Meril

Dafodil™

Pericardial Bioprosthesis

DDL/PPT/002/20200715

Dafodil™
Pericardial Bioprosthesis

Global Med-Tech Group

Meril

CORE OBJECTIVE

To develop, manufacture & distribute clinically relevant, state-of-the-art & best-in-the-class products to alleviate human suffering & improve quality of life.

Global Med-tech Hub For High Quality, Next Generation Technologies

Dafodil™
Pericardial Bioprosthesis

Meril Infrastructure

Meril

Robust R&D, Ultra-modern, Large Manufacturing & Commitment to Clinical Research

- Large, hi-tech, mfg. capacity
- Dedicated R&D Complex at Meril Park with more than 150 professionals
- Global clinical program to establish safety and efficacy of products

Dafodil™
Pericardial Bioprosthesis

Meril's DNA

Meril

Wide patient access

Global Market Presence

Creating Long Term Partnership

Strong R&D Focus

Meril

Highest Quality Control

Strong Organizational Band Width

Commitment to Training & Education

Large Scale Manufacturing

Presence in 4 Large Business Verticals

Cardiovascular
24 Product Families
- Cardio,
- Peripheral &
- Neuro vascular
- Structural Heart Disease
- Congestive Heart Failure

Orthopedic
10 Product Families
- Total Knee Replacement
- Total Hip Replacement
- Spine implants
- Trauma implants

Endo- Surgery
30 Product Families
- Sutures
- Staplers
- Adhesives
- Hernia Repair
- Women's health

Diagnostics
45 Product Families
- Analyzers
- Reagents
- Biochemistry
- Hematology
- Immunology
- Rapid testing
- POCT

100+ Technologies

- Largest dedicated training academy for Med-Tech in Asia Pac
- Our Vision: Transform patient care through professional education
- 10,000+ HCPs engaged for various educational programs
- Over 1,000 Interventional Cardiologists from over 20 countries have visited us in last few years
- Dedicated TAVR & Complex PCI (CIT) programs are organized
- Live case transmissions & hands-on simulator models for Ortho, Cardio, Surgery

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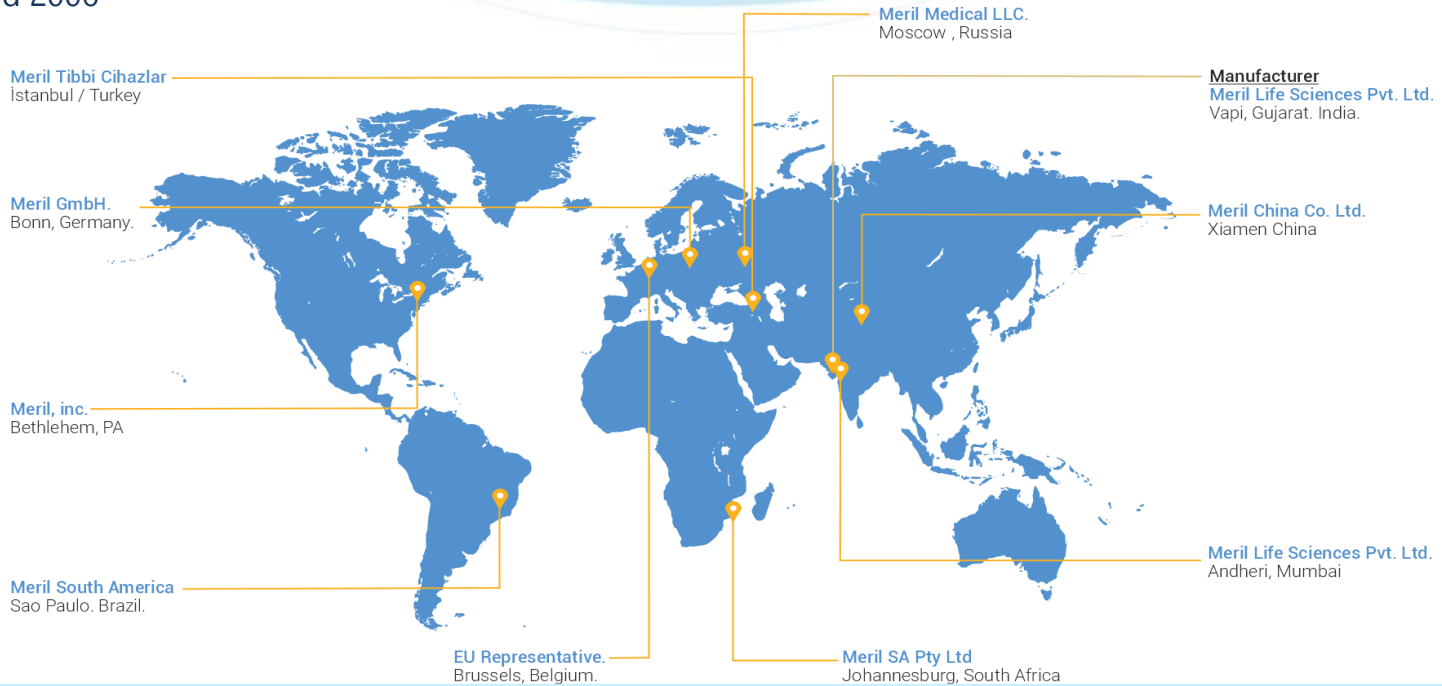
Over a Decade of Growth and Innovation

Meril

Established 2006



- Business in 100+ countries
- 4,000+ employees
- DCGI, CE, USFDA, CFDA, KFDA, ANVISA, INVIMA, Russia MoH, TGA, Canada, PMDA Japan

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Current & future Cardiovascular portfolio

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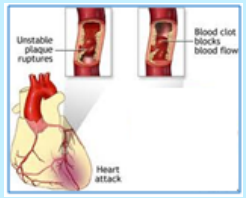
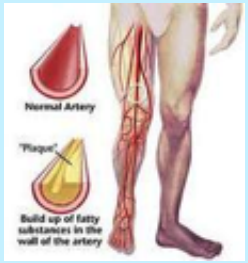
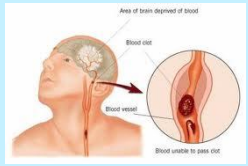
Vascular



Coronary
- Cobalt Chromium Stent
- PTCA Balloon
- Drug Eluting Stent
- Bioresorbable Scaffold
- Drug Coated Balloon

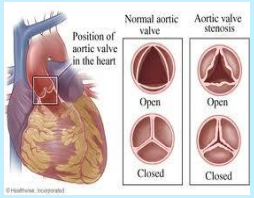


Peripheral
- Peripheral BMS, DES & BRS
- PTA Balloons
- Nitinol Peripheral BMS & DES
- Drug Coated PTA Balloon

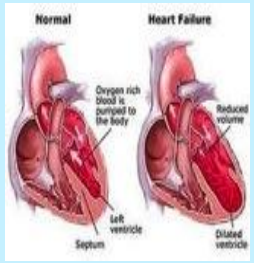


Neurovascular
- Flow modification stents
- Embolisation material
- Micro-catheters
- Accessories

Non-Vascular



Structural Heart
- TAVR
- TMVR
- SVR - Biological / Mechanical
- Valvuloplasty Balloons
- Septal Defect Closure Device



Heart failure
- Intra Aortic Balloon Pump
- Left Ventricular Assist Device

Ablation Therapies
- Renal denervation
- Bronchial thermoplasty

Dafodil™
Pericardial Bioprosthesis

Overview

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- Product and Features Overview
- Architecture
- Durability
- Implantability
- Hemodynamics
- Dafodil-1 First-In Human trial
- Valve Preparation Procedure
- Sizer set
- Ordering Info
- Technical Specification

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Pericardial Bioprosthesis

Product and Features Overview

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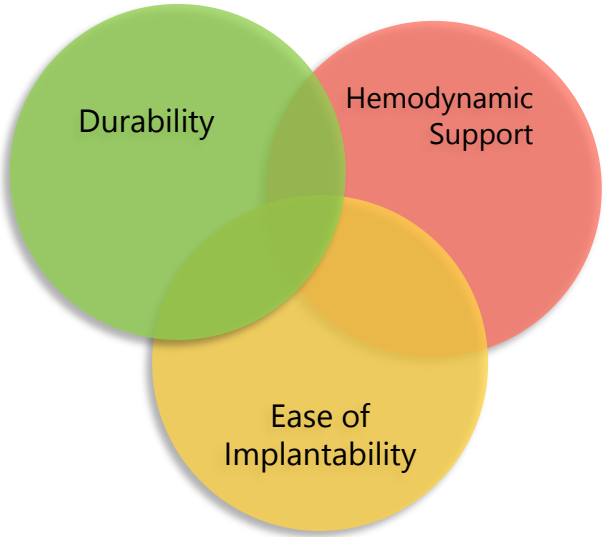
Dafodil is a **Bovine Pericardium** tissue based **Tri-leaflet Stented Valve**.
Scientifically modeled and bioengineered design to optimize:



Position-Specific design answers the challenging requirements of the Mitral & Aortic position

Aortic Bioprosthesis

Mitral Bioprosthesis

Dafodil™
Pericardial Bioprosthesis

Architecture

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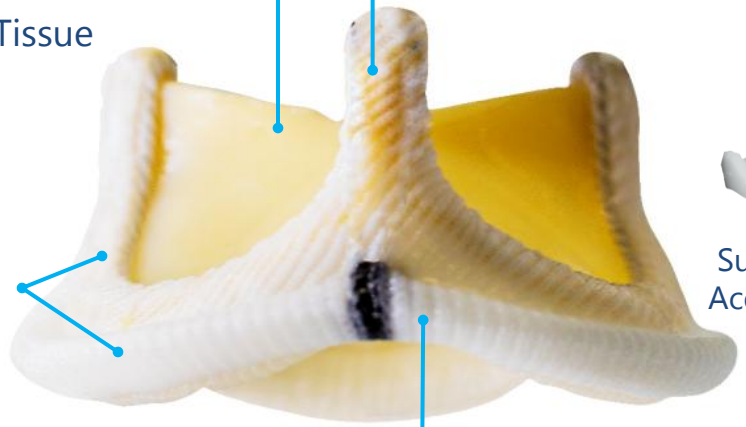
Triple Composite design

Bovine Pericardium Tissue

Polyester knit fabric



Triad Frame Design

Support ring-
Acetal Polymer

Commissures-
PET Film Structure

Wireform-
Elgiloy alloy

Sewing ring

with Commissural markers

(Dafodil Mitral has a Silicone Ring)

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Pericardial Bioprosthesis

Durability

Meril

Triad Frame Design

Commissure : PET Film structure

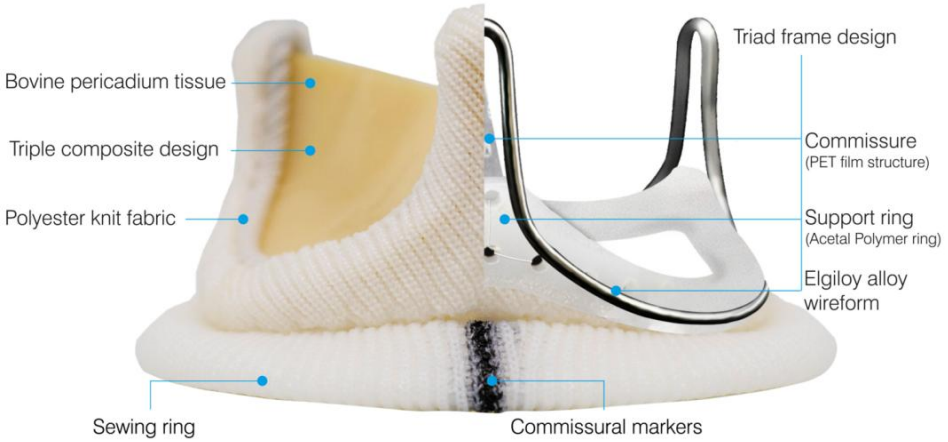
Support Ring : Acetal Polymer ring

Wireform : Elgiloy Alloy

- Superior Spring Efficiency
- Fatigue resistant Characteristics
- Corrosion Resistant alloy

Polyester Knit Fabric

- Designed to minimize Para-Valvular leak
- Promotes tissue in-growth



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Pericardial Bioprosthesis

Durability

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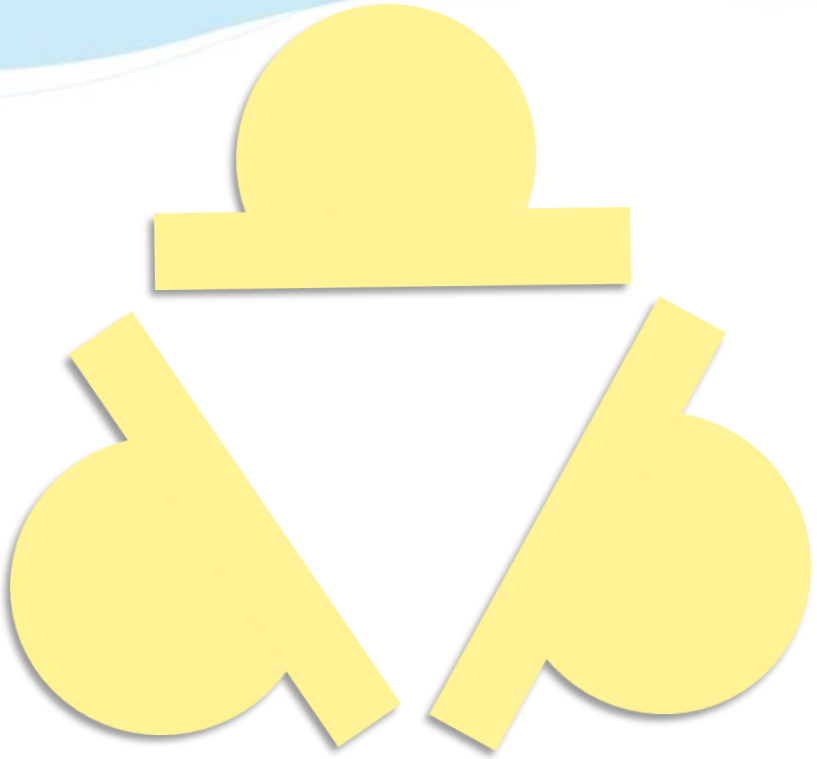
Triple Composite Leaflet Design

- Advanced Tissue Thickness Matching Technology
- Tissue Deflection Testing to match Size and Shape
- Better Hemodynamics and Durability

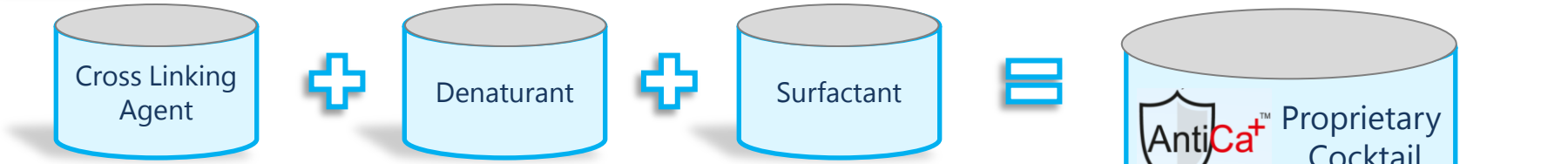


Durability : AntiCa+ ™

AntiCa+™ is Meril's own Patented Anti-calcification process to mitigate the risk of calcification .

Glutaraldehyde Fixed Bovine Pericardium

Process



Functions

- Chemically extracts phospholipids from cellular components of pericardial tissue &
- Inactivates the Glutaraldehyde resistant organisms.

Process Outcomes

- Reduces bio-burden
- Renders the tissue resistant to calcification
- Increases Valve's Long term Durability

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Pericardial Bioprosthesis

Implantability: Position Specific Design

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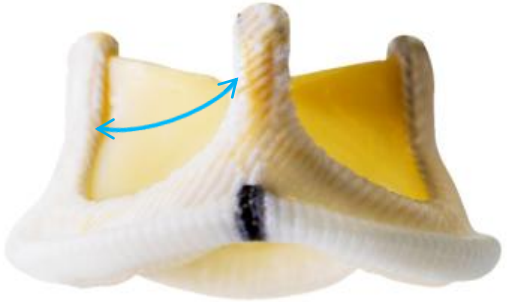
Aortic Valve

Specially designed Commissure posts ensure :

- Ease of Insertion
- Widen Ostia Clearance
- Compliments more space for better knot tying experience
- Differential Sewing ring with contour design



Mitral Valve

•Sewing ring with additional Silicone ring helps in mitigating Para Valvular leak

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Pericardial Bioprosthesis

Implantability: Dafodil Mitral Delivery System

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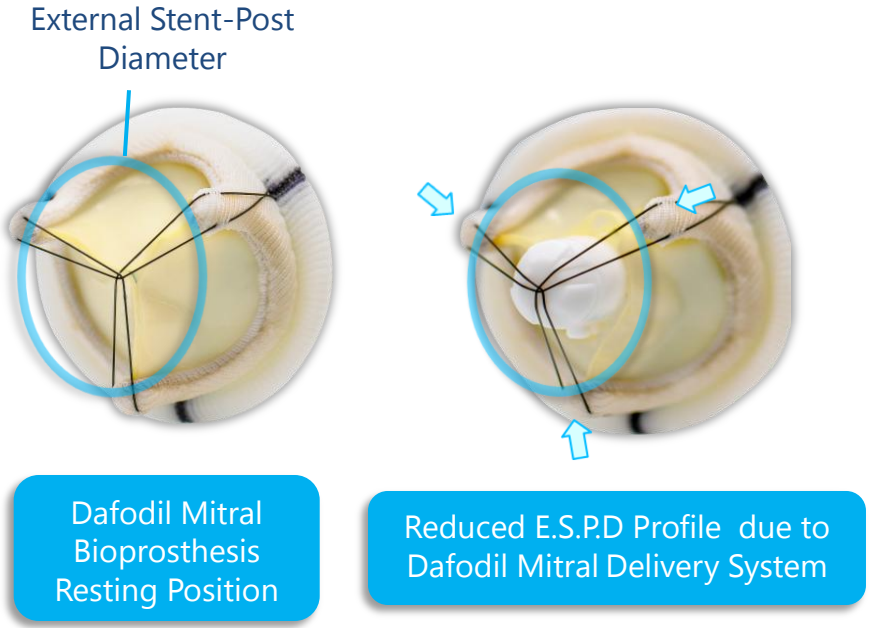
Position-Specific Design

Unique Dafodil Mitral Delivery System for Ease of Implant at Mitral position

Surgeons can **Actively Modify** the External Stent Post Diameter (E.S.P.D) to reduce its profile aiding Implantation in the Mitral Annulus.

This is possible by **Locking threads** and **Rotator** unique to mitral valves. When Inserted it creates tension onto the black sutures running over the commissures.



Dafodil Mitral Bioprosthesis Resting Position

Reduced E.S.P.D Profile due to Dafodil Mitral Delivery System

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Implantability: Sewing Ring

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Sewing Ring

- Polyester fabric Sewing ring
  - -Soft and Pliable
  - - Provides optimal natural fit
- Commissural markers
  - - Aid in Proper valve orientation during implantation
  - - Helps for Uniform placement of sutures

Sewing Ring - Mitral

- Position-specific design answers the challenging requirements of the Mitral position - additional Silicone ring helps in mitigating Para-Valvular leak

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Pericardial Bioprosthesis

Implantability

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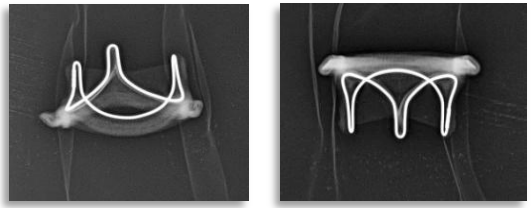
Elgiloy alloy wireform

- Provides Exceptional handling characteristics
- Excellent Radio-Opacity



Dafodil Aortic and Mitral Valve Placement

MRI Compatibility

- MR conditional in a magnetic field of upto 3.0 Tesla

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Pericardial Bioprosthesis

Hemodynamics

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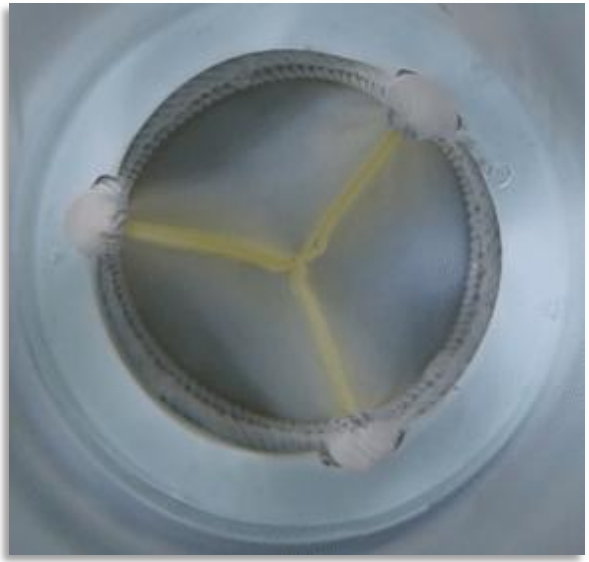
Specifically designed for **Supra-Annular** placement ensuring improved Hemodynamics

Triple-Composite design provides larger **Effective Orifice Area (EOA)**

Leaflet Co-aptation helps minimize Intra-Valvular Regurgitation



Excellent Effective Orifice Area & Leaflet Co-aptation

To be viewed in Fullscreen.

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Dafodil-1 First-In-Human Trial

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Purpose

The purpose of Dafodil-1 first-in-human trial was to evaluate clinical safety and performance (including hemodynamic parameters) of the Dafodil pericardial bio-prosthesis in patients who underwent aortic or mitral valve replacement

Method

This prospective, multicenter clinical trial enrolled 60 patients (Aortic: 30 patients; Mitral: 30 patients) from seven sites across India.

- Safety endpoints were early (≤30 days) and late (> 30 days) mortality and valve-related morbidity.
- Performance End Points and
- Other End Points

Hiremath *et al. Journal of Cardiothoracic Surgery* (2020) 15:140
https://doi.org/10.1186/s13019-020-01154-7

Journal of Cardiothoracic Surgery

RESEARCH ARTICLE Open Access

Check for updates

Clinical outcomes and hemodynamic performance of Dafodil™ aortic and mitral pericardial bioprosthesis: 1-year results from Dafodil-1 first-in-human trial

C. S. Hiremath[1], Anil R. Jain[2], Anurag Garg[3], Nirmal Gupta[4], Yugal K. Mishra[5], Zile Singh Meharwal[6], Nityanand Thakur[7], Atul A. Maslekar[8] and Naman Shastri[9*]

Dafodil™ Pericardial Bioprosthesis

Study Endpoints

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Key safety endpoints

- MACE
- All cause mortality
- Myocardial infarction
- All stroke

Performance endpoints

- NYHA
- Hemodynamic performance
- Device success
- Quality of life
- (SF-12 questionnaire)

Other end points

- Cardiovascular mortality
- Stroke and TIA
- Major and minor bleeding
- Acute kidney injury
- Valve thrombosis
- Structural valve deterioration
- Prosthetic valve endocarditis
- Major paravalvular leak
- Conduction disturbances and arrhythmia
- Non structural valve dysfunction
- Aortic/mitral apparatus damage or dysfunction
- Hemolysis
- Explant
- Trial valve related reoperation

https://doi.org/10.1186/s13019-020-01154-7

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Enrolment Details (60/60)

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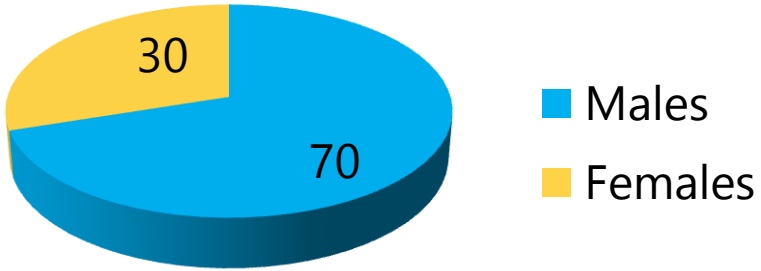
Sr. No.	Principal Investigator	Institute	Enrolled	Aortic	Mitral
1.	Dr. Devi Prasad Shetty	Narayana Institute of Cardiac Sciences, Bangalore	8	6	2
2.	Dr. Nirmal Gupta	Sanjay Gandhi Post Graduate Institute, Lucknow	3	1	2
3.	Dr. Nityanand Thakur	Sassoon Hospital, Pune	1	0	1
4.	Dr. C. S. Hiremath	Sri Sathya Sai Institute of Higher Medical Sciences, Bangalore	22	6	16
5.	Dr. Yugal Mishra*	Fortis Escorts Heart Institute, Delhi	3	2	1
6.	Dr. Anil Jain	SAL Hospital & Medical Institute, Ahmedabad	13	8	5
7.	Dr. Anurag Garg	Dr. D Y Patil Hospital, Pune	10	7	3
Total			60	30	30

*Dr. Yugal Mishra is no more associated with the Fortis Escorts Heart Institute, Delhi.
Presently, the study is been conducted at Fortis Escorts Heart Institute, New Delhi with Dr. Z. S. Meherwal as Principal Investigator.

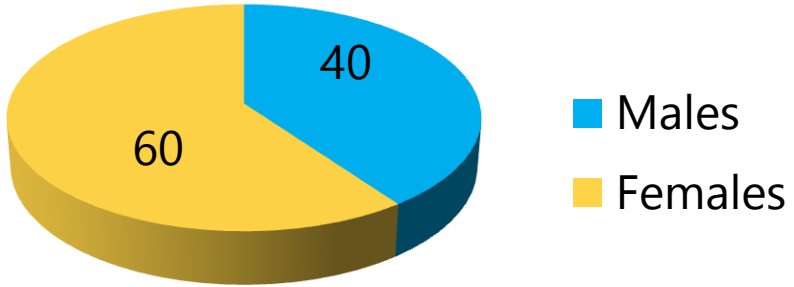
Gender Ratio

Demographics	AVR	MVR
Age years (mean ± SD)	59.83 ± 8.33	48.57 ± 12.63

Aortic Valve Gender Ratio



Mitral Valve Gender Ratio

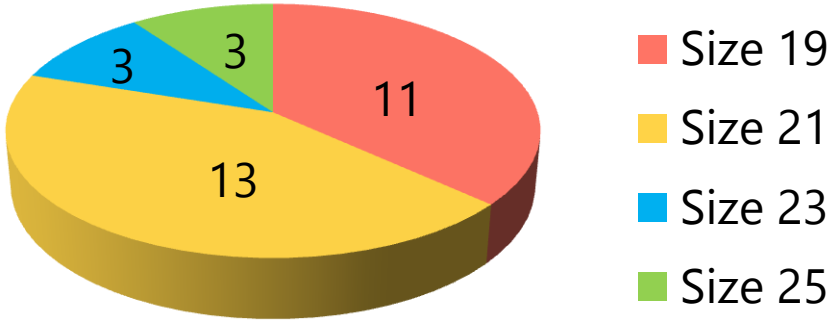


https://doi.org/10.1186/s13019-020-01154-7

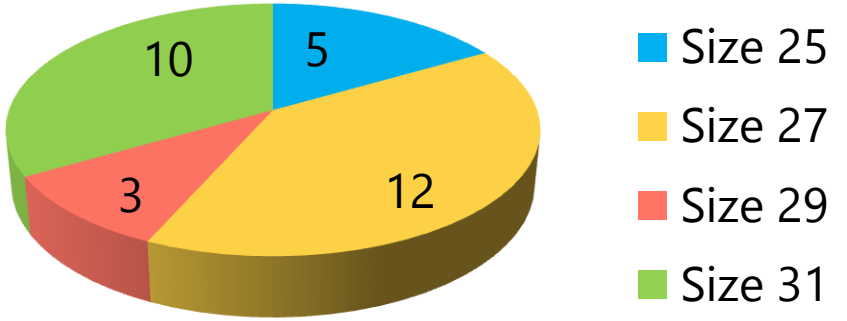
Valve Sizes Used

Dafodil Aortic and Mitral Pericardial Bioprosthesis
n= 60 (30:30 Aortic:Mitral)

Aortic Valve Size Split



Mitral Valve Size Split



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Dafodil™ Pericardial Bioprosthesis

Summary : Results at 12 months

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Safety	
Freedom from All-cause Mortality	93.33%
Freedom from Valve related mortality	100%
Freedom from Stroke	100%
Freedom from Valve thrombosis	100%
Freedom from Structural Valve deterioration	100%
Freedom from Permanent Pacemaker Implantation	98.33%

Performance	
Device Success	95%

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Dafodil™ Pericardial Bioprosthesis

Serious Adverse Events (SAE) Details:

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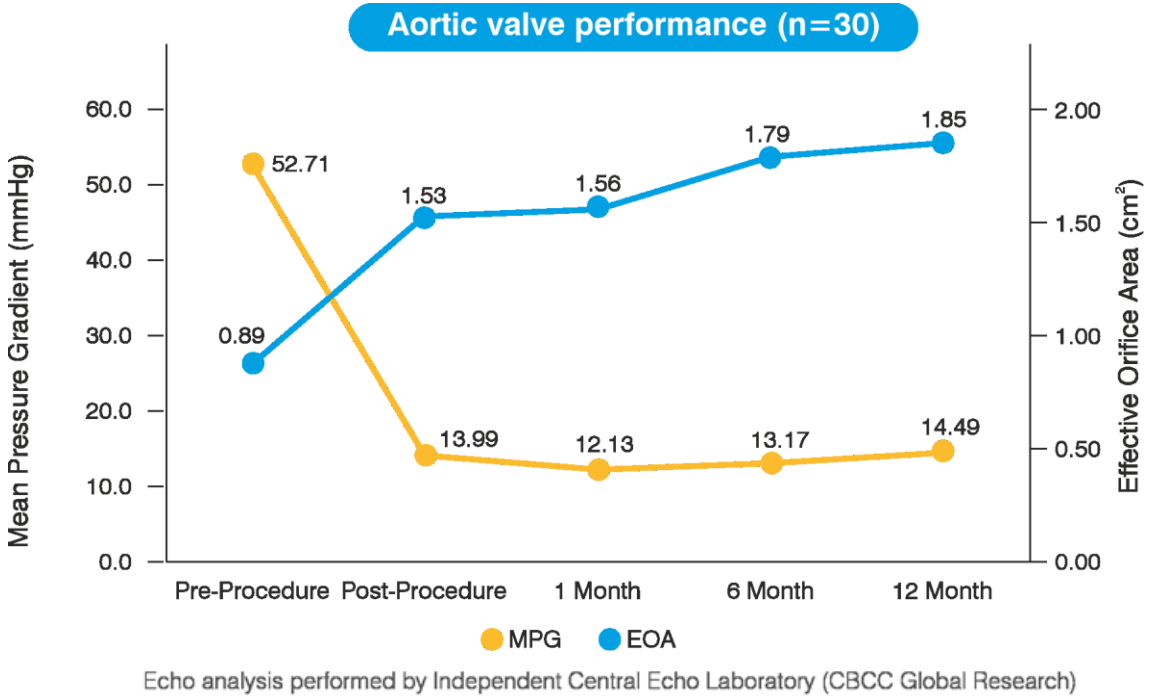
Sr. No.	Patient ID	Type of SAE
1	Patient 1	Congestive cardiac failure followed by death
2	Patient 2	Death due to cardiopulmonary arrest due to low cardiac output due to biventricular dysfunction
3	Patient 3	Septicemia and multi organ failure leading to death
4	Patient 4	Multi-organ dysfunction syndrome leading to death

All Mortality have been adjudicated as
'Not Related to Study Device' by independent Clinical Event Committee (CEC) of Dafodil-1 FIH Trial

https://doi.org/10.1186/s13019-020-01154-7

Aortic Valve performance



Echo analysis performed by Independent Central Echo Laboratory (CBCC Global Research)

~72.5% ↓
Reduction in Mean Pressure gradient*

~107% ↑
Increase in EOA values*

https://doi.org/10.1186/s13019-020-01154-7

*Values compared at Pre-procedure and at 12 months

Dafodil™ Pericardial Bioprosthesis

Aortic Valve performance

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Parameter	Valve Size	Pre-procedure	Discharge	1 Year Data	% Increase at 1 Year
Effective Orifice Area (mm^2)	19 (11)	0.72 ± 0.21	1.59 ± 0.67	1.78 ± 0.28	~147%
	21 (13)	0.68 ± 0.10	1.47 ± 0.55	1.83 ± 0.23	~169%
	23 (3)	1.32 ± NA	1.38 ± 0.11	2.32 ± 0.13	~75.7%
	25 (3)	2.48 ± 1.97	1.60 ± 0.24	1.84 ± 0.11	~-25.8% *
	Overall (30)	0.89 ± 0.70	1.53 ± 0.54	1.85 ± 0.27	~107%

* These patients were a case of dominant Moderate AR with Low Gradients and Higher EOA at Baseline (Pre-Implant)

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Dafodil™ Pericardial Bioprosthesis

Mitral Valve performance

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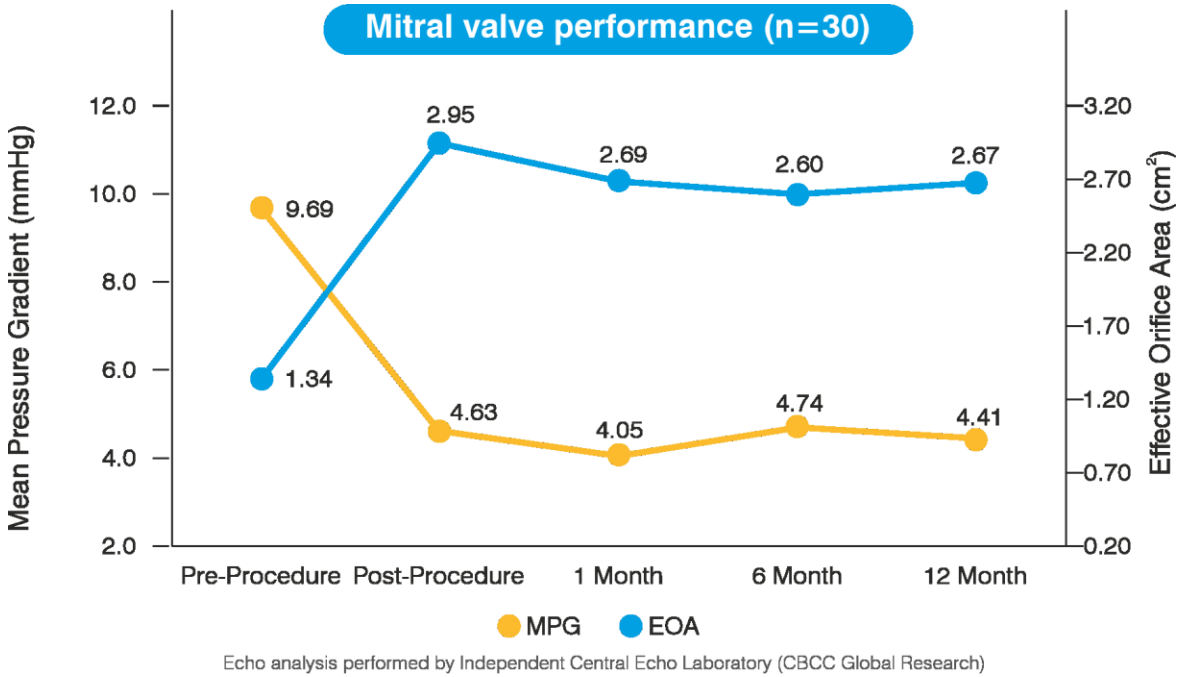

Echo analysis performed by Independent Central Echo Laboratory (CBCC Global Research)

~54.4% ↓
Reduction in Mean Pressure gradient*

~91.7% ↑
Increase in EOA values*

https://doi.org/10.1186/s13019-020-01154-7

*Values compared at Pre-procedure and at 12 months

Dafodil™ Pericardial Bioprosthesis

Mitral Valve performance

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Parameter	Valve Size	Pre-procedure	Discharge	1 Year Data	% Increase at 1 Year
Effective Orifice Area (mm^2)	25 (5)	0.98 ± 0.13	2.50 ± 0.48	2.37 ± 0.44	~141%
	27 (12)	1.20 ± 0.61	3.10 ± 0.64	2.68 ± 0.55	~123%
	29 (3)	1.93 ± 0.24	3.85 ± 1.38	2.86 ± 0.43	~48%
	31 (10)	1.50 ± 1.13	2.67 ± 0.70	2.78 ± 0.42	~85%
	Overall (30)	1.34 ± 0.77	2.95 ± 0.80	2.67 ± 0.48	~99%

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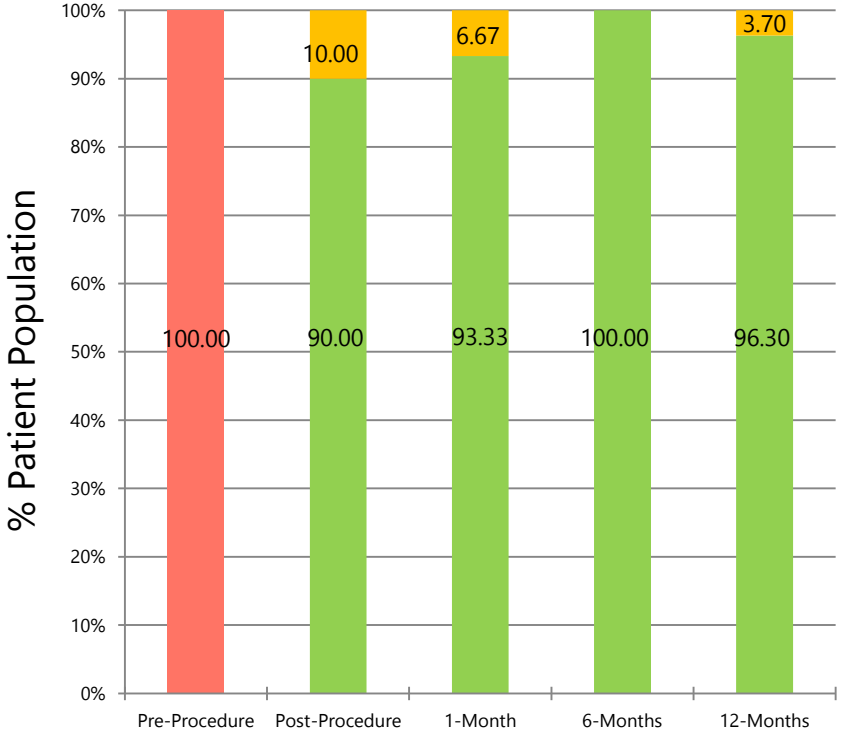
Functional NYHA

Aortic NYHA class



NYHA class

- Class IV
- Class III
- Class II
- Class I

Mitral NYHA class

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Dafodil™ Pericardial Bioprosthesis

Dafodil-1 Study Conclusion

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Clinical outcomes of Dafodil-1 study at one-year demonstrate **acceptable preliminary safety and performance** of the Dafodil Pericardial Bioprosthesis implanted at aortic and mitral positions.

Moreover, hemodynamic profile of Dafodil Pericardial Bioprosthesis confirmed favorable performance of the valve at aortic and mitral positions

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Valve Preparation Procedure

Dafodil™ Pericardial Bioprosthesis

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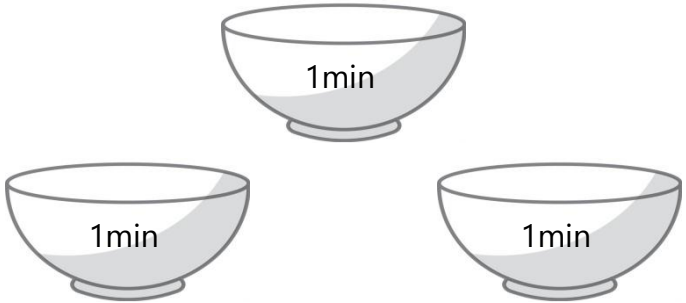
Objective

To thoroughly rinse the Glutaraldehyde sterilant used as storage solution for the bioprosthesis .

Rinse Procedure

- Place the bioprosthesis in the first bowl of sterile, physiological saline. The saline solution should completely cover the bioprosthesis and holder.
- With the bioprosthesis and holder submerged, slowly agitate (gently swirl) back and forth for a minimum of 1 minute.
- Transfer to 2nd rinsing bowl and gently agitate for a minimum 1 more minute.
- Transfer to 3rd rinsing bowl and gently agitate for a minimum 1 more minute.
- Finally, keep the bioprosthesis and holder in a 4th bowl of saline until implantation to prevent the tissue from drying.

500ml Saline in each Bowl



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Sizer set

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Aortic sizer set

Mitral sizer set

Dafodil™
Pericardial Bioprosthesis

Ordering Information

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Available Bioprosthesis Diameter (mm)	Reference Catalogue	
	Aortic Model	Mitral Model
19	DDL19A	N/A
21	DDL21A	N/A
23	DDL23A	DDL23M
25	DDL25A	DDL25M
27	DDL27A	DDL27M
29	N/A	DDL29M
31	N/A	DDL31M

Available Sizer Set	Reference / Catalogue Number
Aortic sizer set	DFA1927
Mitral sizer set	DFM2331

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Technical Specification
Aortic Valve

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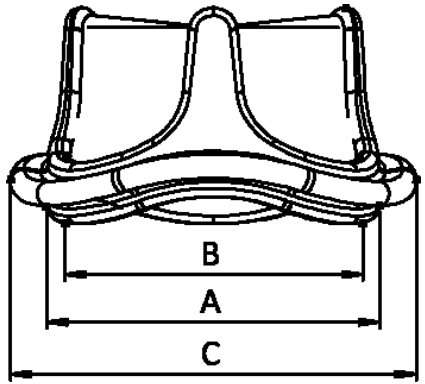
Aortic	Size	19	21	23	25	27
	A. Tissue Annulus Diameter	20	22	24	26.5	28.5
	B. Internal Stent Post Diameter (Base)	18	20	22	24	26
	C. External Sewing ring Diameter	27	28	31	33	36

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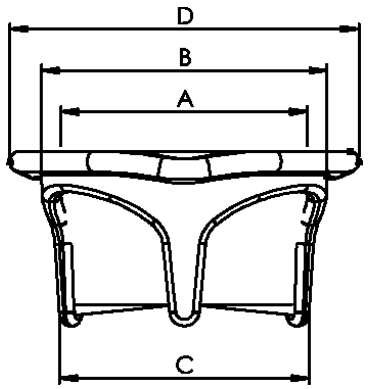
Technical Specification
Mitral Valve

Meril

Mitral	Size	23	25	27	29	31
	A. Stent Diameter (Wire Form)	23	25	27	29	29
	B. External Stent Post Diameter (Base)	26.5	28.5	29.5	32.5	32.5
	C. External Stent Post Diameter (Tip)	27	29	31	33	33
	D. External Sewing Ring Diameter	33	36	38	41	43

Dafodil™
Pericardial Bioprosthesis

General Product Information

Meril

Storage Temperature	10˚ C to 25 ˚ C (50-77˚ F)
Storage Solution	Glutaraldehyde
MRI Safety	MR conditional in a magnetic field of upto 3.0 Tesla
Recommendation	Use only Dafodil Aortic/Mitral Sizer Set with Dafodil Aortic/Mitral bioprosthesis

Thank you