifice area,  $A_2$  = IMA area,  $A_3$  = LAD area at toe site,  $A_4$  = LAD area 3 mm distal to toe site, IMA = internal mammary artery, LAD = left anterior descending coronary artery.

### Post-mortem human hearts

External recipient coronary artery diameter ranged from 1.5 to 2.5 mm (median 2.0 mm).

In one control anastomosis, the complete outline of the anastomotic site could not be visualized due to the presence of abundant plaque with severe calcification. All constructed errors were properly visualized in longitudinal and transverse images. One oversutured toe anastomosis showed an adventitial flap waving up and down in the anastomotic orifice closing it off almost completely. This was confirmed by the cast. Presence and extent of coronary pathology was well visualized and quantifiable. In all anastomoses, ultrasound geometry corresponded qualitatively with cast geometry.



**Figure 2.** Longitudinal and transverse ultrasound images and corresponding cast of (from top to bottom) a control, oversutured toe, oversutured heel, cross-over and purse string anastomosis. Arrows indicate ridges in the oversutured toe and heel anastomoses, a suture in the cross-over anastomosis as well as the severely narrowed anastomotic orifice in the purse string anastomosis. IMA = internal mammary artery, LAD = left anterior descending coronary artery.

## DISCUSSION

The principal results of this study are: (1) In the porcine hearts, all four standardized anastomosis construction errors presented with a significant reduction in anastomotic orifice area; (2) In the ex-vivo porcine heart, all 25 anastomoses were visualized properly, including the anatomy of the LAD at the anastomosis site; (3) In the post-mortem human heart, all 10 but one (due to calcification) anastomoses were visualized properly, including the complete outline of the anastomosis site and presence of plaque.

The four constructed errors did not influence the in- or outflow corner area ratios of the anastomoses (table 1), in contrast to the anastomotic orifice ( $A_1$ ) area ratios which were significantly reduced for all the error groups except the oversutured heel (table 2).

The 13 MHz resolution of the mini-transducer proved sufficient to visualize the complete outline and characteristics (septal perforators, coronary pathology) of the anastomotic site. Based on measurements made with the electronic calipers of the ultrasound system, calculations could be made to assess the impact of the specific construction error on anastomotic geometry. Apart from the intentional construction errors, two unintended technical abnormalities (ridge due to extra stitch and adventitial flap) were revealed. Both unintended errors mimic clinical practice too. Thus, 13 MHz epicardial ultrasound may be a valuable diagnostic tool to assess anastomotic quality prior to chest closure. The small size of the present mini-transducer allows its application in between the suction pods of a cardiac stabilizer [7,10].

Besides the use for anastomotic geometry assessment [5,8,9], epicardial ultrasound may help to localize the target artery and choose the anastomotic site based on the evaluation of its wall thickness, plaque morphology (calcifications) and lumen diameter [4,5,10]. We expect high-frequency epicardial ultrasound to become a useful intraoperative diagnostic modality that is a non-invasive, fast, simple, and relatively inexpensive method in both on- and off-pump coronary artery bypass surgery. Angiography, currently considered the gold standard, is invasive, time consuming, expensive and not always immediately available in the operating room [1]. An additional disadvantage is the uncertain significance of early abnormal findings, which could lead to unnecessary revisions. Quantitative analysis of the angiogram is possible, but time consuming and displays far less anatomical detail of the anastomosis. Epicardial ultrasound in contrast, clearly displays the anatomy and dimensions of the anastomosis and therefore can differentiate for example between gross anastomotic construction errors, adventitial flaps and thrombus or spasm, which resolves after the immediate postoperative period.

Another widely used non-invasive method to assess bypass graft function is transit time flowmetry. However, flowmetry provides no anatomical information of the anastomosis. The observed flow depends on other factors as well. A crucial limitation is that flowmetry will only detect a severely stenosed anastomosis ( $> 75\%$ ) [11].

Next to flowmetry, ultrasound can easily be employed as a complementary quality control method to provide information about bypass graft function and anastomotic geometry, respectively. For example, epicardial ultrasound may detect an adventitial flap in the anastomotic orifice in the presence of a normal flow recording. Flowmetry, on the other hand, may detect reduced volume flow in the presence of a flawless anastomosis, indicating either a proximal anastomosis problem, graft kinking, graft spasm, or reduced distal runoff.

The limitation of this study is its laboratory setting, with pressure perfusion by saline of the bypass graft. In addition, the merits and limitations of the present transducer for detection of anastomosis construction errors in the clinical setting and in an observer blinded experimental setting remain to be established.

In conclusion, ex-vivo, epicardial 13 MHz ultrasound was successful in accurately visualizing and assessing the geometry of four different construction errors in the distal coronary anastomosis. All errors reduced the anastomotic orifice area.

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# Detection of construction errors in ex-vivo coronary artery anastomoses by 13 MHz epicardial ultrasound



6

R.P.J. Budde, R. Meijer, T.C. Dessing, C. Borst, P.F. Gründeman.

Heart Lung Center Utrecht, University Medical Center Utrecht, Utrecht, the Netherlands

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## ABSTRACT

**Objective:** Intraoperative detection of suboptimal coronary anastomoses allows revision before chest closure. We evaluated an epicardial 13 MHz ultrasound mini-transducer as a means to detect three different coronary anastomosis construction errors.

**Methods:** In total, 120 internal mammary artery to coronary artery anastomoses were constructed correctly (n=60) or incorrectly (n=60) with one technical error: suture cross-over, purse string or deep toe stitch (n=20 each) using ex-vivo pressure perfused porcine (96 anastomoses) and human hearts (24 anastomoses). Two blinded observers scanned and scored the anastomoses using epicardial ultrasound. In 24 human and 24 porcine anastomoses, angiograms were made of 24 correct and 24 incorrect anastomoses and scored by two other blinded observers. Angioscopy and cast injection served as a reference.

**Results:** Overall, 119/120 anastomoses were accurately scored as correct or incorrect within 67 s (8-381) (median with range) by both observers (sensitivity 0.98, specificity 1.00, kappa 1.00, (1.00, 1.00 and 1.00 in angiography subset, respectively)). One deep toe stitch that induced outflow corner stenosis was spotted by both observers but regarded insignificant and hence, inaccurately scored as correct. In 5 anastomoses, unintended irregularities were detected. By angiography anastomoses were accurately scored with a sensitivity of 0.75 and specificity of 0.81 ( $p < 0.001$ , vs. ultrasound) and kappa of 0.54. Angioscopy and cast confirmed ultrasound findings and did not reveal irregularities other than detected by ultrasound.

**Conclusions:** Ex-vivo, epicardial 13 MHz ultrasound allowed rapid and accurate evaluation of coronary anastomoses and detected technical construction errors with higher sensitivity and specificity than angiography.

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## INTRODUCTION

There is concern about the increased risk of anastomosis construction errors in (minimally invasive) off-pump coronary artery bypass grafting (CABG) because the suturing process is technically more demanding than surgery on the arrested heart [1]. In on-pump CABG, total occlusion or stenosis >50% is seen in up to 9% of grafts at short term angiographic follow up [1]. Angioscopy reveals irregularities and technical errors, that include purse string effect, intimal flaps, thrombus formation and misplaced sutures, in up to 24% of anastomoses [2,3].

An intraoperative technique to assess anastomotic quality may improve patency rates in all approaches to CABG, because suboptimal anastomoses may be revised before chest closure [4]. Currently, angiography is the gold standard, but it is scarcely used intra-operatively [5]. Epicardial ultrasound for anastomosis visualization and assessment was described in the 1980s [6]. Despite promising results [6], technical limitations prevented widespread use. Recently, we described a new high frequency epicardial ultrasound mini-transducer (15 x 9 x 6 mm) for assessment of the left anterior descending coronary artery (LAD) in patients [7] and geometry assessment of anastomoses [8,9]. Due to its small size and high frequency (up to 13 MHz in B-mode), this mini-transducer has potential for routine intra-operative assessment of anastomoses at all locations on the heart.

The aim of this study was to investigate the ability of two blinded observers to detect and characterize three different standardized construction errors in coronary anastomoses on ex-vivo hearts using the 13 MHz mini-transducer and compare it to the gold standard angiography.

## MATERIAL AND METHODS

### Ex-vivo porcine and post-mortem human hearts

On 46 ex-vivo porcine hearts, 96 internal mammary artery (IMA) to LAD anastomoses were constructed. On 4 isolated post-mortem human hearts, a total of 24 anastomoses were constructed on the LAD, diagonal branches, right coronary artery and circumflex coronary artery. All grafts were porcine IMA's.

The coronary arteries were cannulated proximally to pressurize (80 mm Hg) the anastomoses with saline using a Langendorff setup.

### Anastomosis construction

All 120 anastomoses were randomly constructed by a single investigator (RPJB) either correctly (n=60) or with one standardized construction error (n=60), either a suture cross-over, purse string or a deep toe stitch (n=20 each). The distribution of anastomosis types is summarized in table 1. The cross-over anastomosis was constructed by interlocking two suture bites on opposite sides of the arteriotomy, approximately one third of the anastomotic orifice length from the toe. The purse string anastomosis was made by pulling heavily on the suture-ends before fashioning the suture. In the deep toe suture bite anastomosis, the suture was passed through the posterior wall of the coronary artery at the toe.

Anastomotic sites on the porcine LAD were chosen at random. In the human hearts (24 anastomoses), the anastomosis was deliberately placed in sites with (n=12) and without (n=12) atherosclerotic disease as determined by digital palpation and epicardial ultrasound scanning (table 1).

**Table 1.** Number and distribution of anastomosis types.

Anastomosis type	Porcine hearts	Human hearts	Total
Control	48 (12)	12 (12) {6}	60 (24) {6}
Suture cross-over	16 (4)	4 (4) {2}	20 (8) {2}
Purse string	16 (4)	4 (4) {2}	20 (8) {2}
Deep toe stitch	16 (4)	4 (4) {2}	20 (8) {2}
Total	96 (24)	24 (24) {12}	120 (48) {12}

Numbers in brackets represent anastomoses in which angiography was performed, numbers in accolades represent anastomoses constructed in vessel area with plaque.

### **Ultrasound equipment**

As before [8,9], a commercially available, high frequency (up to 13 MHz in B-Mode), linear array mini-transducer (Aloka, Tokyo, Japan; transducer dimensions: 15 x 6 x 9 mm) was used. The image scan width is 10 mm. The mini-transducer was placed in a handling tool that can be held like a pencil [7]. Imaging was performed with an Aloka SSD 5000 Prosound ultrasound system. Ultrasound transmission gel (Parker Laboratories, Fairfield, NJ) was applied directly onto the anastomosis for proper contact.

### **Ultrasound scanning**

Two observers (RM and TCD) blinded for the anastomosis type, scanned and scored all anastomoses as described below. Both had extensive experience in echocardiographic scanning of coronary anastomoses. Scan time needed to obtain sufficient information for scoring was recorded.

### **Angiography**

In a subgroup of 24 porcine anastomoses (12 correct, 4 of each error) and all 24 human heart anastomoses (12 correct, 4 of each error), angiography (C-arm, Pulsera, Philips Eindhoven, the Netherlands) of the graft and anastomosis was performed in at least two different oblique projections by selectively injecting contrast media through the IMA (table 1).

Two independent observers (JMPGE and CB) blinded for the anastomosis type, scored the angiograms as described below.

### **Anastomosis scoring by ultrasound and angiography**

Anastomoses were scored as either correct or construction error. The location and appearance of detected technical errors and irregularities were indicated in a schematic drawing of the anastomosis. The location was categorized into one or more of the following categories: IMA, anastomotic orifice, inflow corner, outflow corner or the recipient coronary artery.

### **Angioscopy and cast**

During perfusion, a 2.4 mm angioscope (11281A, Karl Storz, Germany) was introduced through the free proximal end of the IMA to visualize the anastomosis [2,3].

A polyvinylsiloxane impression material (Kerr Co, Romulus, MI, USA) was injected into the IMA to fill the coronary artery, anastomosis and the IMA

itself. The resulting 3D cast of the anastomosis was removed from the vessels after hardening and visually inspected at 3.5x magnification. Angioscopy and cast findings combined served as a reference for ultrasound and angiography findings.

### **Statistical analysis**

Kappa value was calculated to rate the agreement between observers and interpreted according to Landis and Koch [10]. Sensitivity and specificity were calculated based on the scoring of both observers combined. Scores were compared using chi-square test. Scan times are presented as median with range and compared using the Wilcoxon rank sum test.

## RESULTS

### Anastomosis construction

External inspection could not discriminate incorrect from correct anastomoses.

### Ultrasound scanning and scoring

All 120 anastomoses were easily visualized within 67 s (8-381) [median (range)]. Visualization of the porcine anastomoses (61 s (8-381)) was faster than the human anastomoses (92 s (14-256),  $p < 0.001$ ). Representative ultrasound images of a control anastomosis are presented in figure 1.

Both observers accurately scored 119/120 (99%, table 2) anastomoses as correct or construction error (sensitivity 0.98, specificity 1.00 and kappa 1.00). In most anastomoses, the presence of a construction error was detected directly upon the first visualization of the anastomosis. In the one inaccurately scored anastomosis (deep toe stitch anastomosis), slight narrowing of the outflow corner was spotted, but considered insignificant and hence scored as correct by both observers.

Each of the construction errors presented with a distinct appearance on the ultrasound image. The cross-over anastomosis presented with an echodense spot in the anastomotic orifice (Figure 2). In the purse string anastomosis, the anastomotic orifice was narrowed (Figure 3). In the deep toe stitch anastomosis, narrowing of the outflow corner was seen (Figure 4). All errors were seen in both the longitudinal and transverse scan plane.

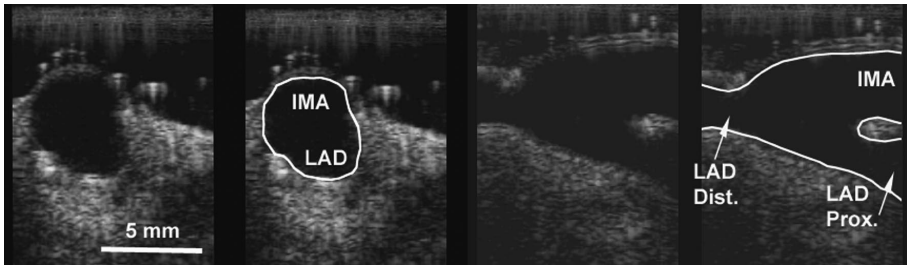
One purse string anastomosis presented as a control anastomosis on ultrasound and was scored as such by both observers. In 5 anastomoses, unintended irregularities were detected by both observers: outflow corner

**Table 2.** Scoring results of both observers combined.

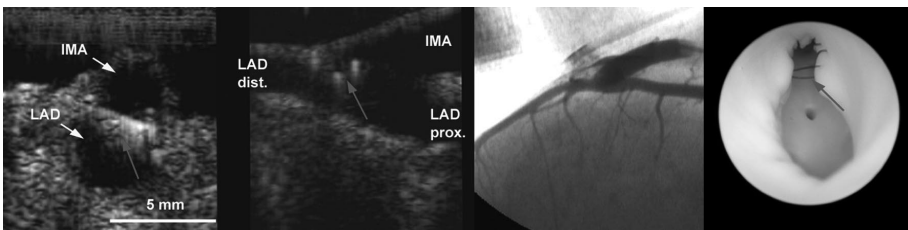
Scoring		Ultrasound	Angiography	P-value
Correct/Construction error	% accurate	99 % (100 %)	78 %	] <0.001
	Sensitivity	0.98 (1.00)	0.75	
	Specificity	1.00 (1.00)	0.81	
	Kappa	1.00 (1.00)	0.54	
Location of error	% accurate	100 % (100 %)	68 %	-

Percentages given as the mean of the percentages of the two observers. Percentages in brackets are based on the subset of anastomoses in which angiography was performed.



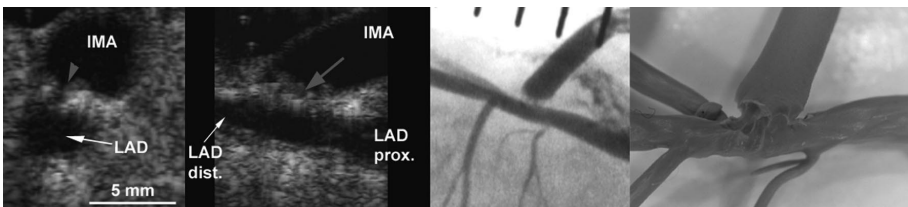


**Figure 1.** Correctly constructed control anastomosis: transverse (left panels) and longitudinal ultrasound image (right panels). IMA, internal mammary artery; LAD, left anterior descending coronary artery; Prox, proximal; Dist, distal.



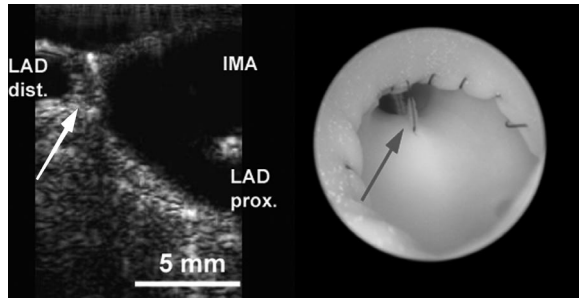
**Figure 2.** Suture cross-over anastomosis: panels from left to right, transverse and longitudinal ultrasound image, angiogram and angioscopic image taken from the IMA towards the outflow corner. Note in the longitudinal ultrasound image the suture traversing twice the anastomotic orifice (arrow). The transverse image was taken at the level of the overcrossing suture. The anastomosis appeared normal on the angiogram. IMA, internal mammary artery; LAD, left anterior descending coronary artery; Prox, proximal; Dist, distal.

(Color image: page 168)

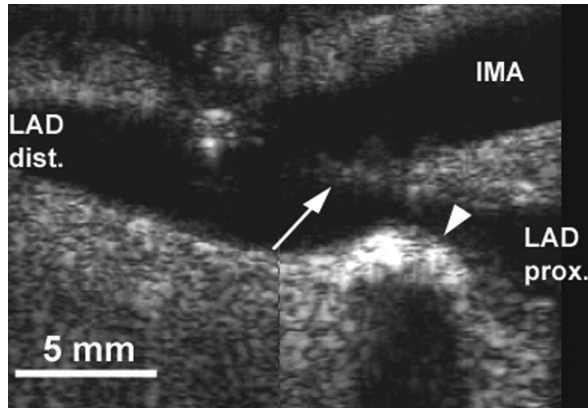


**Figure 3.** Purse string anastomosis: panels from left to right, transverse and longitudinal ultrasound image, angiogram and cast. Note in the transverse ultrasound image the severe narrowing of the anastomotic orifice (arrow) and the small resulting lumen (arrowhead). IMA, internal mammary artery; LAD, left anterior descending coronary artery; Prox, proximal; Dist, distal.

(Color image: page 168)



**Figure 4.** Deep toe stitch anastomosis: longitudinal ultrasound image (left panel) and angioscopic image from the IMA towards the outflow corner (right panel). Note in the angioscopic image the suture passing through the posterior wall of the LAD (arrow). IMA, internal mammary artery; LAD, left anterior descending coronary artery; Prox., proximal; Dist, distal. (Color image: page 168)



**Figure 5.** Composite longitudinal ultrasound image of calcification in a purse string anastomosis (arrowhead). Note its bright appearance and distinct echo shadowing. In the anastomotic orifice the lateral wall can be seen due to narrowing by the pursestring effect (arrow).

narrowing with LAD disruption in a purse string anastomosis, additional purse string effect of various degrees in 3 anastomoses and an inflow corner narrowing in one anastomosis. All these findings were confirmed by angioscopy and cast and analyzed as such.

In several anastomoses, tissue was detected in the anastomosis by only the second observer. It is conceivable that sometimes tissue was introduced during the angioscopy procedure that was performed in between scanning by the two observers. This is a known complication of angioscopy [2]. These findings were not used in the analysis.

In all anastomoses scored as construction error, the error location was accurately scored by both observers (kappa 1.0). The sort of error was correctly identified in 58/60 anastomoses by observer #1 and in 54/60 anastomoses by observer #2 (93% overall).

Presence of calcifications in the human hearts was not a confounding factor for image interpretation as calcifications presented with clear echocardiographic shadowing (Figure 5) making them easy to discriminate from construction errors.

### Angiography

Of the 48 anastomoses in which angiography was performed, 36 and 39 were accurately scored as correct or construction error by observer #3 and #4, respectively (sensitivity 0.75, specificity 0.81, kappa 0.54, table 2). In these 48 anastomoses, the sensitivity and specificity of ultrasound was 1.0 and 1.0, respectively ( $p < 0.001$  vs. angiography). The suture cross-over error proved to be particularly difficult to detect by angiography (figure 2). Of the inaccurately scored anastomoses, five were inaccurately scored by both observers.

The error location in anastomoses accurately scored as construction error was accurately identified in 10/18 and 14/18 anastomoses (68 % accurate, overall) by observer #3 and #4, respectively. Three anastomoses were inaccurately scored due to the presence or presumed presence of plaque and calcification.

Angiographically, the specific kind of construction error could not be determined reliably. Only distinction between outflow corner and orifice narrowing could be made.

### Angioscopy and cast

Angioscopy and cast findings corresponded with ultrasound findings and no irregularities other than those detected by ultrasound were noted.

## DISCUSSION

The principal findings of this study are: (1) Epicardial ultrasound enabled detection of construction errors in coronary anastomoses with significantly higher sensitivity and specificity than by angiography; (2) Using epicardial ultrasound the location and type of error could be accurately determined in 100% (68% by angiography) and 93%, respectively, of the anastomoses in which an error was detected; (3) Ultrasound scanning required only a median of 67 seconds to assess an anastomosis.

### Anastomosis quality control

With the advent of off-pump and minimally invasive CABG there has been a renewed interest in techniques to intra-operatively assess distal anastomosis quality [4,11,12]. Currently, only graft flow measurement is used on a large scale [11]. Graft flow measurement, however, can only detect severe stenosis (>75%) and provides no information about its location. Furthermore, there is no clear cut-off point for adequate graft flow and thus it may underestimate the number of suboptimal anastomoses. For various reasons, the gold standard angiography is not used frequently, the most important ones being that it is invasive, not readily available in the OR and time consuming [5].

The potential of epicardial ultrasound for coronary anastomosis assessment has been recognized almost 20 years ago [6]. Technical transducer limitations, however, have prevented widespread clinical introduction. The current mini-transducers allow access more easily. To date, no detailed evaluation has been reported of the ability of epicardial ultrasound to detect and characterize different technical errors in coronary anastomoses in comparison to the gold standard angiography.

In the subgroup of 48 anastomoses, epicardial ultrasound enabled detection of construction errors with significantly higher sensitivity (1.00) and specificity (1.00) than achieved with angiography (0.75 and 0.81, respectively). When calculated from all 120 anastomoses in the study, the sensitivity and specificity of epicardial ultrasound was 0.98 and 1.00, respectively.

In addition, epicardial ultrasound enabled discrimination between narrowing due to suture errors or due to calcifications that present with a distinct echo shadowing (Figure 5), whereas by angiography this was not possible. Anastomosis evaluation with epicardial ultrasound required only a median of 92 seconds in human anastomoses, which is clinically acceptable. In most cases, the detection of the error was instantaneous and subsequent scanning time was spent characterizing the error and looking for additional irregular-

ities. Clinically, revision would be performed directly after spotting a serious error.

As we have shown before [7], the mini-transducer can also be used to locate the coronary artery and select the optimal anastomotic site. Combined with its use for anastomotic quality assessment and possibly epi-aortic scanning as well, the ultrasound mini-transducer may prove a multipurpose diagnostic tool to improve the quality of CABG surgery.

A concern with the use of epicardial ultrasound for anastomosis quality assessment is that image interpretation is subjective and operator dependent [4]. In the present study, however, the two observers scored all anastomoses identically with regard to the presence of a construction error ( $\kappa$  1.0), indicating an almost perfect agreement [10], whereas by angiography  $\kappa$  was 0.54 (indicating a moderate agreement). The observers did have extensive previous experience with the interpretation of ultrasound images of anastomoses though. Preferably, the surgeon is trained in a laboratory setting which includes scanning of anastomoses on ex-vivo hearts perfused by saline and performs image interpretation of off-line images on a computer. This may take a couple of hours. Alternatively, the surgeon may teach him/herself by starting to acquire images during cardioplegic arrest and study the images off-line later on. This permits peer review by a radiologist.

### Limitations

The experimental set-up in ex-vivo hearts presents several limitations compared to the in-vivo situation. First, exposure of the anastomosis for ultrasound scanning was not hampered by motion artifacts. We have experience, however, with scanning IMA-LAD anastomoses on the beating porcine heart. Image quality was comparable to the present study and allowed successful detection of anastomotic irregularities requiring comparable scan times [9]. Second, build-up of angiographic contrast in the ex-vivo hearts due to lack of wash-out made the angiograms less easy to interpret. Third, 96/120 anastomoses were constructed on healthy porcine coronary vessels. However, 12 of the 24 human anastomoses were deliberately constructed in a diseased part of the coronary artery. The plaque and calcification did not impair the ability to assess the anastomosis by ultrasound.



## **CONCLUSION**

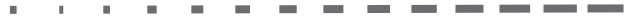
Using an epicardial 13 MHz ultrasound mini-transducer, three technical errors in coronary anastomoses constructed *ex vivo* were detected in about one minute with a higher sensitivity (1.00) and specificity (1.00) than angiography (0.75 and 0.81, respectively). Therefore, epicardial ultrasound is a promising technique for routine clinical intra-operative, non-invasive quality control of coronary anastomoses.

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# Assessment by 13 MHz epicardial ultrasound of distal connector anastomosis in the pig



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R.P.J. Budde<sup>1</sup>, W.J.L. Suyker<sup>2,3</sup>, P.T.W. Suyker<sup>3</sup>, C.W.J. Verlaan<sup>1</sup>, R. Meijer<sup>1</sup>,  
C. Borst<sup>1</sup>, P.F. Gründeman<sup>1</sup>

Heart Lung Center Utrecht, University Medical Center Utrecht<sup>1</sup>,  
Utrecht, the Netherlands, Isala Clinics<sup>2</sup>, Zwolle, the Netherlands, iiTech BV<sup>3</sup>,  
Amsterdam, the Netherlands.

Submitted for publication.

**ABSTRACT**

**Objective:** During application of a distal coronary bypass connector, we employed 13 MHz epicardial ultrasound to evaluate quantitative caliper measurements for vessel size matching and assess anastomosis quality after connector deployment.

**Methods:** Two S<sup>2</sup>AS connector anastomoses were constructed on ex-vivo pressure perfused porcine hearts. Epicardial ultrasound measurements of the connector ring and anastomosis were compared to intravascular ultrasound measurement and cast dimensions. In 22 pigs, anastomotic sites with internal diameter of 2.25-3.0 mm (internal mammary artery) and 1.8-2.2 mm (left anterior descending coronary artery) were selected using external caliper and epicardial ultrasound measurements. Anastomoses were visualized and assessed intraoperatively (beating heart, n=21) and at 3 and 6 months follow-up (explanted heart, n=10 each).

**Results:** Epicardial ultrasound underestimated connector dimension by  $\leq 5\%$  vs. intravascular ultrasound and deviated  $\leq 13\%$  from cast dimensions for other anastomotic measurements. Caliper estimates of internal IMA and LAD diameter differed from ultrasound by  $-4\% \pm 6$  and  $-2\% \pm 7$  (mean  $\pm$  SD), respectively. Intraoperatively, in all animals the anastomotic orifice was flawless. It remained fully patent at 3 and 6 months by ultrasound which was confirmed by histology. The connector to LAD percentage diameter stenosis changed from  $-12\% \pm 5$  intraoperatively to  $-1\% \pm 7$  at 3 months and from  $-7\% \pm 4$  intraoperatively to  $-16\% \pm 13$  at 6 months, in the growing pig model.

**Conclusions:** In the pig, external caliper measurements provided a reliable quantitative estimate of inner graft and coronary diameter for connector size matching. Epicardial 13 MHz ultrasound is a promising method to assess coronary anastomosis quality even when connector metal is present.

## INTRODUCTION

The value of epicardial ultrasound for assessment of hand-sewn anastomoses [1,2,3] and coronary arteries [4] has been shown previously. As novel, facilitated anastomotic techniques emerge and are evaluated in animals [5] and humans [6,7], epicardial ultrasound would be a valuable intraoperative diagnostic modality for qualitative vessel wall assessment to help select an optimal anastomotic site, as well as for verification of the integrity of the constructed anastomosis.

We evaluated the feasibility and validity of epicardial ultrasound to assess anastomoses constructed with one specific metal connector [5] on the ex-vivo and beating porcine heart and to validate quantitative caliper measurement for size matching.

## **MATERIAL AND METHODS**

### **S<sup>2</sup>AS anastomotic system**

The S<sup>2</sup>AS coronary connector (iiTech, Amsterdam, the Netherlands) was described in detail recently [5]. In brief, the graft is connected side-to-side to the coronary artery by an intraluminal expanding metal ring with closing staples that appose donor and recipient vessel wall. By clipping the graft's distal free end, the anastomosis is converted into an end-to-side configuration (cf. figures 1 and 2 in reference 5).

### **Ultrasound equipment**

A commercially available, high frequency (up to 13 MHz in B-Mode) ultrasound mini-transducer (dimensions: 15 x 9 x 6 mm) was used as before [2,3,8]. Imaging was performed with an SSD-5000 ultrasound system (Aloka, Tokyo, Japan). Measurements were performed with the electronic calipers of the system (increments of 0.1 mm, phantom lateral resolution <0.25 mm).

### **Epicardial ultrasound measurement validation**

Two S<sup>2</sup>AS internal mammary artery (IMA) to left anterior descending coronary artery (LAD) anastomoses were constructed, each on a single ex-vivo porcine heart. The anastomosis was pressure perfused at both 80 and 100 mm Hg with saline using a Langendorff set-up and visualized and measured with epicardial ultrasound (Figure 1) as described below.

Subsequently, a 40 MHz intravascular ultrasound probe (IVUS) (Atlantis SR Plus Coronary Imaging Catheter, Boston Scientific, Natick, MA, USA) was advanced through the IMA to visualize the anastomosis, and measure connector diameter in triplicate (Galaxy II IVUS Imaging System, Boston Scientific, Natick, MA, USA).

Impression material (Kerr Co, Romulus, MI, USA) was introduced into the IMA to fill the IMA, anastomosis and LAD. Introduction pressure was measured intraluminally in the IMA, just above the level of the anastomosis. After hardening, the resulting 3D cast was removed and measured under 3.5 x magnification using electronic sliding calipers (accurate to 0.01 mm) (Figure 1, L2, T2 and T3 measurement, each performed in triplicate).

### **Animals and surgery**

Epicardial ultrasound was included in the evaluation of 22 Dalling pigs (62-

94 Kg) that were part of a study to investigate the S<sup>2</sup>AS constructed left IMA (LIMA) to LAD anastomosis at 3 and 6 months that is to be reported separately. The anastomosis was constructed off-pump using a median sternotomy approach as before [5].

The specific S<sup>2</sup>AS system used, can accommodate coronary artery inner diameters of 1.8-2.5 mm. However, to adjust for expected vessel growth during follow-up in the growing pig model, LIMA and LAD sites with inner vessel diameter of 2.25-3.0 mm and 1.8-2.2 mm, respectively, were required. This practically corresponds to an outer diameter of 2.75-3.5 and 2.3-2.7, respectively, due to the 1/7 inner diameter to wall thickness ratio in this species. The LAD was clipped proximal to the anastomosis. To prevent inadvertent occlusion of side branches, an LAD section of at least 7 mm without side branches was required proximal to the anastomotic site.

The LAD was exposed by dissecting the overlying epicardial tissue at a site appearing to be in the diameter range by visual inspection. The distal part of the semi-skeletonised LIMA was cleared of all loose periadventitial tissue. After 5 minutes of soaking in a diluted papaverine solution (5 mg/mL), pressurized LIMA and LAD external diameter was first measured using a custom made caliper (0.2 mm increments, Figure 2).

Subsequently, in still transverse B-Mode epicardial ultrasound images of these sites, the internal diameter was measured (horizontal and vertical axis) in triplicate. For each measurement the transducer was positioned anew.

After construction, the stabilized anastomosis was scanned as described below. Graft flow and the reactive hyperemic peak response after 30 seconds of ischemia were measured as before [5] using a transit time flow probe (Transonic, Ithaca, NY, USA).

After 3 and 6 months follow-up, the animals were sacrificed as before [5] and the heart was taken out. The LIMA was cannulated to perfuse the anastomosis with formalin at 80 mm Hg. The anastomosis was scanned as described below. Subsequently, histologic processing was performed as before [5].

### **Anastomosis visualization**

After ultrasound gel application, the anastomosis proper was visualized in longitudinal and transverse scan planes, as well as the LAD until approximately 15 mm downstream and the IMA until approximately 15 mm upstream of the anastomosis. The inner diameter of the anastomotic orifice and of the LIMA and LAD just proximal and distal to the anastomosis was measured.



### Statistical analysis

The mean of the triplicate measurements was used for further analysis. The difference between both intravascular ultrasound and cast measurements and corresponding epicardial ultrasound measurements is presented as a percentage of intravascular ultrasound and cast dimensions. Data are presented as mean  $\pm$  standard deviation (SD).

## RESULTS

### Epicardial ultrasound measurement validation

Epicardial ultrasound underestimated the connector ring dimension by  $\leq 5\%$  compared to IVUS measurements. All other epicardial ultrasound measurements according to figure 1 differed  $\leq 13\%$  from cast dimensions (table 1). In the transverse scan image, the LAD diameter at the anastomosis could not be measured due to shadowing by the overlying metal connector. Macroscopically, cast geometry corresponded to ultrasound geometry.

### Animal study

Both LIMA and LAD were easily measured by both caliper and ultrasound. Caliper estimates of internal LIMA and LAD diameter differed from ultrasound by  $-4\% \pm 6$  and  $-2\% \pm 7$ , respectively (table 2). In 20/22 animals a LIMA diameter within the specified study range was found. In 18/22 animals an LAD site within the study range without sidebranches within 7 mm proximally could be found. A partial intramyocardial LAD course in one animal and sidebranches in 3 animals dictated use of sites outside the originally intended diameter range.

All 22 device deployments were successful. The one animal with an LAD size below the lower limit of 1.8 mm was excluded, whereas the animals with an LAD slightly above the originally intended inner diameter of 2.2 mm, but still within the acceptable range of the device (1.8-2.5 mm), were accepted.

Intraoperatively, all anastomoses were easily visualized and measured (figures 3 and 4, table 3). No tissue ridges, intimal flaps or thrombus were observed. In one anastomosis, a hard to interpret non-obstructive “fold” of the LAD posterior wall was observed in the transverse scan image. Graft flow was  $14 \pm 7$  ml/min (range 6 - 29 ml/min); the reactive hyperemic peak response was  $6.7 \pm 2.9$  times baseline flow (range 2.5 - 13.3).

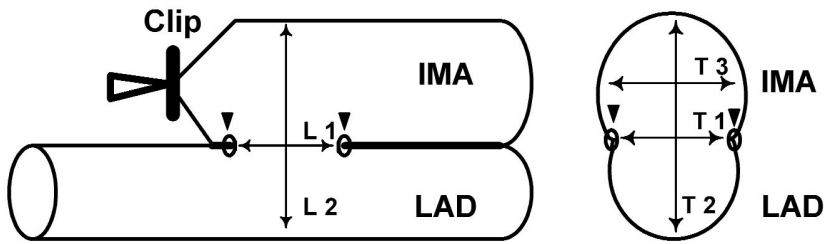
The 3 and 6 month follow-up period was completed by 10 animals each (table 3). The one death was not cardiac related. On the formalin perfused hearts, the anastomoses were difficult or impossible to locate visually. The connector ring and the clip on the distal IMA provided echocardiographic landmarks to locate the anastomosis under the fibrotic tissue. The “fold” seen at implantation at the floor of one anastomosis had disappeared without causing apparent narrowing on both ultrasound and histology, thus making vessel spasm a likely explanation.

**Table 1.** Dimensions (mm) of ex-vivo heart S<sup>2</sup>AS anastomoses measured by epicardial ultrasound, intravascular ultrasound and sliding calipers for cast dimensions. The difference is presented as percentage of intravascular ultrasound or cast measurements

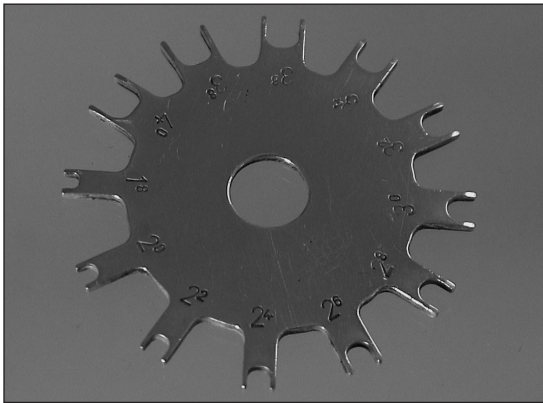
Ultrasound scan plane	Measurement	Epicardial Ultrasound	Intravascular Ultrasound	Cast	% difference	Epicardial Ultrasound	Intravascular Ultrasound	Cast	% difference
	Connector	2.5	2.62	-	-5	2.6	2.61	-	0
	L1 and T1								
Longitudinal	L2	5.3	-	6.10	-13	6.3	-	6.38	-1
Transverse	T2	6.0	-	6.10	-2	6.7	-	6.38	+5
Transverse	T3	4.0	-	3.75	+7	4.1	-	3.74	+10

See figure 1 for explanation of L1, L2, T1, T2 and T3 measurements. Connector diameter is presented as the measurement at 100 mm Hg for both epicardial and intravascular ultrasound. Intraluminal cast injection pressure was 90 mm Hg in heart #1 and 110 mm Hg in heart #2. For heart #1, the mean of ultrasound measurements at 80 and 100 mm Hg was compared to cast measurements and for heart #2, ultrasound measurements at 100 mm Hg were used





**Figure 1** Schematic drawing of S<sup>2</sup>AS IMA-LAD anastomosis. The arrowheads point at the connector ring. Dimensions were measured both in longitudinal (L1,L2) and transverse (T1, T2, T3) epicardial ultrasound images by electronic calipers of the ultrasound system and in the cast (L2, T2, T3) by sliding calipers.

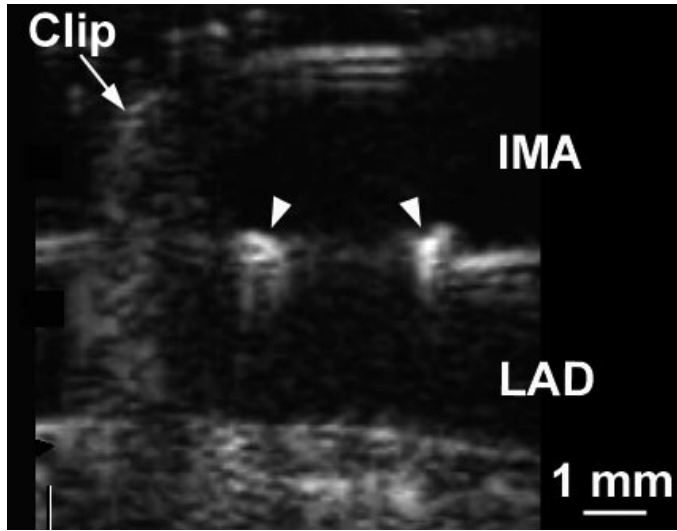


**Figure 2.** Custom made caliper for external vessel diameter: the slots in which the vessel is placed increase in size by 0.2 mm.

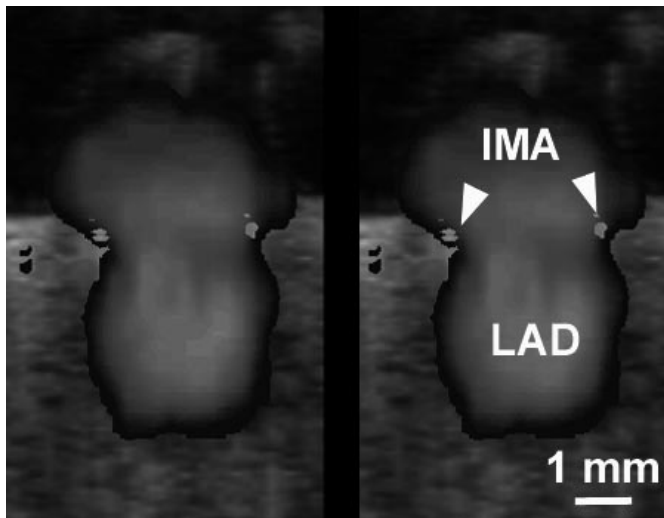
**Table 2** Internal LIMA and LAD dimensions (mm) before anastomosis construction measured by ultrasound and estimated by caliper.

	IMA	LAD
Ultrasound	2.7 ± 0.2	2.1 ± 0.2
Caliper	2.6 ± 0.2	2.0 ± 0.1
Difference	-0.1 ± 0.2	-0.1 ± 0.2
Difference range	-0.4 to 0.2	-0.3 to 0.2

Values are presented as mean ± SD (n=22). Ultrasound values are the average of triplicate measurements. Caliper outer diameter measurements were adjusted for vessel wall thickness by subtracting 2 x 0.25 mm to represent inner diameter.



**Figure 3**  $S^2AS$  anastomosis: Longitudinal 13 MHz ultrasound image of coronary connector anastomosis constructed on the ex-vivo heart. The  $S^2AS$  connector presented as two bright reflections (arrowheads) that border the anastomotic orifice. In the longitudinal image, the clip (arrow) on the distal IMA caused ring-down artefacts that make the underlying section of the outflow corner difficult to assess. Note that the metal connector ring itself generated limited echo artefacts.



**Figure 4.**  $S^2AS$  anastomosis: transverse powerflow ultrasound image. The metal coronary connector is clearly seen (arrowheads). (Color image: page 169)

**Table 3** IMA, orifice and LAD dimensions (mm) measured with ultrasound at implantation and at follow-up.

Group	IMA just proximal to orifice		Orifice		LAD just distal to orifice		% diameter stenosis orifice vs. LAD	
	Implantation	Follow-up	Implantation	Follow-up	Implantation	Follow-up	Implantation	Follow-up
3 months follow-up group (n=10)	2.7 ± 0.3	2.8 ± 0.3	2.4 ± 0.0	2.4 ± 0.1	2.1 ± 0.1	2.4 ± 0.2	-12% ± 5	-1% ± 7
6 months follow-up group, (n=10)	2.7 ± 0.4	2.4 ± 0.2	2.3 ± 0.2	2.4 ± 0.1	2.2 ± 0.2	2.1 ± 0.2	-7% ± 4	-16% ± 13

Values are presented as mean ± SD.

## DISCUSSION

The principal findings of this study are: (1) epicardial 13 MHz ultrasound allowed assessment of anastomotic quality in the presence of a metal coronary connector; (2) in healthy vessels, caliper measurements provided a reliable indication of inner vessel diameter; (3) epicardial ultrasound was an easy to use tool to select coronary anastomotic sites and estimate the inner diameter.

### Facilitated coronary anastomosis

Target vessel assessment is important to select the optimal anastomotic site and match connector size. In healthy vessels, external diameter was easily measured by caliper and correlated well with internal diameter measured by ultrasound. Caliper measurement, however, does not provide information about the presence of plaque and/or calcifications that should be avoided at the anastomotic site to minimize the risk of dissection during introduction of the anastomotic device into the coronary artery [7]. The two techniques are complementary: a standardized caliper for obtaining a diameter measurement fast; ultrasound to assess wall pathology [4].

Similar to hand-sewn anastomoses, intra-operative quality control after facilitated anastomosis construction is important to allow intra-operative revision of suboptimal anastomoses. Carrel et al. [7] describe one patient in which re-operation was necessary to revise a connector constructed anastomosis that, despite adequate intra-operative graft flow, presented unsatisfactory immediate post-operative angiography findings due to capture of the coronary posterior wall by the connector. It is conceivable that intraoperative epicardial ultrasound would have detected that error. In the present study, however, no anastomotic errors were detected. With ample laboratory experience in visualizing conventional anastomoses with construction errors [2,3], we feel that the image quality was sufficient to detect abnormalities in connector anastomoses. Furthermore, it is unlikely that we missed severe narrowing of the anastomosis because in all animals, intraoperative graft flow (range: 6-29 ml/min) and reactive hyperemia peak response ( $6.7 \pm 2.9$ ) were satisfactory, and quantitative histology showed fully patent anastomoses at follow-up.

Connectors are being developed to facilitate off-pump and minimally invasive coronary surgery. A method to assess anastomotic quality intraoperatively needs to be applicable in these settings. First, the ultrasound mini-transducer fits between the suction pods of a coronary stabilizer [4]. Secondly, it can pass an 11 mm trocar and be used endoscopically on the

anterior and posterior side of the heart in the pig model [8]. In limited access approaches with angled visualization, epicardial ultrasound may be used for internal diameter measurement of a target artery that is difficult to access and assess by a caliper.

The ability to visualize the anastomosis under a layer of fibrous tissue at follow up indicates that epicardial ultrasound may help during re-operation in locating and assessing the pre-existing anastomoses including the graft and native artery.

### **Limitations of the study**

All anastomoses were constructed on healthy porcine coronary arteries. The human coronary wall thickness at the anastomotic site is likely to be more variable. However, results of 24 (conventional) anastomoses on the post-mortem human heart indicate that plaque and calcifications do not prevent assessment of coronary anastomoses by epicardial ultrasound [3].

It is conceivable that vascular connectors with a relatively large amount of metal [6] can not be evaluated properly by epicardial ultrasound because of metal induced imaging artefacts.



## **CONCLUSION**

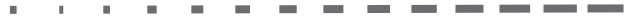
Epicardial 13 MHz ultrasound enabled intraoperative assessment of the S<sup>2</sup>AS coronary connector anastomosis in considerable detail, in spite of some metal induced echo artefacts. To match connector size to graft and coronary size in open-chest procedures, caliper measurement provided a reliable estimate of inner vessel diameter. Epicardial ultrasound was easy to use in addition for qualitative vessel assessment, and may be used for quantitative assessment as well, particularly in limited access procedures.

### **Acknowledgements**

We acknowledge the contributions of J. Matonick, PhD, M.P. Buijsrogge, MD, PhD and colleagues of the central animal facilities of the Utrecht University.

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# Intraoperative coronary artery and graft assessment by epicardial ultrasound



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R.P.J. Budde, P.F.A. Bakker, R. Meijer, C. Borst, P.F. Gründeman

Heart Lung Center Utrecht, University Medical Center Utrecht, Utrecht,  
the Netherlands

Submitted for publication.

**ABSTRACT**

**Objective:** A 13 MHz epicardial ultrasound mini-transducer (15x9x6 mm) was evaluated to assess the target coronary artery and anastomosis on all sides of the heart, in 8 patients undergoing coronary artery bypass surgery.

**Methods:** The mini-transducer was equipped with a custom made malleable handling tool. On indication, scanning was performed of 8 coronary arteries as well as of 27 coronary anastomoses on the arrested heart.

**Results:** All sides of the heart were easily accessible with the mini-transducer. Based on intraoperative coronary artery scanning, the anastomotic site was altered (n=4), the decision was made to graft the coronary artery (n=2) and the LAD identified after incorrect conventional selection of the diagonal (n=1). No anastomosis construction errors were detected. In one anastomosis, a calcified plaque was seen in the outflowcorner.

**Conclusions:** Using an epicardial ultrasound mini-transducer, coronary arteries and anastomoses on all sides of the heart were successfully assessed. Ultrasound information greatly aided in intraoperative decision making that resulted in anastomotic site changes and prevented grafting of the wrong vessel.

## INTRODUCTION

In coronary artery bypass grafting (CABG), epicardial ultrasound enables intraoperative assessment of the coronary artery and the anastomosis [1-8]. Despite promising results in early studies on the anterior side of the heart, widespread adoption of the technique has been prevented by the inability to scan on the lateral and posterior side, due to the bulky transducers at the time [1,2].

Indications for intraoperative evaluation include: discrepancies between pre-operative angiographic and intraoperative findings, decision making problems in optimal distal anastomosis site selection in diffuse coronary disease, impaired intraoperative assessment of the coronary vessels in reoperations and an intramural vessel course. Poor vessel wall quality, small diameter and back bleeding may hamper anastomosis construction and creates the need for intraoperative assessment to diagnose anastomotic construction errors, allowing immediate intraoperative correction. Particularly, bypass grafts anastomosed to coronary arteries on the lateral and posterior cardiac surface are at risk for construction errors because of less optimal exposure.

We previously described a high-frequency epicardial ultrasound mini-transducer (15x9x6 mm, Aloka, Tokyo, Japan) for the assessment of coronary arteries and anastomoses on ex-vivo hearts [8], at all sides of the beating porcine heart [6,7], and the anterior side of the beating heart in patients [5].

In the present study we evaluated the use of the epicardial ultrasound mini-transducer on all sides of the heart to assess coronary arteries and coronary artery anastomoses in patients undergoing CABG surgery, in whom we felt that this investigation was indicated based on intraoperative findings.

## PATIENTS AND METHODS

### Patients

In 8 patients undergoing CABG surgery, epicardial ultrasound scanning was performed upon indication. The preoperative coronary angiogram was reviewed by the surgeon (PFAB) to determine the target arteries and sites for grafting. A median sternotomy approach, cardio-pulmonary bypass, single aortic cross-clamping, and ante- and retrograde tepid blood cardioplegia were applied. The left internal mammary artery (LIMA) was used for grafting of the left anterior descending (LAD) coronary artery and diagonal branches. All other coronary arteries were grafted using the greater saphenous vein.

### Ultrasound equipment

A high-frequency (upto 13 MHz in B-mode) linear array epicardial ultrasound mini-transducer (Aloka, Tokyo, Japan) was used [6-8]. It measures 15x9x6 mm, has a 10 mm image scanwidth and offers both B-Mode and color Doppler imaging [6-8]. Two sternal wires were fixed to the mini-transducer by a custom made snap on clip [6,7] and wrapped around its cable to act as a handling tool (Figure 1, top panel). By bending the wires, the probe handling tool could be adjusted to any desired shape for optimal access to the areas to be scanned (Figure 1, bottom panel). The mini-transducer was placed in a gel filled sterile protective cover (Ultracover, International Medical Products, Inc, Zutphen, the Netherlands) to act as both a sterile and electrical barrier. Sterile ultrasound gel (Parker Laboratories, Fairfield, NJ, USA) was applied directly onto the epicardial surface and/or anastomosis for improved visualization.

Imaging was performed with an SSD 5000 Prosound ultrasound system (Aloka, Tokyo, Japan), positioned at the head end of the operating table. The continuous scan image was recorded on videotape for retrospective time analysis.

Scanning was performed by one of two persons (RPJB or RM) with experience in epicardial ultrasound scanning.

### Coronary artery pre-scan

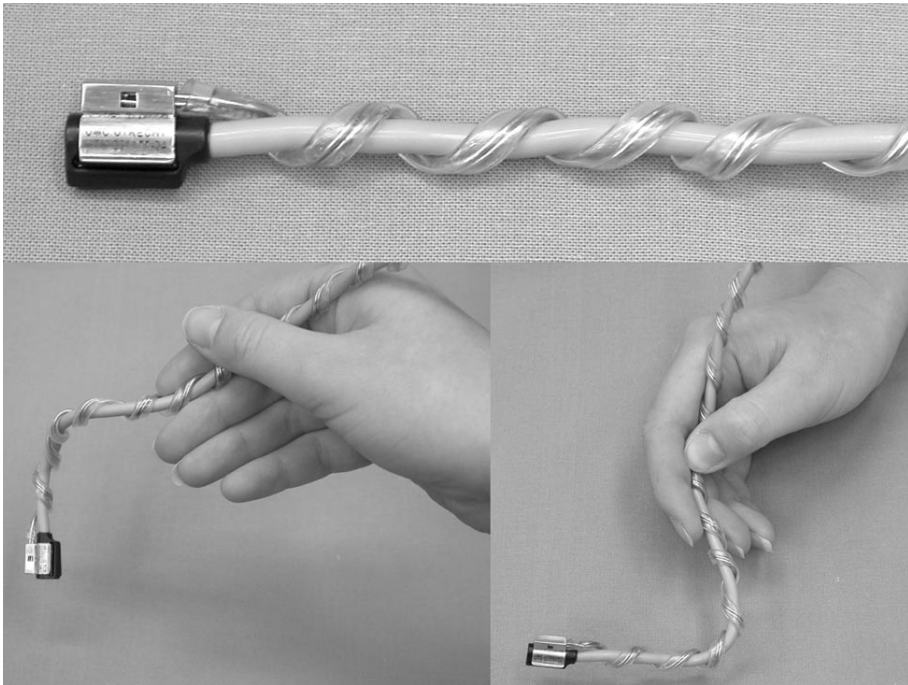
When intraoperative findings prevented optimal distal anastomotic site selection based on findings of target vessel inspection and palpation, scanning of the coronary arteries was performed prior to arteriotomy on the arrested heart during continuous retrograde blood cardioplegia. If severe

calcifications or plaques were detected by scanning, another anastomotic site, free of (or with limited) disease and distal to the most severe stenosis, was selected by epicardial ultrasound. Additional anastomoses were constructed when an unexpected significant stenosis was observed during scanning, in contrast with the angiographic findings.

### Anastomosis scan

Using a standard approach, all anastomoses were evaluated. First, vein graft anastomoses were scanned during continuous antegrade blood cardioplegia perfusion (approximately 100 mm Hg) before construction of the proximal anastomosis on the aorta. The LIMA-(diagonal)-LAD anastomosis was subsequently constructed and scanned on the arrested heart during cardio-pulmonary bypass, after removal of the bulldog clamp on the LIMA, immediately prior to removal of the aortic cross-clamp.

The anastomoses were imaged in both longitudinal and transverse scan planes using B-mode and power Doppler imaging.



**Figure 1.** The Aloka 13 MHz mini-transducer with custom made probe handling tool. The probe is placed in a sterile probe cover for clinical use (not shown).

## RESULTS

### Coronary artery pre-scanning

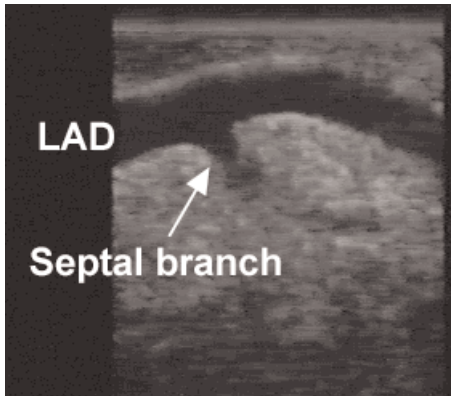
Indications for, and results of pre-scanning are listed in Table 1. Pre-scanning of 8 coronary arteries in 5 patients required 196 seconds (median, range 57-375). In 2 cases, ultrasound findings affected the number of coronary artery anastomoses, and in 2 patients the distal anastomosis site was changed (n=4). In one patient with parallel running intramural diagonal branches and LAD, ultrasound scanning revealed that the diagonal had been incorrectly identified as LAD. Echocardiographically, the LAD was identified by the underlying ventricular septum and septal perforators (Figure 2).

**Table 1** Coronary artery pre-scan indications and results.

Patient#	Coronary artery	Indication	Results
1	LAD	Angiogram difficult to interpret	No alteration of conventionally selected site.
4	LAD	Excessive epicardial fat	Correct identification of LAD after conventional unintended selection of diagonal
5	LAD	Angiogram difficult to interpret	Scanned on the beating heart. Severe disease seen by ultrasound, based on which the LIMA was harvested and grafted.
7	LAD	Angiogram difficult to interpret	Anastomosis site changed
	Diagonal	Angiogram difficult to interpret	Grafted based on ultrasound findings
	OM	Angiogram difficult to interpret	Anastomosis site changed
8	LAD	Angiogram difficult to interpret	Anastomosis site changed
	OM	Angiogram difficult to interpret	Anastomosis site changed

LAD: left anterior descending coronary artery,

LIMA: left internal mammary artery, OM: obtuse marginal branch.

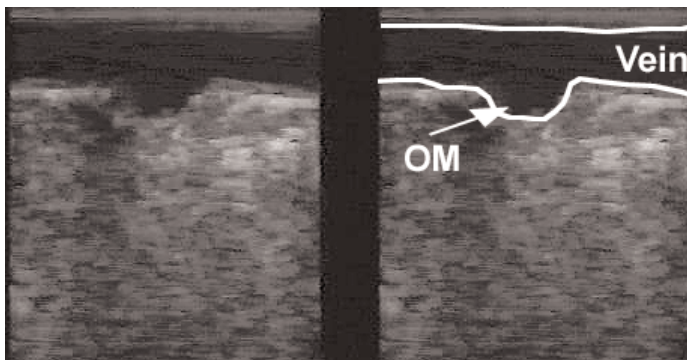


**Figure 2.** Longitudinal ultrasound image of the LAD. Note the ventricular septum and the septal perforating branch (arrow).

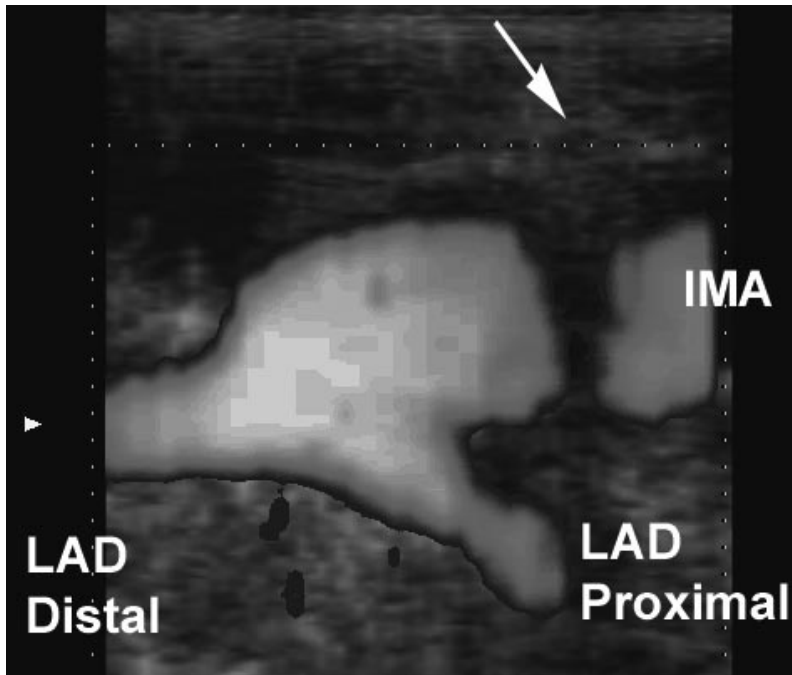
### Anastomosis scanning

A total of 27 anastomoses, on all sides of the heart, was successfully visualized in 150 seconds (median, range 54-335) (Figures 3 and 4, table 2). No damage to any of the anastomoses or leakage of the probe cover was observed.

No anastomosis construction errors were detected. In one LIMA-diagonal-LAD jump graft, a large calcified plaque was detected in the outflow corner on the posterior LAD wall (Figure 5). It was not observed on the preoperative angiogram, nor intraoperatively detected despite careful inspection and palpation. In this patient, there was no indication for pre-scanning. However, after anastomosis scanning, the LAD was visualized and several disease free sites were detected distal to the anastomosis. Transit time measured flow was 23 ml/min for the LAD anastomosis alone and 44 ml/min both anastomoses combined, and the constructed graft was accepted. In three other anastomoses (no pre-scanning), small calcified plaques were observed.



**Figure 3.** Fully patent side-to-side vein to OM anastomosis.



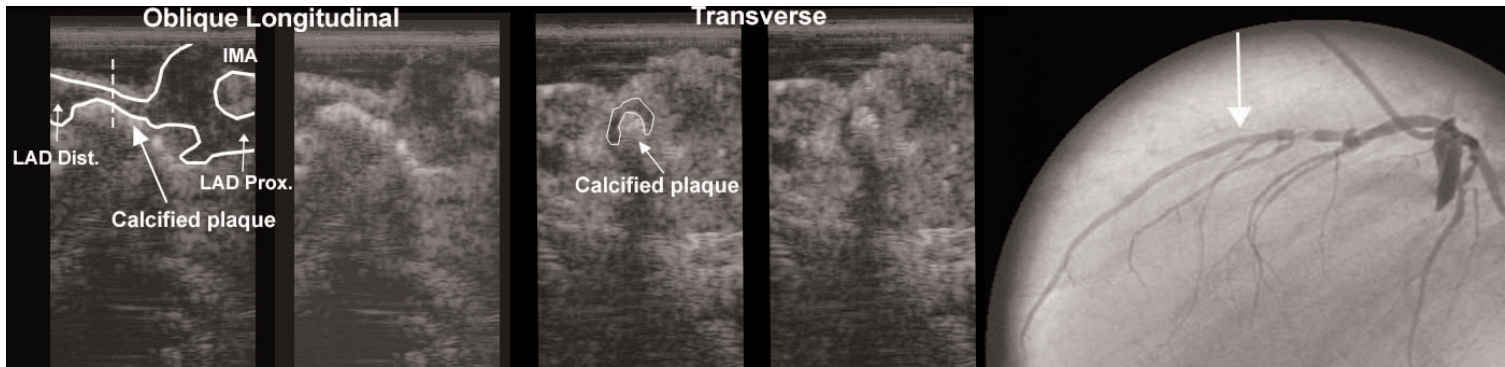
**Figure 4.** Fully patent LIMA-LAD anastomosis: power Doppler imaging. Ultrasound shadowing was caused by a clip (arrow) on an IMA sidebranch. (Color image: page 169)

**Table 2** Number and type of anastomoses scanned

Anastomosis type	Configuration	Number	Remarks
LIMA-LAD	End-to-side	8	Severe calcified plaque detected on the bottom of outflow corner (n=1)
LIMA-diagonal	Side-to-side	1	-
Vein-RDP	End-to-side	7	Some plaque in coronary artery at and distal to anastomosis (n=1)
Vein-OM	End-to-side	3	Some plaque in coronary artery at and distal to anastomosis (n=2)
Vein-OM	Side-to-side	8	-
Total	-	27	No construction errors observed

LIMA: left internal mammary artery, LAD: left anterior descending coronary artery, RDP: right posterior descending coronary artery, OM: obtuse marginal branch.





**Figure 5.** LIMA-LAD anastomosis. Left panels: oblique longitudinal ultrasound image showing large calcification in the outflow corner; Middle panels: transverse image at the level of the outflow corner; Rightmost panel: pre-operative angiogram, with the anastomotic site indicated (arrow).

## DISCUSSION

The principal findings of this study are: (1) The 13 MHz epicardial ultrasound mini-transducer enabled successful assessment of coronary arteries and anastomoses on all sides of the arrested heart; (2) intraoperative epicardial ultrasound scanning greatly aided in optimal anastomotic site selection and prevented grafting of the wrong vessel.

### Access to the lateral and posterior side of the heart

To our knowledge, this is the first study that describes the successful visualization of coronary arteries and anastomoses by epicardial ultrasound on all sides of the heart. In previous studies [1-4], the relatively bulky epicardial ultrasound transducers prevented scanning of the lateral and posterior sides of the heart. Owing to its small size and the custom made malleable handling tool, the present mini-transducer enabled optimal visualization at all sides of the heart, including sections of the obtuse marginal (OM) branches located close to the base of the heart and anastomoses constructed on these sites.

### Anastomotic site selection

In a previous study of epicardial ultrasound scanning of the LAD, with a 10 MHz mini-transducer on the beating heart [5], the anastomotic site was changed in 3/13 patients. In the present study where pre-scanning was performed on indication in patients on cardiopulmonary bypass, the anastomotic site was altered in 4/8 arteries.

One LAD appeared to be misidentified after scanning. The combined preliminary experience supports the routine intraoperative application of epicardial ultrasound prior to anastomosis construction. Given the shift of CABG patient characteristics towards a population with a high incidence of diffuse coronary artery disease, there is a growing need for intraoperative evaluation of coronary arteries and graft patency, which is supported by the results presented herein. We regard the 196 seconds (57–375) seconds scanning time acceptable for routine use in relation to the diagnostic benefit.

Grafting of the wrong vessel (diagonal in stead of LAD) has been reported [9]. The underlying ventricular septum and septal perforating branches (Figure 2) may serve as distinctive echocardiographic landmarks for discrimination between the LAD and diagonal branches.

### **Anastomosis scanning**

No construction errors were detected in 27 anastomoses (9 arterial and 18 vein grafts). It is unlikely that we missed an error as epicardial ultrasound is a remarkably effective method to detect such errors [7,8]. In one anastomosis, at first, no flow was seen in the anastomosis during power Doppler imaging. After repositioning of a retraction sling, power Doppler flow was detected. Conduit compression or kinking needs to be excluded if no power Doppler flow is observed in the anastomosis.

The detection of a large protruding calcified plaque in the outflow corner of a LIMA-LAD anastomosis in a patient in which LAD pre-scanning was not performed further supports the routine use of epicardial ultrasound prior to the arteriotomy. It is conceivable that a fraction of the anastomotic stenoses seen at postoperative angiography [10] is due to grafting at suboptimal anastomotic sites rather than to suture errors. A study, in which intraoperative ultrasound scanning is combined with post-operative angiography may provide more insight in this matter.

### **Scanning in general**

For accurate interpretation of the ultrasound image it is necessary that the ultrasound machine, with the monitor, are placed as close as possible to the scanning person. Alternatively, the ultrasound image could be displayed on a flat screen monitor mounted on an articulating arm that can be positioned at the head end during scanning and stored out of way during the rest of the operation.

### **Limitations**

Scanning was performed on the arrested heart using antegrade and retrograde blood cardioplegia. Under these conditions it was quick and easy. Scanning on the stabilized beating heart may be more difficult due to motion artefacts. However, it appeared to be no problem for accurate visualization in previous animal [6,7] and patient studies [3-5].

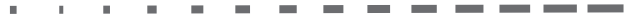


## **CONCLUSION**

Using a 13 MHz epicardial ultrasound mini-transducer, coronary arteries and anastomoses on all sides of the heart were successfully visualized and assessed. Epicardial ultrasound information aided in intraoperative decision making that resulted in changes of anastomotic site and number of anastomoses. In one patient it prevented grafting of the wrong vessel. The absence of anastomosis construction errors was demonstrated intraoperatively in all distal coronary anastomoses.

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# Study protocol

**Evaluation of coronary arteries and anastomoses by 13 MHz epicardial ultrasound, angiography and multislice CT: A pilot study in 30 patients undergoing coronary artery bypass grafting**



9

## Investigators:

P.F.A. Bakker, C. Borst, R.P.J. Budde, P.A. Doevendans, P.F. Gründeman, R. Meijer, W.M. Prokop<sup>1</sup>, P.R. Stella

Heart Lung Center Utrecht, Department of Radiology<sup>1</sup>  
University Medical Center Utrecht, Utrecht, the Netherlands

The protocol described in this chapter has been approved by the medical ethics committee of the University Medical Center Utrecht (Study #04-143).

## INTRODUCTION

In coronary artery bypass grafting (CABG), the early (<1 month) patency rate for the left internal mammary artery (LIMA) to left anterior descending coronary artery (LAD) bypass varies between 94% and 99% [1]. A potential aid to improve early patency is intraoperative visualization of the distal coronary anastomosis by high frequency epicardial ultrasound [2,3]. Epicardial ultrasound provides anatomical information about the anastomotic geometry and can detect technical construction errors, allowing intraoperative revision of suboptimal anastomoses [2,3]. The predictive value, however, of detected irregularities in the coronary anastomosis for its short and long term patency is unknown. Multislice CT is being explored as a non-invasive alternative for coronary angiography which is currently the gold standard for preoperative assessment of the coronary anatomy and post-operative anastomotic patency in patients undergoing CABG [4,5,6]. Recently, a new generation multislice CT scanner has become available that theoretically provides a superior resolution. We will correlate the intraoperative ultrasound findings with both coronary angiography and multislice CT scan findings at discharge for evaluation of the coronary anastomosis.



## OBJECTIVE

To assess (1) whether intraoperative findings during scanning of the coronary anastomosis by epicardial ultrasound predict the angiographic and multislice CT findings at discharge in patients undergoing CABG.

## HYPOTHESIS

- Intraoperative epicardial ultrasound will visualize the LIMA-LAD anastomosis in sufficient detail to predict angiographic and multislice CT findings at discharge.

### Anastomosis quality score

- A. intraoperatively: anastomotic quality (good/satisfactory/poor)
  - surgeon score
  - epicardial ultrasound score
- B. at discharge: anastomotic quality
  - angiographic score (good/satisfactory/poor)
  - multislice multislice CT score (good, satisfactory/poor)
- C. comparisons
  - correlation intraoperative echo score and surgeon score
  - correlation CT score at discharge and intraoperative echo score
  - correlation angio score at discharge and intraoperative echo score
  - correlation angio score at discharge and multislice CT score at discharge

### Secondary end point

- Time required to determine the epicardial ultrasound score

## MATERIALS AND METHODS

### Patient selection

Patients who are scheduled for elective on-pump CABG in the UMC Utrecht, with the preoperative intent to construct at least a LIMA-LAD anastomosis, are approached preoperatively. Patients are enrolled in the study after written informed consent has been obtained. A total of 30 patients will be included. Patients can indicate on the informed consent form whether or not they want to be informed about the individual study results.

### Rationale for total number of patients included

The literature on the occurrence of construction induced abnormalities in coronary anastomosis is limited. Furthermore, the exact number will be surgeon dependant.

By angiography (minor) abnormalities are detected in 17/72 (24%) anastomoses by Siegel et al. [7] and in 6/43 (14%) by Chaux et al. [8]. With the experience gained in the laboratory setting using epicardial ultrasound, detecting minor abnormalities in the anastomosis with ultrasound will indicate that major abnormalities that require intraoperative revision will also be detected [3]. Assuming that (minor) abnormalities are present in 15% of anastomoses and that we want to have at least 2 (minor) abnormalities in the series that can be detected by ultrasound with 95% certainty, 30 patients (= 30 LIMA-LAD anastomoses) have to be included.

For the angiography and multislice CT there is 100% chance to have at least two (minor) abnormalities in 30 patients assuming 3 to 4 anastomoses per patients. In 30 patients a total of 90-120 anastomoses will be available for assessment by angiography and multislice CT.

### Patient exclusion criteria

- Contrast allergy or contraindication for contrast administration
  - Concomitant other cardiac surgery
  - Renal failure (serum creatinine > 1,5 mg/dl (>133  $\mu\text{mol.l}^{-1}$ ))
  - Severe claustrophobia
  - Inability to comply with 25 seconds breathhold commands
  - Atrial fibrillation
  - Heart failure
  - Women of childbearing age
  - Pregnancy
  - Inability to stabilize the anastomosis with an Octopus tissue stabilizer

### Surgical and epicardial scanning procedure

- After cannulation of the patient for cardiopulmonary bypass, depending on the intraoperative findings, the LAD may be scanned with the ultrasound mini-transducer before anastomosis construction. The scan is performed during stabilization of the LAD with an Octopus cardiac stabilizer (Medtronic, Inc, Minneapolis, MN, USA). Due to the cannulation, cardiopulmonary bypass can be immediately started in case of hemodynamic compromise.
- During construction of the anastomosis, the length of the arteriotomy and the diameter of the IMA and the LAD at the anastomotic site are measured.
- After construction of the LIMA-LAD anastomosis, the surgeon evaluates the bypass as usual and scores the anastomotic quality as good, satisfactory, or poor (i.e. requires revision), based on the routine intra-operative findings that may include graft flow measurement. The arguments for scoring the anastomosis as good, satisfactory, or poor are recorded.
- If the anastomosis requires revision, the anastomosis is first scanned with the mini-transducer, before the graft is revised. A revised anastomosis will be scored anew.
- Subsequently, the LIMA-LAD anastomosis is stabilized with an Octopus cardiac stabilizer (Medtronic, Inc, Minneapolis, MN, USA) and the anastomosis and the LAD distal to the anastomosis are scanned by ultrasound as described below. The ultrasound findings will lead to an ultrasound score of anastomosis quality (good, satisfactory or poor). Due to the cannulation, cardiopulmonary bypass can be immediately started in case of hemodynamic compromise.
- Other anastomoses than the LIMA-LAD anastomosis may be scanned during cardioplegia perfusion depending on intraoperative accessibility.
- The surgeon is blinded for the epicardial scanning information, and intraoperative decisions will not be influenced by ultrasound findings. Since anastomotic geometry depends on the transmural pressure, systolic, diastolic and mean arterial pressure is recorded during scanning.

### Echocardiographic equipment

A 13 MHz linear array color-Doppler mini-transducer (UST-5531, Aloka, Tokyo, Japan), measuring 15 mm in length, 6 mm in width and 9 mm in height, is used. After being swapped with ethanol, the transducer is wrapped in a gel filled sterile sleeve (Ultracover, 86593, International Medical Products B.V., Zutphen, The Netherlands, CE 0336). A metal handling tool (MP-2750, Aloka, Tokyo, Japan) is used to manipulate the transducer.

Imaging is performed with an Aloka SSD 5000 Prosound ultrasound system (Aloka, Tokyo, Japan). The ultrasound system, transducer and handling tool are CE marked under number CE 0123. Images are stored on videotape and on the ultrasound machine to enable retrospective review and analysis. The transducer is cleared for epicardial use in a gel filled sterile sleeve by the “Medische Technologie en Multimedia” department of the UMC Utrecht.

### Echocardiographic scan procedure

The surgeon aligns the LIMA with the LAD course for optimal scan results. The anastomosis is first visualized (B-Mode and color-Doppler) in the longitudinal axis, with the anastomotic orifice, inflow and outflow corner captured in one image. If it is not possible to capture the whole anastomosis in one image, specific parts are visualized in several images. Subsequently, a transverse sweep and a transverse image at the maximum width of the anastomotic orifice as well as at the level of the outflow corner are obtained in both B-mode and color-Doppler. If irregularities are detected, the location, appearance and possible cause of the irregularity are described on a standardized form. Based on the ultrasound findings the anastomosis is scored as good, satisfactory or poor (requires revision), according to the parameters in Table 1.

The time is recorded that is required to perform the epicardial ultrasound scans and determine the echo score of anastomosis quality. We expect this time to be several minutes.

**Table 1.** Ultrasound score

	Good	Satisfactory	Poor
Stenosis of outflow corner	0 %	0% - 30%	>30 %
Adventitia debris	-	-	+
Purse string	-	Mild	Severe
Suture cross-over	-	-	+
Tissue ridges	-	Small, no visually reduction significant diameter	Large, visually significant diameter reduction
Thrombus formation	-	-	+
Ratio anastomotic orifice to coronary artery approximately 3mm distal to toe	>1	1,0-0,7	<0.7

### Postoperative multislice CT

Postoperative medically refractory atrial fibrillation excludes patients from this examination. Patients are positioned in the CT scanner. If the heart rate exceeds 80 beats per minute, metoprolol is administered under supervision of a physician of the cardiology department and monitoring of blood pressure and the ECG. Scanning will take place during a breathhold period of approximately 25 seconds. After the image acquisition, a three dimensional reconstruction of the coronary anatomy and the LIMA-LAD anastomosis is made. The quality of the anastomosis is scored as good/satisfactory or poor, according to the parameters in Table 2.

The total amount of received radiation during a multislice CT is expected to be approximately 5-12 mSv.

**Table 2.** Multislice CT score

	Good/Satisfactory	Poor
Stenosis of outflow corner	<30%	>30 %
Anastomotic orifice narrowing	<30%	>30 %
Ratio anastomotic orifice to coronary artery approximately 3mm distal to toe	>0,7	<0.7

### Angiography

Before discharge a standard angiogram of all grafts and anastomoses is made by selectively injecting contrast media into the graft. The anastomosis is visualized in standard projections for anastomosis assessment. Systolic, diastolic and mean arterial pressure is recorded. The angiogram is evaluated for stenosis in the graft, anastomosis and in the coronary artery distal to the anastomosis by an observer who is unaware of the intraoperative ultrasound findings. If a stenosis is present the degree of diameter stenosis (%) is estimated. The quality of the anastomosis is scored as good, satisfactory or poor, according to the parameters in Table 3.

The total amount of received radiation during a coronary angiogram of the LIMA-LAD anastomosis is expected to be approximately 10-15 mSv.

**Clinical follow-up**

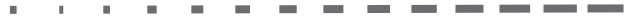
After the operation, clinical follow-up until discharge.

**Table 3.** Angiography score

	Good	Satisfactory	Poor
Stenosis of outflow corner	0 %	0% - 30%	>30 %
Anastomotic orifice narrowing	0 %	0% - 30%	>30 %
Ratio anastomotic orifice to coronary artery approximately 3mm distal to toe	>1	1,0-0,7	<0.7
Contrast run-off	Good	Good	Poor

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## Coronary artery bypass grafting

Coronary artery bypass grafting (CABG) for ischemic heart disease is traditionally performed through a median sternotomy on the arrested heart using cardio-pulmonary bypass (CPB). In the last decade, beating heart off-pump CABG (OPCAB) [1-4], minimally invasive [5,6] and even robot-assisted totally endoscopic CABG (TECAB) [7-9] have been developed, aimed at reducing CPB and median sternotomy related morbidity.

Intra-operative high-frequency (7-15 MHz) epicardial ultrasound may aid the surgeon during CABG surgery to: (1) locate the target coronary artery, (2) assess the target coronary artery, (3) assess the quality of the constructed anastomosis and (4) assess the wall quality of the aorta.

The use of epicardial ultrasound in CABG was first described in the 1980s with promising results [10-15]. However, the bulky transducers at the time limited their use to the anterior side of the heart [10-15]. This prevented widespread adoption and application of epicardial ultrasound.

In the mid 1990s, the development of OPCAB and minimally invasive approaches to CABG, in which anastomosis suturing is considered more challenging, revived interest in the technique and boosted development of smaller, higher resolution transducers [16-21].

The literature on epicardial ultrasound in CABG surgery was reviewed and the (potential) applications and current status of the technique are discussed.

## Epicardial ultrasound equipment

There are several requirements for an epicardial ultrasound transducer. First of all, visualization of the small (1-4 mm) coronary arteries, requires a relatively high imaging frequency ( $\geq 7$  MHz). Secondly, the transducer must be small and connected to the ultrasound system by a flexible cable to allow scanning on the lateral and posterior sides of the heart where the space between the epicardial surface and the adjacent structures inside the chest is limited. The transducer must have a handling tool that can be adjusted for optimal access to each individual target site on the heart that is to be scanned. Ideally, the transducer offers B-mode, color-Doppler and power Doppler imaging.

Because the transducer is in direct contact with the operating field, the transducer should be sterilized or, alternatively, be placed in a sterile cover. The imaging system must have a CF (cardioflux) mark, if the probe itself is sterilized and used without a cover directly on the heart. Alternatively, a

sterile cover can also act as an electrical barrier.

Over time, the transducer size has significantly decreased [10-21]. In 2001, we started using a mini-transducer (initially up to 10 and later 13 MHz in B-Mode, Aloka, Tokyo, Japan) that measures only 15 x 9 x 6 mm (Chapter 1, figures 1&3) [19,20,22-25]. It has color-Doppler imaging capability, is small enough to reach all parts of the heart [Chapter 8], easily fits between the suction pads of a coronary stabilizer [19], and can also pass a trocar for endoscopic use [20,24].

## **Intraoperative applications of epicardial ultrasound in CABG surgery:**

### **1. Localization of the target coronary artery**

Preoperatively, the target coronary arteries and sites for revascularization are determined on the coronary angiogram. Intraoperatively, the target coronary arteries are located by visual inspection of the epicardial surface. Visual localization may be difficult due to covering of the epicardial surface by fat and/or an intramyocardial vessel course. In re-operations the presence of fibrosis also obscures the epicardial surface. If visual localization is not possible, time consuming and potentially dangerous (inadvertent entering of the right ventricle) dissection of the epicardial tissue (and ventricular wall) is needed to locate the target artery. Inadvertent grafting of the wrong vessel, especially a diagonal branch instead of the left anterior descending coronary artery (LAD), has been reported [26,27].

Several studies describe the successful localization of the LAD with epicardial ultrasound in patients where the LAD could not be located by visual inspection and palpation [12,16,17,21,28]. By manipulating the epicardial ultrasound transducer over the heart, the LAD was located within only a few minutes. For the LAD, the underlying ventricular septum and the presence of septal perforators serve as distinctive landmarks for identification [16, Chapter 8]. The coronary artery can be discriminated from accompanying veins by the presence of calcifications and plaque and in color Doppler imaging by the different color filling due to opposite flow directions [20]. After echocardiographic localization of the artery, targeted dissection of the epicardial fat can be performed, which minimizes risk and time consumption. In one patient we prevented unintended grafting of a diagonal branch that was erroneously identified as the LAD by visual inspection [Chapter 8]. By epicardial ultrasound this was discovered and the true LAD was identified and successfully grafted [Chapter 8].

## 2. Assessment of the target coronary artery.

After target artery localization, the optimal anastomotic site (distal to the main stenosis identified on the coronary angiogram and free from coronary pathology) has to be selected. On the angiogram not all sites of stenosis are accurately depicted [10,14,29-31] and the vessel distal to a large stenosis may not always be visible due to poor contrast filling [10]. Intraoperatively the surgeon relates visual information about anatomical landmarks to the stenosis seen on the angiogram. By subsequent digital palpation of the coronary artery to detect calcifications and taking into account the surgical access and exposure, an anastomotic site is chosen. Digital palpation is subjective and may easily miss soft plaques and disease on the posterior vessel wall. For the reasons described above, the anastomotic site may appear suboptimal (plaque and calcifications present) after the arteriotomy has been performed. In OPCAB, in addition, the coronary artery has to be clamped proximal and distal to the anastomotic site during suturing. Backbleeding through the arteriotomy from septal perforators and sidebranches in the isolated coronary segment may severely hamper visibility on the suture line. Septal perforators can not be detected by visual inspection or by palpation before opening of the vessel. With epicardial ultrasound, the coronary artery can be rapidly and accurately assessed [12-15,17-19,20,22, Chapter 8]. Plaque, calcifications and side branches are easily spotted. Epicardial ultrasound is especially helpful in assessing sections of the coronary artery that are not well visualized on the angiogram [10, Chapter 8]. After intraoperative assessment by epicardial ultrasound, the decision whether or not to graft the artery can be made (16, Chapter 8).

Measurement of the resulting coronary lumen can be accurately performed by epicardial ultrasound and correlates well with histological and angiographic dimensions [17,18,31]. However, using color Doppler imaging, epicardial ultrasound tends to overestimate moderate stenoses and underestimates more severe stenoses [18]. The Doppler gain setting may be of influence for these measurements.

Suematsu et al. [17] describe intraoperative deviation from the initial conventionally selected anastomotic site in 3/12 patients, after epicardial ultrasound scanning of the recipient coronary artery. This corresponds well with our own findings in off-pump patients (change in 3/13 patients) [19] and on-pump patients (change in 4/8 arteries) [Chapter 8]. In one patient, we detected a large calcified plaque, just distal to the anastomosis during epicardial ultrasound scanning. Pre-arteriotomy scanning of the coronary artery had not been performed in this patient. This would have allowed deviation to a more distal site where the artery was

free of pathology as seen by epicardial ultrasound after anastomosis construction [Chapter 8].

Based on these findings, it is conceivable, that a fraction of anastomosis irregularities seen on postoperative angiography [32,33] are actually due to selection of suboptimal anastomotic sites rather than suture errors. It is conceivable that careful selection and assessment of the anastomotic site by epicardial ultrasound, may decrease the number of anastomosis irregularities seen postoperatively.

### 3. Quality control of the constructed anastomosis

An optimally constructed distal anastomosis is of paramount importance for longterm graft patency. However, by intraoperative angiography, (minor) irregularities are detected in upto 24% of anastomoses [34]. In a review by Mack et al. [32], the angiographic patency of the LIMA-LAD anastomosis is 94%-99% at  $\leq 1$  month follow-up, 88%-93% at intermediate (1 month-1 year) follow-up and between 51% and 98% at long term (upto 15 years) follow-up. Patency, however, is non-specific term. In a study by Berger et al. [33], angiographic patency of LIMA-LAD grafts at short term follow-up is 98.8%. But, stenosis of  $\geq 50\%$ - $\leq 99\%$  was seen in 7.8% of grafts, so only 91% of the grafts had  $\leq 50\%$  stenosis [33]. In the study by Berger [33], all patients underwent CABG on the arrested heart via median sternotomy access, which is considered to be the most optimal setting for anastomosis suturing.

The suturing process in minimally invasive CABG and OPCAB is considered more technically demanding because of one or more of the following factors: residual motion of the target area, blood obscuring the arteriotomy edge, suboptimal angle of view, absence of force feedback on the telemanipulation systems and lack of an assistant to present the graft [7,9,35,36]. The reported data on the number of intra-operative anastomosis revisions is limited, but varies widely (between 0.6 % and 8.5% revision of all anastomoses) [37]. When described as the percentage of patients in which at least one anastomosis was revised, the numbers are between 2% and 8.5% of patients [37]. Clearly, intraoperative anastomotic quality assessment would aid to increase anastomotic patency, as suboptimal anastomoses may be revised before chest closure.

The potential of epicardial ultrasound to assess anastomosis quality was recognized simultaneously with its use for coronary artery assessment in the 1980s [11,13]. Several animal studies [11,17,24] demonstrate that control anastomoses are accurately discriminated from anastomoses with deliberately introduced construction errors when evaluated with epicardial ultrasound by blinded observers. High frequency epicardial ultra-

sound allows visualization of the anastomosis in such detail that individual sutures (7-0 Prolene) can be identified [24,25]. In a study on ex-vivo hearts, two experienced blinded observers scored anastomoses as control or construction error by using epicardial ultrasound with a sensitivity of 0.98 and specificity of 1.00 [25]. This is higher than achieved with the gold standard angiography (sensitivity 0.75, specificity 0.81,  $p < 0.01$ ) [25].

Haaverstad et al. [38] report that, in a series of 24 patients, in one patient the LIMA-LAD anastomosis was revised because of outflow corner narrowing seen on epicardial ultrasound, despite adequate intraoperative graft flow (22 ml/min) measured by a transit-time flow probe. Other authors [13,17] describe anastomosis revision based on epicardial ultrasound detected irregularities as well.

Assessment of an anastomosis by epicardial ultrasound requires only several minutes, so it does not excessively lengthen the operation [17,24,38,Chapter 8].

Although the focus is mainly on the distal anastomosis, the proximal aorta-to-graft anastomosis can be equally well visualized and assessed [11].

#### 4. Assessment of the aorta before cannulation and clamping

To initiate CPB and/or construct the proximal anastomosis the aorta is cross- or side-clamped. This may dislodge aortic calcifications and plaques that may embolize to the brain. Knowledge about the location and extend of aortic disease may aid in choosing the most optimal site for clamping to minimize the risk of microemboli.

Epicardial ultrasound scanning of the aorta (epi-aortic scanning) provides information on the location and extend of calcification [39,40]. Epicardial ultrasound is more sensitive than transesophageal echocardiography and digital palpation [41] that both underestimate the extend of disease. Clamping and cannulation can be performed at those sites that have little or no calcifications. Systematic use of ultrasound guided aortic clamping and cannulation improves the outcome of patients undergoing CABG [42].

#### Emerging Applications

Epicardial ultrasound may also be of use to aid in the application of new and emerging techniques in the field of cardiac surgery.

### **Totally endoscopic coronary artery bypass grafting**

In minimal access and totally endoscopic procedures, the lack of overview adds to the problem of coronary artery localization. Inability to locate the LAD alone, is reason for conversion to an open-chest approach in upto 9% of TECAB patients, and one of the major difficulties prohibiting further expansion of TECAB [8]. Furthermore, anastomosis suturing is more demanding. In the closed-chest pig, the major target arteries for bypass grafting can be located by manipulating an epicardial ultrasound mini-transducer over the heart using robot-assisted instruments [20,43]. Anastomoses can also be accurately visualized [24]. Using picture-in-picture technology, the operator was provided with the camera and real-time ultrasound image at the same time to allow direct integration of the ultrasound information to the visual information from the camera [20,24]. The endoscopic application of epicardial ultrasound awaits clinical application in TECAB patients.

### **Facilitated coronary anastomosis connectors**

Automated vascular connectors to facilitate construction of the distal anastomosis are currently under intense investigation and likely to boost (minimally invasive) OPCAB surgery [44-46]. Assessment of the anastomotic site on the coronary artery is just as important just as it is for constructing conventional sutured anastomoses. Furthermore, anastomosis quality assessment is important, because even with connectors anastomotic irregularities may occur that are not otherwise directly evident intraoperatively [46].

In the pig model, epicardial ultrasound was successfully used for patency assessment of anastomoses constructed with one specific connector [45,Chapter 7]. However, not all connectors may be candidates for assessment with epicardial ultrasound as some consist of a considerable amount of metal that is likely to cause distortion of the ultrasound image [44].

### **Left ventricle to coronary stent**

Left ventricle to coronary stents, that supply blood directly from the left ventricle into the coronary artery, are being evaluated as an alternative for conventional CABG surgery [47].

Epicardial ultrasound allows guided placement of the stent into the ventricle between the ventricular septum and the papillary muscles in the porcine model [48]. Correct placement can be checked by demonstrating bi-directional flow in the stent using color-Doppler imaging. [48,49].



### Concerns/limitations

There is some concern about the operator dependency and subjectivity of epicardial ultrasound [50]. In a study on the ex-vivo heart, 2 experienced ultrasound observers independently of each other scanned and subsequently scored all anastomoses (n=120) identical (kappa 1.00) [25]. This indicates that, in experienced hands, epicardial ultrasound is reproducible and operator independent. However, a study in which the agreement of more, unrelated observers is investigated, will provide more insight into this matter.

For accurate interpretation of the ultrasound images it is very important that the surgeon has a good view of the monitor whilst scanning. We don't think it is necessary to have a radiologist to operate the ultrasound machine as the anesthetist or an OR nurse can likely be taught how to do this in a limited amount of time.



## **Future developments and directions**

### **On-pump versus off-pump CABG**

The debate about the anastomosis quality in off-pump CABG still continues [3,4,35-37]. The high sensitivity and resolution of epicardial ultrasound in visualization of the anastomosis may be integrated in a study with an equal number of patients operated on-pump and off-pump by the same surgeon, to investigate this issue. It may provide hard data to fuel, or even settle the debate.

### **3D imaging**

The ability to obtain (real-time) three dimensional ultrasound images of coronary arteries and anastomoses would make intra-operative epicardial ultrasound an even more appealing and illustrative technique. Computer software is available, that reconstructs a 3D image from a sequence of successive 2D ultrasound images obtained by a high frequency epicardial ultrasound transducer. However, many factors (residual motion, pulsatile flow) influence image quality and further refinement is needed before high quality images can be obtained.

Recently, Suematsu reported on the first attempts to use of a novel real-time 3D ultrasound system for intracardiac navigation on the beating heart [51,52]. Eventually these developments may prove an important part of the technology that enables intracardiac beating heart surgery.

### **Multislice CT**

Multislice CT scanners are under intense evaluation as an alternative for coronary angiography to visualize and assess the coronary arteries preoperatively and assess anastomotic patency postoperatively [53,54]. Multislice CT has the potential for more detailed visualization (including differentiation between soft and hard plaques) than angiography [53]. The relation between intraoperative epicardial ultrasound findings and pre- and postoperative CT findings has never been described thus far. We have devised a study protocol (Chapter 9) that will relate preoperative and postoperative angiography, intraoperative epicardial ultrasound and postoperative multislice CT scanning for coronary artery and anastomosis assessment. This study is expected to provide some interesting insights in this era.



## Conclusions

The improvements in epicardial ultrasound transducer size and technology over the last 20 years has resulted in smaller higher resolution transducers that can be used as a multipurpose intraoperative tool. At least one mini-transducer can be used on all sides of the heart, in all approaches currently used for CABG. Epicardial ultrasound helps the surgeon in (1) locating the target coronary artery, (2) selecting the optimal anastomotic site on the coronary artery, (3) assessing and documenting the quality of the constructed anastomosis, (4) selecting the optimal site for aortic clamping and cannulation. Routine intraoperative use of epicardial ultrasound during CABG surgery may improve patient outcome.

## Epicardial ultrasound as an anastomosis quality assessment technique

Ten characteristics of an ideal anastomotic quality assessment technique were formulated in chapter 1. Based on the research described in this thesis, the following can be said about how epicardial ultrasound complies with these characteristics.

### 1. Non invasive

Clearly epicardial ultrasound is a non-invasive technique. Furthermore, we never damaged an anastomosis by epicardial ultrasound scanning.

### 2. High sensitivity and specificity

With epicardial ultrasound, construction errors in coronary anastomoses on the ex-vivo heart were detected with higher sensitivity (0.98) and specificity (1.00) than achieved with the current gold standard angiography (sensitivity 0.78, specificity 0.81)(Chapter 6).

### 3. Easy to use

Manipulating the epicardial ultrasound transducer is not difficult. We feel, that a surgeon can be trained to successfully perform the scanning procedure within a limited amount of time (several hours).

### 4. Provides easy to interpret results

Epicardial ultrasound provides highly detailed images and major irregularities, that necessitate anastomosis revision, are easily spotted (Chapters 4,5,6). For surgeons that want to start using this technique, a laboratory training is suggested, that includes scanning of anastomoses on ex-vivo hearts and image interpretation of off-line images on a computer.

However, further research is needed to determine which (minor) anastomotic irregularities detected during epicardial ultrasound scanning do not necessarily require anastomosis revision, because they do not induce a functional anastomotic stenosis during follow-up.

#### **5. Reproducible / Operator independent**

On the ex-vivo heart, 2 experienced ultrasound observers independently of each other scanned and subsequently scored 120 anastomoses identical ( $\kappa$  1.00) as control or presence of a construction error (Chapter 6). This indicates that the technique is both reproducible and operator independent. However, a study in which the agreement of more, unrelated observers is investigated, will provide more insight into the amount of operator dependency.

#### **6. Applicable on all sides of the heart and all types of anastomoses**

In porcine open- and closed-chest beating heart CABG and in patients undergoing CABG on the arrested heart, visualization of coronary arteries and anastomoses at all common sites for bypass grafting on all sides of the heart, was performed with the mini-transducer (Chapters 3,4,8). Clinically, side-to-side jump anastomoses as well as distal end-to-side anastomoses can be successfully visualized with epicardial ultrasound (Chapter 8).

#### **7. Fast**

Anastomosis assessment on the ex-vivo heart required a median of 67 seconds (Chapter 6). On the beating porcine heart mean open chest scan time, for a series of images of an anastomosis in standardized scan planes, was just over 2 minutes (Chapter 4). Clinically, median scan time per anastomosis was 2.5 minutes, which is acceptable.

#### **8. Provides both anatomical and functional information**

Epicardial ultrasound provides anatomical information in such detail that very small structures (i.e. 7-0 Prolene sutures) are accurately visualized (Chapters 4,5,6). Using Doppler imaging and assessment, the flow pattern in a graft can be visualized from which the mean graft flow (ml/Min) can be calculated, which provides some functional information. Thus far, however, we have not been able to perform these calculations reproducibly for coronary anastomoses.

#### **9. Applicable in reduced access and totally endoscopic approaches**

In the porcine model, the mini-transducer was successfully manipulated

endoscopically using a tele-manipulation system, for scanning on all sides of the heart of both coronary arteries and anastomoses (Chapters 3 and 4). However, the endoscopic applicability of the mini-transducer in patients undergoing TECAB remains to be established.

#### **10. Inexpensive**

The initial investment for the epicardial ultrasound equipment is high. However, most cardiac surgery centers will already have an ultrasound machine available, so only a suitable epicardial ultrasound probe needs to be purchased. The probe (like most ultrasound transducers) can be reused many times. The added procedural costs per patient consist of the cost per use for the ultrasound system and probe, one sterile probe cover and one package of sterile ultrasound transmission gel.

## OVERALL CONCLUSIONS

The aim of the thesis was to evaluate epicardial ultrasound as a means to locate and assess coronary arteries and assess the quality of the distal coronary anastomosis in (totally endoscopic, off-pump) coronary artery bypass grafting.

The main conclusions of the studies in this thesis are:

1. The 13 MHz epicardial ultrasound mini-transducer enables successful endoscopic localization and assessment of the major target coronary arteries for bypass grafting within a median of 3 minutes per artery.
2. The conventionally sutured distal coronary anastomosis can be assessed in high detail by 13 MHz ultrasound in both open- and closed-chest (off-pump) CABG. Anastomosis construction errors are detected by epicardial ultrasound with higher sensitivity and specificity than by the gold standard angiography.
3. Epicardial 13 MHz ultrasound enables intraoperative assessment of the S<sup>2</sup>AS coronary connector anastomosis in considerable detail, in spite of some metal induced echo artefacts.
4. The 13 MHz epicardial ultrasound mini-transducer can be used on all sides of the heart for coronary artery and coronary anastomosis assessment and provides valuable information to aid in intraoperative decision making.

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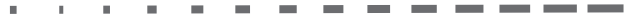
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# SUMMARY



## SUMMARY

### Chapter 1

Coronary artery bypass surgery (CABG) is traditionally performed via a median sternotomy approach on cardiopulmonary bypass (arrested heart). Since the mid 1990s, beating heart, minimally invasive and even totally endoscopic CABG have been continuously (re)explored. Anastomosis suturing is considered more difficult in these approaches.

In all approaches to CABG, the surgeon may face several intraoperative difficulties:

1. Localization of the target coronary artery for bypass grafting. The coronary arteries may be embedded in the epicardial fat or run intramyocardially, making them invisible to the eye, necessitating time consuming and potentially harmful dissection.
2. Selection of the optimal anastomotic site on the target coronary artery. Visual inspection and digital palpation are the only means available and provide only limited information.
3. Assessment of the quality of the constructed anastomosis. Technical construction errors may go unnoticed intraoperatively and may lead to bypass graft failure.

In this thesis an epicardial ultrasound mini-transducer was evaluated to aid in all the intraoperative difficulties described above in both open- and closed-chest CABG surgery.

### Chapter 2

Three enabling devices were employed for closed-chest multivessel robot-assisted beating heart CABG in a porcine model: 1) a sternum lift for the creation of additional workspace inside the thorax; 2) an EndoStarfish for closed chest exposure of the posterior side of the heart, and; 3) an EndoOctopus for closed chest stabilization of the coronary artery. Employing Trendelenburg positioning, mean arterial pressure remained above 70 mm Hg (without additional inotropic support) during exposure of posterior and inferior branches which enabled arterial grafting of these arteries on the beating heart.

### Chapter 3

The epicardial ultrasound mini-transducer was used in the closed-chest beating heart porcine model described in chapter 2, in order to endoscopically

locate and assess the major target coronary arteries (LAD, OM3 and RDP) for bypass grafting. The mini-transducer was introduced through a port and manipulated over the heart using robot-assisted instruments. The ultrasound image was displayed picture-in-picture on the master console of the tele-manipulation system. After proper endoscopic exposure and stabilization, robot-assisted epicardial ultrasound scanning enabled successful endoscopic identification and assessment of the major coronary branches within a median of 169 seconds per artery.

#### **Chapter 4**

The mini-transducer was also evaluated for the (endoscopic robot-assisted) assessment of coronary anastomoses on the beating porcine heart. Coronary anastomoses were constructed as control or with a suture cross-over construction error. The anastomoses were successfully visualized on the beating heart in both the open- and closed-chest approach. During off-line assessment, all anastomoses were accurately identified as correct or incorrect by two blinded observers.

#### **Chapter 5**

In pressure perfused porcine and human hearts, we investigated the epicardial ultrasound presentation and geometry alteration of specific construction errors in coronary artery anastomoses. The construction errors consisted of an oversutured toe, an oversutured heel, a cross-over and a purse string. Using epicardial 13 MHz ultrasound, accurate visualization and assessment of all four different construction errors was possible. All errors reduced the area of the anastomotic orifice, but not the inflow or outflow corner.

#### **Chapter 6**

Next, on ex-vivo hearts, the sensitivity and specificity of epicardial ultrasound for the detection of coronary anastomosis construction errors was determined and compared to the gold standard angiography. We found that using epicardial ultrasound construction errors were detected with a sensitivity of 0.98 and specificity of 1.00 which is significantly higher than achieved by angiography (0.75 and 0.81, respectively). There also was a better agreement between observers using ultrasound than the angiography observers.

#### **Chapter 7**

During application of the S<sup>2</sup>AS distal coronary bypass connector in porcine beating heart CABG, we employed the mini-transducer to evaluate quantitative caliper measurements for vessel size matching and assess the quality of

the anastomosis after connector deployment. The external caliper measurements provided a reliable quantitative estimate of inner graft and coronary diameter for connector size matching. Epicardial 13 MHz ultrasound enabled intraoperative assessment of the S<sup>2</sup>AS coronary connector anastomosis in considerable detail, in spite of some metal induced echo artefacts.

### Chapter 8

After its thorough evaluation and validation in the laboratory, the successful initial results of the application of the mini-transducer, on all sides of the arrested heart, in patients undergoing CABG surgery is described. The information obtained by epicardial scanning was of great value as it resulted in changes of the selected anastomotic site, affected the number of constructed anastomoses, in one patient prevented grafting of the wrong vessel and confirmed the absence of anastomosis construction errors.

### Chapter 9

To build on the initial clinical findings, a study protocol was set-up that will evaluate the relation between intraoperative epicardial ultrasound findings and preoperative and postoperative coronary angiography findings and postoperative multislice CT scan findings, in patients undergoing CABG surgery. The protocol has been approved by the medical ethics committee of the University Medical Center Utrecht.

### Chapter 10

The improvements in epicardial ultrasound transducer size and technology over the last 20 years has resulted in smaller transducers with higher resolution that can be used as a multipurpose intra-operative tool. The mini-transducer used in the studies described in this thesis, can be used on all sides of the heart, in all approaches currently used for CABG. Epicardial ultrasound may aid in (1) locating the target coronary artery, (2) selecting the optimal anastomotic site on the coronary artery, (3) assessing and documenting the quality of the constructed anastomosis, (4) selecting the optimal site for aortic clamping and cannulation. Routine intraoperative use of epicardial ultrasound during CABG surgery may improve patient outcome.

# SAMENVATTING



## SAMENVATTING

### Hoofdstuk 1

Coronaire (kransslagader) omleidings operaties worden traditioneel uitgevoerd via een mediane sternotomie (doornemen van het borstbeen) met gebruik van de hart-long machine om het hart stil te kunnen leggen.

Sinds de midden jaren negentig, is de kloppend hart, minimaal invasieve en zelfs totaal endoscopische (opereren via enkele kleine toegangswegen) benadering continu ge(re)exploreerd. Het hechten van de anastomose (vaatverbinding) wordt in deze benaderingen moeilijker geacht.

Bij alle benaderingen voor een omleidings operaties kan de chirurg tijdens de operatie verschillende moeilijkheden tegenkomen:

1. Het lokaliseren van de kransslagader waarop de anastomose moet worden aangelegd. Wanneer de kransslagader verborgen ligt in het vetweefsel dat op het hart aanwezig is of in de hartspier verloopt, kan deze niet visueel gelokaliseerd worden. Tijdrovende en potentieel gevaarlijke dissectie van het hartweefsel is dan noodzakelijk om de kransslagader te vinden.
2. Het selecteren van de optimale plaats op de kransslagader om de anastomose aan te leggen. Inspectie en palpatie zijn de enige manieren om het bloedvat te beoordelen en geven slechts weinig informatie.
3. Beoordelen van de kwaliteit van de aangelegde anastomose. Technische constructie fouten kunnen intraoperatief onopgemerkt blijven en kunnen leiden tot het dicht gaan zitten van de anastomose na de operatie.

In dit proefschrift werd een epicardiale (direct op het hart) echocardiografische (ultrageeluid) mini-transducer geëvalueerd, om tijdens de operatie de chirurg te helpen bij alle bovenstaande problemen, in zowel de open als gesloten borstkas benadering voor omleidings chirurgie.

### Hoofdstuk 2

In dit hoofdstuk worden drie chirurgische hulpmiddelen beschreven die het mogelijk maken om zonder het borstbeen te openen, met behulp van een operatie robot, anastomoses aan te leggen op alle kanten van het kloppende hart. De drie hulpmiddelen zijn: (1) een “sternum lift” waarmee het borstbeen omhoog kan worden getild, waardoor er meer ruimte in de borstkas ontstaat; (2) een “EndoStarfish”, waarmee de achterkant van het hart endoscopisch geëxposeerd kan worden, en (3) een “EndoOctopus” om in de gesloten borstkas de kransslagader te stabiliseren. Door gebruik te maken van Trendelenburg positionering, bleef de arteriële bloeddruk gemiddeld boven de 70 mm Hg (zonder ionotropica toe te dienen) tijdens het



exposeren van de achterkant van het hart in de gesloten borstkas van het varken. Dit maakt het mogelijk met gesloten borstkas op alle kanten van het kloppende hart anastomoses aan te leggen.

### Hoofdstuk 3

De epicardiale echo mini-transducer werd toegepast in het varkens model van gesloten borstkas coronair chirurgie, zoals beschreven in hoofdstuk 2, om endoscopisch de meest belangrijke takken van de linker en rechter kransslagaderen voor omleidings chirurgie te lokaliseren en beoordelen. Via een trocar poort werd de mini-transducer in de borstholte gebrachte om vervolgens met behulp van de robot instrumenten over het hart te manipuleren. Het echobeeld werd middels beeld-in-beeld technologie op de chirurgische console in het beeld van de operatiecamera geprojecteerd. Na adequate endoscopische expositie en stabilisatie konden de belangrijkste kransslagaderen binnen een mediane tijdsduur van 169 seconden per kransslagader gelokaliseerd en beoordeeld worden.

### Hoofdstuk 4

De bruikbaarheid van de mini-transducer voor het evalueren van de kwaliteit van coronaire anastomoses in een (endoscopische, robot geassisteerde) setting op het kloppende hart werd geëvalueerd in varkens experimenten. De coronaire anastomoses werden aangelegd hetzij als een controle anastomose zonder fouten of met een specifieke hechtfout (twee in elkaar gehaakte hechtdraden (cross-over)). Op het kloppende hart konden de anastomoses succesvol in beeld gebracht worden in zowel de open als in de gesloten borstkas benadering. Achteraf werden alle anastomoses correct beoordeeld door twee geblindeerde beoordelaars.

### Hoofdstuk 5

De invloed van specifieke anastomose constructie fouten op de geometrie van de anastomose werd bestudeerd met behulp van epicardiale echografie op ex-vivo, druk geperfuseerde varkens en post-mortem humane harten. De bestudeerde constructie fouten bestonden uit: een overhechte “teen” van de anastomose, een overhechte “hiel” van de anastomose, het in elkaar haken van twee hechtsteken (cross-over), en het zeer ernstig aansnoeren van de hecht draad voor het afknopen van de hechting. Met de 13 MHz epicardiale mini-transducer konden alle vier de specifieke constructie fouten accuraat in beeld gebracht worden en was beoordeling van de invloed op de geometrie mogelijk. Alle fouten verminderden de oppervlakte van de anastomose opening maar niet die van de uitstroom openingen naar distaal en proximaal.

## Hoofdstuk 6

Vervolgens werd op ex-vivo harten, de sensitiviteit en de specificiteit van epicardiale echocardiografie voor het detecteren van constructie fouten in coronaire anastomoses bepaald en vergeleken met de huidige “gouden standaard” angiografie. Constructie fouten werden met behulp van epicardiale echocardiografie gedetecteerd met een sensitiviteit van 0.98 en een specificiteit van 1.00 wat significant hoger was dan met behulp van angiografie (respectievelijk 0.75 en 0.81). Ook was er een betere overeenstemming tussen de echo beoordelaars onderling dan tussen de angiografie beoordelaars onderling.

## Hoofdstuk 7

De epicardiale mini-transducer werd gebruikt tijdens de toepassing van de S<sup>2</sup>AS vaatconnector voor omleidings chirurgie op het kloppende hart in het varken. Met behulp van echo werden kwantitatieve metingen van de vaaddiameter met behulp van een speciaal ontworpen meetinstrument gevalideerd. Tevens werd de kwaliteit van de coronaire anastomose na het afvuren van de connector beoordeeld. Uit het onderzoek bleek dat met behulp van het meetinstrument een betrouwbare schatting van de interne vaaddiameter gemaakt kan worden. Met de 13 MHz epicardiale echo mini-transducer kan intraoperatief de kwaliteit van de S<sup>2</sup>AS anastomose beoordeeld worden, ondanks minimale artefacten die geïnduceerd worden door het metaal van de connector.

## Hoofdstuk 8

Na de grondige evaluatie en validatie van de mini-transducer in het laboratorium, worden in dit hoofdstuk de eerste succesvolle resultaten beschreven van de toepassing van de mini-transducer op alle kanten van het hart, bij patiënten die een omleidings operatie ondergaan.

De informatie die met behulp van de epicardiale echo werd verkregen was van grote waarde omdat dit resulteerde in het veranderen van de anastomose plaats op de kransslagader, van invloed was op het totale aantal anastomoses dat werd aangelegd en in één patiënt door de echo informatie werd voorkomen dat er op een verkeerde kransslagader een anastomose werd aangelegd. Tevens werd de afwezigheid van constructie fouten in de anastomoses bevestigd.

## Hoofdstuk 9

Om de succesvolle bevindingen in patiënten uit te bouwen, werd er een studie protocol opgezet waarbij in patiënten die een omleidingsoperatie moeten ondergaan de intraoperatieve echo bevindingen worden vergeleken

met pre- en postoperatieve angiografie informatie en postoperatieve bevindingen bij een multislice CT onderzoek. De medisch ethische toetsingscommissie van het Universitair Medisch Centrum Utrecht heeft haar toestemming voor deze studie gegeven.

### Hoofdstuk 10

De verbeteringen gedurende de laatste 20 jaar van de epicardiale echocardiografie transducer afmetingen en technologie hebben geresulteerd in kleinere transducers met een hogere resolutie die gebruikt kunnen worden als een veelzijdige intraoperatieve tool tijdens coronaire omleidingschirurgie. De mini-transducer die gebruikt is in het onderzoek beschreven in dit proefschrift, kan op alle kanten van het hart worden gebruikt, tijdens alle chirurgische benaderingen die op dit moment voor coronaire omleidingsoperaties worden gebruikt.

Epicardiale echocardiografie helpt intraoperatief bij: (1) het lokaliseren van de kransslagader, (2) het beoordelen en vastleggen van de kwaliteit van de kransslagader, (3) het beoordelen en vastleggen van de kwaliteit van de aangelegde anastomose, en (4) het selecteren van de optimale plaats voor het afklemmen en cannuleren van de aorta. Routinematig gebruik van epicardiale echocardiografie kan de resultaten van coronaire omleidingsoperaties verbeteren.

## DANKWOORD

Velen hebben bijgedragen aan de totstandkoming van dit proefschrift en een woord van dank is dan ook op zijn plaats:

Prof. dr. C. Borst, mijn promotor. Beste Kees, vanaf het allereerste begin was mijn promotietraject een race tegen de klok, om op tijd met de co-schappen te kunnen beginnen. Je begeleiding is van cruciaal belang geweest voor het welslagen. Je razendsnelle, minutieuze correcties van manuscripten en abstracts zijn reeds door vele AIO's voor mij geroemd en ook het werk in dit proefschrift was geen uitzondering. Je maakte me snel wegwijs in de wetenschappelijke taal en mores. Dit alles gecombineerd met je vermogen om aandachtig en rustig te luisteren naar ieders verhaal en vervolgens tot een afgewogen besluit te komen, maken je de ideale promotor. Ik beschouw het dan ook als een eer om als een van de laatste promovendi, onder je te mogen promoveren. Veel succes bij alle uitdagingen na je emeritaat.

Dr. P.F. Gründeman, mijn co-promotor. Beste Paul, je enthousiasme tijdens de experimenten is ongeëvenaard en werkt aanstekend. De vrijheid die gaf in het doen van onderzoek heb ik als erg prettig ervaren. Helaas ben je door ziekte niet bij alle delen van het promotie onderzoek even betrokken kunnen zijn. Het stimuleren van, en mogelijkheden die bood tot, congresbezoek heb ik altijd zeer gewaardeerd. Veel succes in het nieuwe huis en met alle nieuwe wetenschappelijke uitdagingen.

Dr. P.F.A. Bakker, cardio-thoracaal chirurg en co-promotor. Beste dr. Bakker, ondanks de overvolle klinische agenda had u altijd tijd voor onderzoek waarbij er altijd een onthaal met koffie en koek was. Mijn dank voor uw intensieve medewerking aan de klinische toepassing van de epicardiale echo en de prettige samenwerking.

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Thomas (zoooooo) Dessing, (bijna) afgestudeerd medisch student. Beste Thomas, mondiale oorden zijn na je tijd in het lab geen onbekende meer voor je. Ik denk met veel plezier terug aan de mooie tijden die we in London (Tiger-Tiger, champagne en de meeste mooie auto's per vierkante meter in Bond street) en Los Angeles (kick down automatic transmission) hebben beleefd. Ook mijn oprechte dank voor je toewijding aan het onderzoek, blijkende uit de lange dagen die je maakte en je bereidheid om 's avonds na je co-schappen op het lab te komen scannen. Binnenkort weer eens een biertje en een nootje?

John Dries en Elly van Zwol, (voormalig) biotechnici. Beste John en Elly, dank voor de ondersteuning en gezelligheid tijdens de vaak zeer lange robot experimenten.

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Niels Boone, paranimf, sportauto rijder en pillendraaiër. Beste Niels, we kennen elkaar al zeer lang en ik waardeer het dat je me nu als paranimf wilt bijstaan. Een goede tijd toegewenst in die “mooie stad achter de duinen”.

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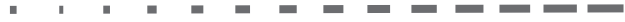
Beste Ria en Walter, mijn dank voor jullie interesse, steun en natuurlijk de gezelligheid in Slikgat.

Beste Opa en Oma, ondanks dat de gezondheid jullie soms in de steek liet, waren jullie altijd geïnteresseerd.

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Lieve Miron, de afgelopen jaren waren een zeer turbulente tijd waarin hoogte- en dieptepunten elkaar in rap tempo afwisselden. Samen kwamen we er altijd weer uit. Hopelijk zijn we nu in wat rustiger vaarwater gekomen. Dank je wel voor alle steun, begrip en ondersteuning als ik weer eens moest werken.

Ricardo

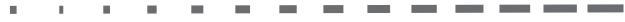




## Curriculum Vitae

Ricardo P.J. Budde was born on September 30, 1978 in Goes, the Netherlands. In 1996, he obtained his high school diploma (VWO) from the Buys Ballot College in Goes. In the same year he entered medical school at Utrecht University where, in 1997, he also started studying Medical Biology. The master's degree in Medicine was obtained in 2001. In 2002, after completing two internships at the Experimental Cardiology Laboratory (head: prof. C. Borst) at Utrecht University he obtained his master's degree (met genoegen) in Medical Biology as well. From 2002 to August 2004 he stayed at the Experimental Cardiology Laboratory to work on his PhD thesis. In 2004 he was awarded the prize for the best presentation during the meeting of the Netherlands Association for Cardio-Thoracic Surgery. In September 2004 he has started his clinical internships to obtain the medical degree.

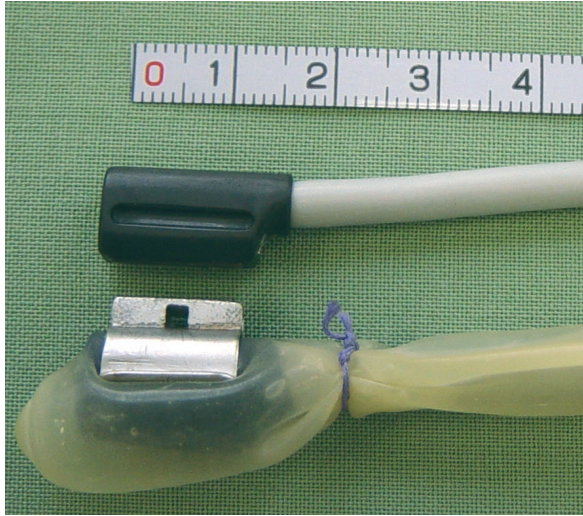
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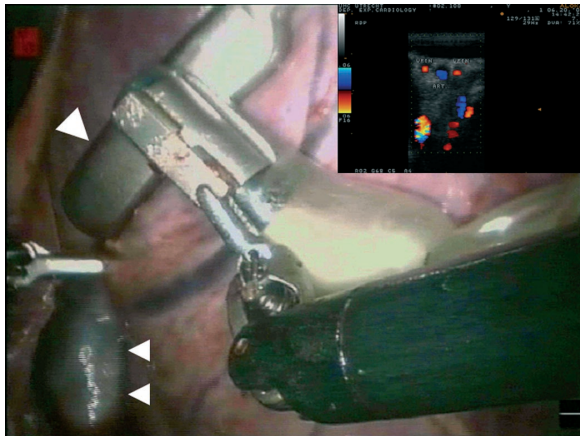
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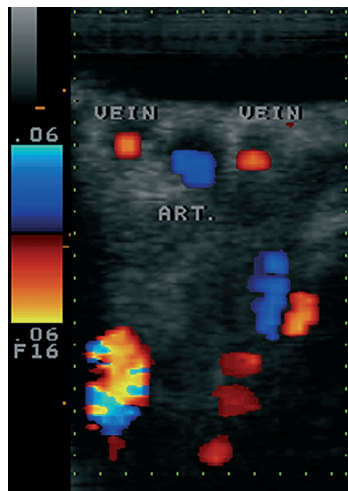
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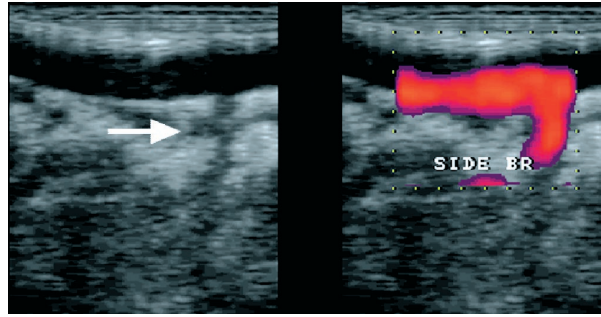
Chapter 3, Figure 1



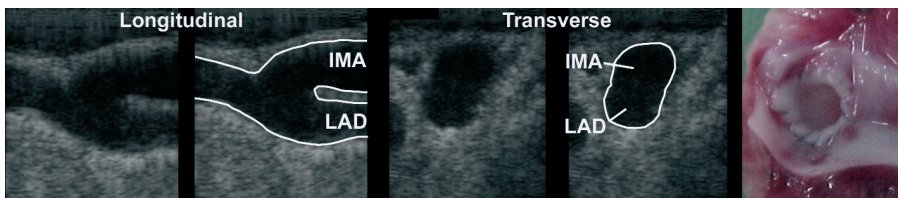
Chapter 3, Figure 2



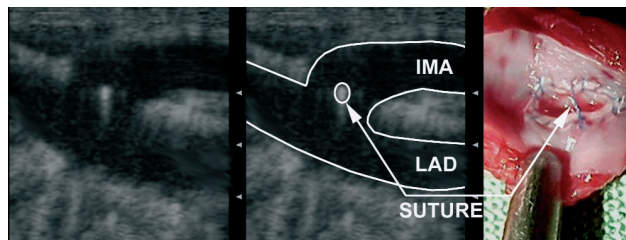
Chapter 3, Figure 4



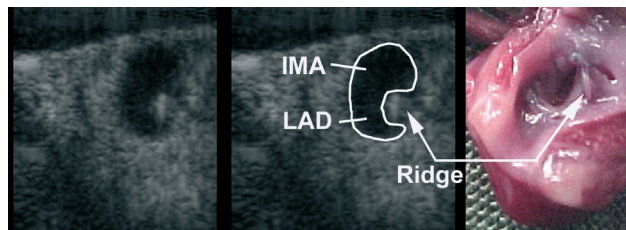
Chapter 3, Figure 6



Chapter 4, Figure 1



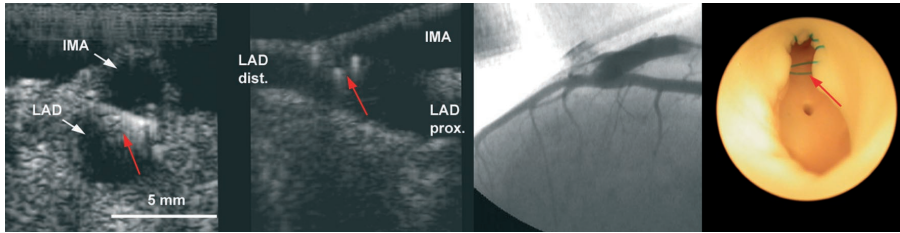
Chapter 4, Figure 2



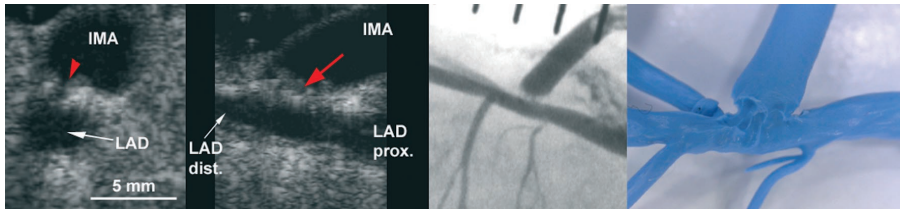
Chapter 4, Figure 3



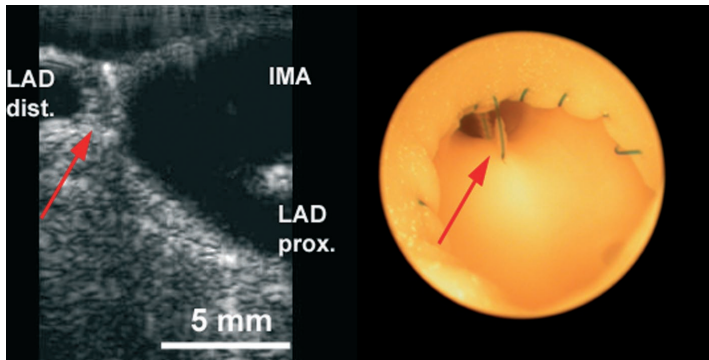




Chapter 6, Figure 2

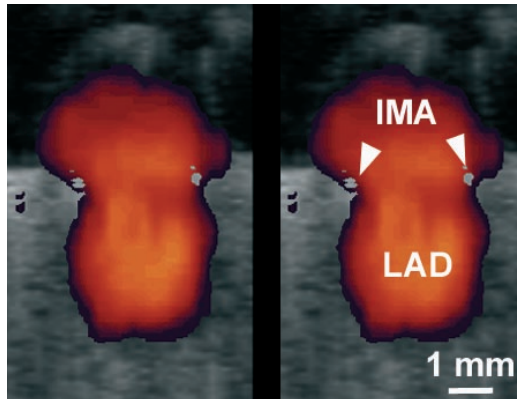


Chapter 6, Figure 3

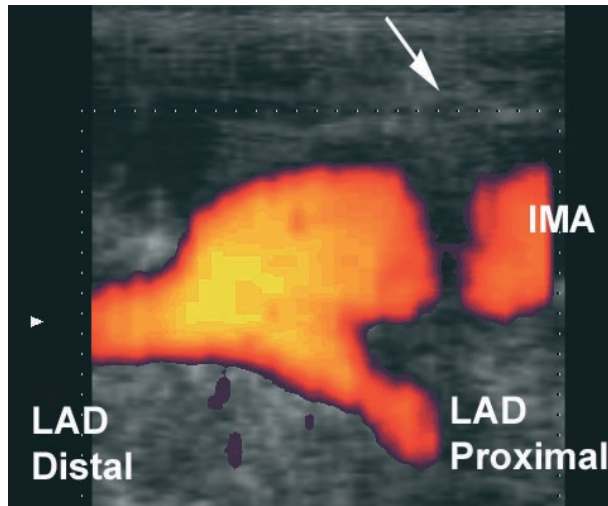


Chapter 6, Figure 4





Chapter 7, Figure 4



Chapter 8, Figure 4

