

New transfemoral TAVI Devices

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Eberhard Grube, MD

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
Boston Scientific: C, SB, AB
Biosensors: E, SB, C, AB
Cordis: AB
Abbott Vascular: AB
Capella: SB, C, AB
Valtech: E, SB,
Claret: SB

Key

G - Grant and or Research Support E - Equity Interests S - Salary, AB - Advisory Board
C - Consulting fees, Honoraria R - Royalty Income I - Intellectual Property Rights
SB - Speaker's Bureau O - Ownership OF - Other Financial Benefits'

Background

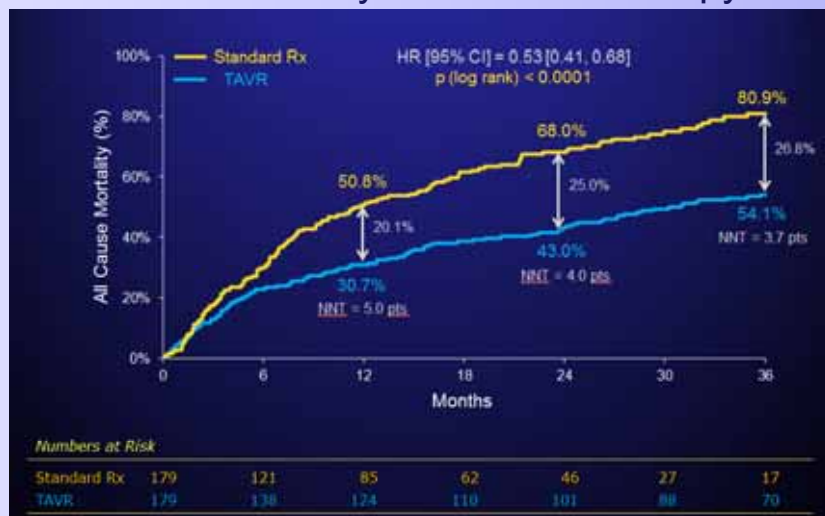
Transcatheter Aortic Valve Implantation / Replacement (TAVI/R)

Epidemiological data suggest

- ~2-5% of adults >65 years old have severe aortic valve stenosis
- ~30% - 40% of patients requiring aortic valve replacement do not undergo surgery:

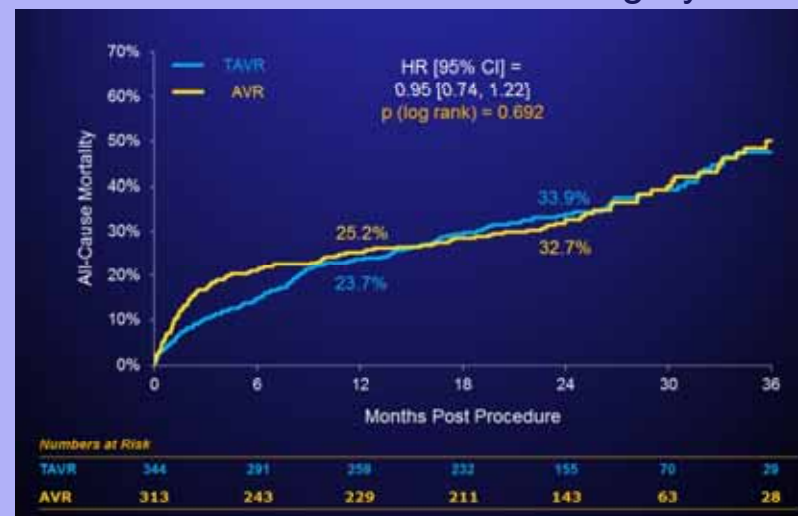
TAVI/R provides an alternative treatment for patients with severe symptomatic aortic stenosis

Lower mortality vs. medical therapy



PARTNER Cohort B Presented by S Kapadia at TCT 2012

Similar survival rate vs. surgery



PARTNER Cohort A Presented by S Kodali at ACC 2012

Limitations with early TAVR devices

Stroke, bleeding & vascular complications

Challenges with device positioning

Paravalvular leakage (associated with increased mortality*)

*Kodali, et al. NEJM 2012;366:1685; Tamburino, et al. Circ 2011;123:299; Abdel-Wahab, et al. Heart 2011;97:899

Building on Success

First generation devices provide significant clinical benefit,
but opportunities for improvement remain



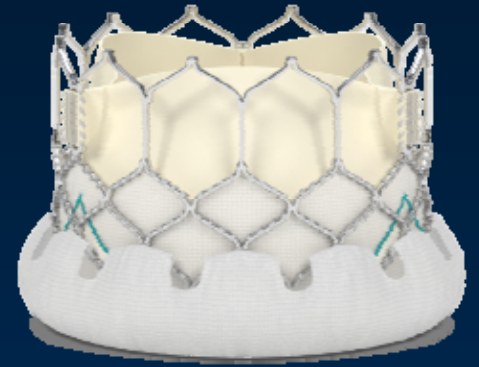
- Controlled deployment
- Simple, precise and atraumatic aortic/ventricular repositioning
- No or trivial paravalvular leakage
- Full atraumatic retrieval
- Decrease complication rate
- Simple preparation and loading of valve

New Generation TAVI Devices:

- Edwards Sapien/Centera Evolution
- Medtronic CoreValve Evolution
- Direct Flow Medical
- St. Jude Portico
- BSC Lotus Valve
- Symetis Acurate Valve
- Valve Medical

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Edwards – SAPIEN Evolution



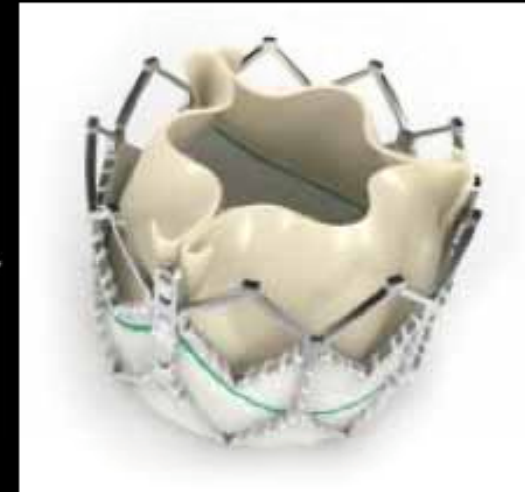
2002

Cribier-Edwards THV



2006

Edwards SAPIEN THV

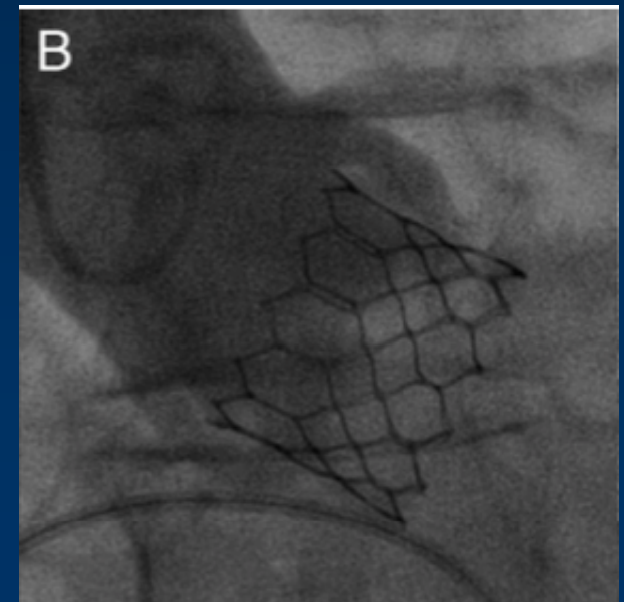
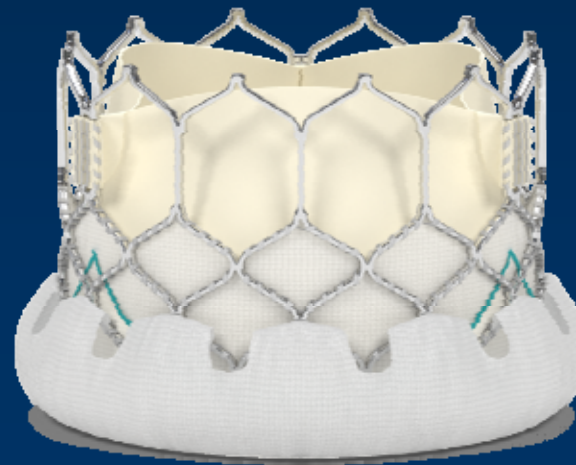


2010

Edwards SAPIEN XT* THV

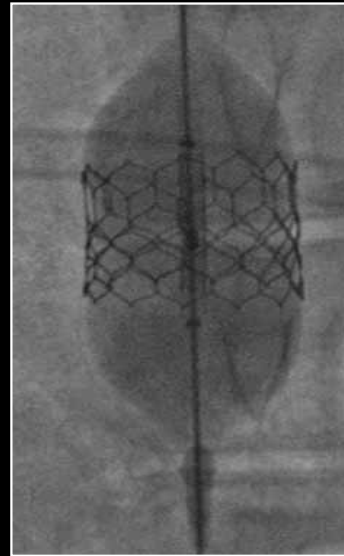


2012
SAPIEN 3



SAPIEN 3

Edwards SAPIEN 3 Valve

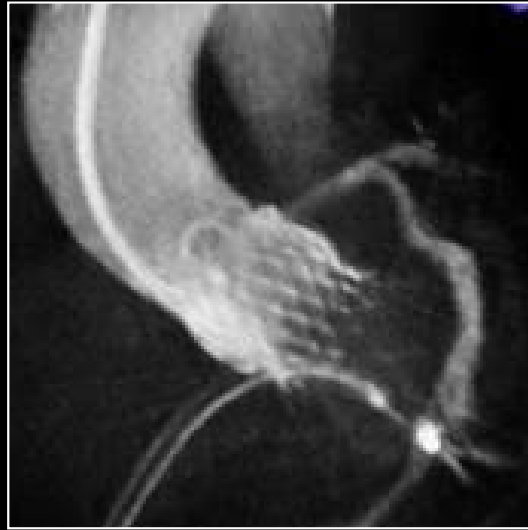


Balloon-expandable

- ✓ Potentially further reduces PV leaks
- ✓ Lower profile valve delivered through a 14 Fr eSheath
- ✓ Treated bovine pericardial tissue

Edwards Centera Valve

Edwards **CENTERA** Valve



Self Expanding

Edwards Centera

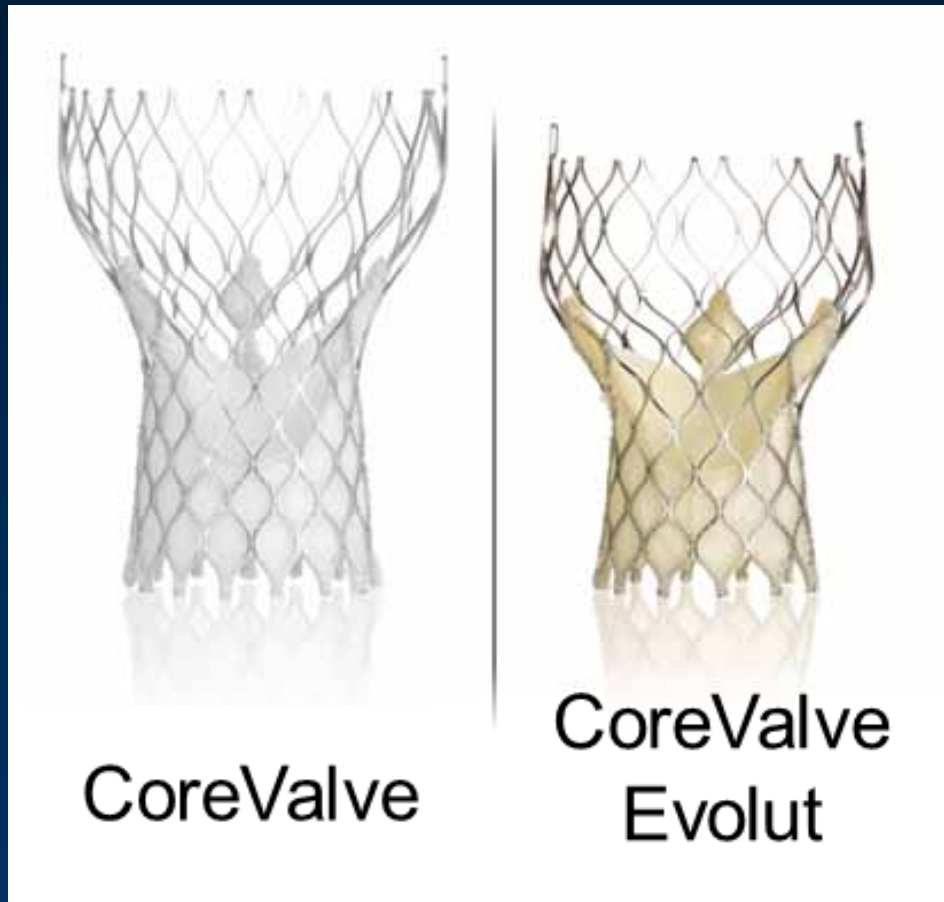


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CoreValve Evolut Design Goals



True Anatomical Fit:

- Tailored height and shape
- Conformability and sealing with optimized radial force and interference across annular ranges
- Coaptation in non-circular anatomy with supra-annular valve position

AOA[®] Anti-Mineralization Treatment:

- Reduce both early and late valvular calcification

CoreValve Evolut

Refined height and shape

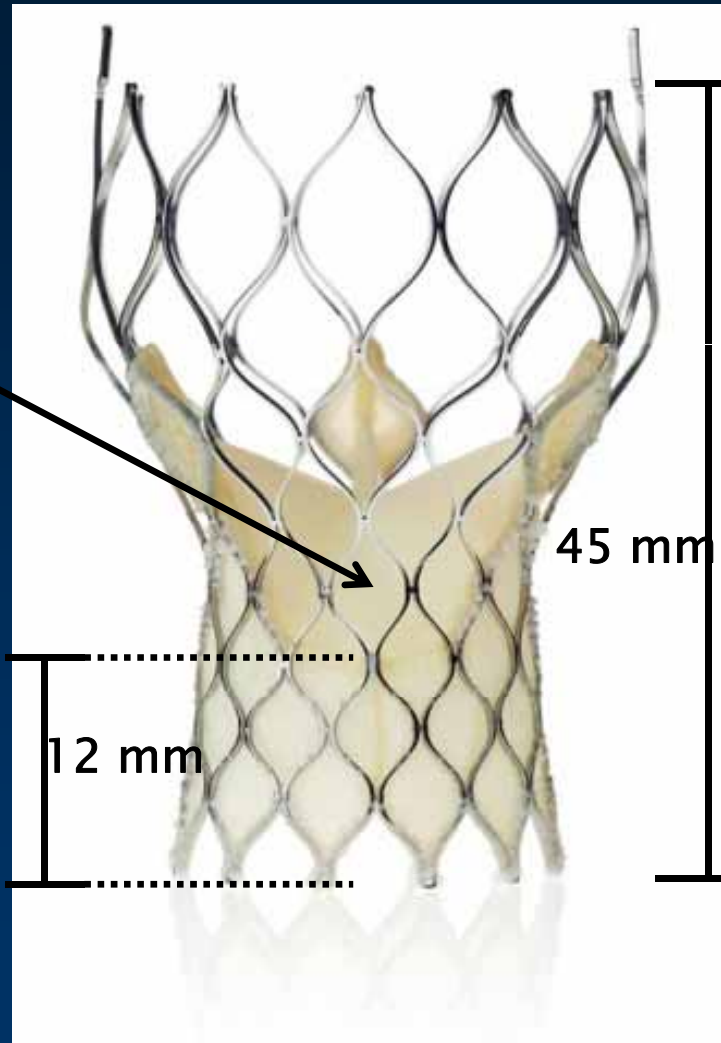
Preserved coronary access

Maintains CoreValve cell geometry for coronary access

(smallest cell accommodates 12Fr catheter)

Preserved skirt length

Provides seal against paravalvular leak



Reduces overall height 9–10 mm

Reduced height

Reduce height of outflow for better fit, especially in angulated anatomy

Serves annulus range

18mm–20mm

(23mm Valve)

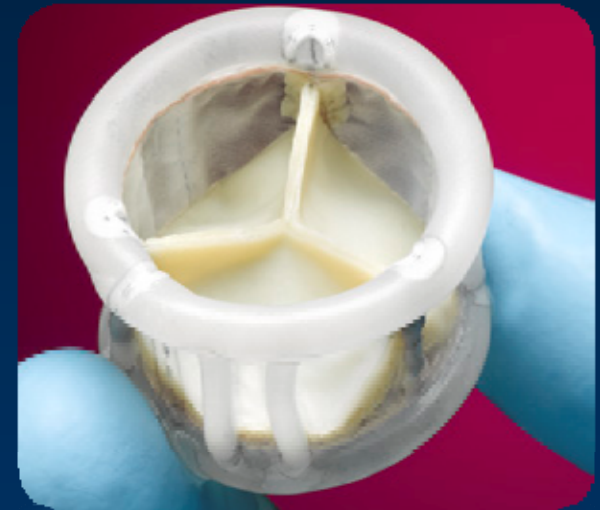
Engager™ Valve Design

- Control arms
- Self-expanding nitinol frame and polyester skirt
- Supra-annular valve function
- Bovine pericardial tissue



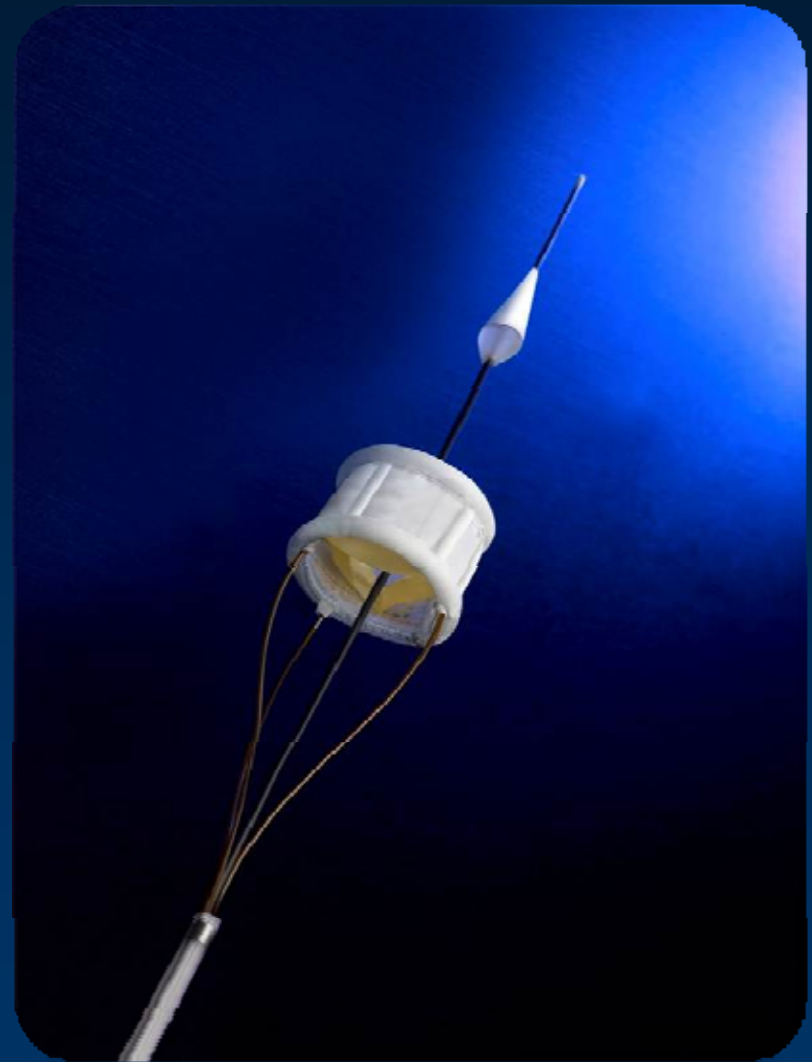
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DFM System Components

- Non-metallic Frame
 - Expandable Dacron polyester double-ring design containing non-compliant PCI technology
 - Tri-leaflet bovine pericardial tissue
- 18Fr delivery and retrieval for all sizes
 - Compatible with 0.035" guidewire
 - 3 positioning wires used for expansion
- Treatment range 19–26mm
 - 25mm valve treats 19–24mm annulus
 - 27mm valve treats 24–26mm annulus



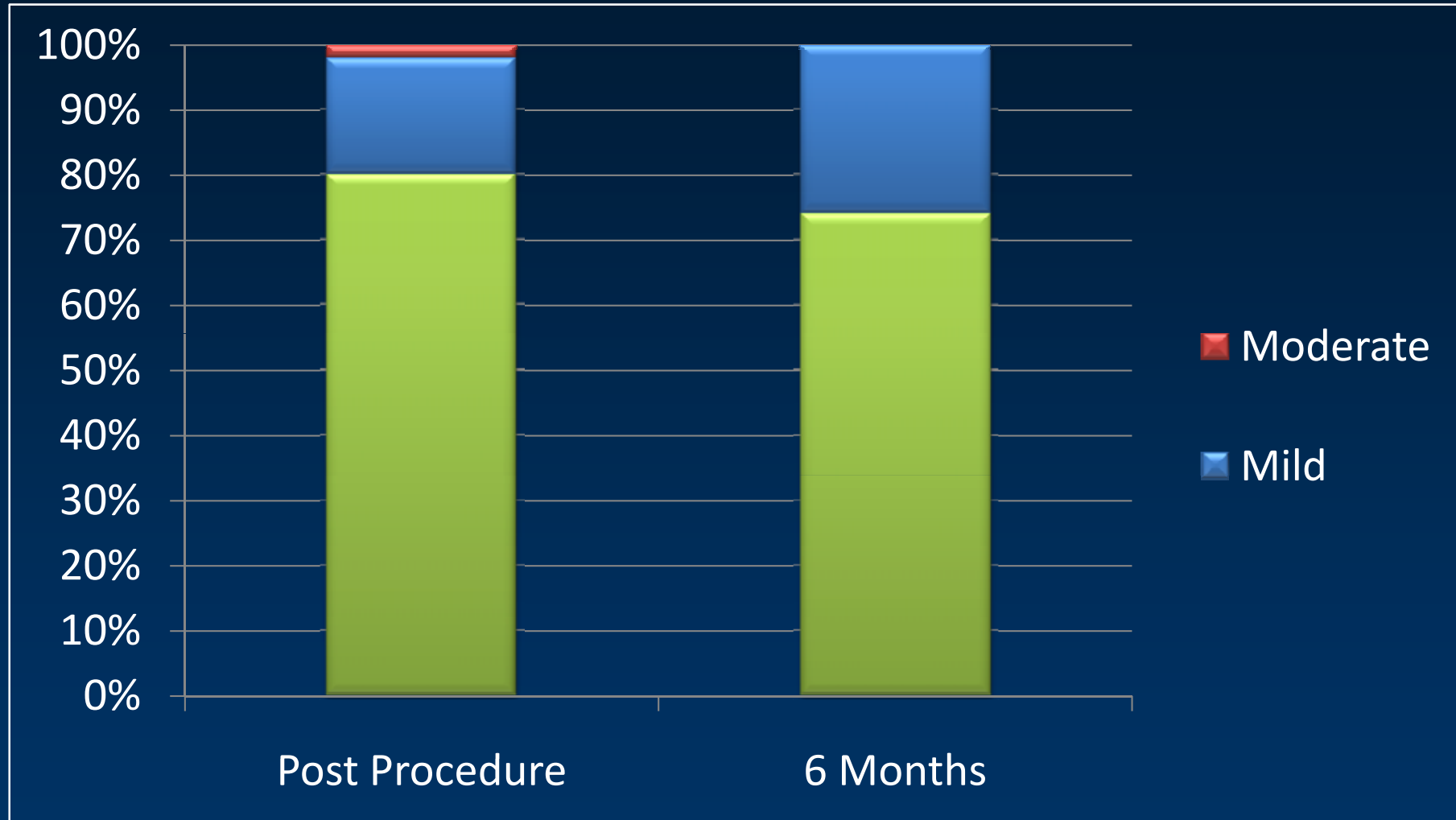
DISCOVER CE Trial: Conclusions

The Direct Flow Medical Valve:

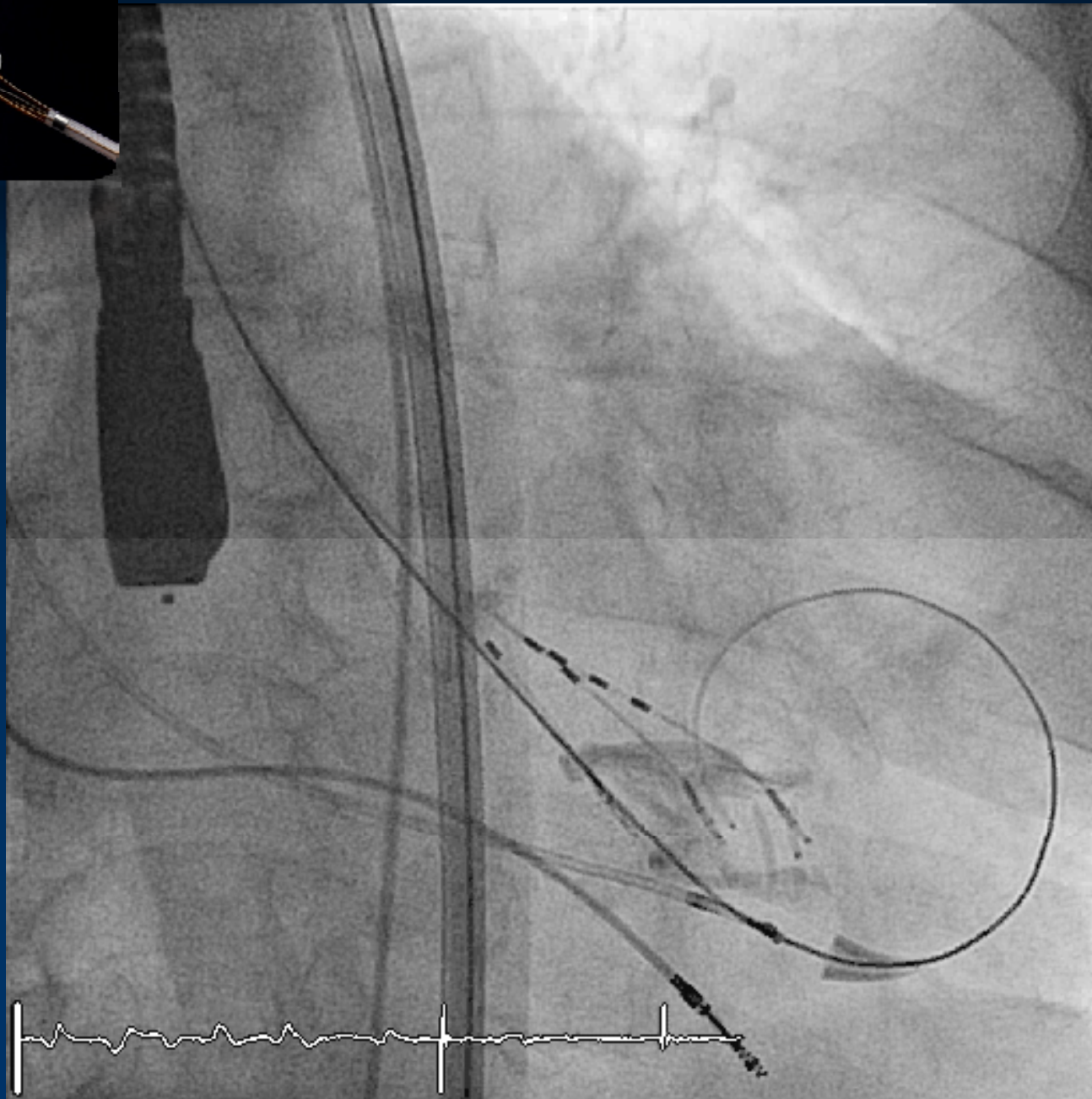
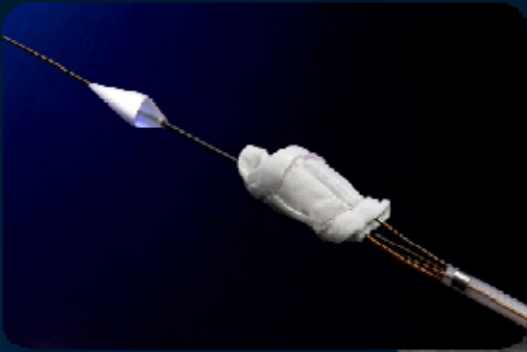
- Achieved 98% freedom from all cause mortality at 30 days and 91% at 6 months
- Can be safely and effectively used to treat high and extreme surgical risk patients with aortic stenosis
- Provides hemodynamic stability during implantation
- Allows controlled positioning, repositioning and safe retrieval
- Virtually eliminates aortic regurgitation

DISCOVER Trial:

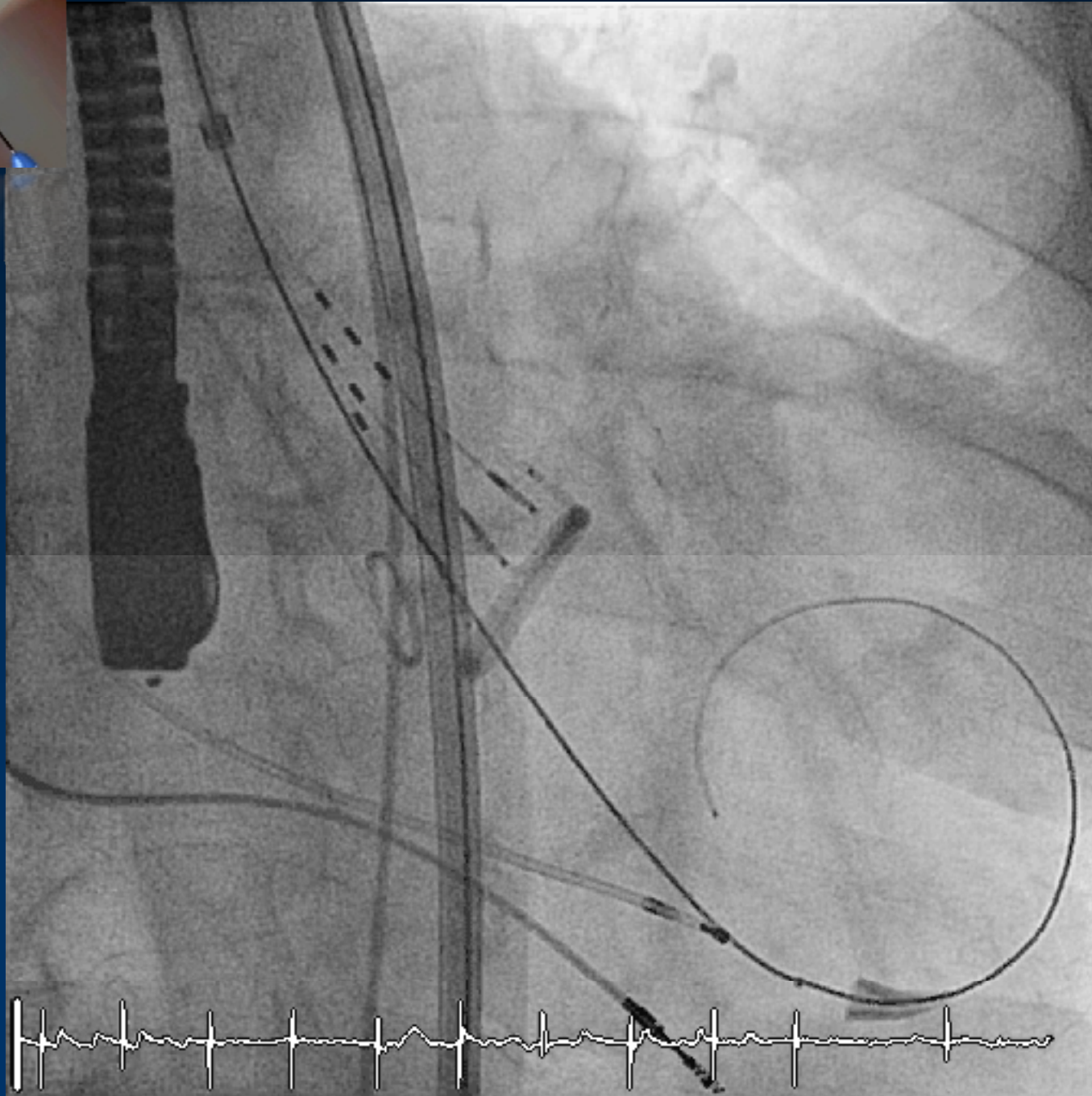
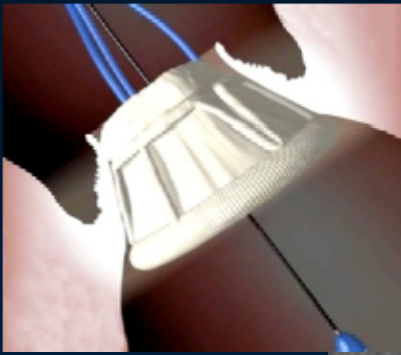
Echocardiographic Aortic Regurgitation by Core Lab



Direct Flow – Positioning LVOT



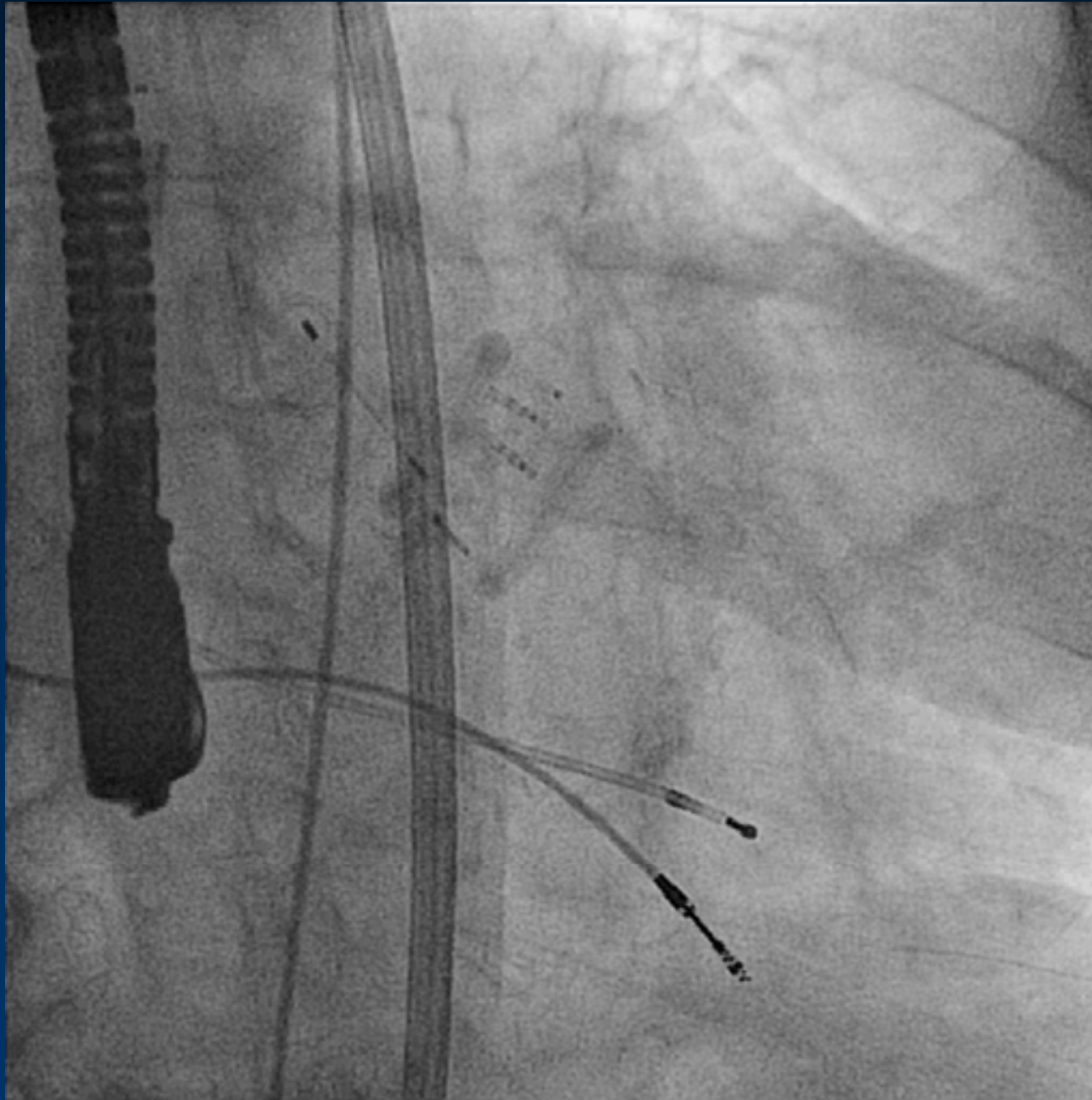
Direct Flow – Positioning Annulus



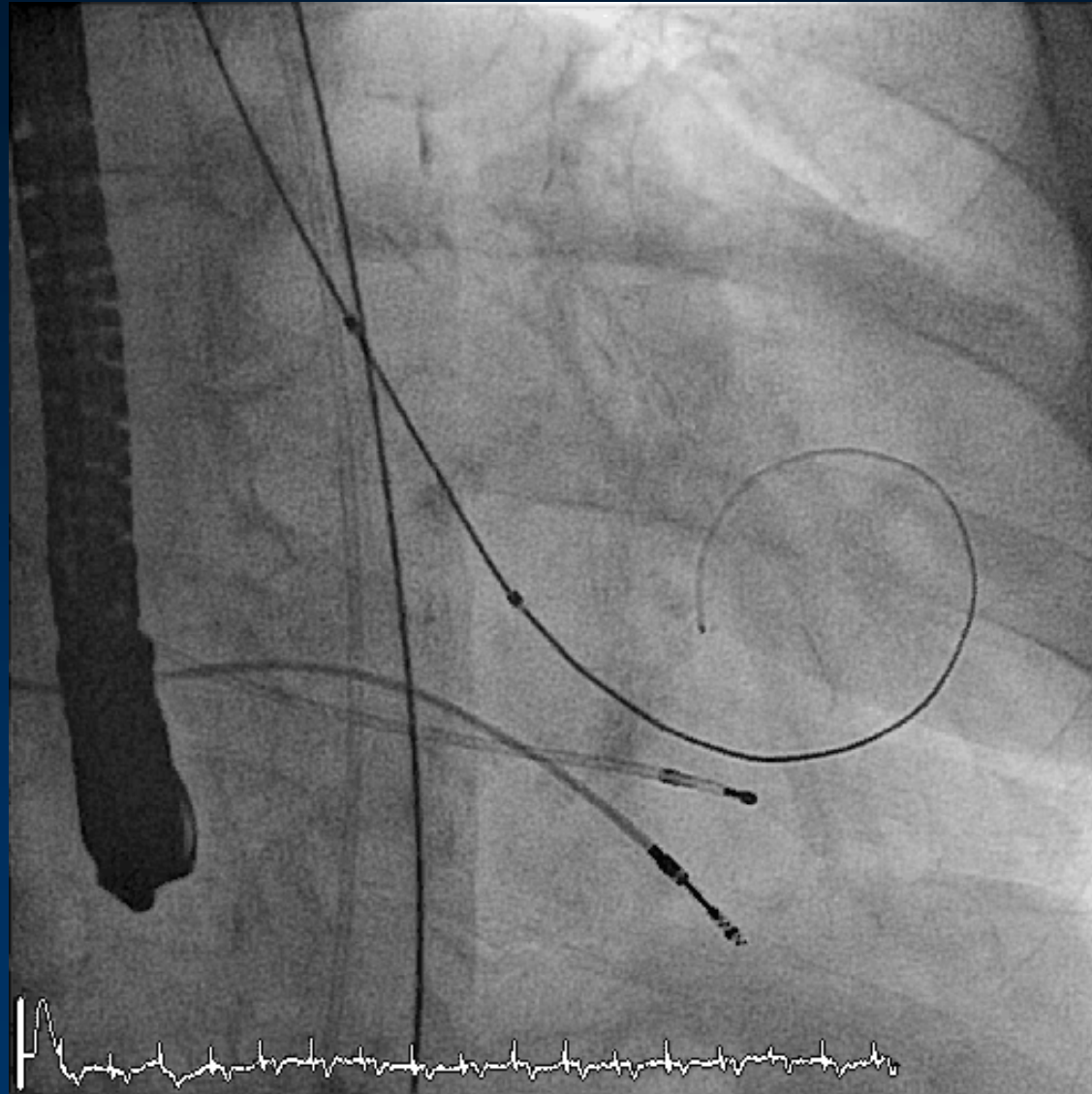
Direct Flow Medical – „Bonn View“



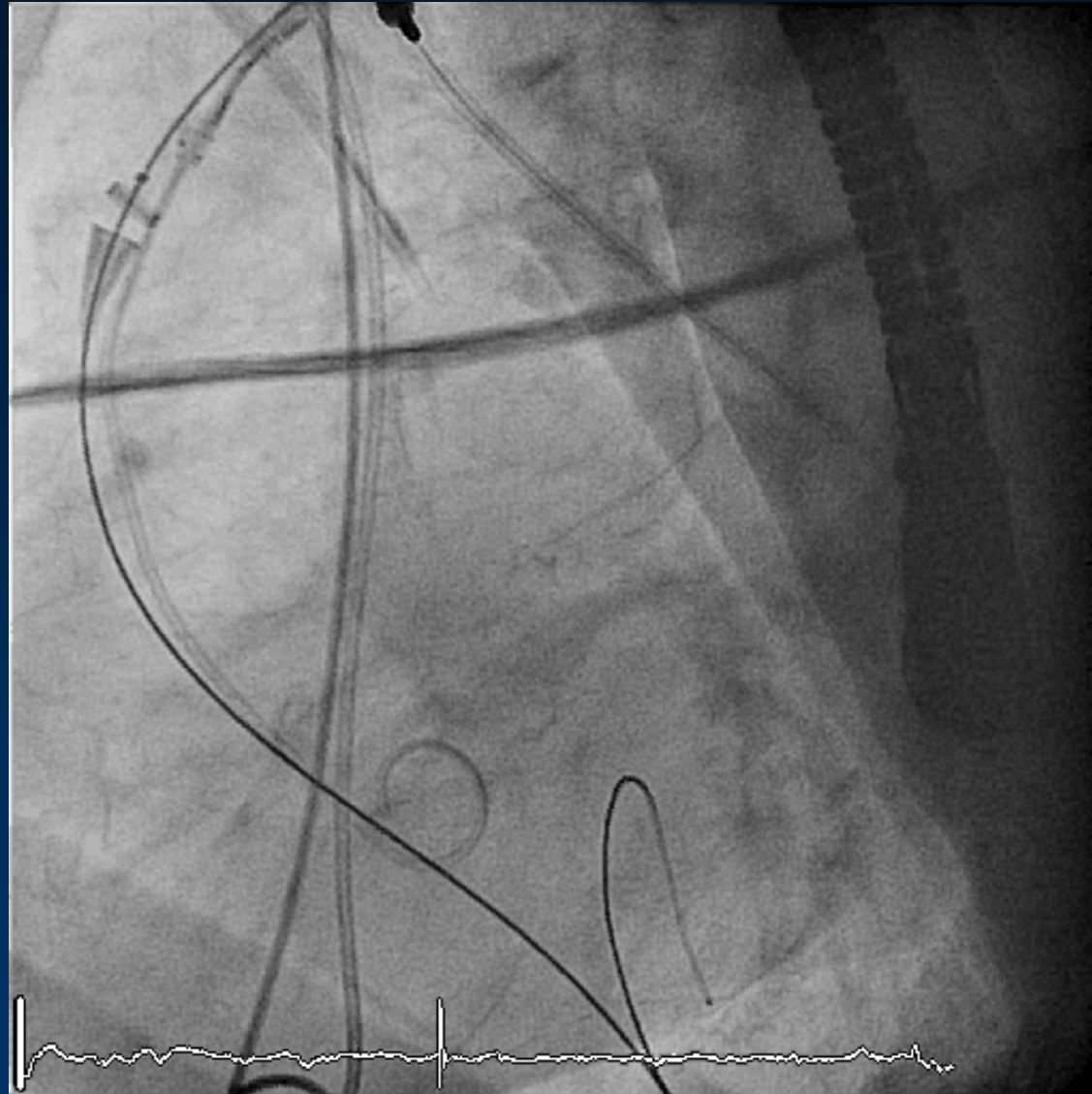
Direct Flow Medical – Final



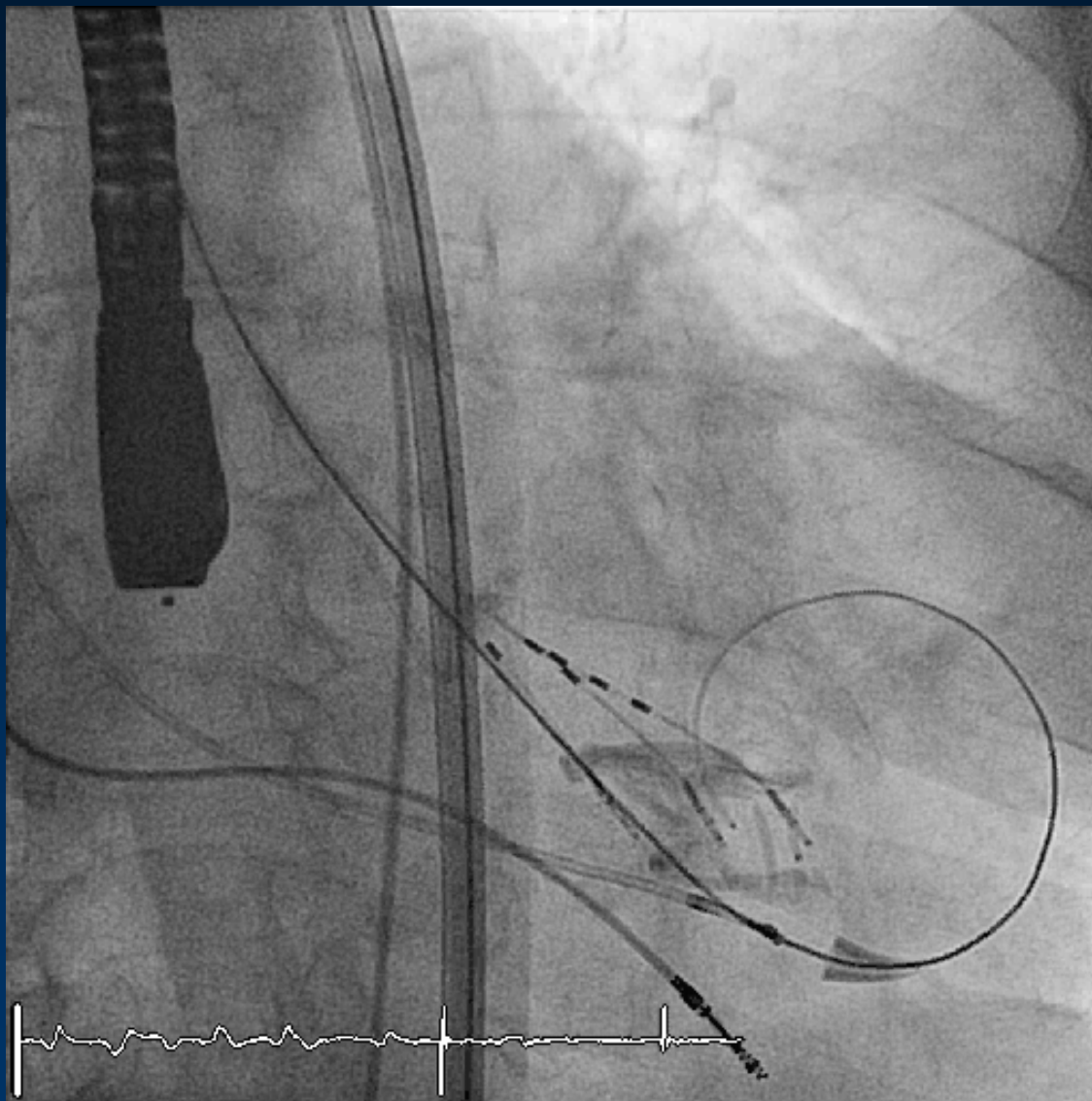
Direct Flow – BAV



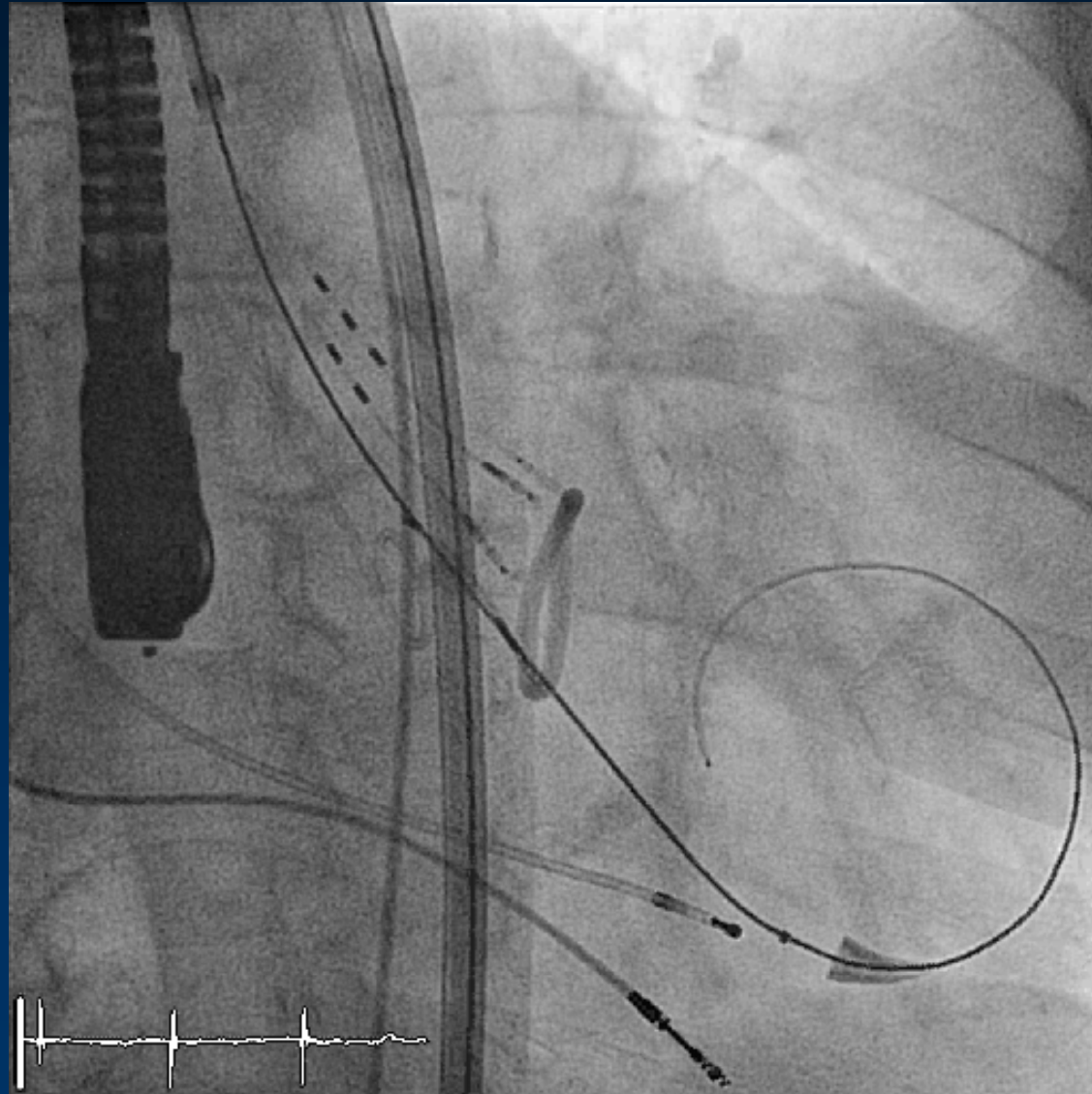
Direct Flow – Passing Annulus



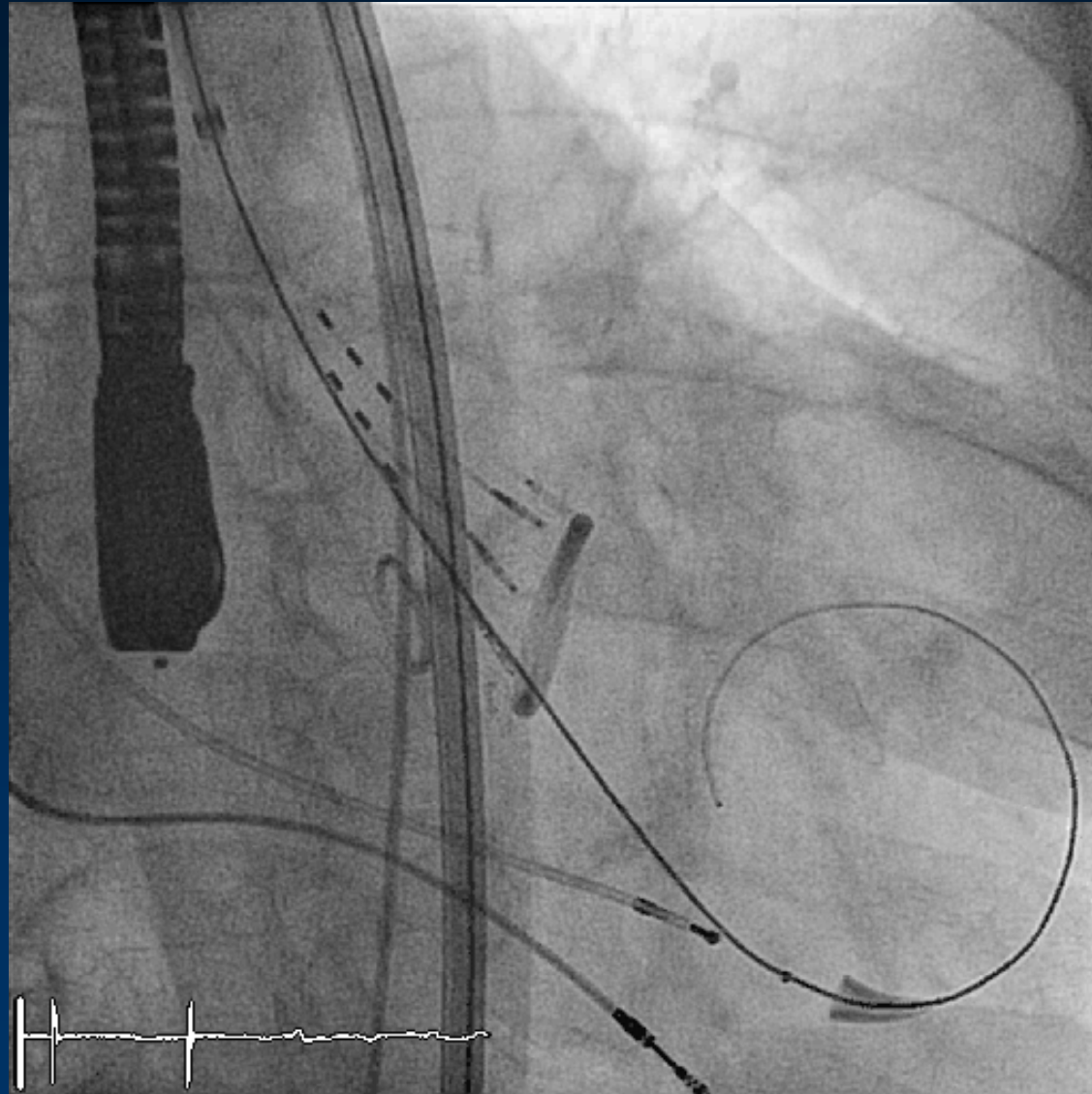
Direct Flow – Positioning LVOT



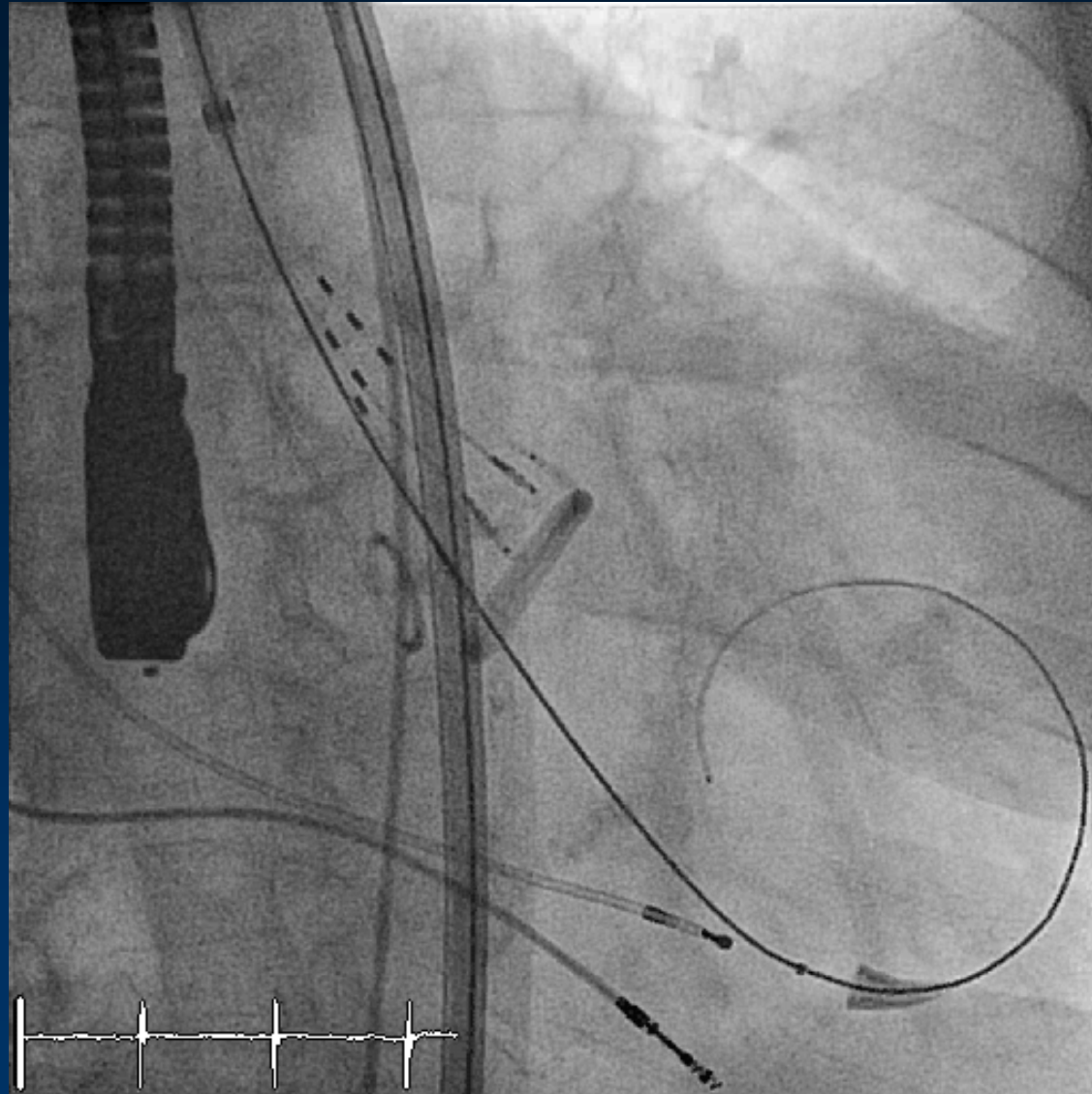
Direct Flow – Positioning Annulus



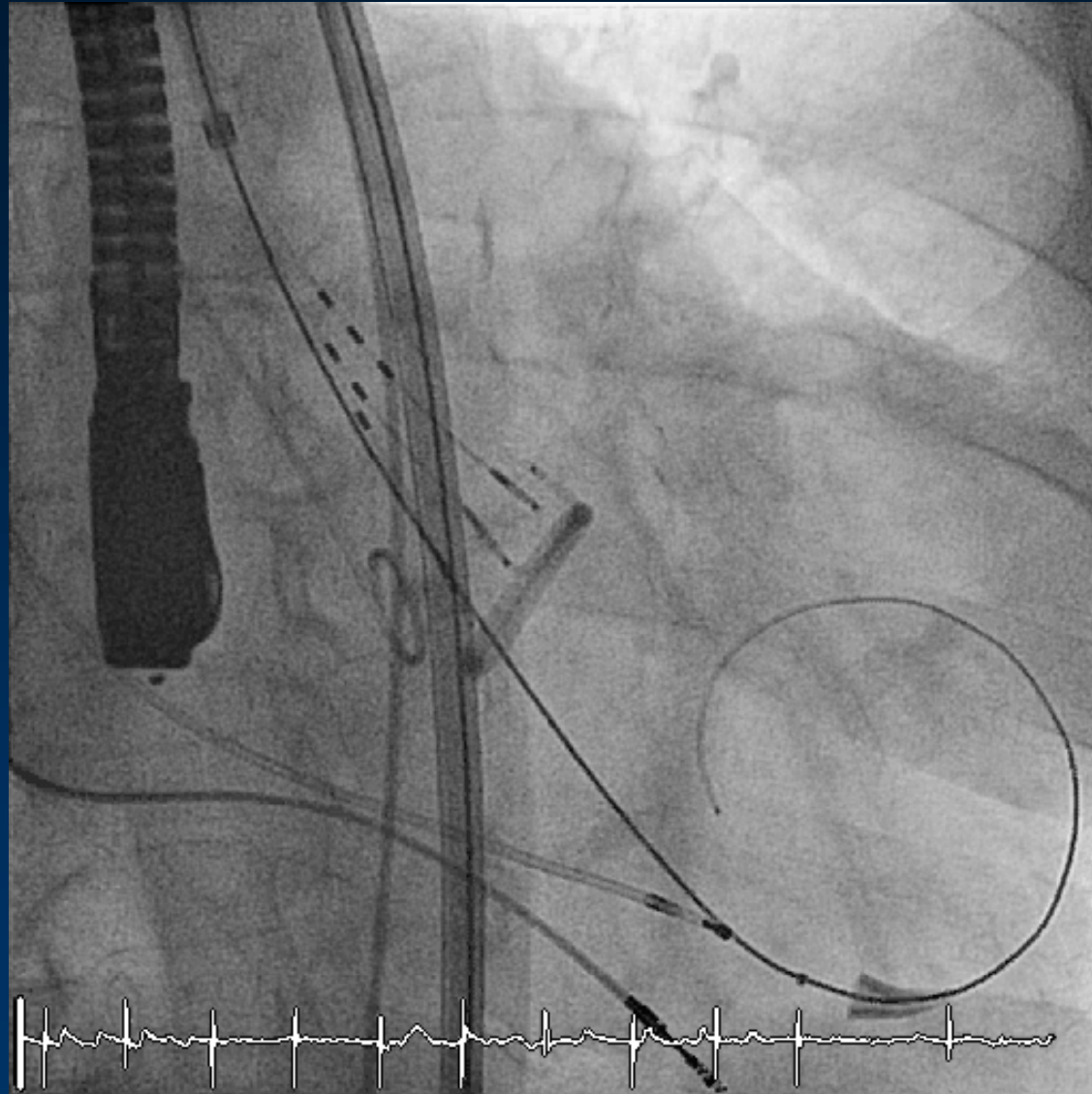
Direct Flow – „Squaring“



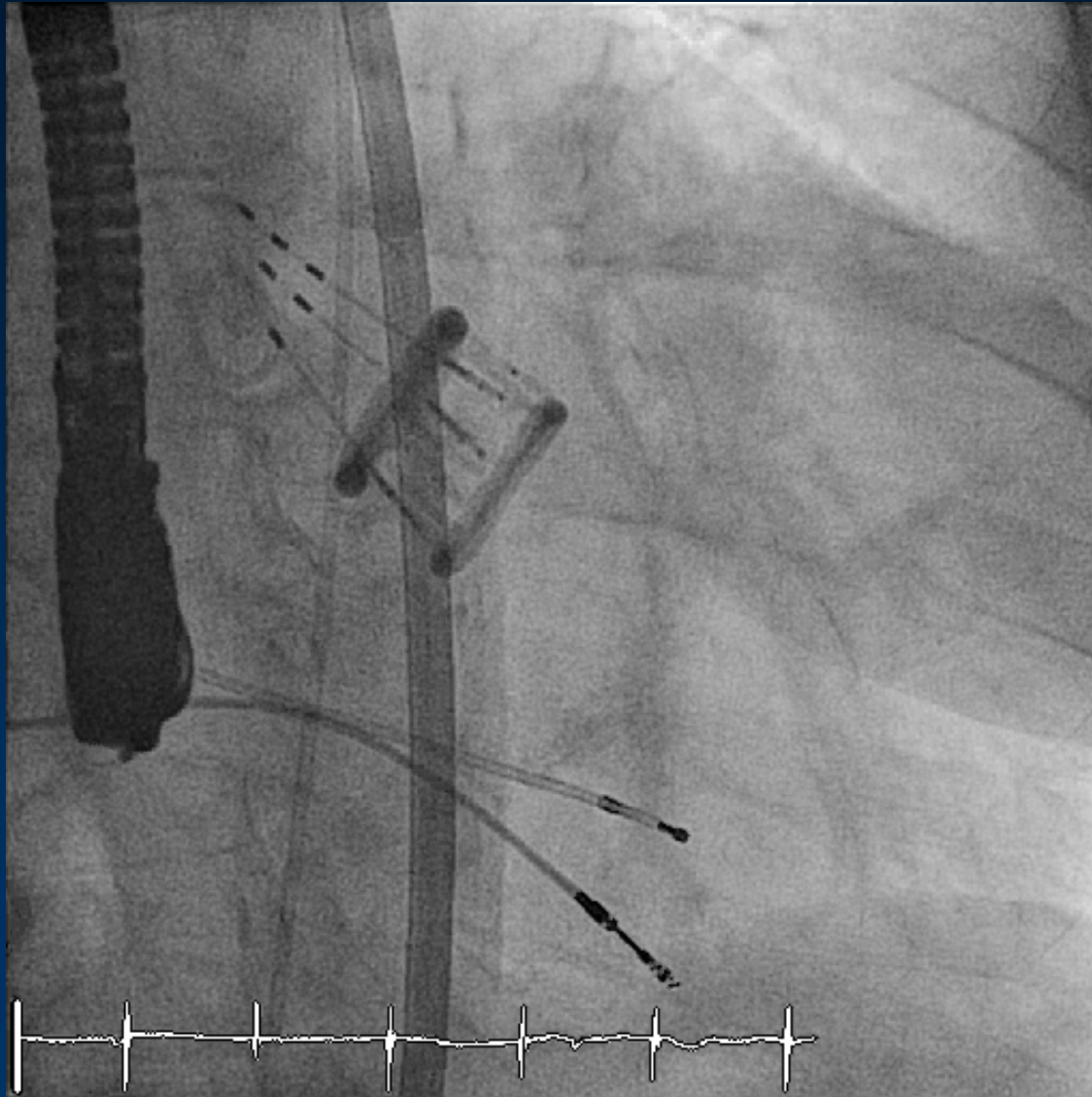
Direct Flow – Positioning Annulus



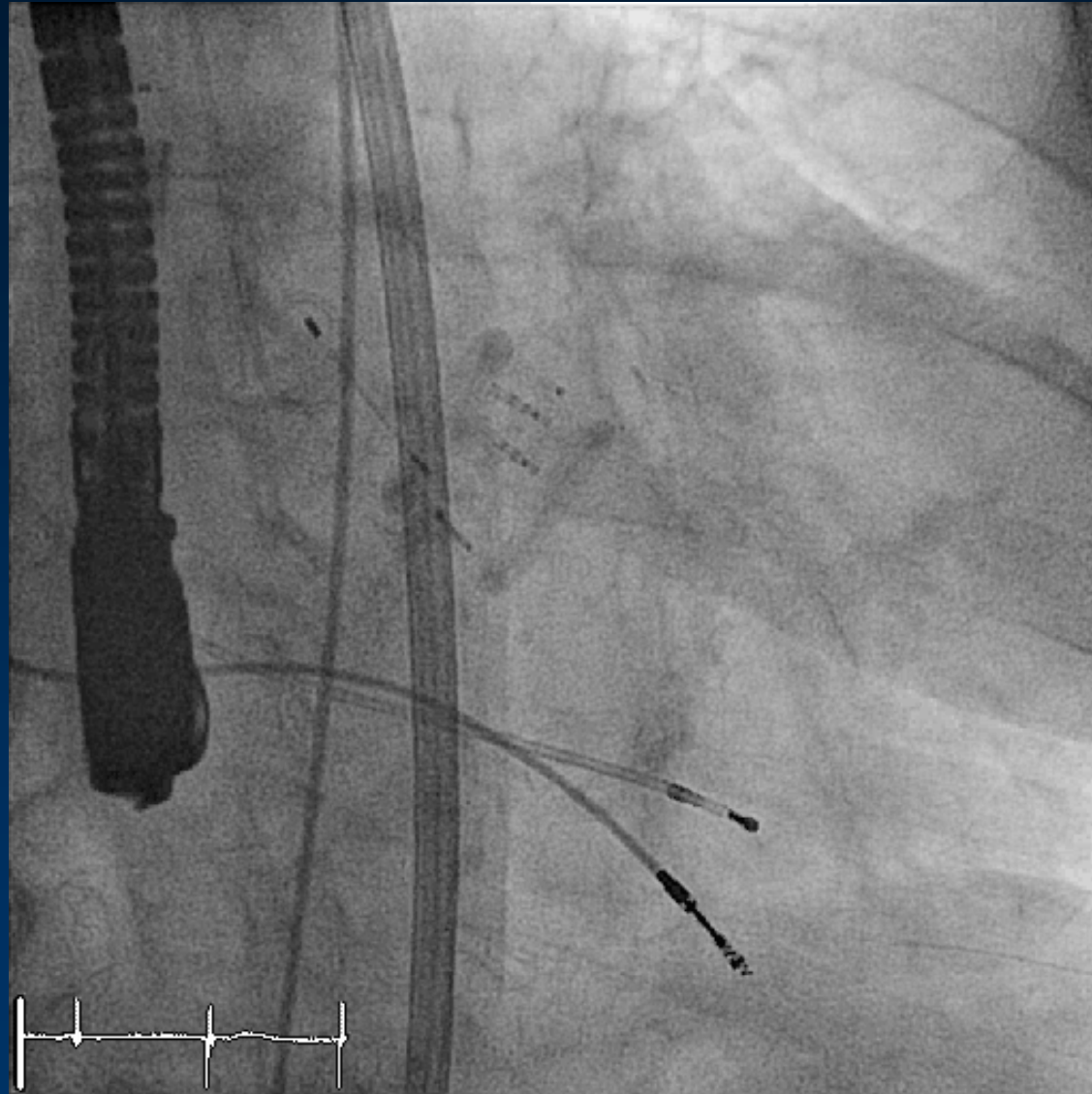
Direct Flow – Positioning Annulus



Direct Flow – Pre Release Control



Direct Flow – Release



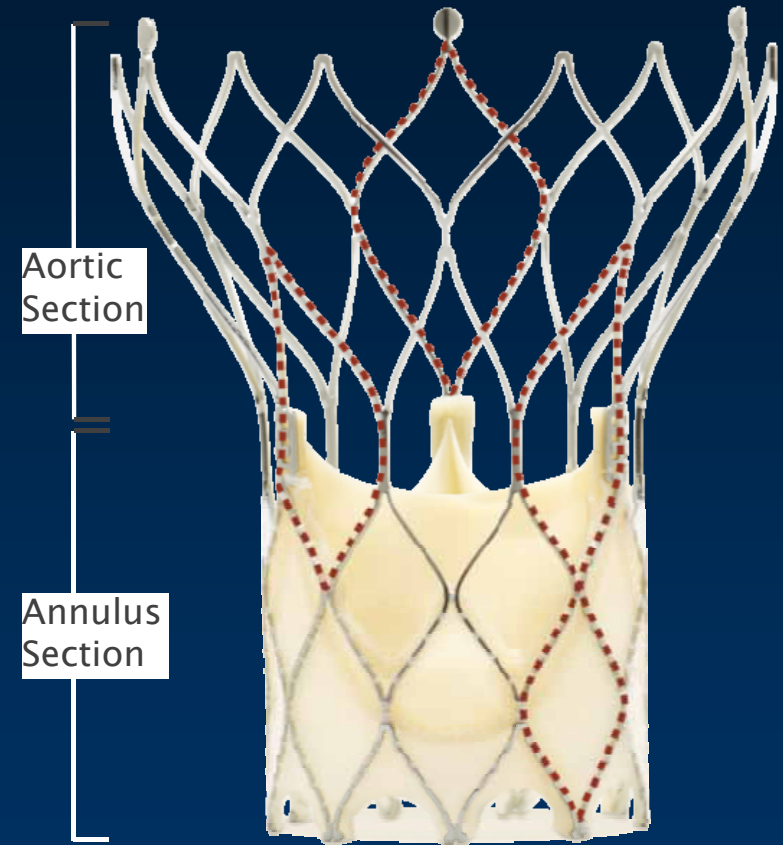
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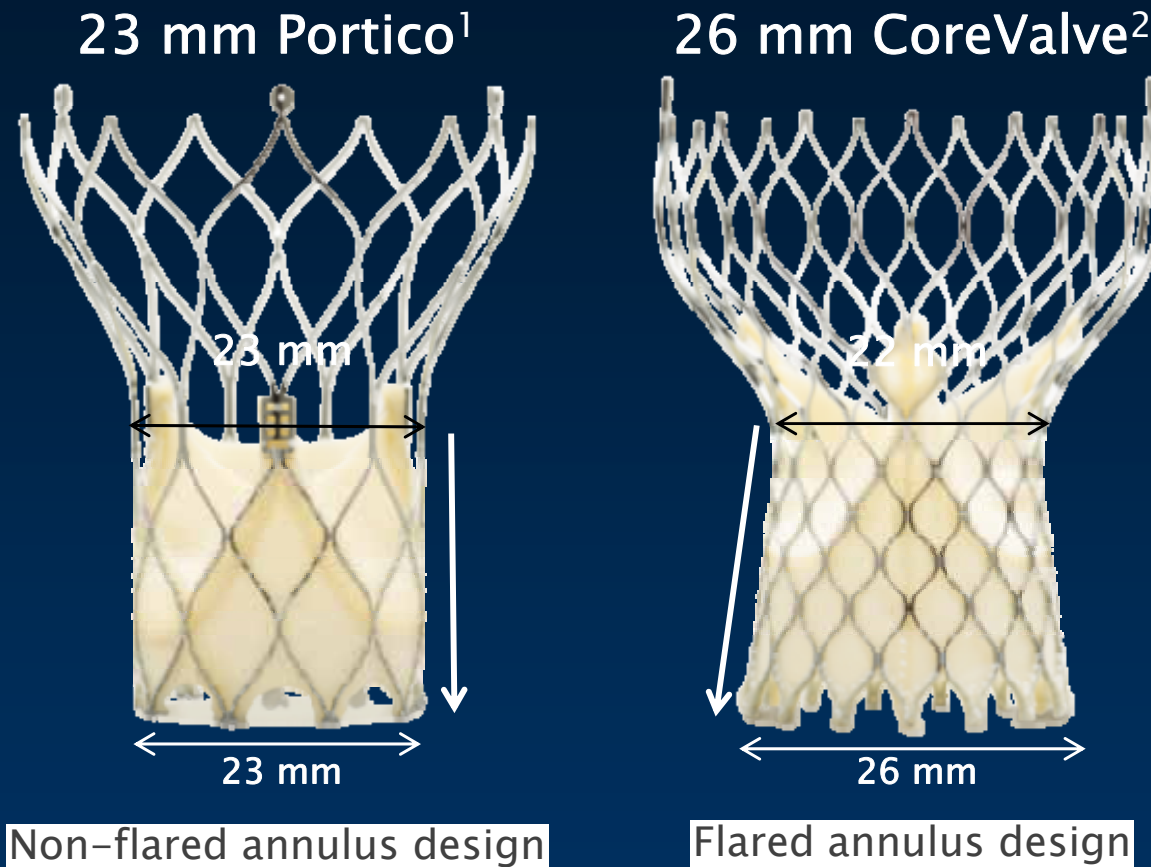


Portico Overview: Valve Design

- The large cells in the annulus section of the stent are designed to minimize the risk of PV leak
 - Less metal — minimizing the potential of a stent strut resting against a calcific nodule
 - More tissue — allowing the tissue to conform around calcific nodules
- Rapid pacing not required to deploy the valve



Portico and CoreValve Design Comparison



The annulus section of the Portico stent is not flared when compared to the flared annulus section of the CoreValve. Designed to minimize the risk of interfering with the conduction system and mitral valve apparatus.

1. St. Jude Medical Data on File.
2. Medtronic, CoreValve brochure, PN090401 V1 April 2007

TAVR with the Portico Valve

First-in-Human Experience

Table 4 Hemodynamic Function After Implantation and at 30-Day Follow-Up

| Case # | Pre-TAVR | | | Post-TAVR, Pre-Hospital Discharge | | | | 1-Month Post-TAVR | | | |
|-----------|----------------------|-------------|-------------|-----------------------------------|------------|----------|---------|----------------------|------------|----------|---------|
| | AVA, cm ² | MG, mm Hg | LVEF, % | AVA, cm ² | MG, mm Hg | PAR | TAR | AVA, cm ² | MG, mm Hg | PAR | TAR |
| 1 | 0.5 | 59 | 65 | 1.0 | 14 | Mild | None | 1.0 | 15 | Mild | None |
| 2 | 0.5 | 28 | 30 | 1.8 | 4 | Moderate | Trivial | 1.6 | 4 | Moderate | Trivial |
| 3 | 0.7 | 35 | 70 | 1.5 | 6 | Trivial | None | 1.5 | 10 | Trivial | None |
| 4 | 0.6 | 38 | 35 | 1.4 | 13 | Mild | Severe | 1.4 | 14 | Trivial | None |
| 5 | 0.8 | 39 | 60 | 1.5 | 8 | Trivial | None | 1.3 | 8 | Trivial | None |
| 6 | 0.4 | 56 | 58 | 1.3 | 10 | Trivial | None | 1.2 | 10 | Trivial | None |
| 7 | 0.6 | 40 | 60 | 1.1 | 16 | Mild | None | 1.1 | 11 | Mild | None |
| 8 | 0.6 | 45 | 60 | 1.3 | 10 | Trivial | None | 1.2 | 15 | Trivial | None |
| 9 | 0.5 | 82 | 70 | 1.4 | 18 | Mild | None | 1.6 | 7 | Mild | None |
| 10 | 0.8 | 27 | 69 | 1.4 | 8 | Mild | None | 1.3 | 10 | Mild | None |
| Mean ± SD | 0.6 ± 0.1 | 44.9 ± 16.7 | 54.7 ± 14.3 | 1.4 ± 0.2 | 10.7 ± 4.5 | | | 1.3 ± 0.2 | 10.9 ± 3.8 | | |

Aortic valve area, cm²

Pre-TAVR

0.6 ± 0.1

Post-TAVR

1.4 ± 0.2

Mean gradient, mmHg

44.9 ± 16.7

10.7 ± 4.5

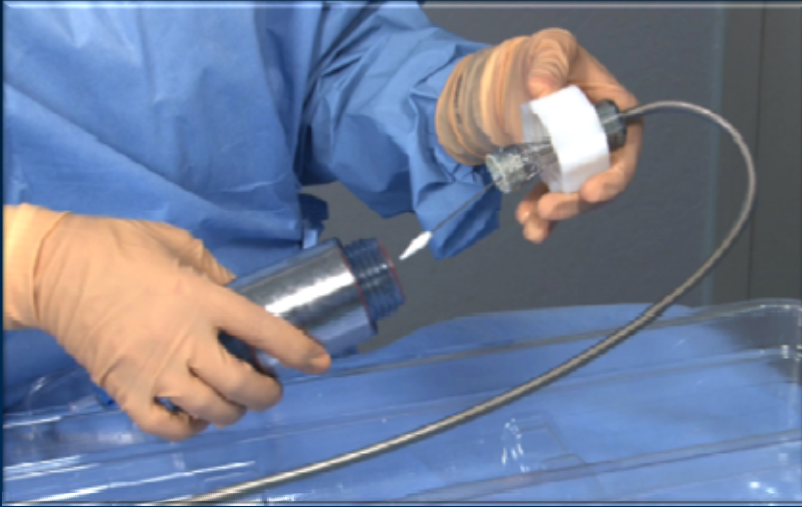
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Lotus Valve System

1. Preloaded delivery system



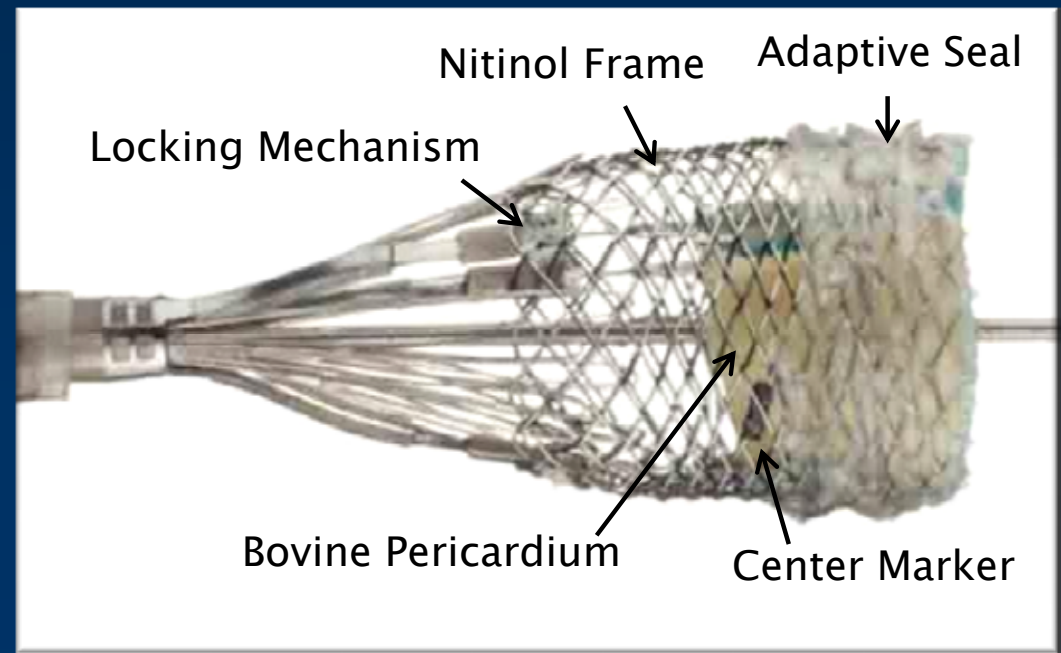
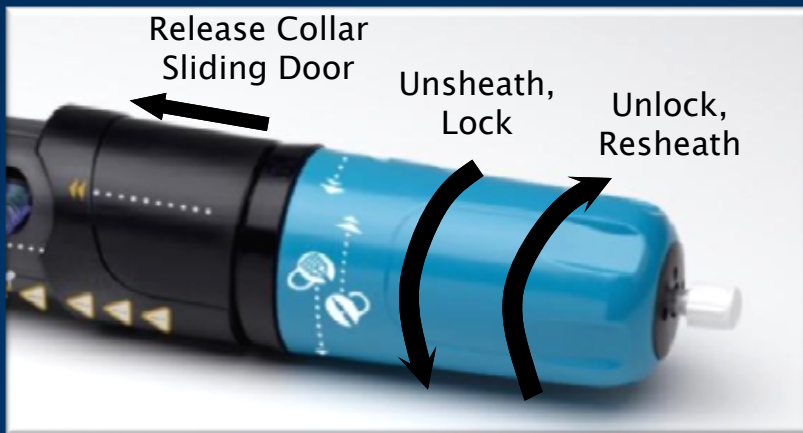
3. Central radiopaque marker to aid precise positioning

4. Functions early enabling controlled deployment

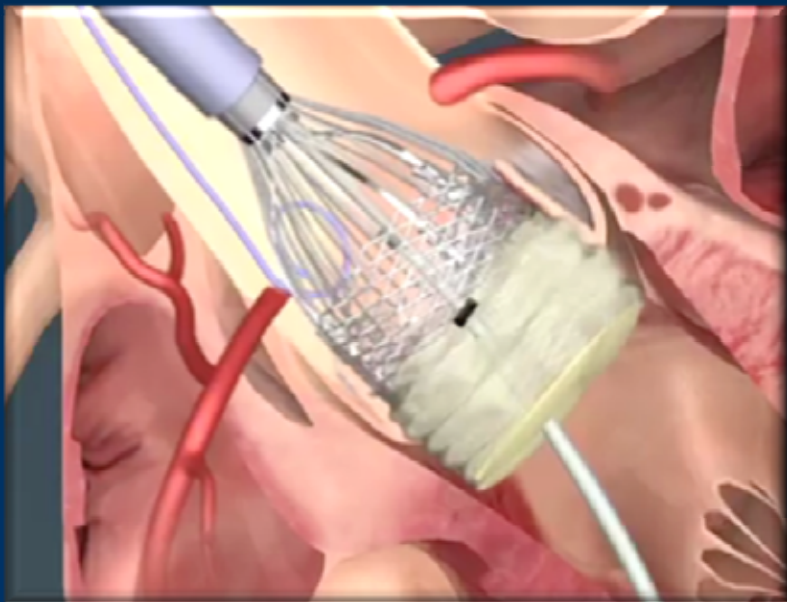
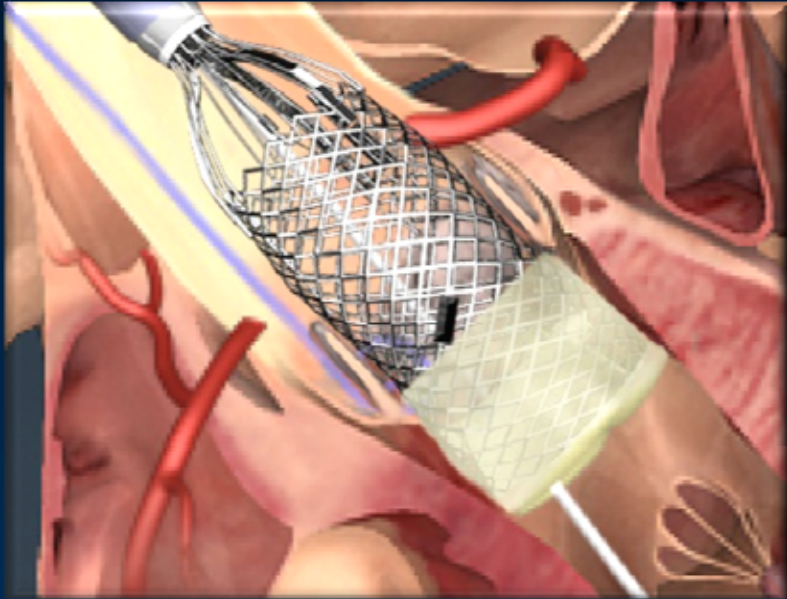
5. Fully retrievable and repositionable

6. Adaptive seal designed to minimize paravalvular leak

2. Simple handle design

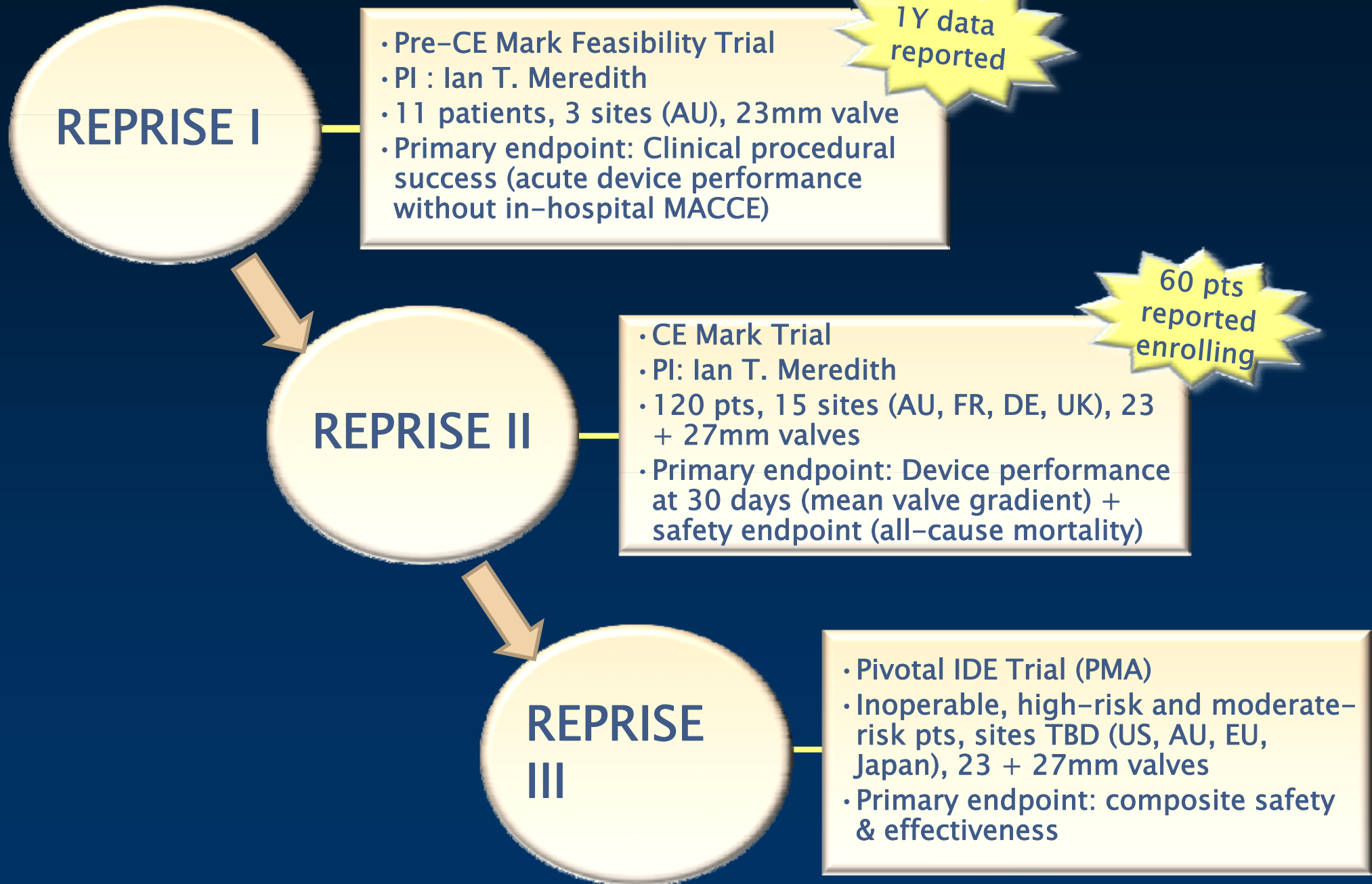


Lotus™ Valve

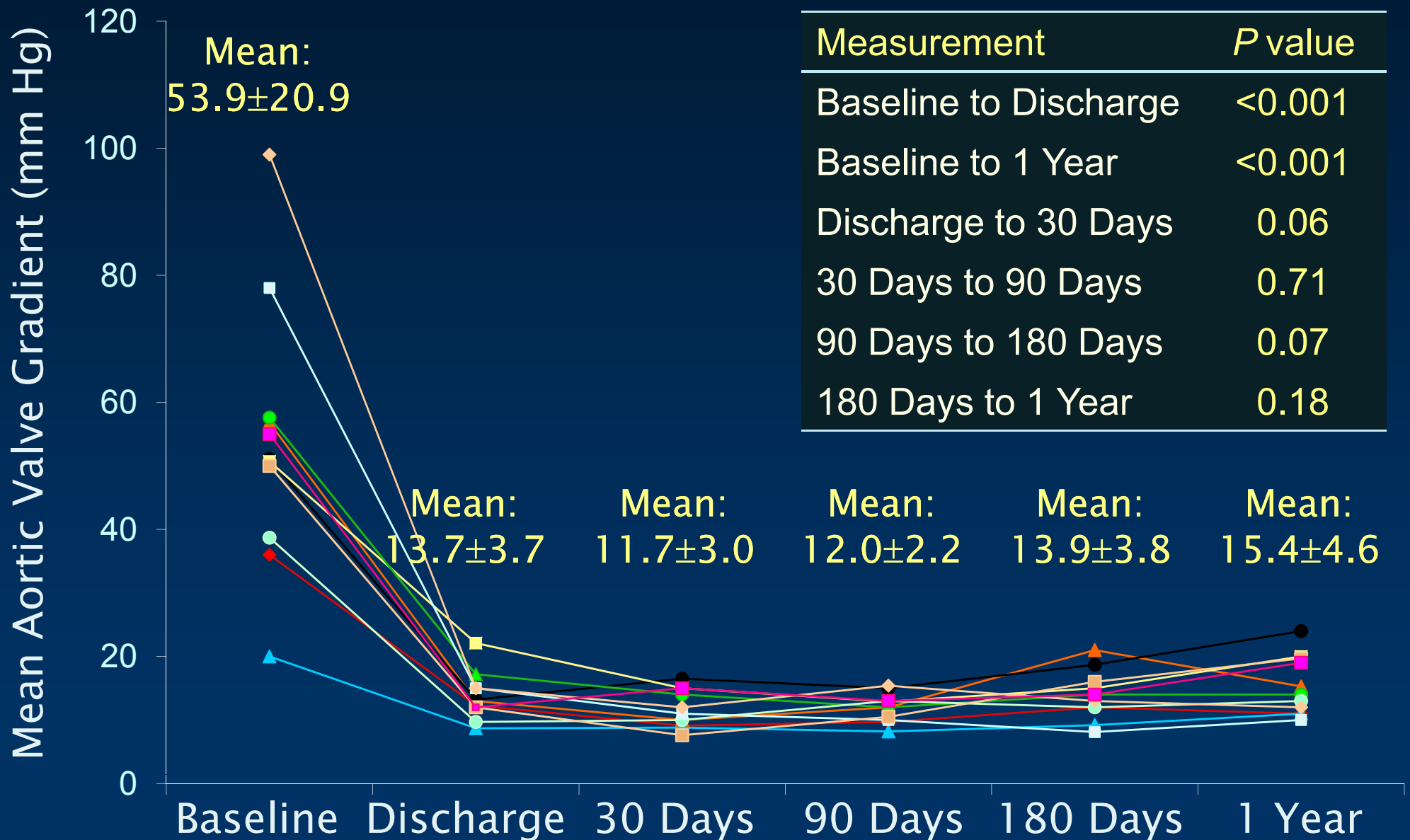


- Central radiopaque positioning marker aids precise placement
- Valve expands radially as it shortens
- Valve functions very early in deployment aiding controlled positioning
- Valve can be repositioned and redeployed at any time during procedure and is fully recapturable at 100% deployment
- Precise, predictable and controlled placement potentially reduces risk of coronary obstruction, valve embolization, malpositioning and valve in valve
- Adaptive Seal conforms to annular anatomy and minimizes paravalvular leakage

The Lotus Aortic Valve Program

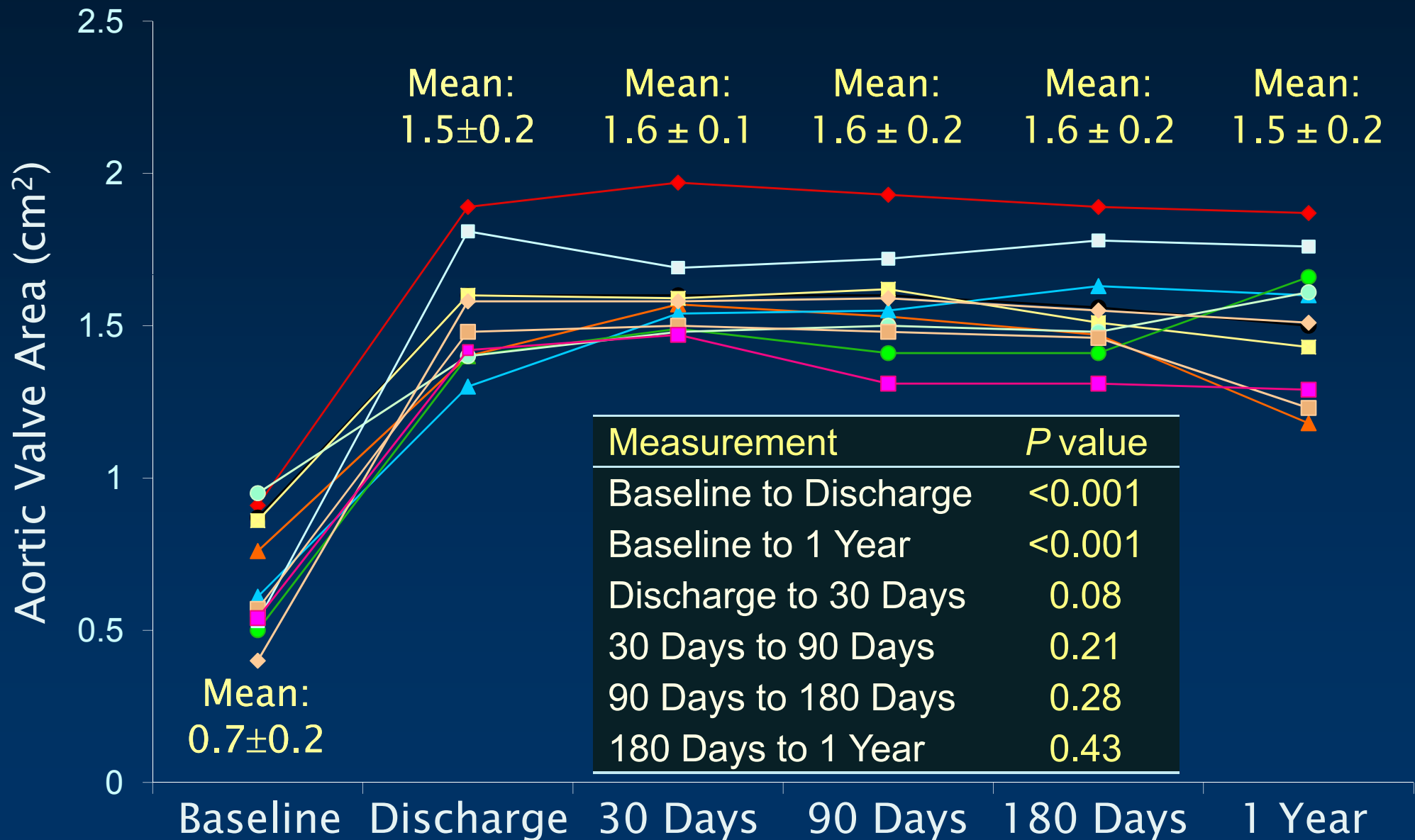


Mean Aortic Valve Gradient by Patient REPRISE I

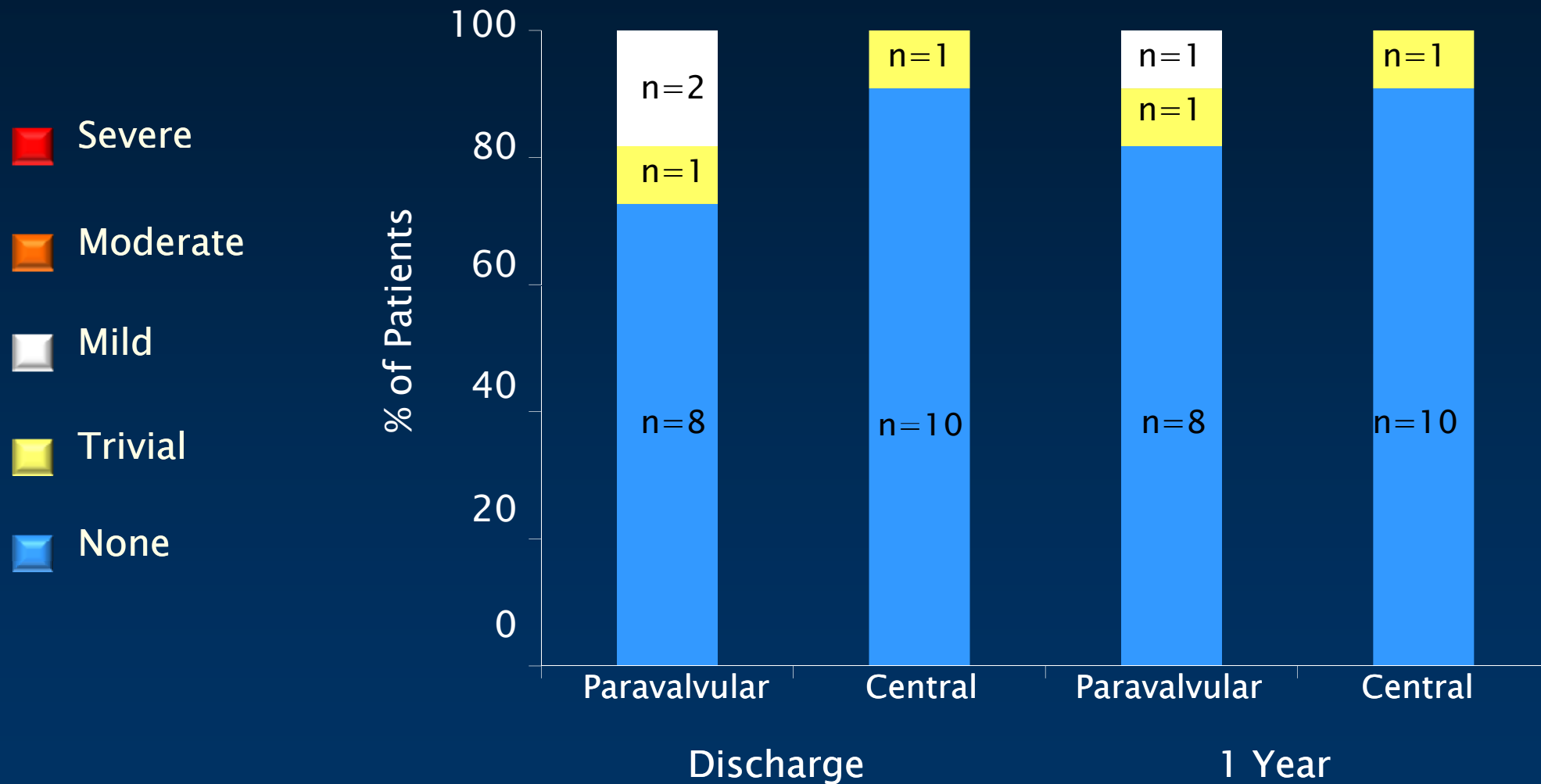


Effective Orifice Area by Patient

REPRISE I

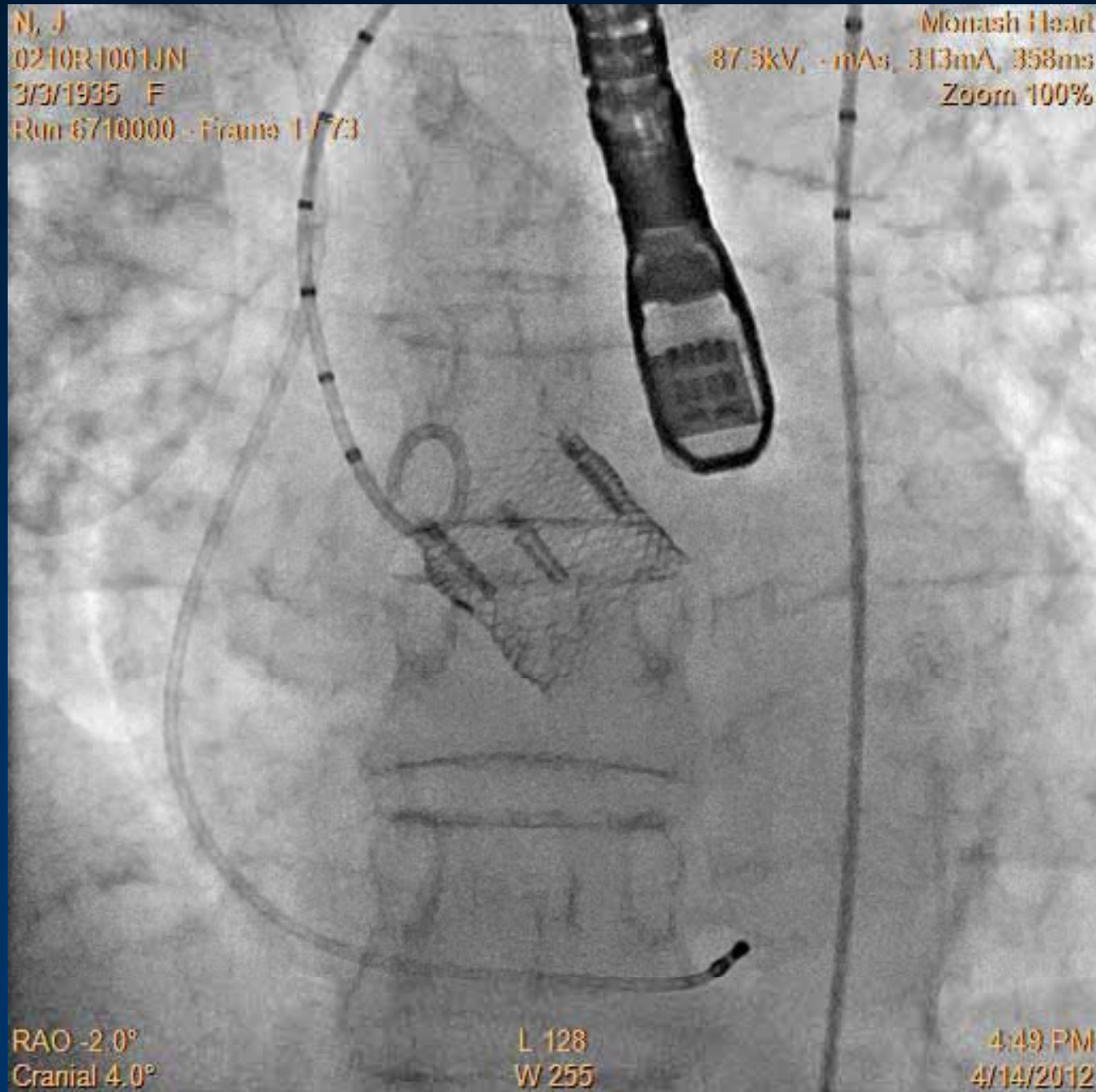


REPRISE 1 – Aortic Regurgitation Transthoracic Echocardiography

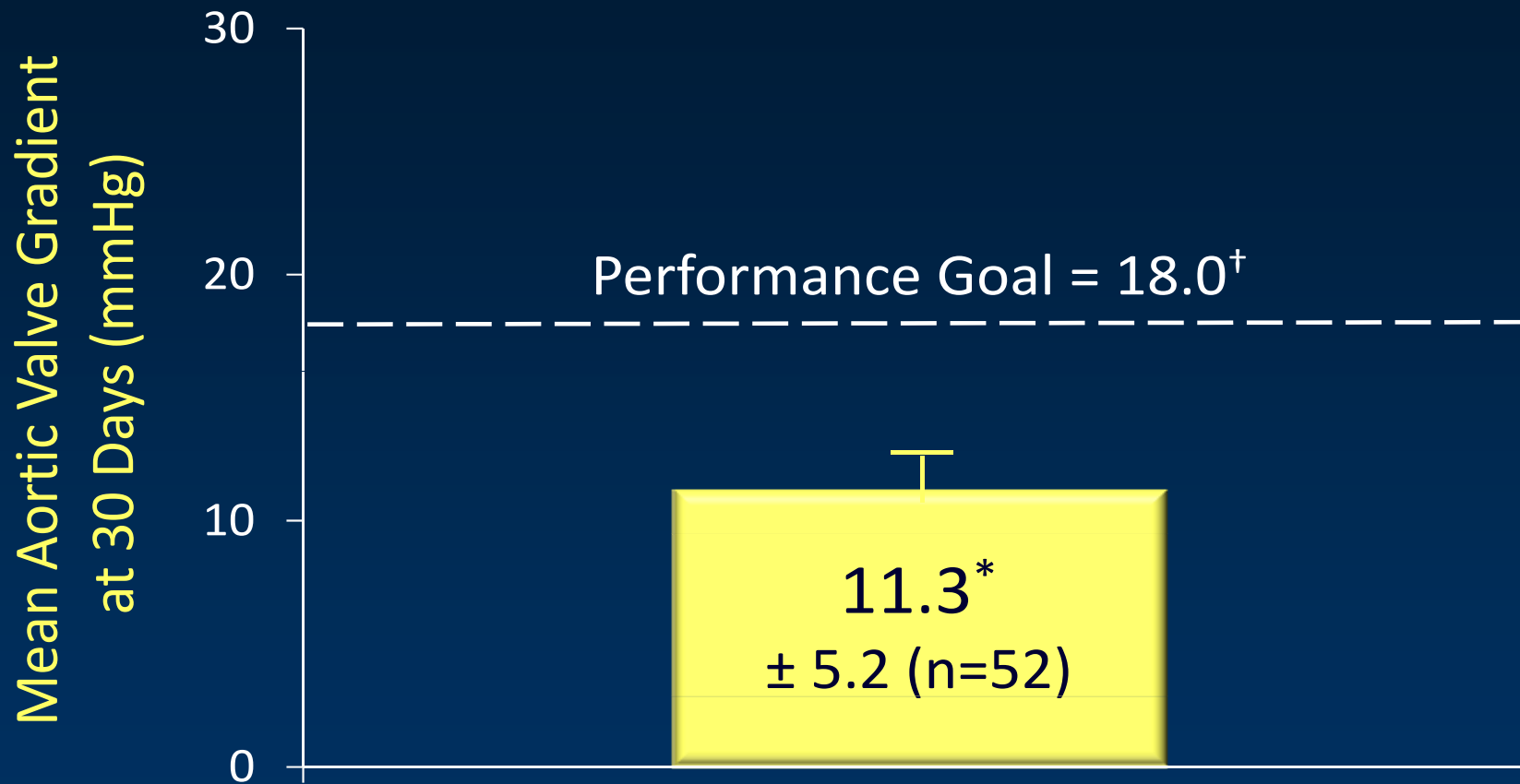


No Moderate / Severe AR by Independent Adjudication

BSC Lotus Valve Final Angiogram



Primary Device Performance Endpoint *REPRISE II – First 60 Patients*



* Value of 11.3 with a 99.2%[‡] UCB of 13.1
is significantly less than the performance goal ($P < 0.001$)

[‡] Alpha-level adjustment for interim analysis

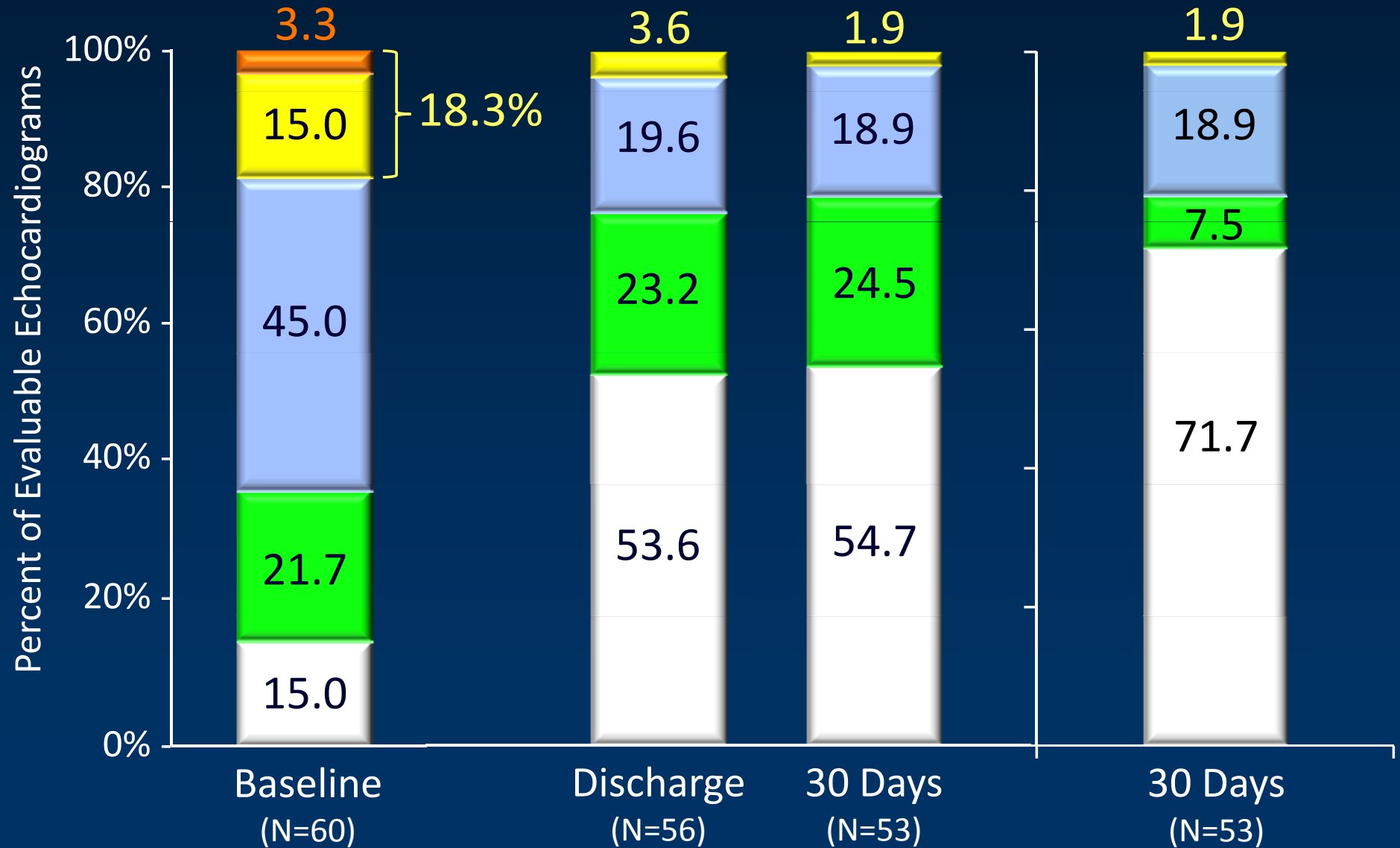
[†] Based on an expected mean of ≤ 15 mmHg (literature review) plus a test margin of 3 mmHg

REPRISE II Aortic Regurgitation Over Time

None Trace Mild Moderate Severe

Combined

Paravalvular



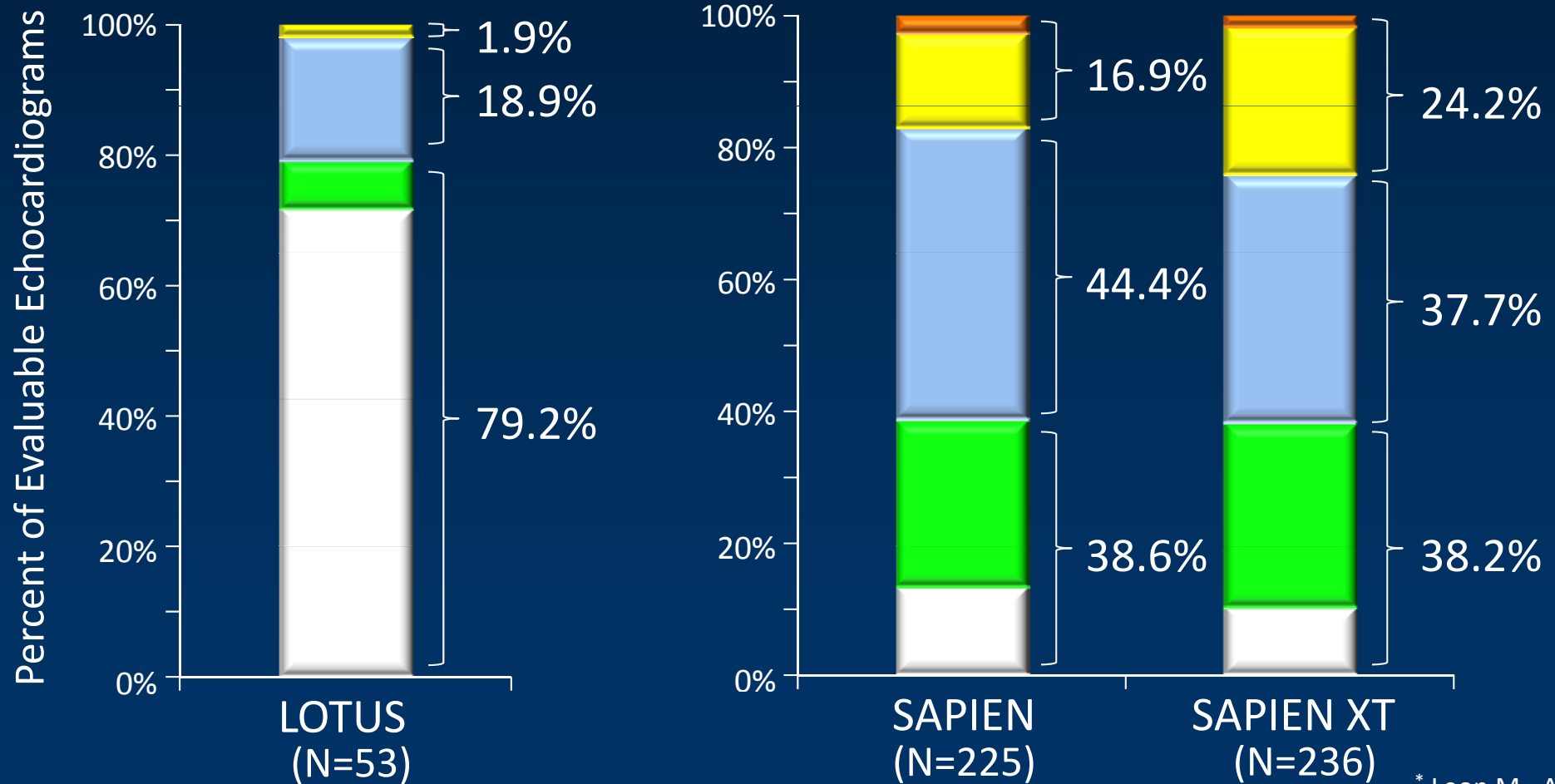
Paravalvular Aortic Regurgitation–30 Days

REPRISE II Comparison with Edwards Valves

None Trace Mild Moderate Severe

REPRISE II

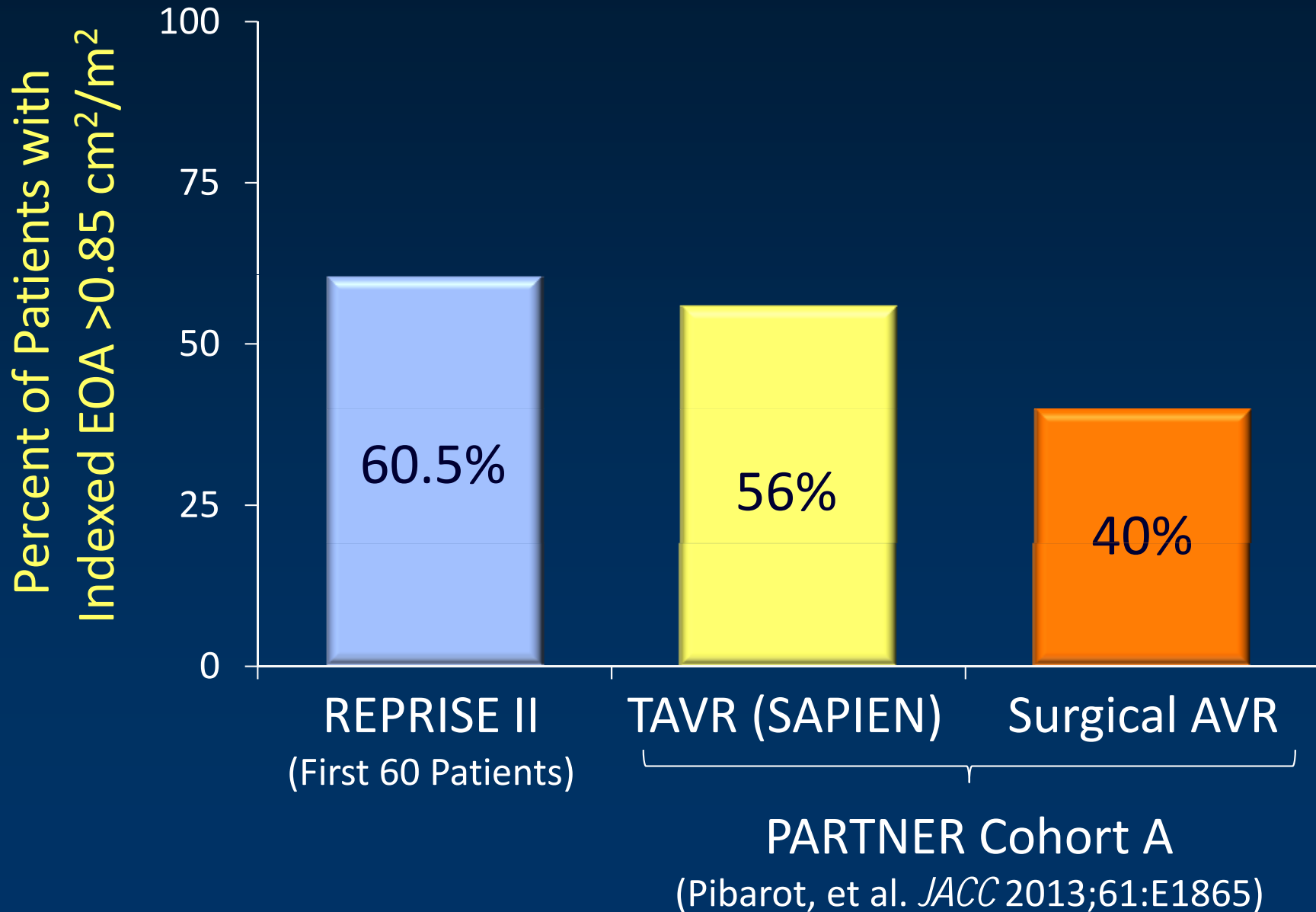
PARTNER II, Inoperable Cohort*



* Leon M., ACC 2013

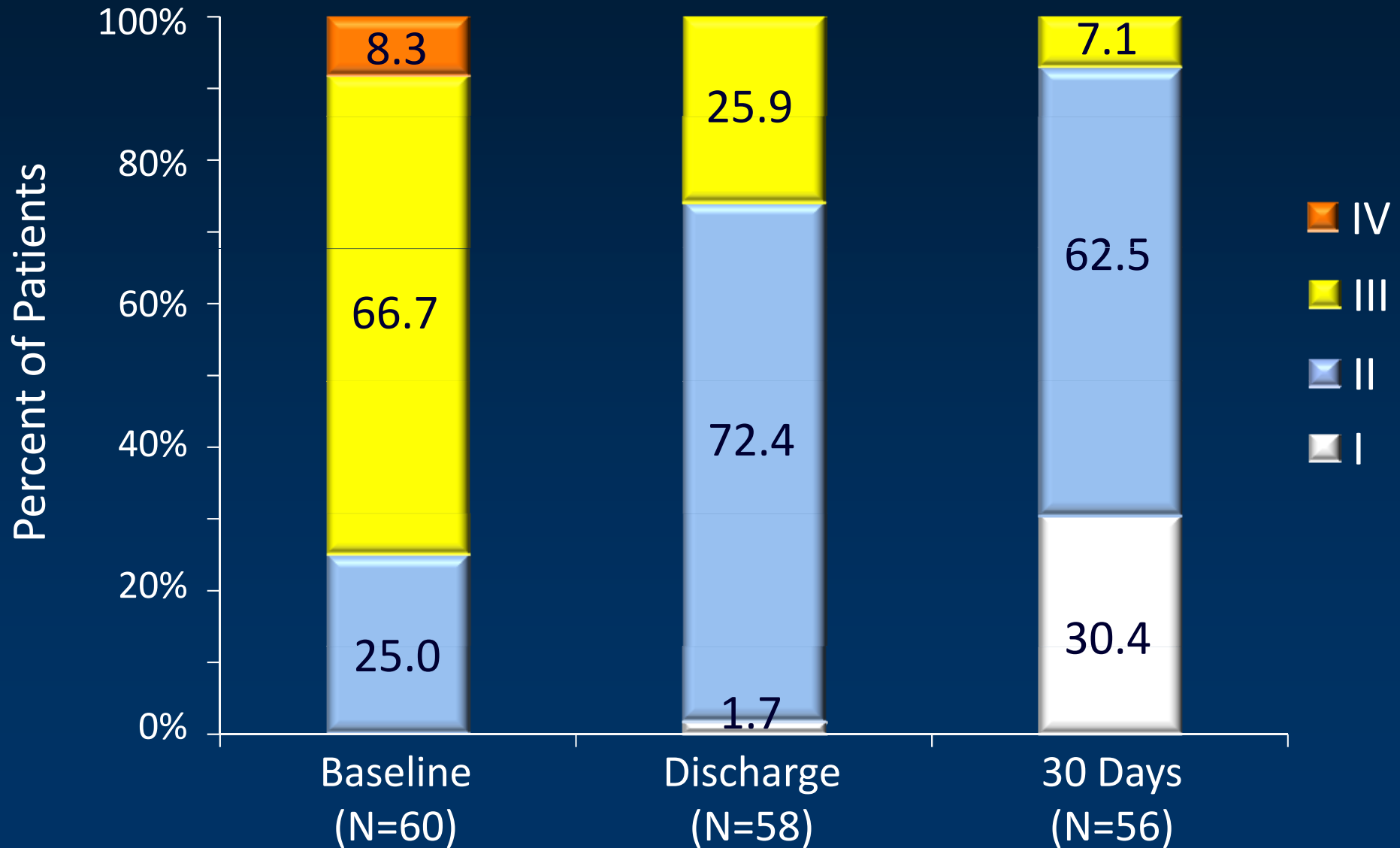
Indexed Effective Orifice Area Post Implant

REPRISE II Comparison with PARTNER Cohort A



NYHA Class Changes Over Time

REPRISE II - First 60 Patients



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ACURATE TF™ Aortic Bioprosthesis

SELF-EXPANDING NITINOL

Conforms to native anatomy
3 sizes: 21mm to 27mm

STABILIZATION ARCHES

Flexible
Self-aligning

UPPER CROWN

Supra-annular anchoring
Stable positioning
Tactile feedback

LOWER CROWN

Minimal LV protrusion
Low risk of conduction defects



PERICARDIAL LEAFLETS

Porcine pericardium
Lower profile

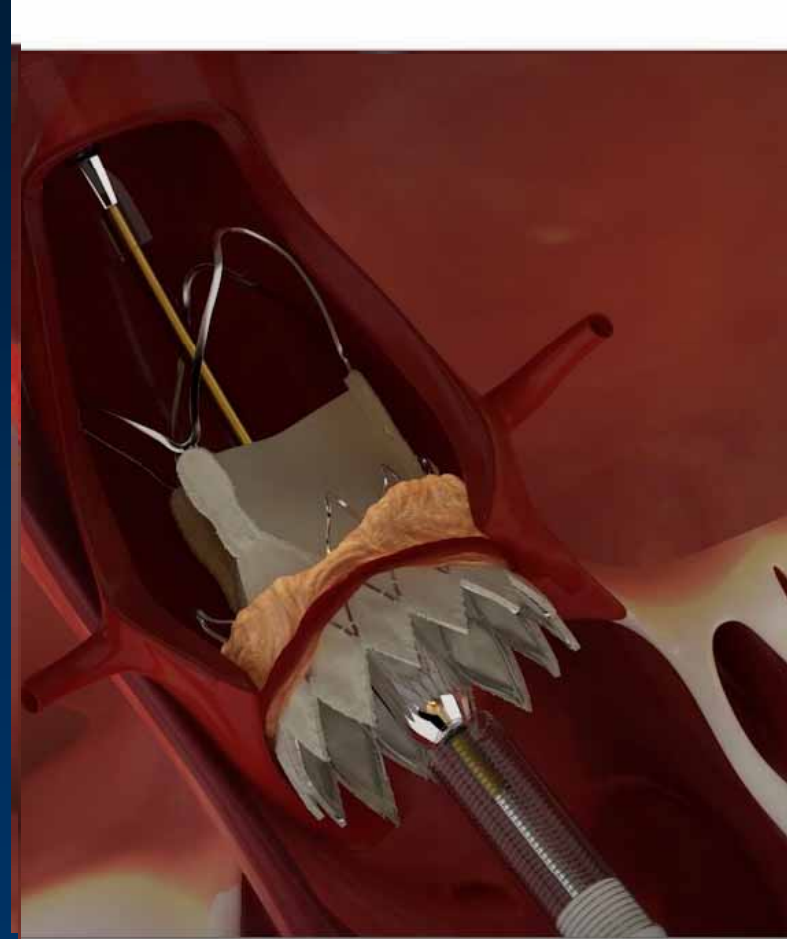
PERICARDIAL SKIRT

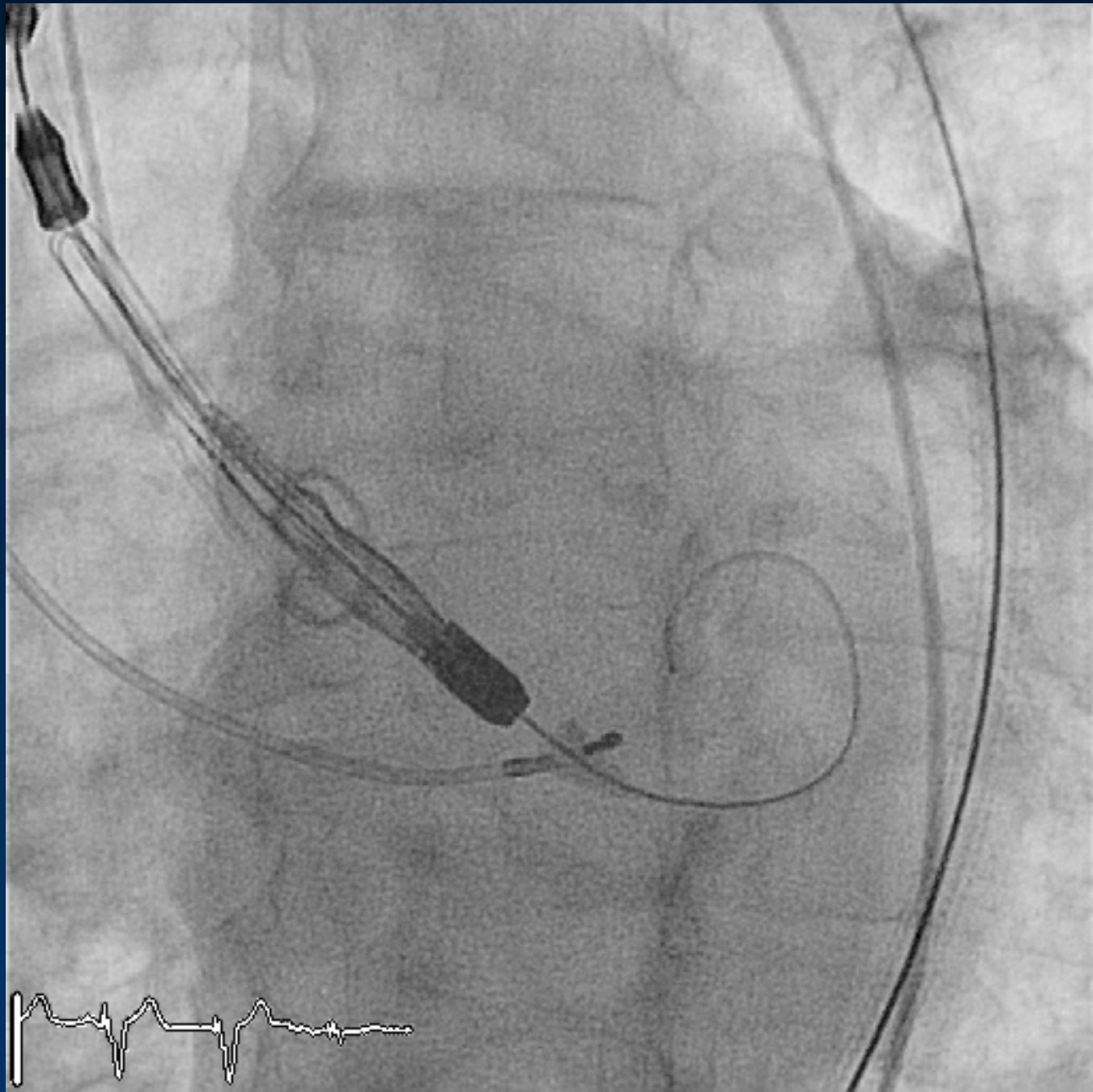
Inner & outer skirt acts as seal to prevent PVL

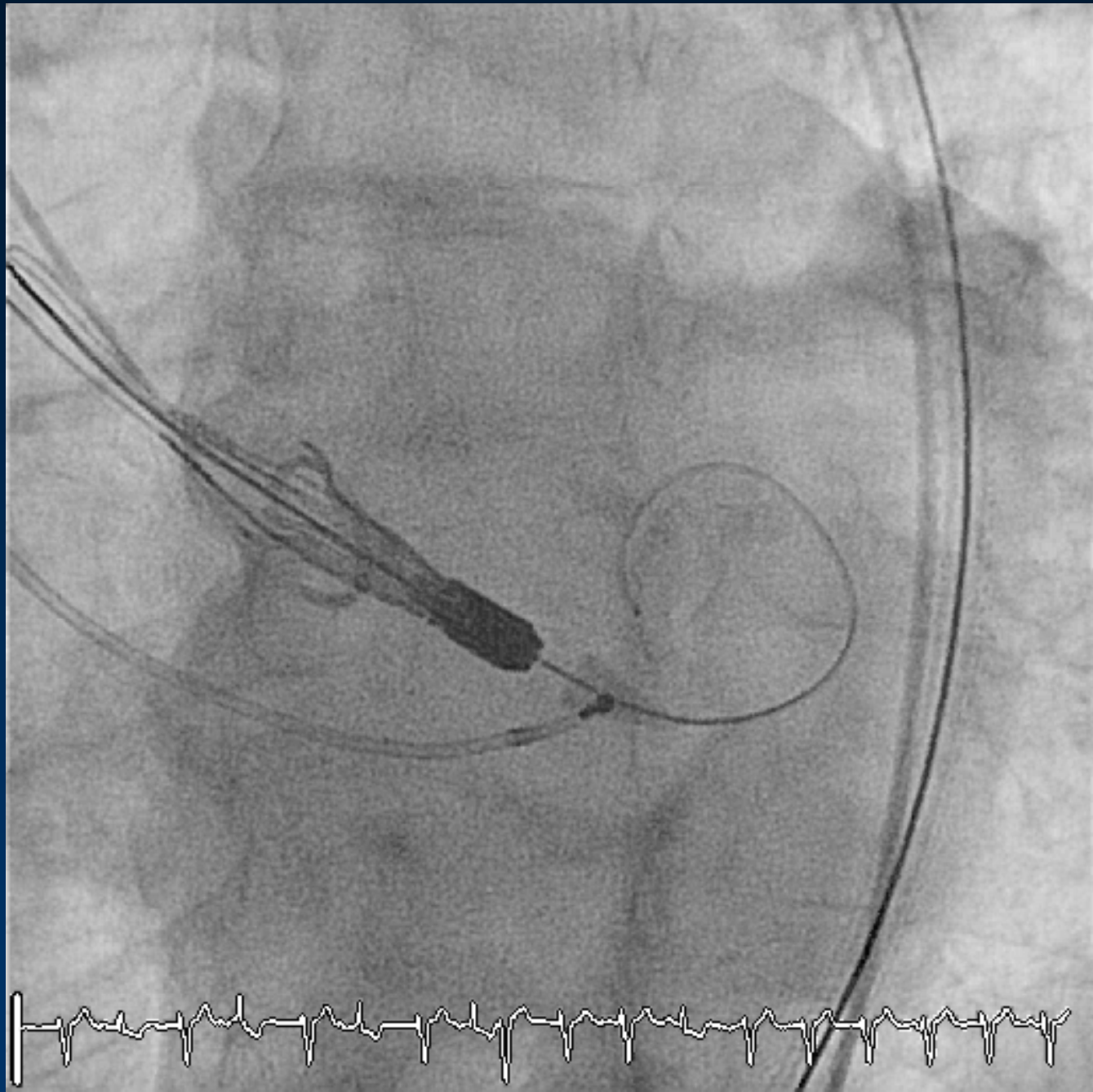
ACURATE TF™ 3-Step Implantation

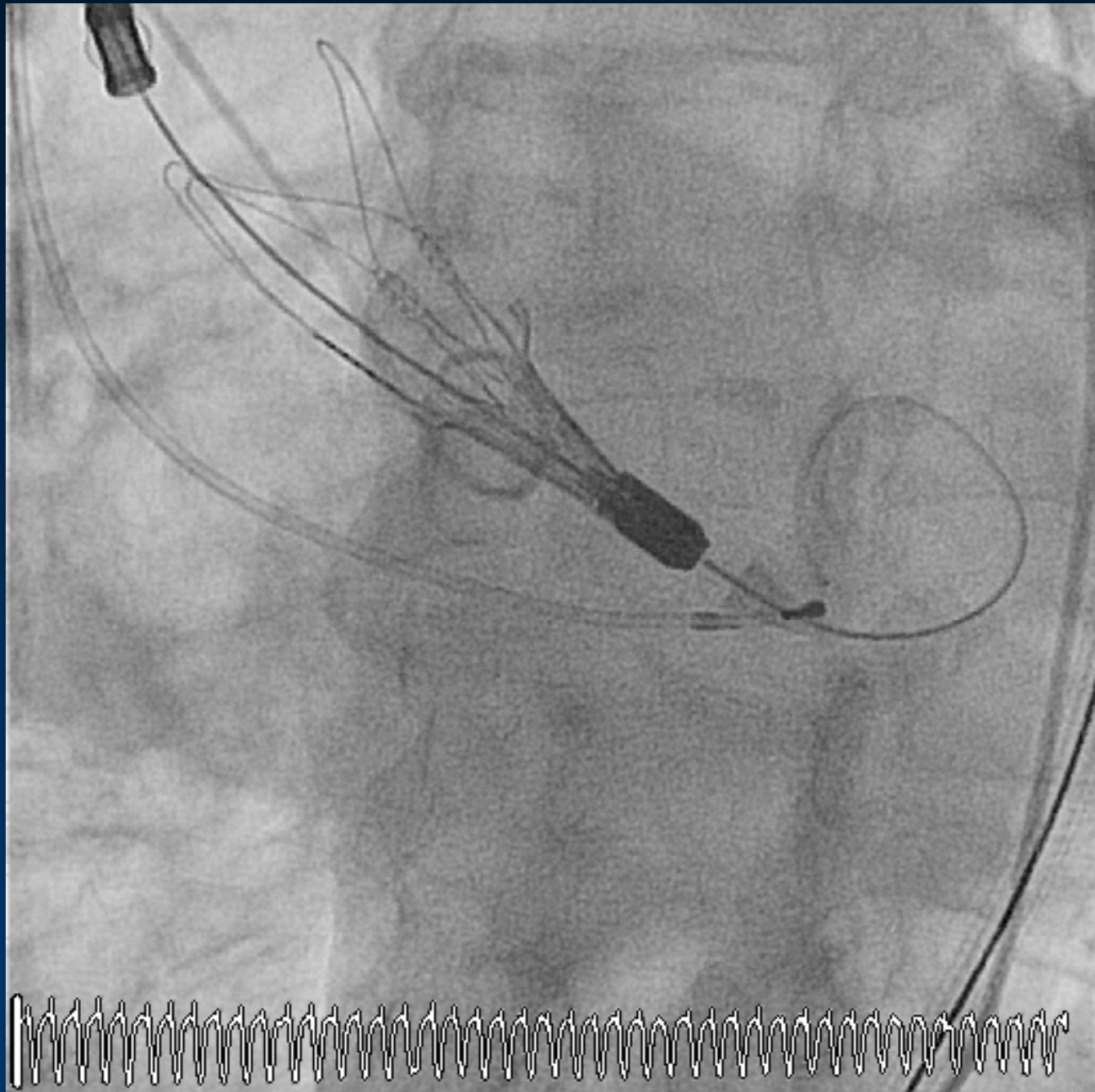
Initial Alignment

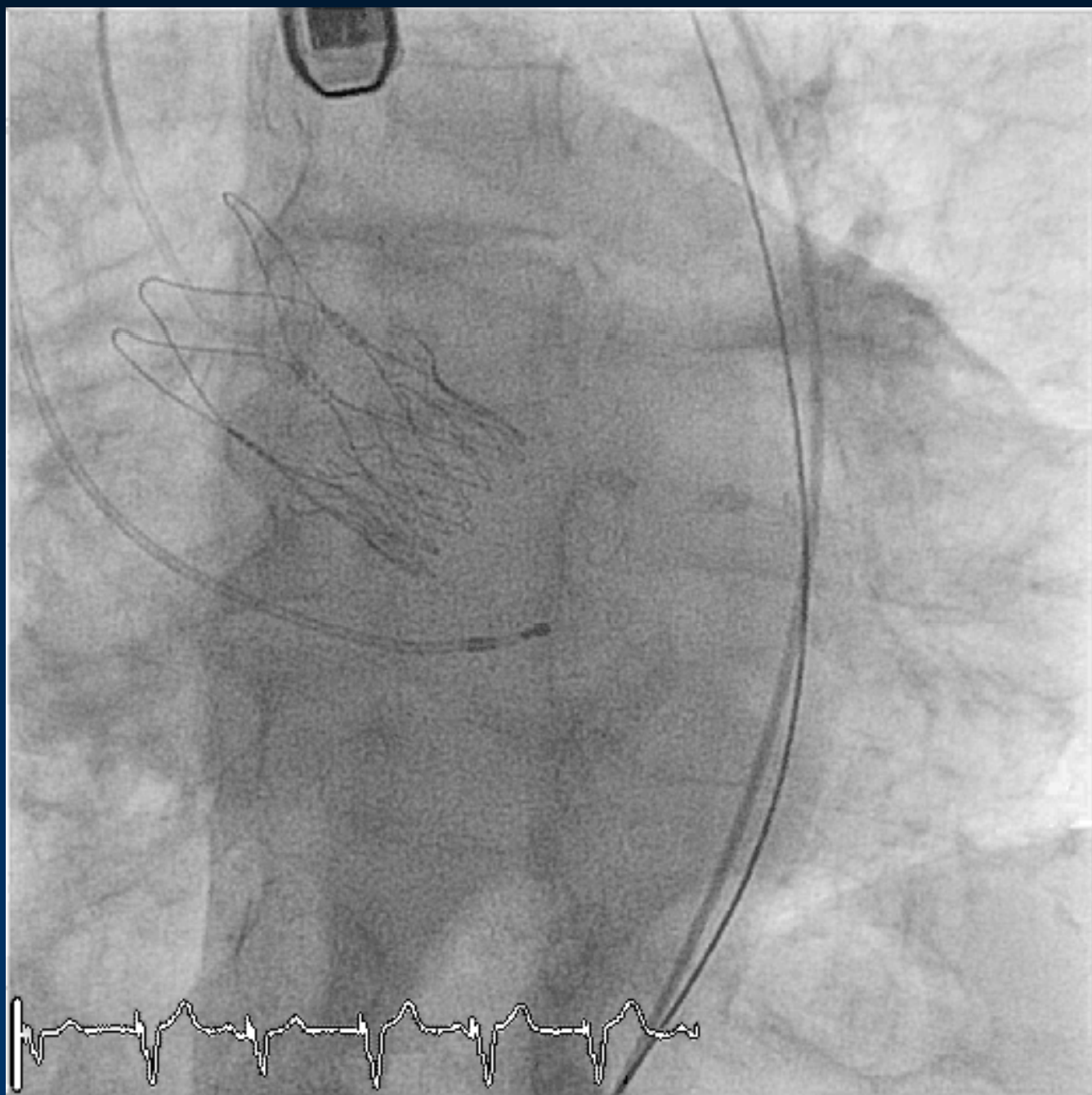
1. Open upper crown & gentle pressure forward
2. Open stabilization arches
3. Open lower crown for full deployment



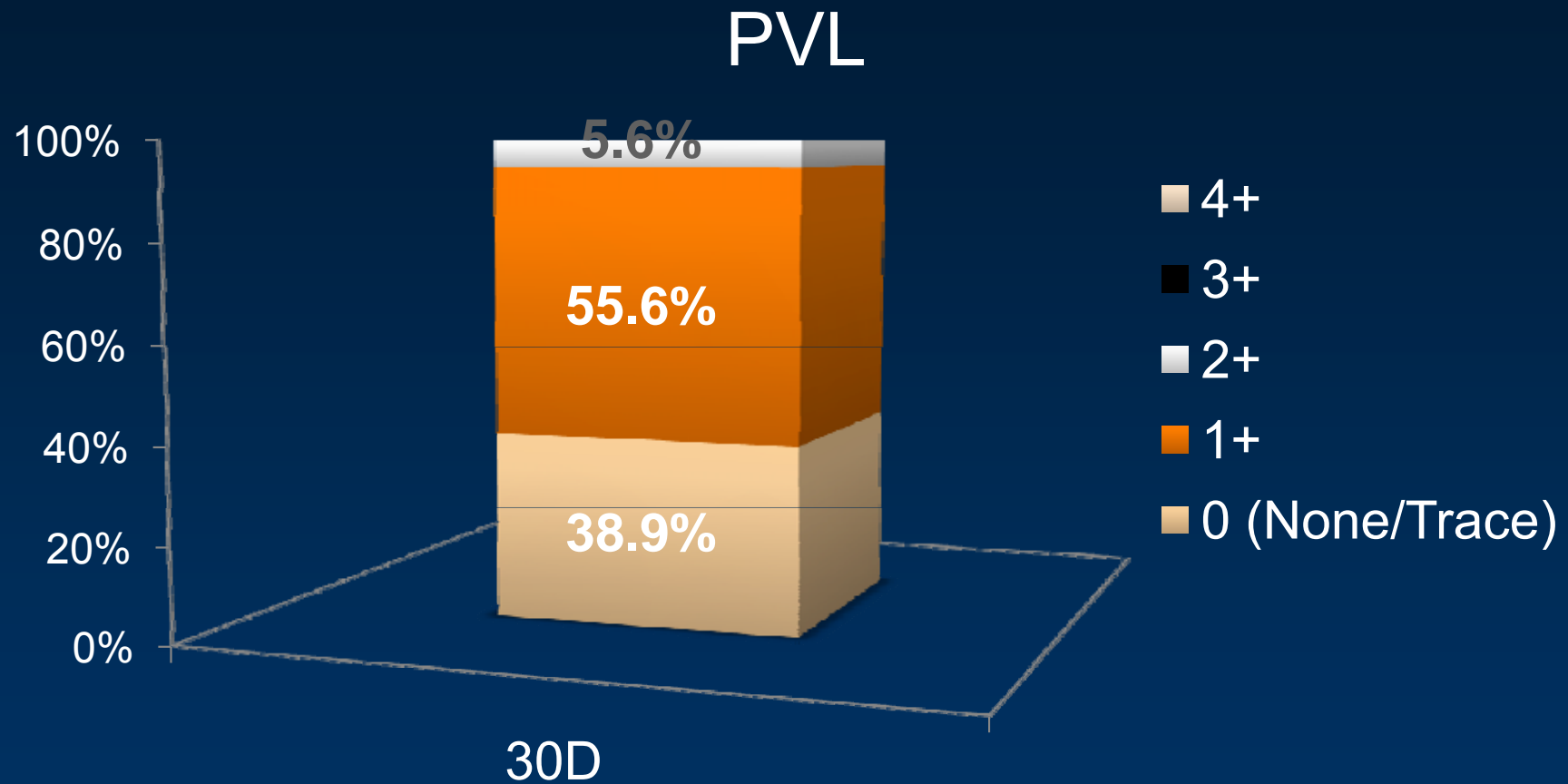








30D Paravalvular Leak



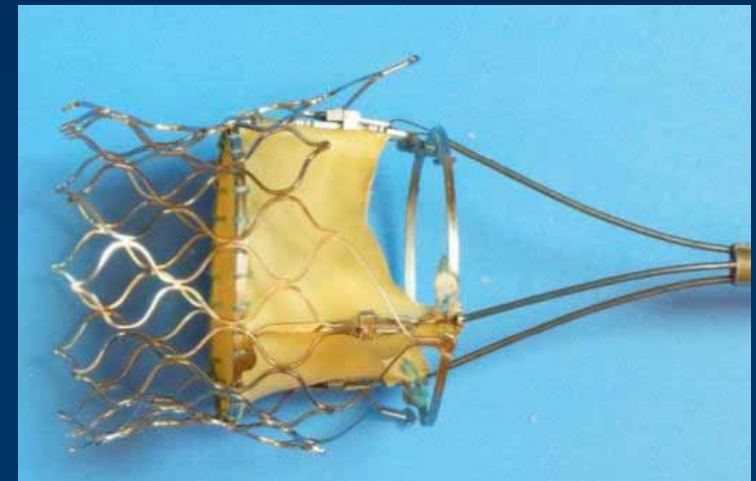
Only 1 patient with a moderate PV leak (+2)

ACURATE TF™ Take Away

- Completed TF FIM (n=20)
 - 4 different operators
 - 4 different centers
 - 3 valve sizes implanted (21 mm – 27mm)
 - Very good results at 30 days
 - Feasibility proven
- Currently enrolling in TF 50
 - LPI: JAN 2013
- TF 100 (Pivotal) to begin MAR 2013
- CE Mark submission H1 2013
- CE Mark H2 2013

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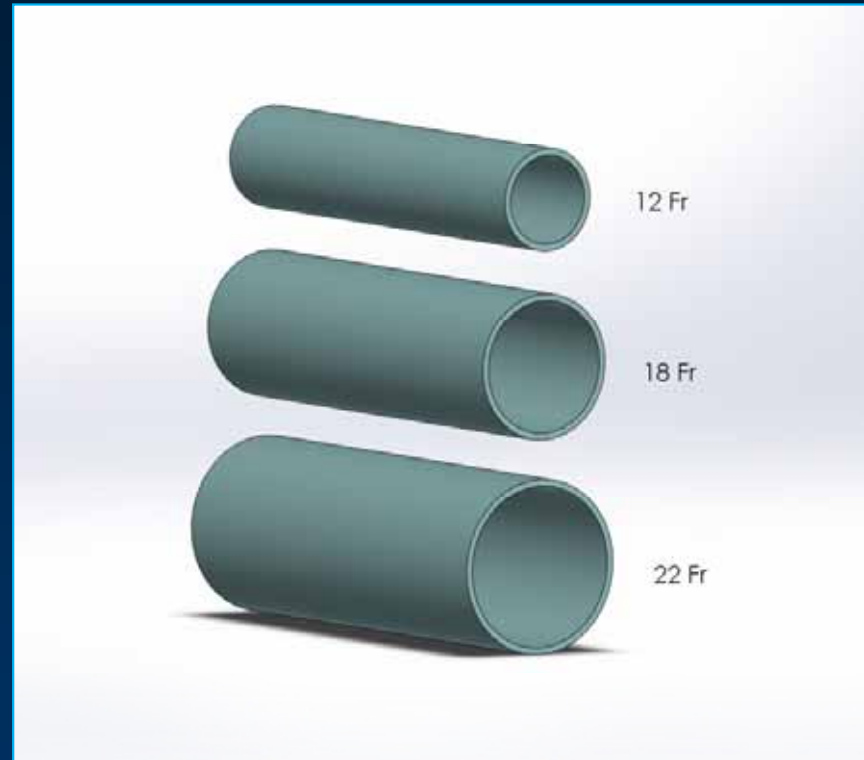


“Unique” Valve Medical Design Features

- Modular concept – frame and valve separate
- Folded valve design (not crimped)
- 3-D valve leaflet construction (single piece)
- *In-situ* docking (valve to frame in ascending Ao)
- Coating to reduce Para-valvular regurgitation
- Temporary valve (in descending Ao) for safety
- Ultra-low profile – 12 Fr delivery system (1st gen)

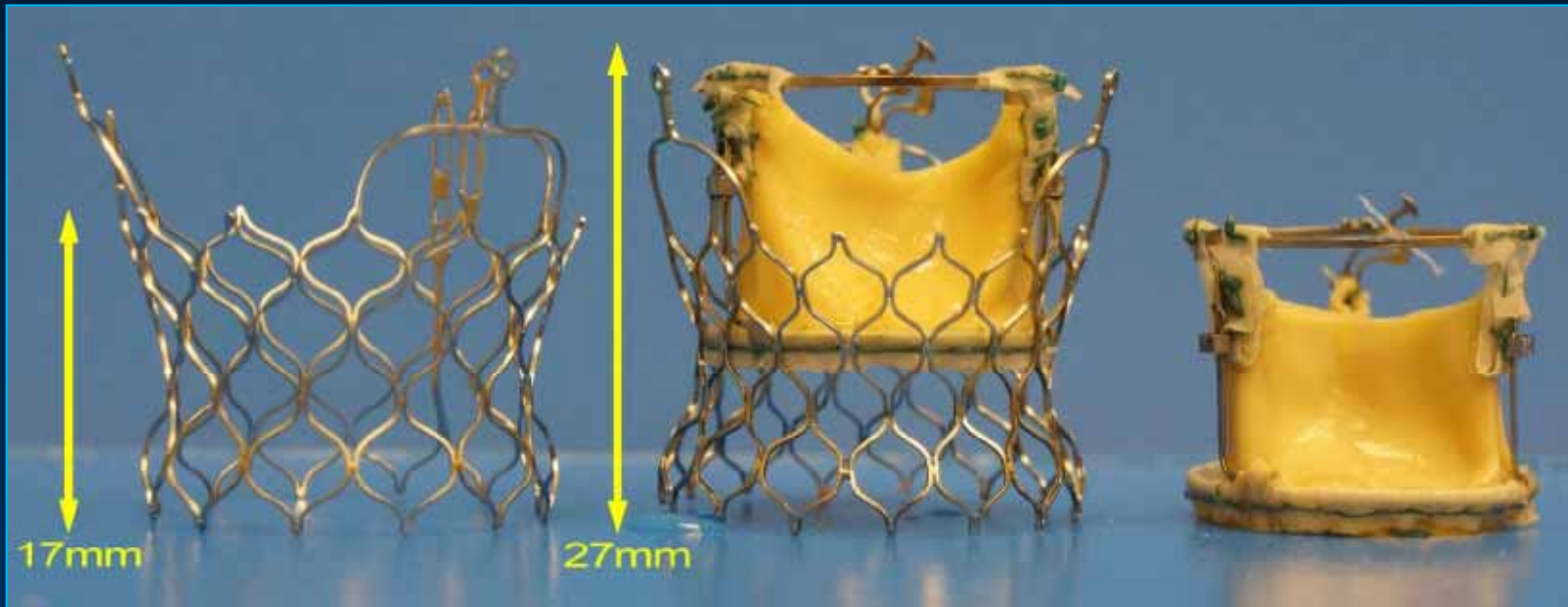
Valve Medical TAVI

An Ultra-low Profile System



- *True 12Fr (catheter O.D.) profile (3.8 mm diameter) for all valve sizes (1st generation)*

Device Components



Frame Module



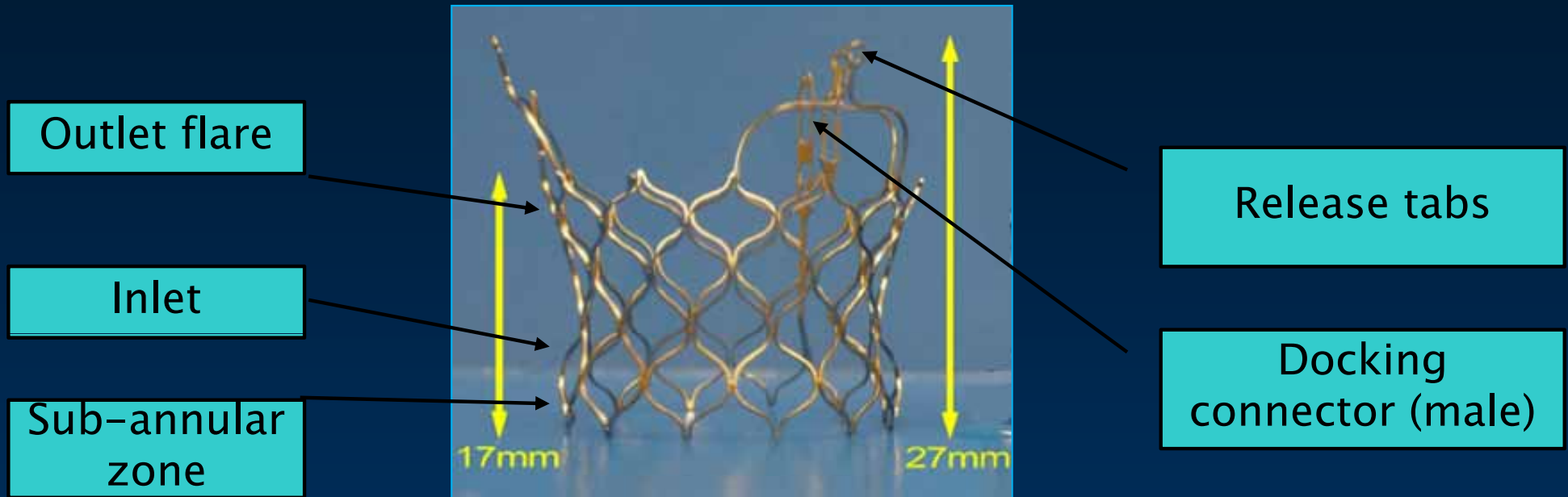
Assembled Device



Valve Module

1. Nitinol self-expanding frame module inserted in optimal annular location
2. Valve module is reconstituted in ascending Ao
3. Valve module is docked to frame

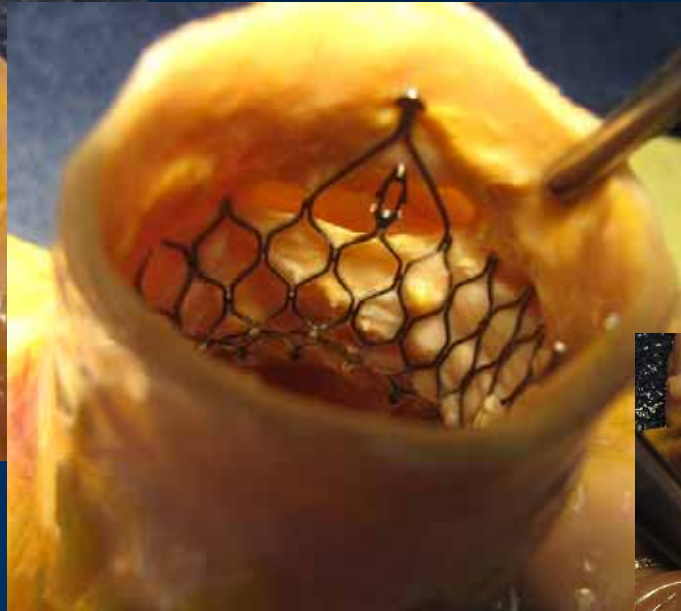
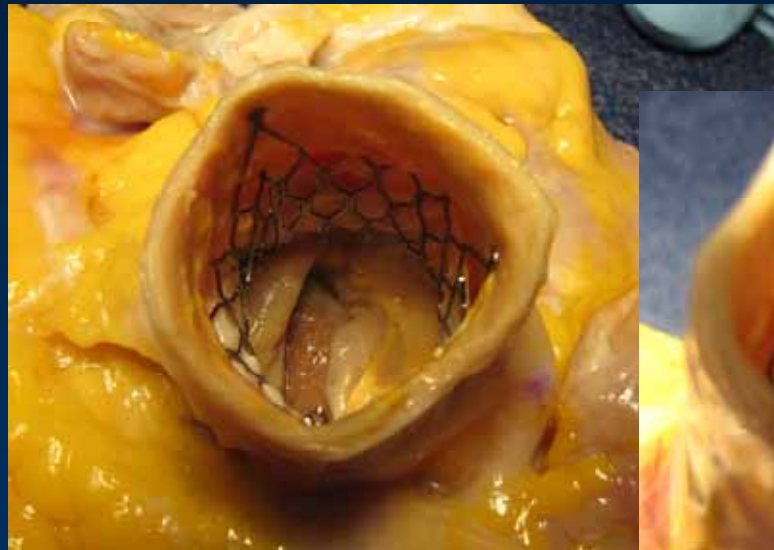
Frame Module



- Displaces native leaflets & anchors device
- Nitinol & encapsulated polymer coating
- Shape is optimized to conform to anatomy (sub-annular fixation to reduce PVL)

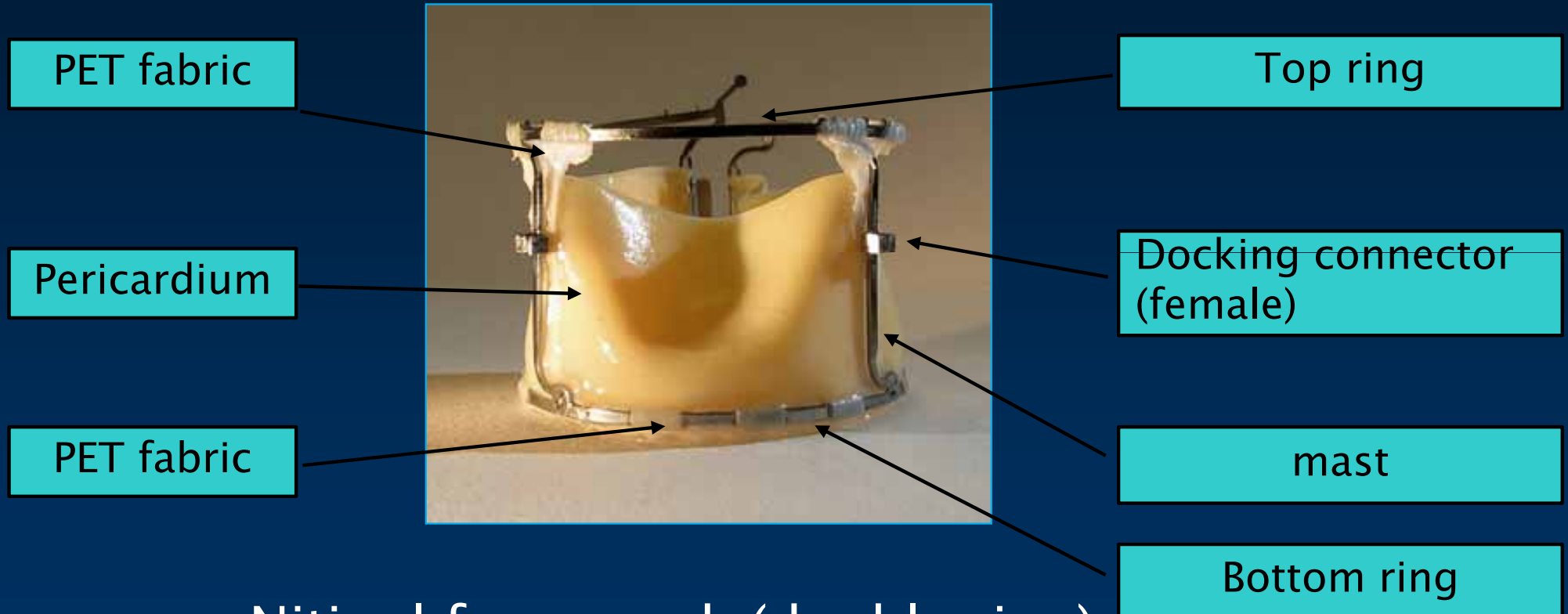
Frame Module Testing in Cadaver AS Specimens

Ex-vivo frame shape study



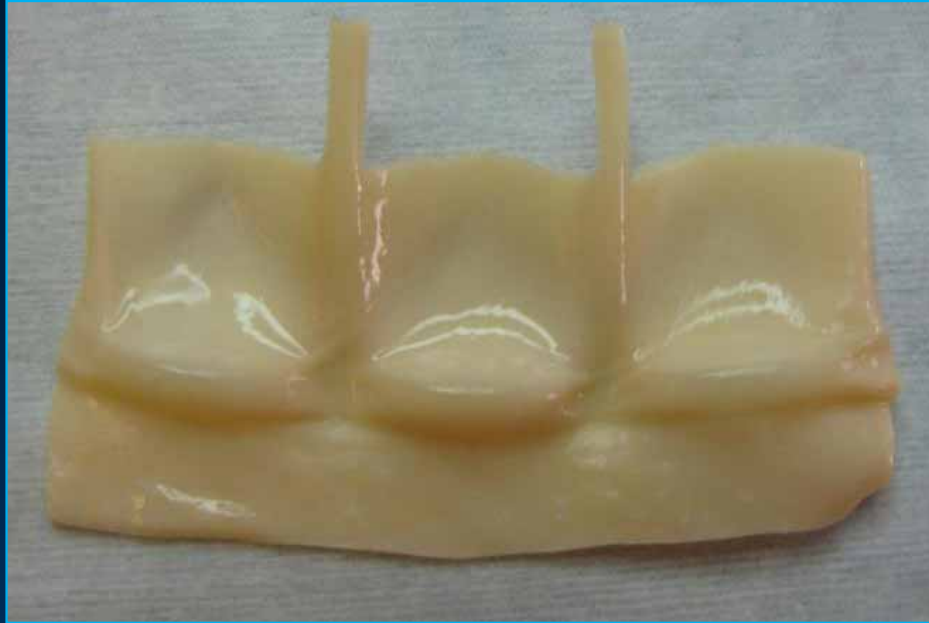
Seattle Science Foundation
(Mark Reisman and John Webb)

Valve Module



- Nitinol framework (double ring)
- Bovine pericardium (full thickness)
- PET fabric (valve sewn to PET)

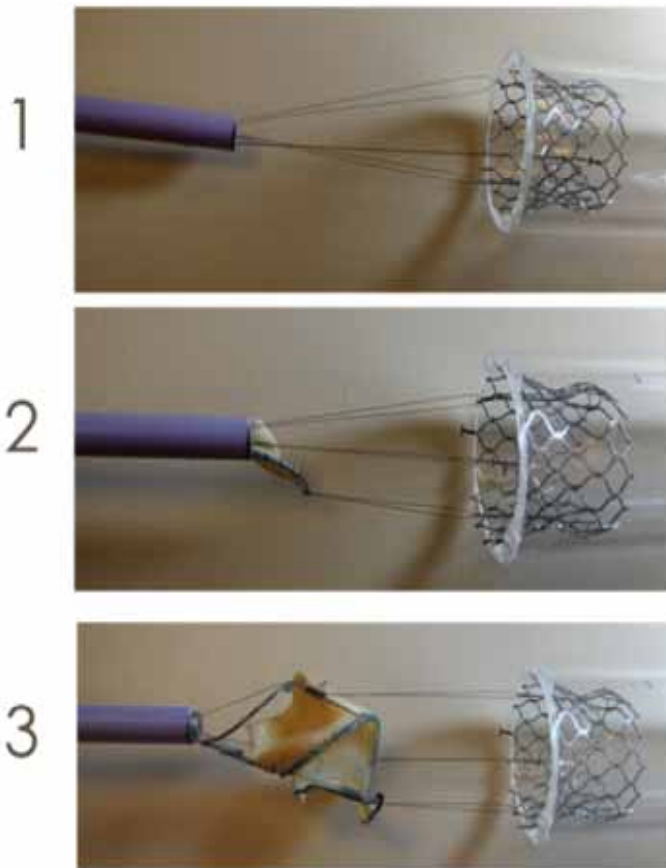
3-D Valve Leaflets



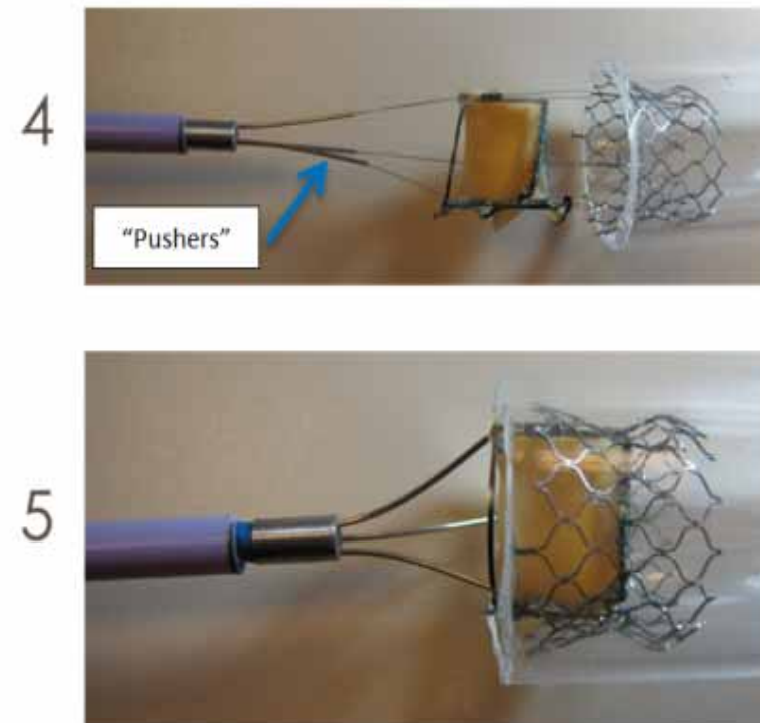
- Single piece of pericardium is fixed 3D on a mandrel
- Fewer stitches → improved manufacturability and durability
- Enhanced coaptation → wider opening and improved hemodynamics
- Full thickness bovine pericardium (500 microns)

Frame and Valve Module Docking and Assembly

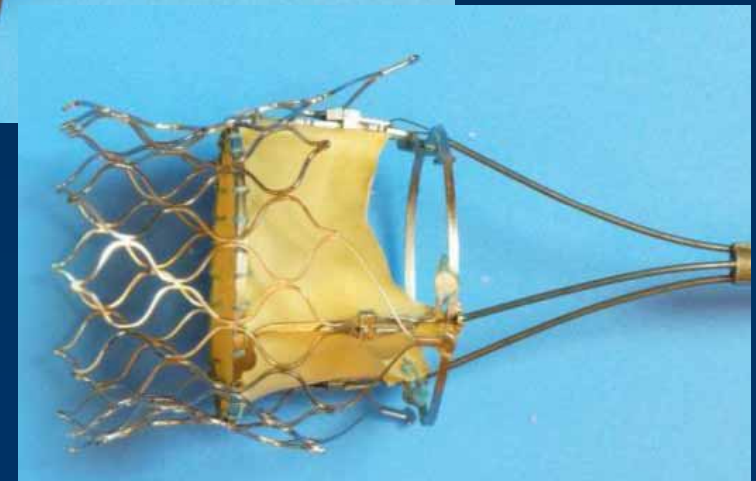
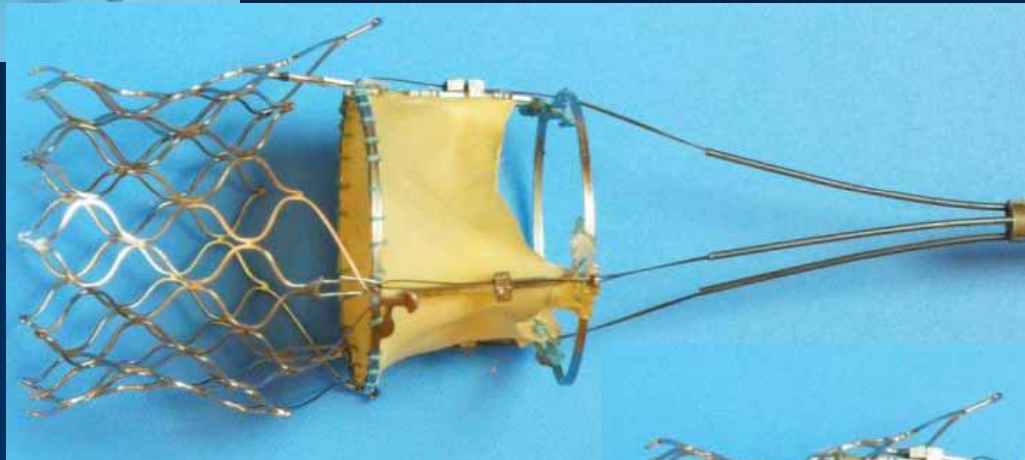
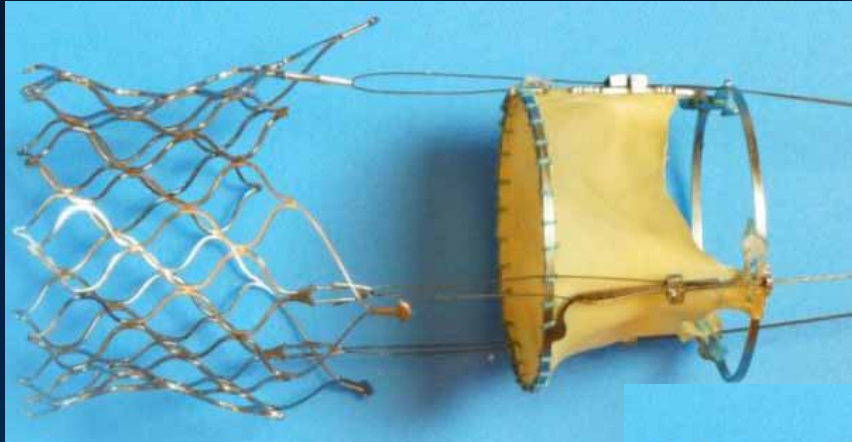
Ring Release



Ring advanced on wires

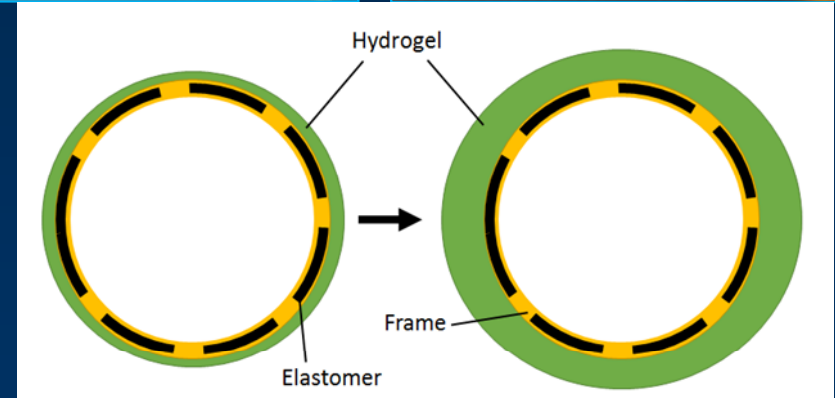
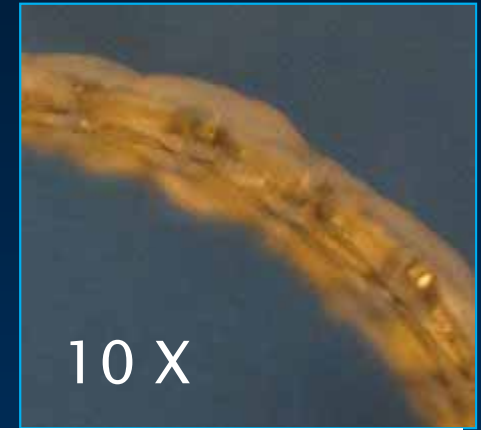
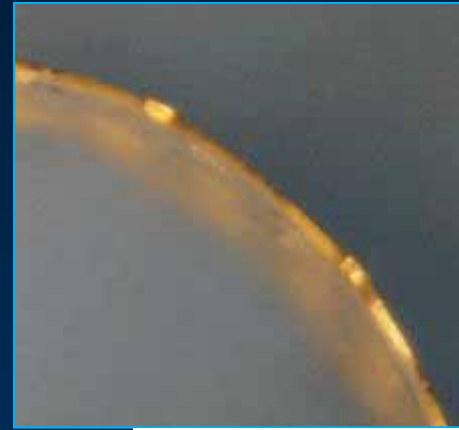


Valve Module Docking to Frame



Polymer Coating

Para-valvular leak prevention



- Two-layer polymer coat
- External hydrogel-based layer
- Frame stored dry
- Following implantation, the hydrogel swells outwards (extended “seal zone”)

Temporary Valve



- Provides patient safety; hemodynamic stabilization with transient AR during docking
- Placed in descending Ao ('Hufnagel' position)
- Incorporated into dedicated 12Fr introducer sheath
- Mono-leaflet, polymeric 'parachute' type valve

Conclusions

- A fully optimized TAVR system which addresses most of the current limitations requires a radical design change which temporarily dissociates the support frame from the valve component.
- The resulting ultra-low profile Valve Medical TAVR system (≤ 12 Fr) should provide immediate solutions to the problems of vascular access considerations, accurate valve positioning, and moderate-severe PVL.

New Generation TAVR Devices:

| | Fr Size (ID) | Reposit. | Leak | TA/ TF |
|-----------------|--------------|----------|--------|--------|
| ▪ Sapien 3 | (14) | - | ++ | Yes |
| ▪ CoreValve | 16/18 | + | ++ | No |
| ▪ Direct Flow | 18 | ++ | ++ | No |
| ▪ Portico | 18 | ++ | ++ | No |
| ▪ Sadra | 18 | +++ | +++ | No |
| ▪ Symetis | 18 | ++ | +++ | Yes |
| ▪ Valve Medical | 12 (OD) | - | (++++) | No |