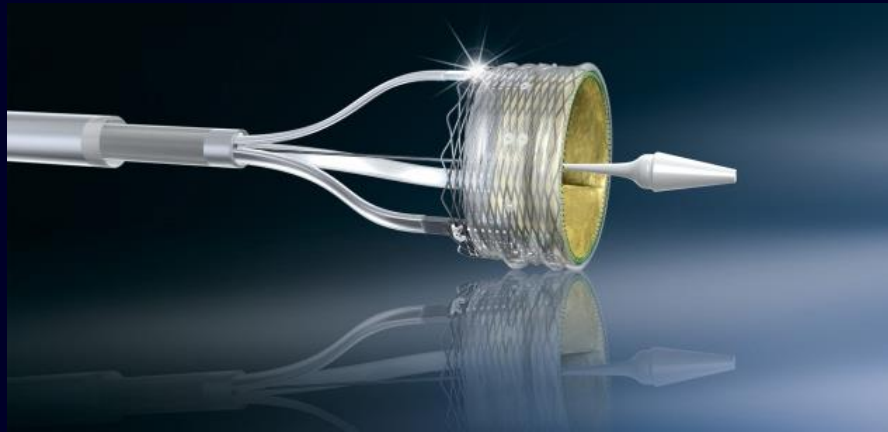


Lotus™ Valve System for Transcatheter Aortic Valve Implantation/Replacement (TAVI/R)



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Stanford University, School of Medicine, Palo Alto, California, USA

Eberhard Grube, MD

Financial Disclosure

<u>Physician Name</u>	<u>Company/Relationship</u>
Eberhard Grube, MD	Medtronic, CoreValve: C, SB, AB, OF Direct Flow: C, SB, AB Mitralign: AB, SB, E Boston Scientific: C, SB, AB Cordis: AB Abbott Vascular: AB Valtech: E, SB, In Seal Medical: SB, E Claret: SB Keystone, SB Shockwave: E, 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

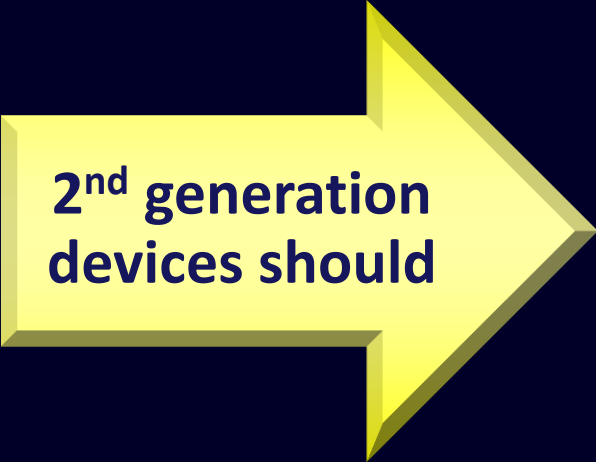
Early TAVI Devices for Severe Aortic Stenosis

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 aposition
- Stroke

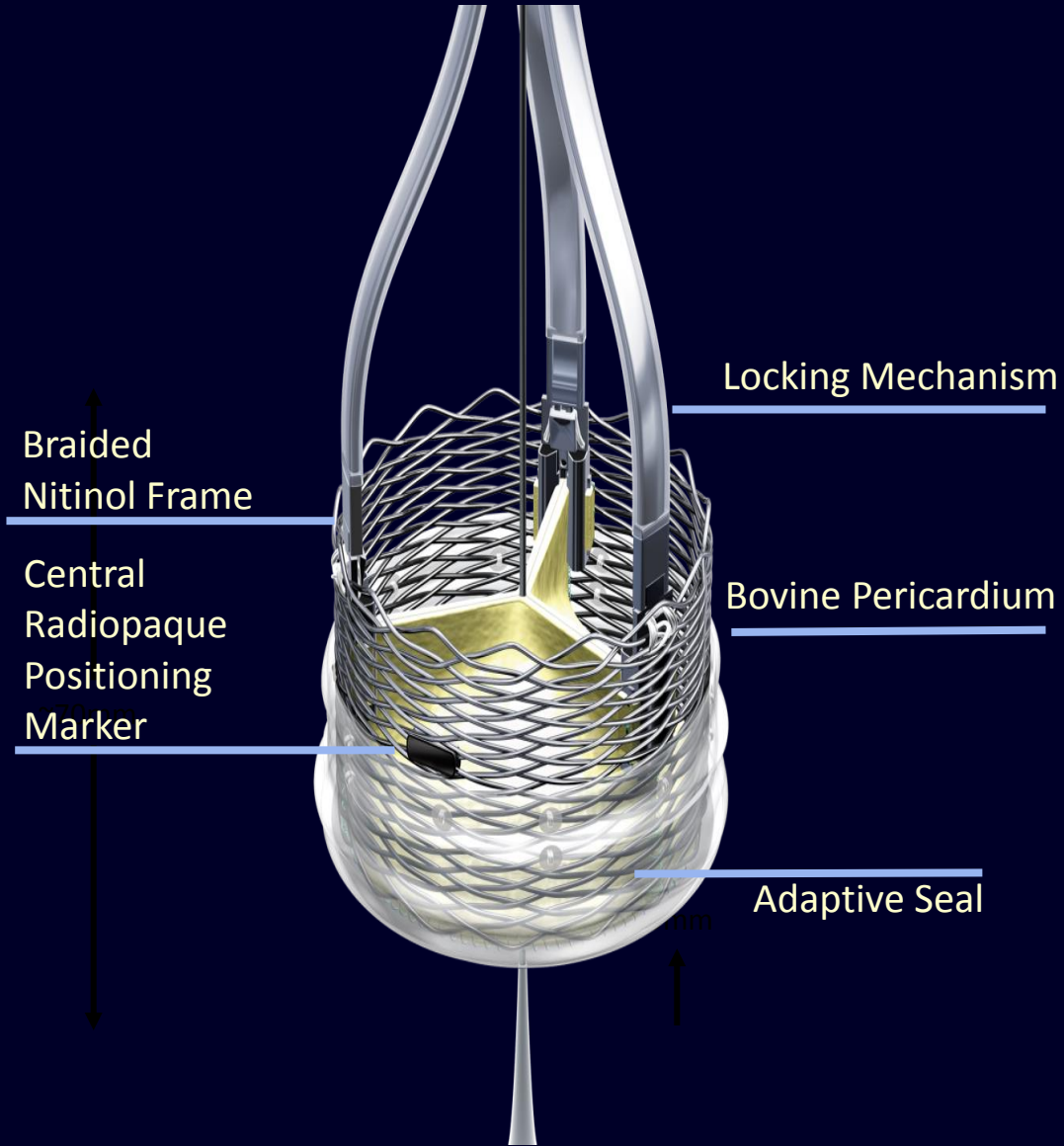


**2nd generation
devices should**

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

Lotus Valve System Design Goals

Controlled Mechanical Expansion

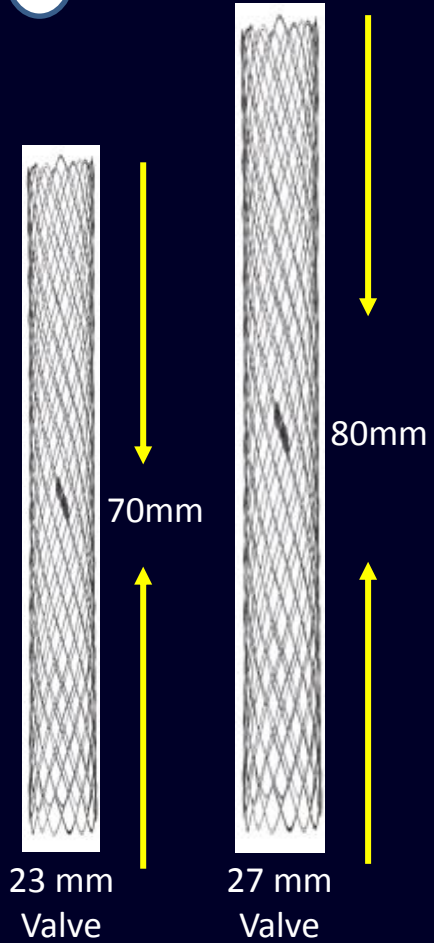


- Valve deployed via controlled mechanical expansion
- No rapid pacing during deployment
- Valve functions early enabling controlled deployment
- Ability to assess valve in final configuration before release

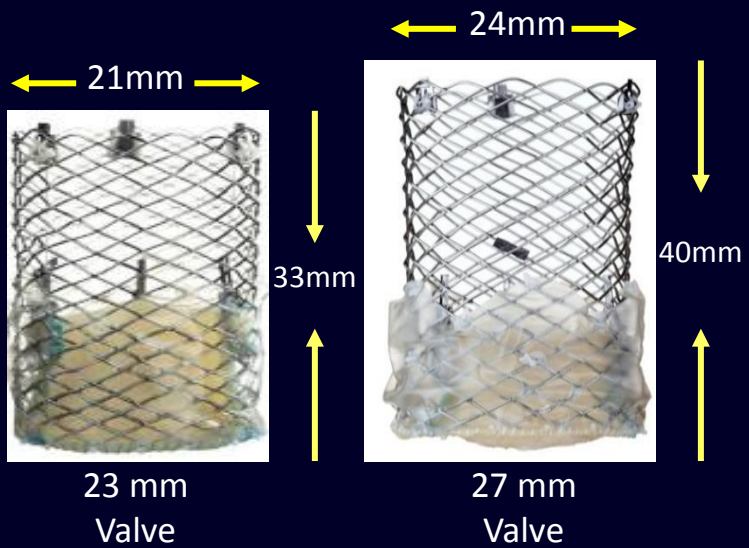
Lotus Valve System

Deployment Phases

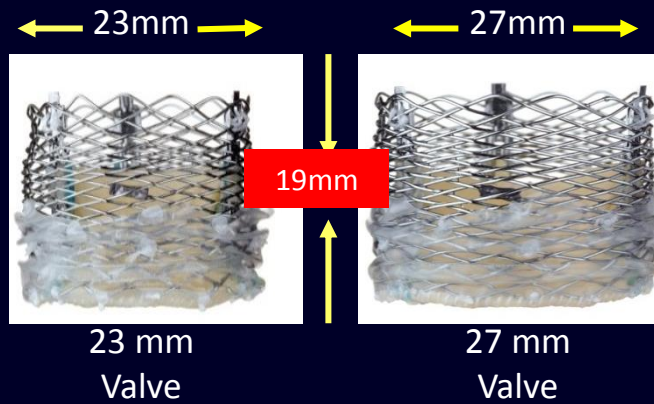
1 Elongated Configuration (for Delivery)



2 Intermediate Configuration

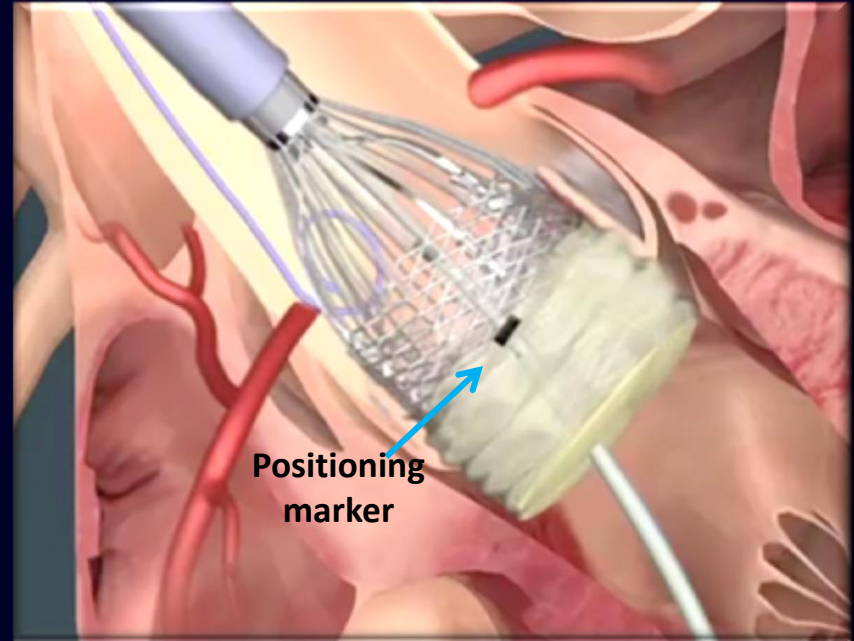
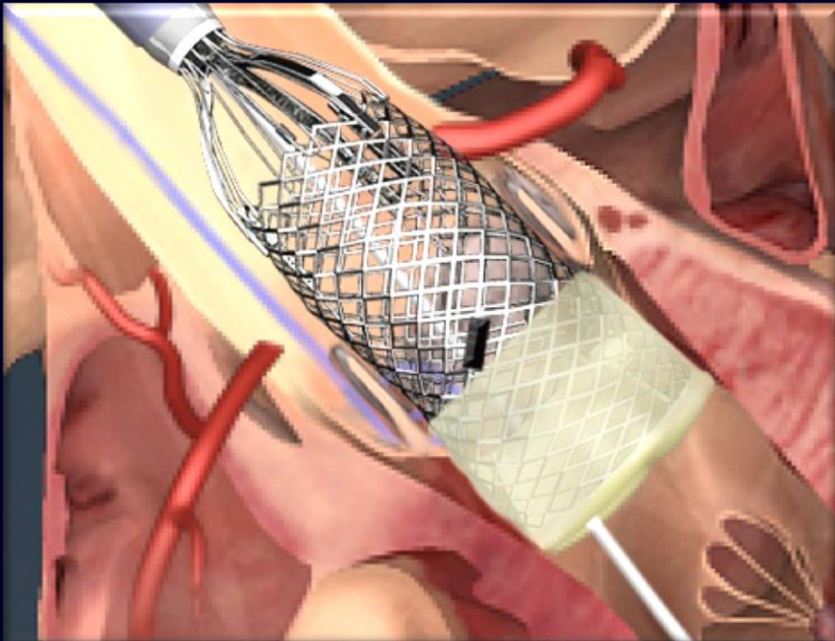


3 Final Locked Configuration



Lotus Valve System Design Goals

Controlled, Accurate, and Predictable Positioning



- Central radiopaque positioning marker to guide placement
- Valve is repositionable throughout entire deployment process
- Fully retrievable prior to release, including after locking in final configuration

Lotus Valve System Design Goals

Controlled Mechanical Expansion

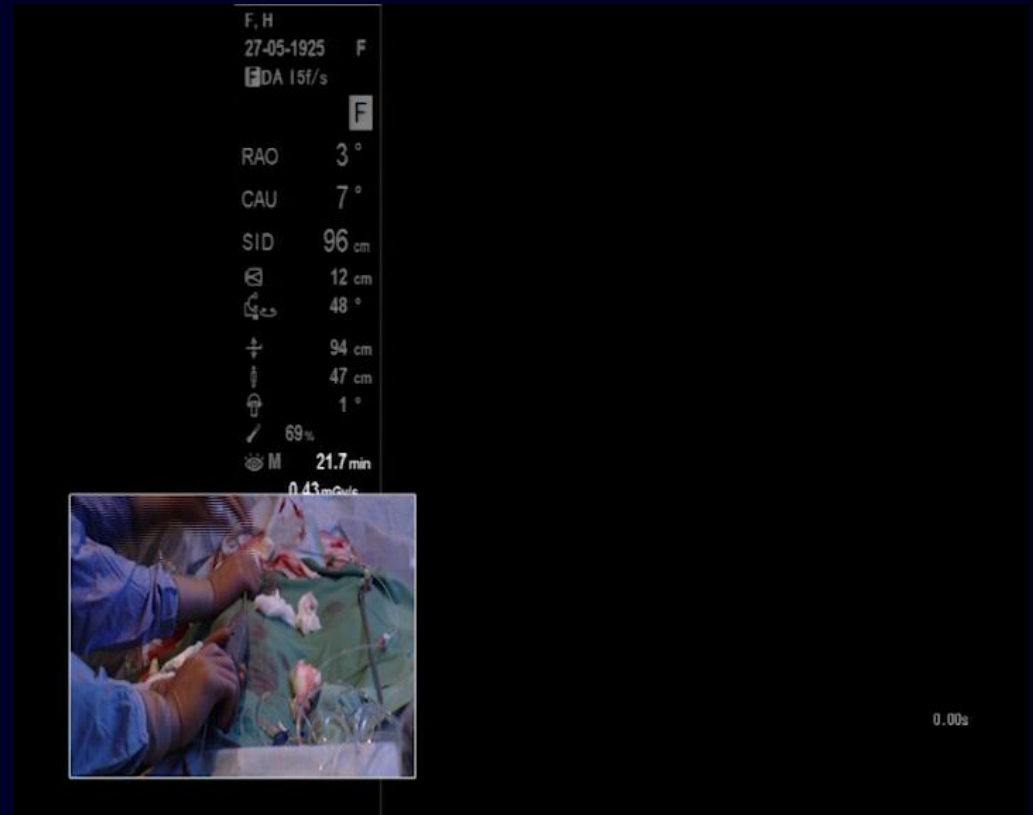
- Valve deployed via controlled mechanical expansion.
 - ➔ *It is neither balloon expandable nor self-expanding.*
- No rapid pacing during deployment
- Valve functions early
- No valve movement on release



Lotus Valve System Design Goals

Controlled, Accurate, and Predictable Positioning

- Central radiopaque positioning marker to guide placement
- Valve is repositionable throughout entire deployment process

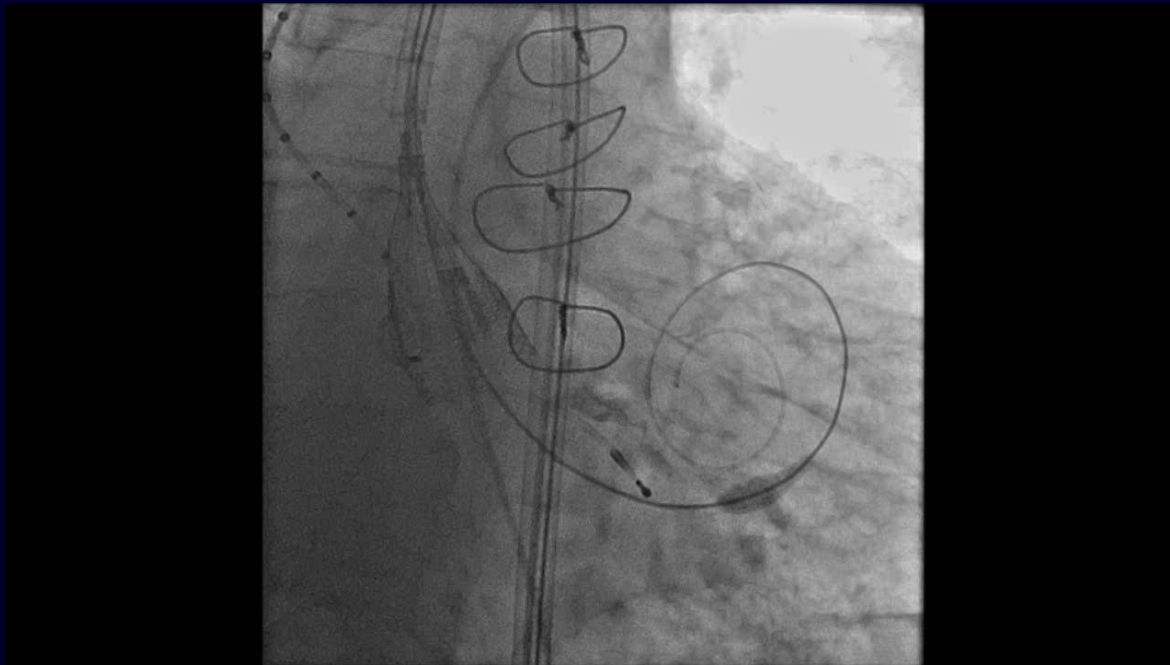


Partial Re-sheathing to Reposition
(Focus on the marker)

Lotus Valve System Design Goals

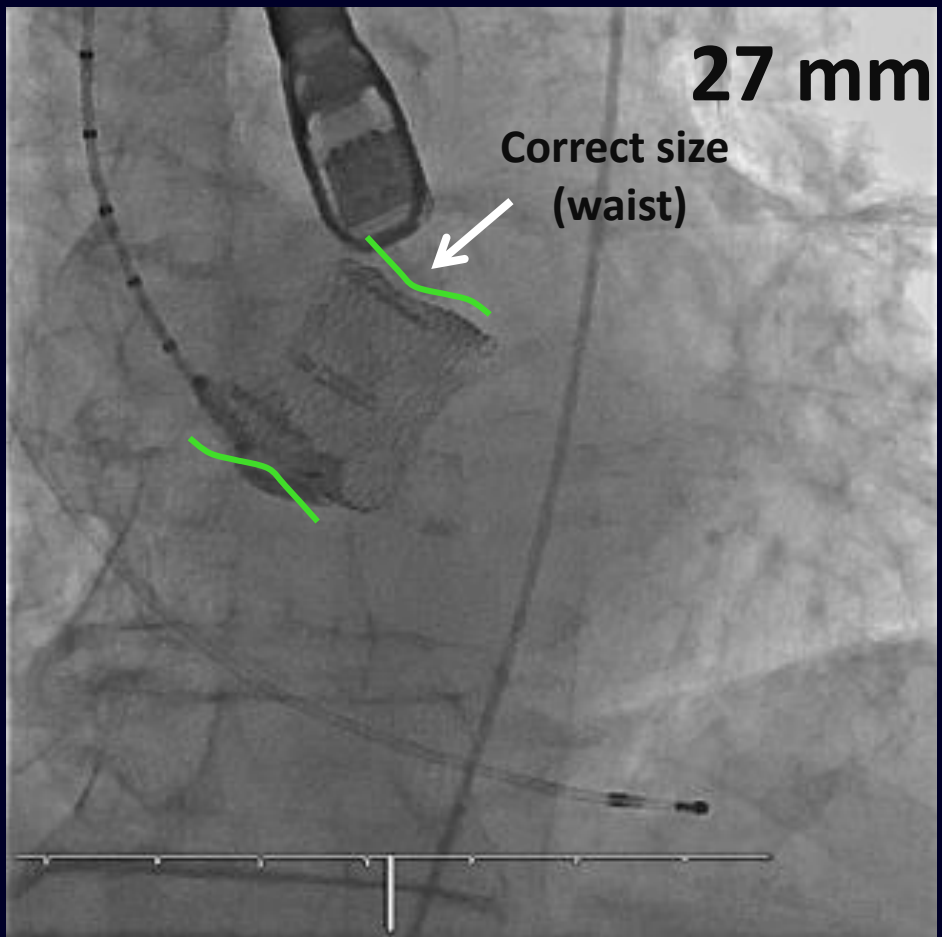
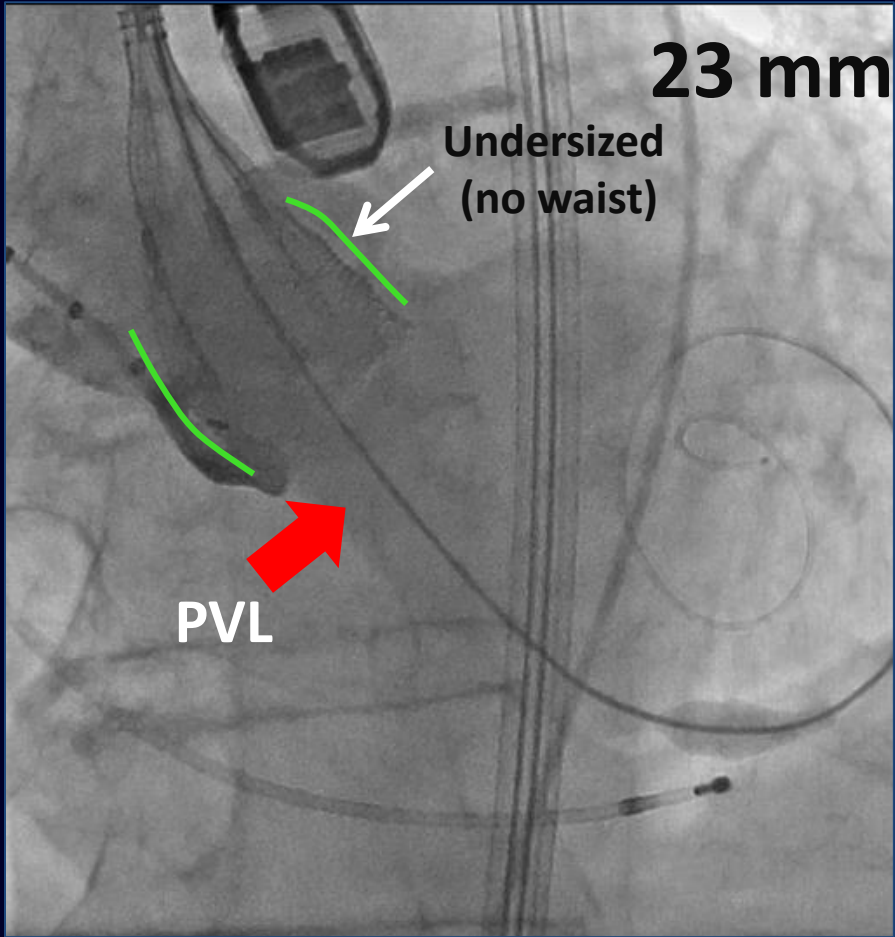
Controlled, Accurate, and Predictable Positioning

Fully retrievable prior to release,
including after locking in final configuration



REPRISE II Case Example

23 mm Lotus valve retrieval and exchange for 27 mm Lotus valve



Lotus valve is repositionable throughout entire deployment process

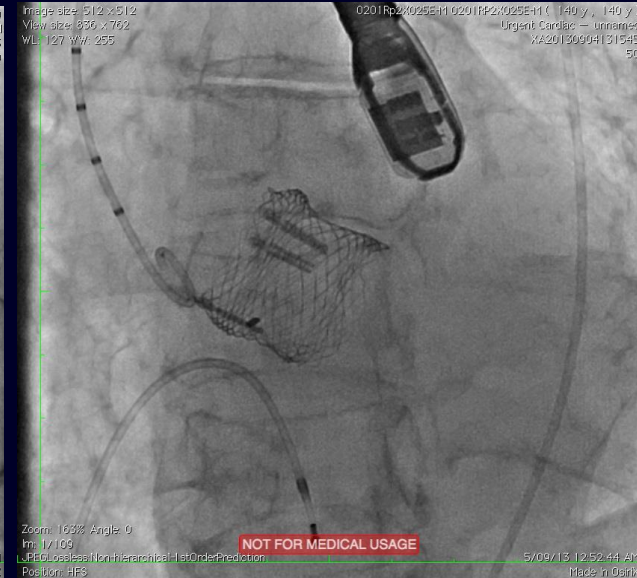
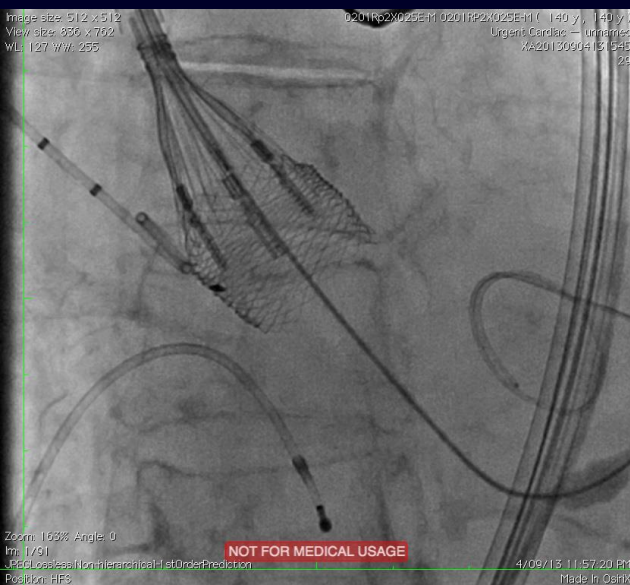
REPRISE II Case Example

23mm Lotus Valve Retrieval and Exchange for 27mm Valve

23 mm valve deployed.
Too small; significant PVL

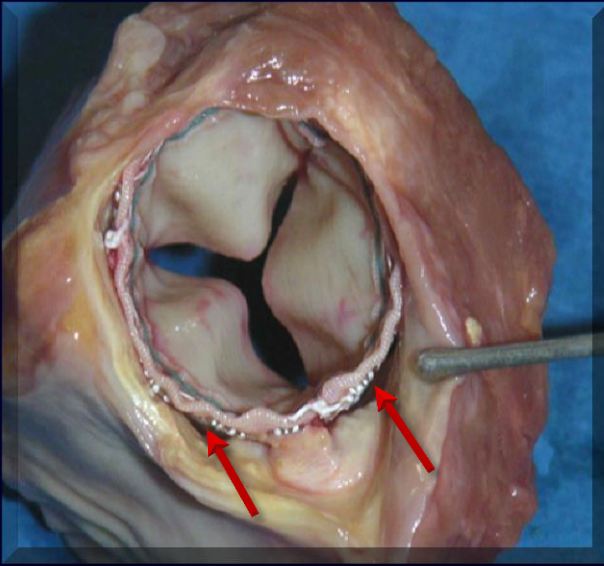
Atraumatic resheathing to
retrieve and remove

Replaced with 27mm valve
No PVL



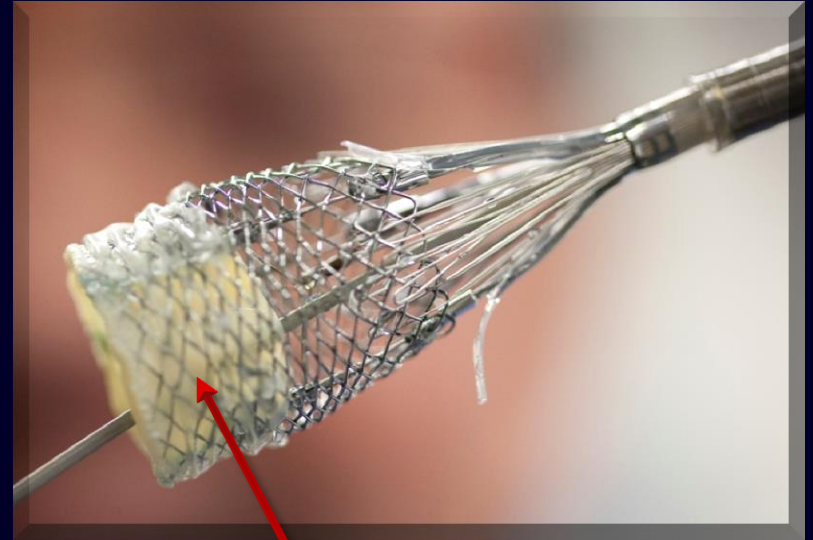
Lotus Valve System Design Goals

Minimize Paravalvular Leakage (PVL)



Non – Circular Annulus
+
Irregular Calcification
=
PVL

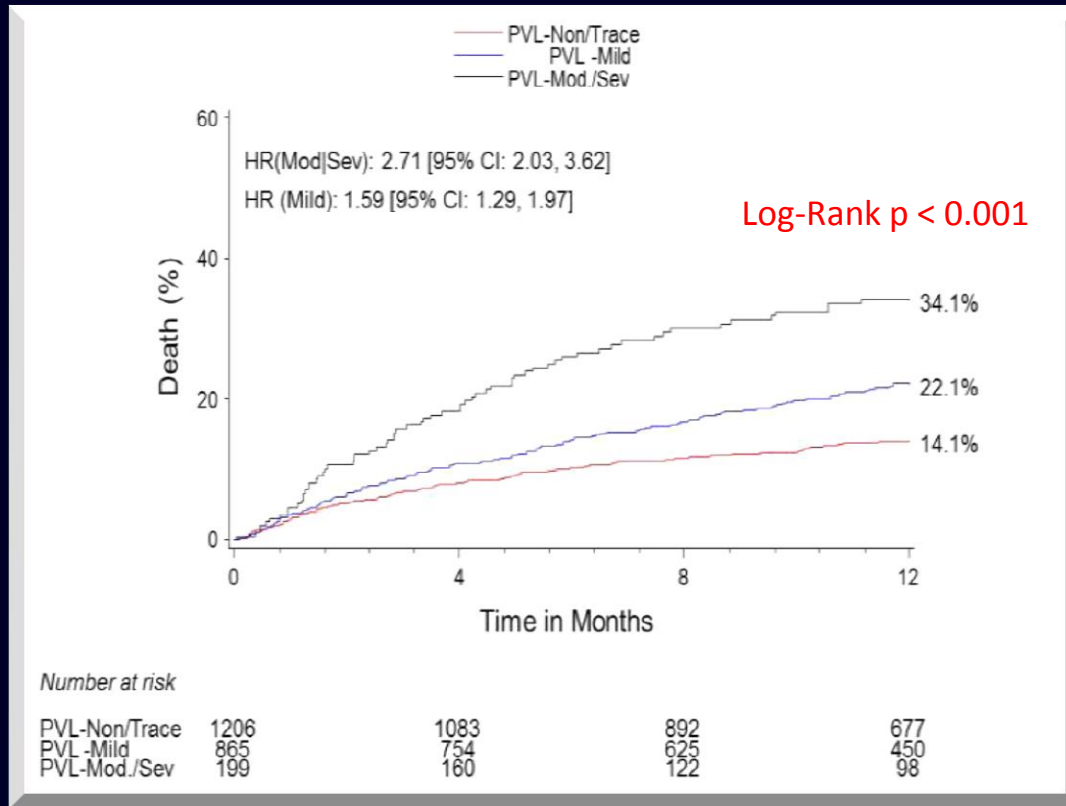
Adaptive seal to mitigate PVL



Adaptive
Seal

PVL is a Significant Predictor of Mortality

PARTNER Trial 1-Year Outcomes Stratified by PVL

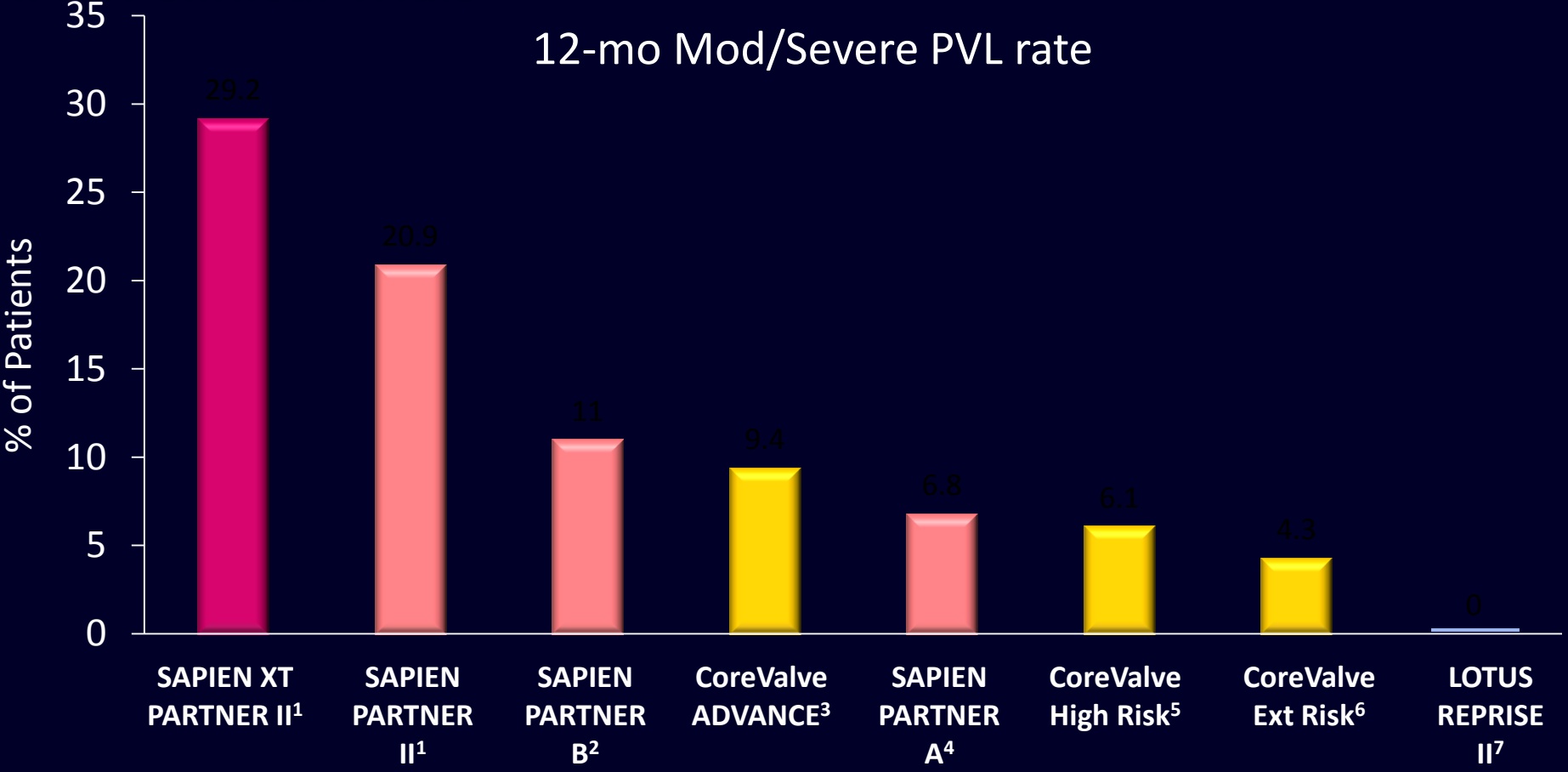


Multivariate Analysis – Predictors of One Year Mortality

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

12 Month Moderate & Severe PVL

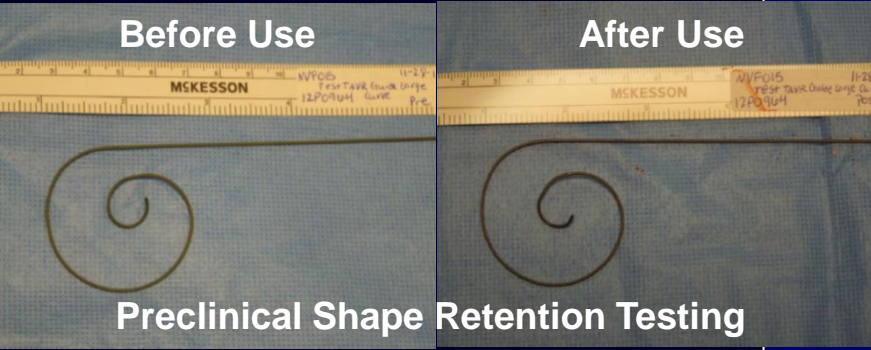
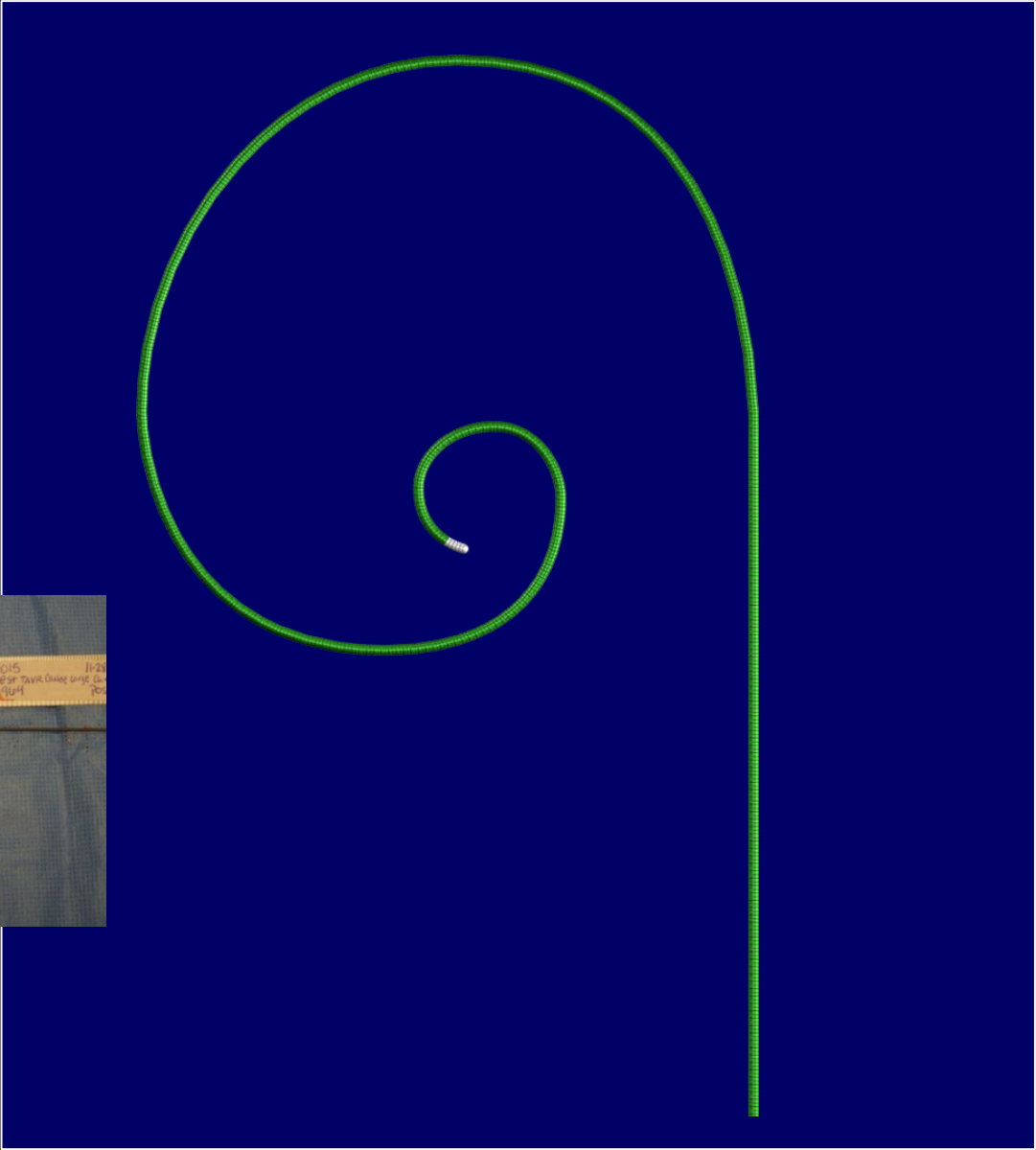
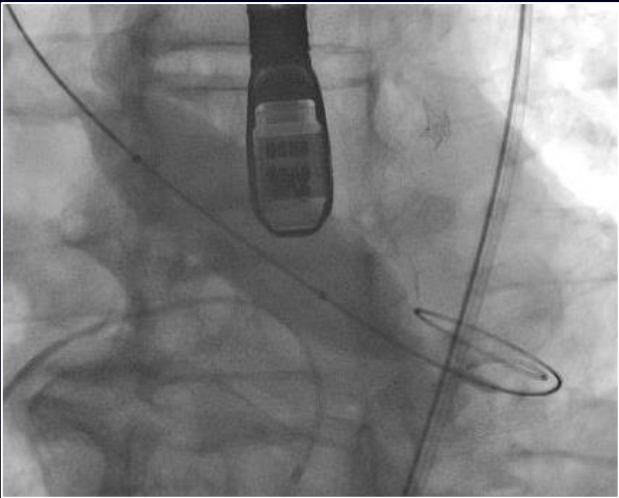
TAVR Clinical Trials



STS Score:	10.3	11	11.2	5.3	11.8	7.3	10.3	7.1
N:	284	276	179	996	348	390	489	120

¹Leon M, ACC 2013., ²Leon, NEJM 2010., ³Linke A, PCR 2014., ⁴Smith, NEJM 2011., ⁵Adams D, *N Engl J Med* 2014., ⁶Popma J, *JACC* 2014., ⁷Ian Meredith, TCT 2014., Results from different studies not directly comparable. Information provided for educational purpose only.

Safari Guidewire

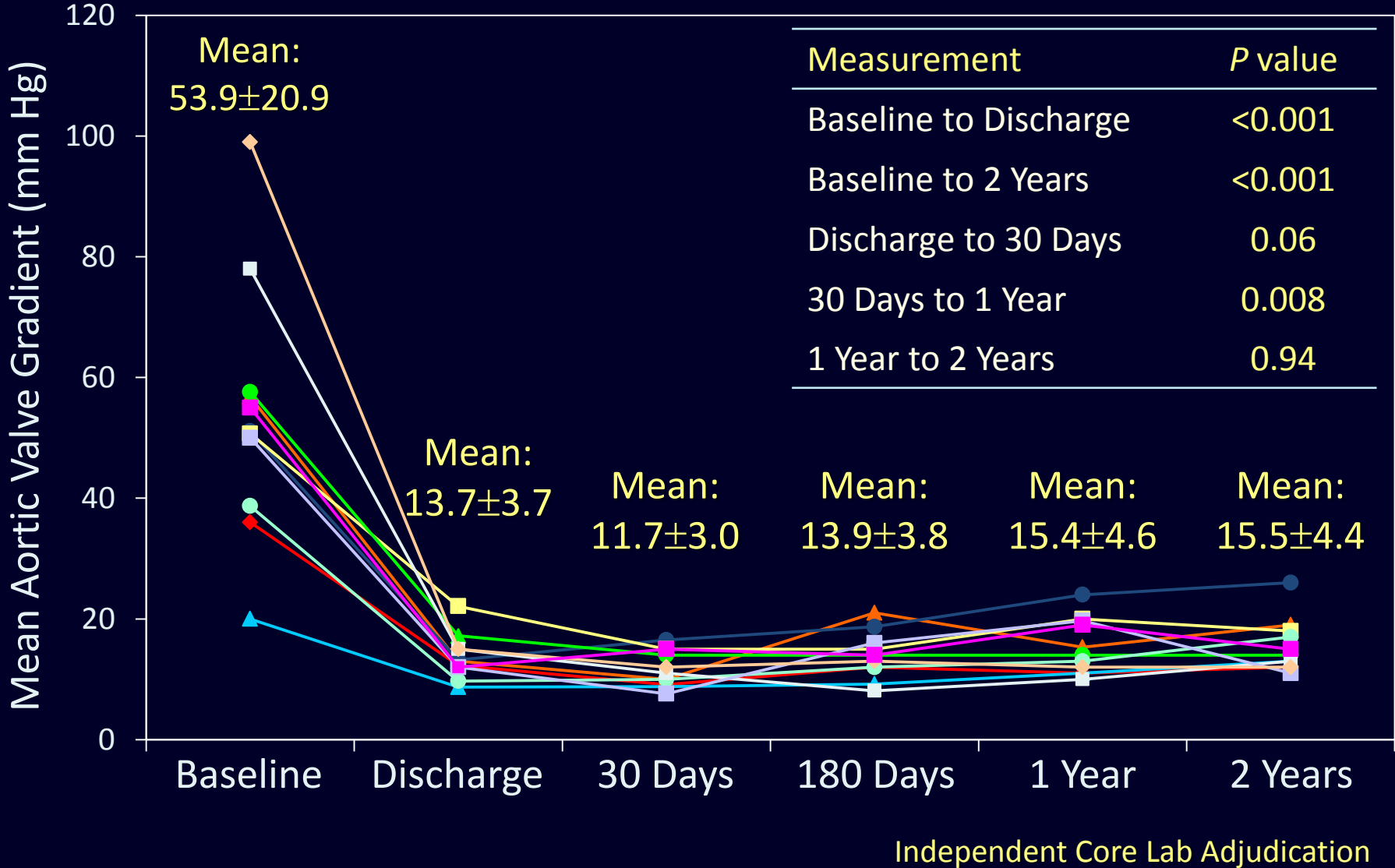


LOTUS Clinical Program



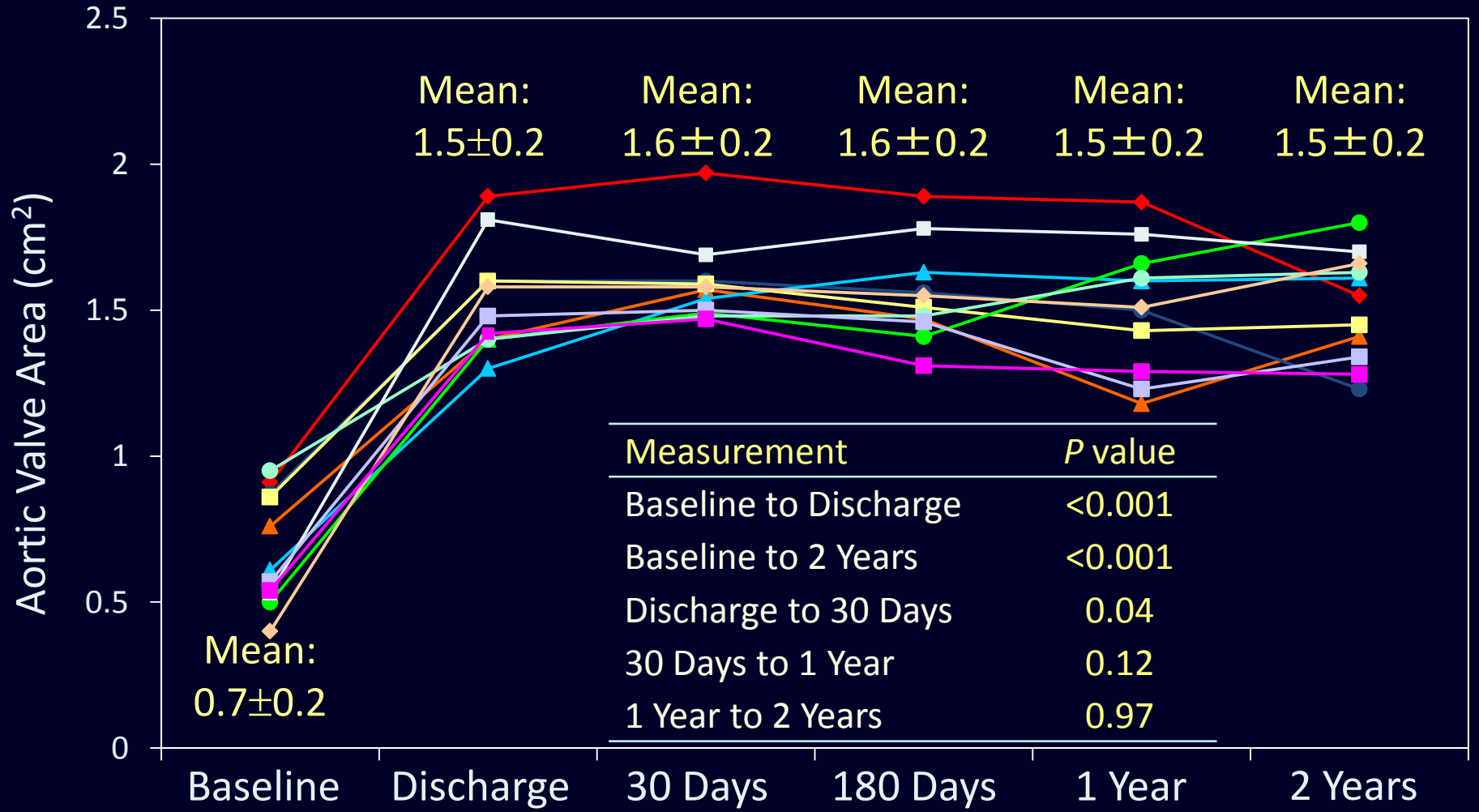
REPRISE I at 2 years

Mean Aortic Valve Gradient by Patient



REPRISE I at 2 Years

Effective Orifice by Patient



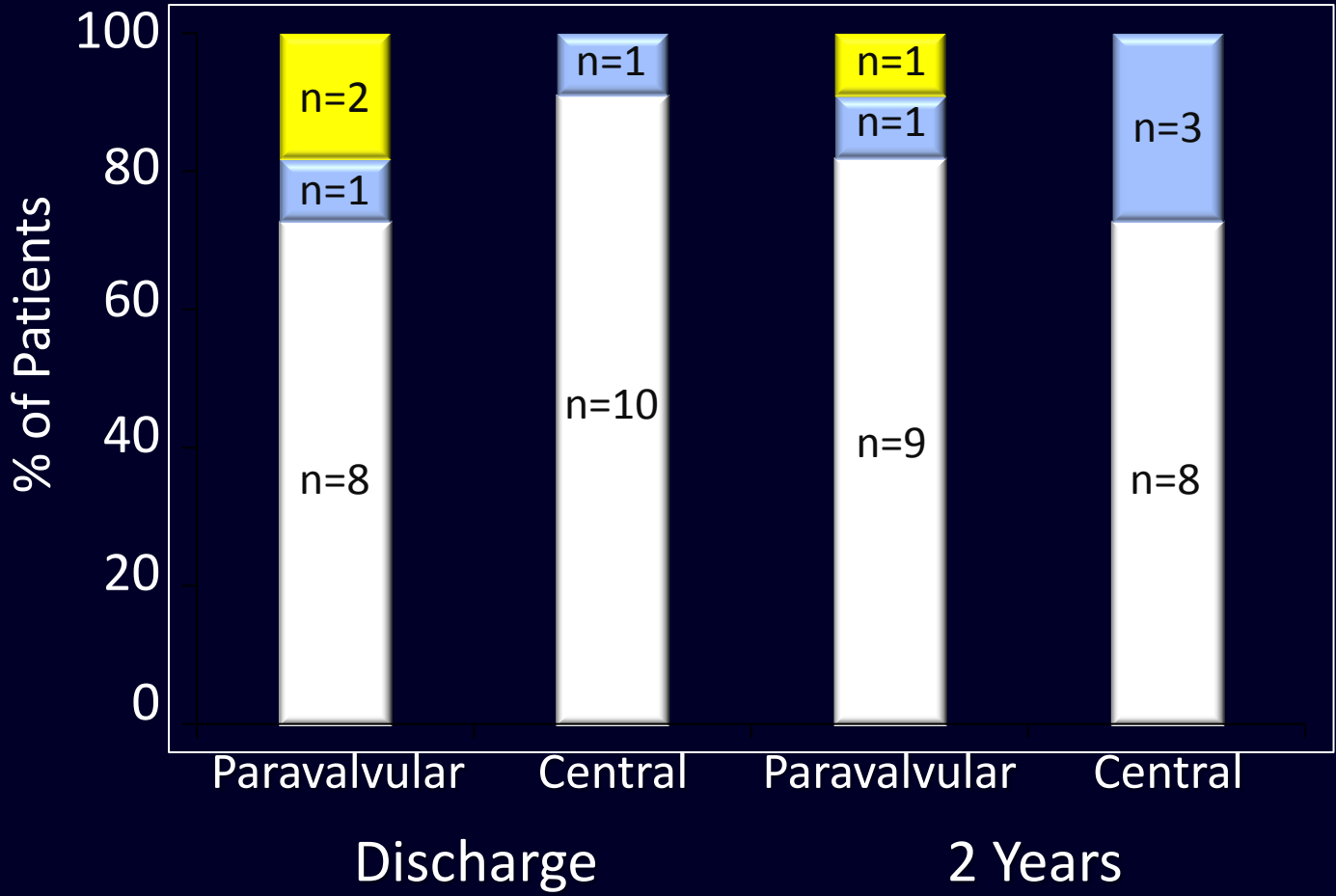
P values: Repeated measures and random effects ANOVA model

Independent Core Lab Adjudication

REPRISE I at 2 Years

Aortic Regurgitation

- Severe
- Moderate
- Mild
- Trivial
- None



No Moderate / Severe AR by Independent Adjudication

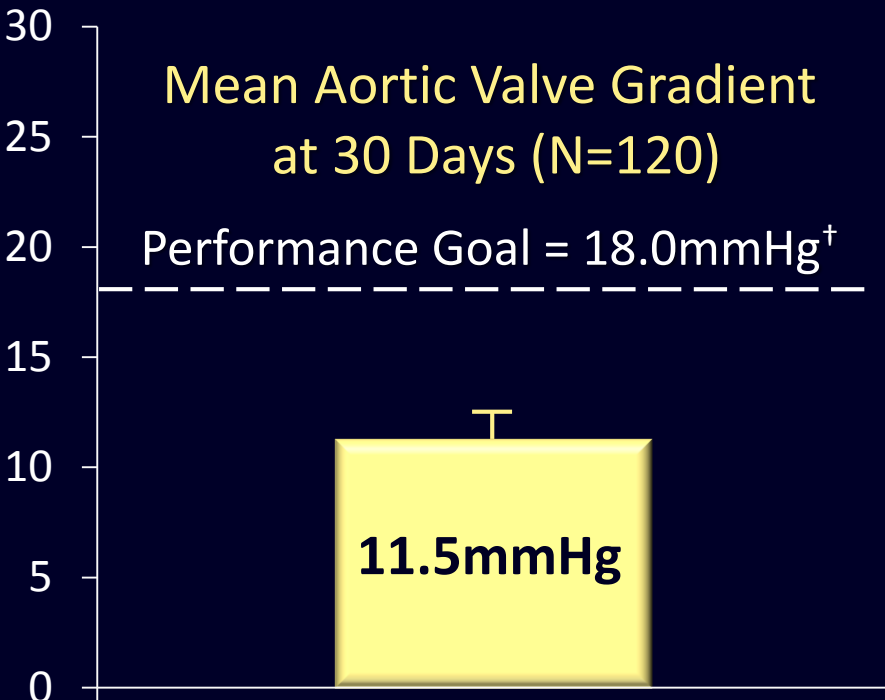
REPRISE II with Extended Cohort (N=250)

Device Performance

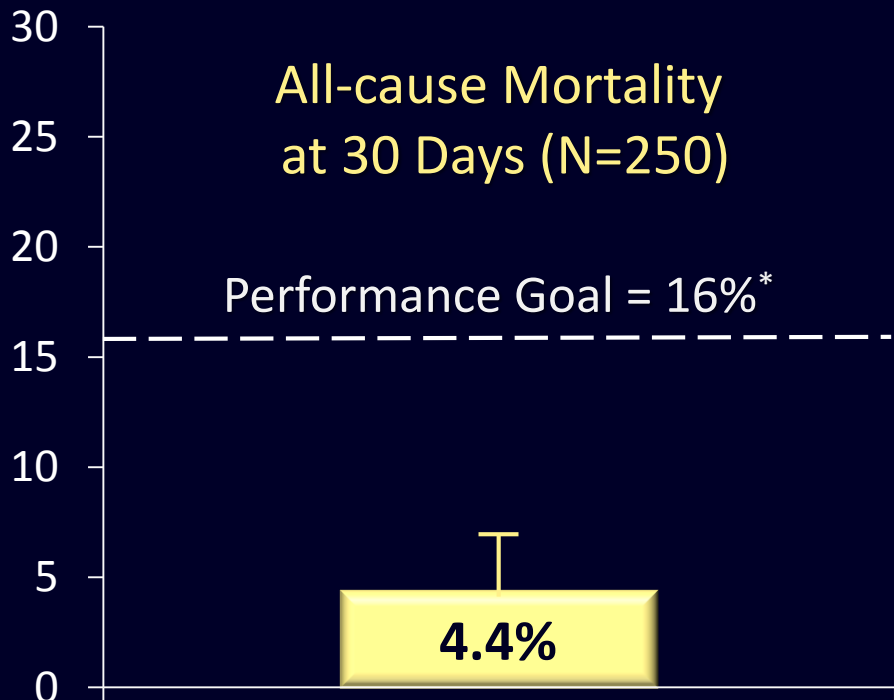
Successful access, delivery, deployment & system retrieval	98.8%*
Successful valve repositioning, if attempted (n=85)	100.0%
Partial valve resheathing (n)	71
Full valve resheathing (n)	14
Successful valve retrieval, if attempted (n=13)	92.3%*
Aortic valve malpositioning	0.0%
Valve migration	0.0%
Valve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

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

Primary Endpoints



*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)*

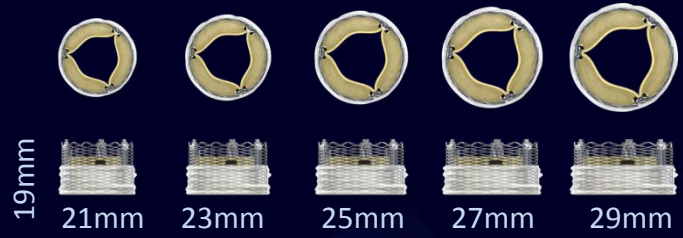
Summary

Lotus Valve Design Goals

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

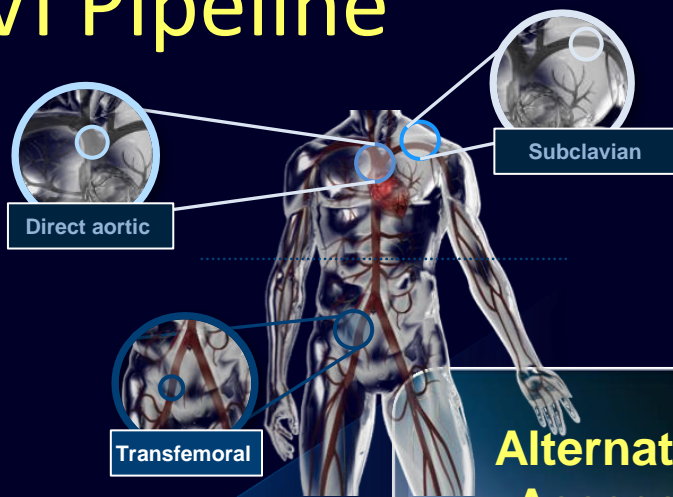
Thank You for Your Kind Attention

Boston Scientific Future TAVI Pipeline



Complete Size Matrix

FUTURE PIPELINE



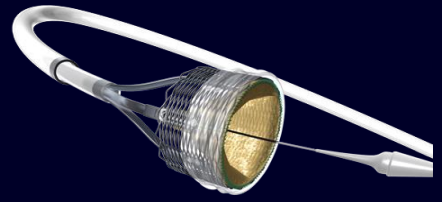
Alternate Access Routes



TAVI-Dedicated Wires

Enhanced Delivery System

Next Gen Focus Areas
BAV
Profile Reduction
Embolic Protection
Expandable Sheath
Large Bore Closure



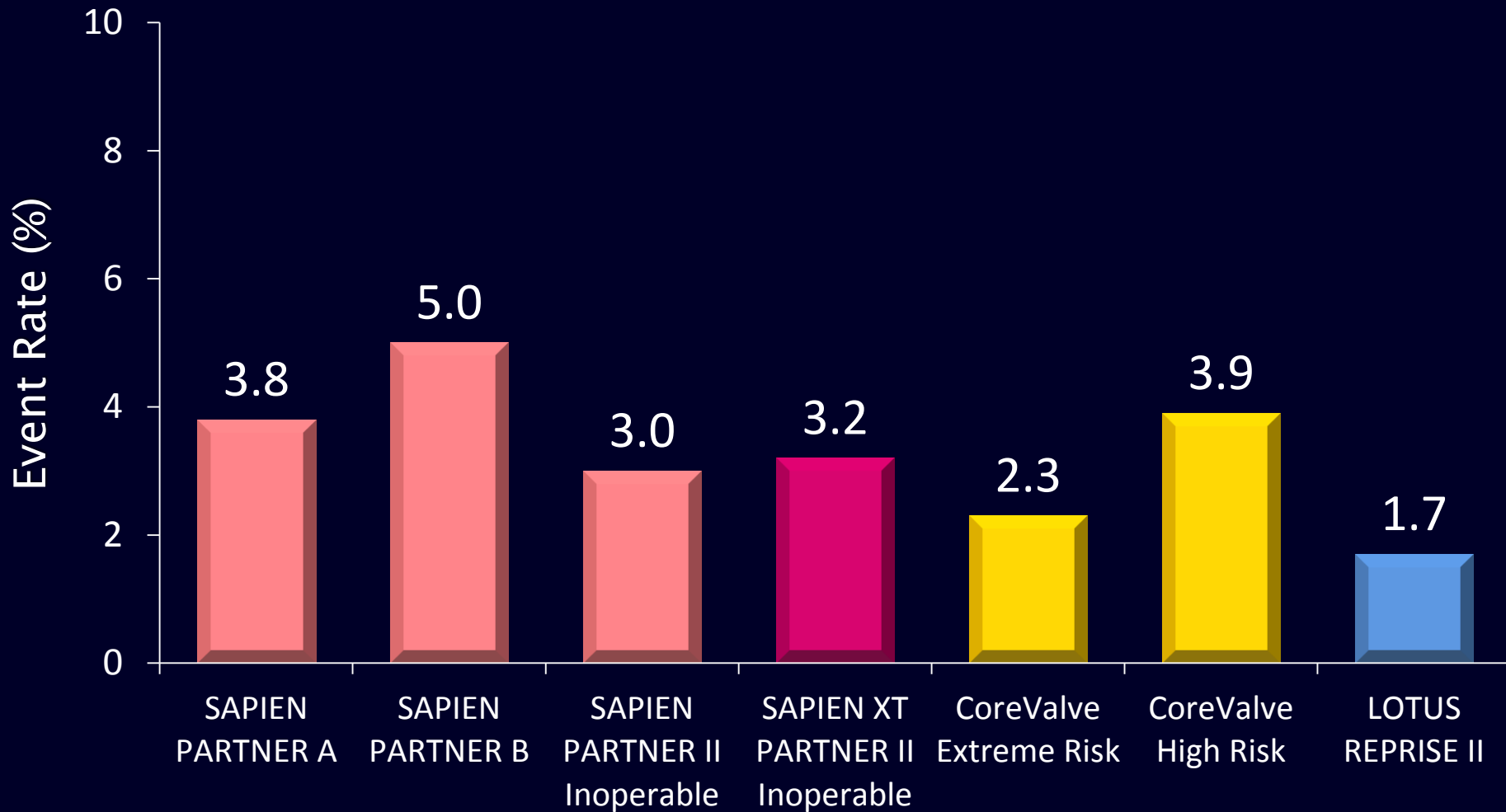
Summary

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 implants
-
- Second generation TAVI technologies show promise in reducing PVL and improving clinical outcomes

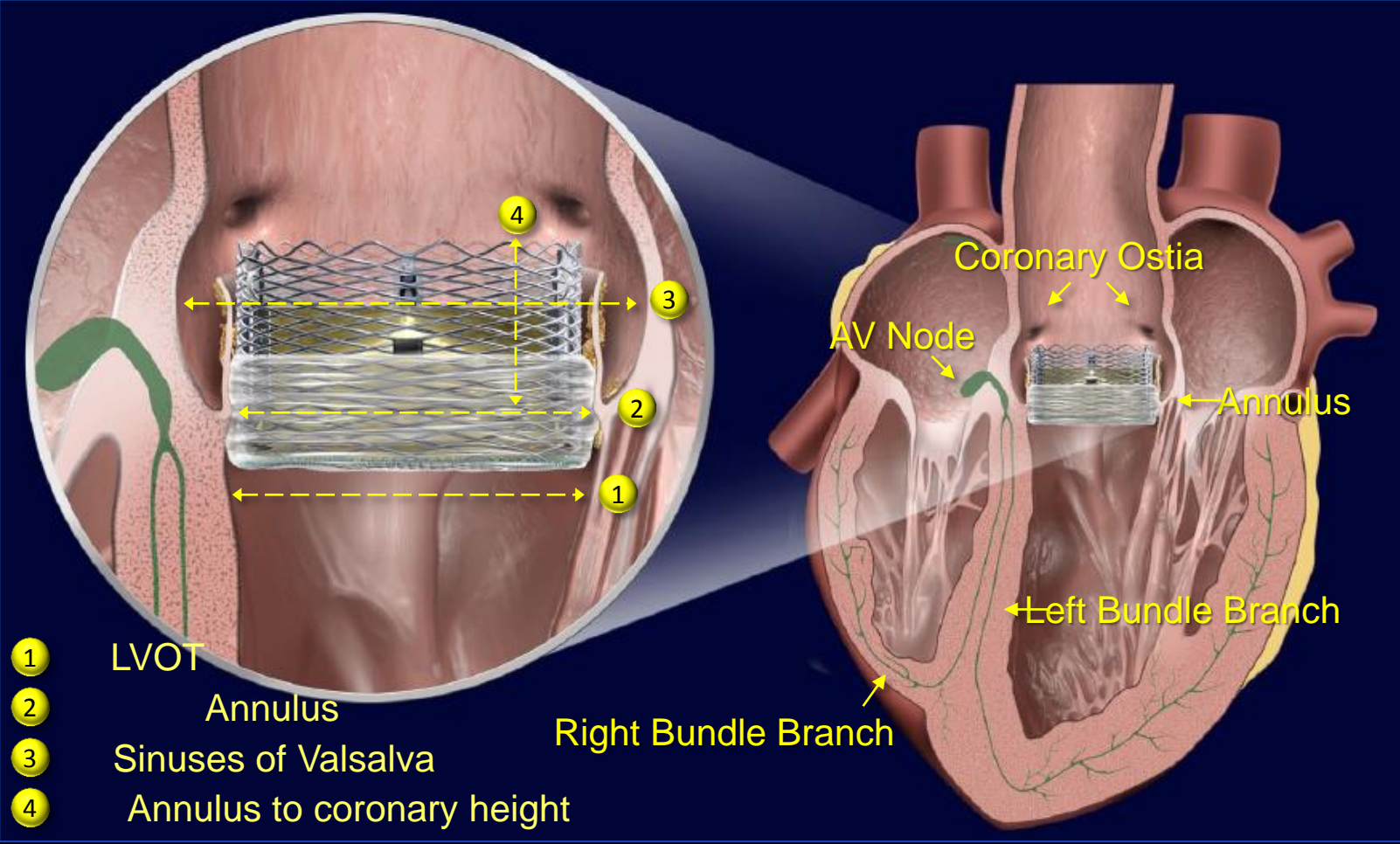
Major/Disabling Stroke at 30 Days

REPRISE II & Other TAVR Studies



PARTNER A: Smith, et al. N Engl J Med 2011;364:2187; PARTNER B: Leon, et al. N Engl J Med 2010;363:1597;
PARTNER II Inop: Martin Leon, MD at ACC 2013; CoreValve Extreme Risk: Popma J, JACC 2014 [ePub ahead of print]
REPRISE II: Meredith I et al, JACC 2014 (In Review). Results from different studies are not directly comparable.

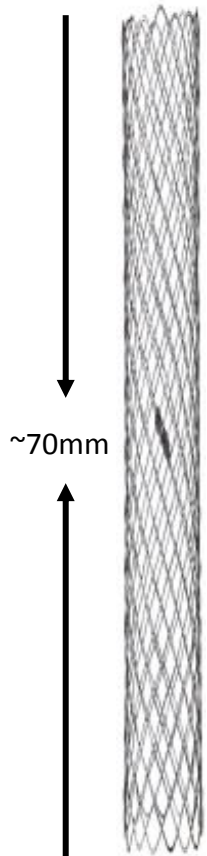
LOTUS Valve In Situ



Lotus Valve System Design Goals

Controlled Mechanical Expansion

Valve elongated in catheter for delivery



Step 1:
Unsheathing

Valve
unsheathed
into
intermediate
configuration



Step 2 :
Locking

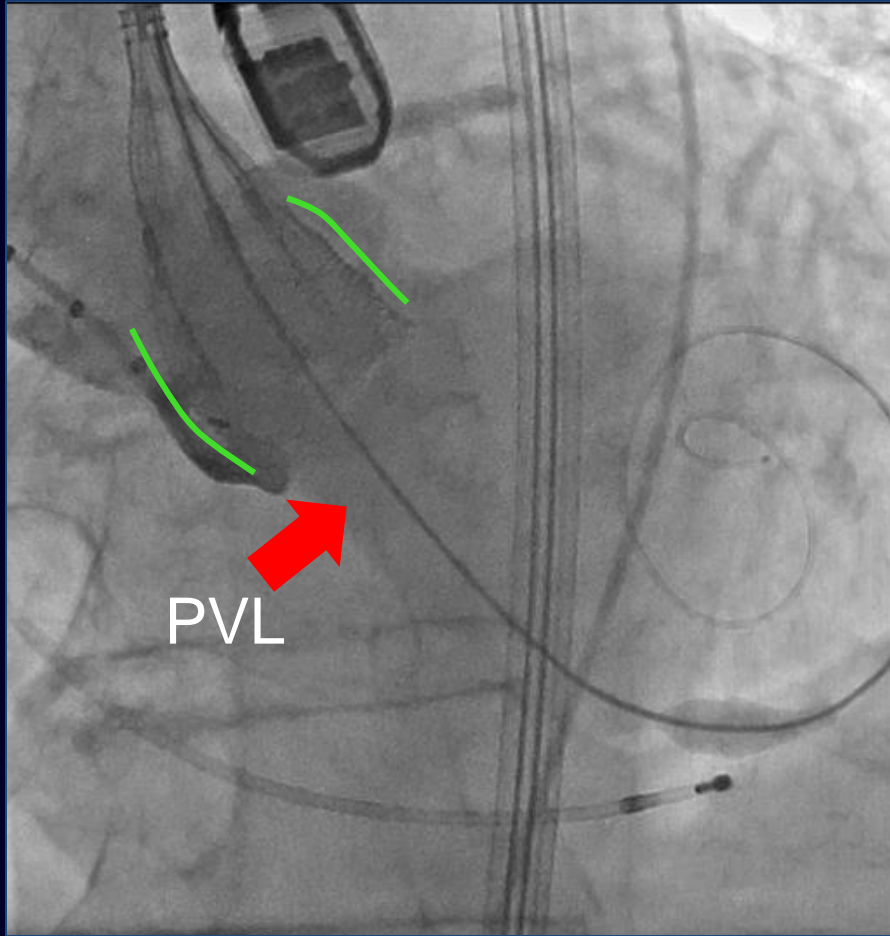
Valve expands
radially as it
shortens and
locks into final
configuration



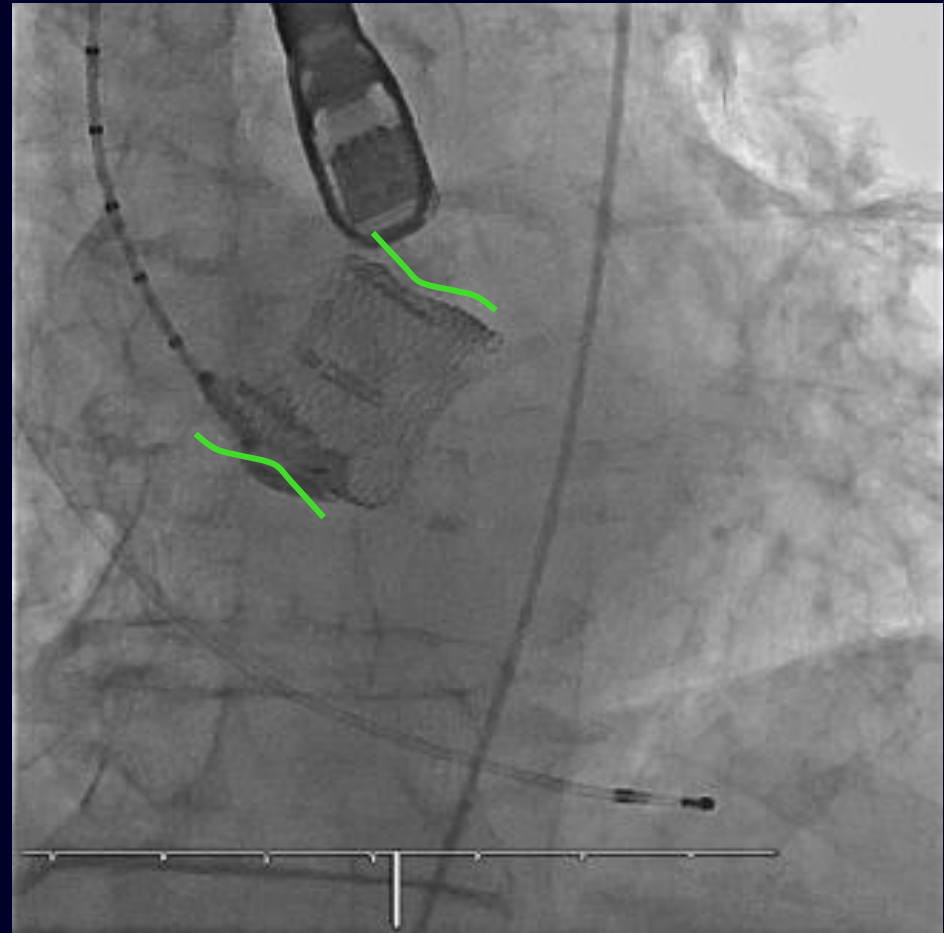
- Valve deployed via controlled mechanical expansion.
 - It is neither balloon expandable nor self expanding.
- No rapid pacing during deployment
- Valve functions early enabling controlled deployment
- No valve movement on release

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