Balloon Expandable Valve. New Understanding about Sizing, Positioning and Repeating

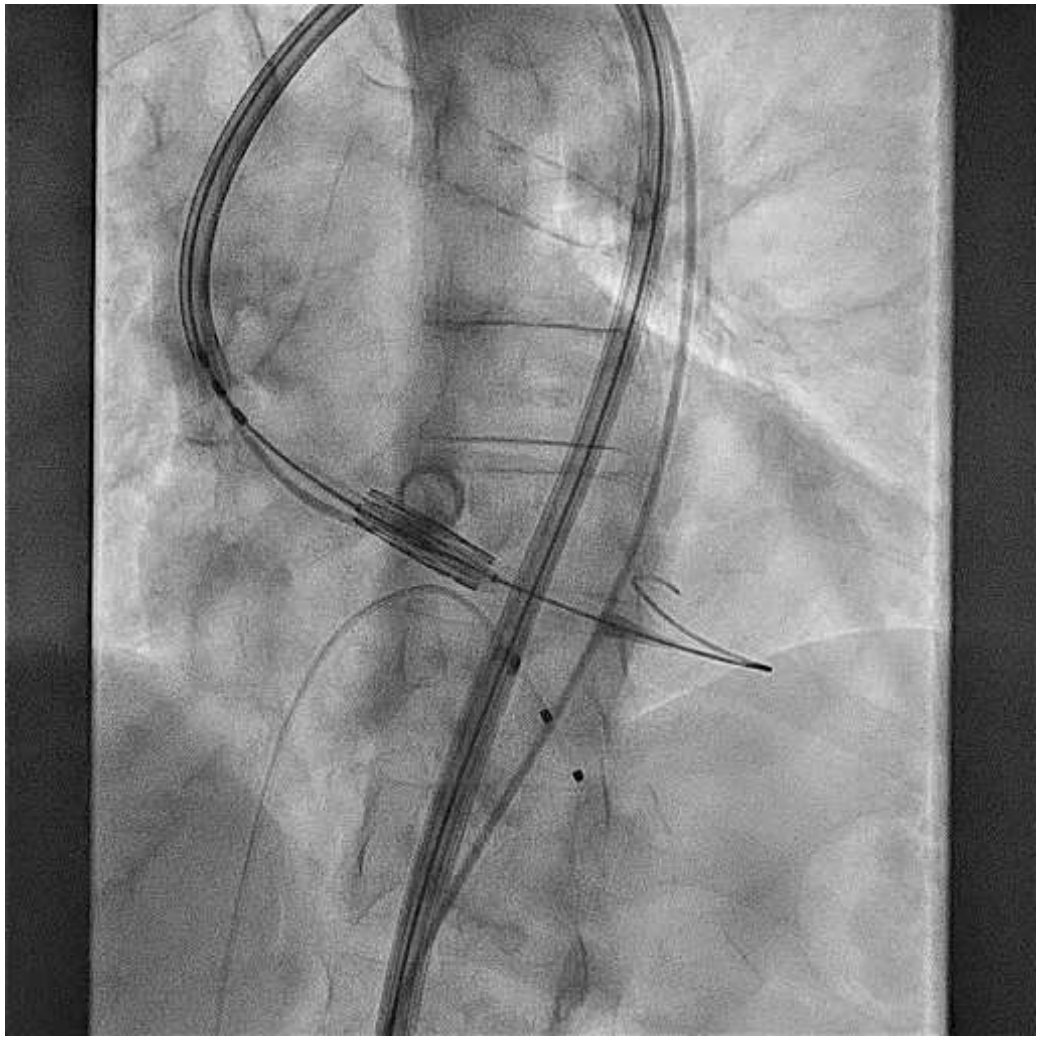
Alan C. Yeung, MD
Li Ka Shing Professor of Medicine
Medical Director, Cardiovascular Health
Stanford University School of Medicine
Stanford Medicine

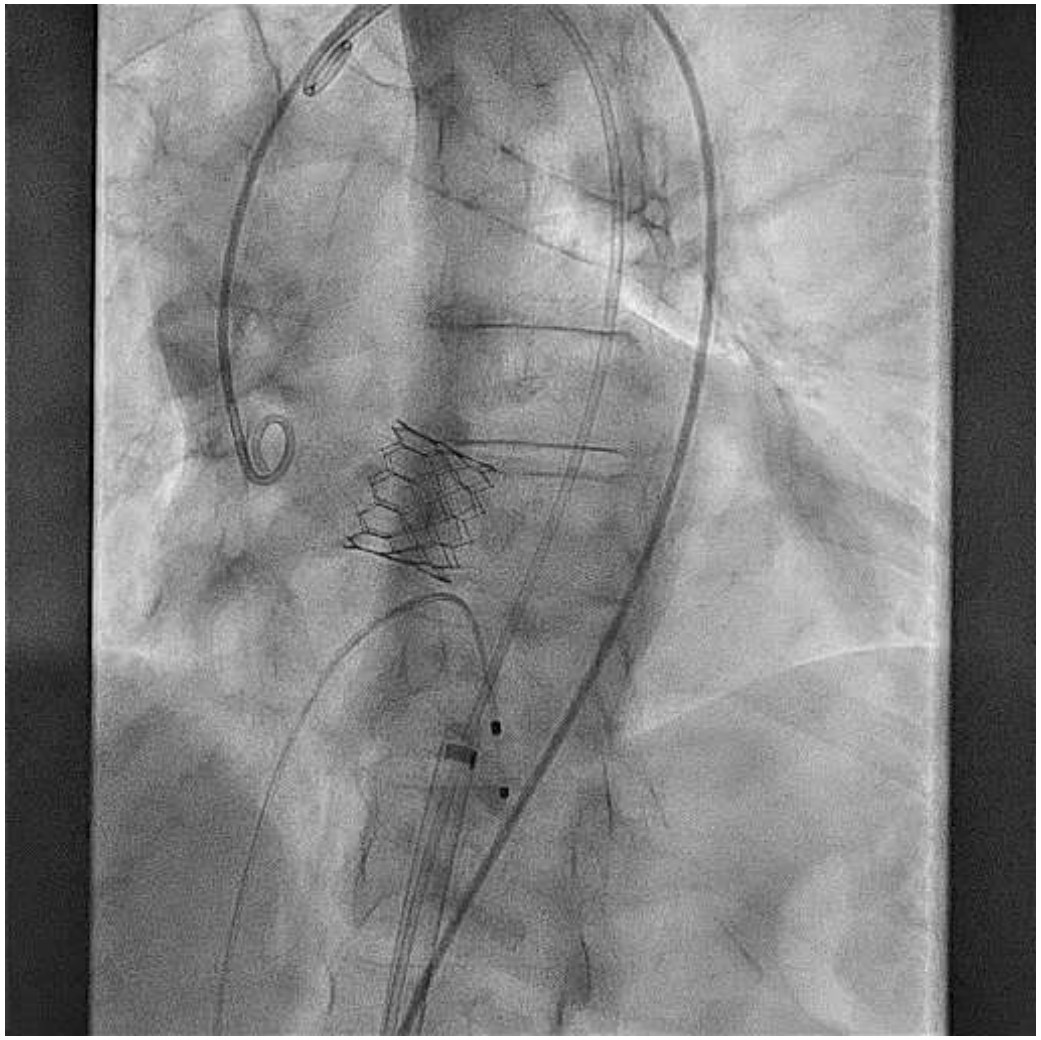
Disclosure Statement of Financial Interest

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

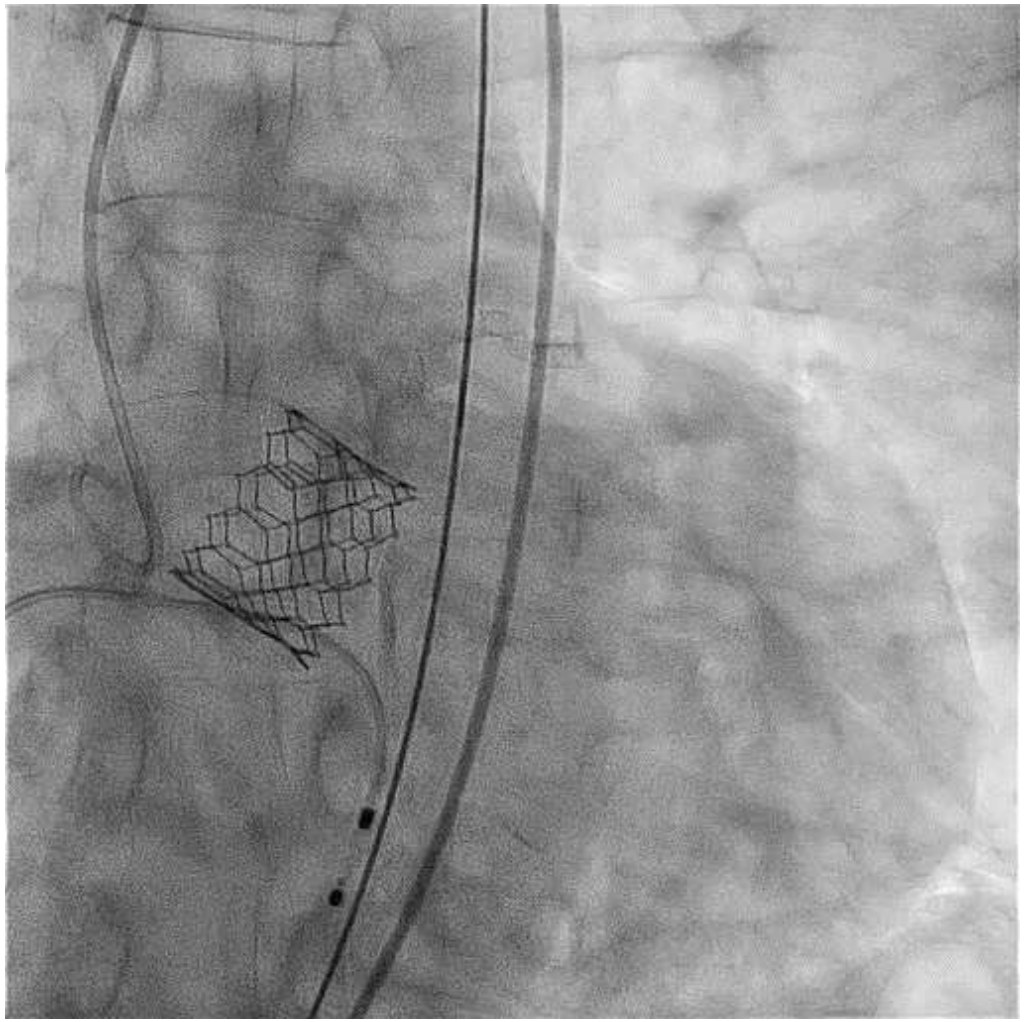
Affiliation/Financial Relationship	Company
• Grant/Research Support	• Edwards Lifesciences, Abbott
• Scientific Advisory Board	• Medtronic
• Executive Physician Council	• Boston Scientific Corp

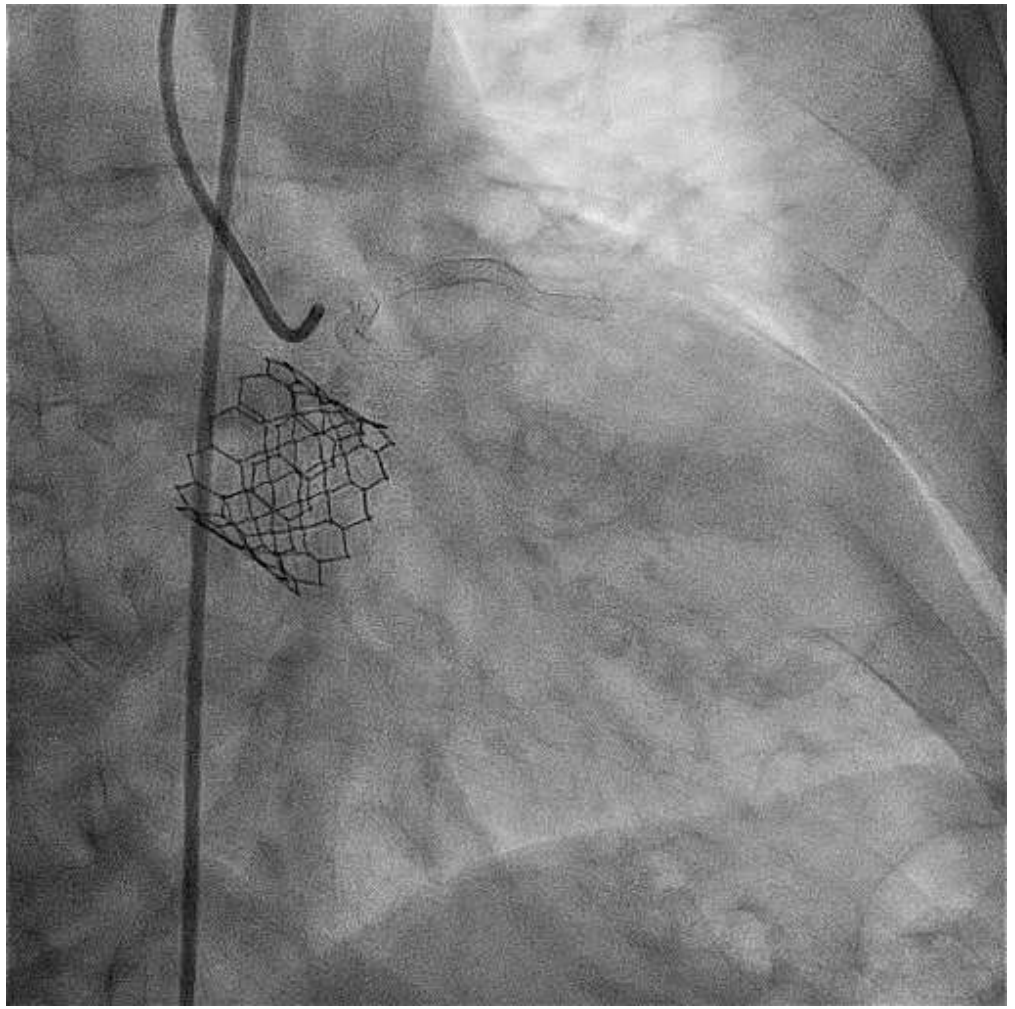
One and Done



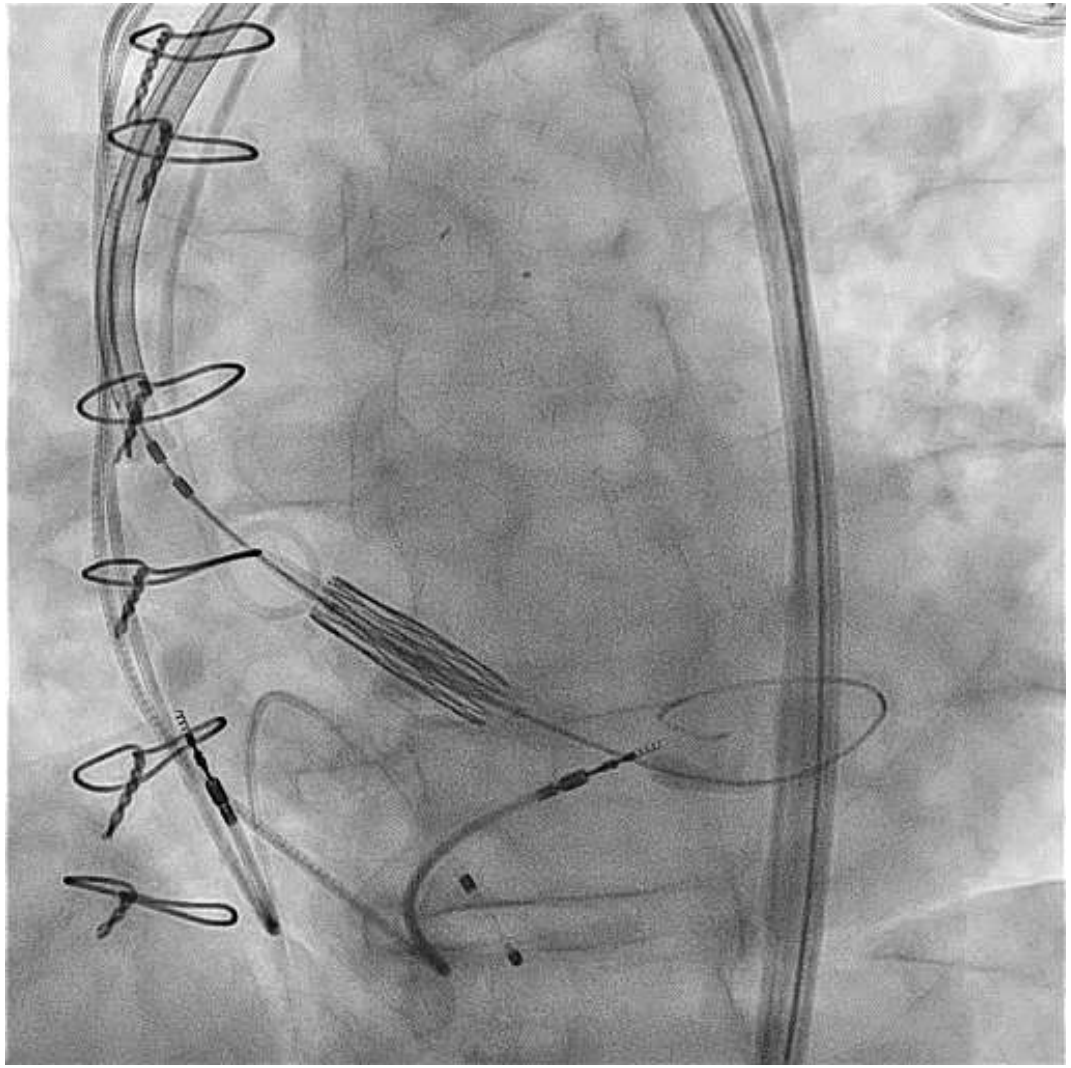


Annular Rupture



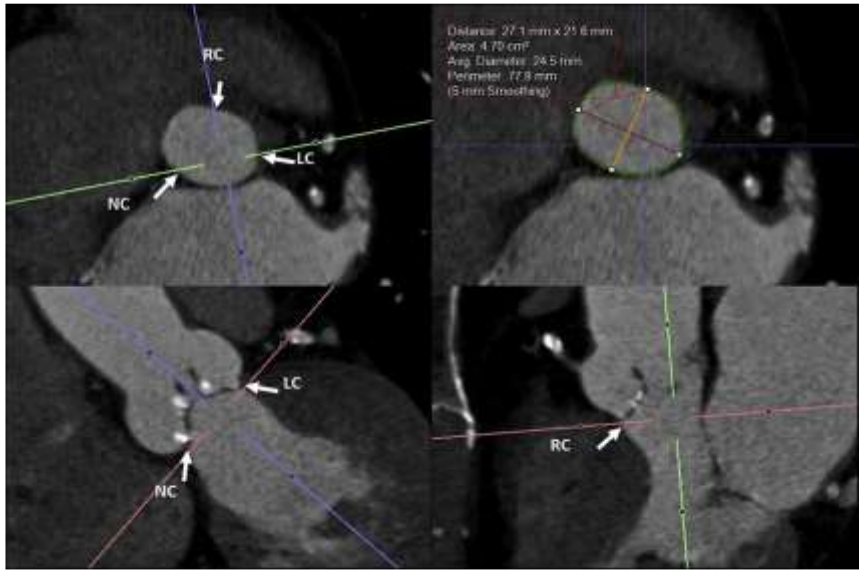


Valve Embolization



Optimal MDCT-Sizing of the SAPIEN 3 THV

- Sizing



Systolic/maximum annular area

SAPIEN 3 Dimensions (nominal area)

$$\text{Oversizing \%} = \frac{\text{nominal SAPIEN 3 area}}{\text{systolic annular area}} \times 100$$

Optimal MDCT-Sizing of the SAPIEN 3 THV

- SAPIEN - Influence of Sizing on the Prevalence of PAR

Inverse proportional relationship of oversizing and occurrence of PAR

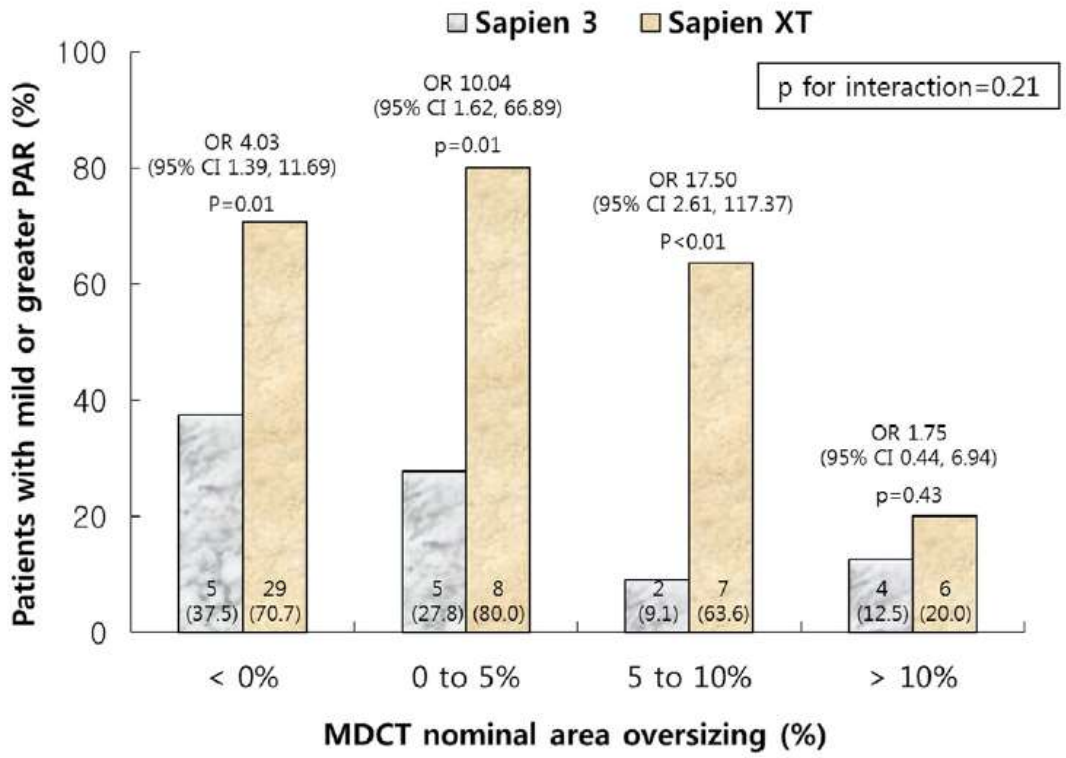
- Higher with undersizing
- Less with oversizing
- Low with oversizing >10% (by area)

Willson et al. JACC 2012

Optimal MDCT-Sizing of the SAPIEN 3 THV

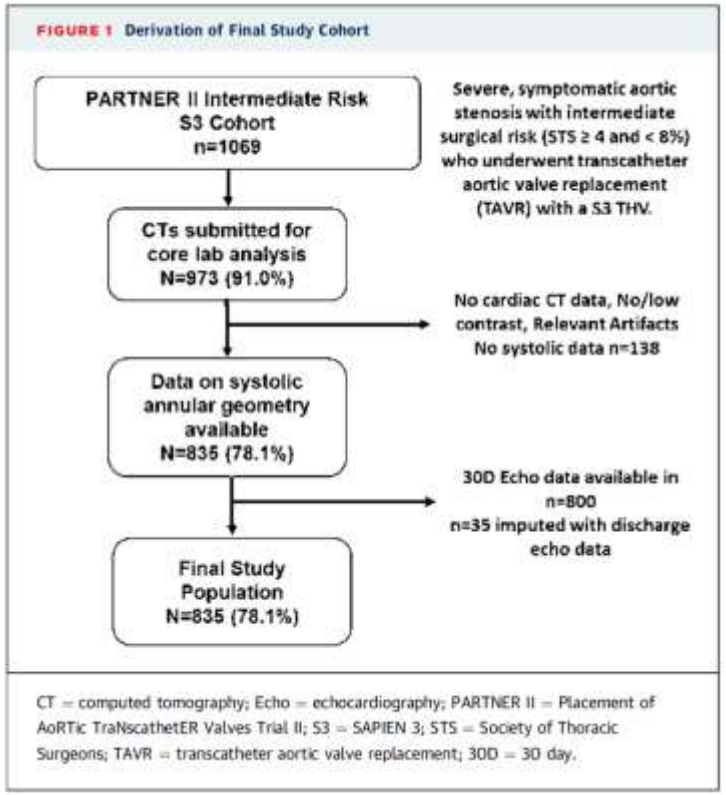
- Less oversizing needed SAPIEN 3 vs SAPIEN XT

FIGURE 5 Rates of Mild or Greater PAR According to MDCT Nominal Area Oversizing Group in Patients With Systolic MDCT Measurements

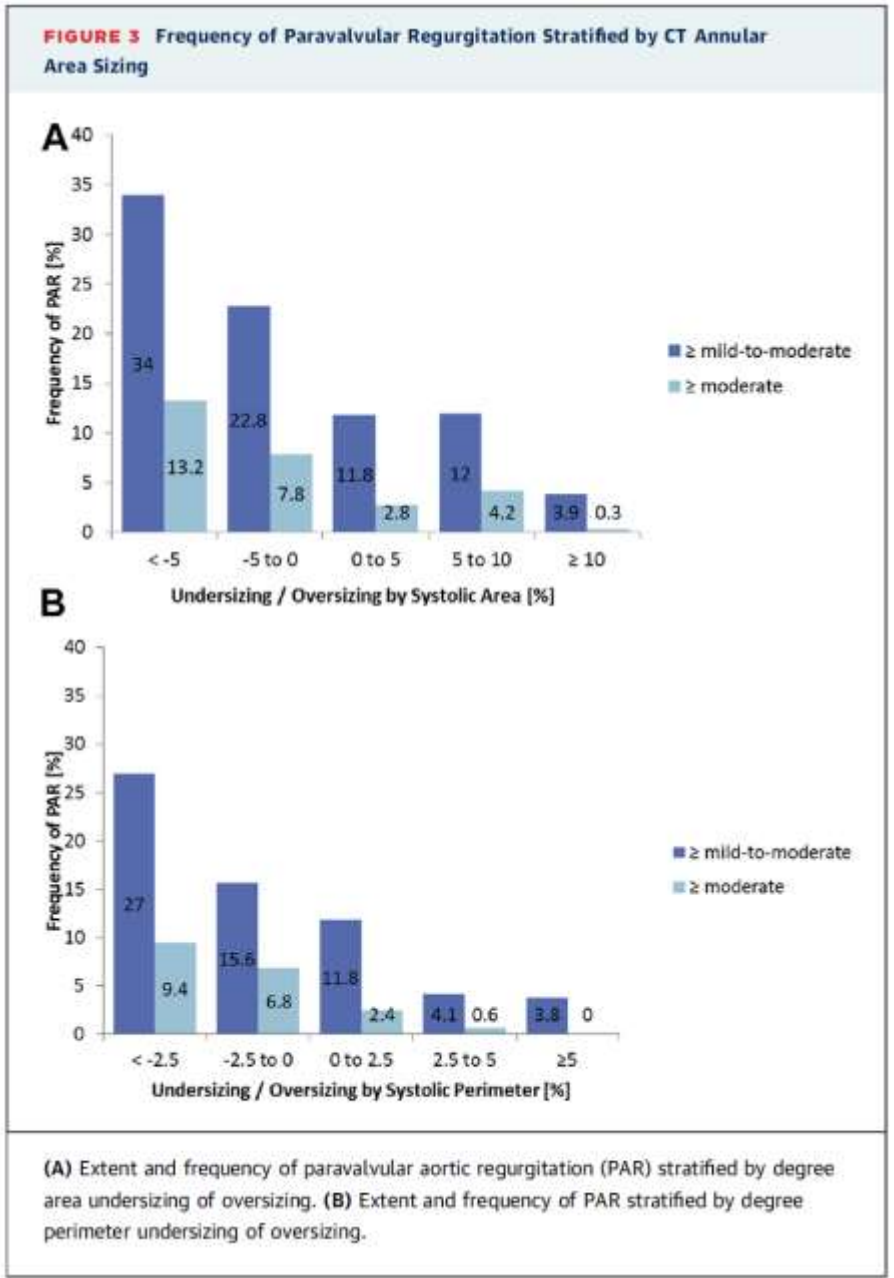


Optimal MDCT-Sizing of the SAPIEN 3 THV

- PARTNER 2 S3 Intermediate Risk

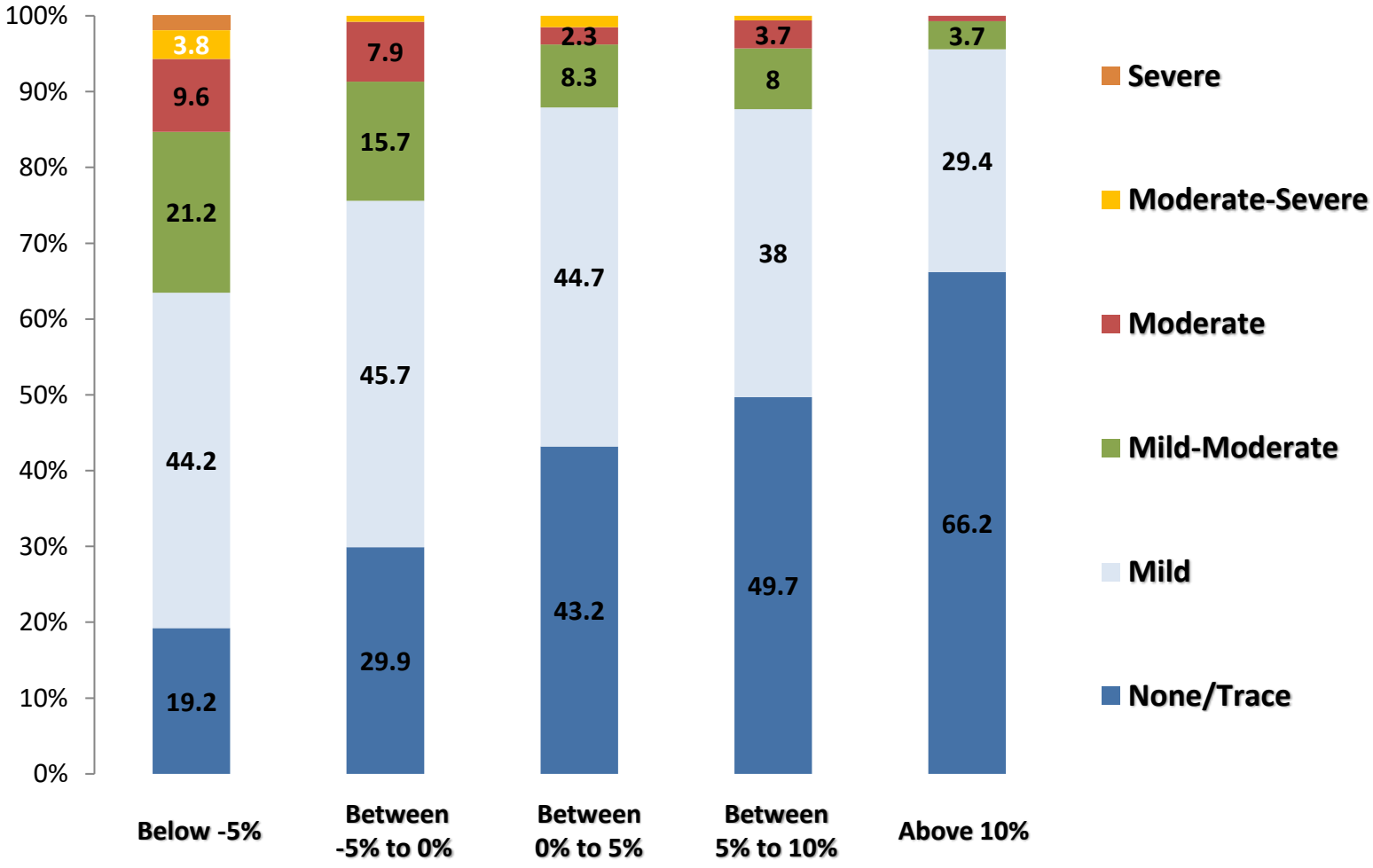


Blanke et al JACC Cardiovasc Interv. 2017



PAR Stratified by % Oversizing by Area

from Blanke and Leipsic, PII S3i Blanke et al JACC Cardiovasc Interv. 2017



Propensity-Matched Comparison | S3 vs. S3 Ultra

Paravalvular Regurgitation

Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

Real-World Experience With the SAPIEN 3 Ultra Transcatheter Heart Valve

A Propensity-Matched Analysis From the United States

Tamim M. Nazif, MD; Thomas J. Cahill, MBBS, DPhil; David Daniels, MD; James M. McCabe, MD; Mark Reisman, MD; Tarun Chakravarty, MD; Raj Makkar, MD; Amar Krishnaswamy, MD; Samir Kapadia, MD; Bassem M. Chehab, MD; John Wang, MD; Christian Spies, MD; Evelio Rodriguez, MD; Tsuyoshi Kaneko, MD; Rebecca T. Hahn, MD; Martin B. Leon, MD; Isaac George, MD

BACKGROUND: Paravalvular regurgitation (PVR) after transcatheter aortic valve replacement is associated with adverse clinical outcomes. The SAPIEN 3 Ultra (Ultra) is a new generation balloon-expandable transcatheter heart valve with a modified external skirt that is designed to reduce PVR, but reports of clinical and echocardiographic outcomes are limited. The aim of this study was to compare short-term outcomes of patients undergoing transcatheter aortic valve replacement with the Ultra and the original SAPIEN 3 (S3) transcatheter heart valve in a large national registry.

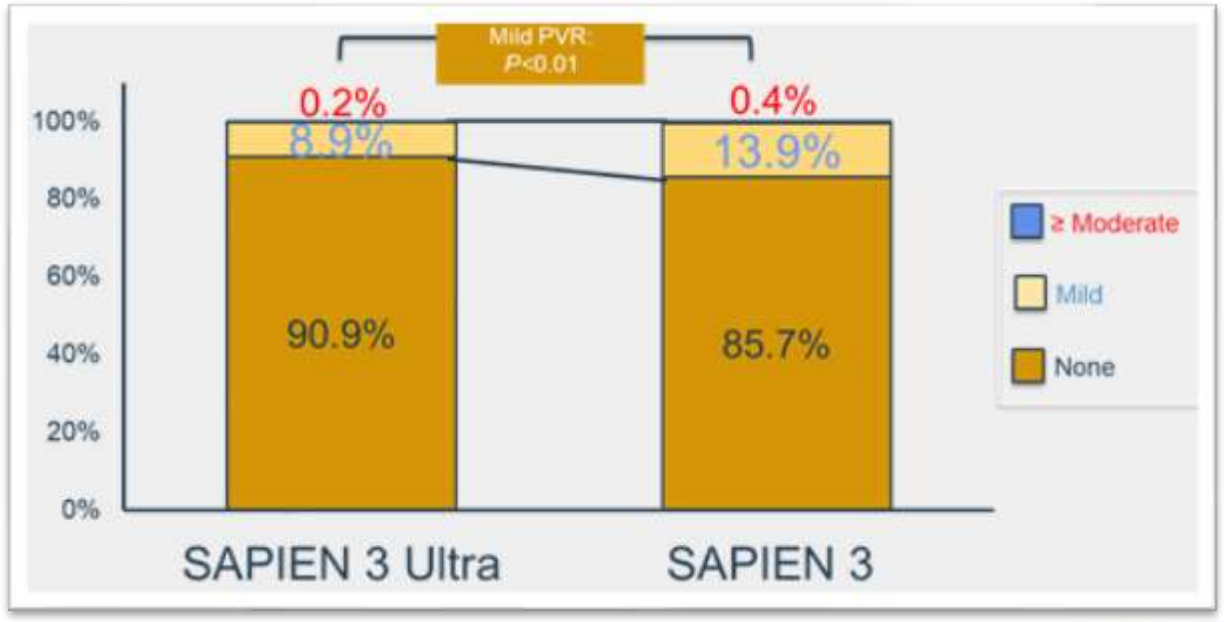
METHODS: Data from The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry was used to compare patients who underwent elective, transfemoral transcatheter aortic valve replacement with the Ultra or S3 transcatheter heart valve. Clinical and echocardiographic outcomes were analyzed in a propensity-matched cohort at discharge and 30 days.

RESULTS: Patients who underwent transcatheter aortic valve replacement with Ultra (N=1324) from January 2019 to February 2020 were propensity score–matched with patients treated with S3 (N=32 982) during the same period, resulting in 1324 matched pairs. There was no difference in the rate of device success between patients treated with Ultra and S3 (97.1% versus 98.0%, P=0.11). At hospital discharge, PVR was significantly reduced with Ultra compared with S3, with mild PVR in 9.0% versus 13.9% and moderate or greater PVR in 0.1% versus 0.4% (overall P<0.01). At 30 days, there were no differences between Ultra and S3 recipients in the rates of all-cause mortality or stroke (1.8% versus 2.8%, P=0.10), major vascular complications (1.1% versus 1.0%, P=0.84), or permanent pacemaker implantation (6.4% versus 6.2%, P=0.81).

CONCLUSIONS: In this propensity-matched analysis from the Transcatheter Valve Therapy Registry, the Ultra transcatheter heart valve was associated with similar procedural and 30-day clinical outcomes, but reduced incidence of PVR, compared with S3. The clinical benefit of less PVR should be evaluated in longer-term studies.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: heart valve ■ paravalvular regurgitation ■ transcatheter aortic valve replacement ■ United States



SAPIEN 3 versus SAPIEN 3 Ultra

7 Observational Studies [n=4107 patients (S3U: 1996; S3: 2111)]

SAPIEN 3

SAPIEN 3 Ultra

All-Cause Mortality

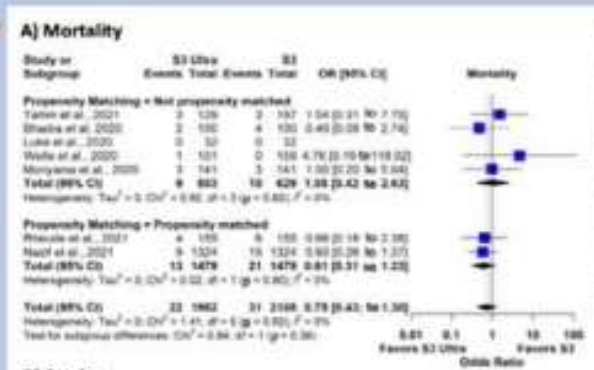
S3:1.5% vs **S3U**: 1.1%

Stroke

S3:1.65% vs **S3U**:1.49%

Bleeding

S3:0.76% vs **S3U**: 0.45%



Moderate/Severe PVL

S3: 1.71% vs **S3U**: 0.71%

Mild PVL

S3: 28.4% vs **S3U**: 13.4%

Pacemaker

S3: 6.17% vs **S3U**: 5.84%

Abdelfatlehet al AJC 168. 2022

Optimal MDCT-Sizing of the SAPIEN 3 THV

- SAPIEN 3 Sizing Chart

It may not always be possible to implant the larger THV size for borderline annulus diameters. Consider the smaller THV in the following special situations:

- Severe annulus calcification
- Narrow root and low coronary ostia
- Narrow sinotubular junction
- Mitral annular calcification
- Porcelain aorta
- Bulky leaflet and low coronary ostia

If/when outside of recommended range:

1) Reference alternative sizing modalities (echocardiography, balloon sizing)
2) Consider the following factors in valve size selection
   - Clinical: very advanced age, corticosteroids, chest radiation, extensive calcification, calcium extending into the LVOT, etc

Bold = recommended Sealing Zones relate only to valves that are deployed with nominal volumes

3D Area-derived Diameter (mm)		20.0	20.2	20.5	20.7	21.0	21.1	21.4	21.7	22.0	22.3	22.6	22.8	23.0	23.1	23.4	23.7	23.9	24.0	24.2	24.5
3D Annular Area (mm²)		314	320	330	338	346	350	360	370	380	390	400	410	415	420	430	440	450	452	460	470
% Annular Area Over (+) or Under (-) Nominal by 3D CT	23 mm	29.3	26.9	23.0	**20.1**	**17.3**	**16.0**	**12.8**	**9.7**	**6.8**	**4.1**	**1.5**	**-1.0**	**-2.2**	**-3.3**	**-5.6**	-7.7	-9.8			
	26 mm											29.8	26.6	25.1	23.6	**20.7**	**18.0**	**15.3**	**14.8**	**12.8**	**10.4**
	29 mm																				

ALL VALUES PRESENTED ARE BASED ON NOMINAL/RECOMMENDED INFLATION VOLUMES.

SYSTOLIC MEASURES ARE RECOMMENDED

24.5	24.7	25.0	25.2	25.5	25.7	26.0	26.2	26.4	26.5	26.7	26.9	27.2	27.4	27.6	27.9	28.0	28.1	28.3	28.5	28.8	29.0	29.2	29.4	29.5	29.6	29.9	30.1	30.3
470	480	490	500	510	520	530	540	546	550	560	570	580	590	600	610	615	620	630	640	650	660	670	680	683	690	700	710	720
10.4	**8.1**	**5.9**	**3.8**	**1.8**	**-0.2**	**-2.1**	**-3.9**	**-4.9**	-5.6	-7.3	-8.9																	
			29.8	27.3	24.8	22.5	**20.2**	**18.9**	**18.0**	**15.9**	**13.9**	**11.9**	**10.0**	**8.2**	**6.4**	**5.5**	**4.7**	**3.0**	**1.4**	**-0.2**	**-1.7**	**-3.1**	**-4.6**	-5.0	-5.9	-7.3	-8.6	-9.9

Optimal MDCT-Sizing of the SAPIEN 3 THV

- SAPIEN 3 Sizing Chart

It may not always be possible to implant the larger THV size for borderline annulus diameters. Consider the smaller THV in the following special situations:

- Severe annulus calcification
- Narrow root and low coronary ostia
- Narrow sinotubular junction
- Mitral annular calcification
- Porcelain aorta
- Bulky leaflet and low coronary ostia

If/when outside of recommended range:

1) Reference alternative sizing modalities (echocardiography, balloon sizing)
2) Consider the following factors in valve size selection
   - Clinical: very advanced age, corticosteroids, chest radiation, extensive calcification, calcium extending into the LVOT, etc

Bold = recommended Sealing Zones relate only to valves that are deployed with nominal volumes

3D Area-derived Diameter (mm)		20.0	20.2	20.5	20.7	21.0	21.1	21.4	21.7	22.0	22.3	22.6	22.8	23.0	23.1	23.4	23.7	23.9	24.0	24.2	24.5
3D Annular Area (mm²)		314	320	330	338	346	350	360	370	380	390	400	410	415	420	430	440	450	452	460	470
% Annular Area Over (+) or Under (-) Nominal by 3D CT	23 mm	29.3	26.9	23.0	**20.1**	**17.3**	**16.0**	**12.8**	**9.7**	**6.8**	**4.1**	**1.5**	**-1.0**	**-2.2**	**-3.3**	**-5.6**	-7.7	-9.8			
	26 mm											29.8	26.6	25.1	23.6	**20.7**	**18.0**	**15.3**	**14.8**	**12.8**	**10.4**
	29 mm																				

ALL VALUES PRESENTED ARE BASED ON NOMINAL/RECOMMENDED INFLATION VOLUMES.

SYSTOLIC MEASURES ARE RECOMMENDED

24.5	24.7	25.0	25.2	25.5	25.7	26.0	26.2	26.4	26.5	26.7	26.9	27.2	27.4	27.6	27.9	28.0	28.1	28.3	28.5	28.8	29.0	29.2	29.4	29.5	29.6	29.9	30.1	30.3
470	480	490	500	510	520	530	540	546	550	560	570	580	590	600	610	615	620	630	640	650	660	670	680	683	690	700	710	720
10.4	**8.1**	**5.9**	**3.8**	**1.8**	**-0.2**	**-2.1**	**-3.9**	**-4.9**	-5.6	-7.3	-8.9																	
			29.8	27.3	24.8	22.5	**20.2**	**18.9**	**18.0**	**15.9**	**13.9**	**11.9**	**10.0**	**8.2**	**6.4**	**5.5**	**4.7**	**3.0**	**1.4**	**-0.2**	**-1.7**	**-3.1**	**-4.6**	-5.0	-5.9	-7.3	-8.6	-9.9

Larger or Smaller Size Valve?

Larger Valve

- Lower gradient
- AV block
- Peri-aortic hematoma
- Annular rupture (including septum, AML)

Smaller Valve

- Paravalvular leak
- Malposition or embolization

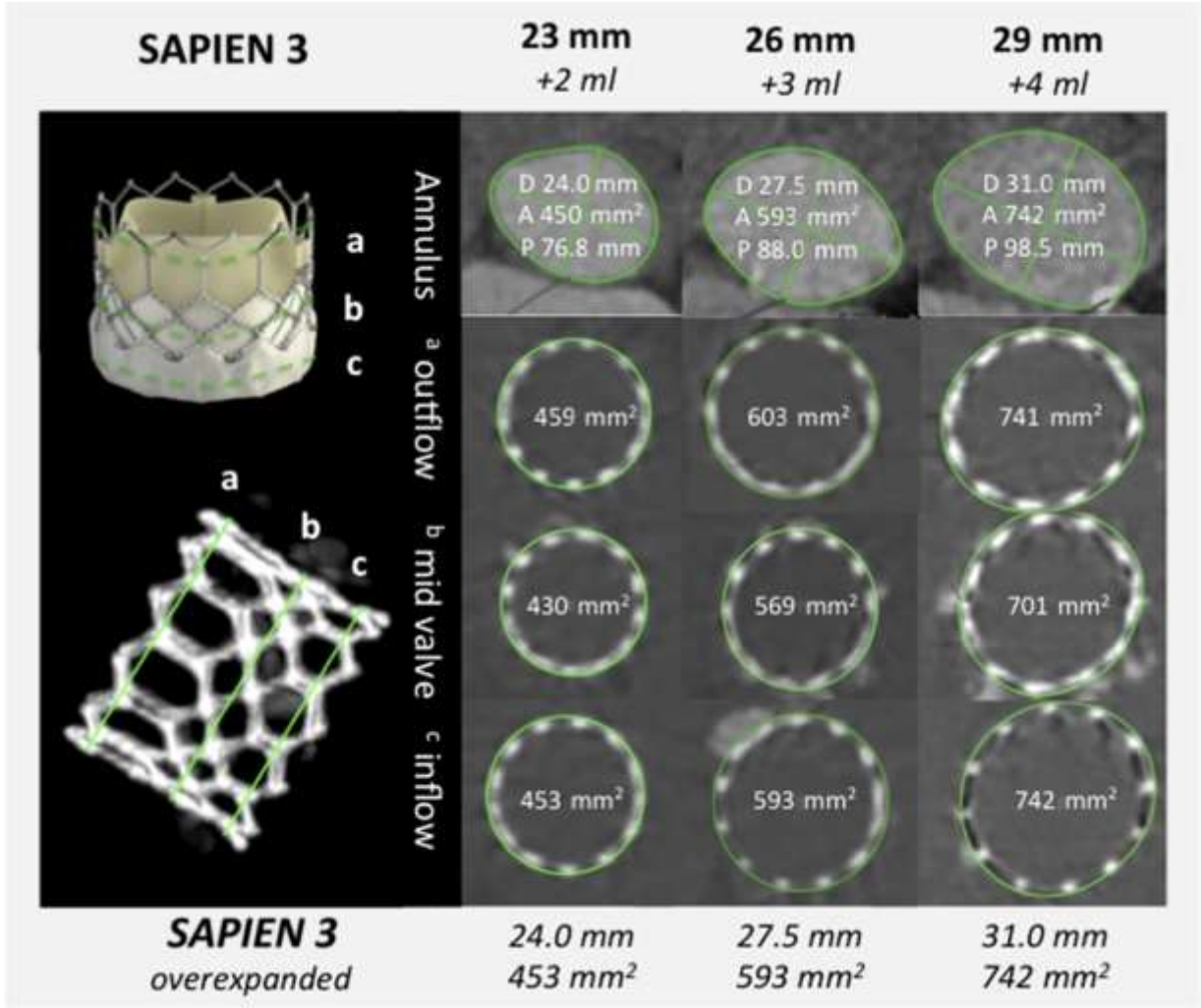
Annular Rupture is not Random

	Univariate	
Predictors	Odds Ratio (95%CI)	P value
LVOT calcification ≥ moderate	10.92 (3.23-36.91)	<0.001
Prosthesis area oversizing ≥ 20%	8.38 (2.67-26.33)	<0.001

Consider a oversizing a smaller valve due to anatomical factors:

- Annular calcium
  - LVOT calcification, porcelain aorta
- Coronary obstruction concerns
  - (Narrow root, bulky leaflets, low coronary ostia)
- Narrow STJ
- Anterior mitral leaflet calcification

Over-Sizing of the Smaller SAPIEN 3 THV



- 23mm+2 ml = 5% oversize for area of 430mm2 (instead of 5% undersize)
- 26mm+3 ml = 9% oversize for area of 546mm2 (instead of 5% undersize)
- 29mm+4 ml = 9% oversize for area of 680mm2 (instead of 5% undersize)

Under-Sizing of the Larger SAPIEN 3 THV

Very roughly underfill the balloon by 5-10% (1 to 2cc)…

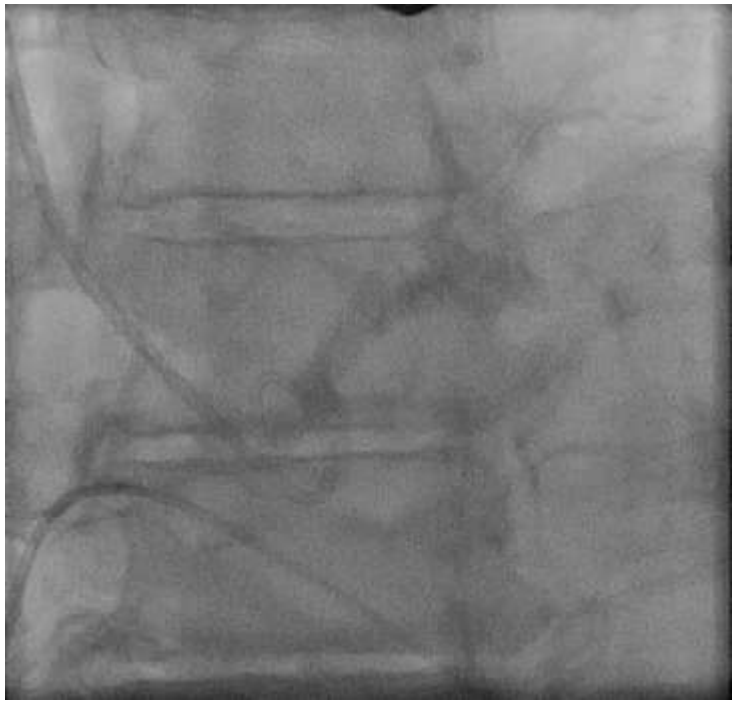
- Annular stretch will be reduced
- THV inflow size will be reduced slightly
- Little effect on symmetry, gradients
- Less risk of annular injury?
- Reduced durability?

“Tunable” valve strategy

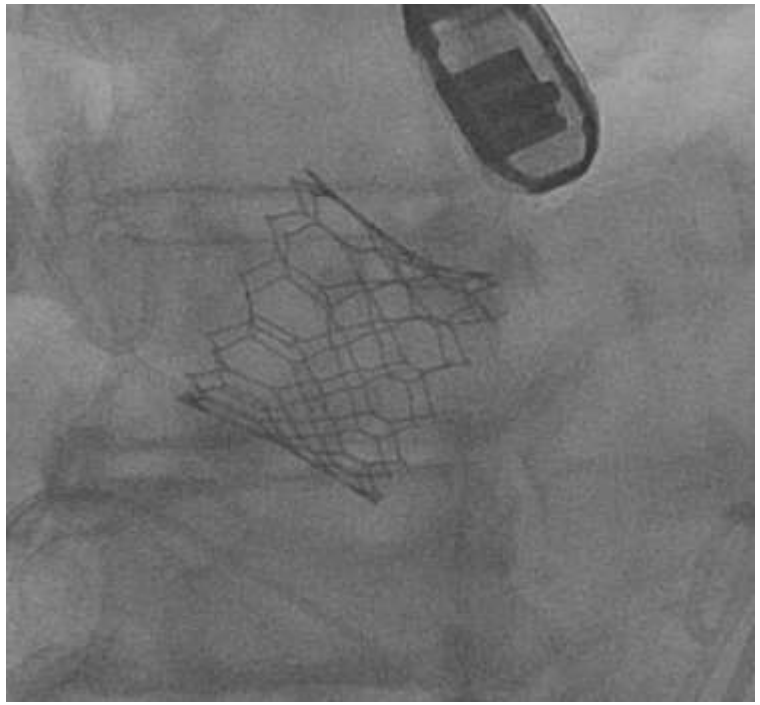
- Select the larger valve
- Underfill 5% to <10% (1 to 2cc):
  - if oversizing >20% by area
  - if high risk for rupture
    (eg. LVOT calcification, very elderly, XRT)
- If there is a leak, then add in removed contrast and post-dilate

SAPIEN 3
LVOT calcium, oversizing >20% by area

- LVOT calcium



- Underfilled 9%



Slightly underexpanded
No leak

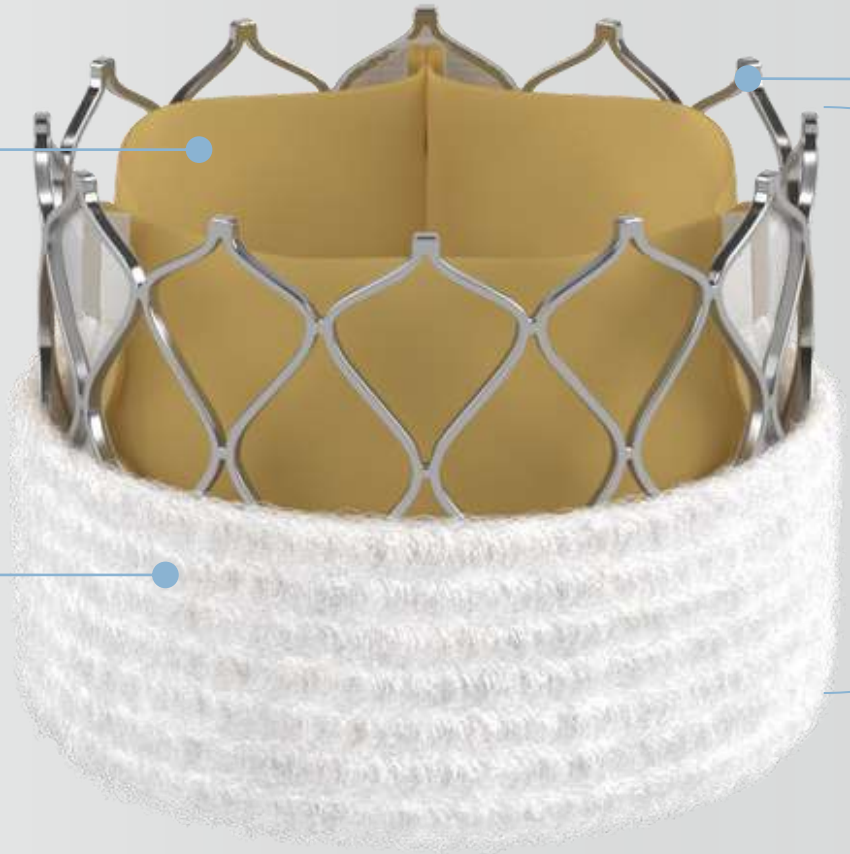
SAPIEN X4 Transcatheter Heart Valve System

RESILIA tissue

- Offers enhanced anti-calcification technology and enables dry storage
- Maintains bovine pericardial leaflets matched for thickness and elasticity

Enhanced PET outer skirt

- Designed to further minimize PVL
- Maintains low profile access



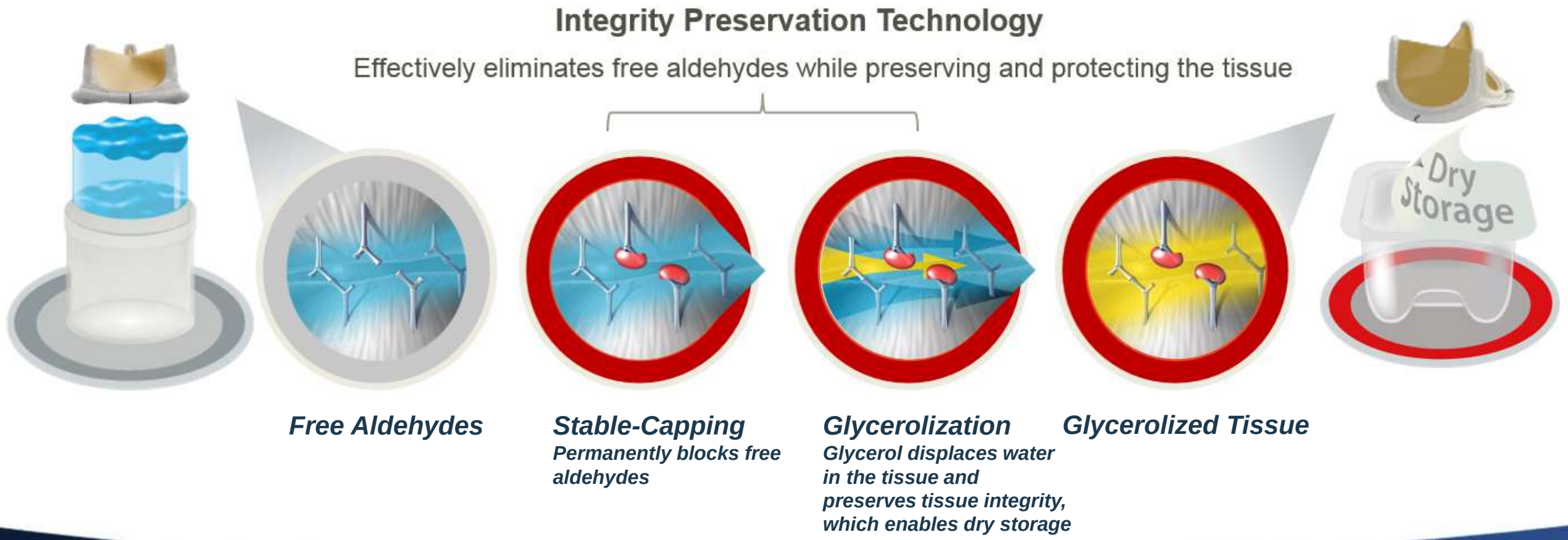
Novel frame and leaflet design

- Enables adjustable sizing while maintaining valve performance over the deployment diameter range
- Maintains high radial strength cobalt chromium balloon-expandable design

Low frame height and large cells

- Facilitates future coronary access

RESILIA tissue is bovine pericardial tissue transformed by the addition of a novel integrity preservation technology



SAPIEN X4: Provides Adjustable Valve Sizing

SAPIEN 3 Ultra

4 valve sizes (3 mm increments)

20 mm

23 mm

26 mm

29 mm

SAPIEN X4

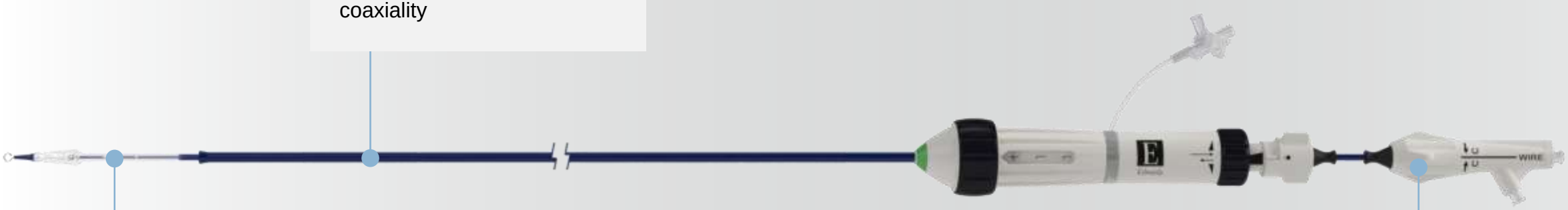
3 valve sizes, 16 unique deployment diameters (0.5 mm increments)


480
470
490
460
300
450
310
440
320
430
330
420
340
410
350
400
360
390
370
380
% Oversizing
Deployed valve diameter in mm
Bolded cells represent the recommended % oversizing consideration range based on deployed valve diameters and annular areas. However, chosen % oversizing/under sizing is determined by the treating physician and is dependent upon each patient's individual anatomical considerations.
Systolic measurements are recommended
Valve Size
23 mm
26 mm
All values presented are based on deployed diameter ranges of the THV
SAPIEN X4 Valve Sizing Chart
Edwards

SAPIEN X4 Delivery System

Commander-like system

- Articulation for tracking and coaxiality

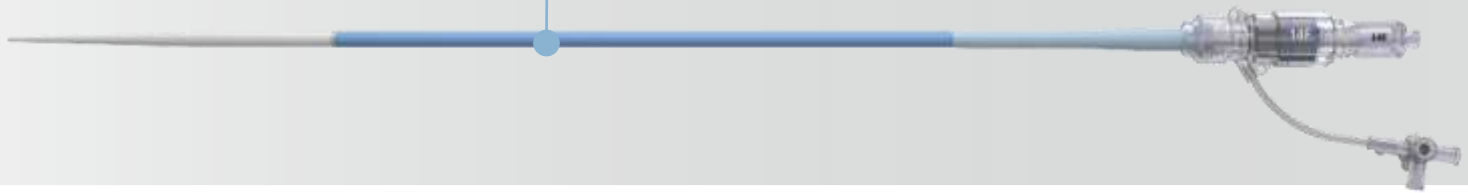


On-balloon valve preparation

- Enables commissural alignment
- Streamlines procedure

Low profile access

- Maintains 14/16F expandable sheath compatibility

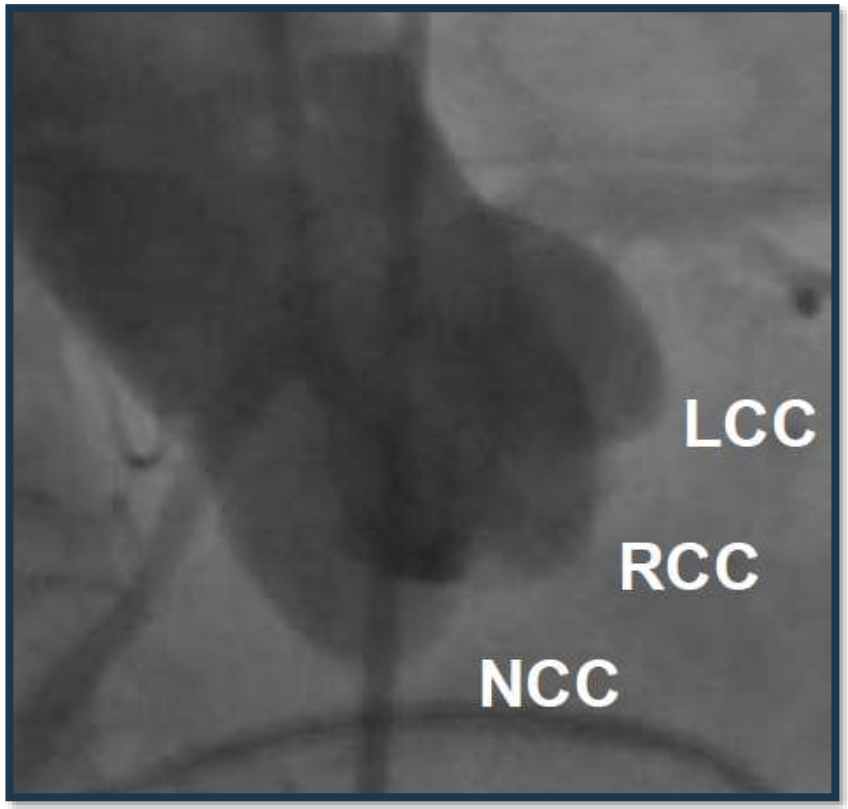


Valve Rotation Control

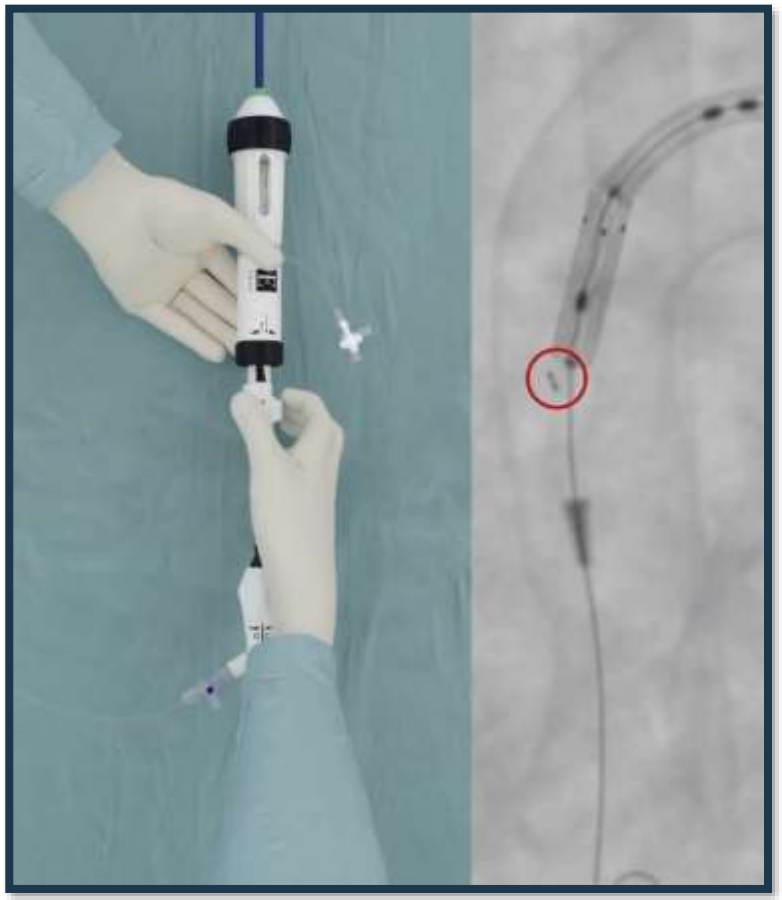
- Enables commissural alignment
- Independent control of valve orientation

Commissural Alignment with SAPIEN X4

1. ***Standard 3 cusp view***



2. ***Align radiopaque marker prior to deployment***



SAPIEN X4 Clinical Research Program

ALLIANCE Study

ALLIANCE "Native" Trial
n=765

Bicuspid Registry
n= 150

VIV
n= 150

- Prospective, single arm, multicenter, study
- Severe, aortic stenosis
- Any surgical risk level
- Symptomatic (NYHA ≥2)
- Trileaflet valve morphology

Primary Endpoint: Non-hierarchical composite of death and stroke at 1 year
Compared to historical control (primarily PARTNER 2 and PARTNER 3)

Key Secondary Endpoints:
- Favorable outcome per VARC-3
- Paravalvular regurgitation at 30 days
- New permanent pacemaker implant at 30 days

Follow-up *(Annually Through 10 years)*

Study Committee

NATIVE STUDY PI's

Tamim Nazif , MD
Columbia University

Rahul Sharma, MBBS
Stanford Hospital

AVIV STUDY PI

Pradeep Yadav, MD
Piedmont Heart Institute

STEERING COMMITTEE

Martin Leon, MD, Chair
Columbia University

Vinod Thourani, MD
Piedmont Heart Institute

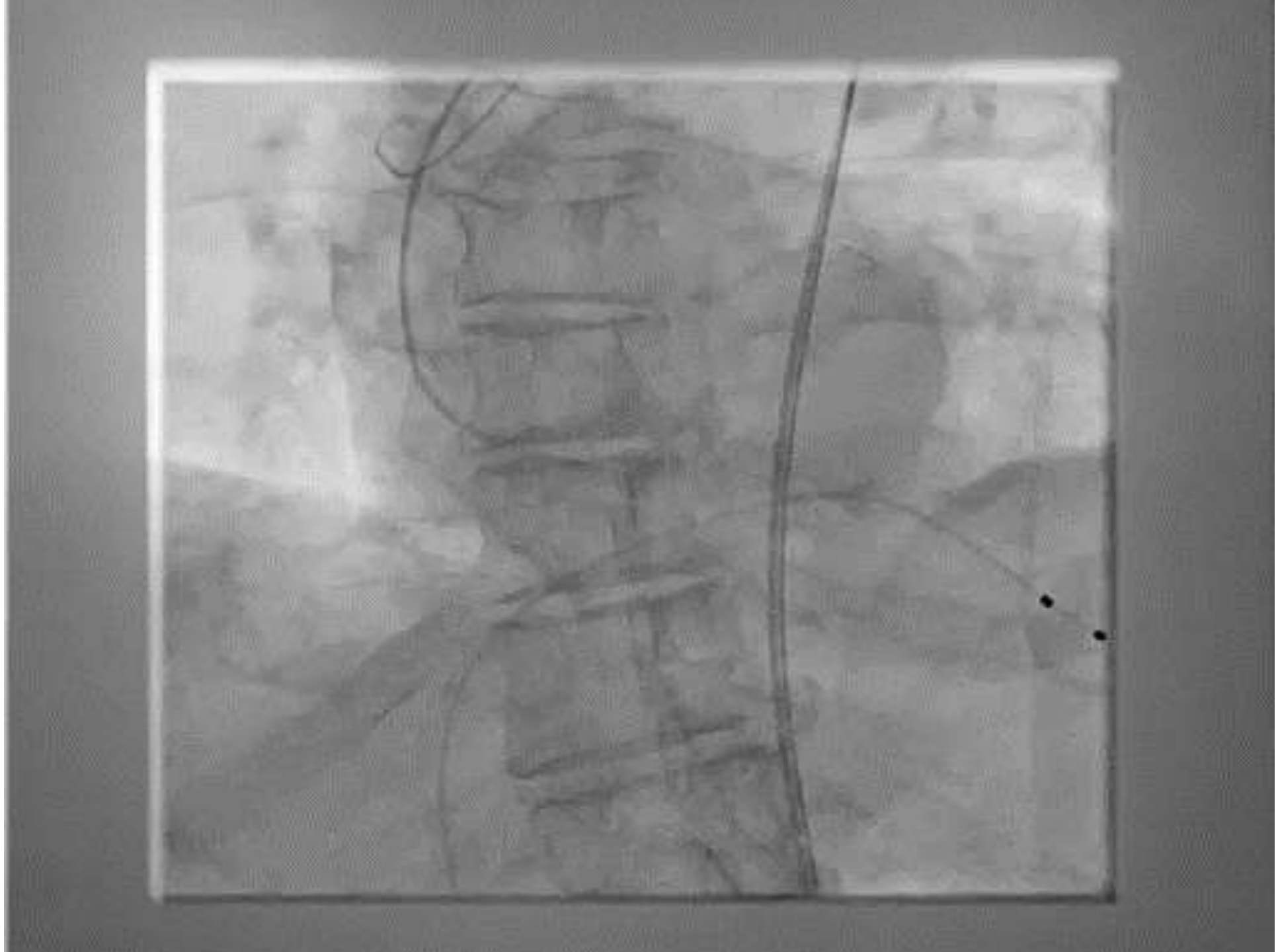
David Wood, MD
St. Paul's Hospital

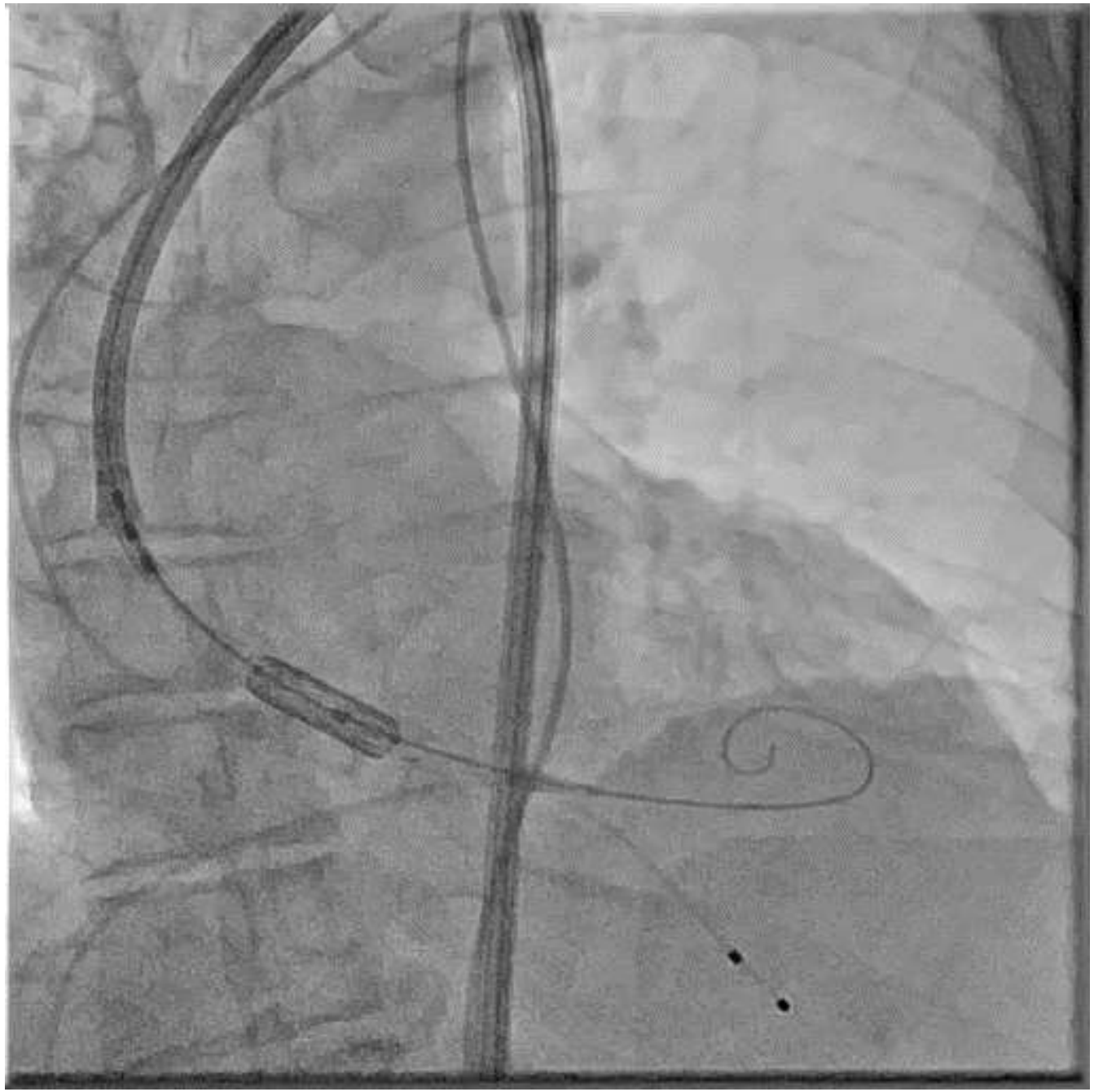
Santiago Garcia, MD
The Christ Hospital

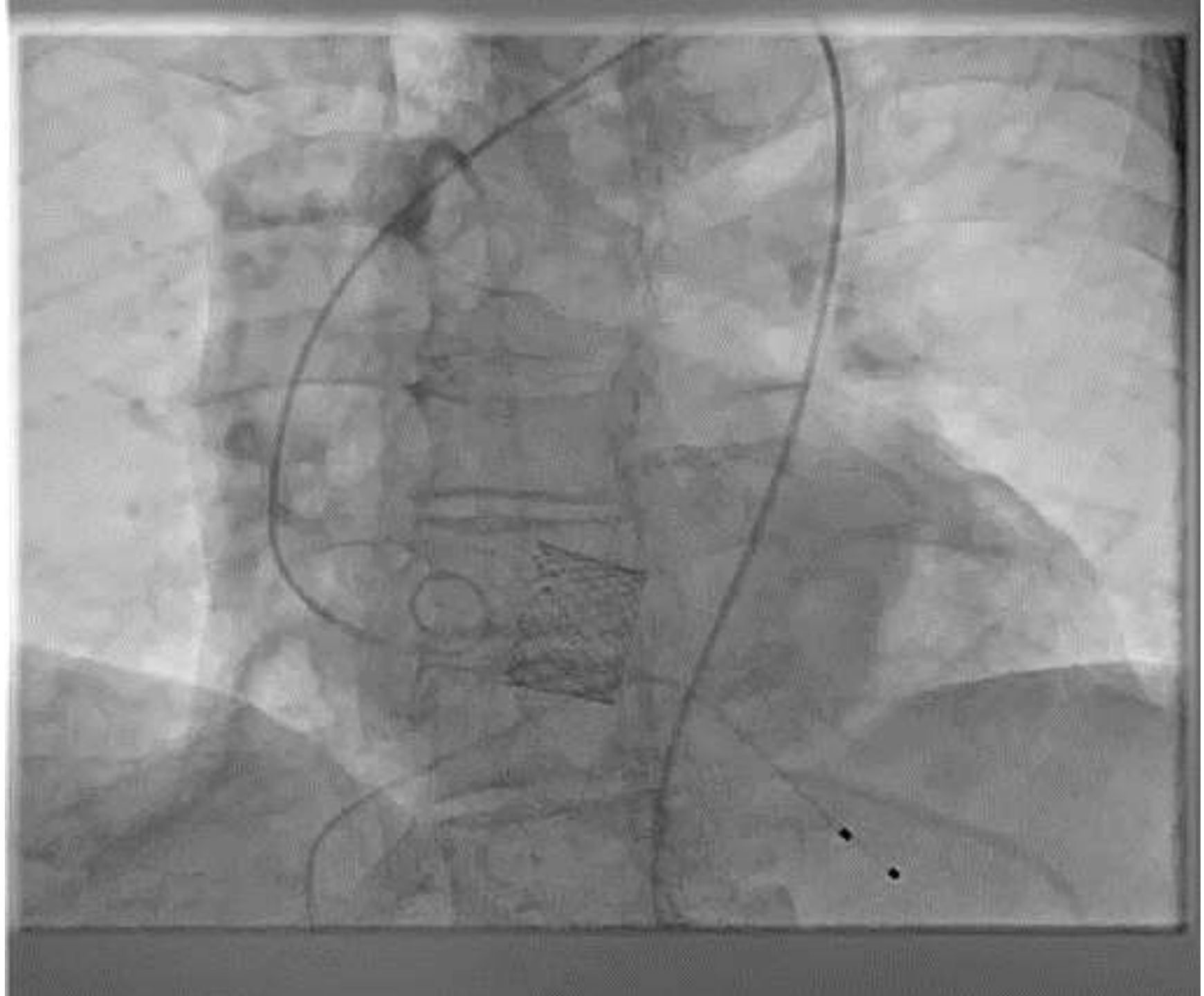
Katherine Harrington, MD
Baylor Scott & White

Study Sites


St. Paul's Hospital
University of Washington Medical Center
Providence St. Vincent Medical Center
St. Patrick Hospital
CentraCare
Mayo Clinic
Rush University Medical Center
Alexian Brothers Hospital Network
NorthShore University Health System
Northwestern
Medical Center of the Rockies
Kaiser San Francisco
Bay Area Sutter Health
UC Davis Medical Center
Stanford Hospital and Clinics
Saint Luke Hospital
Cardiovascular Research Institute of Kansas
Cedars-Sinai Medical Center
Scripps Memorial
Oklahoma Heart Institute
Baylor Plano
Baylor Heart
University of Texas Memorial Hermann
Austin Heart
HCA Houston Medical Center (SCRI)
Hamilton Hospital
Henry Ford Hospital
Cleveland Clinic
Allegheny General Hospital
The Christ
Vanderbilt
Saint Thomas Health
Methodist Le Bonheur
Emory
Piedmont Heart Institute
Institut Universitaire de Cardiologie et de Pneumologie de Québec (IUCPQ) - Laval
Dartmouth-Hitchcock Medical Center
Rochester General
University at Buffalo
Hartford Hospital
Columbia University Medical Center
Montefiore
Cornell Medical Center
Atlantic Health Morristown Hospital
Rutgers Robert Wood Johnson
Pinnacle Health
MedStar Union Memorial Hospital
Sentara Cardiovascular Research Institute







Conclusions

- Sizing of balloon expandable valve is “tunable” balancing between valve gradient, PVR and annular injury.
- Calcium load likely determines risk of complication
- Sapien X4 standardizes this adaptive sizing strategy with a new frame design