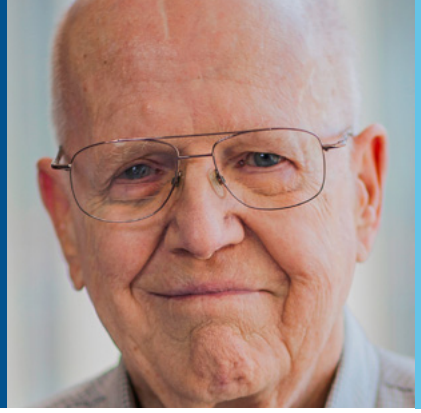
# MOSAIC™ MITRAL BIOPROSTHESIS

## 16-year Clinical Compendium

Medtronic
Further, Together



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## PREFACE

The Medtronic Mosaic™ aortic and the Medtronic Mosaic™ mitral bioprostheses are third generation porcine stented tissue valves. They consist of porcine valves that are crosslinked in a buffered 0.2% glutaraldehyde solution using a tissue fixation method unique to Medtronic — Physiologic Fixation™ — in which the valve is pressurized to its natural dimensions while the leaflets are allowed to float freely at zero net differential pressure. The valves are then treated with alpha-amino oleic acid (AOA™), which has been shown to mitigate porcine leaflet calcification in animal studies,[1,2] and are mounted on flexible stents.*

## INTRODUCTION

The original Medtronic Mosaic™ Investigational Device Exemption (IDE) study was conducted in 1,617 patients (1,252 in the aortic position and 365 in the mitral position) at 17 centers. In order to obtain long-term durability and survival data, patients from six of these centers were invited to participate in a long-term post approval study, in which a total of 1,029 patients (797 in the aortic position and 232 in the mitral position) agreed to participate.

## THE CLINICAL STUDY

### Design:

The Mosaic™ Long-Term Post Approval Study (PAS) was a prospective, multi-national, multi-center, nonrandomized clinical study of the Mosaic™ bioprosthesis.

### Objectives:

The primary objectives were to evaluate long-term survival of patients following valve replacement with the bioprosthesis and the long-term durability of the bioprosthesis.

### Methods:

Patients from six centers from the Mosaic™ IDE study were invited to participate. Those who gave written informed consent to participate were included.

Patients were contacted by telephone on an annual basis, for up to 16 years, to obtain follow-up information. Annual interviews were conducted between one month prior to and two months after the anniversary dates of the implants. Patients were monitored for valve-related reoperations, explants, and deaths, and the reasons for each were documented, when available.

If an annual evaluation was unobtainable, after repeated attempts to contact the patient, that evaluation was considered missing. If two consecutive evaluations were missed and no evaluation was completed prior to the the time of the database closure on May 22, 2014, the patient was considered lost to follow-up (LTFU). If an evaluation was successfully completed before study closure, prior missed evaluations were considered permanently missed.

*No clinical data is available which evaluates the long-term impact of the Physiologic Fixation process or the impact of AOA treatment in patients.

### Data Analysis:

Separate evaluations were performed for aortic valve replacement (AVR) and mitral valve replacement (MVR). Descriptive statistics were used to summarize the data. For continuous variables, the number of patients, mean, standard deviation, minimum, median, and maximum are provided. For categorical variables, the number and percentage of patients are provided. Survival analyses using the Kaplan-Meier method3 were used to estimate survival, freedom from reoperation, and freedom from explant due to structural valve deterioration (SVD). Peto's formula4 was used for the calculation of the standard errors of these estimates. Events that occured in the early and late postoperative periods were included in these analyses.

### Mortality and Study Bioprosthesis-related Morbidity:

Mortality and valve-related reoperations were reported through 16 years post implant. The reporting of adverse events follows the guidelines of the Society of Thoracic Surgeons (STS) and the American Association for Thoracic Surgery (AATS).[5]

**Early (operative) mortality** is defined as deaths that occurred within 30 days of implant if the patient was discharged from the hospital, or at any time after implant if the patient was not discharged from the hospital. Hospital-to-hospital transfer is not considered a hospital discharge.

**Early morbid events** are those events that occurred within the first 30 days of implant. Early event rates are calculated as the number of patients having the event divided by the total number of patients, expressed as a percentage.

**Late mortality** is defined as all deaths that occurred after 30 days postoperative, if the patient was discharged from the hospital.

**Late morbid events** are those events that occurred after 30 days postoperative. Linearized rates (percentage per patient-year) are used to summarize late events. These rates are useful for reporting multiple events in individual patients and are calculated as the number of late events divided by the cumulative late postoperative patient-years, expressed as a percentage.

## PATIENT CHARACTERISTICS

A total of 232 patients underwent MVR. At implant, the mean age was 67.9 ± 10.5 years (median 71 years; range 17 to 84 years). Table 1 displays the age of patients at implant. Fifty-two percent of the patients were female. The distribution of patients with cardiac rhythm disturbance, mitral lesions, risk factors, and previous cardiovascular surgeries is listed in Tables 2 and 3. Nearly 74% of the patients were in New York Heart Association (NYHA) class III or IV prior to MVR surgery, and the most frequently reported primary etiologies of valvular dysfunction were myxomatous degenerative and ruptured chordae tendineae.

**Table 1. Age of Patients at Implant (Years)**

| Age | n | % |
|---|---|---|
| ≤ 40 | 7 | 3.0 |
| 41 - 50 | 3 | 1.3 |
| 51 - 60 | 27 | 11.6 |
| 61 - 70 | 76 | 32.8 |
| 71 - 80 | 113 | 48.7 |
| > 80 | 6 | 2.6 |

Note: Mean patient age at implant 67.9 ± 10.5 years.

**Table 3. Risk Factors and Previous CV Surgery**

| Risk Factor | n | % |
|---|---|---|
| Left Atrial Enlargement | 138 | 59.5 |
| Coronary Artery Disease | 129 | 55.6 |
| Congestive Heart Failure | 116 | 50.0 |
| **Previous CV Surgery** | **n** | **%** |
| Any Surgery | 54 | 23.3 |

Note: Patients may have had more than one risk factor or more than one CV surgery.

**Table 2. Patient Characteristics**

| Gender | n | % |
|---|---|---|
| Female | 121 | 52.2 |
| Male | 111 | 47.8 |
| **NYHA** | **n** | **%** |
| I | 0 | 0.0 |
| II | 61 | 26.3 |
| III | 147 | 63.4 |
| IV | 24 | 10.3 |
| **Cardiac Rhythm** | **n** | **%** |
| Sinus | 156 | 67.2 |
| Atrial Fibrillation/Flutter | 61 | 26.3 |
| Heart Block | 10 | 4.3 |
| Paced | 5 | 2.2 |
| **Mitral Lesion** | **n** | **%** |
| Stenosis | 20 | 8.6 |
| Insufficiency | 181 | 78.0 |
| Mixed | 31 | 13.4 |
| **Primary Etiology of Valvular Dysfunction** | **n** | **%** |
| Myxomatous Degeneration | 90 | 38.8 |
| Ruptured Chordae Tendineae | 58 | 25.0 |

Note: Patients may have had more than one etiology of valvular dysfunction. The two most frequently reported etiologies are listed.

## OPERATIVE DATA

### Concomitant Procedures

Nearly 54% of the patients underwent a concomitant procedure with the most common procedure being coronary artery bypass grafts (CABG) at 43.5%. See Table 4.

### Valve Size Distribution

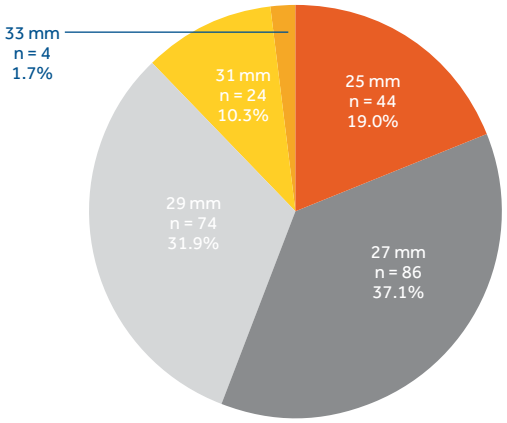
Of the 232 mitral valves implanted, the most common sizes were 27 mm (37.1%) and 29 mm (31.9%). See Figure 1.

**Table 4. Concomitant Procedures**

| Procedure | n | % |
|---|---|---|
| Any Concomitant Procedure | 125 | 53.9 |
| Coronary Artery Bypass Grafts (CABG) | 101 | 43.5 |

Note: Patients may have had more than one concomitant procedure. The most frequently reported procedure is listed.

**Figure 1. Mosaic™ Bioprosthesis Size**




## SUMMARY OF FOLLOW-UP

A total of 1,969.4 patient-years of follow-up were obtained from 232 patients at six centers. See Table 5. The mean follow-up was 8.5 ± 4.8 years (range 0 to 18.0 years).

**Table 5. Long-Term Study Centers**

| Center | City | Country | n | Total Follow-Up (patient-years) |
|---|---|---|---|---|
| Vancouver Hospital and Health Science Centre/St. Paul's Hospital | Vancouver | Canada | 70 | 623.4 |
| Regina General Hospital | Regina | Canada | 66 | 563.7 |
| Albertinen Krankenhaus | Hamburg | Germany | 47 | 381.3 |
| Hôpital Laval | Sainte-Foy | Canada | 27 | 198.5 |
| Green Lane Hospital | Auckland | New Zealand | 14 | 136.2 |
| Monash Medical Centre* | Clayton | Australia | 8 | 66.3 |
| Total | | | 232 | 1,969.4 |

*The center withdrew from the study in 2004.

## VALVE-RELATED COMPLICATIONS

### Early Events

The operative mortality rate for all patients was 3.0%. There were no early valve-related deaths reported.

### Late Events

The late valve-related complication rates at 16 years are presented in Table 6. The 31 reoperations performed were due to structural valve deterioration (16), other/not specified (6), primary paravalvular leak (4), endocarditis (2), mitral stenosis (2), and primary valve thrombosis (1). The 10 late valve-related deaths were due to endocarditis (3), bioprosthetic valve dysfunction (3), permanent neurological event (3), hemorrhage (1).

**Table 6. Valve-Related Complications at 16 Years**

| Event | Number of late events | Percent per patient-year | Freedom from ± SE (%) |
|---|---|---|---|
| Reoperation | 31 | 1.6% | 71.7 ± 13.5 |
| Explant due to SVD | 16 | 0.8% | 79.7 ± 12.7 |
| Valve-related or unexplained death | 24 | 1.2% | 69.0 ± 13.6 |
| Valve-related death | 10 | 0.5% | 91.2 ± 9.6 |

Note: There were a total of 1,957.5 late patient-years and 1,956.8 late death patient-years of follow-up.

### Survival and Durability

Table 7 displays the freedom from all death and freedom from death due to valve-related or unexplained death (also see Figures 2 and 4). Table 8 displays the durability of the Mosaic™ Bioprosthesis as freedom from reoperation, explant, and explant due to SVD (see also Figure 6 for explant due to SVD and Figure 8 for reoperation). There were a total of 118 deaths, which included 7 (3.0%) hospital deaths, and 111 (5.7% per-patient year) late deaths. Twenty-four of the total deaths (all late) were valve-related or unexplained. No reoperations occurred within 30 days of surgery. A total of 31 (1.6% per patient-year) late reoperations occurred, which included one repair.

### Survival and Durability by Patient's Age at Implant

At the time of implant, there were 37 patients 60 years of age or less, 76 patients 61 to 70 years of age, and 119 patients greater than 70 years of age. Figures 3, 5, and 7 summarize survival, freedom from valve-related or unexplained death, and freedom from explant due to SVD by patient's age at implant.

## VALVE REPLACEMENT

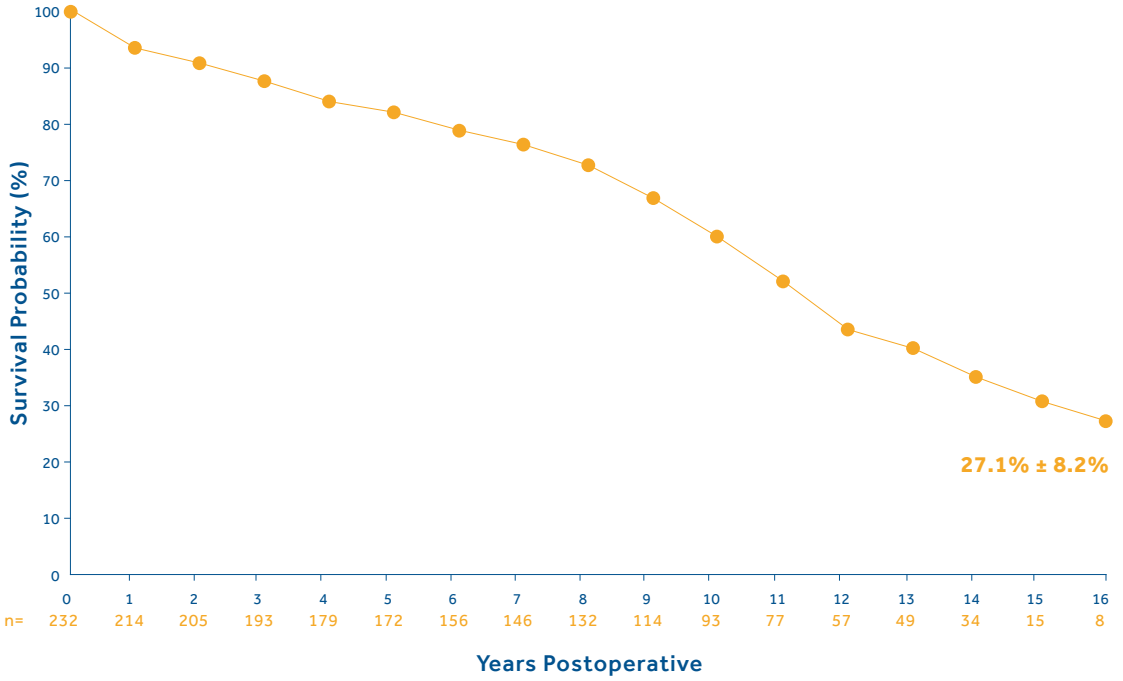
### Table 7. Survival

| | Freedom from ± SE (%) | | | | | |
|---|---|---|---|---|---|---|
| | 1 Year | 5 Years | 10 Years | 12 Years | 15 Years | 16 Years |
| All Deaths | 93.5 ± 1.6 | 82.5 ± 2.6 | 59.8 ± 3.9 | 43.7 ± 4.3 | 30.5 ± 6.6 | 27.1 ± 8.2 |
| ≤ 60 Years | 94.6 ± 3.8 | 88.6 ± 5.8 | 72.3 ± 9.2 | 62.8 ± 11.5 | 62.8 ± 19.2 | 62.8 ± 22.1 |
| > 60 and ≤ 70 Years | 92.1 ± 3.1 | 81.0 ± 4.7 | 58.7 ± 6.7 | 47.5 ± 7.2 | 24.5 ± 9.5 | 16.3 ± 10.6 |
| > 70 Years | 94.1 ± 2.2 | 81.7 ± 3.7 | 56.8 ± 5.6 | 35.3 ± 5.7 | 24.1 ± 8.6 | 24.1 ± 12.1 |
| Valve-Related or Unexplained Death | 98.6 ± 0.8 | 97.1 ± 1.3 | 92.2 ± 2.7 | 83.2 ± 4.4 | 77.6 ± 9.5 | 69.0 ± 13.6 |
| ≤ 60 Years | 100.0 ± 0.0 | 100.0 ± 0.0 | 95.5 ± 4.9 | 95.5 ± 6.1 | 95.5 ± 10.2 | 95.5 ± 11.8 |
| > 60 and ≤ 70 Years | 97.2 ± 1.9 | 95.5 ± 2.7 | 93.6 ± 4.2 | 90.6 ± 5.8 | 84.6 ± 14.9 | 56.4 ± 26.3 |
| > 70 Years | 99.1 ± 0.9 | 97.2 ± 1.7 | 90.3 ± 4.2 | 73.0 ± 7.6 | 65.2 ± 15.7 | 65.2 ± 22.2 |

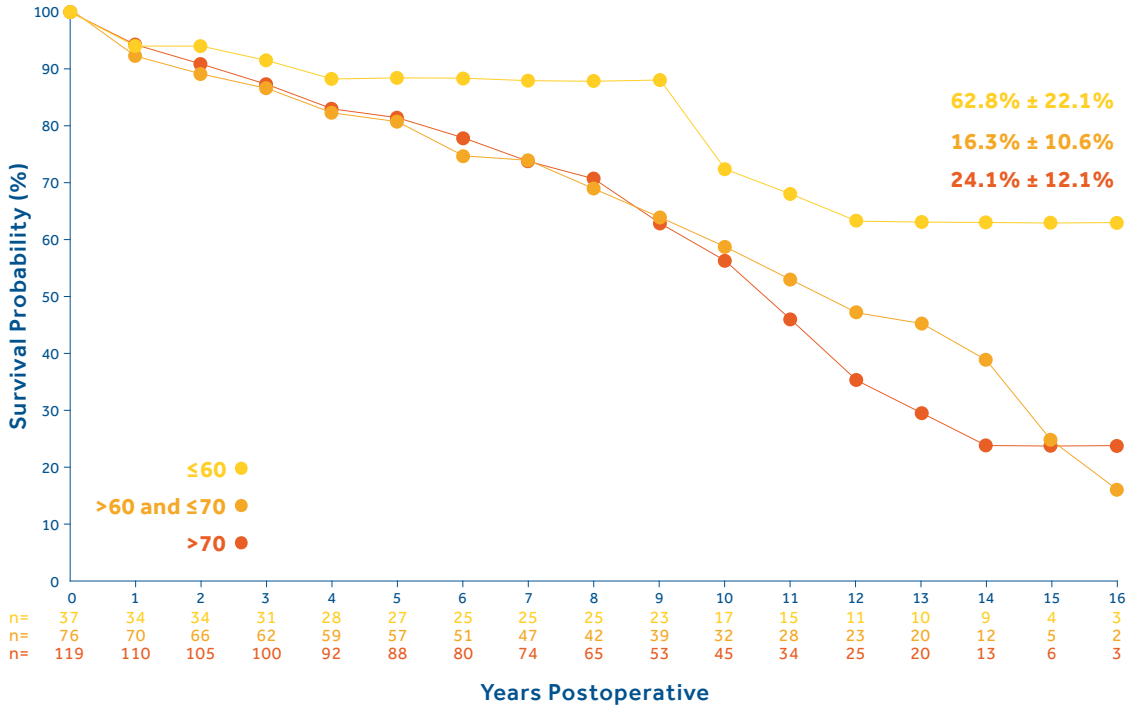
### Table 8. Durability

| | Freedom from ± SE (%) | | | | | |
|---|---|---|---|---|---|---|
| | 1 Year | 5 Years | 10 Years | 12 Years | 15 Years | 16 Years |
| Reoperation | 99.1 ± 0.6 | 96.1 ± 1.4 | 86.9 ± 3.3 | 79.5 ± 4.8 | 71.7 ± 9.8 | 71.7 ± 13.5 |
| ≤ 60 Years | 97.1 ± 2.8 | 94.0 ± 4.4 | 78.9 ± 8.8 | 68.4 ± 11.6 | 51.8 ± 18.0 | 51.8 ± 20.8 |
| > 60 and ≤ 70 Years | 100.0 ± 0.0 | 95.6 ± 2.7 | 89.0 ± 5.2 | 78.7 ± 7.9 | 70.6 ± 17.1 | 70.6 ± 27.1 |
| > 70 Years | 99.1 ± 0.9 | 97.1 ± 1.8 | 88.5 ± 4.6 | 86.2 ± 6.5 | 86.2 ± 13.1 | 86.2 ± 18.5 |
| Explant | 99.1 ± 0.6 | 96.6 ± 1.4 | 90.5 ± 2.9 | 82.9 ± 4.5 | 74.8 ± 9.7 | 74.8 ± 13.3 |
| ≤ 60 Years | 97.1 ± 2.8 | 94.0 ± 4.4 | 82.2 ± 8.4 | 71.2 ± 11.5 | 54.0 ± 18.3 | 54.0 ± 21.1 |
| > 60 and ≤ 70 Years | 100.0 ± 0.0 | 97.0 ± 2.2 | 92.0 ± 4.6 | 81.3 ± 7.7 | 73.0 ± 17.0 | 73.0 ± 26.8 |
| > 70 Years | 99.1 ± 0.9 | 97.1 ± 1.8 | 92.4 ± 3.8 | 90.0 ± 5.7 | 90.0 ± 11.6 | 90.0 ± 16.5 |
| Explant Due To SVD | 100.0 ± 0.0 | 99.5 ± 0.5 | 94.4 ± 2.3 | 86.5 ± 4.2 | 79.7 ± 9.3 | 79.7 ± 12.7 |
| ≤ 60 Years | 100.0 ± 0.0 | 100.0 ± 0.0 | 90.8 ± 6.7 | 78.7 ± 11.0 | 65.6 ± 19.2 | 65.6 ± 22.2 |
| > 60 and ≤ 70 Years | 100.0 ± 0.0 | 98.4 ± 1.6 | 93.3 ± 4.3 | 82.5 ± 7.5 | 74.0 ± 16.9 | 74.0 ± 26.7 |
| > 70 Years | 100.0 ± 0.0 | 100.0 ± 0.0 | 96.5 ± 2.7 | 94.0 ± 4.6 | 94.0 ± 9.4 | 94.0 ± 13.3 |

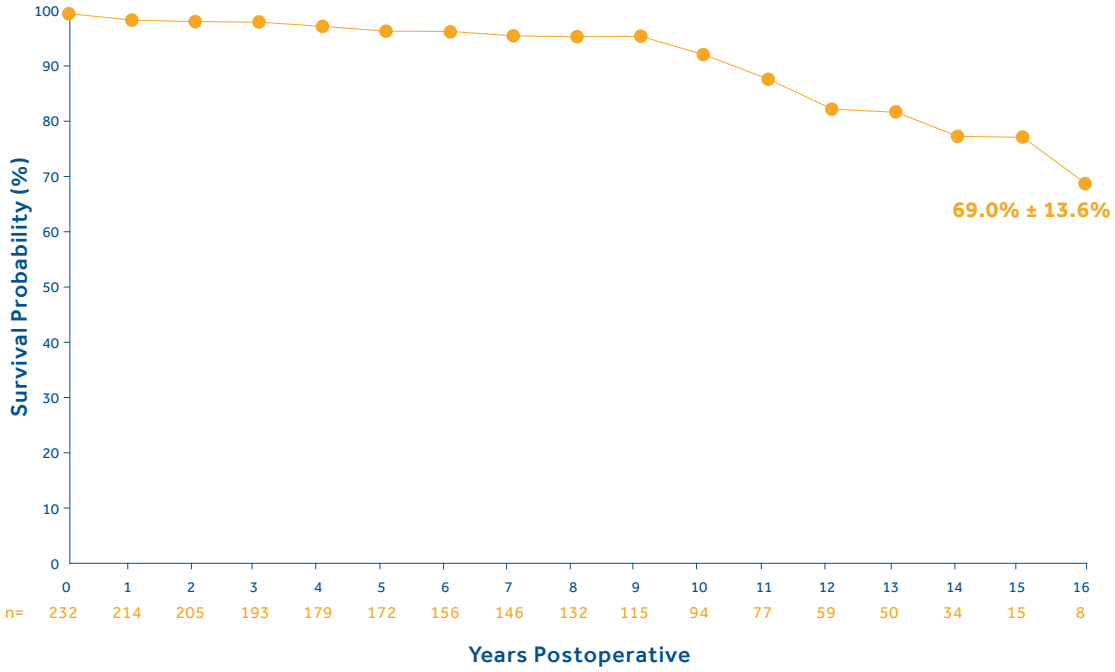
## Figure 2. Survival



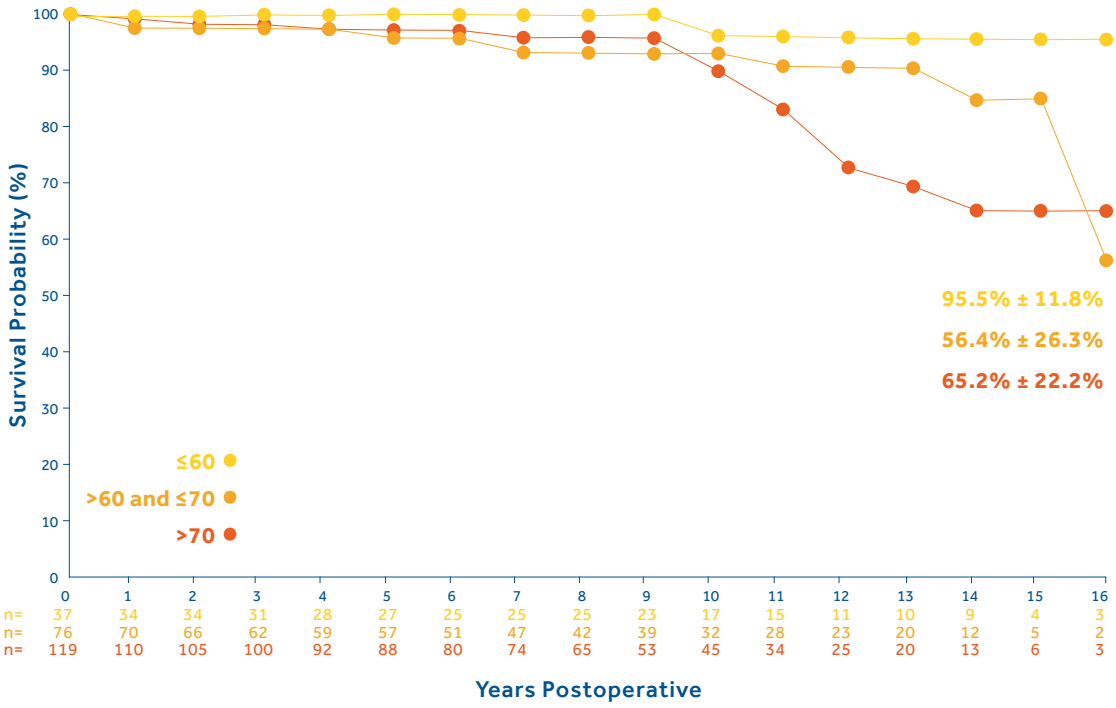

## Figure 3. Survival by Patient's Age at Implant



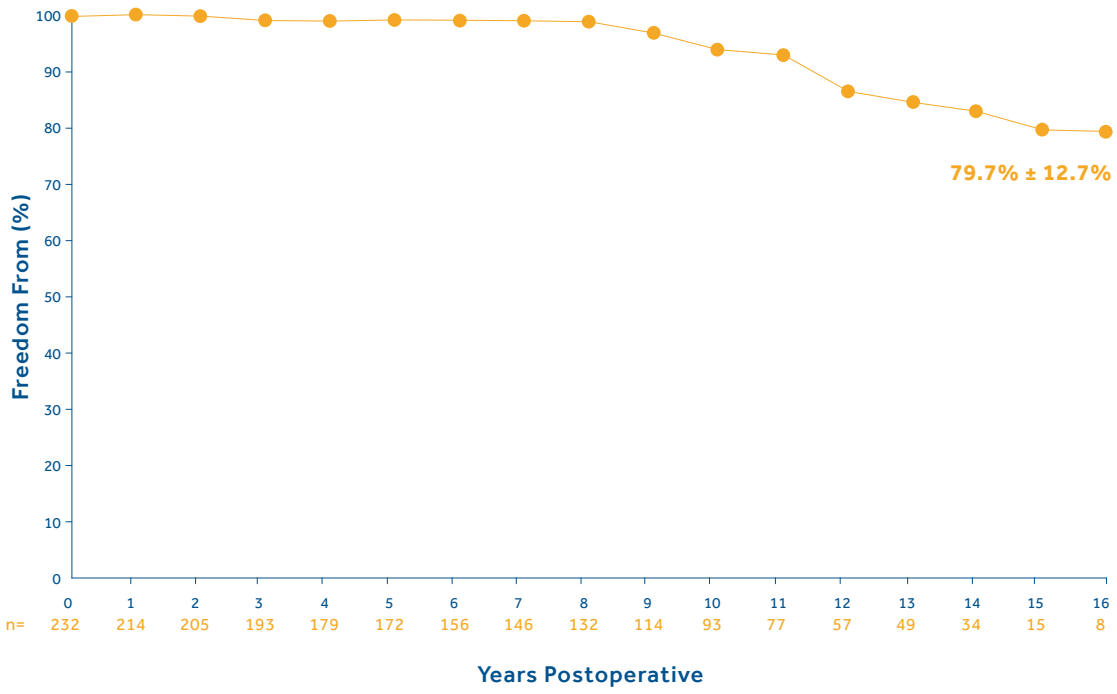
## Figure 4. Freedom from Valve-Related or Unexplained Death



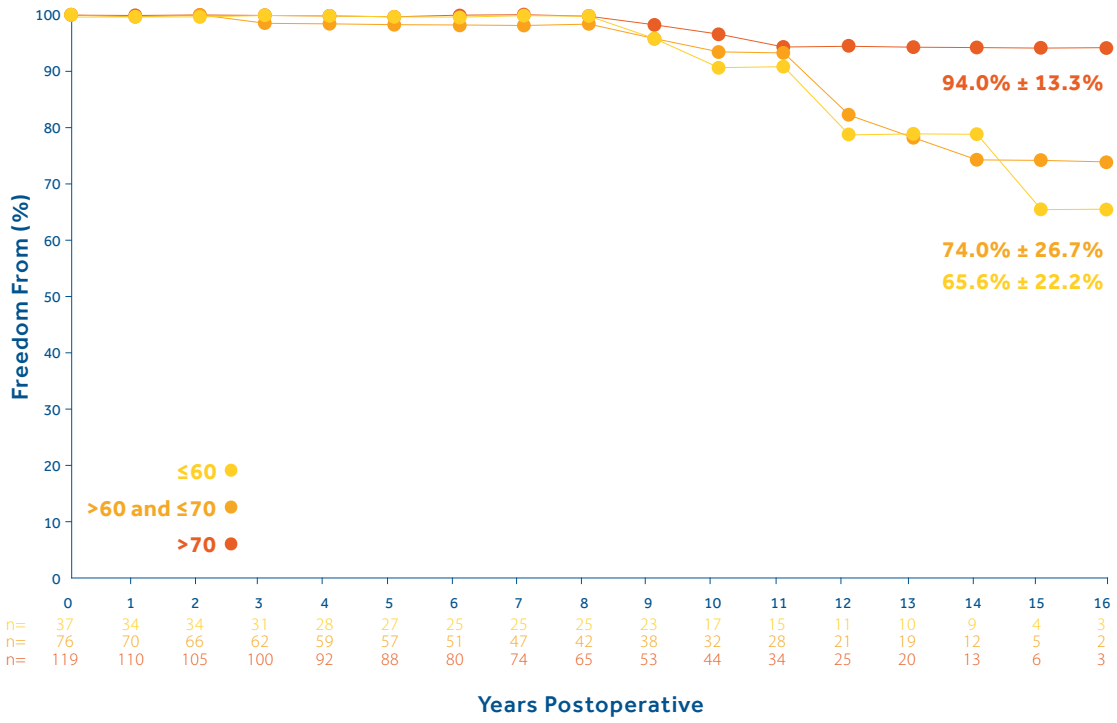

## Figure 5. Freedom from Valve-Related or Unexplained Death by Patient's Age at Implant



## Figure 6. Freedom from Explant due to SVD

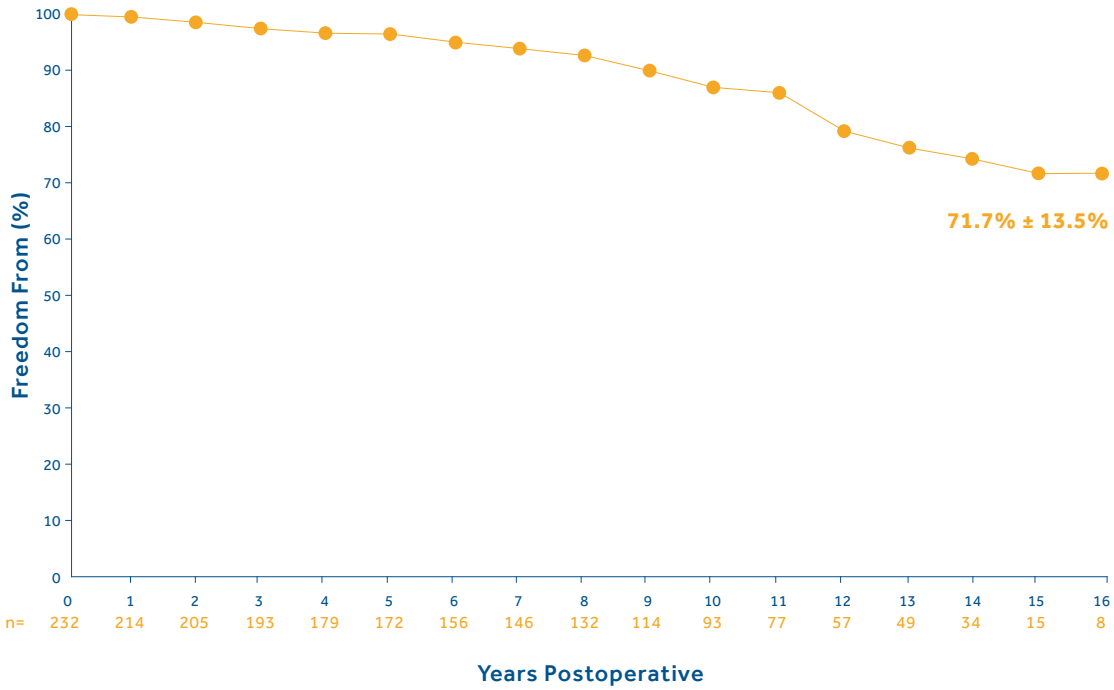



## Figure 7. Freedom from Explant due to SVD by Patient's Age at Implant



## VALVE REPLACEMENT

**Figure 8. Freedom from Reoperation**




## SUMMARY FOR MITRAL VALVE

The Mosaic™ bioprosthesis in the mitral position has demonstrated outstanding long-term results — at 16 years, survival from all death is 27.1% and freedom from explant due to SVD is 79.7%.

## **BIBLIOGRAPHY** | REFERENCES

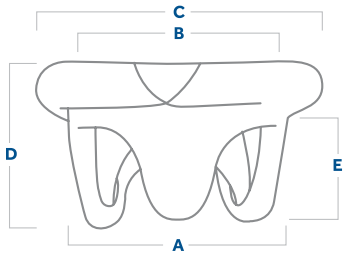

1. Gott JP, et al. Refinement of the alpha aminooleic acid bioprosthetic valve anticalcification technique. *Ann Thorac Surg*, 1997;64(1):50-8.
2. Walther T, et al. Comparison of different anticalcification treatments for stentless bioprostheses. *Ann Thorac Surg*, 1998;66(6 Suppl): S249-54.
3. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association*, 1958;53:457-81.
4. Peto R, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. I. Introduction and design. *Br J Cancer*, 1976;34(6):585-612.
5. Guidelines for Reporting Morbidity and Mortality After Cardiac Valvular Operations. *Ann Thorac Surg*. 1988;46(3):257-9.


## **BIBLIOGRAPHY** | RELEVANT PUBLICATIONS


1. Blauwet LA, Malouf JF, Connolly H, et al. Comprehensive echocardiographic assessment of normal mitral Medtronic Hancock II, Medtronic Mosaic, and Carpentier-Edwards Perimount bioprostheses early after implantation. *J Am Soc Echocardiogr*. 2010;23(6):656-66.
2. Duarte IG, MacDonald MJ, Cooper, et al. In vivo hemodynamic, histologic, and antimineralization characteristics of the Mosaic bioprosthesis. *Ann Thorac Surg*. 2001;71(1):2-9.
3. Eichinger WB, Botzenhardt F, Gunzinger R, et al. European experience with the Mosaic bioprosthesis. *J Thorac Cardiovasc Surg*. 2002;124(2):333-9.
4. Fradet G, Bleese N, Busse E, et al. The Mosaic valve clinical performance at seven years: results from a multicenter prospective clinical trial. *J Heart Valve Dis*. 2004;13(2):239-46; discussion 246-7.
5. Fradet GJ, Bleese N, Burgess J, Cartier PC. Mosaic valve international clinical trial: early performance results. *Ann Thorac Surg*. 2001;71(5 Suppl):S273-7.
6. Jamieson WR, Fradet GJ, MacNab J, et al. Medtronic Mosaic porcine bioprosthesis: investigational center experience to six years. *J Heart Valve Dis*. 2005;14(1):54-63.
7. Jamieson WR, Riess FC, Raudkivi PJ, et al. Medtronic Mosaic porcine bioprosthesis: assessment of 12-year performance. *J Thorac Cardiovasc Surg*. 2011;142(2):302-7 e2.
8. Jasinski MJ, Kadziola Z, Keal R, Sosnowski AW. Mosaic Medtronic bioprosthetic valve replacement clinical results and hemodynamical performance. *J Cardiovasc Surg* (Torino). 2000;41(2):181-6.
9. Mecozzi G, Milano A, De Carlo M, et al. Intravascular hemolysis in patients with new generation prosthetic heart valves: a prospective study. *J Thorac Cardiovasc Surg*. 2002;123(3):550-6.
10. Riess FC, Bader R, Cramer E, et al. Hemodynamic performance of the Medtronic Mosaic porcine bioprosthesis up to ten years. *Ann Thorac Surg*. 2007;83(4):1310-8.
11. Riess FC, Cramer E, Hansen L, et al. Clinical results of the Medtronic Mosaic porcine bioprosthesis up to 13 years. *Eur J Cardiothorac Surg*. 2010;37(1):145-53.
12. Suri RM, Schaff HV, Meyer SR, Hargrove WC, 3rd. Thoracoscopic versus open mitral valve repair: a propensity score analysis of early outcomes. *Ann Thorac Surg*. 2009;88(4):1185-90.
13. Thomson DJ, Jamieson WR, Dumesnil JG, et al. Medtronic Mosaic porcine bioprosthesis satisfactory early clinical performance. *Ann Thorac Surg*. 1998;66(6 Suppl):S122-5.
14. Thomson DJ, Jamieson WR, Dumesnil JG, et al. Medtronic Mosaic porcine bioprosthesis: midterm investigational trial results. *Ann Thorac Surg*. 2001;71(5 Suppl):S269-72.

## **SPECIFICATIONS** | BIOPROSTHESIS PRODUCTS

**Mosaic™ Mitral Valve, Model 310 C**




A polyester felt insert in the sewing ring provides strength with low suture drag.

| Order Number | Valve Size (Stent O.D.†) (A) (± 0.5 mm) | Orifice Diameter (Stent I.D.) (B) (± 0.5 mm) | Suture Ring Diameter (C) (± 1 mm) | Valve Height (D) (± 0.5 mm) | Ventricular Protrusion (E) (± 0.5 mm) |
|---|---|---|---|---|---|
| 310C25 | 25 | 22.5 | 33.0 | 18.0 | 13.5 |
| 310C27 | 27 | 24.0 | 35.0 | 19.0 | 14.0 |
| 310C29 | 29 | 26.0 | 38.0 | 20.5 | 15.5 |
| 310C31 | 31 | 28.0 | 41.0 | 22.0 | 17.0 |
| 310C33 | 33 | 30.0 | 43.0 | 23.0 | 17.5 |

(nominal values, in millimeters) †Equivalent to annulus diameter

### Mosaic™ Bioprosthesis

**Indications:** For the replacement of malfunctioning native or prosthetic aortic and/or mitral heart valves. **Contraindications:** None known. **Warnings/Precautions/Adverse Events:** Accelerated deterioration due to calcific degeneration of bioprosthesis may occur in: children, adolescents, young adults, and patients with altered calcium metabolism (e.g., chronic renal failure, hyperparathyroidism). Adverse events can include: angina, cardiac arrhythmia, cardiac dysrhythmias, death, endocarditis, heart failure, hemolysis, hemolytic anemia, hemorrhage, transvalvular or paravalvular leak, myocardial infarction, nonstructural dysfunction, stroke, structural deterioration, thromboembolism, or valve thrombosis. **Caution:** Federal law (USA) restricts these devices to sale by or on the order of a physician.

For a listing of indications, contraindications, precautions, warnings, and potential adverse events, please refer to the Instructions for Use. For countries that use eIFUs, consult instructions for use at this website **www.medtronic.com/manuals**. Note: Manuals can be viewed using a current version of any major internet browser.

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