Medtronic

MOSAIC® PORCINE BIOPROSTHESIS

Instructions for Use

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician (or properly licensed practitioner).

1. DEVICE DESCRIPTION

MOSAIC Porcine Bioprostheses, aortic model 305 and mitral model 310, are comprised of porcine aortic valves crosslinked and preserved in buffered 0.2% glutaraldehyde and then fitted and secured to cloth covered flexible stents. The crosslinking of the porcine aortic root tissue is accomplished using Physiologic Fixation™, a process in which hydrostatic pressure is applied to the root while maintaining a zero pressure differential across the valve leaflets.

MOSAIC Porcine Bioprostheses are treated with the AOA® process* which uses alpha-amino oleic acid (AOA), a compound derived from oleic acid, a naturally occurring long-chain fatty acid.

The MOSAIC Porcine Bioprosthesis, aortic model is available in 21 mm, 23 mm, 25 mm, 27 mm, and 29 mm diameters. The MOSAIC Porcine Bioprosthesis, mitral model is available in 25 mm, 27 mm, 29 mm, and 31 mm diameters.

Testing has shown that the presence of this device (with the materials described) in a patient undergoing a MRI (magnetic resonance imaging) procedure using a MR system with a static magnetic field of <1.5 Tesla, will present no substantial or increased risk relative to magnetic field interactions, artifacts, and/or heating.

2. INDICATIONS

MOSAIC Porcine Bioprostheses (Models 305 and 310) are indicated for the replacement of malfunctioning native or prosthetic aortic and mitral heart valves.

3. CONTRAINDICATIONS

None known

***No clinical data are available which evaluate the long-term impact of the AOA treatment in patients.**

AOA® is a registered Trademark of Biomedical Design, Inc., Atlanta, Georgia.

4. WARNINGS

FOR SINGLE USE ONLY.

DO NOT RESTERILIZE THE VALVE BY ANY METHOD. Exposure of the bioprosthesis and container to irradiation, steam, ethylene oxide, or chemical sterilization will render the bioprosthesis unfit for use.

Warning: Accelerated deterioration due to calcific degeneration of bioprostheses may occur in:

- children, adolescents, or young adults;
- patients with altered calcium metabolism (e.g., chronic renal failure, hyperparathyroidism).

5. PRECAUTIONS

5.1 Precautions Prior to Use

Do not use the MOSAIC Porcine Bioprosthesis:

- if the tamper evident seal is broken;
- if the glutaraldehyde storage solution does not completely cover the bioprosthesis;
- if the bioprosthesis has been exposed to freezing or has had prolonged exposure to heat.
- if the bioprosthesis is damaged

5.2 Precautions During and After Use

- Do not expose the bioprosthesis to solutions other than the storage solution in which it was shipped, the sterile isotonic saline solution used during the rinsing procedure, or the sterile isotonic saline solution used to irrigate the bioprosthesis.
- Do not allow the tissue of the bioprosthesis to dry. Continuous submersion or irrigation is required.
- Do not add antibiotics to either the storage or the rinse solution. Do not apply antibiotics to the bioprosthesis
- Do not lacerate the tissue. If a bioprosthesis is damaged, it must be explanted and replaced
- Do not attempt to repair a damaged bioprosthesis
- Do not use cutting needles, as they may cause structural damage to the fabric of the bioprosthesis.
- Passing a catheter, surgical instrument, or transvenous pacing lead through the bioprosthesis may damage the bioprosthesis and is, therefore, not recommended.
- Trim suture ends close to the knot to prevent abrasion of leaflet tissue.
- When selecting a bioprosthesis size, consideration of the cardiac anatomy is necessary, and care must also be taken to select a bioprosthesis which adequately provides for the hemodynamic requirements of the patient.

6. ADVERSE EVENTS

A prospective, nonrandomized, multi-center clinical study was conducted to assess the safety and effectiveness of the MOSAIC Porcine Bioprosthesis. Patients were evaluated preoperatively, within 30 days postoperative, 3-6 months postoperative, at one year (11-14 months) postoperative, and annually thereafter. Patients were monitored throughout the postoperative period for possible adverse events. One thousand two hundred fifty-two (1252) patients had isolated aortic valve replacement (AVR) and 365 patients had isolated mitral valve replacement (MVR). Mortality and valve-related morbidity rates after implantation with the MOSAIC Porcine Bioprosthesis are summarized in the tables below.

6.1 Observed Adverse Events

Isolated Aortic Valve Replacement (AVR)

The adverse event rates were based on 1252 bioprostheses implanted in 1252 patients at 17 centers. The cumulative follow-up was 2745.3 patient-years with a mean follow-up of 2.2 years (SD=1.2 years, range=0 - 5.2 years).

Table 1: Observed Adverse Event Rates for AVR

All patients analyzed: N=1252 Cumulative follow-up=2745.3 patient-years

	Early Events[1]		Late Events[2]		Freedom From Event (%) [95% CI][3]			
	n	% of Patients	n	%/Pt.-Yr.	1 Year	2 Years	3 Years	4 Years
All Deaths	41	3.3	82	3.1	93.7 [92.3, 95.2]	91.9 [89.9, 93.8]	88.6 [85.5, 91.7]	85.6 [79.0, 92.1]
Valve-Related or Unexplained	4	0.3	24	0.9	98.7 [98.0, 99.4]	98.2 [97.2, 99.1]	97.1 [95.3, 98.8]	96.5 [92.9, 100.0]
Valve-Related Adverse Events								
Primary Thromboembolism[4]	19	1.4	33	1.25	96.9 [95.8, 98.0]	96.3 [94.9, 97.7]	95.6 [93.5, 97.7]	95.6 [91.5, 99.7]
Permanent Neurological Event	7	0.6	13	0.5	98.7 [98.1, 99.4]	98.4 [97.5, 99.3]	98.0 [96.6, 99.5]	98.0 [95.3, 100.0]
Transient Neurological Event[4]	12	0.9	20	0.8	98.1 [97.2, 98.9]	97.8 [96.8, 98.9]	97.5 [95.9, 99.1]	97.5 [94.3, 100.0]
Primary Valve Thrombosis	0	0.0	5	0.2	99.7 [99.4, 100.0]	99.6 [99.2, 100.0]	99.4 [98.7, 100.0]	99.4 [98.0, 100.0]
Structural Valve Deterioration[5]	0	0.0	1	0.0	100.0	100.0	100.0	100.0
Nonstructural Valve Dysfunction	0	0.0	4	0.15	99.7 [99.4, 100.0]	99.7 [99.4, 100.0]	99.7 [99.2, 100.0]	99.1 [97.3, 100.0]
Leaflet Dysfunction	0	0.0	1	0.0	100.0	100.0	100.0	99.4 [97.8, 100.0]
Patient Prosthesis Mismatch	0	0.0	3	0.1	99.7 [99.4, 100.0]	99.7 [99.4, 100.0]	99.7 [99.2, 100.0]	99.7 [98.7, 100.0]
Endocarditis	1	0.1	19	0.7	99.3 [98.8, 99.8]	98.7 [97.9, 99.5]	97.7 [96.2, 99.2]	97.4 [94.3, 100.0]
All Primary Paravalvular Leak	6	0.5	13	0.5	99.1 [98.5, 99.7]	98.4 [97.5, 99.3]	98.3 [96.9, 99.6]	98.3 [95.7, 100.0]
Major Primary Paravalvular Leak	1	0.1	2	0.1	99.8 [99.4, 100.0]	99.8 [99.4, 100.0]	99.8 [99.2, 100.0]	99.8 [98.8, 100.0]
All Antithromboembolic-Related Hemorrhage	23	1.8	28	1.1	96.5 [95.4, 97.6]	96.3 [94.9, 97.7]	95.3 [93.2, 97.5]	95.3 [91.1, 99.5]
Major Antithromboembolic-Related Hemorrhage	15	1.2	20	0.8	97.6 [96.6, 98.5]	97.5 [96.3, 98.6]	96.5 [94.6, 98.4]	96.5 [92.9, 100.0]
Primary Hemolysis	0	0.0	0	0.0	100.0	100.0	100.0	100.0
Reoperation	0	0.0	20	0.8	99.2 [98.7, 99.8]	99.0 [98.3, 99.7]	98.4 [97.2, 99.7]	95.7 [91.7, 99.6]
Explant	0	0.0	19	0.7	99.3 [98.8, 99.8]	99.1 [98.4, 99.8]	98.5 [97.3, 99.8]	95.8 [91.8, 99.7]

Notes:

1. Early deaths 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. Early valve-related adverse events occurred within the first 30 days of implant. Early event rates were calculated as the percentage of patients.
2. Late deaths occurred after 30 days postoperative, if the patient was discharged from the hospital. Late valve-related adverse events occurred after 30 days postoperative. Late event rates were calculated as linearized rates (%/patient-year). Calculations for late death rates were based on 2642.5 late patient-years. Calculations for late valve-related adverse event rates were based on 2645.2 late patient-years.
3. Freedom from event (early or late) rates were calculated using the Kaplan-Meier method. Peto's formula was used for the calculation of the standard error of the Kaplan-Meier estimate for the confidence interval for adverse events with at least one occurrence.
4. Two early events occurred in one patient.
5. The adverse event occurred after four years postoperative.

Isolated Mitral Valve Replacement (MVR)

The adverse event rates were based on 365 bioprostheses implanted in 365 patients at 17 centers. The cumulative follow-up was 644.2 patient-years with a mean follow-up of 1.8 years (SD=1.3 years, range=0 - 5.2 years).

Table 2: Observed Adverse Event Rates for MVR

All patients analyzed: N=365 Cumulative follow-up=644.2 patient-years

	Early Events[1]		Late Events[2]		Freedom From Event (%) [95% CI][3]			
	n	% of Patients	n	%/Pt.-Yr.	1 Year	2 Years	3 Years	4 Years
All Deaths	15	4.1	25	4.1	92.5 [89.2, 95.7]	89.9 [85.3, 94.5]	85.9 [78.7, 93.0]	80.0 [66.2, 93.7]
Valve-Related or Unexplained	2	0.5	8	1.3	98.4 [96.8, 100.0]	97.3 [94.7, 99.9]	96.4 [92.3, 100.0]	92.2 [82.2, 100.0]
Valve-Related Adverse Events								
Primary Thromboembolism[4]	13	3.0	10	1.6	95.1 [92.3, 97.8]	93.9 [90.0, 97.8]	93.9 [88.5, 99.3]	92.2 [82.0, 100.0]
Permanent Neurological Event	4	1.1	2	0.3	98.6 [97.1, 100.0]	98.6 [96.7, 100.0]	98.6 [96.0, 100.0]	97.0 [90.5, 100.0]
Transient Neurological Event[4]	9	1.9	8	1.3	96.5 [94.1, 98.8]	95.3 [91.9, 98.8]	95.3 [90.5, 100.0]	95.3 [87.1, 100.0]
Primary Valve Thrombosis	0	0.0	1	0.2	100.0	100.0	100.0	98.5 [93.8, 100.0]
Structural Valve Deterioration	0	0.0	0	0.0	100.0	100.0	100.0	100.0
Nonstructural Valve Dysfunction	0	0.0	0	0.0	100.0	100.0	100.0	100.0
Leaflet Dysfunction	0	0.0	0	0.0	100.0	100.0	100.0	100.0
Patient Prosthesis Mismatch	0	0.0	0	0.0	100.0	100.0	100.0	100.0
Endocarditis	2	0.5	6	1.0	98.2 [96.6, 99.9]	98.2 [96.1, 100.0]	98.2 [95.3, 100.0]	95.9 [88.4, 100.0]
All Primary Paravalvular Leak	3	0.8	9	1.5	96.9 [94.7, 99.1]	96.4 [93.4, 99.4]	95.3 [90.7, 100.0]	95.3 [87.1, 100.0]
Major Primary Paravalvular Leak	0	0.0	3	0.5	99.7 [99.0, 100.0]	98.6 [96.7, 100.0]	98.6 [96.0, 100.0]	98.6 [94.1, 100.0]
All Antithromboembolic-Related Hemorrhage	7	1.9	11	1.8	95.8 [93.3, 98.4]	95.3 [91.9, 98.7]	93.4 [87.9, 98.9]	91.0 [80.3, 100.0]
Major Antithromboembolic-Related Hemorrhage	5	1.4	7	1.1	97.3 [95.2, 99.4]	96.7 [93.9, 99.6]	94.8 [89.9, 99.7]	94.8 [86.5, 100.0]
Primary Hemolysis	0	0.0	0	0.0	100.0	100.0	100.0	100.0
Reoperation	0	0.0	5	0.8	99.3 [98.3, 100.0]	98.8 [97.0, 100.0]	98.8 [96.4, 100.0]	94.9 [86.6, 100.0]
Explant	0	0.0	5	0.8	99.3 [98.3, 100.0]	98.8 [97.0, 100.0]	98.8 [96.4, 100.0]	94.9 [86.6, 100.0]

Notes:

1. Early deaths 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. Early valve-related adverse events occurred within the first 30 days of implant. Early event rates were calculated as the percentage of patients.
2. Late deaths occurred after 30 days postoperative, if the patient was discharged from the hospital. Late valve-related adverse events occurred after 30 days postoperative. Late event rates were calculated as linearized rates (%/patient-year). Calculations for late death rates were based on 614.1 late patient-years. Calculations for late valve-related adverse events were based on 615.2 late patient-years.
3. Freedom from event (early or late) rates were calculated using the Kaplan-Meier method. Peto's formula was used for the calculation of the standard error of the Kaplan-Meier estimate for the confidence interval for adverse events with at least one occurrence.
4. Two early events occurred in each of two patients.

6.2 Potential Adverse Events

Adverse events potentially associated with the use of bioprosthetic heart valves include:

- Cardiac dysrhythmias
- death
- endocarditis
- hemolysis
- hemorrhage, anticoagulant/antiplatelet-related
- leak, transvalvular or paravalvular
- nonstructural dysfunction (pannus, suture dehiscence, inappropriate sizing, or other)
- structural deterioration (calcification, leaflet tear, or other)
- thromboembolism
- valve thrombosis

7. CLINICAL STUDIES

The safety endpoints captured in this study were mortality and valve-related morbidity. The effectiveness endpoints in this study were New York Heart Association (NYHA) functional classification and hemodynamic assessments obtained by echocardiography. Patient demographic data and effectiveness data are summarized in the tables below.

Table 3: Patient Demographics

MOSAIC Porcine Bioprosthesis Clinical Study AVR (N = 1252)	
Age at implant in years (mean ± SD, N [min., max.])	70 ± 8, 1252 [21, 89]
Gender (% male / % female)	64% / 36%
Etiology	
Stenosis- % of pts. with stenosis alone (% (number in subgroup/N))	67% (842/1252)
Insufficiency- % of pts. with insufficiency alone (% (number in subgroup/N))	11% (141/1252)
Mixed-% of pts. with stenosis and insufficiency (% (number in subgroup/N))	21.5% (269/1252)
MOSAIC Porcine Bioprosthesis Clinical Study MVR (N = 365)	
Age at implant in years (mean ± SD, N [min., max.])	68 ± 11, 365 [17, 84]
Gender (% male / % female)	47% / 53%
Etiology	
Stenosis- % of pts. with stenosis alone (% (number in subgroup/N))	10% (38/365)
Insufficiency- % of pts. with insufficiency alone (% (number in subgroup/N))	76% (279/365)
Mixed-% of pts. with stenosis and insufficiency (% (number in subgroup/N))	13% (48/365)

Table 4: Effectiveness Outcomes, Functional NYHA

NYHA Class	Preoperative		3-6 Months		1 Year		3 Years	
	n/N	%	n/N	%	n/N	%	n/N	%
MOSAIC Porcine Bioprosthesis Clinical Study AVR (N = 1252)								
I	30/1252	2%	865/1150	75%	812/1090	74.5%	287/498	58%
II	311/1252	25%	266/1150	23%	261/1090	24%	202/498	41%
III	732/1252	58.5%	17/1150	1%	16/1090	1.5%	9/498	2%
IV	179/1252	14%	2/1150	0%	1/1090	0%	0/498	0%
MOSAIC Porcine Bioprosthesis Clinical Study MVR (N = 365)								
I	2/363	1%	190/322	59%	161/260	62%	56/101	55%
II	74/363	20%	119/322	37%	88/260	34%	39/101	39%
III	213/363	59%	11/322	3%	9/260	3.5%	5/101	5%
IV	74/363	20%	2/322	1%	2/260	1%	1/101	1%

Table 5: Effectiveness Outcomes, Hemodynamics, Valvular Regurgitation: AVR
All patients analyzed: N=1252, percent (numerator/N)

Endpoint	≤30 Days	3-6 Months	1 Year	3 Years
Valvular Regurgitation				
% of pts. With no regurgitation	79% (958/1207)	76% (882/1153)	75% (824/1094)	77% (378/490)
% of pts. With trivial regurgitation	13% (155/1207)	15% (172/1153)	16% (175/1094)	15% (73/490)
% of pts. With mild regurgitation	7% (85/1207)	7% (85/1153)	7% (79/1094)	6% (30/490)
% of pts. With mod regurgitation	1% (9/1207)	1% (12/1153)	1% (14/1094)	2% (9/490)
% of pts. With mod severe regurgitation	0% (0/1207)	0% (2/1153)	0% (2/1094)	0% (0/490)
% of pts. With severe regurgitation	0% (0/1207)	0% (0/1153)	0% (0/1094)	0% (0/490)

Note: Data reflect transvalvular, paravalvular and indeterminate regurgitation noted at all locations combined.

Table 6: Effectiveness Outcomes, Hemodynamics, Mean Pressure Gradient: AVR
All patients analyzed: N=1252, number in subgroup/N, mean ± SD [min., max.]

Endpoint	≤30 Days	3-6 Months	1 Year	3 Years
Mean Pressure Gradient (mmHg)				
21 mm	217/240, 14.6 ± 6.5 [2.7, 54.7]	199/240, 13.3 ± 5.3 [3.0, 34.4]	189/240, 14.5 ± 5.3 [2.0, 40.5]	87/240, 15.5 ± 5.6 [4.5, 32.5]
23 mm	456/495, 13.0 ± 5.3 [0.9, 37.0]	446/495, 11.8 ± 4.9 [2.0, 43.1]	425/495, 12.8 ± 5.0 [3.0, 32.7]	198/495, 14.0 ± 5.5 [3.1, 35.5]
25 mm	334/362, 11.6 ± 4.9 [2.0, 32.0]	331/362, 10.6 ± 4.4 [1.1, 35.7]	310/362, 11.8 ± 5.2 [2.0, 38.9]	127/362, 12.1 ± 5.8 [1.4, 43.1]
27 mm	119/130, 11.1 ± 4.1 [2.0, 21.5]	114/130, 9.1 ± 4.0 [2.0, 23.1]	105/130, 10.0 ± 4.0 [3.4, 22.7]	45/130, 10.5 ± 4.1 [3.3, 24.6]
29 mm	24/25, 12.6 ± 5.8 [7.0, 28.8]	21/25, 8.6 ± 2.9 [3.5, 16.8]	21/25, 10.3 ± 2.6 [4.6, 16.0]	16/25, 9.9 ± 2.5 [5.9, 15.1]

Table 7: Effectiveness Outcomes, Hemodynamics, Effective Orifice Area: AVR
All patients analyzed: N=1252, number in subgroup/N, mean ± SD [min., max.]

Endpoint	≤30 Days	3-6 Months	1 Year	3 Years
Effective Orifice Area (cm^2)				
21 mm	217/240, 1.4 ± 0.4 [0.6, 3.7]	199/240, 1.4 ± 0.4 [0.7, 3.8]	189/240, 1.3 ± 0.4 [0.6, 3.1]	86/240, 1.3 ± 0.3 [0.7, 2.5]
23 mm	458/495, 1.6 ± 0.5 [0.7, 3.9]	447/495, 1.6 ± 0.5 [0.8, 5.4]	426/495, 1.5 ± 0.4 [0.7, 3.4]	199/495, 1.5 ± 0.4 [0.7, 3.2]
25 mm	336/362, 1.8 ± 0.5 [0.8, 4.2]	331/362, 1.8 ± 0.5 [0.7, 4.0]	311/362, 1.8 ± 0.5 [0.7, 4.2]	127/362, 1.7 ± 0.4 [0.6, 3.0]
27 mm	119/130, 1.9 ± 0.6 [1.0, 4.3]	114/130, 2.0 ± 0.5 [1.0, 3.4]	105/130, 1.9 ± 0.6 [1.1, 3.7]	45/130, 1.9 ± 0.7 [1.0, 4.2]
29 mm	24/25, 2.0 ± 0.5 [1.0, 2.9]	21/25, 2.3 ± 0.6 [1.4, 3.6]	21/25, 2.2 ± 0.7 [1.3, 4.1]	16/25, 2.2 ± 0.6 [1.2, 3.4]

Table 8: Effectiveness Outcomes, Hemodynamics, Valvular Regurgitation: MVR
All patients analyzed: N=365, percent (numerator/N)

Endpoint	≤30 Days	3-6 Months	1 Year	3 Years
Valvular Regurgitation				
% of pts. With no regurgitation	80% (280/348)	77% (255/331)	77% (206/267)	77% (75/97)
% of pts. With trivial regurgitation	15% (51/348)	15% (51/331)	16% (42/267)	18% (17/97)
% of pts. With mild regurgitation	3% (12/348)	5% (18/331)	5% (13/267)	2% (2/97)
% of pts. With mod regurgitation	1% (5/348)	2% (6/331)	2% (5/267)	1% (1/97)
% of pts. With mod severe regurgitation	0% (0/348)	0% (1/331)	0% (0/267)	2% (2/97)
% of pts. With severe regurgitation	0% (0/348)	0% (0/331)	0% (1/267)	0% (0/97)

Note: Data reflect transvalvular, paravalvular and indeterminate regurgitation noted at all locations combined.

Table 9: Effectiveness Outcomes, Hemodynamics, Mean Pressure Gradient: MVR
All patients analyzed: N=365, number in subgroup/N, mean ± SD [min., max.]

Endpoint	≤30 Days	3-6 Months	1 Year	3 Years
Mean Pressure Gradient (mmHg)				
25 mm	42/48, 5.9 ± 2.2 [3.0, 13.0]	40/48, 5.5 ± 2.1 [1.0, 12.0]	32/48, 5.6 ± 1.6 [3.0, 9.3]	10/48, 5.1 ± 1.8 [1.9, 8.0]
27 mm	107/115, 5.3 ± 2.2 [2.0, 12.0]	104/115, 4.8 ± 2.1 [1.0, 13.1]	83/115, 4.5 ± 2.2 [1.0, 13.0]	33/115, 4.9 ± 3.0 [1.0, 16.2]
29 mm	133/136, 5.0 ± 2.1 [1.0, 15.0]	125/136, 4.4 ± 2.0 [1.0, 12.5]	101/136, 4.3 ± 1.7 [1.0, 8.6]	36/136, 3.9 ± 1.5 [1.0, 8.3]
31 mm	56/57, 4.7 ± 1.9 [2.0, 10.3]	52/57, 4.1 ± 1.6 [1.0, 7.6]	43/57, 3.7 ± 1.4 [1.0, 6.5]	15/57, 4.0 ± 2.1 [2.0, 9.1]

Table 10: Effectiveness Outcomes, Hemodynamics, Effective Orifice Area: MVR
All patients analyzed: N=365, number in subgroup/N, mean ± SD [min., max.]

Endpoint	≤30 Days	3-6 Months	1 Year	3 Years
Effective Orifice Area (cm^2)				
25 mm	39/48, 1.6 ± 0.4 [0.9, 2.9]	36/48, 1.7 ± 0.8 [0.7, 5.6]	27/48, 1.6 ± 0.5 [0.8, 2.3]	7/48, 1.8 ± 0.6 [1.2, 2.8]
27 mm	95/115, 1.7 ± 0.6 [0.8, 4.6]	93/115, 1.7 ± 0.4 [0.9, 2.9]	76/115, 1.7 ± 0.5 [0.7, 3.7]	28/115, 1.6 ± 0.5 [0.3, 3.3]
29 mm	118/136, 1.7 ± 0.5 [0.7, 3.1]	111/136, 1.8 ± 0.5 [0.7, 3.4]	92/136, 1.8 ± 0.5 [0.8, 3.0]	32/136, 1.7 ± 0.5 [1.2, 3.1]
31 mm	53/57, 1.6 ± 0.5 [0.5, 3.0]	47/57, 1.8 ± 0.6 [1.0, 3.1]	37/57, 1.7 ± 0.6 [1.0, 3.2]	14/57, 1.9 ± 0.7 [1.1, 3.8]

8. INDIVIDUALIZATION OF TREATMENT

Long-term anticoagulant and/or antiplatelet therapy should be considered in patients with a dilated left atrium, a history of thromboembolic events, or a cardiac rhythm of atrial fibrillation or atrial flutter.

8.1 Specific Patient Populations

The safety and effectiveness of the MOSAIC Porcine Bioprosthesis has not been established for the following specific populations because it has not been studied in these populations:

- patients who are pregnant;
- nursing mothers;
- patients with altered calcium metabolism (e.g., chronic renal failure, hyperparathyroidism);
- patients with aneurysmal aortic degenerative conditions (e.g., cystic medial necrosis, Marfan's Syndrome);
- children, adolescents, or young adults.

9. PATIENT COUNSELING INFORMATION

Patients may require anticoagulation and/or antiplatelet therapy for an indefinite period based on each patient's condition.

Patients with bioprostheses are at risk for bacteremia (e.g., undergoing dental procedures) and should be advised about prophylactic antibiotic therapy.

10. HOW SUPPLIED

10.1 Packaging

The MOSAIC Porcine Bioprosthesis is chemically sterilized and is supplied STERILE in a buffered 0.2% glutaraldehyde storage solution. Sterility is compromised if the package is opened and damaged. The outside of the container is NOT sterile.

10.2 Storage

The MOSAIC Porcine Bioprosthesis must be stored between 5° and 25°C (41° and 77°F). Refrigeration is not required, and freezing may damage the bioprosthesis. Room temperature storage (up to 25°C or 77°F) is satisfactory; provided the bioprosthesis is not exposed to sunlight or other ultraviolet light sources or placed where significant temperature fluctuations may occur.

The storage life of the MOSAIC Porcine Bioprosthesis is three (3) years from the date of sterilization. Appropriate inventory control should be maintained so that bioprostheses with earlier expiration dates are preferentially implanted and expiration is avoided.

11. DIRECTIONS FOR USE

11.1 Physician Training

No specific training is required to implant MOSAIC Porcine Bioprostheses. The techniques for implanting these bioprostheses are similar to those used for any stented bioprosthesis.

11.2 Device Features

Features of the MOSAIC Porcine Bioprosthesis include:

The stents of the MOSAIC Porcine Bioprosthesis, Aortic Model 305, and the MOSAIC Porcine Bioprosthesis, Mitral Model 310, are constructed from acetal homopolymer. The stents have a slightly lower profile (approximately 2 mm) for all bioprostheses sizes as compared to the Hancock Standard Bioprosthesis and Hancock Modified Orifice Bioprosthesis.

To allow radiographic visualization, both the aortic and mitral stents are fitted with stent post markers. The stent post markers are placed close to the apex of each stent post to allow visualization of the relationship of the stent posts to one another and to the aortic or ventricular wall.

The stents of both the aortic and mitral models are covered with polyester fabric.

The inflow edge of the stent of the aortic bioprosthesis is scalloped, as is the sewing ring. The sewing ring is mounted flush with the inflow edge of the stent. This facilitates implantation in either the supra-annular or intra-annular position. If the supra-annular position is preferred, the entire bioprosthesis can be seated superior to the annulus, allowing the use of a larger MOSAIC Porcine Aortic Bioprosthesis. The inflow edge of the mitral bioprosthesis stent and sewing ring are flat. The mitral bioprosthesis sewing ring contains polyester felt allowing for easy needle penetration and low suture drag.

Disposable acetal polymer holders are sutured to both aortic and mitral bioprostheses. In the case of the mitral bioprosthesis, the suture attaching the bioprosthesis holder prevents looping of the surgeon's sutures during implantation. The mitral bioprosthesis holder incorporates a ratchet mechanism which, after screwing the bioprosthesis holder onto the handle, is actuated by further rotation. This then causes the stent posts to be drawn inward, easing insertion into the annulus.

The disposable holders are designed to fit the reusable Medtronic Handle (Model 0791). The handle is equipped with a knurled locknut to allow the bioprosthesis to be oriented and secured in a given position with respect to the handle. The handle is also used with MOSAIC Porcine Bioprosthesis obturators for measuring the annulus.

11.3 Handling and Preparation Instructions

Proper bioprosthesis size selection is an important part of heart valve replacement. The internal diameter of the patient's aortic root at the annulus and supracommissural areas and at the mitral annulus may be measured preoperatively,

during diastole, using angiographic and/or echocardiographic techniques. The size selection of a MOSAIC Porcine Bioprosthesis is aided by the use of MOSAIC Aortic and Mitral Obturators (Models 7305 and 7310 respectively). Use only a MOSAIC Obturator to select the appropriate size bioprosthesis. For further information refer to the MOSAIC Aortic and Mitral Obturators Instructions for Use.

Because of the complexity and variation in surgical procedures for cardiac valve replacement, the choice of surgical and suturing techniques is left to the discretion of the individual surgeon. In general, interrupted and mattress suturing are the most commonly reported techniques used for stented valve implantation. Spacing of sutures when using the mattress technique must be carefully matched in length between the annulus and sewing ring to prevent sewing ring distortion. When using the interrupted suturing technique, it is important to trim all suture tail remnants close to the knots to prevent contact of suture tails with the leaflets.

Within the sterile field, prepare three rinse basins, each containing 500 ml of sterile normal saline solution.

The exterior of the device container and lid are nonsterile. The circulating nurse should examine the seal to verify that the container has not been damaged or previously opened. Remove and discard the seal. Turn the lid counterclockwise, and open the container (Figures 1 and 2).

> **DO NOT RESTERILIZE** the bioprosthesis by any method. Exposure of the bioprosthesis and container to irradiation, steam, ethylene oxide or other chemical sterilization will render the bioprosthesis unfit for use.

The bioprosthesis and all internal packaging components are sterile and must be handled accordingly. With the thumb and index finger of a sterile, gloved hand, and maintaining aseptic technique, grasp the retainer by the middle bar and slowly lift it out of the jar allowing for drainage of the glutaraldehyde storage solution (Figure 3).

Carefully release the identification tag from the notches at the base of the retainer (Figure 4).

Hold the retainer upright. Remove the retainer cap by turning it counterclockwise using the thumb and index finger (Figure 5). The inflow aspect of the bioprosthesis will be visible.

Hold the identification tag suture between the second and third fingers of the free hand to assure that the tag does not interfere with bioprosthesis removal. While holding the suture, tip the retainer upside down over the first rinse basin. The bioprosthesis will fall into the free hand (Figure 6). The bioprosthesis will have a retainer collar around it. If the bioprosthesis does not fall, gently tap the retainer against the palm of the hand.

Holding the bioprosthesis over the first rinse basin, with the three stent posts facing upward, position the identification tag suture between the collar and bioprosthesis sewing ring.

Using both hands, grasp the collar on each side of the opening. Open the collar by moving the sides away from each other allowing the bioprosthesis to slide into the rinse basin (Figure 7).

If the bioprosthesis does not fall freely from the collar, the index finger may be used to guide it out. **At no time should the tissue portion of the bioprosthesis be touched.**

Retrieve the bioprosthesis from the basin and have an assistant record the bioprosthesis identification number in the patient's record.

Carefully cut the identification tag from the bioprosthesis and discard the tag.

NOTE: Be careful not to cut the cloth or bioprosthesis tissue when removing the identification tag. Remove any remnants of the identification tag suture from the bioprosthesis.

Rinse Procedure
Submerge the bioprosthesis and holder into the first rinse basin. Gently swirl the bioprosthesis and holder in the solution for a minimum of two minutes in each of the three previously prepared rinse basins. In each basin, gently squeeze the sewing cushion to remove residual glutaraldehyde. **Do not touch the tissue portion of the bioprosthesis.** The bioprosthesis should remain in the third rinse basin until required by the surgeon.

If preferred, the rinse steps may be performed with the Medtronic Handle (Model 0791) attached to the bioprosthesis holder.

Screw the sterile locknut completely onto the sterile Medtronic Handle, then screw the handle into the bioprosthesis holder while lightly grasping the sewing ring of the bioprosthesis. Tighten the locknut against the holder (Figures 8 and 9).

Caution: Do not overtighten the handle.

11.4 Device Implantation

Caution: Do not use if the bioprosthesis has been damaged.

Caution: Extreme care must be taken to prevent damage to the delicate bioprosthesis tissue. Do not handle the tissue portion of the bioprosthesis with instruments. Even the most minor perforation may enlarge in time to produce significant impairment of bioprosthesis function. Should a bioprosthesis be damaged during insertion, do not attempt repair.

Caution: Ensure proper orientation of the bioprosthesis.

Caution: Do not use cutting needles, as they may cause structural damage to the fabric of the bioprosthesis.

Caution: Passage of a catheter, surgical instrument or transvenous pacing lead through any bioprosthesis may damage the delicate bioprosthesis tissue and is, therefore, not recommended.

Aortic Bioprosthesis

Caution: Orient the bioprosthesis to avoid obstruction of the coronary ostia.

To change the angular orientation, loosen the locknut, unscrew the holder an appropriate amount, and retighten the locknut.

During implantation, the bioprosthesis should be periodically irrigated with sterile normal saline to prevent drying of the bioprosthesis tissue. Do not use cutting needles as they could cause structural damage to the bioprosthesis. Following placement of the sutures in the sewing ring, and positioning of the bioprosthesis in the annulus, gently remove the holder and retaining sutures by cutting all three sutures with scissors or scalpel in the protected area (Figure 10).

After cutting the three sutures, hold the bioprosthesis in place and gently pull away the handle. The holder and retaining sutures will pull free from the bioprosthesis. Examine the sewing ring and holder to ensure that no suture remnants remain with the bioprosthesis. The holder should then be unscrewed from the handle and discarded.

Mitral Bioprosthesis

Actuate the ratchet mechanism of the holder by lightly grasping the sewing ring of the bioprosthesis and rotating the valve clockwise. The stent posts are thus deflected to facilitate insertion of the bioprosthesis into the patient's annulus. The posts should not be deflected more than surgically necessary.

Caution: Special care should be exercised when implanting a bioprosthesis in the mitral position in a patient with a small left ventricle. Adequate clearance must be available to avoid contact between the prosthesis stent post and the ventricular wall. Repeated contact between these structures could result in perforation of the ventricular wall.

Caution: The bioprosthesis should be oriented so that the largest intercommissural space corresponds with patient's left ventricular outflow tract. From the atrial aspect of the prosthesis, the largest intercommissural space lies between the green suture marker on the sewing ring and the first commissure in the counter-clockwise direction. Proper positioning in the mitral annulus may be approximated by orienting the green suture marker on the atrial aspect of the sewing ring in the direction of the lateral fibrous trigone. This orientation may minimize the potential for obstruction to the aortic outflow.

To change angular orientation, loosen the locknut, unscrew the holder an appropriate amount, and retighten the locknut.

During implantation, periodically irrigate the bioprosthesis with sterile normal saline to prevent drying of the bioprosthesis tissue. Do not use cutting needles as they could cause structural damage to the bioprosthesis. Following placement of the sutures, the bioprosthesis should be lowered into the annulus, taking care to prevent suture entanglement. Maintaining tension on the sutures at this point is helpful. Suture ends must be trimmed close to the knot to prevent abrasion of leaflet tissue.

Following placement of the bioprosthesis in the annulus, the holder should be removed by cutting the three retaining sutures with scissors or scalpel (Figure 10).

After cutting the three sutures, hold the bioprosthesis in place and gently pull away the handle. The holder and retaining sutures will pull free from the bioprosthesis. Examine the sewing ring and holder to ensure that no remnants remain with the bioprosthesis. The holder should then be unscrewed from the handle and discarded.

11.5 Accessories

Use only MOSAIC Aortic and Mitral Obturators (Models 7305 and 7310 respectively) and the Medtronic Handle (Model 0791) to determine the appropriate MOSAIC Porcine Bioprosthesis size. Valve obturators are provided in aortic and mitral configurations for each size bioprosthesis.

Caution: Do not use other manufacturer's valve obturators, or obturators for another Medtronic heart valve to size the MOSAIC Porcine Bioprosthesis.

11.6 Return of Explanted Bioprosthesis

Medtronic, Inc. is interested in obtaining recovered MOSAIC Porcine Bioprostheses. Specific pathological studies of each explant will be determined under the direction of a consulting pathologist. A written report summarizing the findings will be returned to the physician. Product return kits, including an explant information form, are available by contacting Medtronic, Inc. distribution centers or your Medtronic Sales Representative. It is important that the explant form be completely filled out. If a kit is not available, place the explanted bioprosthesis in a container of glutaraldehyde or 10% buffered formalin immediately after excision. For further instructions on the return of an explanted device, contact your Medtronic Sales Representative.

12. PATIENT INFORMATION

12.1 Registration Information

A patient registration form is included in each device package. After implantation, please complete all requested information. The serial number may be found on the package and on the identification tag attached to the bioprosthesis. Return the original form to the Medtronic address indicated on the form and provide the temporary identification card to the patient prior to discharge. For multiple implantations, use a separate form for each bioprosthesis.

An Implanted Device Identification Card is provided to the patient by Medtronic, Inc. The card contains the name and telephone number of the patient's physician, as well as, information that medical personnel would require in the event of an emergency.

12.2 Patient Manual

Medtronic has prepared a Patient Information Pamphlet which the physician should provide to the patient prior to discharge. Copies of these pamphlets may be obtained from your Medtronic Sales Representative.