

# Aortic Root Replacement With Stentless Porcine Xenografts: Early and Late Outcomes in 132 Patients

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**Background.** Traditionally, aortic root replacement has most commonly involved mechanical composite valve grafts, which have excellent durability but necessitate lifelong anticoagulation. Stentless porcine xenografts (bioroots) are a recently developed alternative that enable root replacement without the necessity of long-term anticoagulation. This study examined the early and late outcomes of aortic root replacement with porcine bioroots.

**Methods.** Porcine bioroots were used for root replacement in 132 patients. Of these, 129 (97.7%) required graft extensions for ascending aortic replacement, and 55 (41.7%) underwent aortic arch replacement. Twenty-three operations (17.4%) were reoperations. Twenty-four patients (18.2%) had aortic dissection. Early and late outcomes were ascertained by reviewing medical records. Changes in New York Heart Association (NYHA) class were used to assess improvements in functional status. Follow-up echocardiography results were reviewed to

assess bioprosthetic valve function and changes in left ventricular ejection fraction.

**Results.** There were 10 operative deaths (7.6%), 9 of which were directly related to intraoperative ventricular failure. Nine patients (6.8%) had late valve-related complications, including 5 patients with prosthetic endocarditis (3 died), 1 annular pseudoaneurysm, and 3 sudden, unexplained deaths. Survivors' NYHA status and left ventricular ejection fraction improved significantly. No structural valve dysfunction was evident during follow-up. Actuarial survival was  $85.6\% \pm 3.1\%$  at 1 year and  $77.8\% \pm 4.8\%$  at 5 years.

**Conclusions.** Aortic root replacement with porcine xenografts can be performed with respectable early and late outcomes, even when combined with aortic arch replacement. Further follow-up is necessary to evaluate long-term bioroot durability.

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Despite the increasing popularity of valve-sparing root reconstructions, root replacement remains a standard approach to treating aortic root disease [1, 2]. Although mechanical composite valve grafts (CVGs) are extremely durable, recipients receive lifelong anticoagulation to prevent thromboembolic complications. In patients who might benefit from a bioprosthetic valve, alternatives for aortic root replacement include valved conduits consisting of an aortic valve bioprosthesis attached to a synthetic aortic graft, cryopreserved aortic root homografts, and pulmonary autografts. A recently developed option is the stentless porcine aortic root—or bioroot—prosthesis.

Bioroots are xenografts composed of a thin, stentless, synthetic sewing cuff attached to a glutaraldehyde-preserved porcine aortic root. They were initially developed as customizable prostheses that could be sculpted as needed into various configurations to enable different

degrees of aortic valve replacement, ranging from sub-coronary valve replacement to full root replacement. Their use for aortic valve replacement has gained in popularity since their introduction in the 1990s, and they have been used in an increasingly wide spectrum of aortic valve operations [3–15]. Unlike most other commercially available root prostheses, bioroots have a combination of highly desirable features: they are ready to implant and available off the shelf in a variety of sizes, and lifelong anticoagulation is not required. This retrospective study examined the early and late outcomes of aortic root replacement with bioroots.

## Patients and Methods

### Patients and Data Collection

Institutional Review Board approval was obtained for the collection and analysis of clinical data and waiver of individual consent. Our prospectively maintained clinical database was used to identify 132 consecutive patients

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(Table 1) who had undergone aortic root replacement with porcine bioroots. In all patients the indication for operation was aneurysm or dissection involving the aor-

Table 1. Preoperative Characteristics of 132 Patients Who Underwent Aortic Root Replacement Operations With Porcine Bioroots

Demographics, Cardiovascular Comorbidities	No. (%) or Mean $\pm$ 1 SD (range) <sup>a</sup>
Sex	
Men	108 (81.8)
Women	24 (18.2)
Age, y	54.8 $\pm$ 14.0 (15-80)
Connective tissue disorder <sup>b</sup>	20 (15.2)
History of stroke (permanent or transient)	14 (10.6)
Coronary artery disease	41 (31.1)
Previous myocardial infarction	10 (7.6)
Congestive heart failure	16 (12.1)
Previous cardiac operation	23 (17.4)
Replacement of ascending aorta or aortic arch	13 (9.8)
Valve repair or replacement <sup>c</sup>	13 (9.8)
Coronary artery bypass	5 (3.8)
Aortic disease	
Ascending aortic aneurysm/annuloaortic ectasia	130 (98.5)
Aortic root diameter, mm <sup>d</sup>	53.1 $\pm$ 13.0 (26-90)
Dissection of ascending aorta	24 (18.2)
Acute	10 (7.6)
Chronic	14 (10.6)
Pseudoaneurysm	5 (3.8)
Ruptured aneurysm	1 (0.8)
Valvular disease	
Aortic valve regurgitation	
Mild	17 (12.9)
Moderate	30 (22.7)
Severe	75 (56.8)
Aortic valve stenosis	
Mild	4 (3.0)
Moderate	8 (6.1)
Severe	9 (6.8)
New York Heart Association classification	
I	32 (24.2)
II	52 (39.4)
III	31 (23.5)
IV	17 (12.9)
Bicuspid aortic valve (congenital or functional)	45 (34.1)
Failed bioprosthetic valve requiring reoperation	3 (2.3)
Active endocarditis	3 (2.3)

<sup>a</sup> Data were available for all 132 patients unless otherwise noted. <sup>b</sup> Six of the 20 patients with connective tissue disorders met Ghent diagnostic criteria for Marfan syndrome. The other 14 had Loays-Dietz syndrome, familial thoracic aortic aneurysm and dissection, or a currently undetermined disorder. <sup>c</sup> Includes 2 Ross procedures and 1 root replacement with a composite valve graft. <sup>d</sup> Data were available for 102 patients.

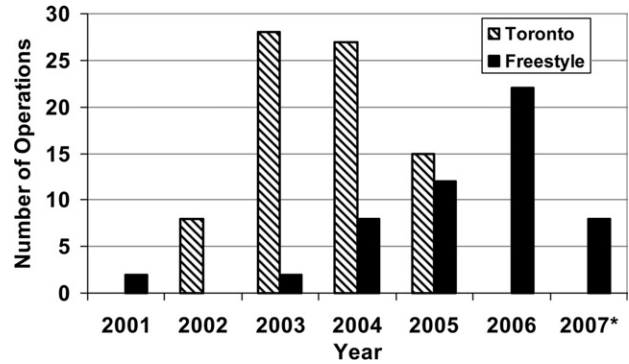


Fig 1. Histogram shows the number of bioroot procedures performed during the study period, stratified by the Toronto (slanted bars) and Freestyle (black bars) bioroots. \*Data for 2007 are from January through July.

tic root; no patient in this series underwent root replacement to treat isolated aortic valve disease [10]. We collected perioperative data after study-specific variables were selected and defined according to relevant reports and reporting guidelines [3-9, 11-21]. Follow-up data were obtained from medical records detailing office visits, hospitalizations, and telephone contacts.

Review of follow-up data focused on identifying potential valve-related complications. Values abstracted from the preoperative and most recent available follow-up (ie, >30 days after operation) echocardiography reports included the lowest raw left ventricular ejection fraction (LVEF) [22]. Current vital status for patients who were lost to follow-up was obtained from the Social Security Death Index (SSDI) database.

#### Bioroot Prostheses

Between March 2001 and July 2007 (Fig 1), 54 patients (40.9%) were implanted with the Medtronic Freestyle Aortic Root Bioprosthesis (Medtronic Inc, Minneapolis, MN). Between May 2002 and November 2005, 78 patients (59.1%) were implanted with the St. Jude Medical Toronto Root Bioprosthesis with BiLinX (St. Jude Medical Inc, St. Paul, MN); data from 26 of these patients were included in a 2004 multicenter report that focused on early outcomes [12].

Patients who received the Toronto bioroot were enrolled in the multicenter investigational device exemption (IDE) clinical trial and provided written informed consent before study enrollment and bioroot implantation. The exclusion criteria for the IDE trial included active endocarditis; need for additional concurrent valve replacement; previous mitral, tricuspid, or pulmonary valve replacement; acute preoperative neurologic event; and renal dialysis. The IDE trial was stopped in 2006, and the Toronto bioroot is no longer being manufactured. The decision to halt progress toward United States Food and Drug Administration approval was reportedly due entirely to business issues and not to any problems with valve safety or performance.

Table 2. Details of 132 Aortic Root Replacement Operations With Porcine Bioroots

Variable	No. (%), or Mean $\pm$ 1 SD (range) <sup>a</sup>
Urgency of operation	
Elective	117 (88.6)
Urgent	4 (3.0)
Emergency	11 (8.3)
Perfusion data and ischemic times	
Cardiopulmonary bypass alone	75 (56.8)
Hypothermic circulatory arrest	57 (43.2)
Without perfusion adjuncts	4 (3.0)
With ACP	37 (28.0)
With RCP	8 (6.1)
With ACP and RCP	8 (6.1)
Right axillary artery cannulation	52 (39.4)
Aortic clamp time, min	109.2 $\pm$ 36.5 (56-321)
CPB time, min	190.3 $\pm$ 65.3 (115-594)
Systemic HCA time, min <sup>b</sup>	29.6 $\pm$ 15.5 (14-85)
Aortic root replacement techniques	
Annular suture technique	
Continuous polypropylene suture	37 (28.0)
Interrupted polyester sutures with pledgets	95 (72.0)
Left coronary artery reattachment technique	
Bentall inclusion	11 (8.3)
Open button	114 (86.4)
Cabrol	1 (0.8)
Hemi-Cabrol	3 (2.3)
Saphenous vein interposition graft	3 (2.3)
Saphenous vein bypass graft	0
Right coronary artery reattachment technique	
Bentall inclusion	5 (3.8)
Open button	115 (87.1)
Cabrol	1 (0.8)
Hemi-Cabrol	1 (0.8)
Saphenous vein interposition graft	3 (2.3)
Saphenous vein bypass graft	7 (5.3)
Ascending aortic and aortic arch management	
Graft extension for ascending aortic replacement	129 (97.7)
Ascending aortoplasty	1 (0.8)
Graft replacement of aortic arch	55 (41.7)
Beveled hemiarch repair	47 (35.6)
Total arch repair	8 (6.1)
Elephant trunk repair	5 (3.8)
Prior reverse elephant trunk repair	1 (0.8)
Bypasses to brachiocephalic arteries	6 (4.5)
Other concomitant procedures	
Coronary artery bypass grafting	32 (24.2)
Placement of intraaortic balloon	7 (5.3)
Ablation procedures for AF (modified Maze)	3 (2.3)
Mitral valve repair or replacement	3 (2.3)

Table 2. Continued

Variable	No. (%), or Mean $\pm$ 1 SD (range) <sup>a</sup>
Placement of ventricular assist device	2 (1.5)
Repair of ventricular septal defect	1 (0.8)
Septal myectomy	1 (0.8)

<sup>a</sup> Data were available for all 132 patients unless otherwise noted. <sup>b</sup> Data were available for 57 patients.

ACP = antegrade cerebral perfusion; AF = atrial fibrillation; CPB = cardiopulmonary bypass; HCA = hypothermic circulatory arrest; RCP = retrograde cerebral perfusion.

### Surgical Techniques

Most of the 132 operations (Table 2) were elective, and 23 procedures (17.4%) were reoperations. Hypothermic circulatory arrest (HCA) was necessary in 57 patients (43.2%), including 10 patients with acute dissection in whom HCA was used to facilitate an open distal anastomosis, most often as a beveled hemiarch. The aortic arch was replaced in 55 patients (41.7%). During the period covered in this series, we used both retrograde and antegrade cerebral perfusion as adjuncts to HCA; our currently favored approach to HCA includes routine use of right axillary artery inflow and antegrade cerebral perfusion [23].

The sizes of the implanted bioroots ranged from 19 to 29 mm; 25-mm bioroots were used in nearly half of the cases. At the time of implantation, the bioroot was rotated so that the noncoronary sinus of the prosthesis was aligned with the right coronary segment of the patient's annulus. The unused left coronary artery stump of the bioroot was often reinforced with a pledgeted polypropylene suture to prevent bleeding. Early in our experience, we used continuous polypropylene sutures to attach the bioroot sewing ring to the aortic valve annulus (Fig 2A). We eventually changed our technique to make it easier to perform the anastomosis, and we currently favor interrupted supraannular polyester mattress sutures with felt pledgets (Fig 2B). The annular anastomosis was often reinforced with a continuous polypropylene suture to prevent bleeding [24].

Whenever possible, both coronary arteries were reattached after being mobilized along with generous buttons of surrounding aortic tissue (Fig 2C). Techniques used to prevent bleeding at the coronary anastomoses have been previously reported in detail [24]. When it was not feasible to use the button technique, an alternative approach to reattachment was used for one or both coronary arteries (Table 2). Alternative methods for reattaching the coronary arteries included the Bentall inclusion technique [1]; the Cabrol technique [25]; the hemi-Cabrol technique, in which one coronary artery was reattached with an 8- or 10-mm polyester interposition graft; and the use of a reversed segment of autologous saphenous vein placed as an interposition graft to a coronary ostium or as a bypass graft to a more distal aspect of the coronary artery. Alternative coronary artery reattachment techniques were used in 9 of 23 patients

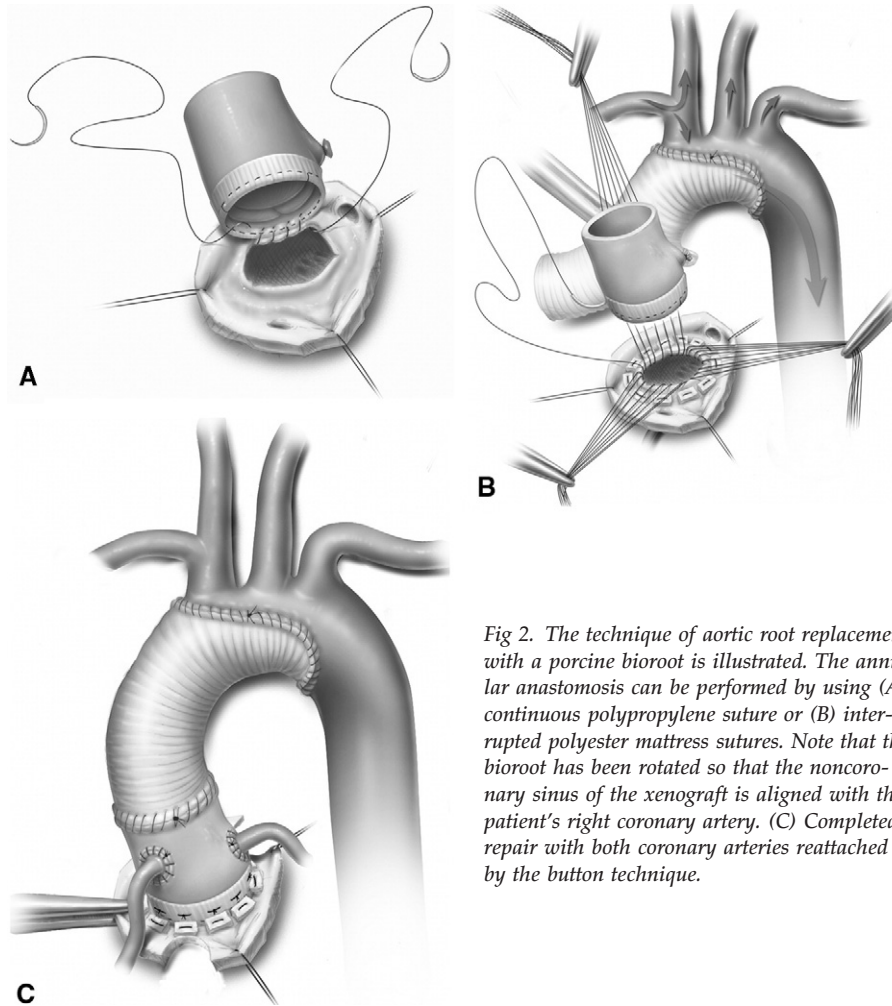


Fig 2. The technique of aortic root replacement with a porcine bioroot is illustrated. The annular anastomosis can be performed by using (A) continuous polypropylene suture or (B) interrupted polyester mattress sutures. Note that the bioroot has been rotated so that the noncoronary sinus of the xenograft is aligned with the patient's right coronary artery. (C) Completed repair with both coronary arteries reattached by the button technique.

(39%) undergoing reoperations compared with 16 of 109 patients (15%) undergoing first-time operations.

In nearly all cases, we used a gelatin-impregnated woven polyester graft (Gelweave, Vascutek Inc, Ann Arbor, MI) to bridge the distance between the bioroot and the distal extent of aortic replacement. Graft sizes varied from 18 to 28 mm, with 24-mm grafts being used most commonly.

The most commonly performed concomitant procedure was coronary artery bypass grafting (CABG). This procedure was used in 7 patients as an alternative approach to coronary reattachment and was needed in another 32 patients to treat coronary artery disease, intraoperative ventricular dysfunction, or severe bleeding from a coronary reattachment site [13]. Placement of an intraaortic balloon, a ventricular assist device, or both, was required in 7 patients (5.3%) because they had difficulty separating from cardiopulmonary bypass.

#### Statistical Analysis

We analyzed only data collected specifically for this retrospective study; no data were obtained from the sponsor of the Toronto bioroot IDE trial. Data were analyzed with SAS 9.2 software (SAS Inc, Cary, NC).

Quantitative variables are presented as mean  $\pm$  1 standard deviation. Overall actuarial survival was estimated by using the Kaplan-Meier survival model.

In a post hoc analysis, we compared the preoperative characteristics, surgical details, and outcomes of patients who received the Freestyle bioroot with those of patients who received the Toronto bioroot. Categorical variables were analyzed with  $\chi^2$  or Fisher exact tests. Continuous variables were first examined for normality of distribution; the *t* test was used for those with normal distributions, and the nonparametric Mann-Whitney *U* test was applied for those with skewed distributions. For survival analysis, we used a Kaplan-Meier survival model in which type of replacement was the factor of comparison. In all tests, two-tailed *p*-values were calculated.

#### Results

##### Early Outcomes

Early complications (Table 3) included 10 operative deaths (7.6%); 8 (6.1%) occurred within 30 days postoperatively (Table 4). Nearly all of the early deaths were directly related to intraoperative ventricular failure; technical problems

**Table 3. Outcomes after 132 Aortic Root Replacement Operations With Porcine Bioroots**

Outcomes	No (%) or Mean $\pm$ 1 SD (range) <sup>a</sup>
<b>Early outcomes</b>	
Operative death	10 (7.6)
Within 30 days of operation	8 (6.1)
During initial hospitalization <sup>b</sup>	10 (7.6)
Stroke <sup>c</sup>	9 (6.8)
Bleeding requiring reoperation	17 (12.9)
Cardiac complications <sup>d</sup>	67 (50.8)
Atrial arrhythmia	45 (34.1)
Ventricular arrhythmia	10 (7.6)
Cardiac failure	16 (12.1)
Pericardial effusion requiring drainage	10 (7.6)
Heart block requiring pacemaker	9 (6.8)
Myocardial infarction	2 (1.5)
Pulmonary complications <sup>e</sup>	28 (21.2)
Renal failure requiring dialysis <sup>f</sup>	8 (6.1)
Survivor hospital LOS, days <sup>g</sup>	13.1 $\pm$ 16.4 (4–108)
<b>Late valve-related complications<sup>h</sup></b>	
Reoperation required	1 (0.8)
Annular pseudoaneurysm	1 (0.8)
Endocarditis	5 (3.8)
Sudden, unexplained death	3 (2.3)

<sup>a</sup> Data were available for all 132 patients unless otherwise noted. <sup>b</sup> Operative mortality was defined as death  $\leq$  30 days of operation or during the initial hospitalization. In accordance with reporting guidelines [19, 20], hospital-to-hospital transfer was not considered discharge, so deaths that occurred after such transfers were counted as operative deaths. Patients who died after being transferred to a nursing home or rehabilitation center were considered as having been discharged unless the death was due to a complication directly related to the operation. Deaths that occurred after this operative period were classified as late deaths. <sup>c</sup> Stroke was defined as a new focal neurologic deficit, whether permanent or transient. <sup>d</sup> Cardiac complications included atrial and ventricular arrhythmias requiring treatment, cardiac failure necessitating mechanical or prolonged inotropic support, heart block requiring pacemaker implantation, myocardial infarction, and pericardial effusion requiring drainage. <sup>e</sup> Pulmonary complications were defined as ventilator dependency lasting  $>$  48 hours, pneumonia, pleural effusion requiring drainage, pneumothorax necessitating evacuation, and atelectasis necessitating bronchoscopy. <sup>f</sup> Includes both temporary and permanent dialysis. <sup>g</sup> Survivors' length of hospital stay (LOS) was computed as the number of days between procedure and discharge; our analyses of this variable excluded patients who died before hospital discharge but included the time patients spent at hospitals or long-term acute care facilities after transfer from our institution. Data were available for 122 patients. <sup>h</sup> Valve-related complications were defined as valve failure necessitating reoperation, annular pseudoaneurysm formation, postoperative endocarditis (including recurrent endocarditis), moderate or severe aortic valve regurgitation (according to echocardiographic findings), and unexplained deaths [16]. (LOS = length of stay.)

with coronary reattachment had occurred in 4 of these patients. Cardiac arrhythmia was the most common early complication, occurring in 55 patients (41.6%); 45 of the 55 arrhythmias (82%) were atrial in origin.

#### Late Outcomes

Clinical follow-up data were available for 119 of the 122 early survivors (97.5%), who had a mean clinical follow-up of  $3.3 \pm 1.5$  years (range, 39 days to 6.8 years). Three patients were lost to follow-up, but their current

vital status data were obtained from the SSDI database; thus, current survival data were available for all patients. Of the 17 late deaths (Table 4), 9 occurred in the first postoperative year. Actuarial survival was  $85.6\% \pm 3.1\%$  at 1 year and  $77.8\% \pm 4.8\%$  at 5 years (Fig 3).

Late valve-related complications have developed in 9 patients (6.8%). In one patient, a pseudoaneurysm arose from the annular and left coronary anastomoses. The bioroot was replaced with a CVG, and the patient remains alive. Endocarditis developed in 5 patients. This complication was fatal in 3 patients and was successfully treated nonoperatively in 2. Three patients died suddenly of unexplained causes (Table 4). Because the causes of death could not be documented, they were classified as valve-related deaths in accordance with the guidelines for reporting adverse events after valve procedures [16]. Therefore, 6 of the late deaths were considered valve-related.

Three patients had late complications due to left main coronary stenosis; although not valve-related, these deaths were attributable to the root-replacement procedure [13]. One of the affected patients died of a myocardial infarction 3 months after operation. In the second patient, severe mitral regurgitation and congestive heart failure developed 2 years after root replacement. This patient was treated with coronary angioplasty and stenting but declined mitral valve repair and ultimately died of heart failure. The third patient remains alive after undergoing emergency CABG 6.5 months after the initial operation.

Follow-up New York Heart Association (NYHA) status was available for 84 of 105 survivors (80%). Comparison of preoperative and follow-up NYHA status showed that after a mean follow-up of  $3.5 \pm 1.3$  years (range, 0.8 to 6.8 years), patients had significant improvement in functional status (Table 5). NYHA status improved in 54 of the 59 patients (92%) who had been in NYHA classes II, III, or IV preoperatively.

Follow-up echocardiography data were available for 99 of 105 survivors (94%). Comparison of preoperative and follow-up LVEF showed that, after a mean follow-up of  $2.8 \pm 1.4$  years (range, 64 days to 6.1 years), patients had significant improvement in ventricular function (Table 5). Of the 39 patients who had reduced LVEF before surgery, LVEF improved in 35 (90%). Valve integrity at follow-up was excellent; only 1 patient had even minimal aortic regurgitation. Mild aortic valve stenosis was found on echocardiography in 8 patients (8.0%), and moderate stenosis was found in 2 (2.0%). No patient had evidence of structural valve deterioration.

#### Comparison of Freestyle and Toronto Bioroot Groups

Our analysis of preoperative characteristics revealed profound differences in the two patient groups (Table 6). Overall, the Toronto bioroot recipients appeared to be at lower risk than the Freestyle bioroot recipients. The more frequent use of HCA in the Freestyle group corresponded to a trend toward longer cardiopulmonary bypass times in this group. Neither early nor late outcomes differed significantly between the two groups.

Table 4. Causes of Early and Late Deaths After 132 Aortic Root Replacement Operations With Porcine Bioroots

Patient Age, Years	Sex	Bioroot Type	Survival, Days	Cause of Death
Early deaths				
64	M	Toronto	0	Intraoperative coagulopathy and left ventricular failure
55	F	Freestyle	0	Intraoperative biventricular failure
64	M	Freestyle	0	Intraoperative left ventricular failure
70	M	Freestyle	0	Intraoperative coagulopathy → biventricular failure
73	M	Freestyle	0	Intraoperative biventricular failure
71	F	Toronto	2	Intraoperative right ventricular failure
52	M	Freestyle	10	Intraoperative left ventricular failure → multiorgan failure
75	F	Toronto	24	Sudden cardiorespiratory arrest
80	M	Freestyle	42	Intraoperative left ventricular failure → multiorgan failure
70	F	Freestyle	58	Intraoperative left ventricular failure → multiorgan failure and sepsis
Late deaths				
34	F	Toronto	39	Sudden, unexplained death <sup>a,b</sup>
42	M	Freestyle	47	Recurrent endocarditis with dehiscence of prosthetic mitral valve, sepsis <sup>a</sup>
66	M	Toronto	67	Sudden, unexplained death <sup>a,c</sup>
66	M	Freestyle	91	Left main coronary stenosis, myocardial infarction
72	M	Toronto	128	Sudden, unexplained death <sup>a,d</sup>
69	M	Toronto	200	Sepsis and respiratory failure
54	M	Freestyle	207	Endocarditis with root abscess → multiple systemic septic emboli <sup>a</sup>
57	F	Freestyle	304	Rupture of descending thoracic aortic pseudoaneurysm
63	M	Toronto	364	Lung cancer, bronchial artery hemorrhage
60	M	Freestyle	463	Sepsis after repair of infected descending thoracic aortic graft and esophageal fistula
61	F	Toronto	793	Left main coronary stenosis, severe mitral regurgitation, congestive heart failure
63	M	Toronto	813	Malignant lymphoma
68	M	Toronto	855	Lung cancer, respiratory failure after lung resection
43	M	Freestyle	877	Myocardial infarction
78	F	Toronto	1711	Endocarditis <sup>a</sup>
72	M	Toronto	2106	Acute myocardial infarction from progressive coronary artery disease
77	M	Freestyle	2431	Pneumonia

<sup>a</sup> Valve-related death. <sup>b</sup> Patient had acute dyspnea and back and abdominal pain after recent thoracoabdominal aortic repair; however, the cause of death could not be documented. <sup>c</sup> Patient had an unrepaired thoracoabdominal aortic aneurysm; however, the cause of death could not be documented. <sup>d</sup> Cause of death was not documented; death was discovered by using Social Security Death Index database after patient was lost to follow-up.

F = female; M = male.

## Comment

The stentless porcine xenograft root is a valuable addition to the surgical armamentarium for aortic root replacement. Our study found encouraging results in a uniquely complex group of patients. Connective tissue disorders were present in a relatively high proportion of patients (15.2%). These diseases are characterized by extensive aortic involvement and thus put patients at increased risk of aortic repair failure [26]. All procedures in our series involved total root replacement, most required extended graft repair of the ascending aorta, and 42% involved aortic arch repair. In contrast, in many previous series of bioroot implantations, often less than 30% of patients underwent full root replacement, and it was rare for repairs to extend into the aortic arch [4, 6–9, 18, 27]. A few reports focused on full root replacement (Table 7), but these series included relatively few patients with aortic dissection, reoperations, or aortic arch repairs [11–15]. Despite the high-risk patient profile in our series,

early and late results were respectable and comparable with those of previous series.

Follow-up results showing improvements in our cohort's functional status and LVEF, as well as bioroot durability, are encouraging: there was no evidence of structural valve failure, and the incidence of late valve-related complications was low (6.8%). Although sudden unexplained deaths meet reporting standards for valve-related mortality [16], given the clinical circumstances in 2 of these patients—1 with an unrepaired thoracoabdominal aortic aneurysm, and 1 with acute back pain after thoracoabdominal aortic repair—it seems unlikely that the bioroots were the cause of death.

Two different types of porcine bioroots have been used in the United States; mid- and long-term data after root replacements are limited for one type and are nonexistent for the other. Follow-up data extending up to 12 years for the Freestyle xenograft have shown excellent clinical outcomes, prosthesis durability, and hemodynamic per-

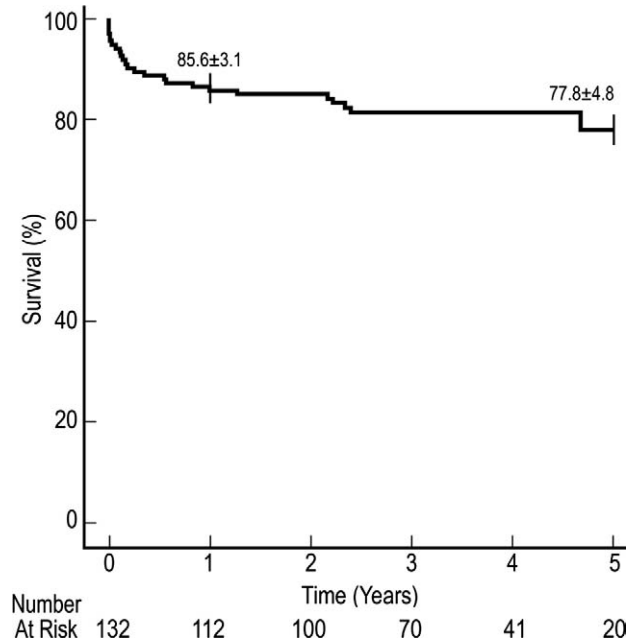


Fig 3. Kaplan-Meier survival curve shows survival after 132 aortic root replacement operations with porcine bioroots.

formance; however, most of the data on this device focus solely on its use for subcoronary aortic valve replacement [3-9]. Mid- and long-term data are emerging for its use in root replacement but remain limited (Table 7). In a randomized trial, Melina and associates [15] found that Freestyle bioroots were about as durable as homografts after a median follow-up of 45 months; 5-year actuarial survival for the bioroot group was 83% ± 5%. Kon and associates [14] reported a similar 5-year actuarial survival of 82.8% after aortic root replacements with Freestyle bioroots.

For the Toronto bioroot, published reports are limited to short-term results culled from the IDE clinical study [11-13]; mid- and long-term outcome data are lacking. Early analysis of the IDE study data revealed outstanding short-term durability and a trend toward a reduction in the transvalvular gradient over time; aortic regurgitation, structural valvular deterioration, and nonstructural dysfunction were not found in any patient [12]. Because the Toronto bioroot has been implanted in more than 600 patients, a careful examination of outcomes in these patients remains important even though the device is no longer available for use.

Although this study was not designed to compare the safety or effectiveness of the 2 devices, we believed that a descriptive post hoc comparison might nevertheless be instructive. We predominately used the Toronto bioroot during our early experience and gradually shifted toward the Freestyle device (Fig 1). In general, the patients who received the Toronto bioroot were healthier preoperatively and had less complicated operations. The most likely explanations for this observation are the constraints of the related IDE study, which prevented enrollment of many high-risk patients, and our own expanding use of bioroots in increasingly complex cases over time. The change from the Toronto device to the Freestyle root also paralleled several changes in our technique; for example, Freestyle recipients were more likely to have axillary artery cannulation and interrupted annular sutures. The higher complexity of operations in the Freestyle group is reflected in the slightly higher incidences of operative death, bleeding, and morbidity in that group; however, none of the outcome variables were significantly different between groups.

Nine of the 10 early deaths were associated with intraoperative ventricular failure, and technical problems related to coronary reattachment occurred in 4 of these cases. It is critical to ensure proper alignment of the

Table 5. Comparison of Preoperative Versus Follow-up New York Heart Association Status and Left Ventricular Ejection Fraction

Postoperative NYHA Class <sup>a</sup>	Preoperative NYHA Class, No. (%)			
	I (n = 25)	II (n = 40)	III (n = 15)	IV (n = 4)
I	22 (88)	35 (88)	9 (60)	1 (25)
II	3 (12)	3 (8)	6 (30)	2 (50)
III	0	2 (5)	0	1 (25)
IV	0	0	0	0

Postoperative LVEF <sup>b</sup>	Preoperative LVEF, No. (%)			
	Normal (n = 55)	Mildly Reduced (n = 27)	Moderately Reduced (n = 11)	Severely Reduced (n = 1)
Normal	51 (93)	23 (85)	7 (64)	0
Mildly reduced	4 (7)	1 (4)	4 (36)	0
Moderately reduced	0	1 (4)	0	1 (100)
Severely reduced	0	2 (7)	0	0

<sup>a</sup> NYHA status significantly improved during follow-up ( $p = 0.004$ ). <sup>b</sup> LVEF was classified as normal ( $\geq 55\%$ ), mildly reduced (41%–54%), moderately reduced (26%–40%), or severely reduced ( $\leq 25\%$ ) [22]. LVEF significantly improved during follow-up ( $p < 0.0001$ ).

LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

Table 6. Comparison of Patients Who Received Toronto vs Freestyle Bioroots<sup>a</sup>

Variable	Toronto Bioroot (n = 78)	Freestyle Bioroot (n = 54)	p-Value
<b>Preoperative</b>			
Age, years	54.1 ± 13.7	55.8 ± 14.5	0.5
Dissection of ascending aorta	6 (8)	18 (33)	<0.001
Acute	0	10 (19)	<0.001
Chronic	6 (8)	8 (15)	0.3
New York Heart Association classification			<0.001
I	25 (32)	7 (13)	
II	34 (44)	18 (33)	
III	18 (23)	13 (24)	
IV	1 (1)	16 (30)	
History of chronic lung or airway disease	12 (15)	18 (33)	0.02
Previous cardiac operation	9 (12)	14 (26)	0.04
<b>Operative</b>			
Urgency of operation			<0.001
Elective	75 (96)	42 (78)	
Urgent	3 (4)	1 (2)	
Emergency	0	11 (20)	
Hypothermic circulatory arrest	23 (29)	34 (63)	<0.001
Without perfusion adjuncts	1 (1)	3 (6)	0.3
With ACP	8 (10)	29 (54)	<0.001
With RCP	8 (10)	0	0.02
With ACP and RCP	6 (8)	2 (4)	0.5
Right axillary artery cannulation	13 (17)	39 (72)	<0.001
Aortic clamp time, min	105.8 ± 20.7	114.2 ± 51.3	0.2
CPB time, min	182.4 ± 44.3	201.8 ± 86.4	0.09
Systemic HCA time, min <sup>b</sup>	33.0 ± 17.4	27.3 ± 13.8	0.2
Aortic arch repair	22 (28)	33 (61)	<0.001
Annular suture technique			0.001
Continuous polypropylene suture	30 (38)	7 (13)	
Interrupted polyester sutures with pledgets	48 (62)	47 (87)	
Left coronary reattachment technique			0.2
Bentall inclusion	4 (5)	7 (13)	
Open button	72 (92)	42 (78)	
Cabrol	0	1 (2)	
Hemi-Cabrol	1 (1)	2 (4)	
Saphenous vein interposition graft	1 (1)	2 (4)	
Right coronary reattachment technique			0.2
Bentall inclusion	2 (3)	3 (6)	
Open button	72 (92)	43 (80)	
Cabrol	0	1 (2)	
Hemi-Cabrol	1 (1)	0	
Saphenous vein interposition graft	1 (1)	2 (4)	
Saphenous vein bypass graft	2 (3)	5 (9)	
<b>Outcomes</b>			
Operative death	3 (4)	7 (13)	0.09
Within 30 days of operation	3 (4)	5 (9)	0.3
Stroke	7 (9)	2 (4)	0.3
Bleeding requiring reoperation	7 (9)	10 (19)	0.1
Cardiac complications	36 (46)	31 (57)	0.2
Pulmonary complications	13 (17)	15 (28)	0.1
Renal failure necessitating dialysis	3 (4)	5 (9)	0.3
Survivor hospital LOS, days <sup>c</sup>	12.5 ± 17.5	14.1 ± 14.7	0.9
Late valve-related complications	6 (8)	3 (6)	0.7

Table 6. Continued

Variable	Toronto Bioroot (n = 78)	Freestyle Bioroot (n = 54)	p-Value
Actuarial survival			0.1
1-year (%)	89.7 ± 3.4	79.6 ± 5.5	
5-year (%)	81.8 ± 5.5	74.1 ± 6.4	

<sup>a</sup> Categorical data are presented as number (percentage) of patients. Continuous data are presented as mean ± 1 standard deviation. Data were available for all 132 patients unless otherwise noted. <sup>b</sup> Data available for 57 patients. <sup>c</sup> Data available for 122 patients.

ACP = antegrade cerebral perfusion; CPB = cardiopulmonary bypass; HCA = hypothermic circulatory arrest; LOS = length of stay; RCP = retrograde cerebral perfusion.

coronary arteries and to carefully select the reattachment sites to prevent kinking of the coronary arteries. Any difficulty weaning the patient from cardiopulmonary bypass raises immediate concern about coronary malperfusion; whenever this is suspected, we expeditiously perform CABG, which can often be done without cross-clamping the aorta. Bleeding from the coronary buttons can also be catastrophic and is notoriously difficult to control. We routinely use adjunctive techniques, such as reinforcement with pericardial rings, to prevent bleeding at these anastomoses [24]. When faced with severe coronary button bleeding, we have a low threshold for reclamping the aorta so that the button can be directly repaired, reattached with an alternative technique (eg, interposition graft), or oversewn after CABG is performed.

This retrospective study has several important limitations. Because of our practice's referral pattern, most of our patients live far away from our center and receive follow-up care from their local physicians. We were fortunate enough to capture basic follow-up information (vital status, need for reoperation, etc) for most patients, but in some cases it was not possible to obtain the other, more detailed information needed to fully assess valve performance. Even when such data were available, the lack of standardization between centers complicated efforts at detailed interpretation of these data. For example, from the echocardiography results, we were able to collect data on LVEF and bioprosthetic valve stenosis and regurgitation, but not on left ventricular hypertrophy, transvalvular gradients, or other important variables. Similar challenges were encountered when we attempted to ascertain the incidence of late thromboembolic complications during follow-up, preventing us from studying this important aspect of prosthetic valve safety.

Although this study showed encouraging early and late outcomes, additional follow-up studies will be necessary to better determine the long-term durability of these devices. The Achilles' heel of bioprosthetic valves remains their poor long-term durability compared with that of mechanical valves. As a consequence, many surgeons remain justifiably reluctant to use bioprosthetic roots in younger patients. Furthermore, the potential difficulty of the inevitable reoperations in young patients is an important consideration. Notably, the ease of valve explantation and replacement during reoperation is one of the cited potential advantages of a new prefabricated valved conduit comprising a stentless porcine aortic valve and a synthetic vascular graft [28]. It is possible that advances in catheter-delivered aortic valve prostheses will affect future decisions about using bioroots in younger patients; the pliable bioroot with structural valve deterioration may be a very suitable landing area for an expandable valve-stent.

In light of these concerns, when valve-sparing root reconstruction is not feasible, we continue to advocate using mechanical CVGs in patients aged younger than 70 years. Most exceptions to this approach are made for patients with contraindications to warfarin therapy, but a growing number are driven by patient demand. The mean age of 54 years in our patient cohort reflects the trend of younger patients requesting bioprosthetic aortic valves in our practice. Patients are increasingly choosing the risk of reoperation over the risks associated with long-term anticoagulation.

In conclusion, although stentless porcine xenografts are not the ideal choice for young patients who need root replacement, they are an important alternative to mechanical CVGs, particularly for patients who either cannot or choose not to tolerate lifelong anticoagulation. As

Table 7. Comparison of Published Series Focusing on Aortic Root Replacement With Porcine Bioroots

First Author, Year	No. of Centers	No. of Patients	Bioroot Type	Full Root Replaced, No. (%)	Dissection, No. (%)	Reoperation, No. (%)	Ascending or Arch, No. (%)	Operative Mortality, No. (%)	Follow-up Survival Rate, %
Kon, 1999 [14]	Single	112	Freestyle	112 (100)	...	...	29 (25.9)	4 (3.6)	82.8 at 5 yrs
David, 2004 [11]	Multiple	191	Toronto	150 (78.5)	...	9 (4.7)	...	7 (3.7)	95.8 at 6 mos
Melina, 2004 [15]	Single	80	Freestyle	80 (100)	...	16 (20)	...	4 (5)	83 at 5 yrs
Gleason, 2004 [12]	Multiple	176 <sup>a</sup>	Toronto	158 (89.8)	14 (8.0)	...	95 (54.0)	7 (4.0)	91.0 at 6 mos
Kincaid, 2007 [13]	Single	503	Both	503 (100)	...	...	180 (35.8)	30 (6.0)	...
Current series, 2009	Single	132	Both	132 (100)	24 (18.2)	23 (17.4)	129 (97.7)	10 (7.6)	77.8 at 5 yrs

<sup>a</sup> Includes 26 patients from the current series.

a consequence, it will be important to continue to collect and report durability data to facilitate valve selection decisions by physicians and patients.

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## References

1. Bentall H, De Bono A. A technique for complete replacement of the ascending aorta. *Thorax* 1968;23:338-9.
2. Davies JE, Sundt TM. Surgery insight: the dilated ascending aorta—indications for surgical intervention. *Nat Clin Pract Cardiovasc Med* 2007;4:330-9.
3. Akar AR, Szafrank A, Alexiou C, et al. Use of stentless xenografts in the aortic position: determinants of early and late outcome. *Ann Thorac Surg* 2002;74:1450-7.
4. Bach DS, Metras J, Doty JR, Yun KL, Dumesnil JG, Kon ND. Freedom from structural valve deterioration among patients aged  $\leq 60$  years undergoing Freestyle stentless aortic valve replacement. *J Heart Valve Dis* 2007;16:649-56.
5. Cartier PC, Dumesnil JG, Metras J, et al. Clinical and hemodynamic performance of the Freestyle aortic root bioprosthesis. *Ann Thorac Surg* 1999;67:345-9.
6. Deleuze PH, Fromes Y, Khoury W, Maribas P, Lemaire S, Bical OM. Eight-year results of Freestyle stentless bioprosthesis in the aortic position: a single-center study of 500 patients. *J Heart Valve Dis* 2006;15:247-52.
7. Doty DB, Cafferty A, Cartier P, et al. Aortic valve replacement with Medtronic Freestyle bioprosthesis: 5-year results. *Semin Thorac Cardiovasc Surg* 1999;11:35-41.
8. Kappetein AP, Braun J, Baur LH, et al. Outcome and follow-up of aortic valve replacement with the Freestyle stentless bioprosthesis. *Ann Thorac Surg* 2001;71:601-7.
9. Mohammadi S, Baillet R, Voisine P, Mathieu P, Dagenais F. Structural deterioration of the Freestyle aortic valve: mode of presentation and mechanisms. *J Thorac Cardiovasc Surg* 2006;132:401-6.
10. Bach DS, Cartier PC, Kon ND, Johnson KG, Deeb GM, Doty DB. Impact of implant technique following Freestyle stentless aortic valve replacement. *Ann Thorac Surg* 2002;74:1107-13; discussion 13-4.
11. David TE, Mohr FW, Bavaria JE, et al. Initial experience with the Toronto Root bioprosthesis. *J Heart Valve Dis* 2004;13:248-51.
12. Gleason TG, David TE, Coselli JS, Hammon JW Jr, Bavaria JE. St. Jude Medical Toronto biologic aortic root prosthesis: early FDA phase II IDE study results. *Ann Thorac Surg* 2004;78:786-93.
13. Kincaid EH, Cordell AR, Hammon JW, Adair SM, Kon ND. Coronary insufficiency after stentless aortic root replacement: risk factors and solutions. *Ann Thorac Surg* 2007;83:964-8.
14. Kon ND, Cordell AR, Adair SM, Dobbins JE, Kitzman DW. Aortic root replacement with the Freestyle stentless porcine aortic root bioprosthesis. *Ann Thorac Surg* 1999;67:1609-15.
15. Melina G, De Robertis F, Gaer JA, Amrani M, Khaghani A, Yacoub MH. Mid-term pattern of survival, hemodynamic performance and rate of complications after Medtronic Freestyle versus homograft full aortic root replacement: results from a prospective randomized trial. *J Heart Valve Dis* 2004;13:972-5; discussion 5-6.
16. Akins CW, Miller DC, Turina MI, et al. Guidelines for reporting mortality and morbidity after cardiac valve interventions. *Ann Thorac Surg* 2008;85:1490-5.
17. Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *Circulation* 2006;114:e84-231.
18. Doty DB, Cafferty A, Kon ND, Huysmans HA, Krause AH Jr, Westaby S. Medtronic Freestyle aortic root bioprosthesis: implant techniques. *J Card Surg* 1998;13:369-75.
19. Edmunds LH Jr, Clark RE, Cohn LH, Grunkemeier GL, Miller DC, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. Ad Hoc Liaison Committee for Standardizing Definitions of Prosthetic Heart Valve Morbidity of The American Association for Thoracic Surgery and The Society of Thoracic Surgeons. *J Thorac Cardiovasc Surg* 1996;112:708-11.
20. Edmunds LH Jr, Cohn LH, Weisel RD. Guidelines for reporting morbidity and mortality after cardiac valvular operations. *J Thorac Cardiovasc Surg* 1988;96:351-3.
21. Westaby S. Stentless bioprostheses in aortic root disease. *Semin Thorac Cardiovasc Surg* 2001;13:273-82.
22. Sweitzer NK, Lopatin M, Yancy CW, Mills RM, Stevenson LW. Comparison of clinical features and outcomes of patients hospitalized with heart failure and normal ejection fraction ( $\geq 55\%$ ) versus those with mildly reduced (40% to 55%) and moderately to severely reduced ( $<40\%$ ) fractions. *Am J Cardiol* 2008;101:1151-6.
23. Coselli JS, Bozinovski J, LeMaire SA. Arch aneurysms. In: Kaiser LR, Kron IL, Spray TL, eds. *Mastery of Cardiothoracic Surgery*. Philadelphia: Lippincott, Williams & Wilkins; 2007: 556-67.
24. Coselli JS, Conklin LD, LeMaire SA. An effective strategy for optimizing hemostasis following aortic root replacement. *J Vasc Br* 2003;2:183-6.
25. Cabrol C, Pavie A, Gandjbakhch I, et al. Complete replacement of the ascending aorta with reimplantation of the coronary arteries: new surgical approach. *J Thorac Cardiovasc Surg* 1981;81:309-15.
26. LeMaire SA, Carter SA, Volguina IV, et al. Spectrum of aortic operations in 300 patients with confirmed or suspected Marfan syndrome. *Ann Thorac Surg* 2006;81:2063-78.
27. Carrel TP, Berdat P, Englberger L, et al. Aortic root replacement with a new stentless aortic valve xenograft conduit: preliminary hemodynamic and clinical results. *J Heart Valve Dis* 2003;12:752-7.
28. Lau KK, Bochenek-Klimczyk K, Galinanes M, Sosnowski AW. Replacement of the ascending aorta, aortic root, and valve with a novel stentless valved conduit. *Ann Thorac Surg* 2008;86:278-81.

## DISCUSSION

**DR JOHN W. HAMMON JR** (Winston-Salem, NC): My colleague, Dr Neal Kon, was invited to discuss this paper and he had to cancel his trip at the last minute, so I am going to present paraphrased remarks from Dr Kon that were altered to fit the time considerations for the discussion.

We congratulate Dr Coselli and his colleagues on an excellent paper and presentation. We also consider the stentless bioroot a superb option for total root replacement. We began implanting stentless bioroots in 1992 and were part of the original Freestyle study group. The vast majority of surgeons in the Freestyle study

group choose to use this valve as a subcoronary implant, but we have always felt it is better utilized if implanted using a full root technique.

I believe our indications and therefore patient population are somewhat different than yours. Our indications for using a stentless bioroot include patients with significant aortic root disease who prefer a tissue valve, the elderly patient with poor tissues, patients with a small aortic root and/or bad ventricles, replacing degenerated stented prostheses, and endocarditis. We can perform AVR [aortic valve replacement] in all patients and not be concerned with patient-prosthesis mismatch. Bioroots offer patients with endocarditis the same advantages as the aortic allograft, the ability to reconstruct the aortic root after extensive débridement of infected tissues. In our series, bioroots have demonstrated very good durability, a 94% freedom from structural valve disease at 14 years, making it an excellent tissue valve replacement option.

We have utilized the simple interrupted suture technique so as to optimize alignment. Why have you chosen to use interrupted mattress sutures or a running technique when each of these techniques might lead to distorting either the bioroot inflow or the left ventricular outflow tract? Have you used the stentless bioroot solely for hemodynamic considerations or do you use it only in patients with significant root disease? Can you elaborate for us, Dr Coselli, what you feel the optimal situations are for implanting a stentless bioroot? Thank you.

**DR COSELLI:** Thank you, Dr Hammon, for your kind comments. With regards to the suture technique, we have not found that the use of the mattress sutures is a problem with regards to distortion of the root, and quite frankly, we just find it easier to use as a teaching technique with the wide variety of individuals in that role that are encountered.

I agree with all of your indications for the use of bioroots. We have used it for all the indications that you have listed. However, I agree that there is a wide variety of patients in whom this approach can be employed, including those with endocarditis, younger individuals wanting to avoid anticoagulation, and patients with small roots in whom the hemodynamic advantages of the stentless valve make it preferable over the mechanical or the stented bioprosthetic valve.

**DR JOHN S. IKONOMIDIS (Charleston, SC):** Can you compare and contrast for us the utility of this device vs use of a composite prosthesis consisting of a stented bioprosthesis sewn to a Dacron [DuPont, Wilmington, DE] graft?

**DR COSELLI:** Quite simply, the superior hemodynamics for any given size is better with the stentless valve than for the same size and virtually any stented valve or mechanical valve. So I think therein lies the primary advantage.