

Lotus Valve System for Transcatheter Aortic Valve Implantation/Replacement (TAVI/R) Evidence



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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
Direct Flow: C, SB, AB
Mitralign: AB, SB, E
Boston Scientific: C, SB, AB
Biosensors: E, SB, C, AB
Cordis: AB
Abbott Vascular: AB
Valtech: E, SB,
Keystone: SB
Claret: E, SB

Key

G – Grant and or Research Support
C – Consulting fees, Honoraria
SB – Speaker's Bureau

E – Equity Interests
R – Royalty Income
O – Ownership

S – Salary, AB – Advisory Board
I – Intellectual Property Rights
OF – Other Financial Benefits

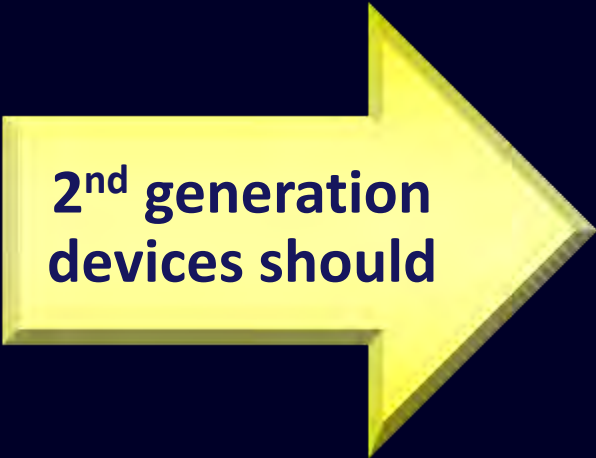
Early TAVI Devices for Severe Aortic Stenosis

Significant benefit for inoperable/high-risk patients, but...



**Current devices
have limitations**

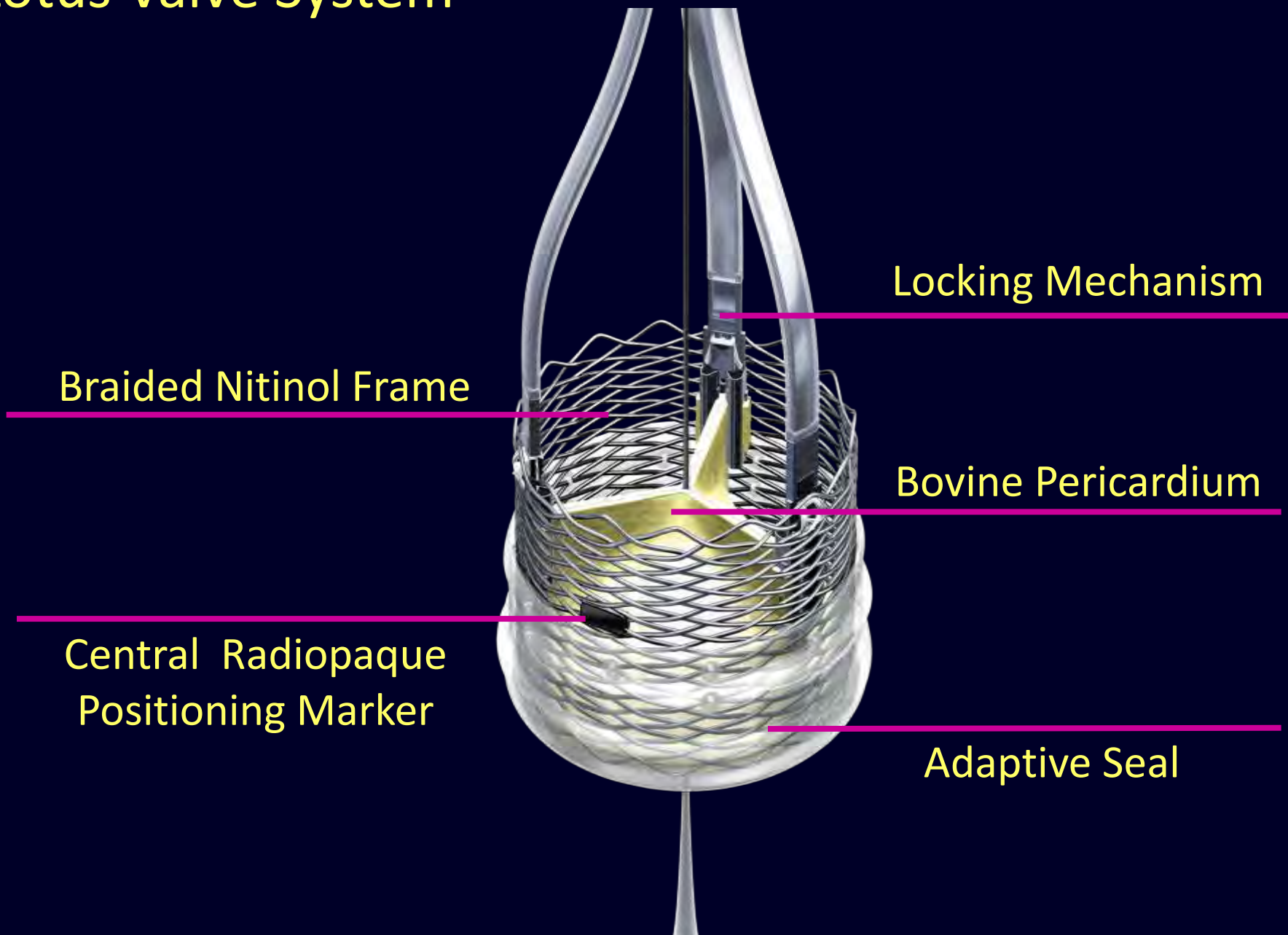
- Paravalvular regurgitation
 - Associated with increased mortality*
- Valve malpositioning
 - Valve migration, embolization, ectopic deployment, TAV-in-TAV, coronary obstruction, incomplete apposition
- Stroke



**2nd generation
devices should**

- Reduce aortic regurgitation
- Have simple, precise & atraumatic aortic/ventricular repositioning
- Allow full atraumatic retrieval

Lotus Valve System



Locking Mechanism

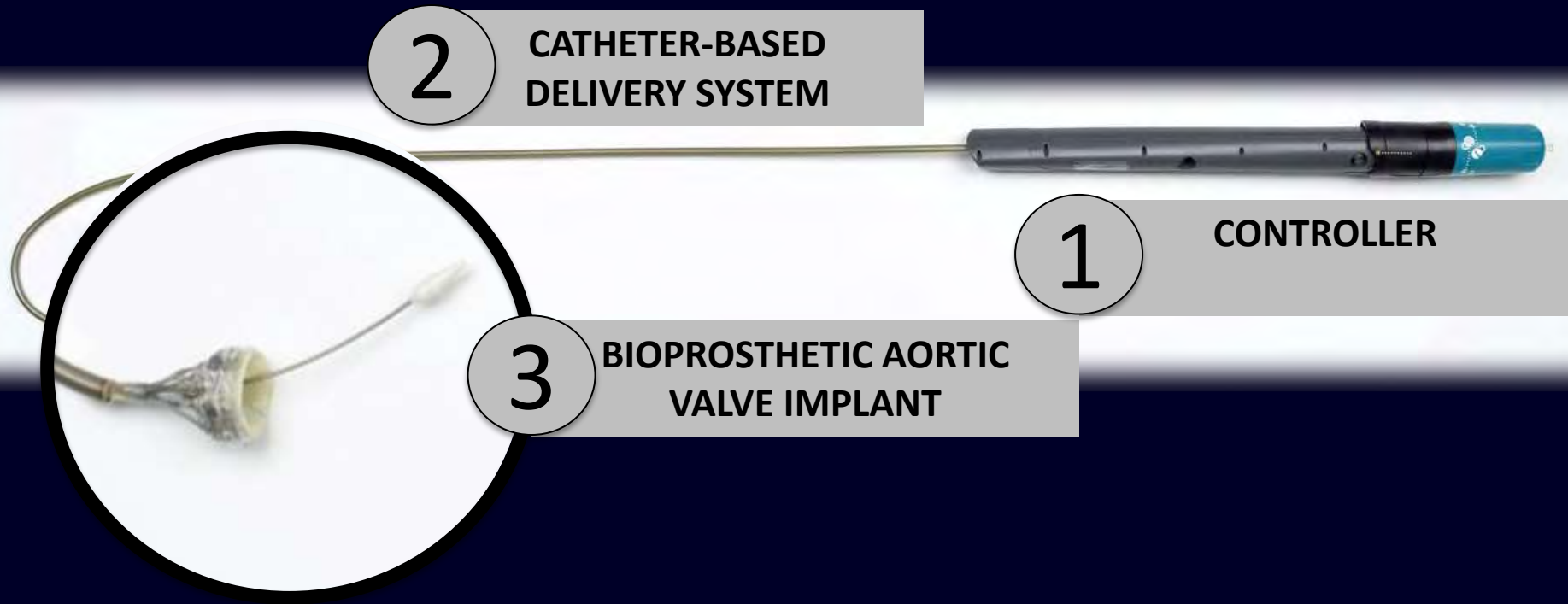
Braided Nitinol Frame

Bovine Pericardium

Central Radiopaque
Positioning Marker

Adaptive Seal

Lotus Valve System Overview



2 CATHETER-BASED DELIVERY SYSTEM

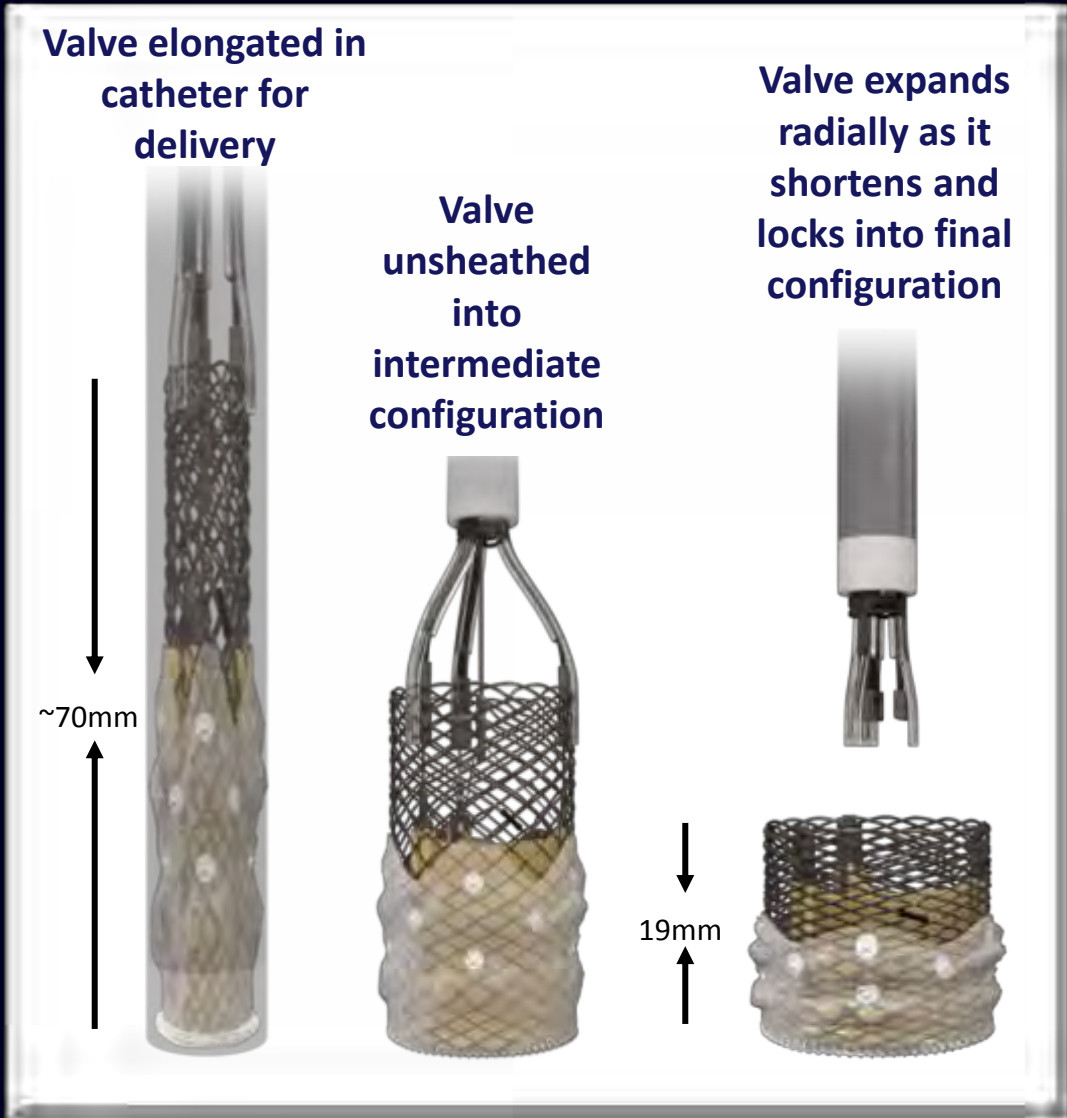
1 CONTROLLER

3 BIOPROSTHETIC AORTIC VALVE IMPLANT

LOTUS VALVE IS PRE-ATTACHED TO DELIVERY SYSTEM

Lotus Valve System Design Goals

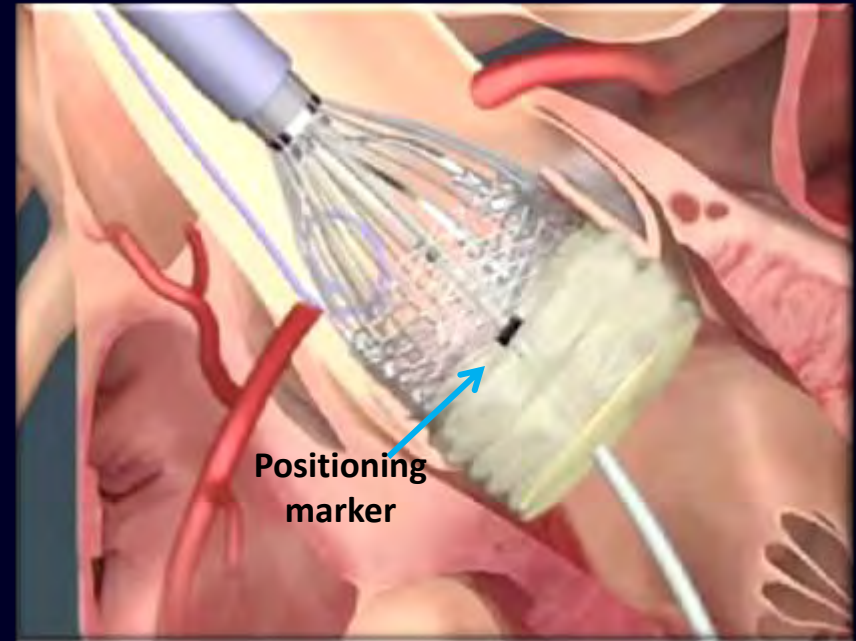
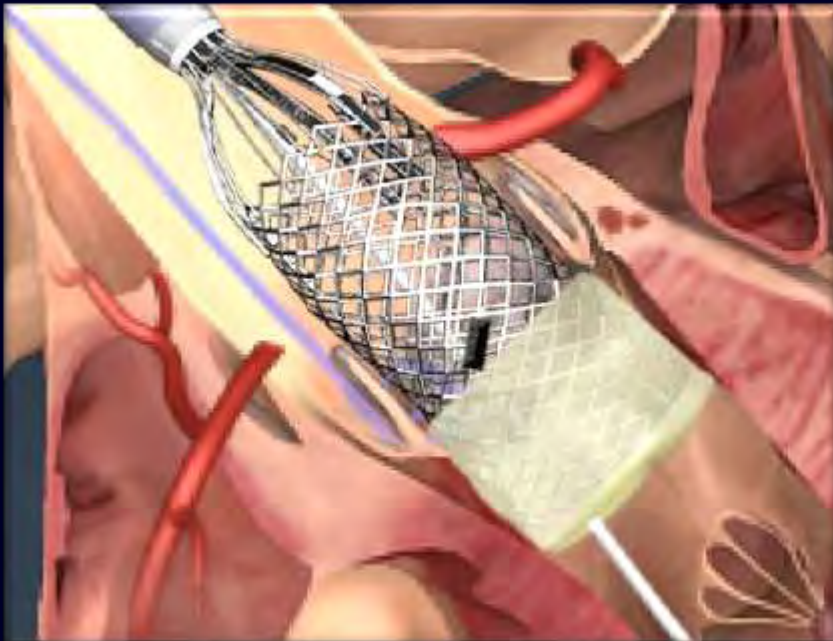
Controlled Mechanical Expansion



- Valve deployed via controlled mechanical expansion.
- No rapid pacing during deployment
- Valve functions early enabling controlled deployment
- No valve movement on release

Lotus Valve System Design Goals

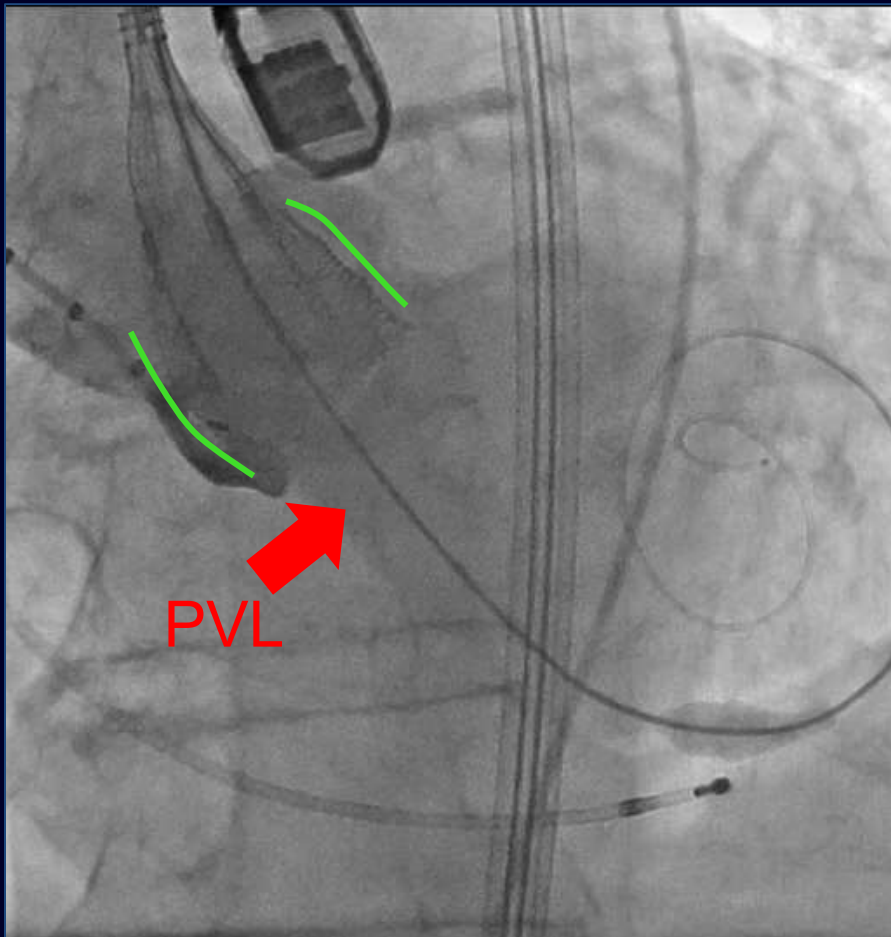
Controlled, Accurate, and Predictable Positioning



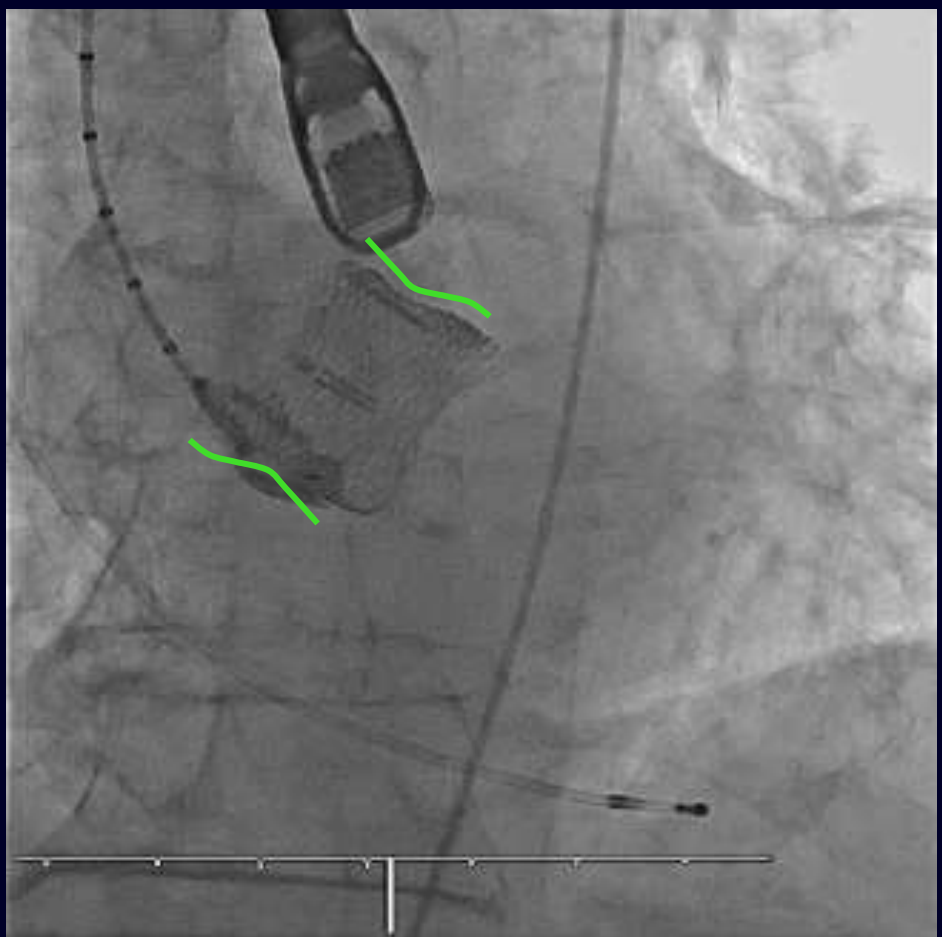
- Central radiopaque positioning marker to guide placement
- Valve is repositionable throughout entire deployment process
- Ability to assess valve in final position
 - Valve still repositionable & retrievable prior to release

REPRISE II Case Example

23mm Lotus Valve Retrieval and Exchange for 27mm Valve



23 mm

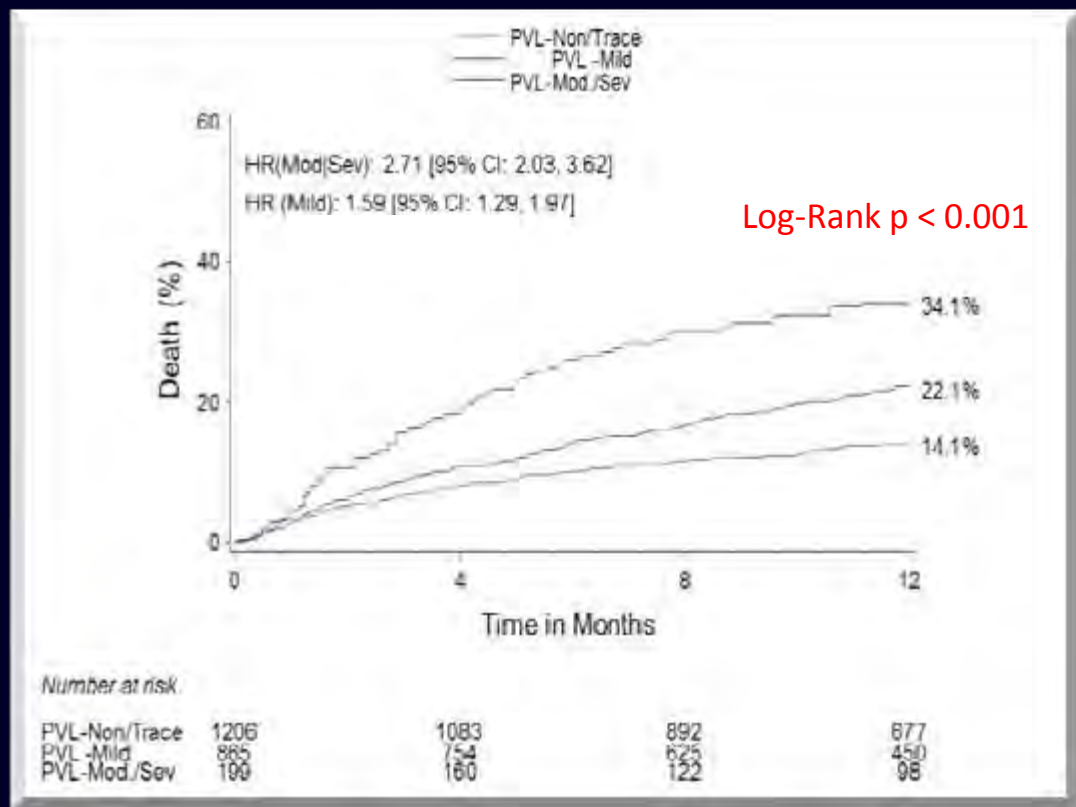


27 mm

Images courtesy of Ian Meredith AM, MBBS, PhD

PVL is a Significant Predictor of Mortality

PARTNER Trial 1-Year Outcomes Stratified by PVL

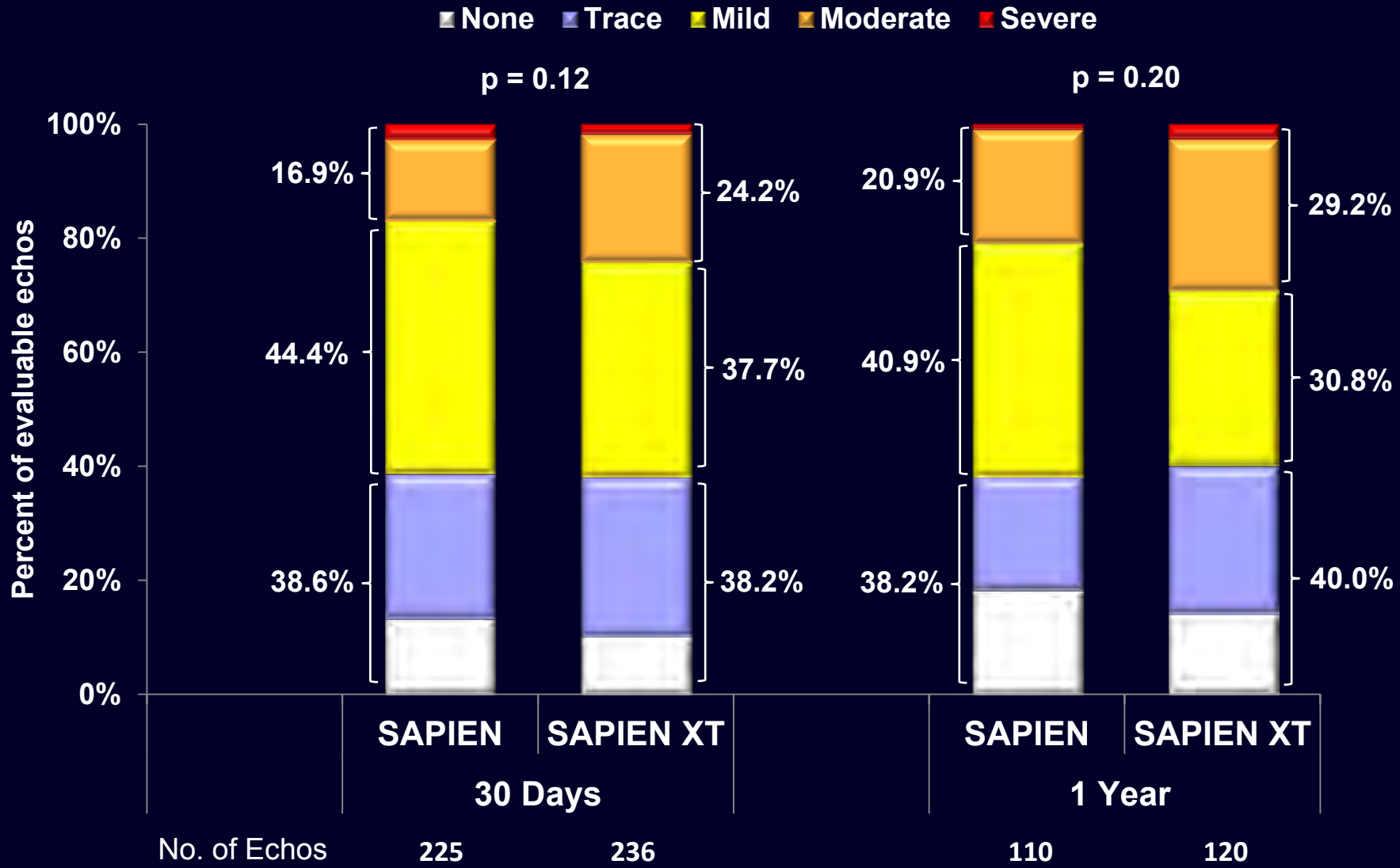


Multivariate Analysis – Predictors of One Year Mortality

Variable	Hazard Ratio	P Value
PVL (Mild vs. None/Trace)	1.47 [1.14, 1.90]	p=0.0034
PVL (Mod/Severe vs. None/Trace)	HR=2.38 [1.69, 3.35]	p<0.0001

PVL in 1st Generation TAVI Systems

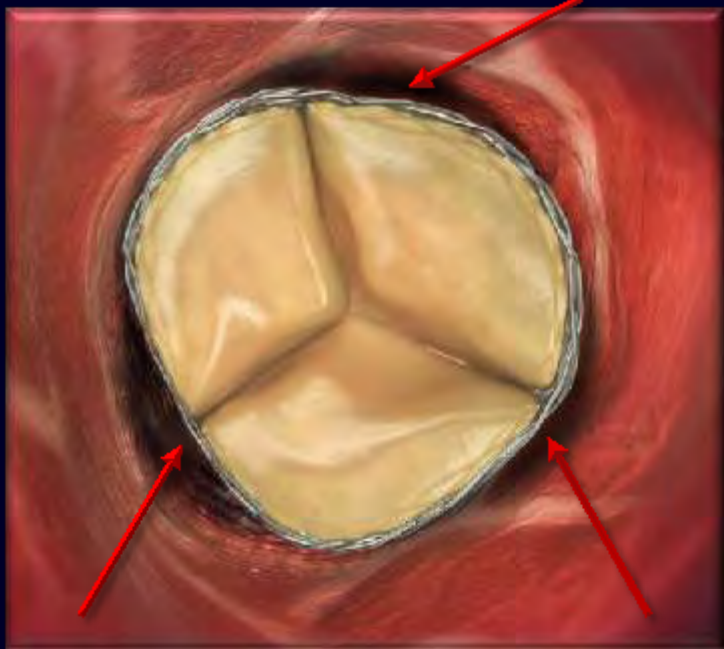
PARTNER II Trial



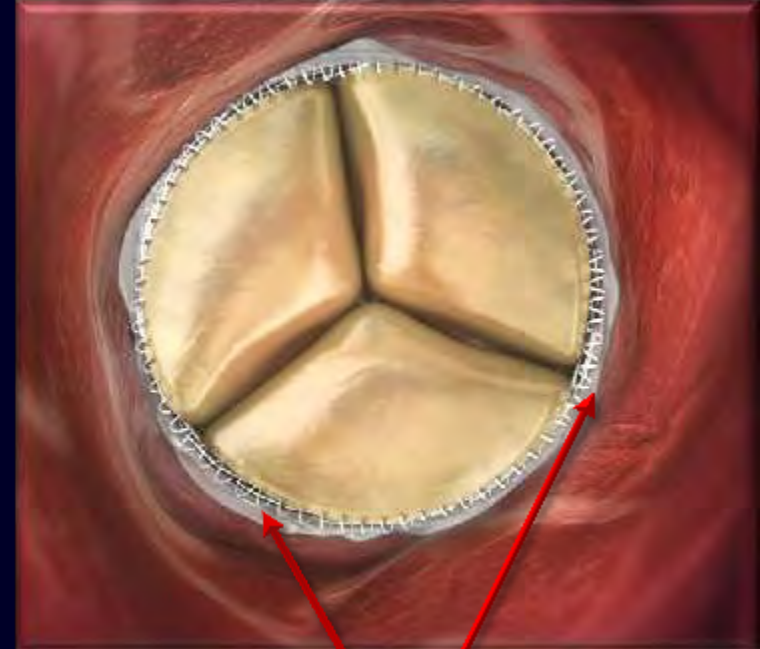
Presented by Martin Leon, MD at ACC 2013

Lotus Valve System Design Goals

Minimize Paravalvular Leak (PVL)



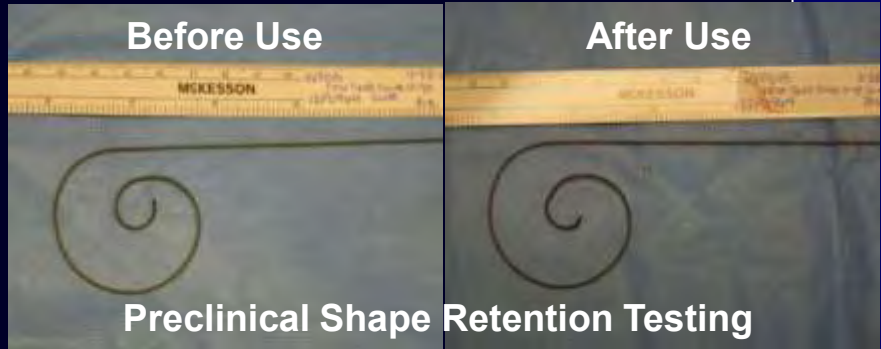
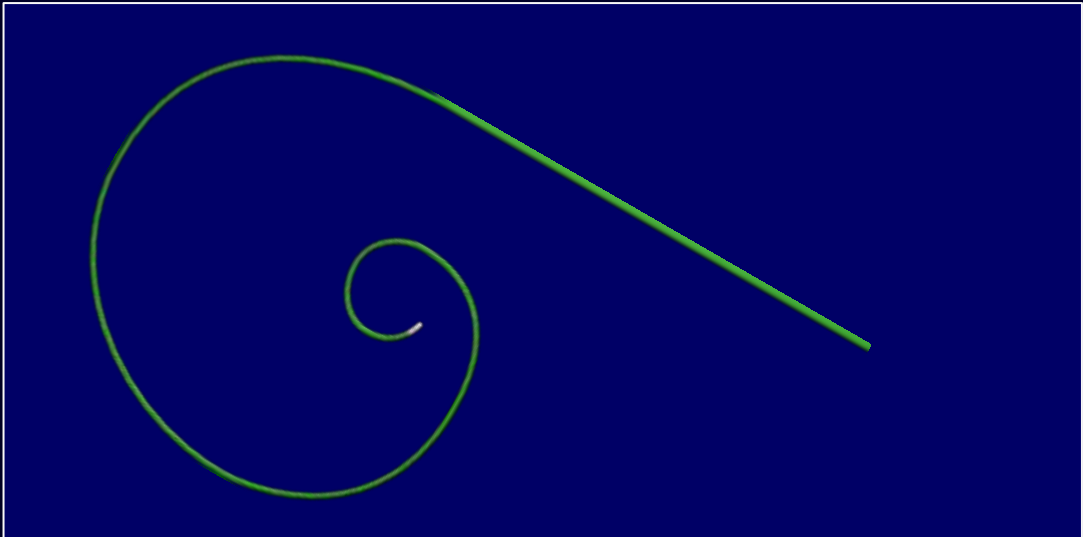
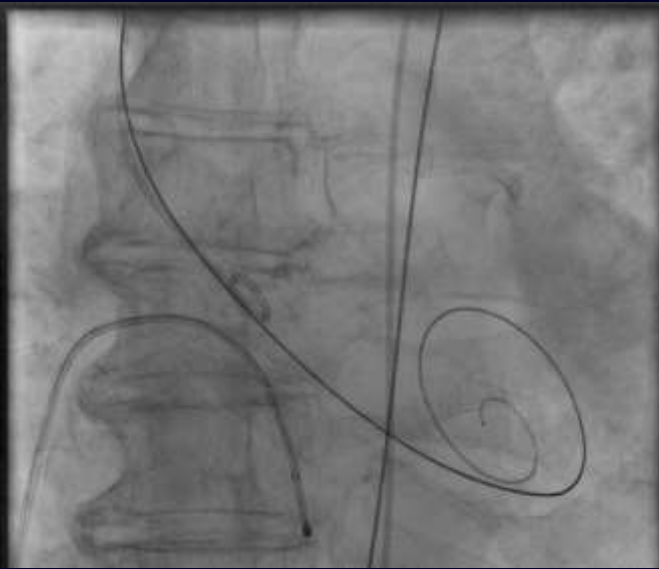
Non – Circular Annulus
+
Irregular Calcification
=
PVL



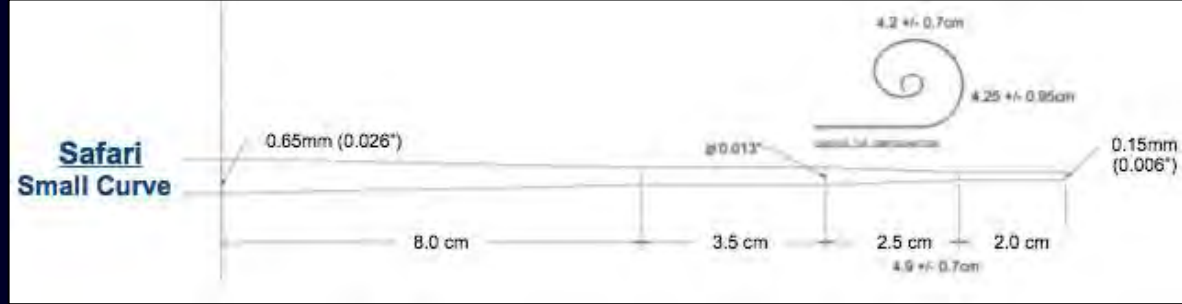
Adaptive
Seal

Adaptive seal to mitigate PVL

Safari Guidewire



- Pre-shaped architecture designed for consistent, reliable performance
- Double curve designed to facilitate stable, atraumatic placement
- PTFE coating allows for less force during device delivery



- Two curve sizes accommodate varying anatomies and systolic contractions of left ventricle

LOTUS Clinical Program

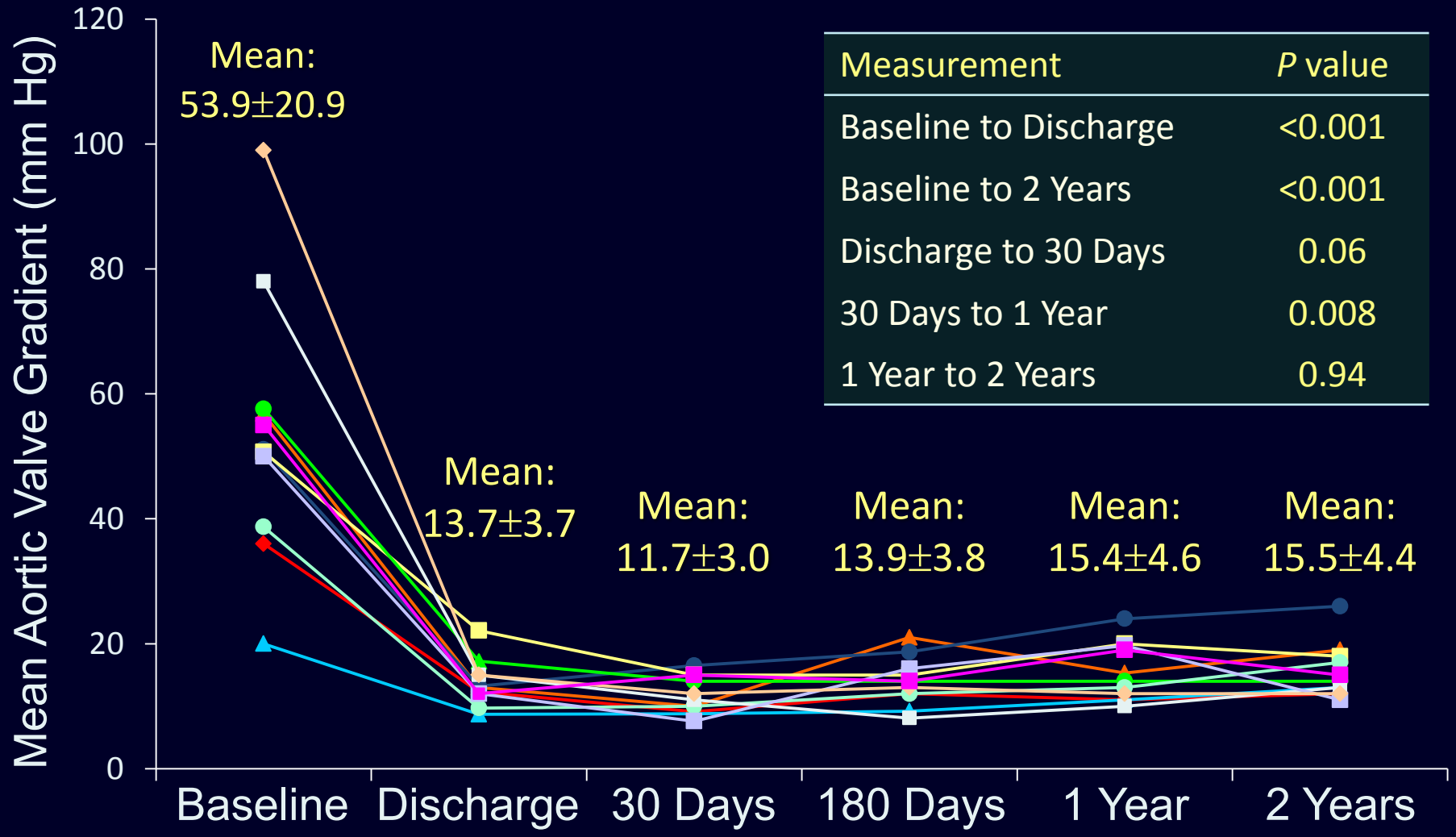


LOTUS Clinical Program



Mean Aortic Valve Gradient by Patient

REPRISE I

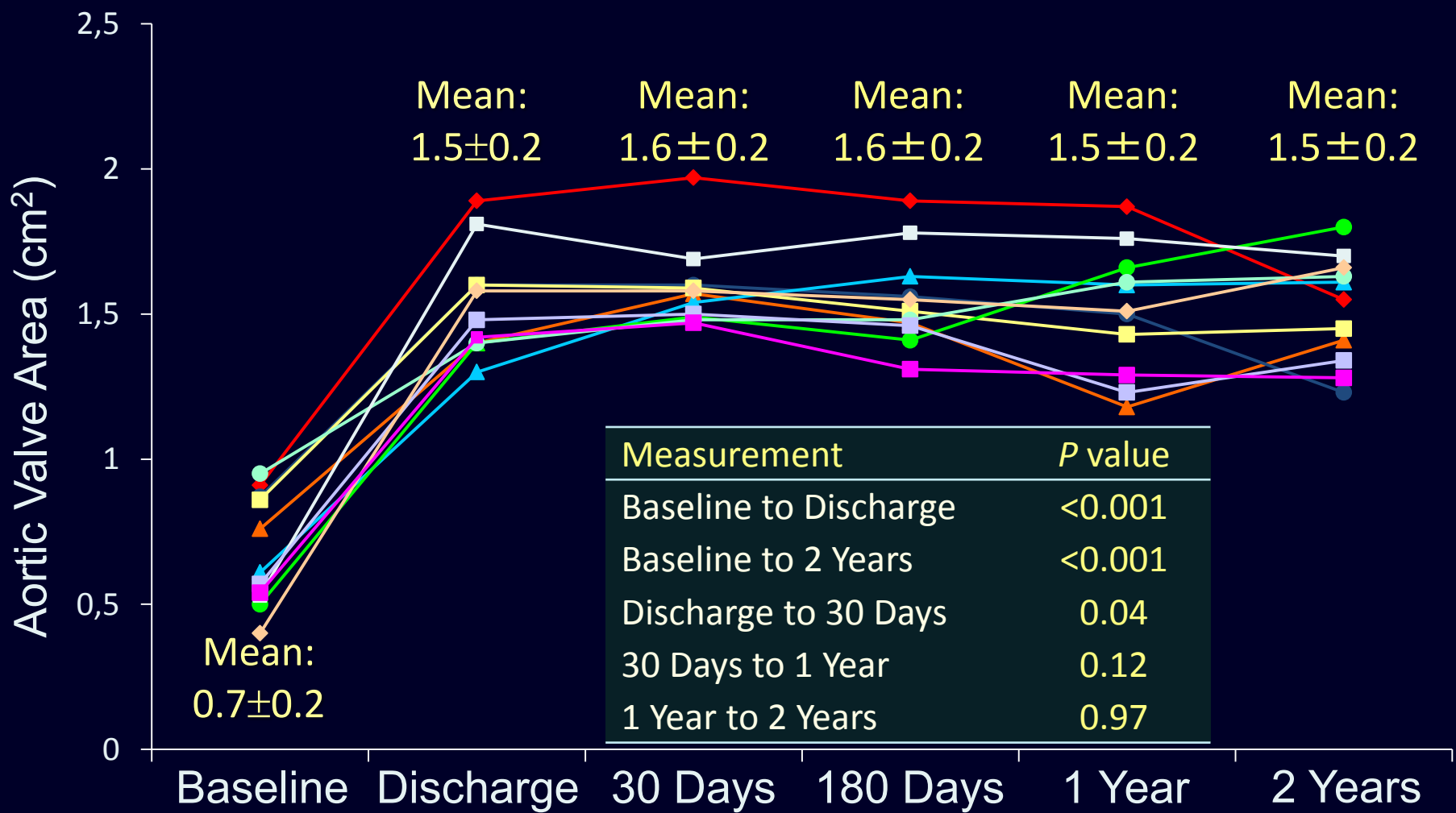


Independent Core Lab Adjudication

Ian Meredith, TCT 2014. *P* values: Repeated measures and random effects ANOVA model

Effective Orifice Area by Patient

REPRISE I



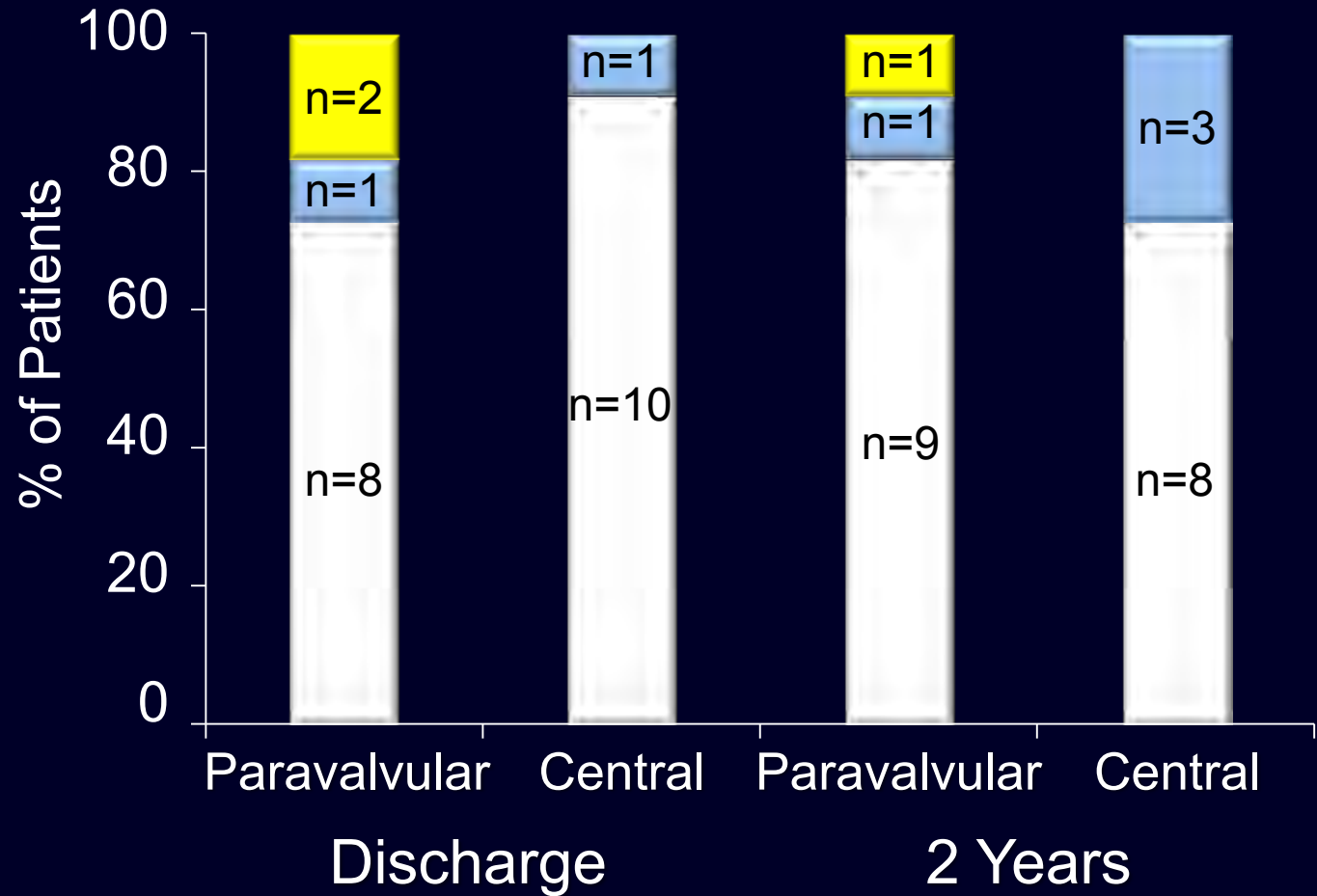
Ian Meredith, TCT 2014. All valve sizes were 23 mm.
 P values: Repeated measures and random effects ANOVA model

Independent Core Lab Adjudication

REPRISE 1 – Aortic Regurgitation

Transthoracic Echocardiography

- Severe
- Moderate
- Mild
- Trivial
- None



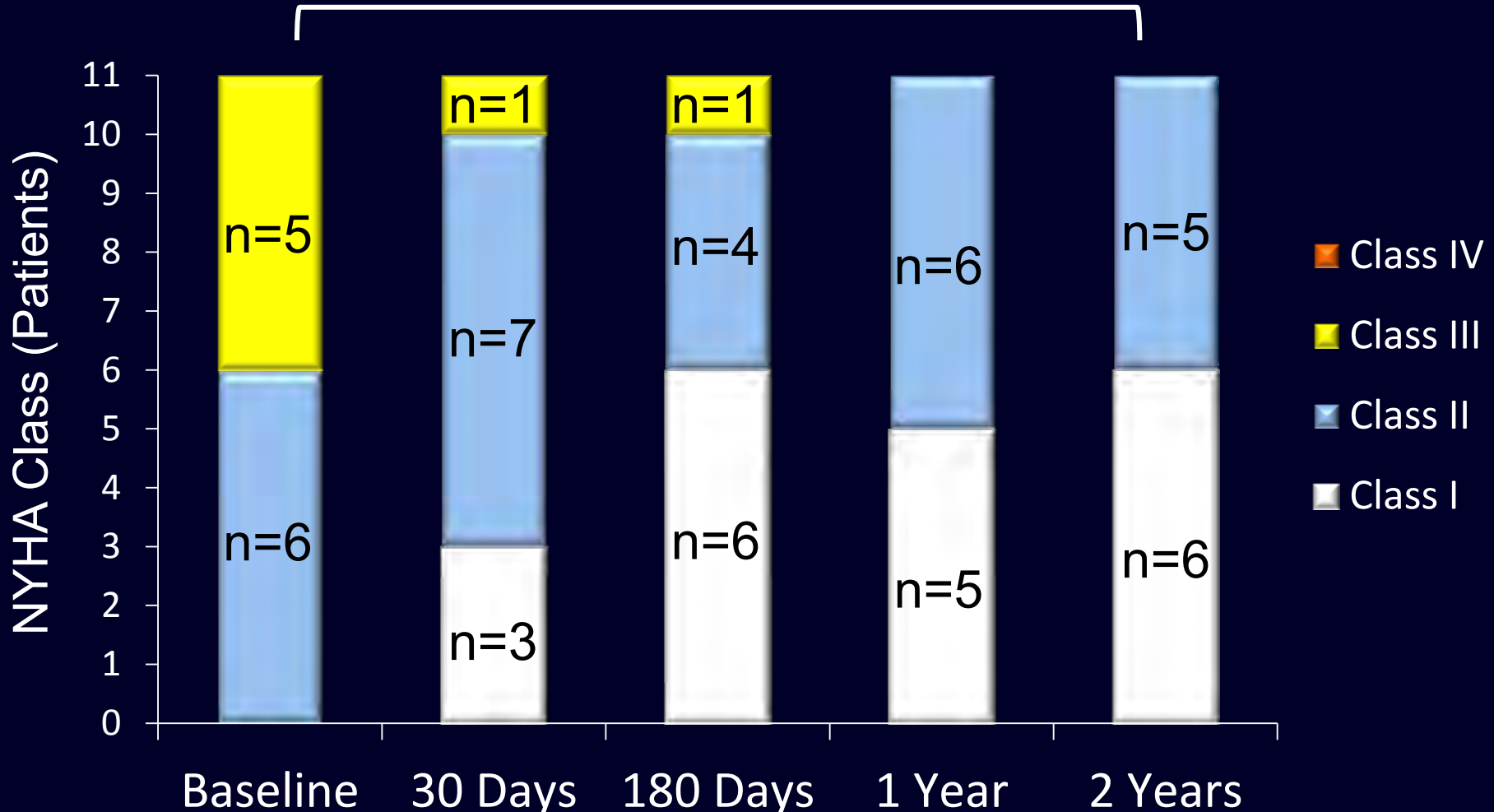
No Moderate / Severe AR by Independent Adjudication

NYHA Assessment



REPRISE I

$P=0.004$



Ian Meredith, TCT 2014.
 P value: Wilcoxon signed rank test for paired data

LOTUS Clinical Program



Device Performance

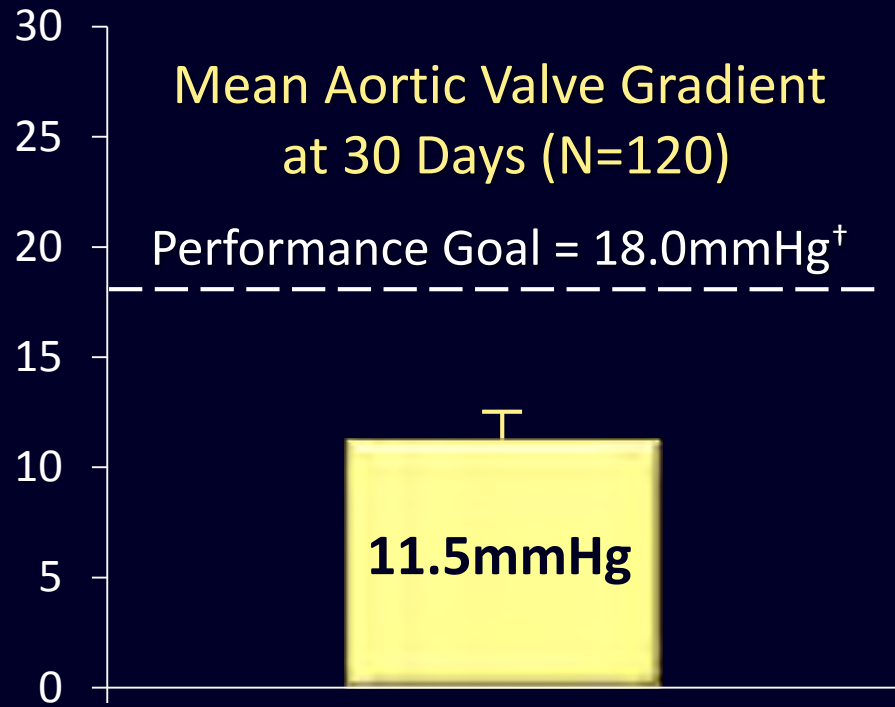
REPRISE II with Extended Cohort (N=250)

Successful access, delivery, deployment & system retrieval	98.8%*
Successful valve repositioning, if attempted (n=85)	100.0%
Partial valve resheathing (n)	71
Full valve resheathing (n)	14
Successful valve retrieval, if attempted (n=13)	92.3%*
Aortic valve malpositioning	0.0%
Valve migration	0.0%
Valve embolization	0.0%
Ectopic valve deployment	0.0%
TAV-in-TAV deployment	0.0%

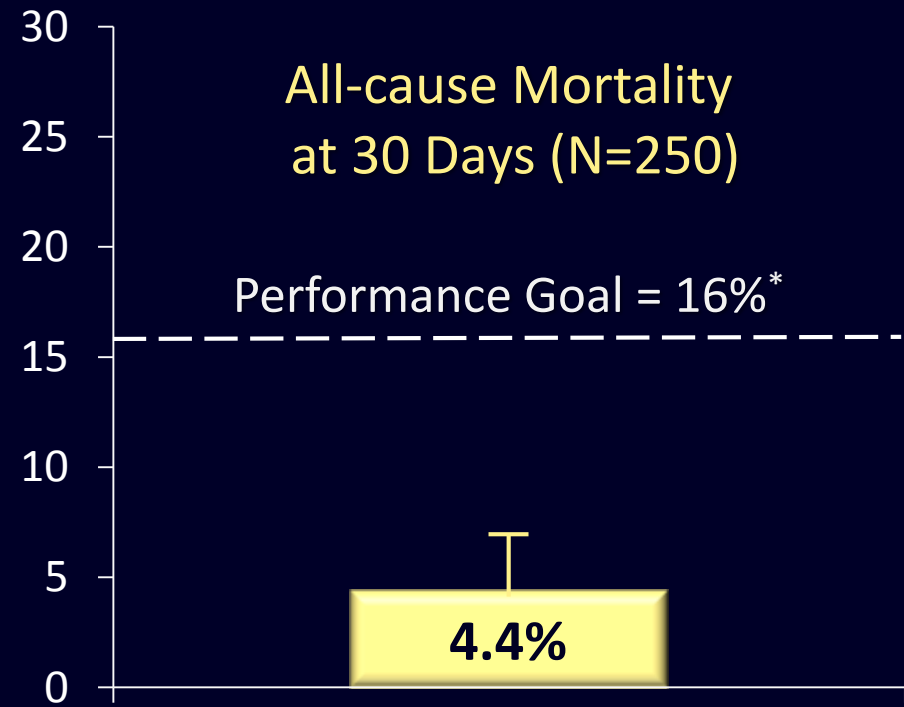
*2 intraprocedural complications occurred prior to valve deployment; 1 retrieval with incomplete retraction into delivery catheter but successfully removed. Lotus valve implanted 42 days afterwards in this patient.

Primary Endpoints

REPRISE II (N=120) & Extended Cohort (N=250)



11.5mmHg ± UCB (12.6mmHg) is significantly below the performance goal (P <0.001)[‡]



4.4% ± UCB (6.97%) is significantly below the performance goal (P <0.001)

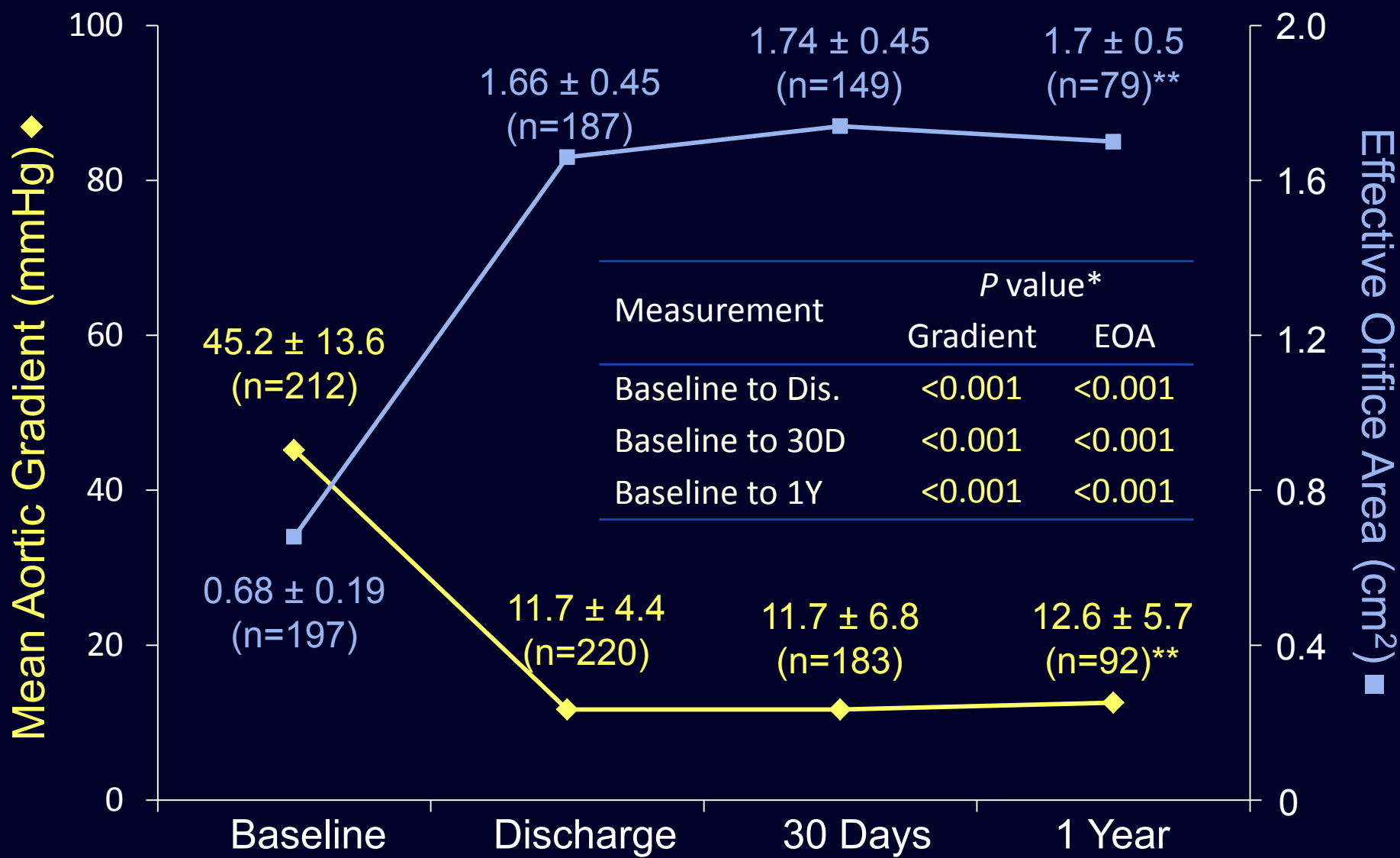
[†] Based on an expected mean of ≤15mmHg (literature review) plus a test margin of 3mmHg

^{*} Based on an expected rate of 9.8% (literature review) plus a test margin of 6.2%

[‡] Meredith, et al. JACC 2014;64:1339. Ian Meredith, London Valves 2014

Mean Aortic Gradient & EOA

REPRISE II with Extended Cohort (N=250)



Ian Meredith, TCT 2014.

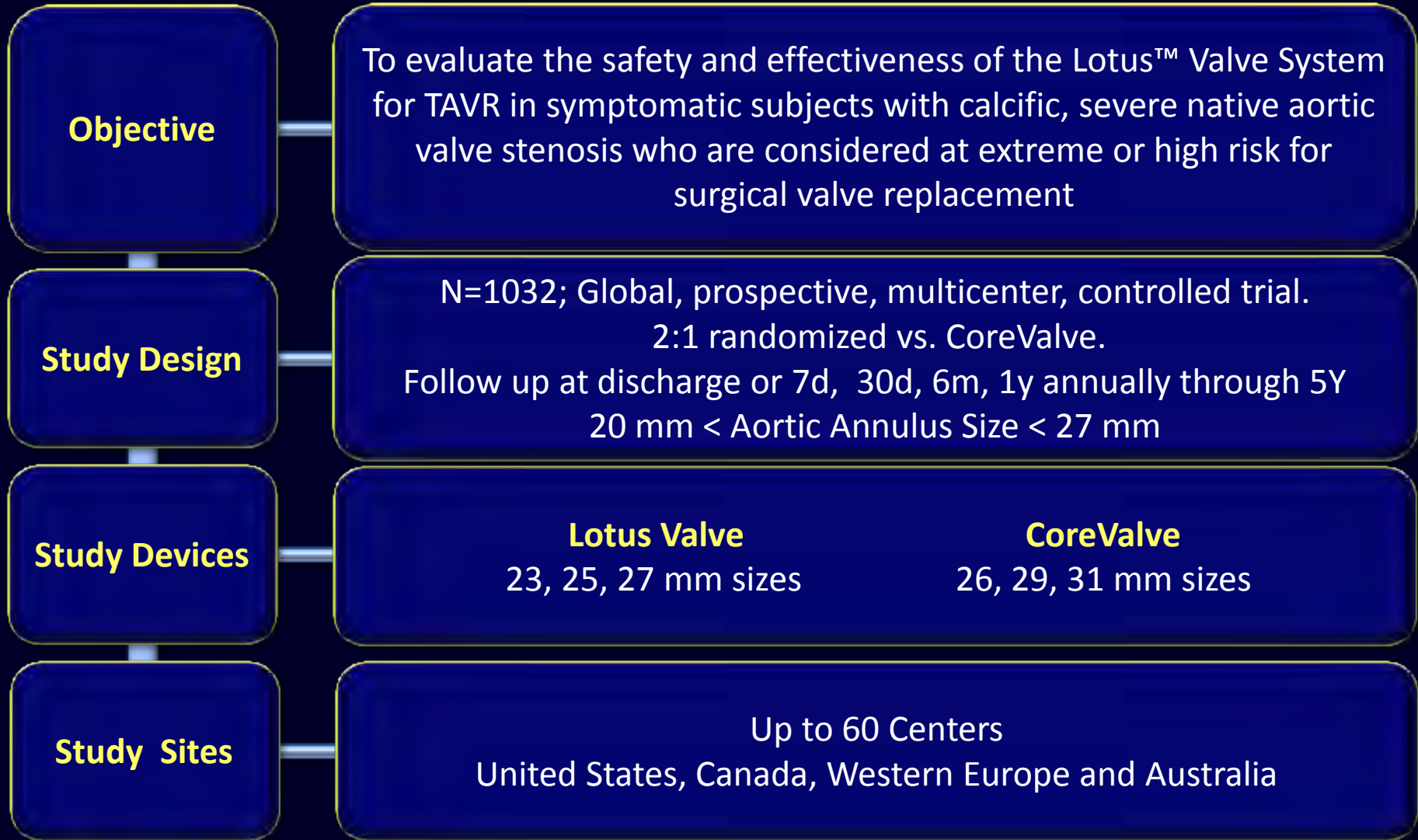
*Repeated measures and random effects ANOVA. **REPRISE II Extended Cohort Excluded.

LOTUS Clinical Program



REPRISE III Trial

REpositionable Percutaneous Replacement of Stenotic Aortic Valve through Implantation of Lotus Valve System – Randomized Clinical Evaluation



REPRISE III Trial

REpositionable Percutaneous Replacement of Stenotic Aortic Valve through Implantation of Lotus Valve System – Randomized Clinical Evaluation

Primary Safety Endpoint

Composite of all-cause mortality, stroke, life-threatening and major bleeding events, stage 2 or 3 acute kidney injury, or major vascular complications at 30 days

Primary Efficacy Endpoint

Composite of all-cause mortality, disabling stroke, or moderate or greater paravalvular aortic regurgitation (based on core lab assessment) at 1 year

Secondary Endpoint

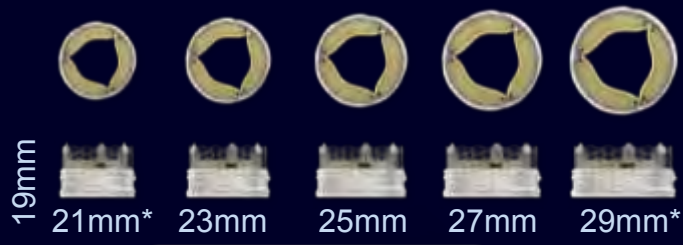
Moderate or greater paravalvular aortic regurgitation (based on core lab assessment) at 1 year

Summary

Lotus Valve Design Goals

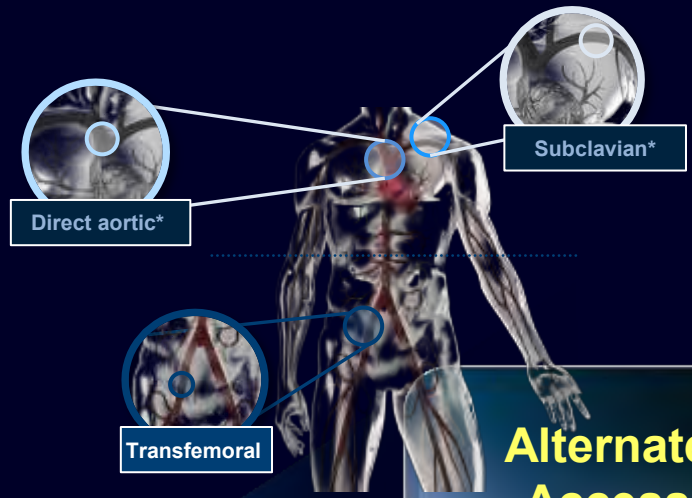
- Adaptive seal to mitigate PVL
 - Controlled mechanical expansion
 - Precise and accurate positioning
 - Repositionable & retrievable any time before release
 - Size matrix expansion to reduce pacemaker implant
 - Significant, clinically meaningful improvement in patient quality of life and health outcomes
-
- Second generation TAVI technologies show promise in reducing PVL and improving clinical outcomes

Boston Scientific Future TAVI Pipeline



Complete Size Matrix

FUTURE PIPELINE

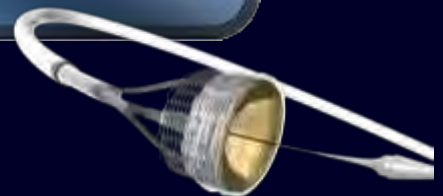


Alternate Access Routes

TAVI-Dedicated Wires*



Enhanced Delivery System*



*Under development, not available for sale.

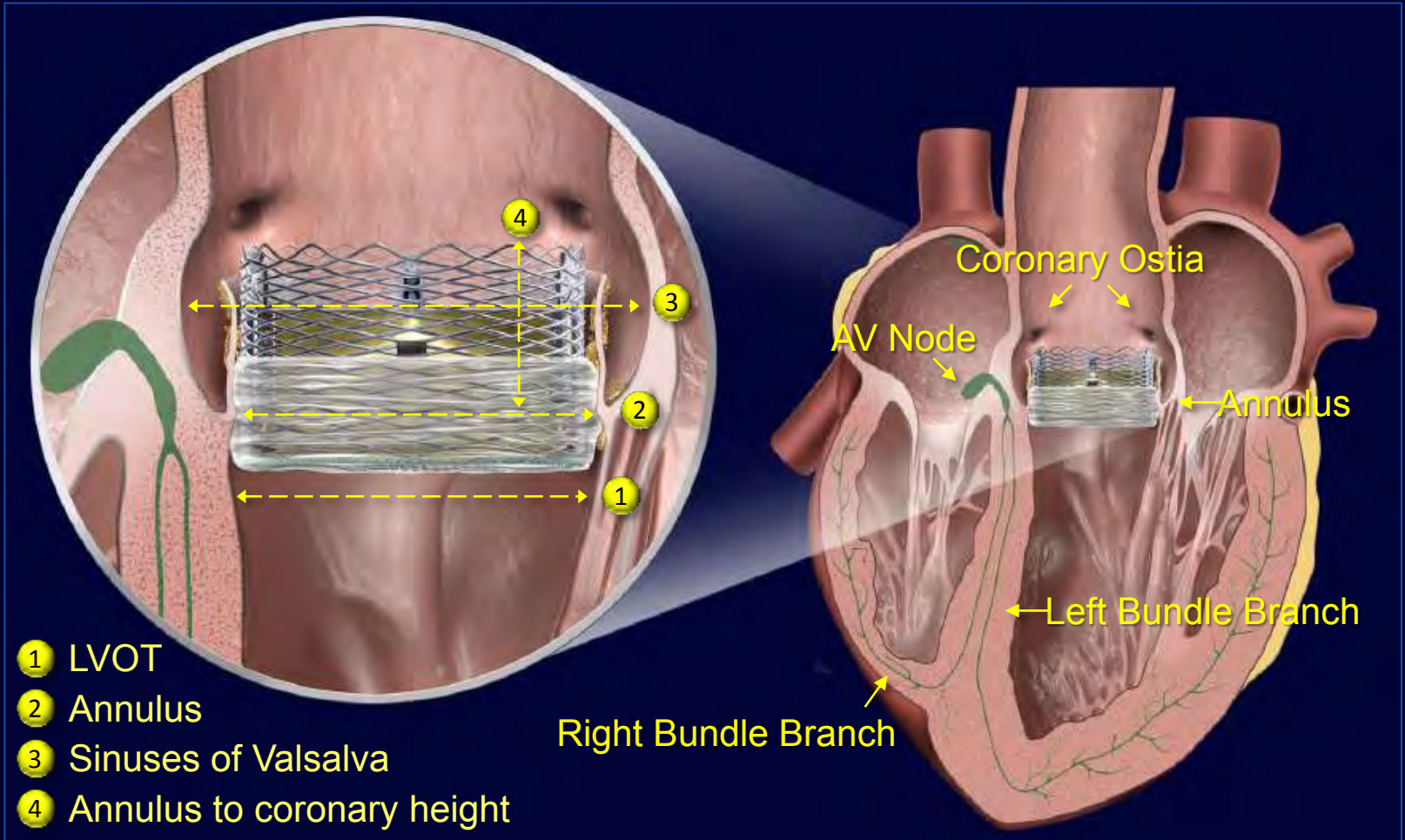
Thank you

Disclaimer:

Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device. Information for the use only in countries with applicable health authority product registrations. Information not intended for use in France.

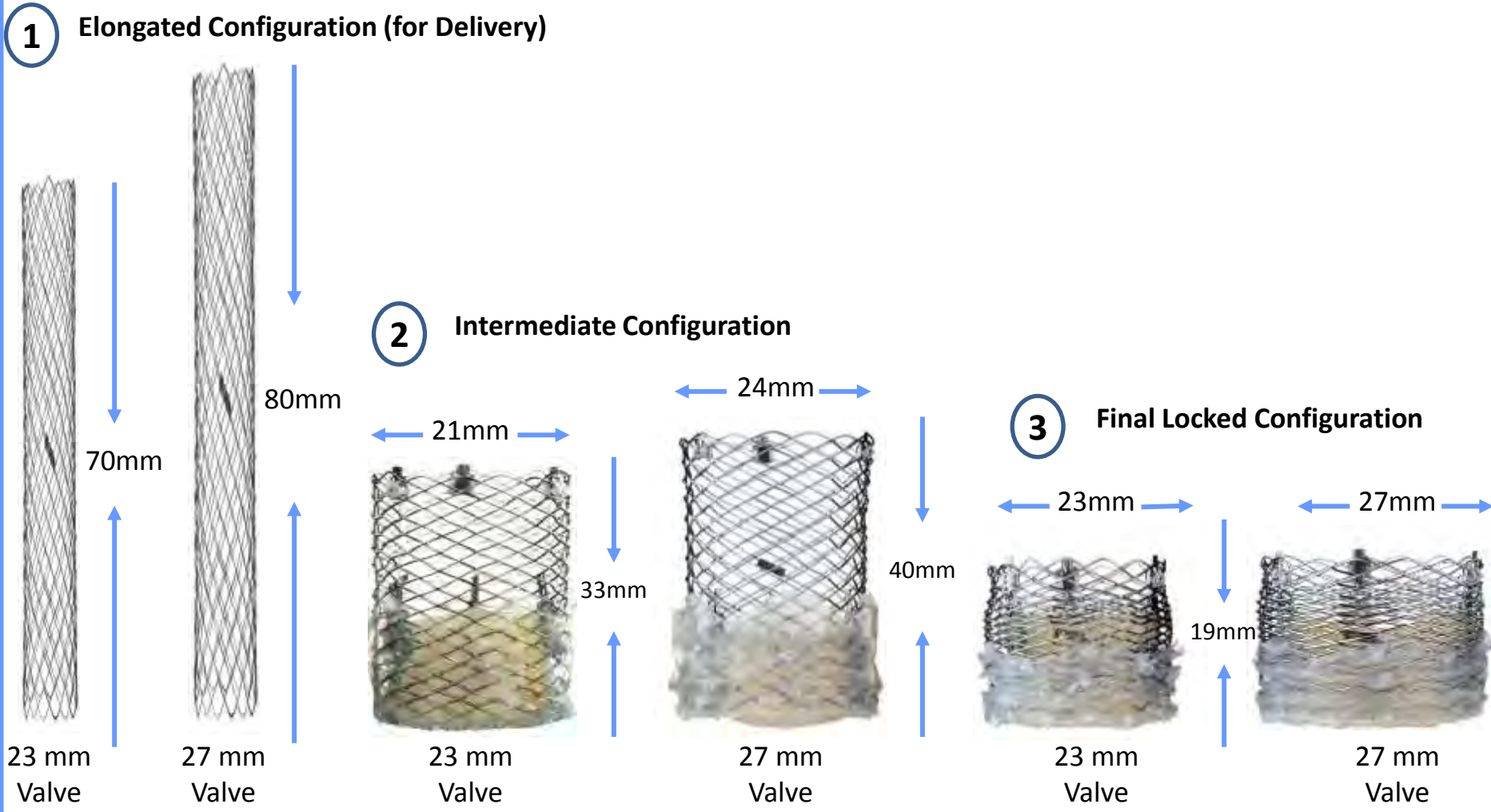
Back-up

Lotus Valve In Situ



Lotus Valve System

Deployment Phases



Safety: Death & Stroke to 1 Year

REPRISE II (N=120)

<i>Event</i>	<i>Discharge/7d</i>	<i>30 Days*</i>	<i>6 Months</i>	<i>1 Year</i>
All-cause death	3.3% (4/120)	4.2% (5/119)	8.4% (10/119)	10.9% (13/119)
Cardiovascular death	3.3% (4/120)	4.2% (5/119)	5.9% (7/119)	6.7% (8/119)
Disabling stroke [†]	1.7% (2/120)	1.7% (2/119)	3.4% (4/119)	3.4% (4/119)
Non-disabling stroke [†]	4.2% (5/120)	4.2% (5/119)	5.9% (7/119)	5.9% (7/119)

Non-CV Deaths 6m to 1y: 1) SCC of the right ear at 314d, 2) pneumonia and sepsis at 336d

CV Deaths 6m to 1y: 1) cardiac failure due to worsened CHF at 266d

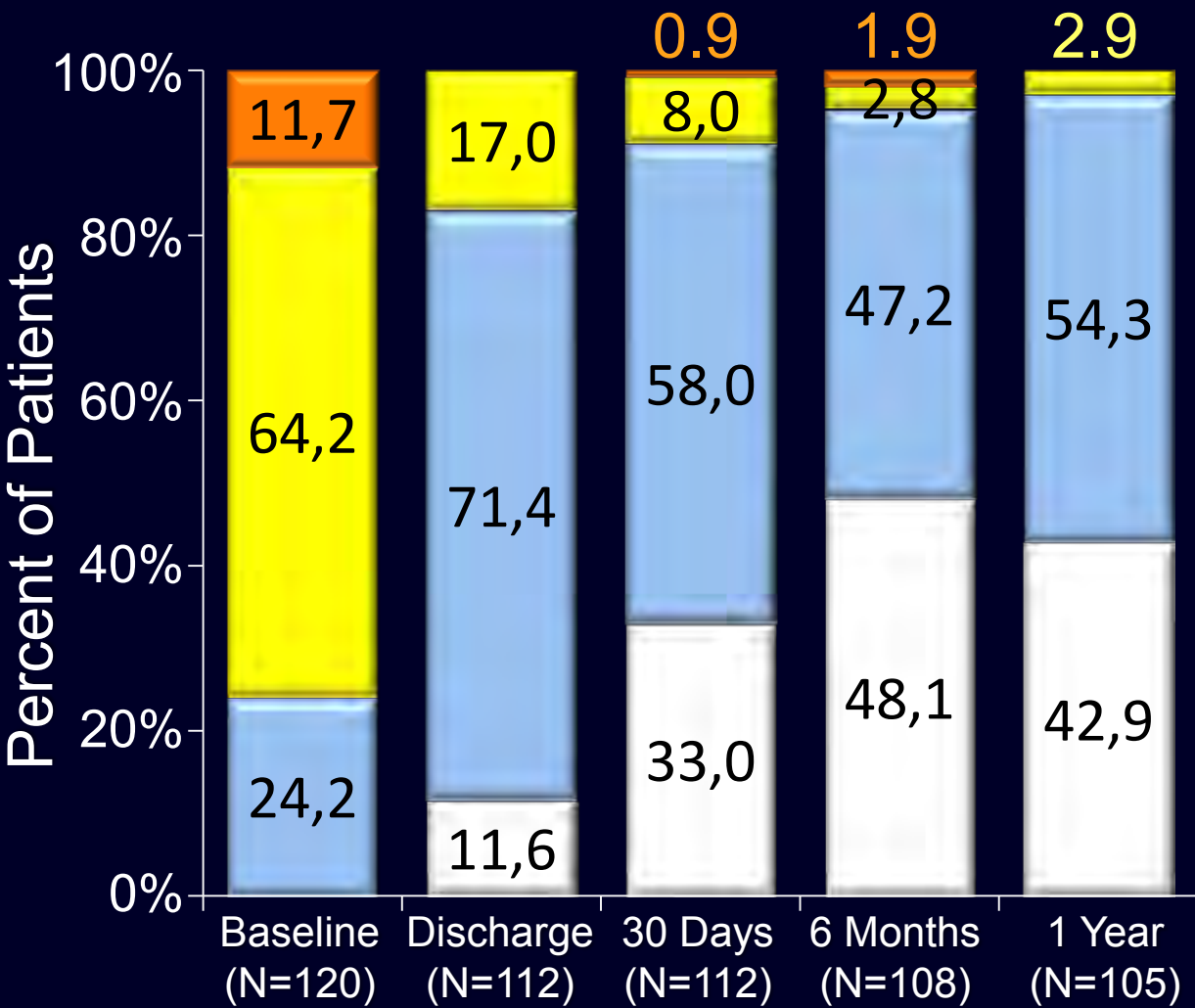
[†] All patients were assessed by a neurologist before and after TAVR . 8/11 pts with stroke at 1y had baseline AF.

* One patient withdrew consent after the discharge/7d time point

Ian Meredith, TCT 2014

NYHA Class Changes Over Time

REPRISE II (N=120)



Measurement	P value
Baseline to Discharge	<0.001
Baseline to 1 Year	<0.001
Discharge to 30 Days	<0.001
30 Days to 1 Year	0.04

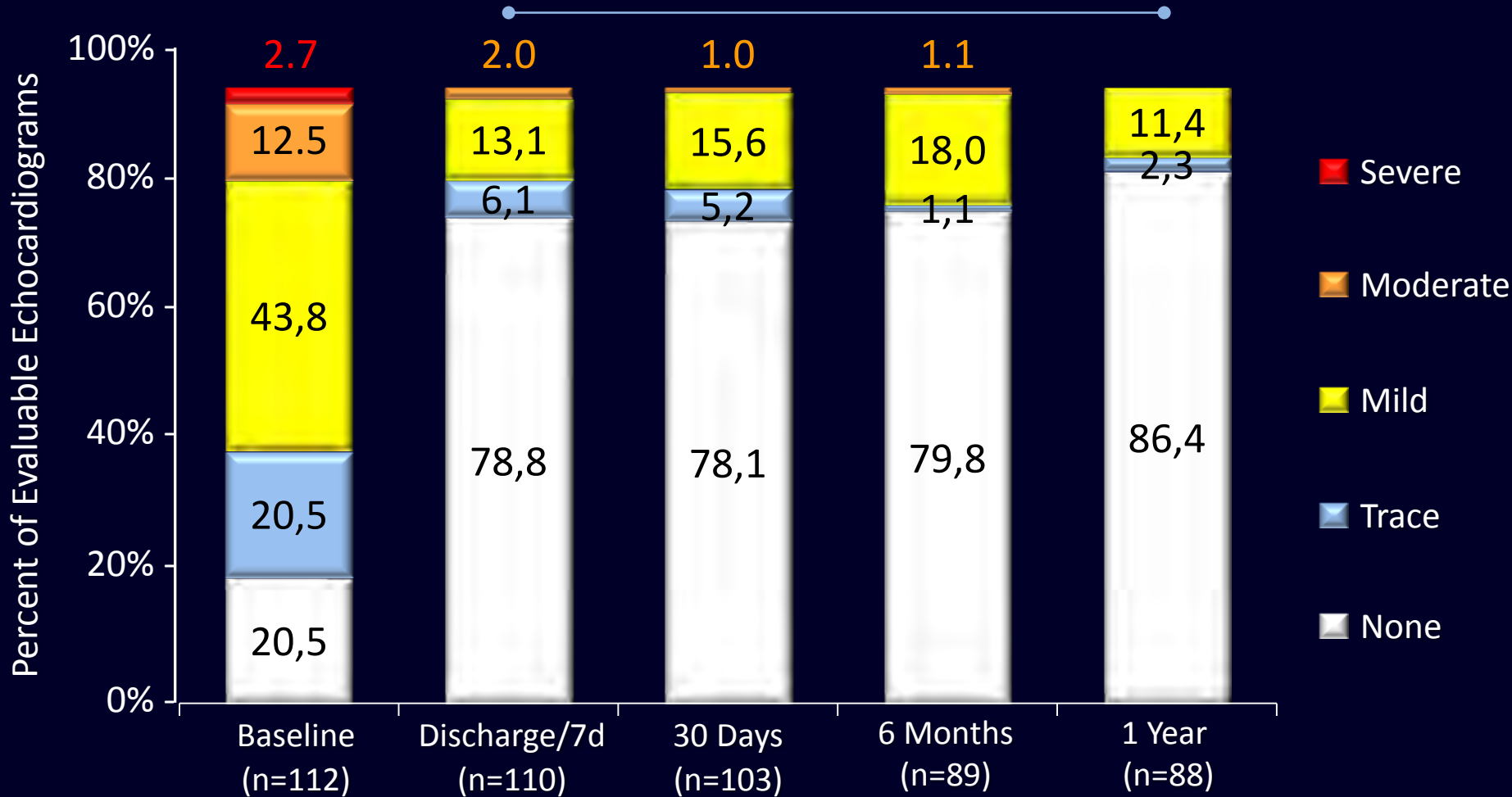


P values calculated from paired Wilcoxon signed-rank test
 Meredith, et al. TCT 2014.

Paravalvular Aortic Regurgitation

REPRISE II (N=120)

Paravalvular

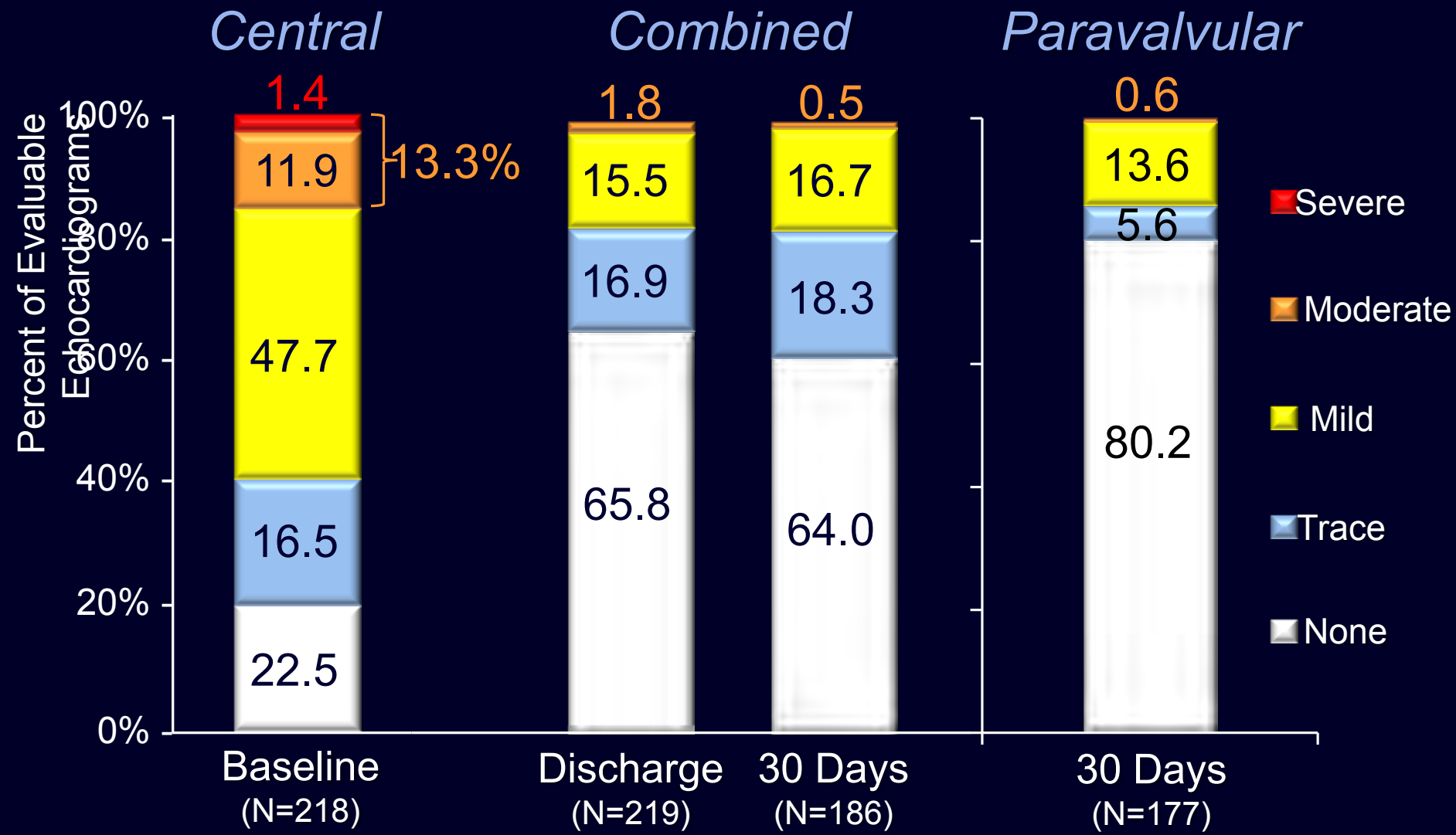


No moderate or severe paravalvular aortic regurgitation at 1 year

Meredith, et al. TCT 2014.

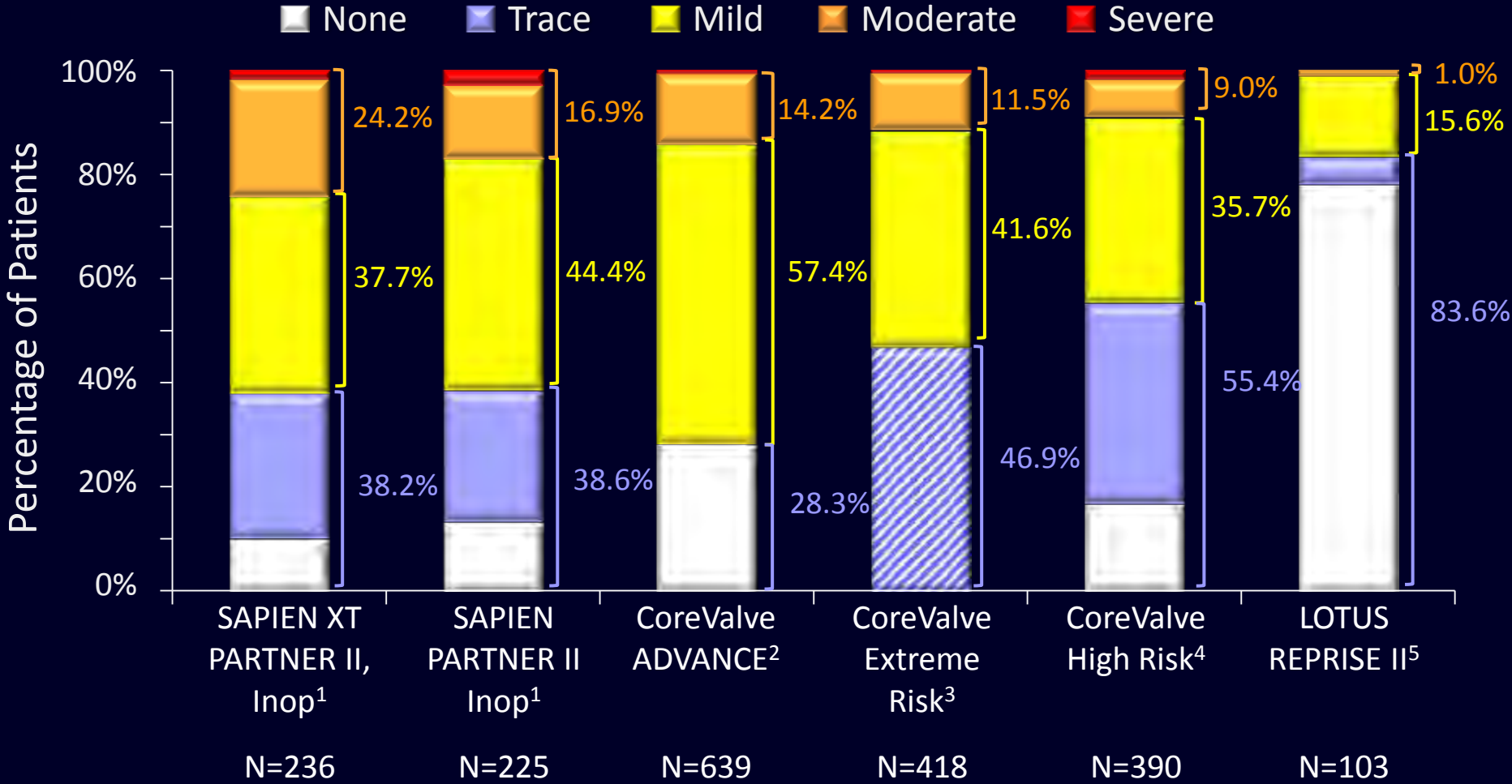
Aortic Regurgitation Over Time

REPRISE II and Extended Cohort (N=250)



| Meredith, London Valves 2014. Post-dilation was not allowed per protocol and was not performed in any case.

1-Month PVL in Core-Lab Adjudicated Clinical Trials



Mod & Sev PVL	24.2%	16.9%	14.2%	11.5%	9.0%	1.0%
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¹Leon M, ACC 2013, ²Linke A, PCR 2014. ³Popma J, JACC 2014; 63(19): 1972-81, ⁴Adams D, N Engl J Med 2014; 370: 1790-98

⁵Meredith I et al, J Am Coll Cardiol 2014;64:1339-48 Results from different studies not directly comparable. Information provided for educational purpose only.

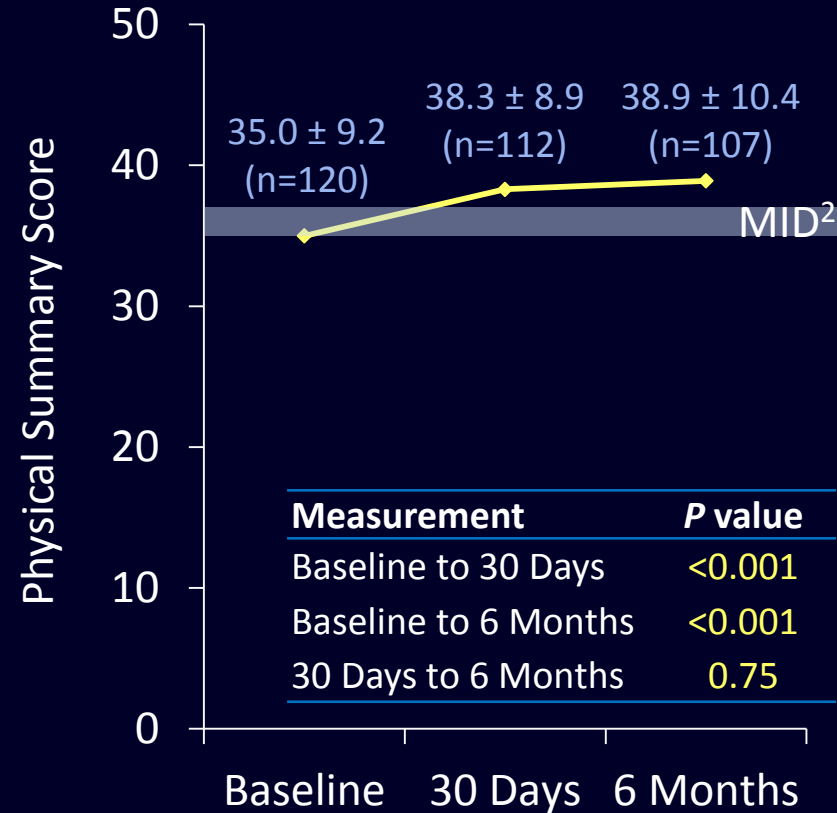
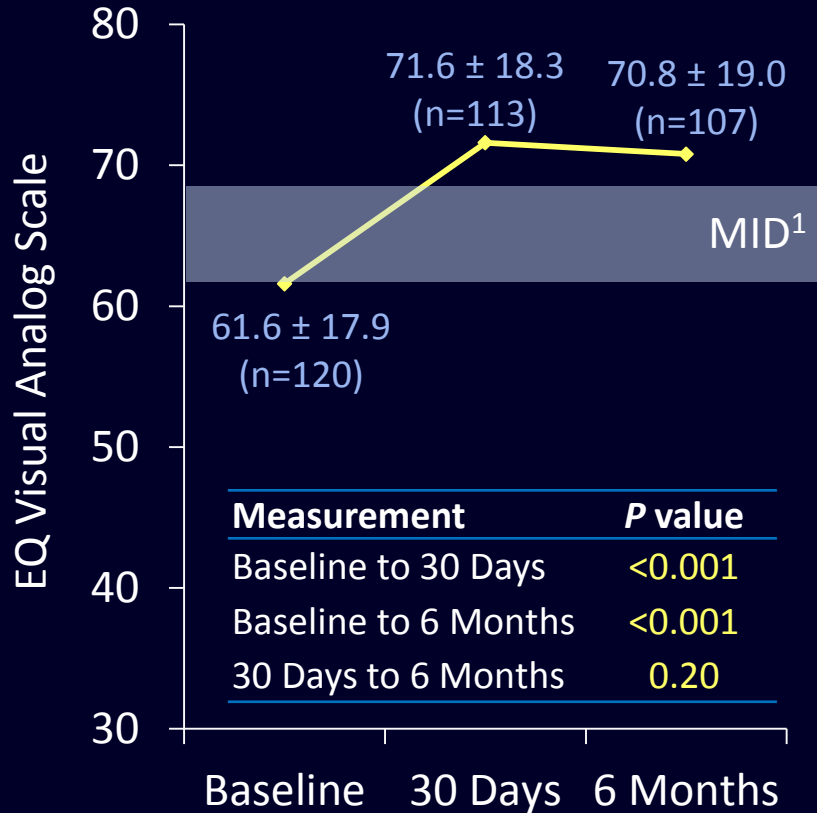
Quality of Life Measures at 6 Months

REPRISE II (N=120)

EQ-5D

SF-12

Higher Scores = Improved QoL



Clinically & statistically significant improvement in health outcomes & QoL

MID = Minimally Important Difference (clinically meaningful change)

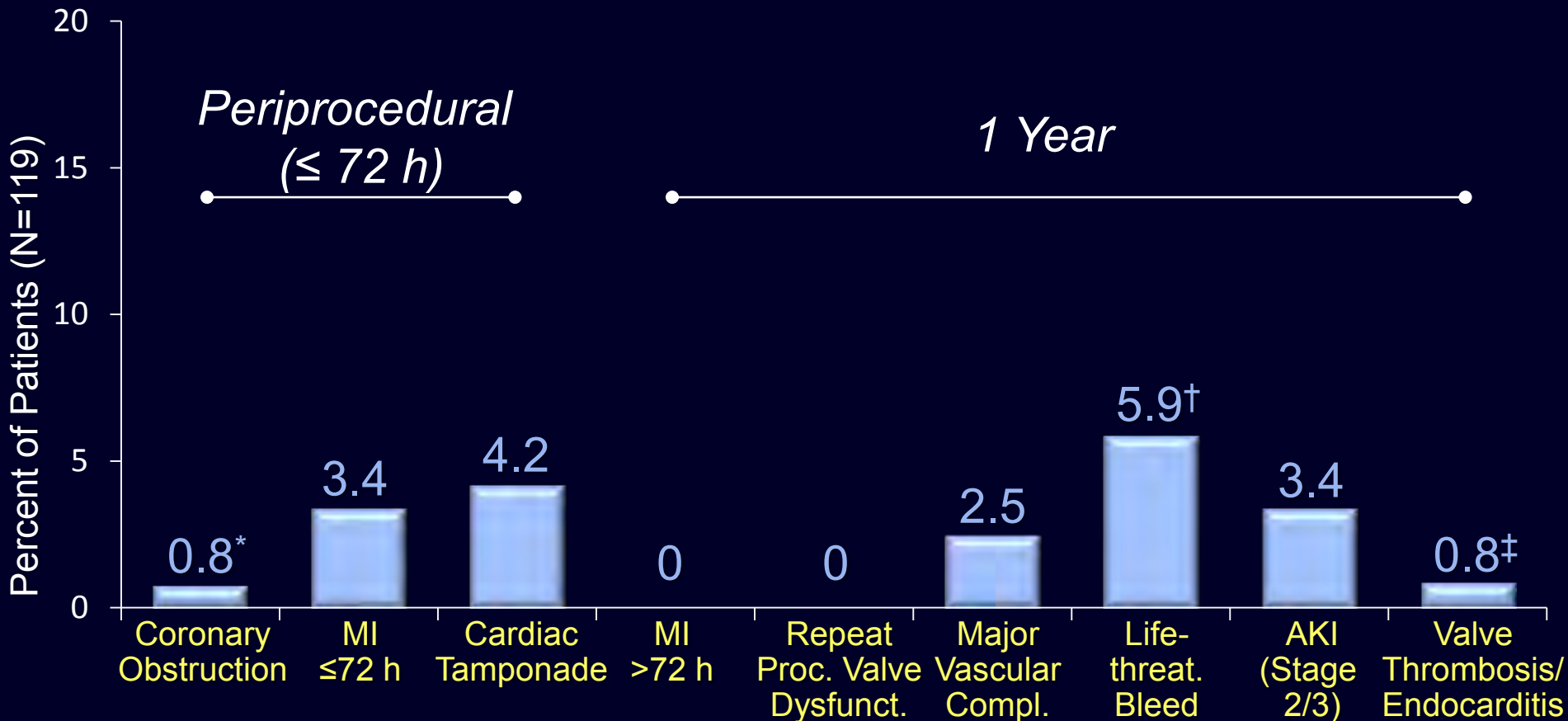
¹Pickard AS, Neary MP, Cella D. Health Qual Life Outcomes. 2007; 5:70 ²Wyrwich et al. Am Heart J. 2004;147:615-622.

Ian Meredith AM, MBBS, PhD at EuroPCR 2014

Additional VARC 2 Safety Endpoints

REPRISE II (N=120)

1 new additional VARC 2 safety event[†] 6m to 1y (disabling bleed after hip surgery)

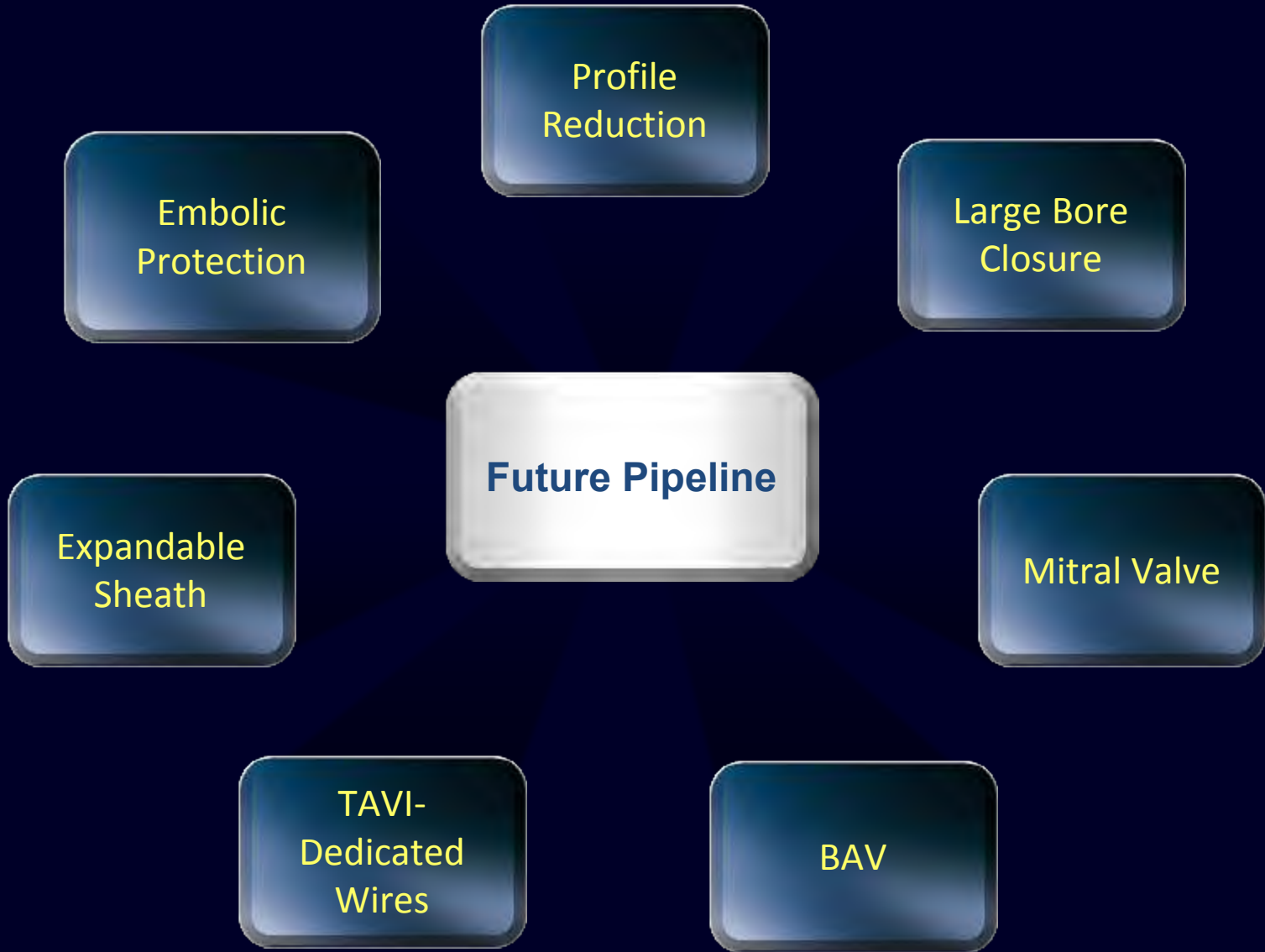


* Stent thrombosis in LAD (implanted >30d previous) that occurred after BAV; rescue PCI performed

[†] Anemia requiring transfusion following hip replacement surgery on day 301; not related.

[‡] Endocarditis associated with urosepsis at day165; not considered related to the index procedure.

Next Generation Focus Areas



* Future Lotus product portfolio and are only displayed for informational purposes, not available for sale

Lotus Valve System

Future Areas of Clinical Focus



* Future Lotus product portfolio and are only displayed for informational purposes, not available for sale