TAVI – Summit 2012
Seoul, September 8, 2012

Next Generation TAVI Systems

Eberhard Grube MD, FACC, FSCAI

University Hospital, Dept of Medicine II, Bonn, Germany
Hospital Alemão Oswaldo Cruz, São Paulo, Brazil
Stanford University, Palo Alto, California, USA

Disclosure Statement of Financial Interest

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

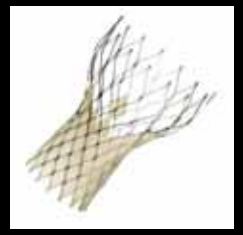
Physician Name	Company/Relationship
Eberhard Grube, MD	Medtronic, CoreValve: C, SB, AB, OF Sadra Medical: E, C, SB, AB Direct Flow: C, SB, AB Mitralign: AB, SB, E Symetis: AB Boston Scientific: C, SB, AB Biosensors: E, SB, C, AB Cordis: AB Kona Medical: E, AB Maya Medical: E, AB Abbott Vascular: AB Capella: SB, C, AB InSeal Medical: AB Valtec: E, SB Claret, SB

TAVI – Current Issues

- Device related Issues
  - Lack in Control and Accuracy in Positioning
  - Lack of Retrievability
  - Paravalvular Leack
  - Access Site Complications
  - Stroke
  - Pacemaker Need
  - Profile size

New TAVI valves are coming to the market in a few year's time

Today

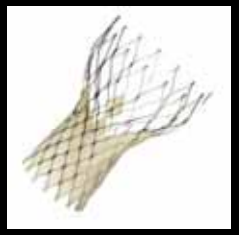


Medtronic CoreValve

Edwards Sapien XT

Edwards Sapien

Tomorrow



Next Gen. Medtronic CoreValve

Boston Sci. Lotus™

HLT

Medtronic Engager

Saint Jude Portico™

Direct Flow

Edwards Sapien XT

JenaValve

Symetis ACCURATE

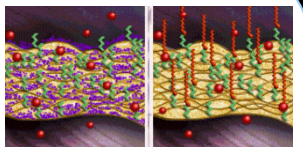
CoreValve Innovation

Focused Efforts on:

- Expansion of patient access
- Further improvement of ease of use
- Continue to advance patient and procedural outcome

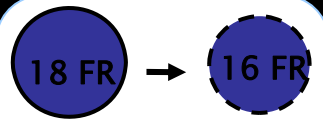
*Delivery System Improvements

Alternative Access Technology



Anti-Mineralization Tissue Treatment

*Greater Annulus Coverage



Profile Reduction

CoreValve Evolut Innovation Pipeline

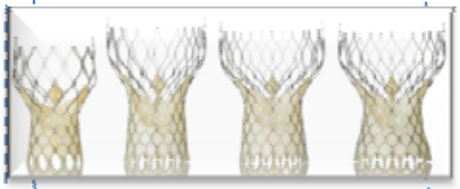
Time →

CoreValve Evolut
23 mm

AccuTrak
Delivery System

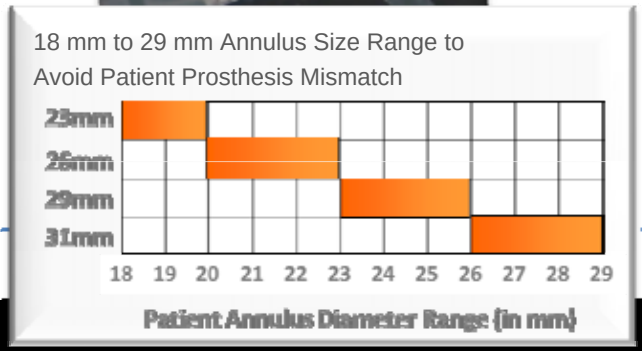
Next Gen
Delivery System

Also compatible with
CoreValve
26/29/31 mm



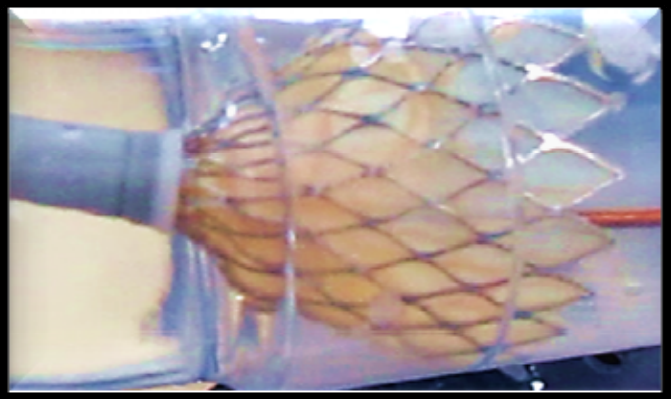
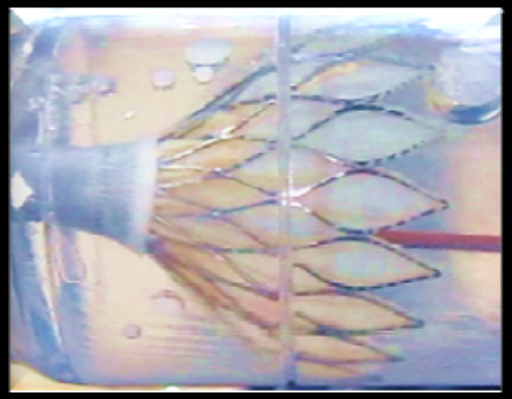
CoreValve Evolut Recaptureable
23 mm

CoreValve Evolut Recaptureable
26/29/31 mm



Recapturable after Valve Deployment

Retrievable, Repositionable, Resheathable


- More control for final valve deployment → Should contribute to reduced PVL and conduction disturbance
- Repositionable system with 18 Fr delivery across full valve size range

…Expect CE Mark Trials on Two New Valve Platforms in 2012

Edwards SAPIEN 3 Valve

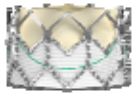
Balloon Expandable

Edwards CENTERA Valve

Self Expanding

Commercial Device*	IDE Trial Enrolling
SAPIEN THV	*SAPIEN XT THV*
	

U.S. Offering

O.U.S. Commercial Offering
SAPIEN XT THV


OUS Offering

12/9/2011

* The Edwards SAPIEN XT valve, the Edwards SAPIEN valve with the Ascendra delivery system, the Edwards SAPIEN 3 valve and the Edwards CENTERA valve are investigational devices and are not available for commercial sale in the U.S.

SAPIEN 3 Advances

Ultra Low-Profile Balloon Expandable Platform

- Designed to further **reduce PV leaks**
- Lower profile valve delivered through a **14 Fr eSheath**
- Discrete valve that anchors in the annulus
- Treated bovine pericardial tissue leaflets
- Dramatically reduced profile for the transapical approach

CENTERA is Edwards' First Self- Expanding Transcatheter Valve

Ultra Low-Profile Self Expanding Platform

- **Motorized delivery system** for stable deployment and single operator use
- **Repositionable**
- Delivered through a **14 Fr eSheath**
- Discrete valve that anchors in the annulus
- Treated bovine pericardial tissue leaflets
- Transfemoral and subclavian approach

First-in-Man Experience Completed

The Lotus™ Valve System

Product Details and Design Goals

Device Delivery:

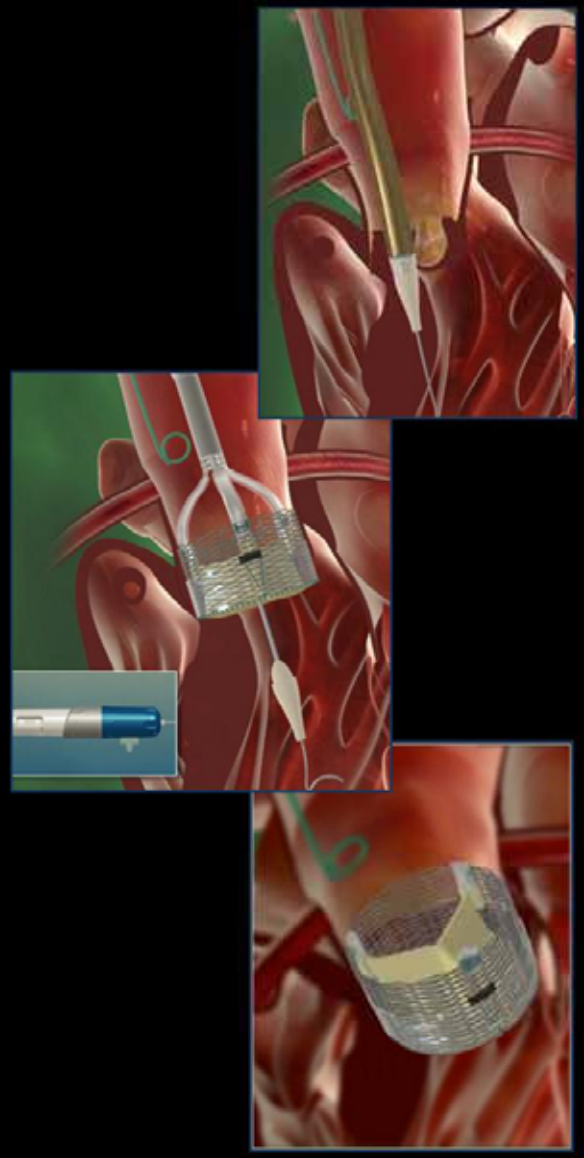
- Nitinol valve frame
- No balloon inflation or rapid pacing of heart for insertion
- Introducer sheath same outer diameter as commercially available 18F sheaths

Device Positioning:

- Self-centering
- Controlled positioning for accurate placement
- Fully retrievable (before release)
- Valve begins functioning early in deployment process

Device Implant:

- Bovine pericardium tri-leaflet aortic valve
- Adaptive™ Seal conforms to irregular surfaces of native anatomy to minimize perivalvular leaks

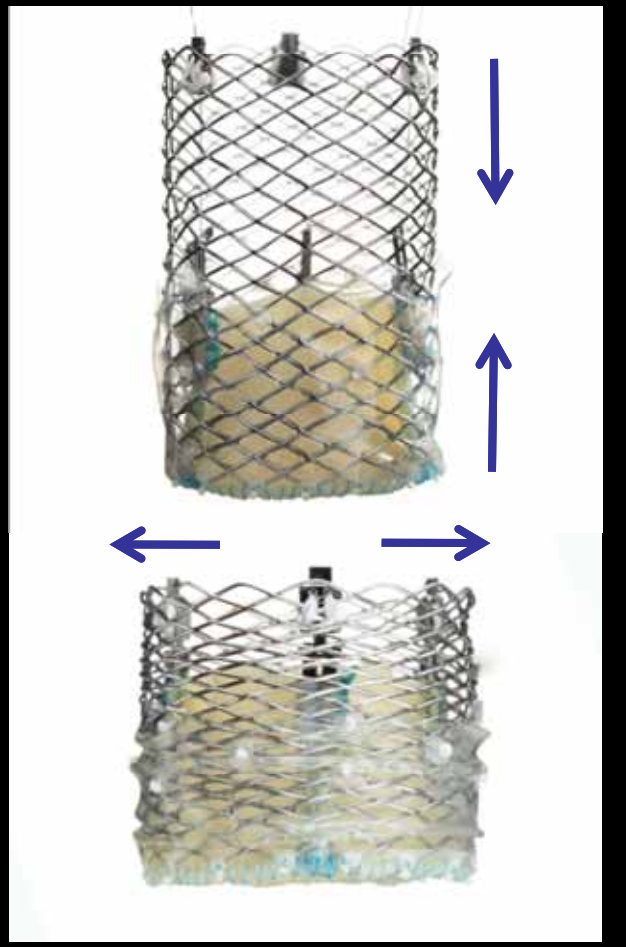


The Lotus Valve System is an investigational device, not available for sale.

See Glossary

Sadra Lotus™ Valve Concept

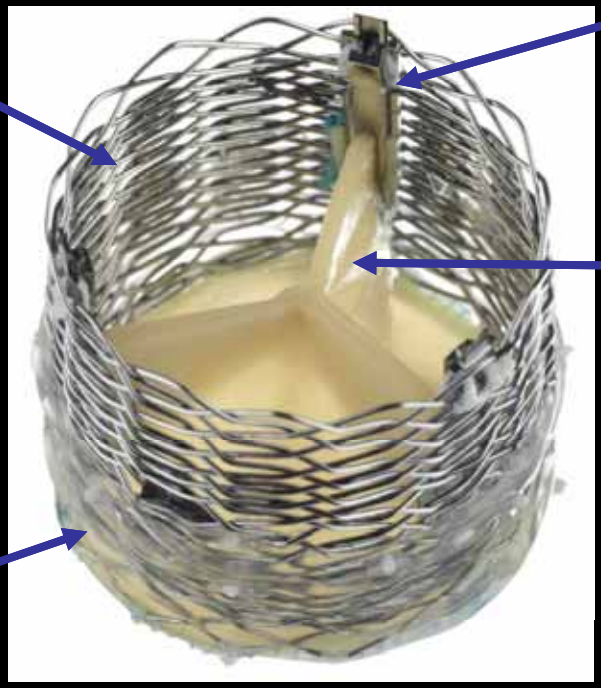
- Braided nitinol stent structure
- Radial expansion as it shortens
  - Enables a more flexible delivery system
  - Enables device repositioning or retrieval
  - Provides significant radial strength



The Lotus™ Valve System

Components and Function

Nitinol Frame
designed for retrieval and repositioning



Locking Mechanism

Bovine Pericardium
Long-Term Proven material

Adaptive Seal
Designed to conform to irregular anatomical surfaces, and to minimize perivalvular leaks

REPRISE Clinical Program

REPRISE I Feasibility	Objectives	To assess the acute safety and performance of the Lotus™ Valve System for transcatheter aortic valve replacement (TAVR) in symptomatic patients with calcified stenotic aortic valves who are considered high risk for surgical valve replacement.
	Primary Endpoint	Clinical procedural success: Device Success without in-hospital MACCE thru discharge or 7d post-procedure
	Valve size	23 mm
	[illegible]nts in Australia	

Principal Investigator: Prof. Ian Meredith

- Prof. Ian Meredith, Monash Heart Center
- Prof. Rob Whitbourn, St. Vincent Hospital
- Prof. Stephen Worthley, Royal Adelaide Hospital

The Lotus Valve System is an investigational device, not available for sale. See glossary.

REPRISE Clinical Program

REPRISE II
CE Mark

Objectives	To evaluate the safety and performance of the Lotus™ Valve System for transcatheter aortic valve replacement (TAVR) in symptomatic subjects with severe calcific aortic stenosis who are considered high risk for surgical valve replacement.
Primary Endpoint	Device Performance Endpoint: Mean aortic valve pressure gradient at 30d Safety Endpoint: All-cause mortality at 30d
Valve size	23 and 27 mm
N	120 patients in Australia, France, Germany, UK

Principal Investigator: Prof. Ian Meredith

- Prof. Ian Meredith, Monash Heart Center
- Prof. Rob Whitbourn, St. Vincent Hospital
- Prof. Stephen Worthley, Royal Adelaide Hospital

- Prof. Thierry Lefevre, Institut Jacques Cartier
- Dr. Didier Tchetche, Clinique Pasteur
- Prof. Gilles Rioufol, Univ. De Lyon
- Prof. Didier Carrie, CHU de Rangeuil

- Dr. Simon Redwood, St. Thomas Hospital
- Dr. Ganesh Manoharan, Royal Victoria, Belfast
- Dr. Daniel Blackman, Spire Leeds Hospital
- Dr. David Hildick-Smith, Royal Sussex

- Prof. Peter Boekstegers, Helios Klinikum, Siegburg
- Prof. Rudiger Lange, German Heart Center, Munich
- Prof. Friedrich Mohr, Herzzentrum, Leipzig

The Lotus Valve System is an investigational device, not available for sale. See glossary.

Primary Endpoint- Discharge/7 Days

REPRISE I (N=11)

Measure	Patients
Clinical Procedural Success (per patient)	9/11
Device Success	10/11
Successful access, delivery, deployment, valve positioning, delivery system retrieval	11/11
Intended valve performance[a]	10/11
One valve implanted	11/11
No MACCE through discharge or 7 days[b]	10/11

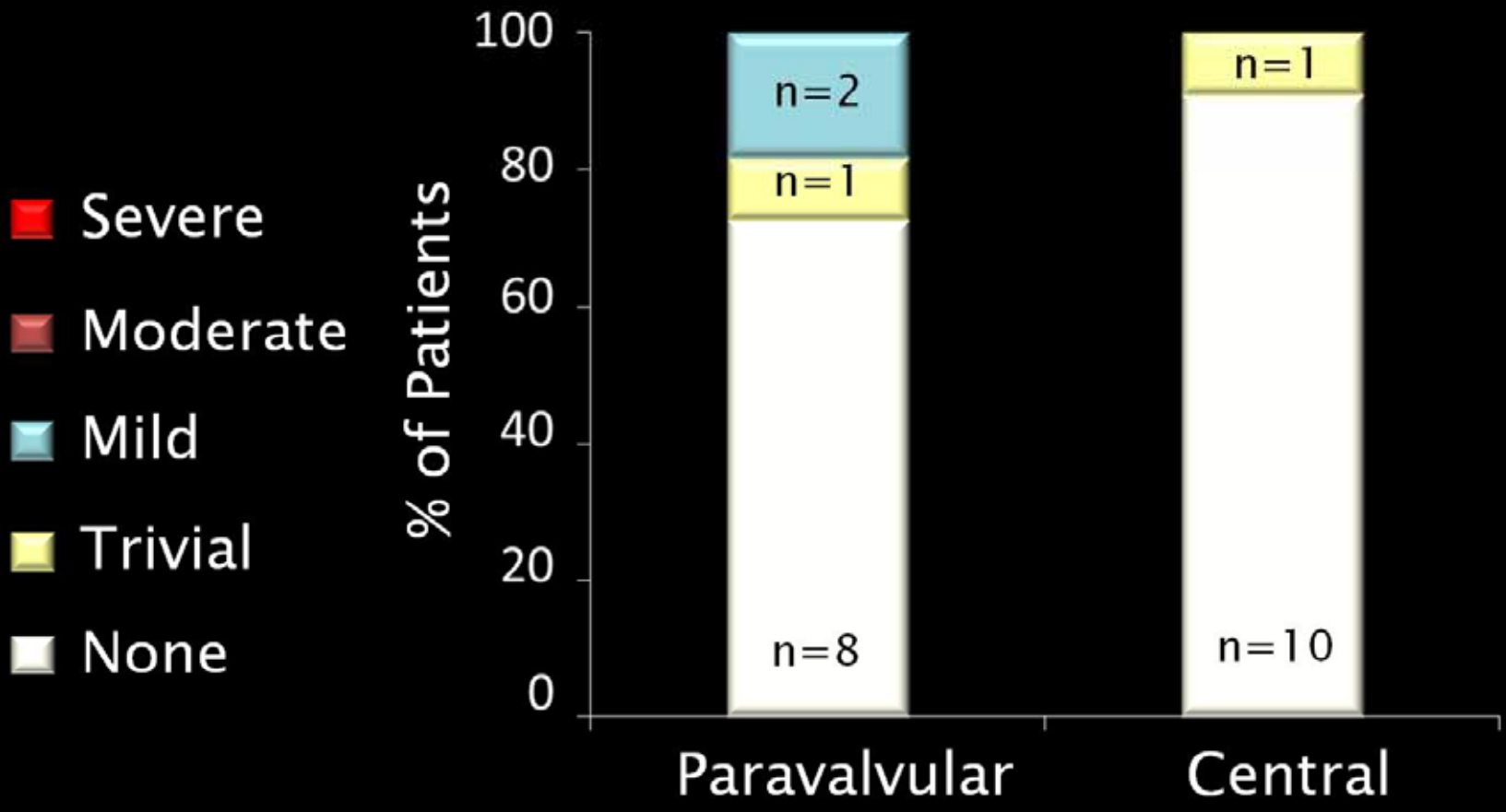
Presented by Ian Meredith, MBBS. PhD. at EuroPCR 2012

a: AVA >1.0 cm^2 plus either a mean aortic valve gradient <20 mmHg or peak velocity <3m/sec, without moderate/ severe prosthetic valve aortic regurgitation

b: Major adverse cardiovascular or cerebrovascular events including all-cause mortality, peri-procedural MI ≤72 hours, major stroke, urgent/emergent conversion to surgery or repeat procedure for valve-related dysfunction

Values are n/N

Aortic Regurgitation
Discharge Transthoracic Echocardiography

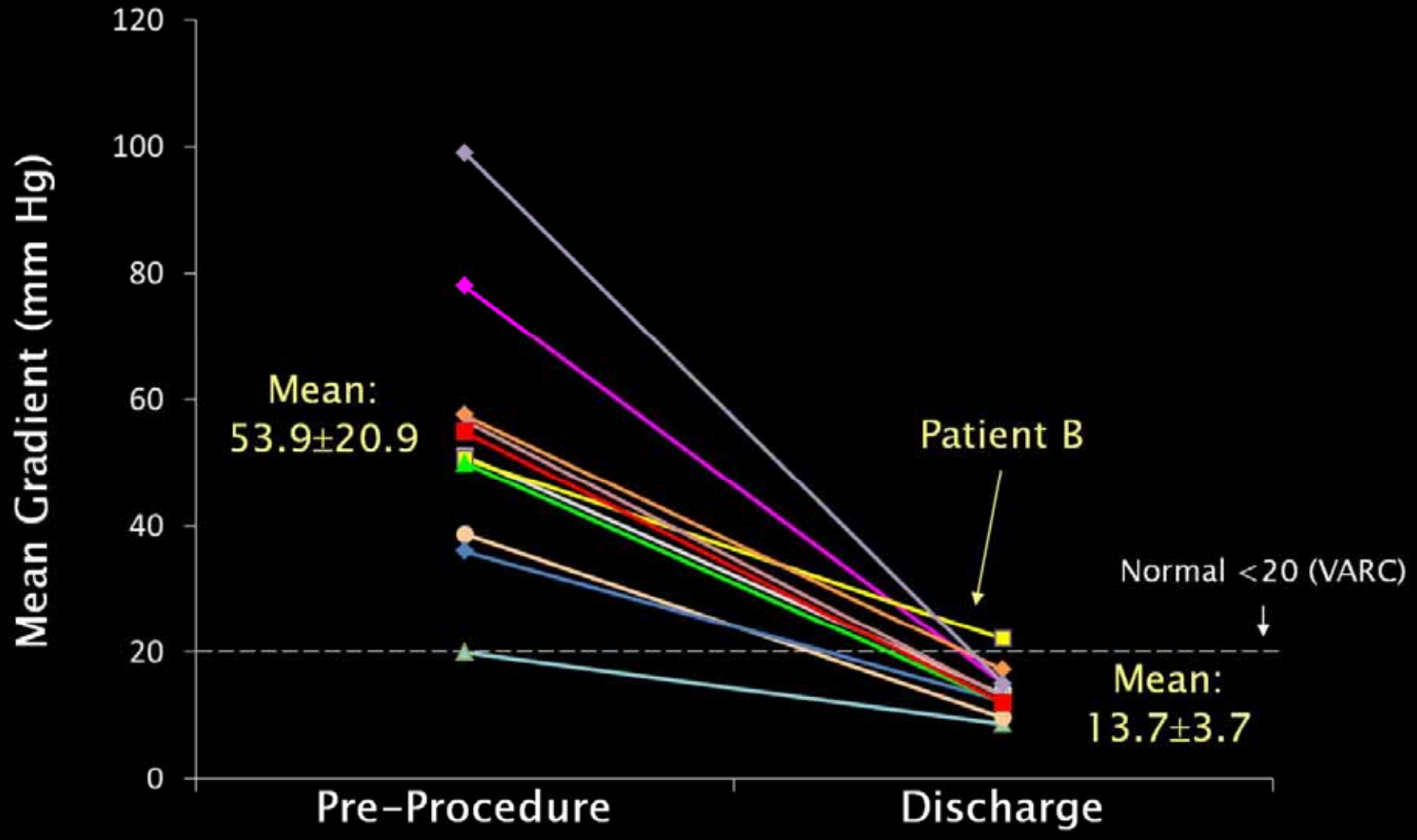


No Moderate / Severe AR by Independent Adjudication

N = 11
Presented by Ian Meredith, MBBS. PhD. at EuroPCR 2012

Mean Aortic Gradient by Patient

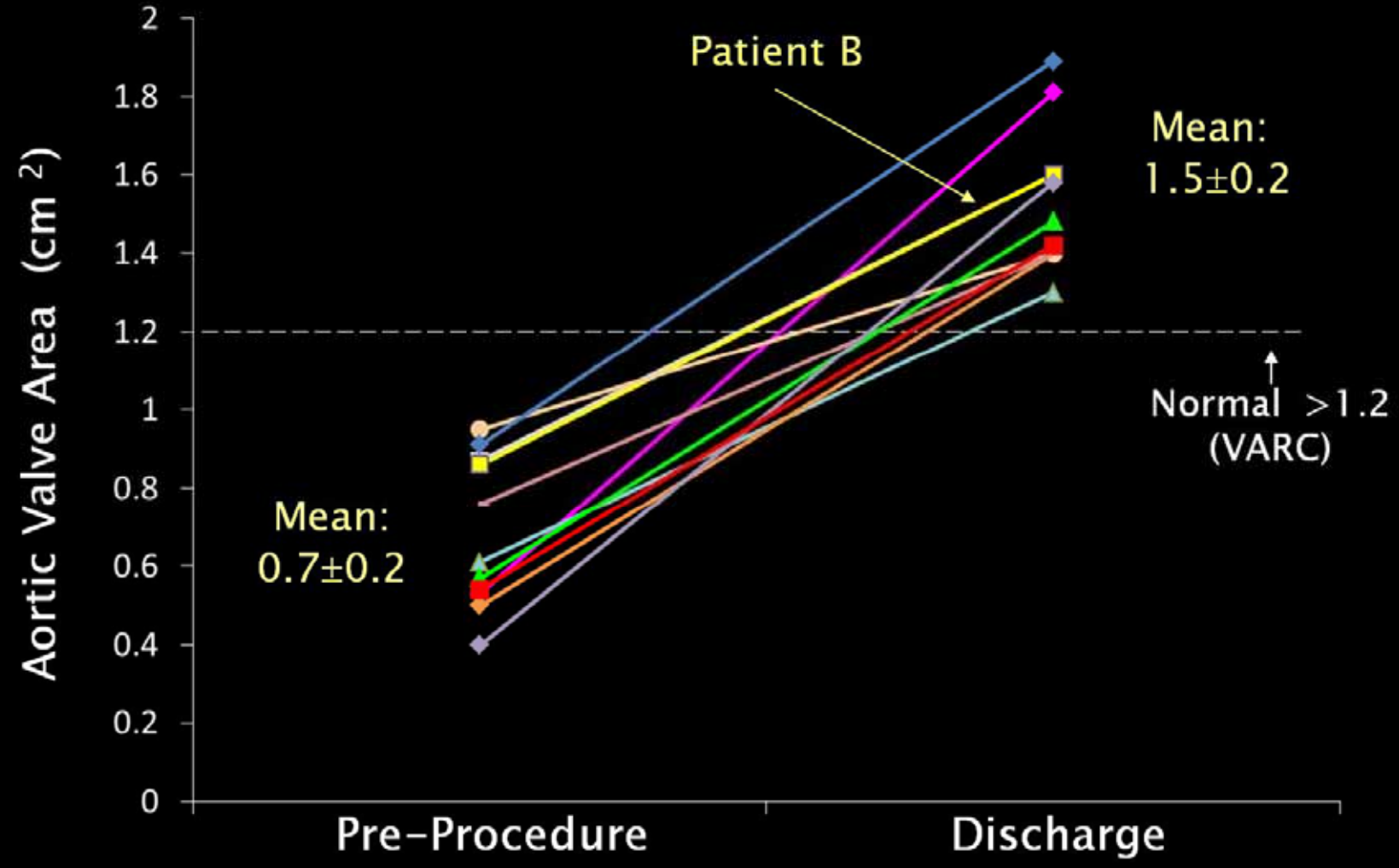
REPRISE I (N=11)



Presented by Ian Meredith, MBBS. PhD. at EuroPCR 2012
VARC=Valve Academic Research Consortium; *J Am Coll Cardiol* 2011, 57:253

Aortic Valve Area by Patient

REPRISE I (N=11)



Presented by Ian Meredith, MBBS. PhD. at EuroPCR 2012
VARC=Valve Academic Research Consortium; *J Am Coll Cardiol* 2011, 57:253
"Discharge" is defined as discharge or 7 days post-procedure, whichever comes first

MACCE

REPRISE I- Discharge/7 Days (N=11)

Characteristic	Patients
In-hospital MACCE	1/11
All cause mortality	0/11
Peri-procedural MI (≤72 hours)	0/11
Major stroke[a]	1/11
Urgent/emergent conversion to surgery or repeat procedure for valve-related dysfunction	0/11

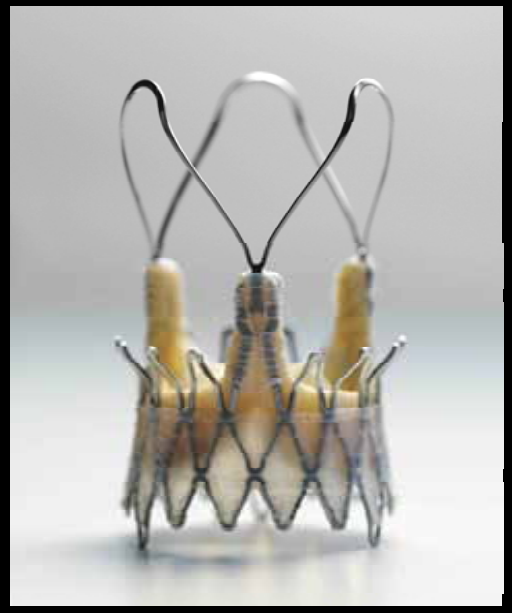
Presented by Ian Meredith, MBBS. PhD. at EuroPCR 2012

a: Preliminary adjudication is major stroke; final adjudication per VARC will occur at 90 days

"Discharge" is defined as discharge or 7 days post-procedure, whichever comes first. MACCE=major adverse cardiovascular and cerebrovascular events; MI=myocardial infarction

Symetis ACURATE TF™ and TA™ Bioprosthesis

- Porcine pericardium
- Self-expanding nitinol stent
- Stent covered inside and out with double porcine pericardium skirt



ACURATE™ Highlights

- Trans Apical:
  - FIM (n=40) 6M results @ EACTS 2011
  - Pilot (n=50) 30D results @ TCT 2011
  - FIM (n=40) 1Y results @ AHA 2011
  - Pivotal (n=150) enrollment start Q4 2011
  - SAVI post-market registry (n=250) with commercial implants
  - Received CE Certification in November 2011 for commercial use
- Trans Femoral:
  - FIM (n=20) enrollment start Q1 2012 (Brazil/Germany/France)
  - Pilot (n=50) enrollment start Q3 2012

ACURATE TF™ 3-Step Implant

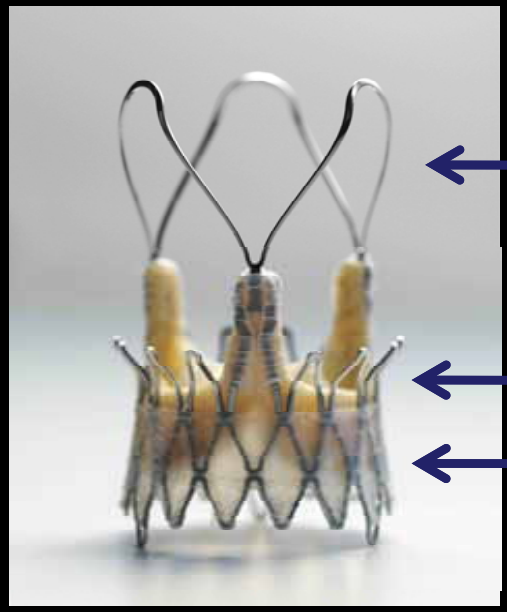
Initial Alignment

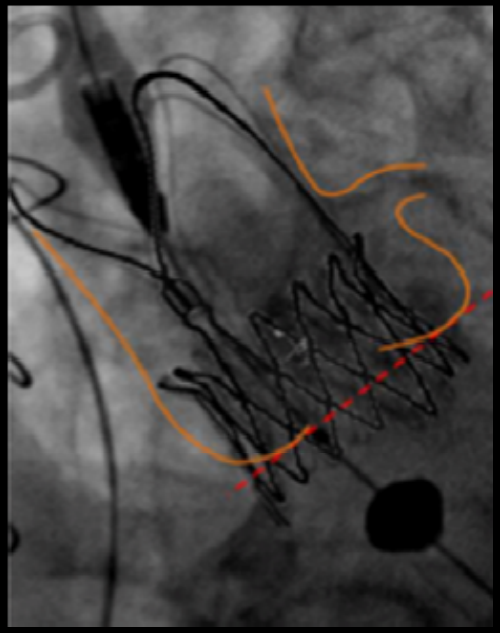
1. Upper Crown & Gentle Push

2. Stabilization Arches

3. Full Release

ACURATE TA™ Bioprosthesis



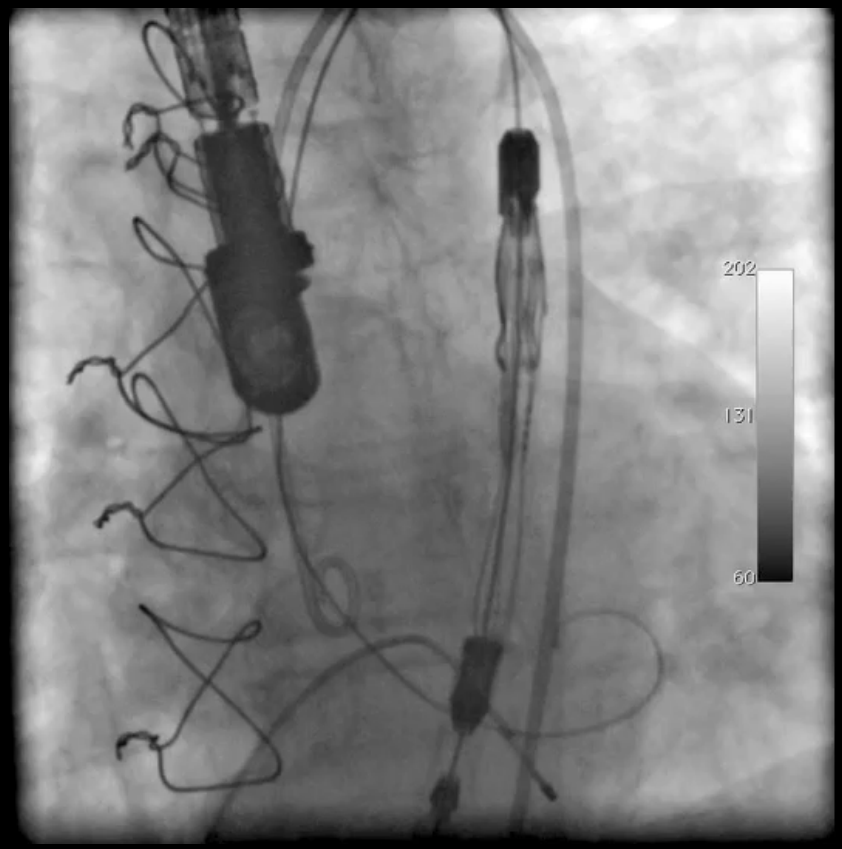


- Treats native annuli from 21mm to 27mm
- Repositionable, self-aligning
- Composed of:
  - Biologic porcine tissue valve for long term durability
  - Self-expandable nitinol stent = form fit
  - PET skirt for ↓ PV leak

First Human Use (FHU)

- 3 patients treated in Sao Paulo by Dr. Alex Abizaid
- Feasibility proven – 3 successful implants
- 3 patients discharged home and well at 5 months
- No reported MACCE to date and follow-up ongoing
- Easy catheter tracking and implantation (tactile feedback)
- No procedure difficulties
- Demonstrates good hemodynamics, low leak
- Green light to start TF FIM!

FHU 001



- Good initial positioning
- Easy upper crown positioning
- Controlled deployment
- Minimal leak
- Low gradient
- First patient, first success

ACURATE TF™ FHU Outcomes

Subject	Assessment	Screening TTE	30D
Patient 001 Male, 78 y/0 STS Score: <6 NYHA Class III AAn: 24.0 cm^2	Mean Gradient	57 mmHg	7.8 mmHg
	AVA/EOA	0.7 cm^2	1.9 cm^2
	Peak jet	4.9 m/s	2.1 m/s
	PVL / IVL	n/a	+1 / 0
Patient 002 Female, 72 y/0 STS Score: <6 NYHA Class III AAn: 22.5 cm^2	Mean Gradient	48 mmHg	11.1 mmHg
	AVA/EOA	0.8 cm^2	1.8 cm^2
	Peak jet	4.3 m/s	2.2 m/s
	PVL / IVL	n/a	0 / 0
Patient 003 Female, 92 y/o STS Score: ≥6 NYHA Class III AAn: 22.4 cm^2	Mean Gradient	65 mmHg	9.6 mmHg
	AVA/EOA	0.4 cm^2	1.9 cm^2
	Peak jet	5.2 m/s	2.4 m/s
	PVL / IVL	n/a	+1 / 0

TF FIM Design

Design	Prospective, multicenter, non-randomized, open
Purpose	Feasibility
Enrollment Number	20 patients
Follow-up Visits	Post-procedure, 7 & 30D and 12M
TeleCheck	6M and 2, 3, 4 & 5Y
Clinical Sites	(1) BR, (3) DE, (1) FR
Study Start	FPI in MAY 2012
Primary Endpoint	ACM @ 30D
Secondary Endpoints	1. MACCE @ 30D and 12M 2. NYHA Class @ 30D and 12M 3. Procedural success post-implant 4. Device success @ 30D and 12M

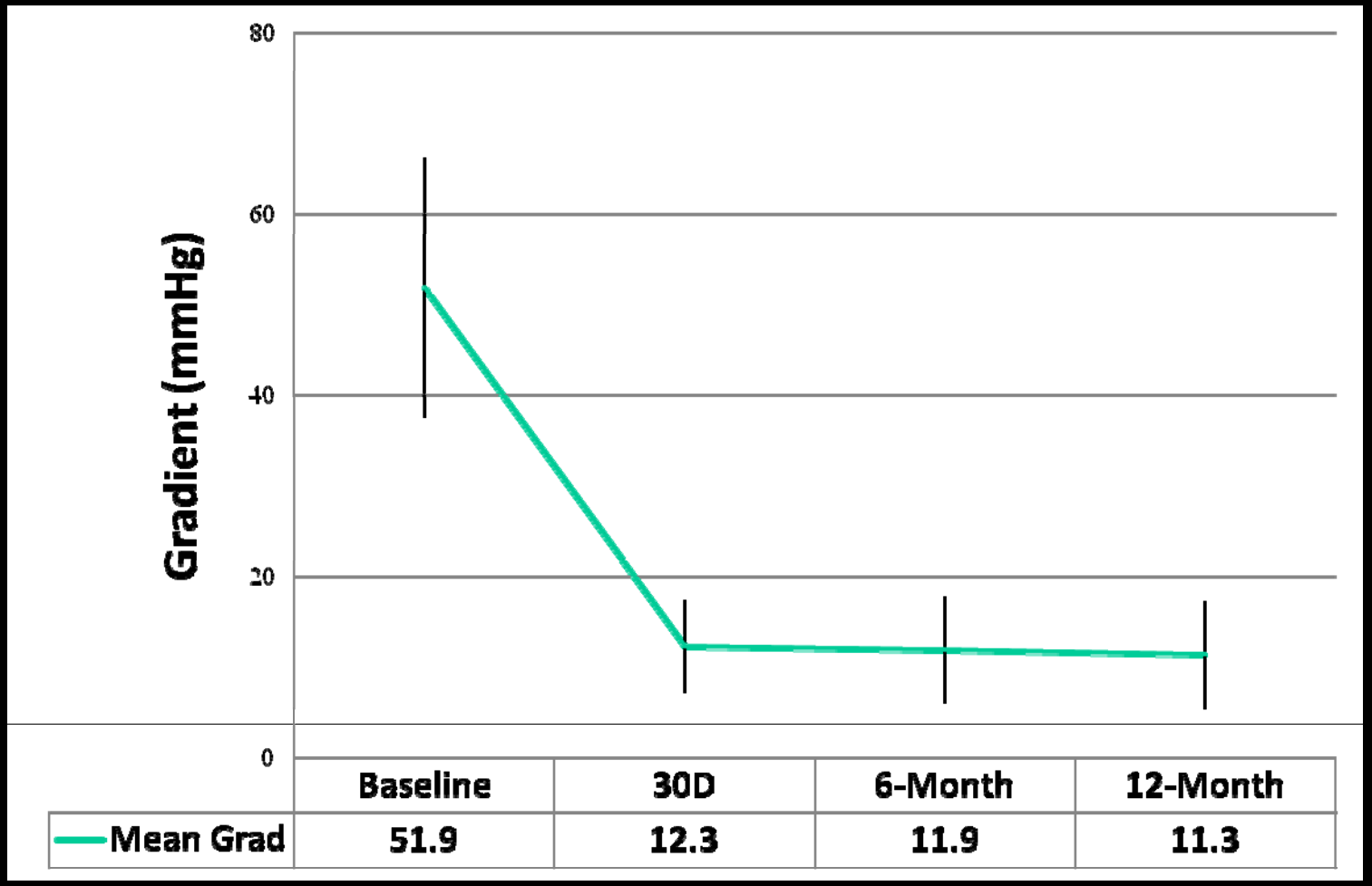
TF FIM Enrollment

SITE	MAY	JUN	Total
Bad Nauheim	2	3	5
Hamburg	1	4	5
Bonn	3	3	5
Sao Paulo	3	2	5
TOTAL	9	10	20

ACURATE TF™ Take Away

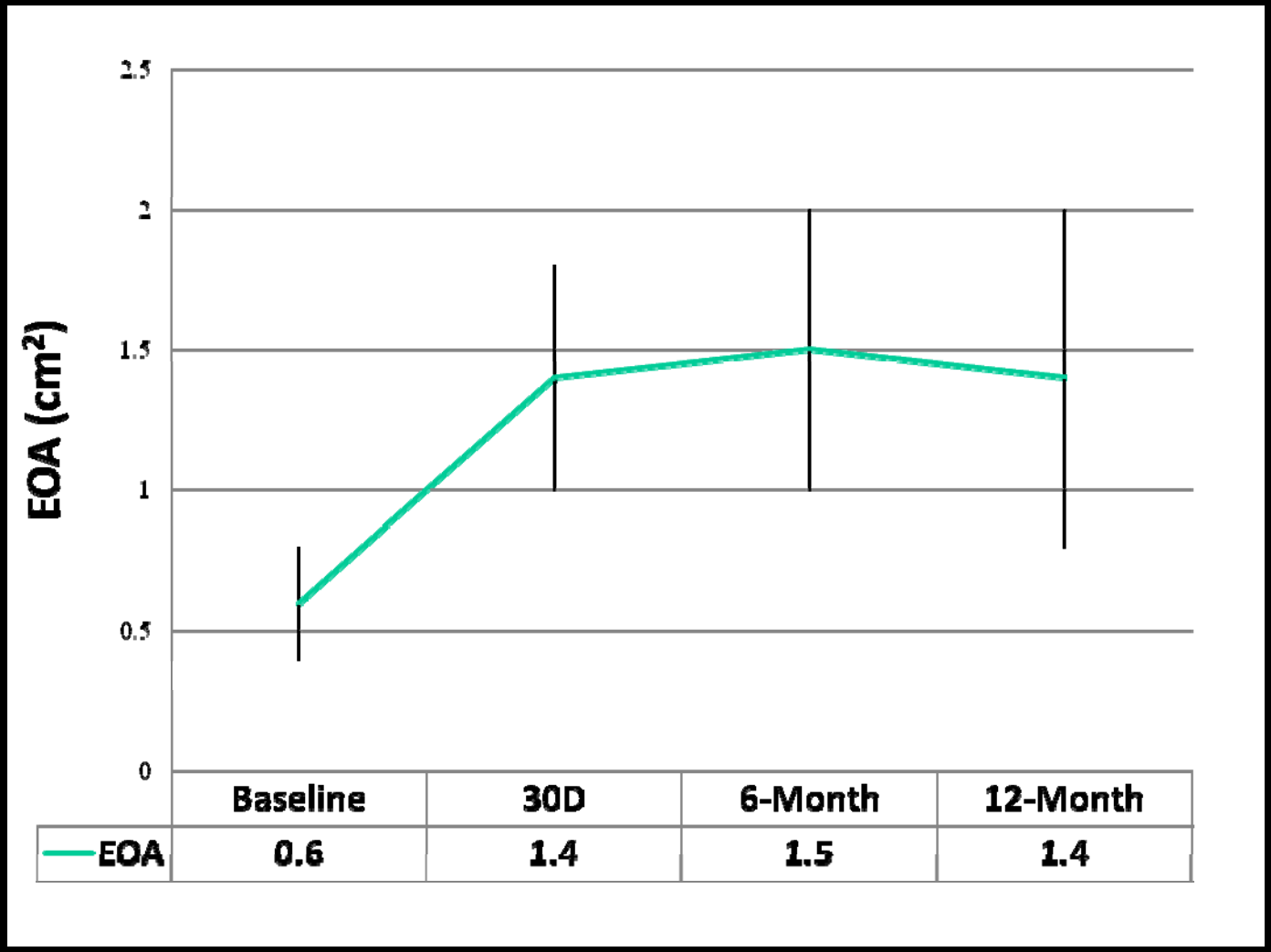
- Successful FHU in Brazil (n=3)
- Currently enrolling in TF FIM trial (n=20)
- 9 patients implanted in Brazil and Germany to date
- TF Pilot (n=50) in Q4
- TF FIM + TF Pilot = TF 70
- TF 70 = CE Mark in 2013

FIM Gradient

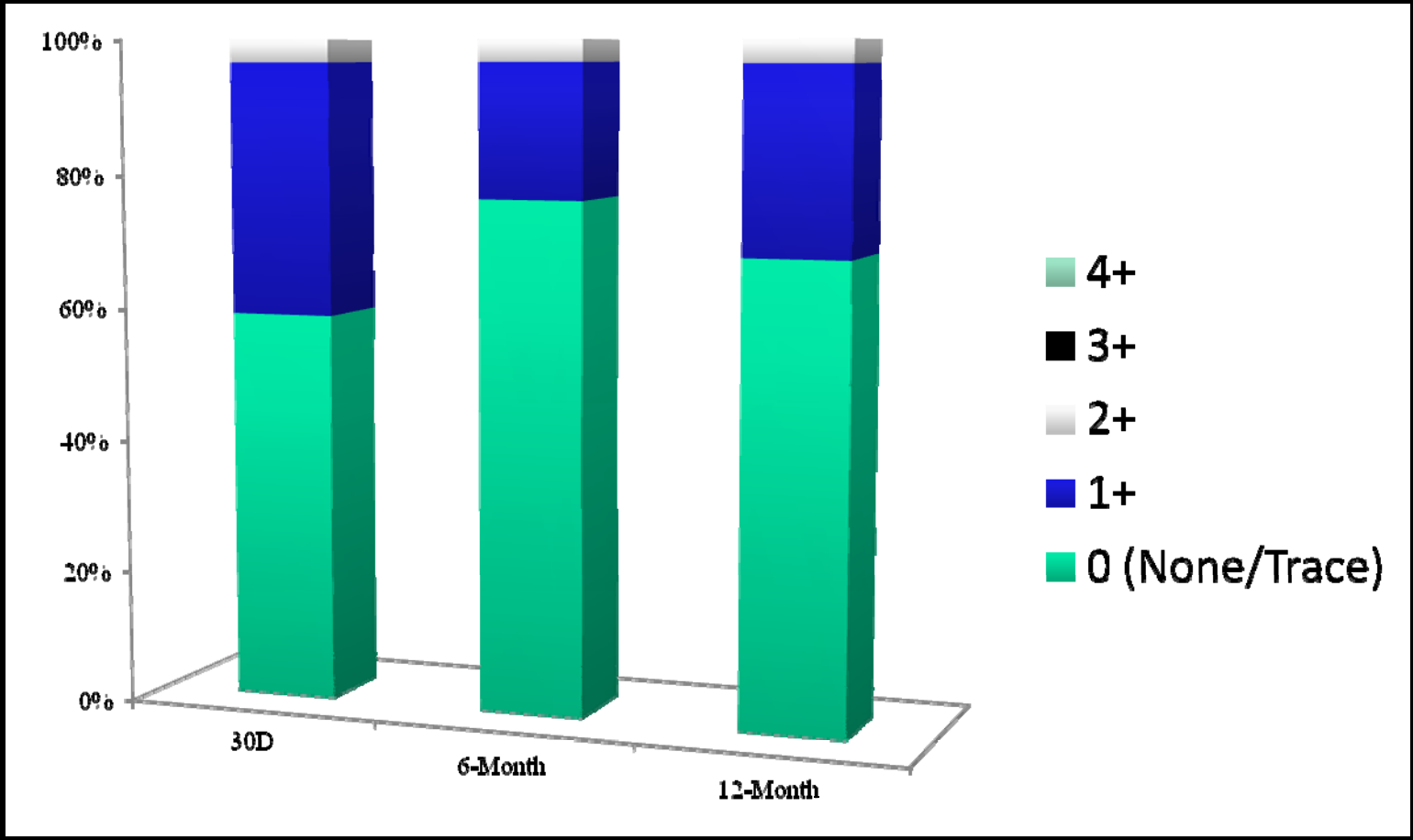


	Baseline	30D	6-Month	12-Month
Mean Grad	51.9	12.3	11.9	11.3

FIM EOA

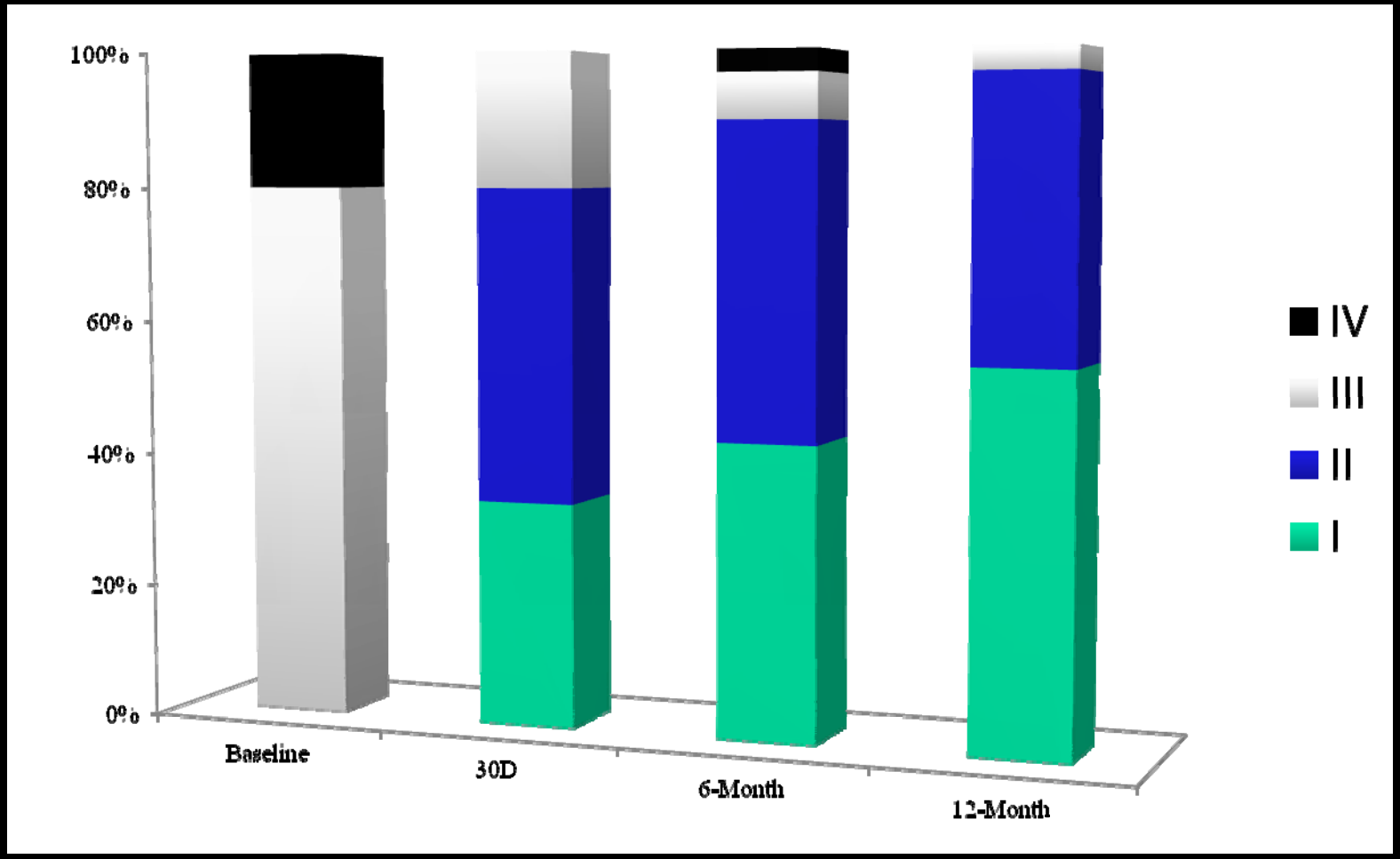

EOA (cm²)
2.5
2
1.5
1
0.5
0
Baseline
30D
6-Month
12-Month
EOA
0.6
1.4
1.5
1.4

FIM PV Leak



12M FU: 96.7% of patients = ≤ +1 PVL
Only 1 patient ≥ +2 PVL

FIM NYHA



12M FU: 90% of patients with improvement from baseline

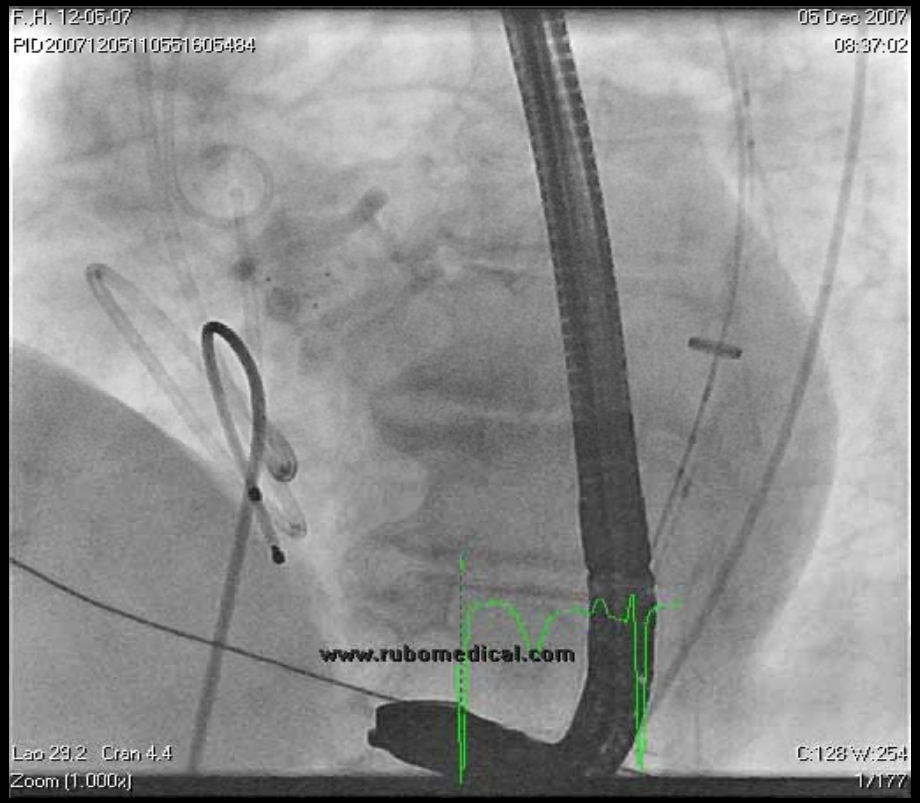
Direct Flow Medical

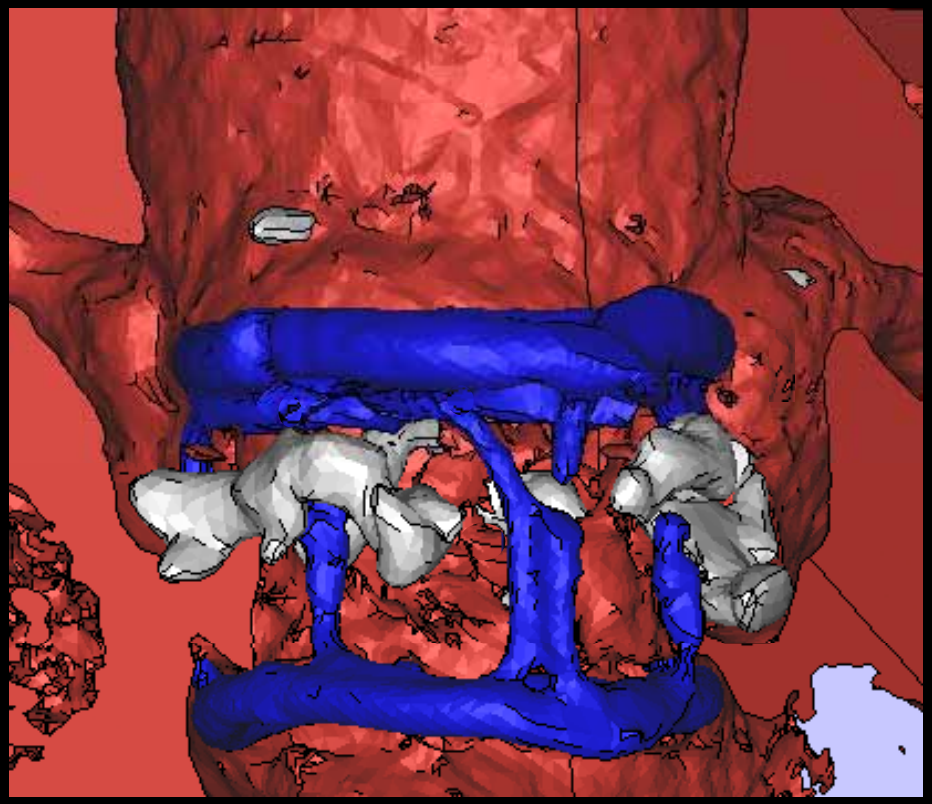
2 sizes matching
valvuloplasty balloons

22F Design

18F Design

DFM Aortic Valve
Aortic Insufficiency – PV Leaks



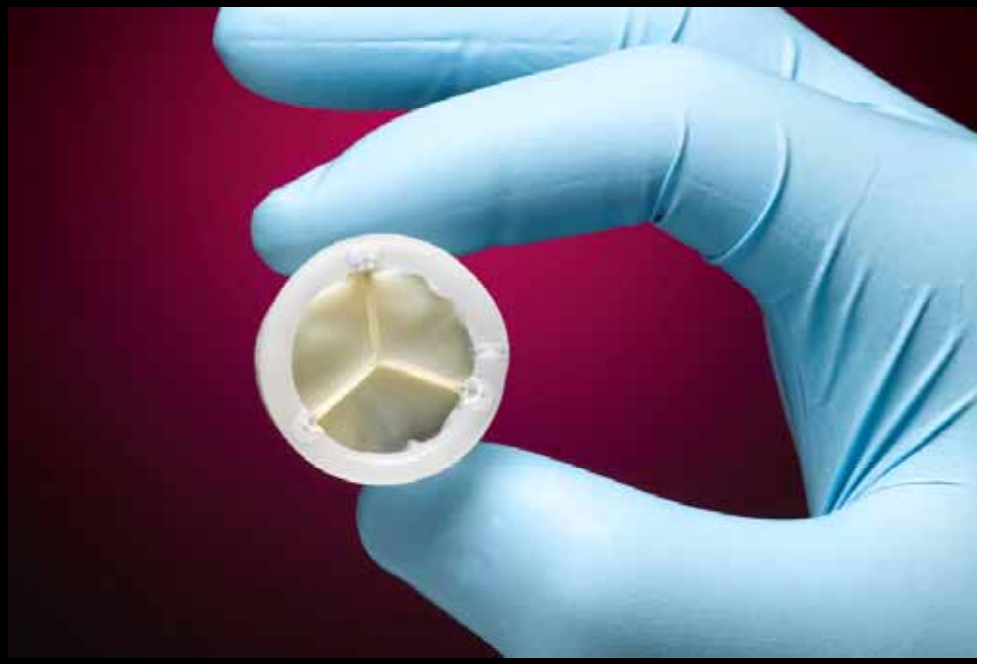


Conformable cuff design and precise positioning maximizes sealing to prevent PV leaks

Direct Flow Valve

Designed for Patient Safety

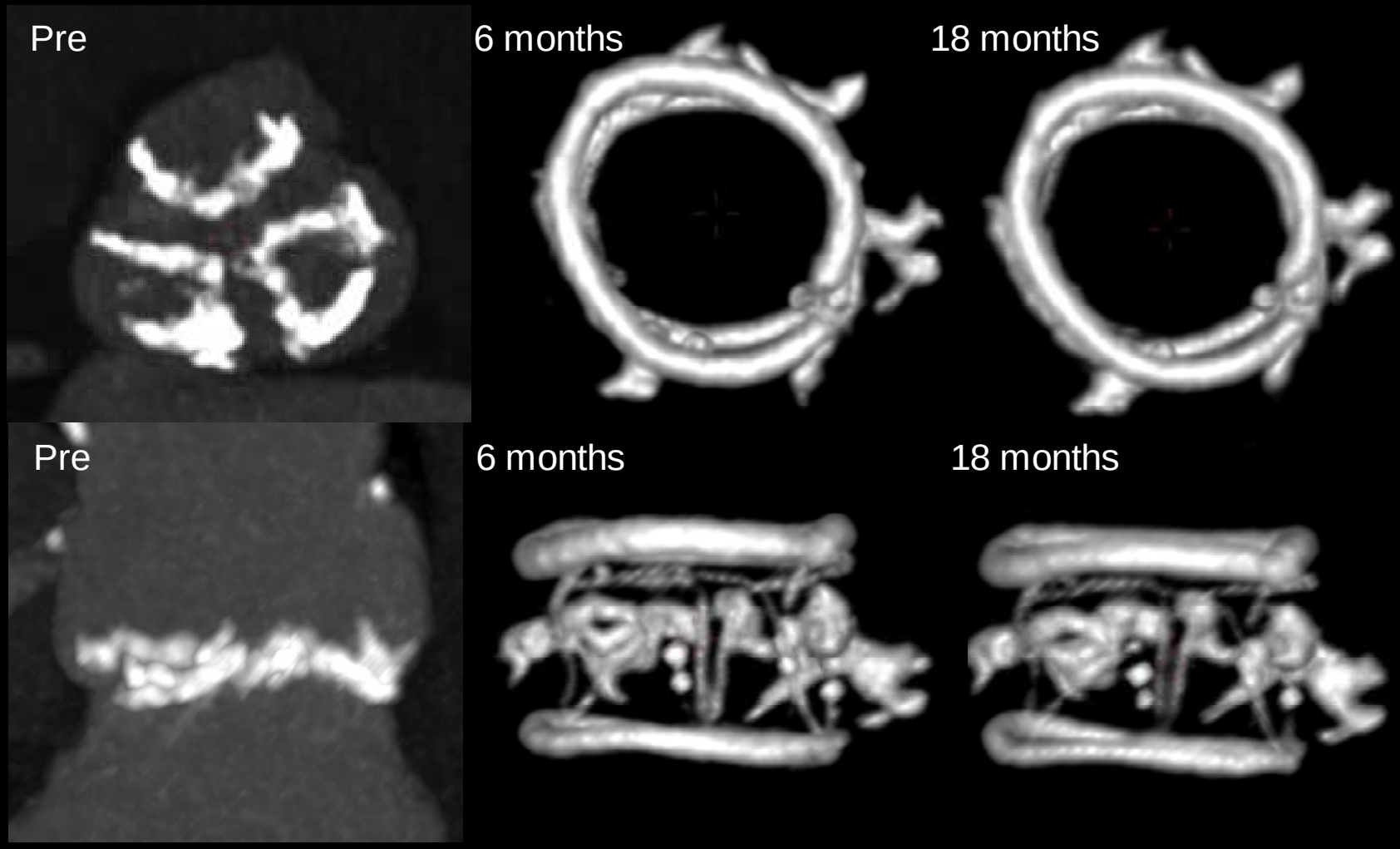
- "Surgical" valve design
- Repositionable & Removable
- Minimizes PV Leaks and AI
- Deliverability/Profile
- Immediately competent
- Durability



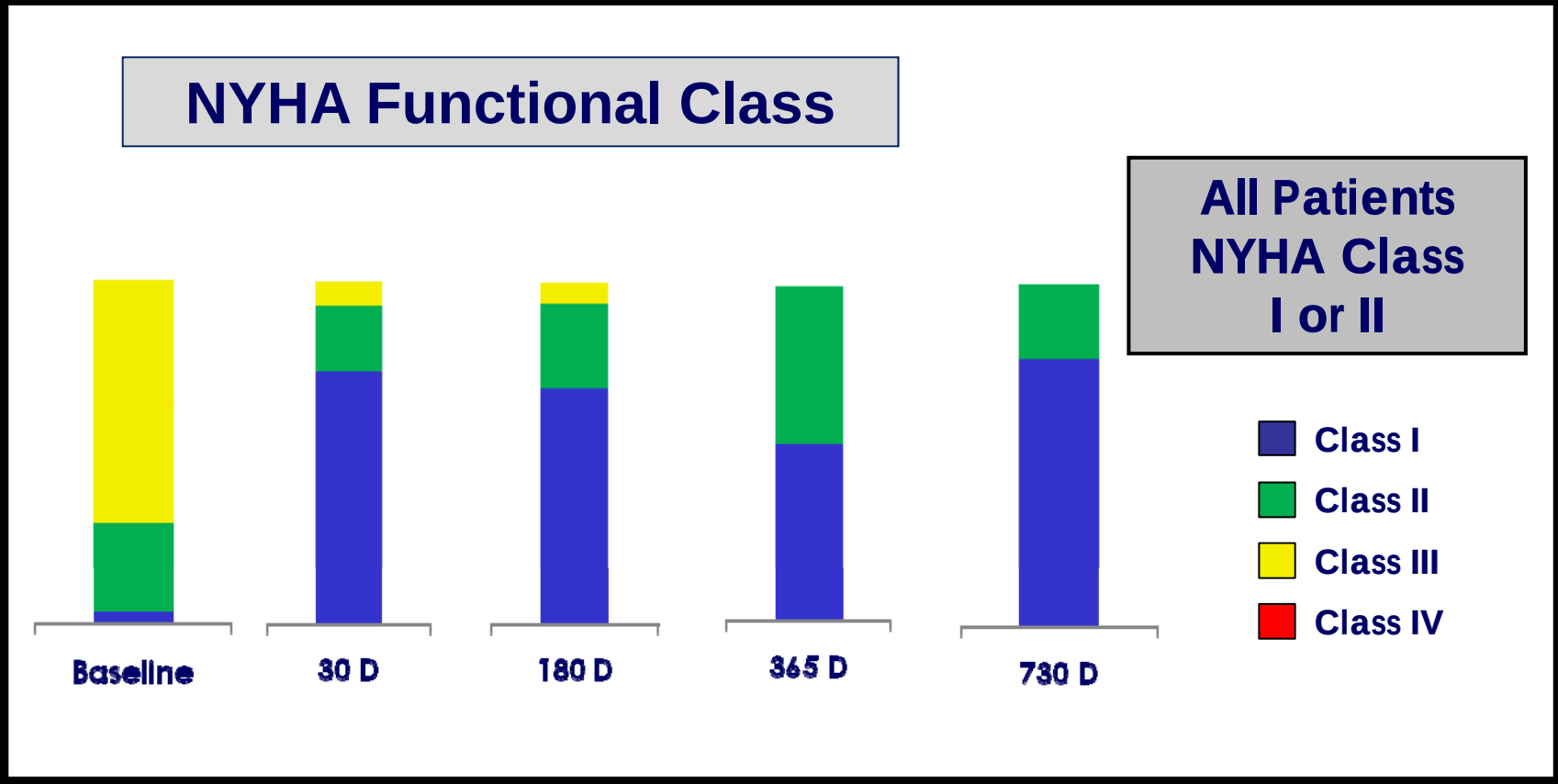
Unique design allows assessment of patient outcomes prior to final device deployment

2 Year Imaging Follow Up

Bijuklic et al, Circulation Cardiovasc Interv, Nov 2011



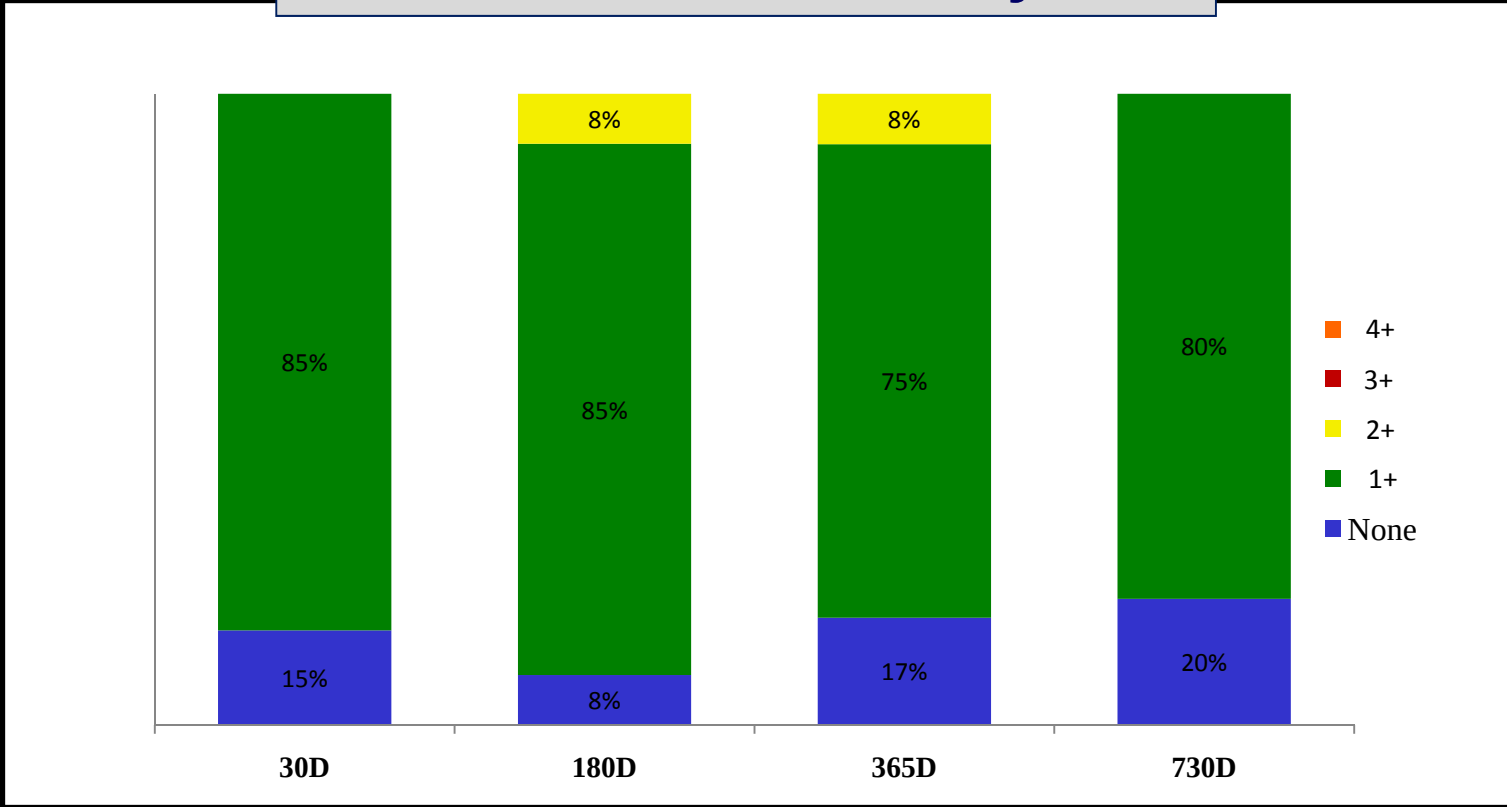
2 Year Data *(EU Feasibility Trial)*



Investigational device not for sale in or outside the United States

2 Year Data *(EU Feasibility Trial)*

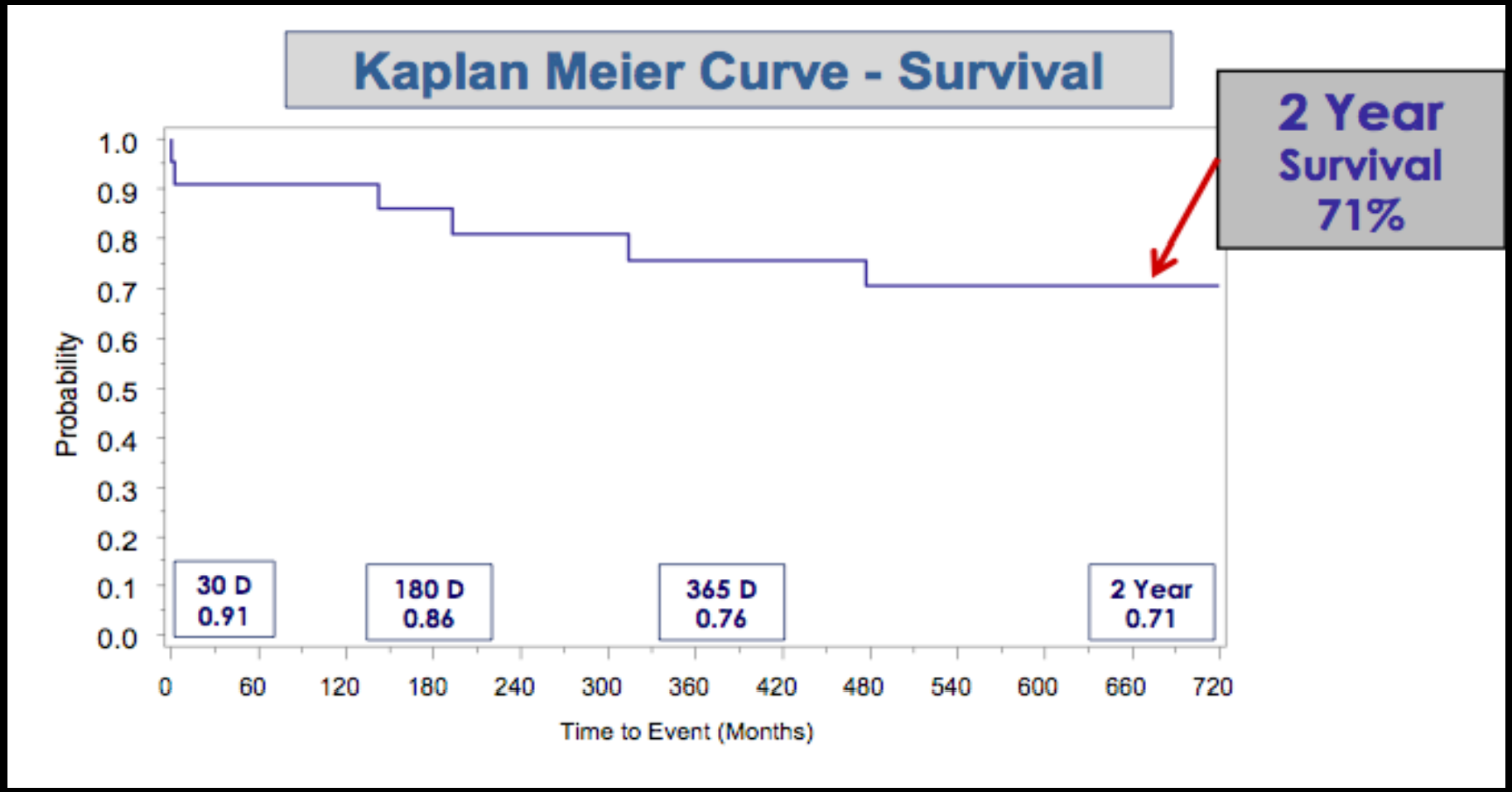
Aortic Insufficiency



* As measured by TTE

Investigational device not for sale in or outside the United States

2 Year Data *(EU Feasibility Trial)*



Investigational device not for sale in or outside the United States

St Jude Medical
(Portico Transcatheter Heart Valve)

St. Jude Medical TAVI System:
Next Generation Design Features

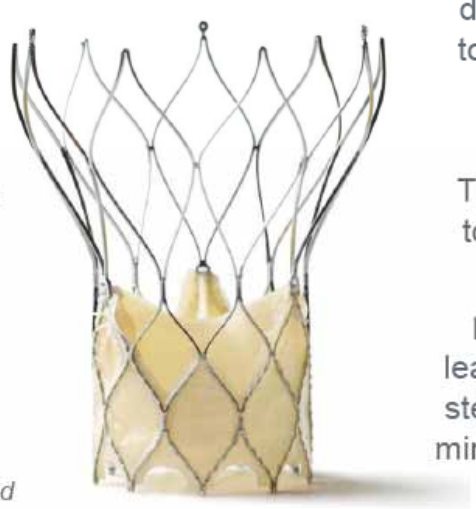
Unique self expanding stent design provides the ability to…

- Re-sheath*
- Reposition
- Retrieve*

… the valve at implant site

Bovine and porcine pericardial valve with Anti-calcification technology **

*Anti-calcification technology is used on SJM Epic™ and Trifecta™*** surgical aortic valves*



Open stent cell design allows access to coronaries and low crimp profile

Tissue cuff designed to minimize PV leak

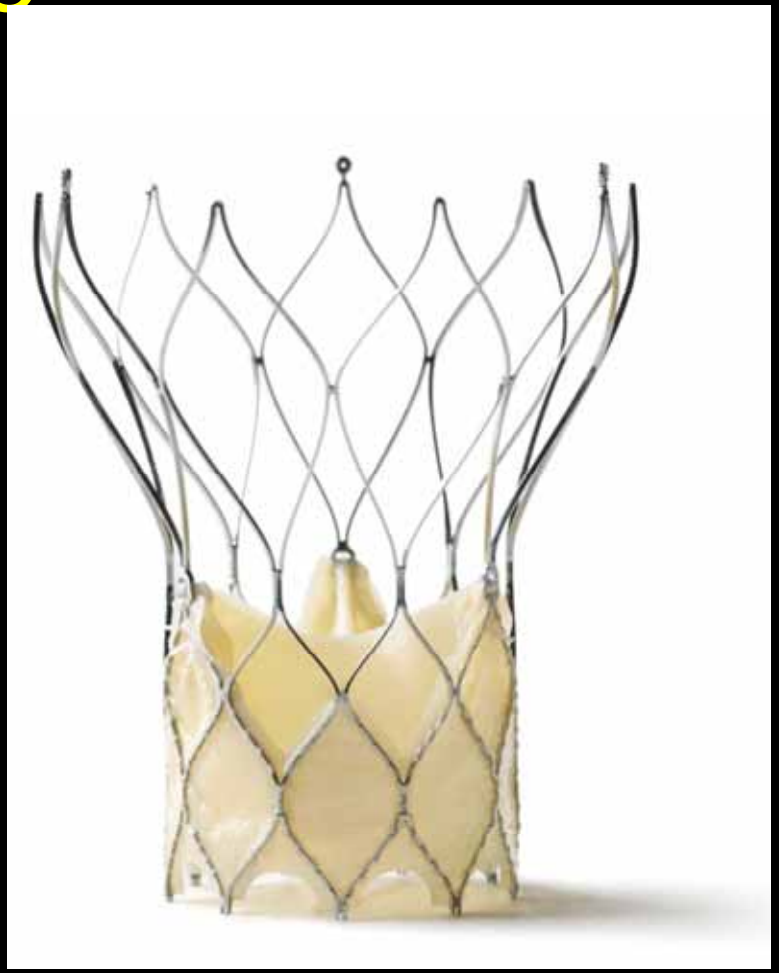
Low placement of leaflets/cuff within the stent frame allows for minimal protrusion into the LVOT

* Until fully deployed
** There is no clinical data currently available that evaluates the long-term impact of anticalcification tissue treatment in humans.
*** Trifecta is an investigational device in the US and is not commercially available.

First Human Implant June 7th, 2011

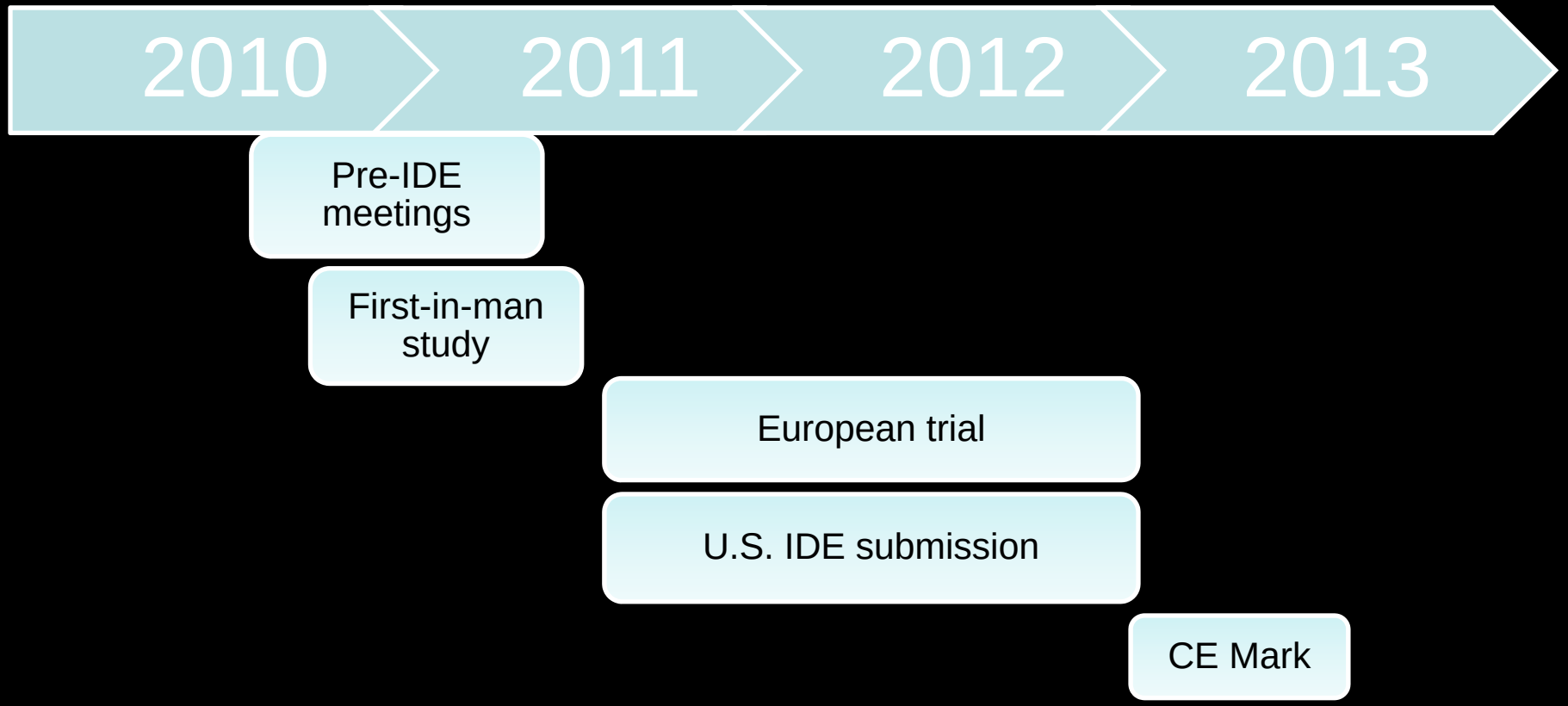
St. Jude Medical TAVI System:
Next Generation Design Features

- Nitinol self expanding stent
- Open stent cell allows access to coronaries and low crimp profile
- Bovine and porcine pericardial valve (Linx™ anticalcification technology*)
- Low placement of leaflets/cuff within stent frame allows for minimal protrusion into the LVOT



*There is no clinical data currently available that evaluates the long-term impact of anticalcification tissue treatment in humans.

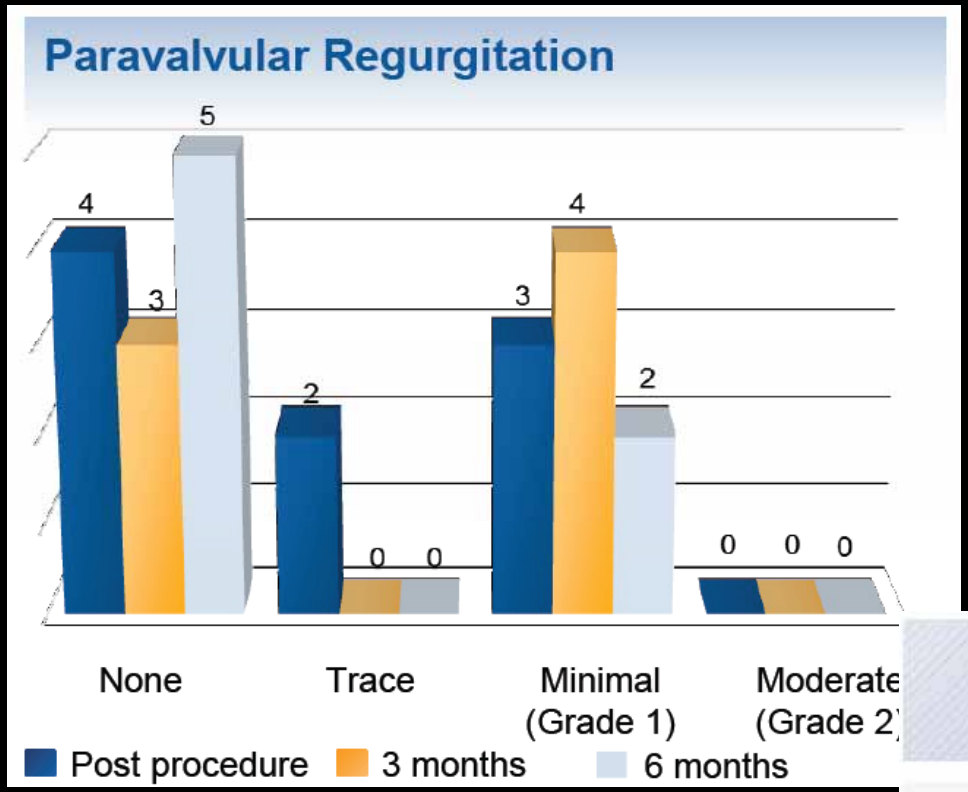
St Jude Medical TAVI System
Program Status



Jena Valve

- Self-expanding nitinol stent with flexible stent posts
- Porcine root valve
- Sizes 23,25,27
- 32F introducer sheath for transapical access

Jena Valve FIM Trial



30 d safety outcomes	FIM pts (N=10)
All cause death (30 d) cardiac death	0 0
Stroke	0
Myocardial infarction	0
Emergent cardiac surgery	1
Onset of AV block	0

Heart Leaflet Technology