My clinical experience with Lotus.

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Clinique Pasteur, Toulouse, France.

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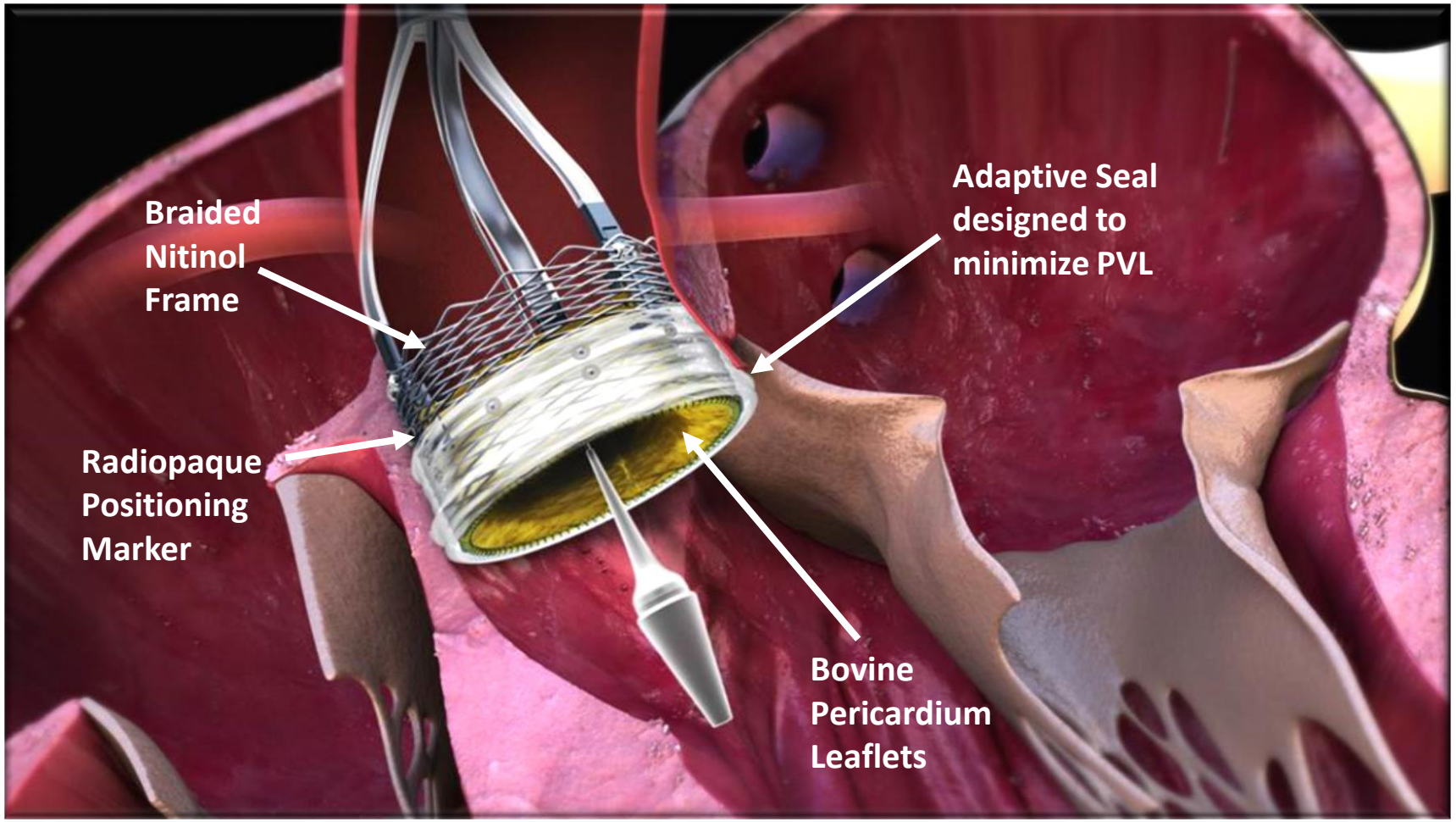
Conflicts of interest:

Consultant for Boston Scientific
Consultant for Edwards LifeSciences
Consultant for Medtronic

Lotus Valve System

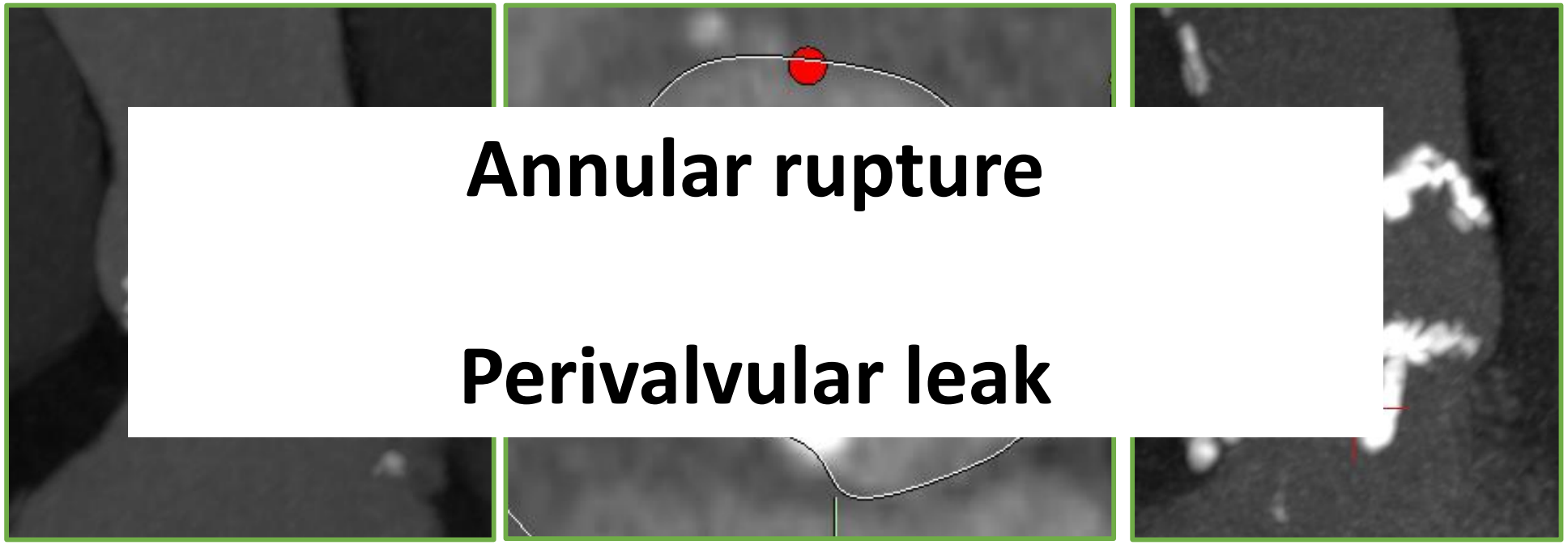
Fully repositionable & retrievable



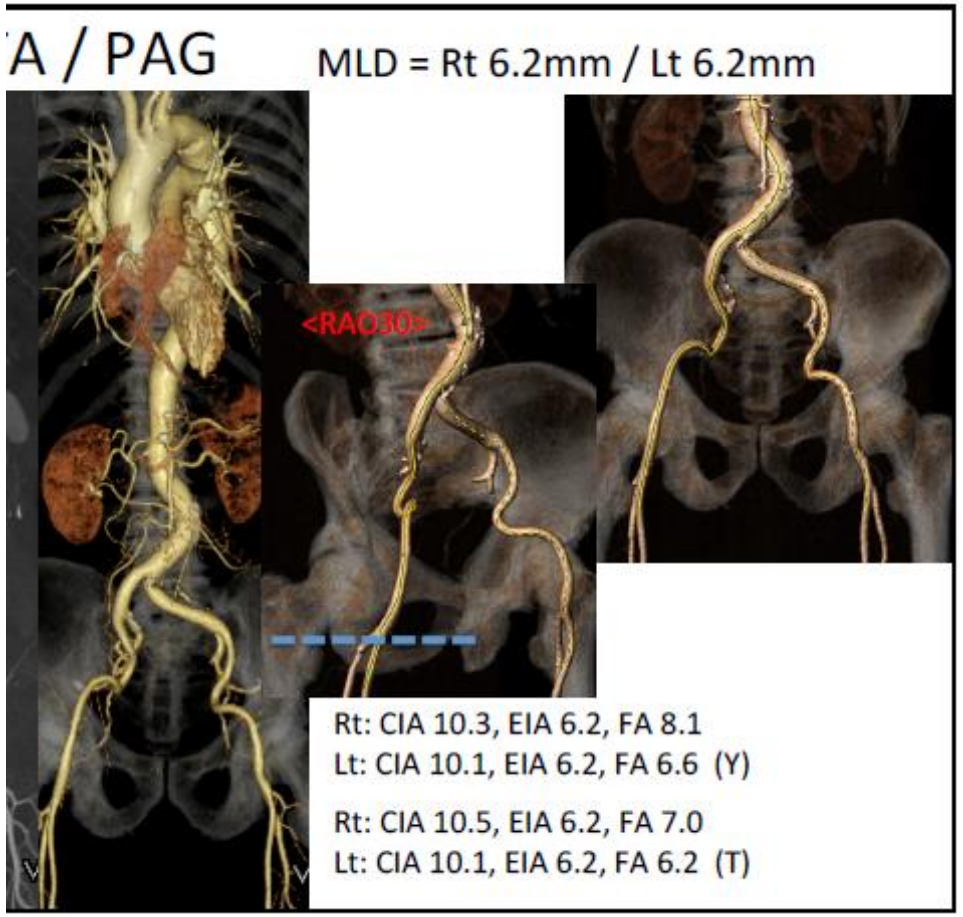
- Controlled mechanical expansion for precise placement
- Early valve function enables hemodynamic stability

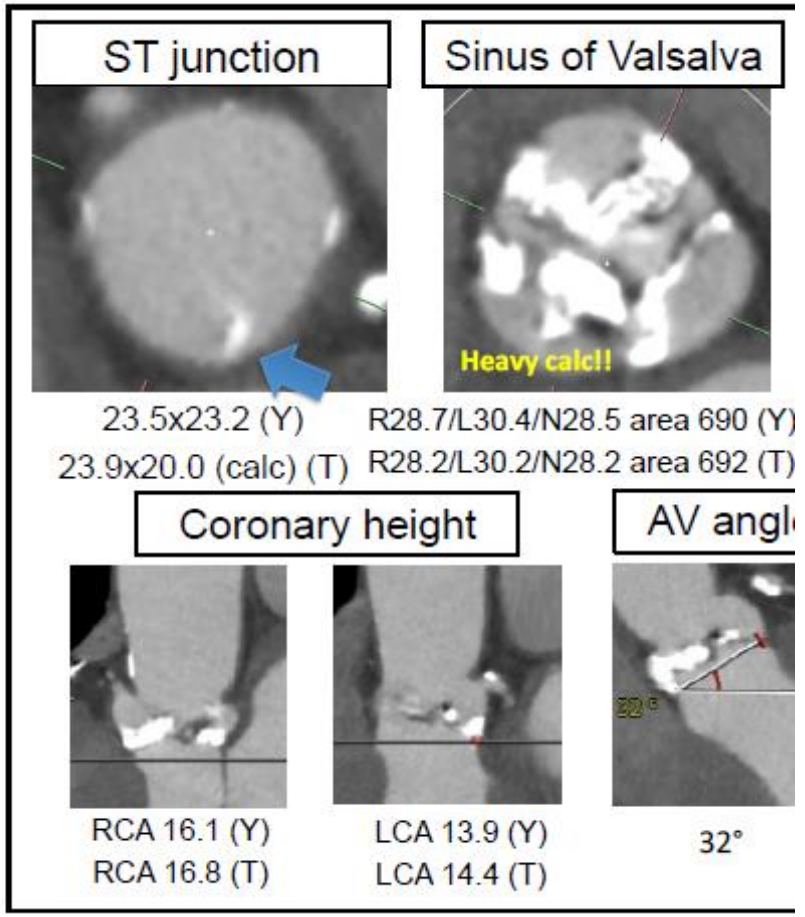
Lotus Valve System Overview

Lotus in heavy calcification



Lotus in heavy calcification





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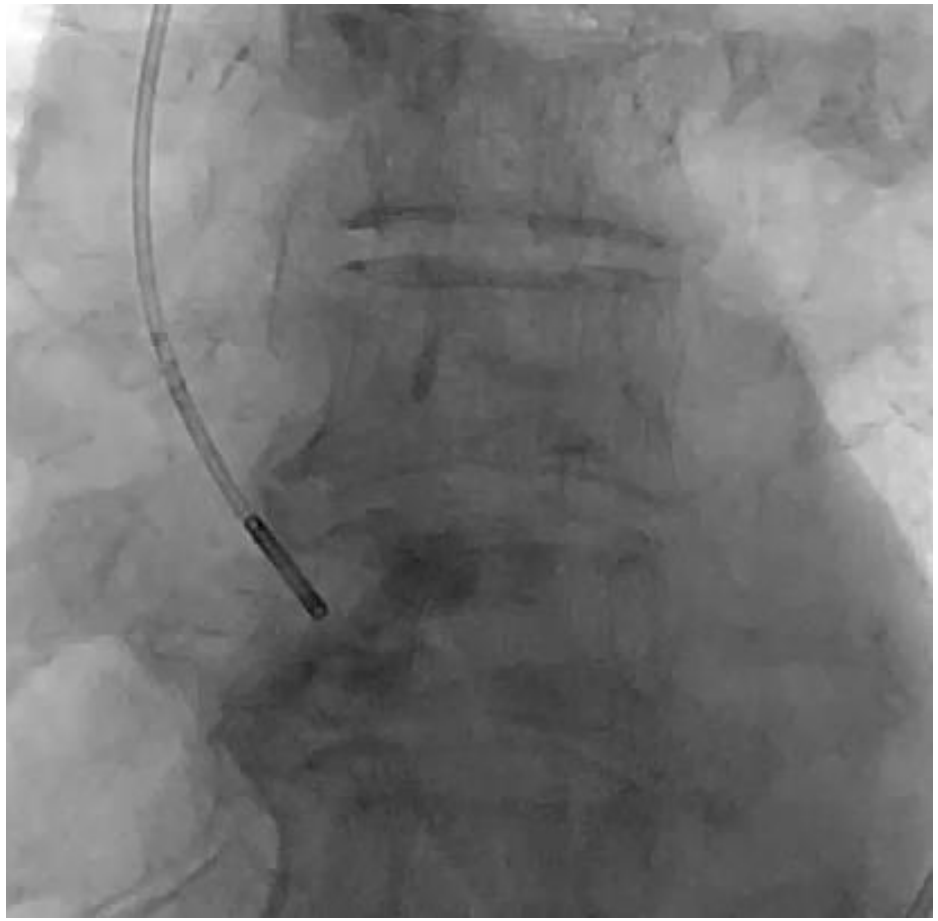
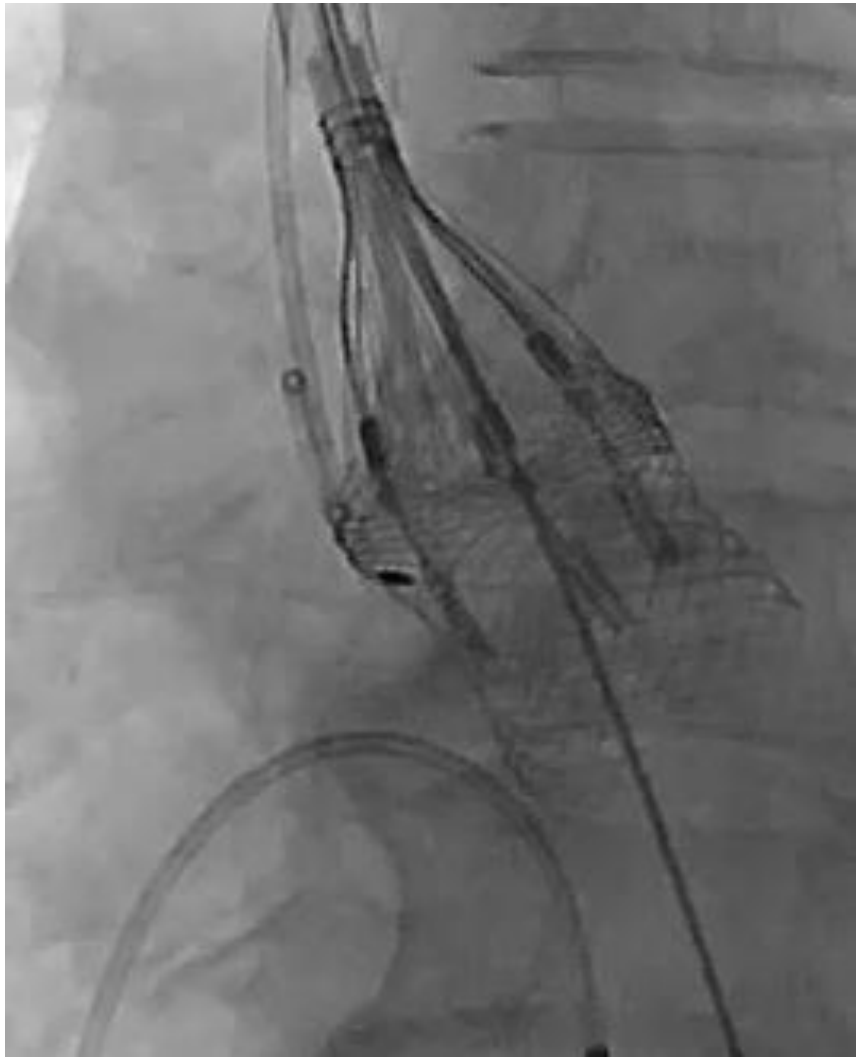
Lotus in heavy calcification



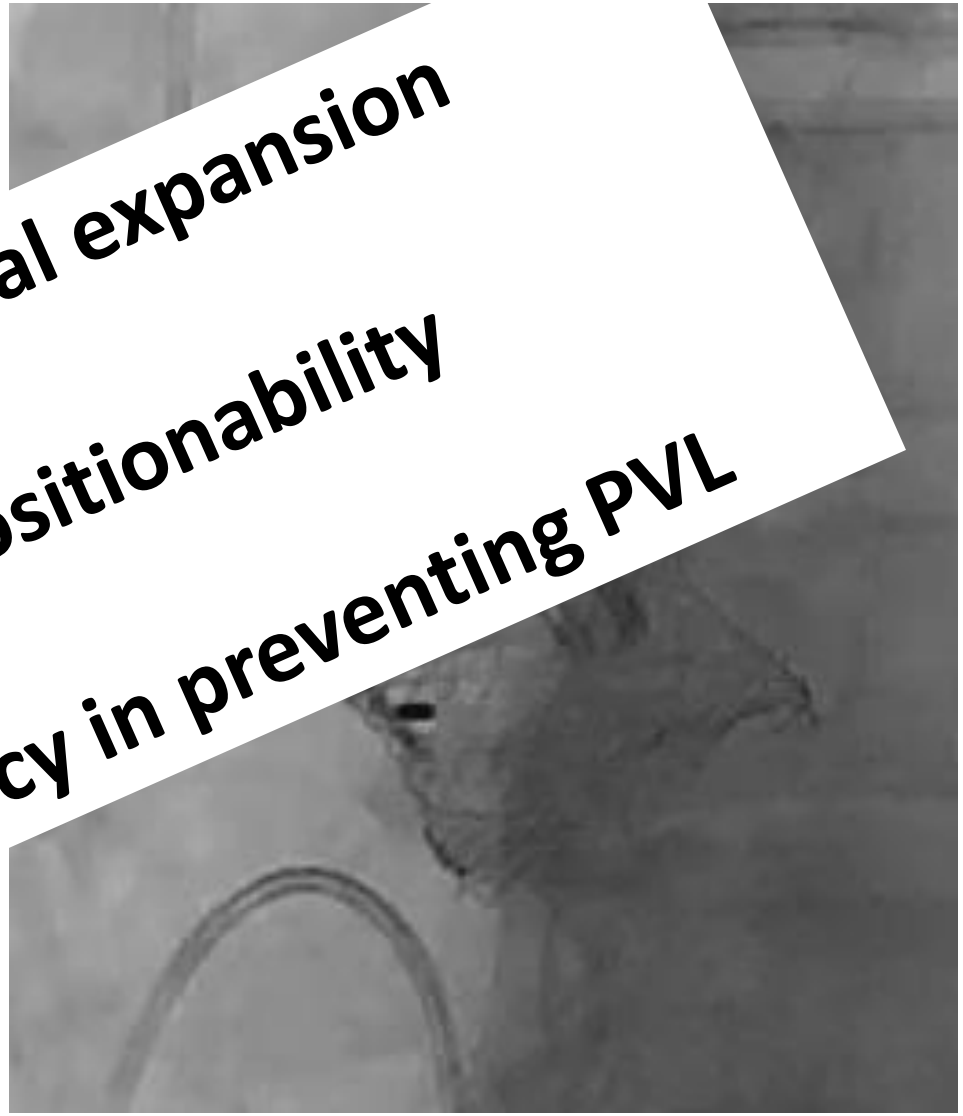


Early click

Mechanical expansion

Repositionability

Efficiency in preventing PVL



Resheath and reposition

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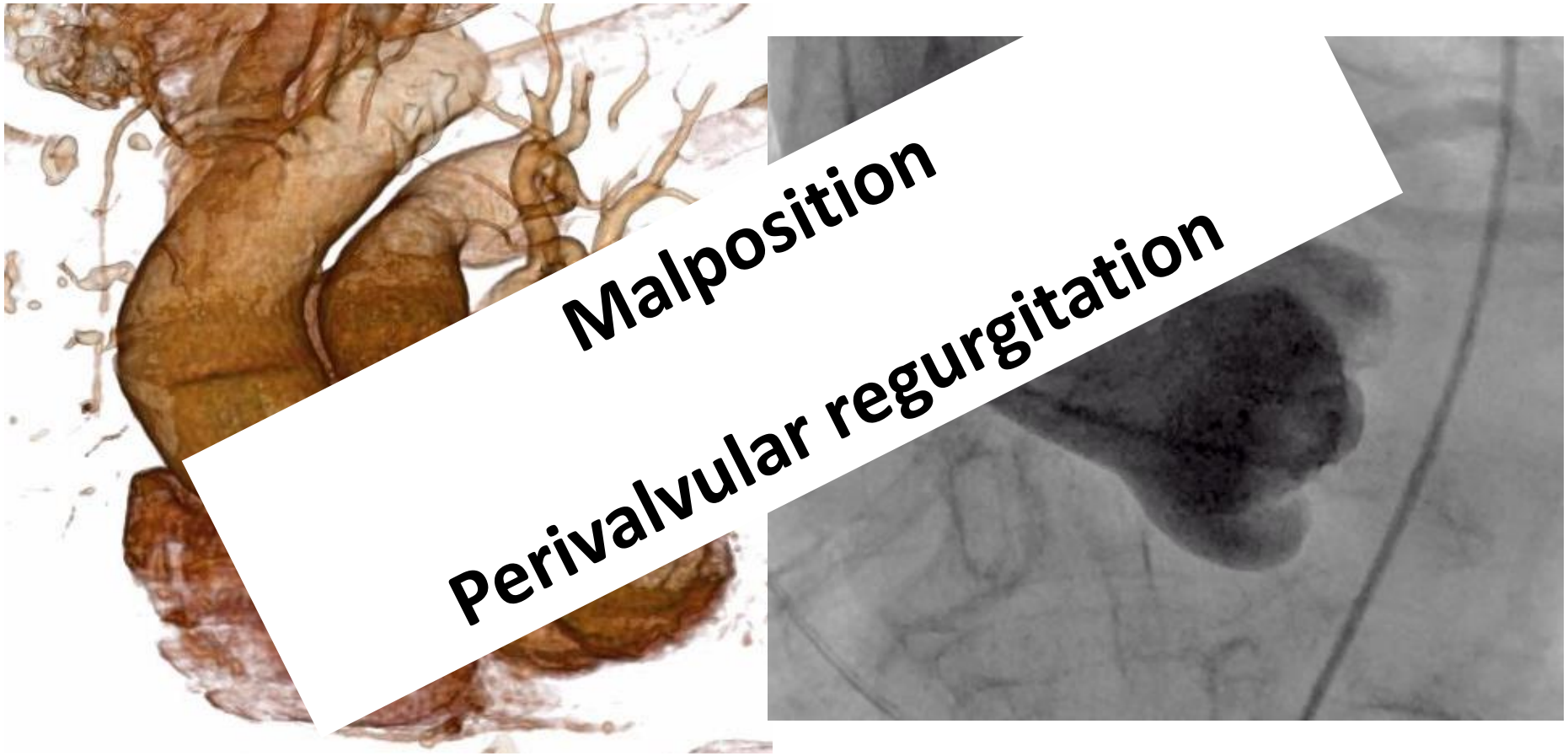
Lotus in horizontal Aorta



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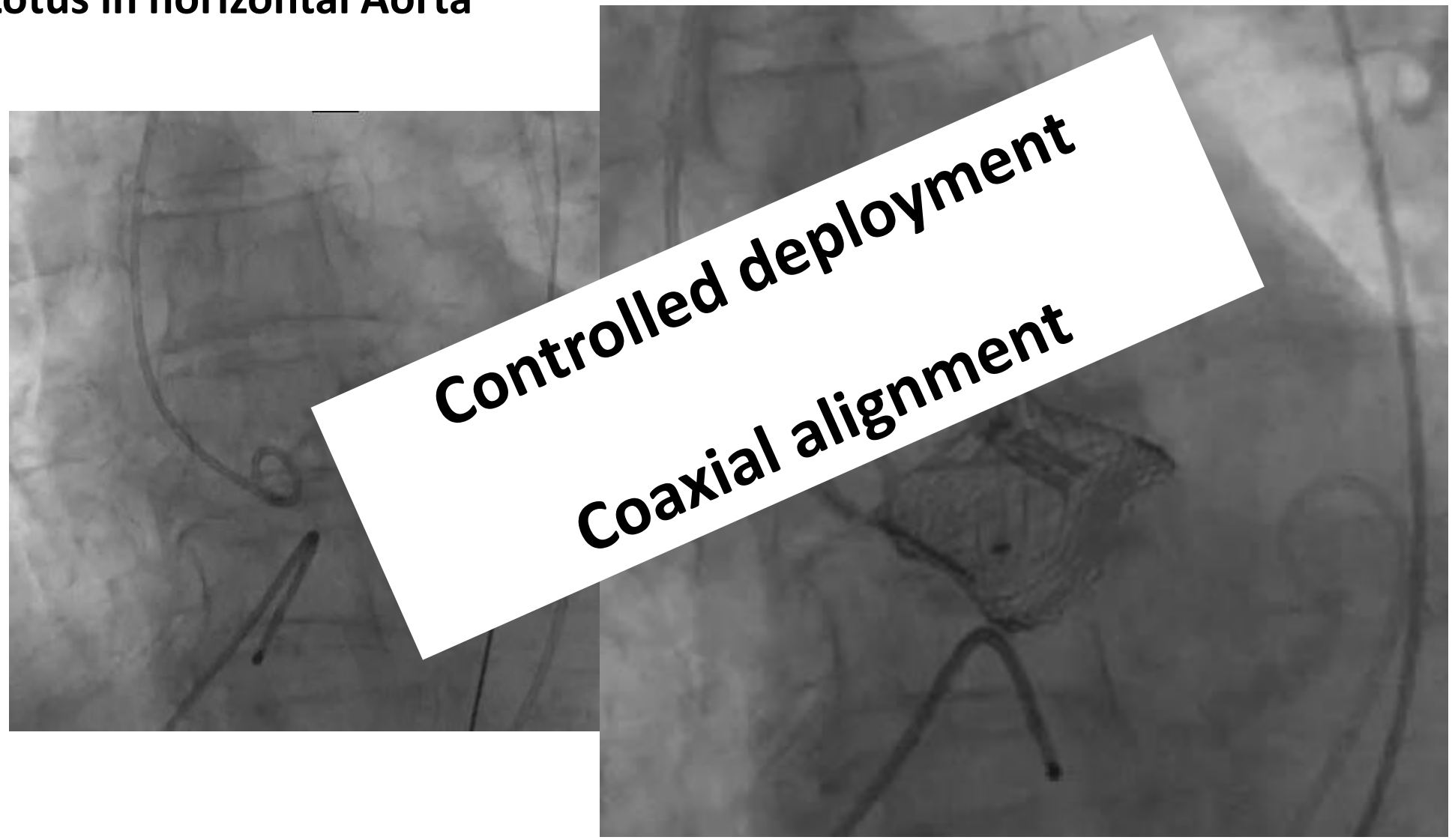
Lotus in horizontal Aorta



Procedural Challenges in bicuspid valves

- Heavily calcified leaflets
- Asymmetric orif
- Hig
- D
- Sizi
  - Ba
  - Inter ice?

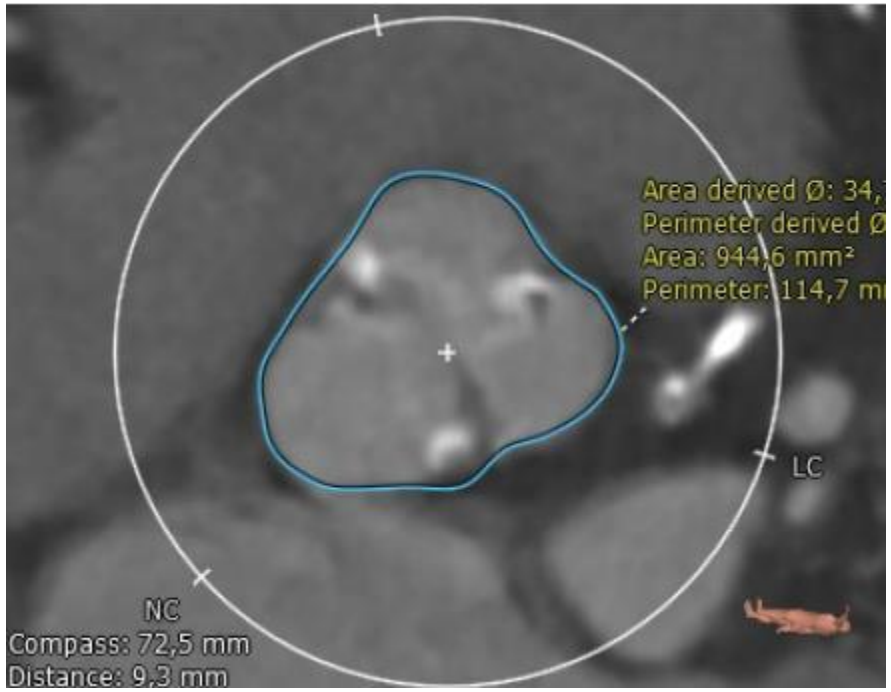
Valve misplacement

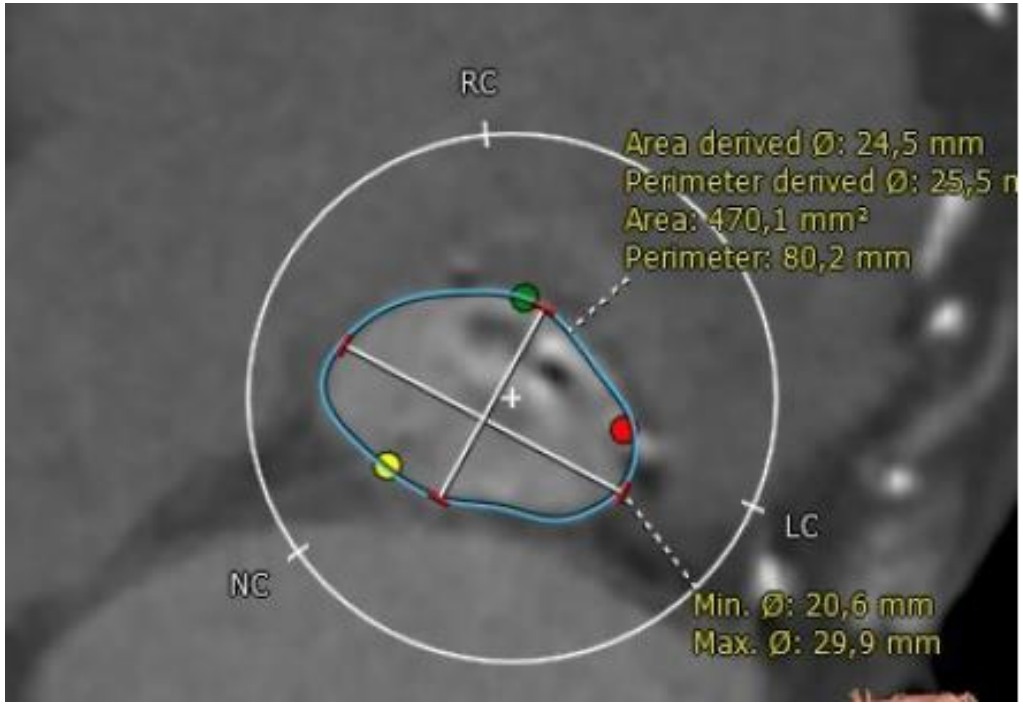
Assymetric valve expansion

High residual gradient

Paravalvular regurgitation

Lotus in bicuspid





Low LVEF: 20%

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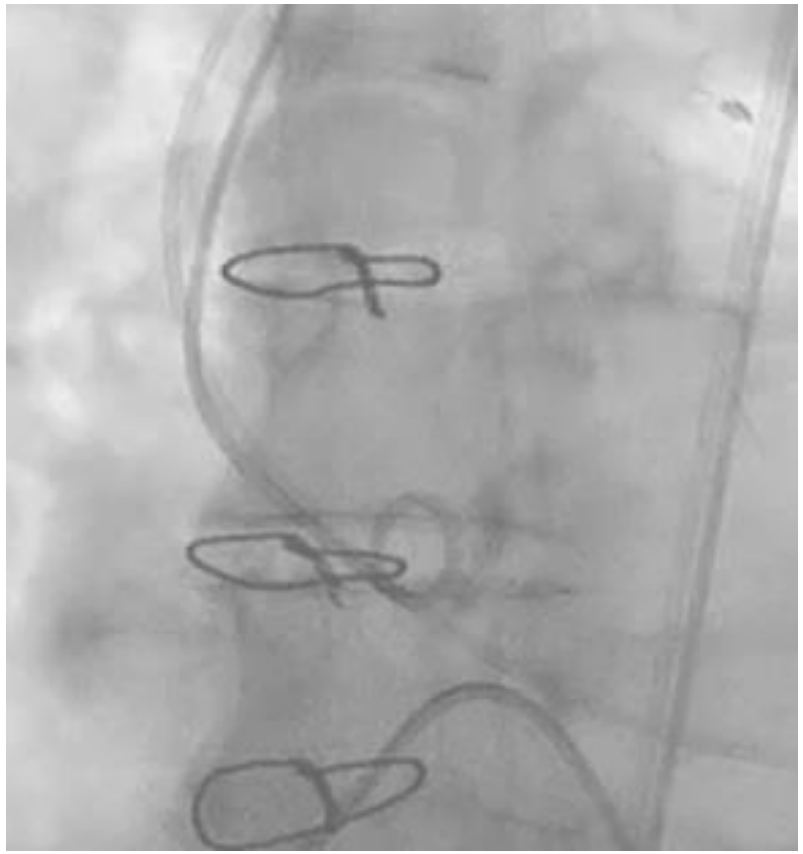
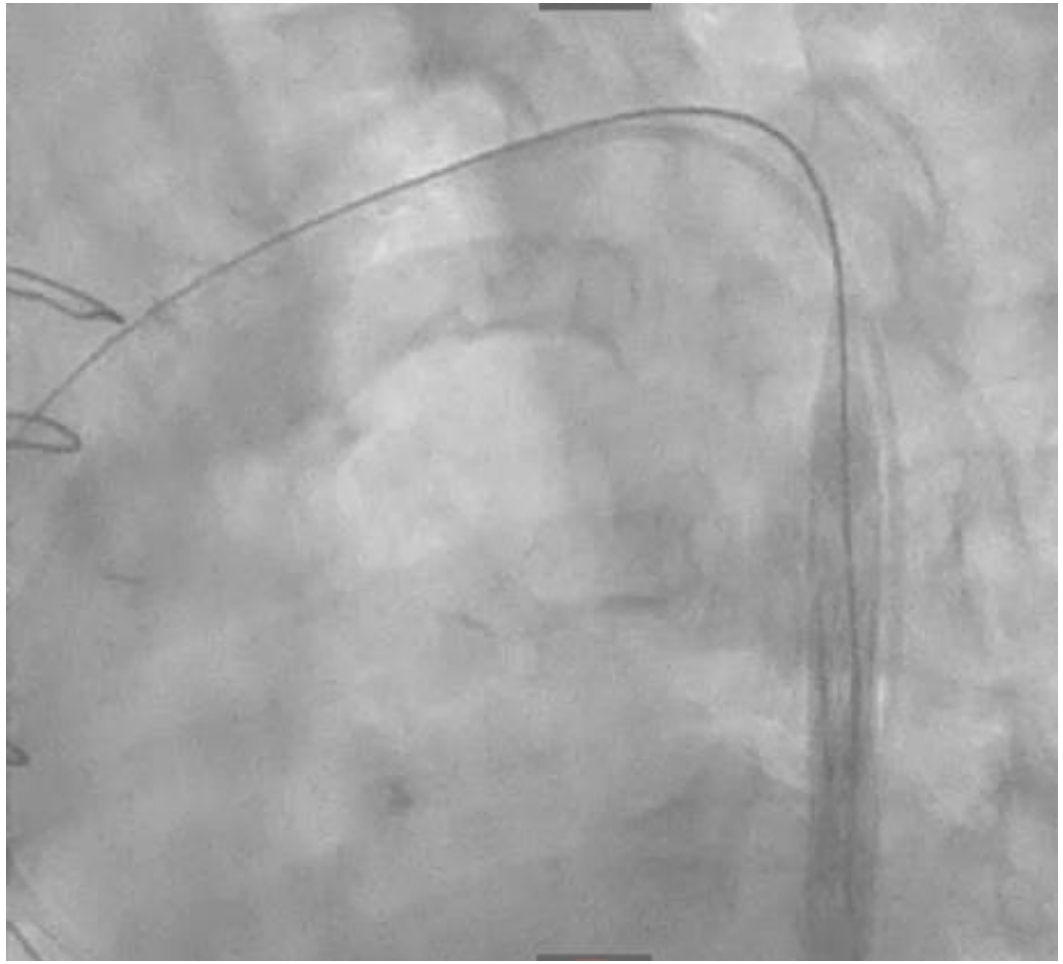
Lotus in bicuspid





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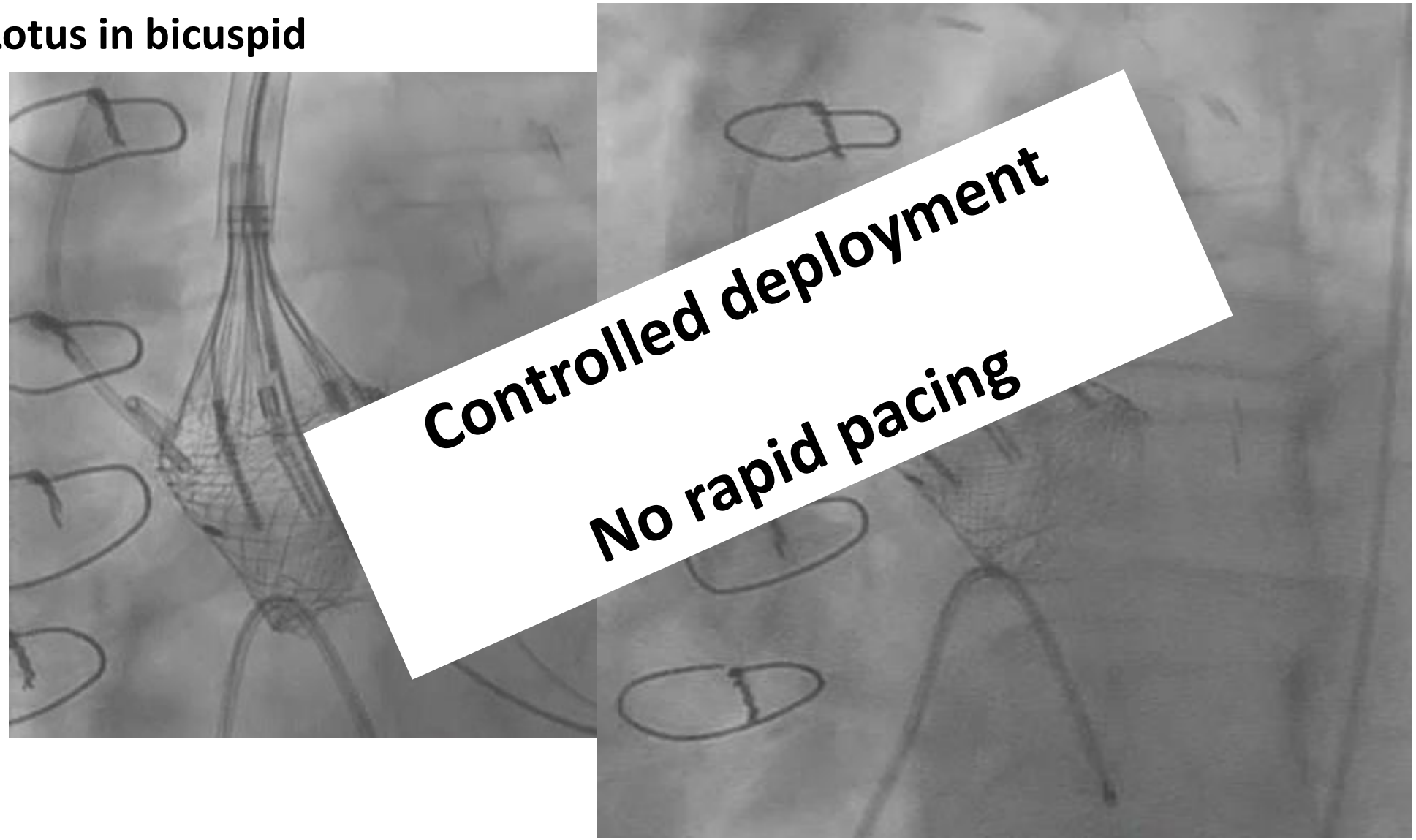
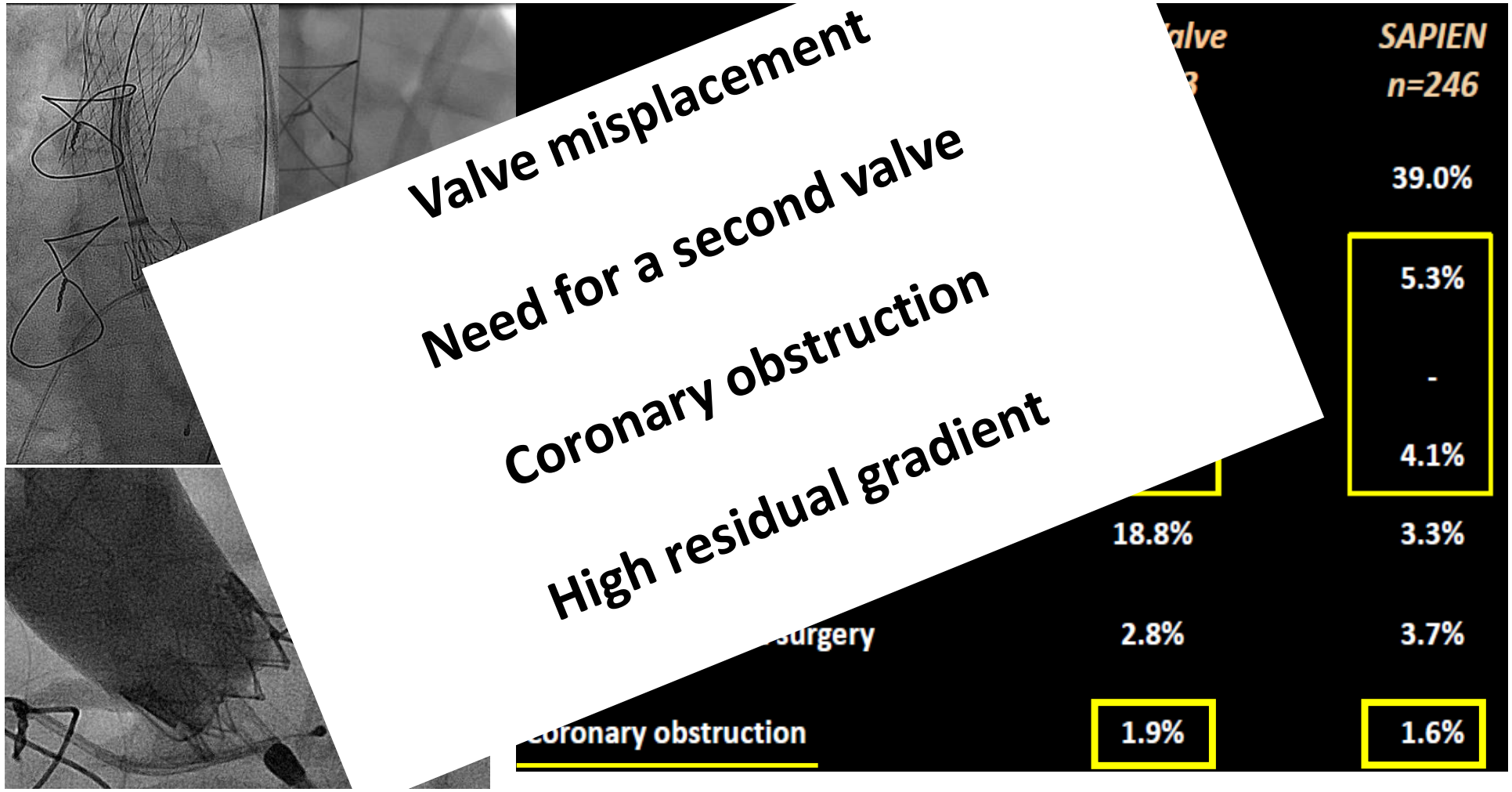
Lotus in bicuspid



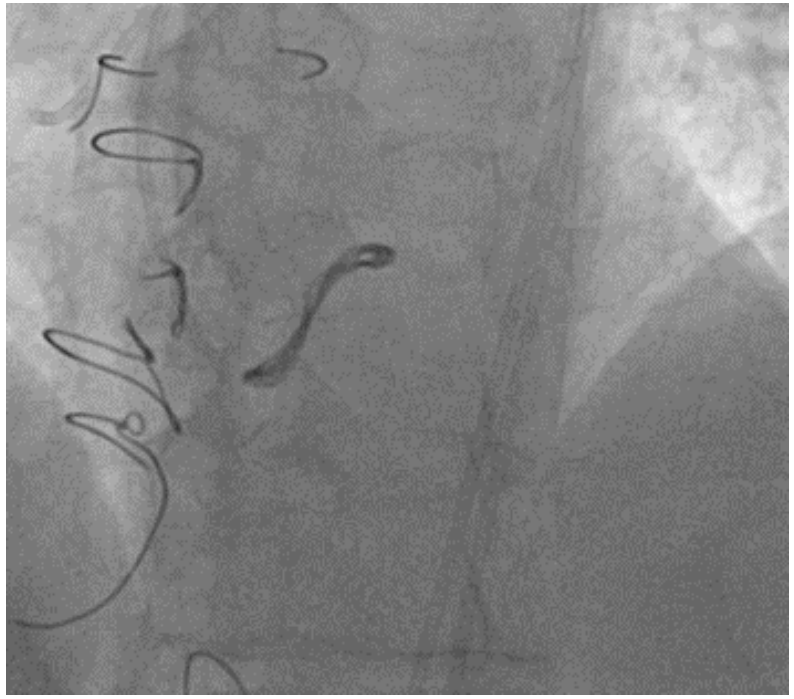
Lotus in valve-in-valve

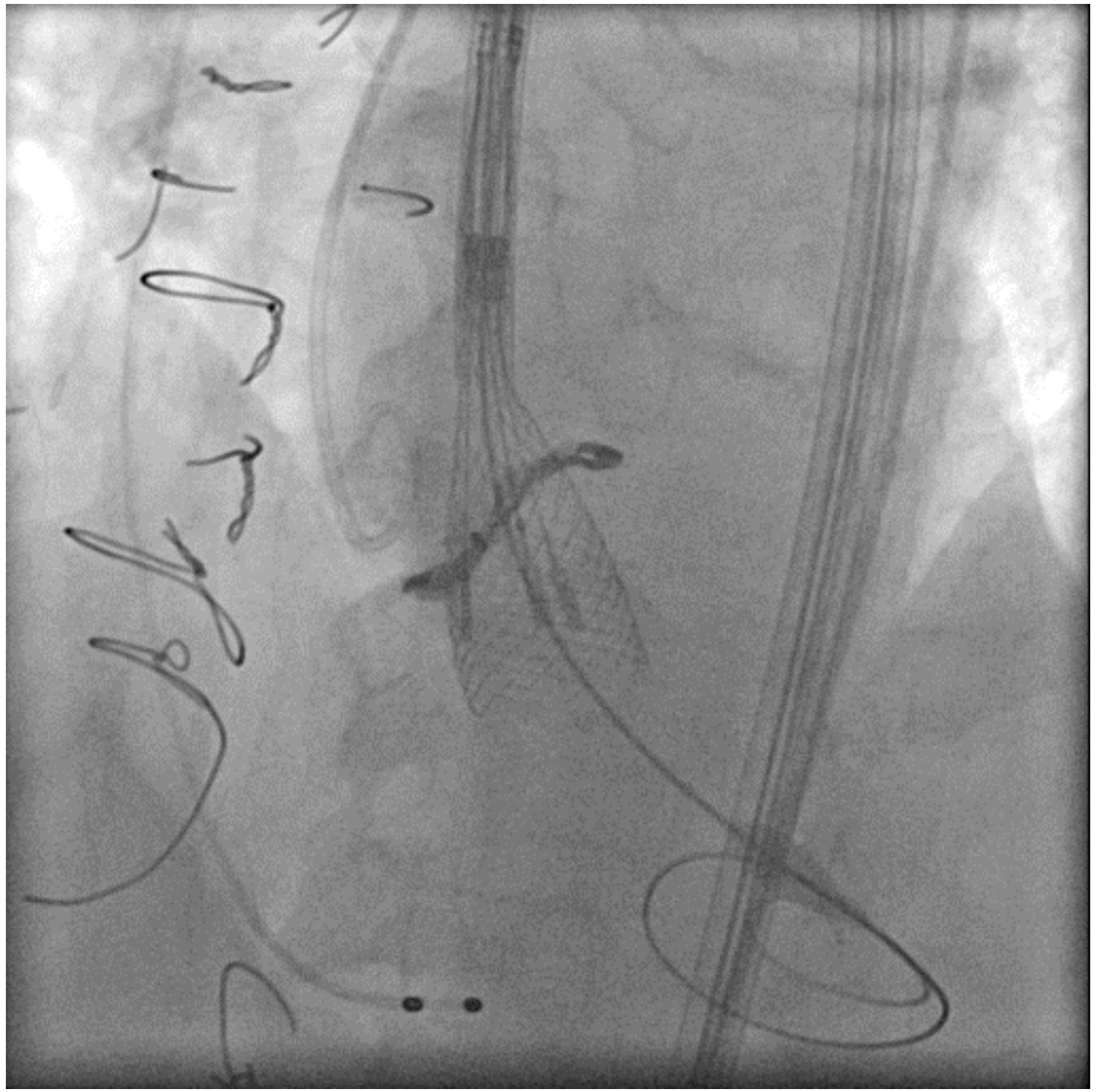


Dvir et al. Circulation. 2012;126:2335-2344.

Lotus in valve-in-valve

19 mm





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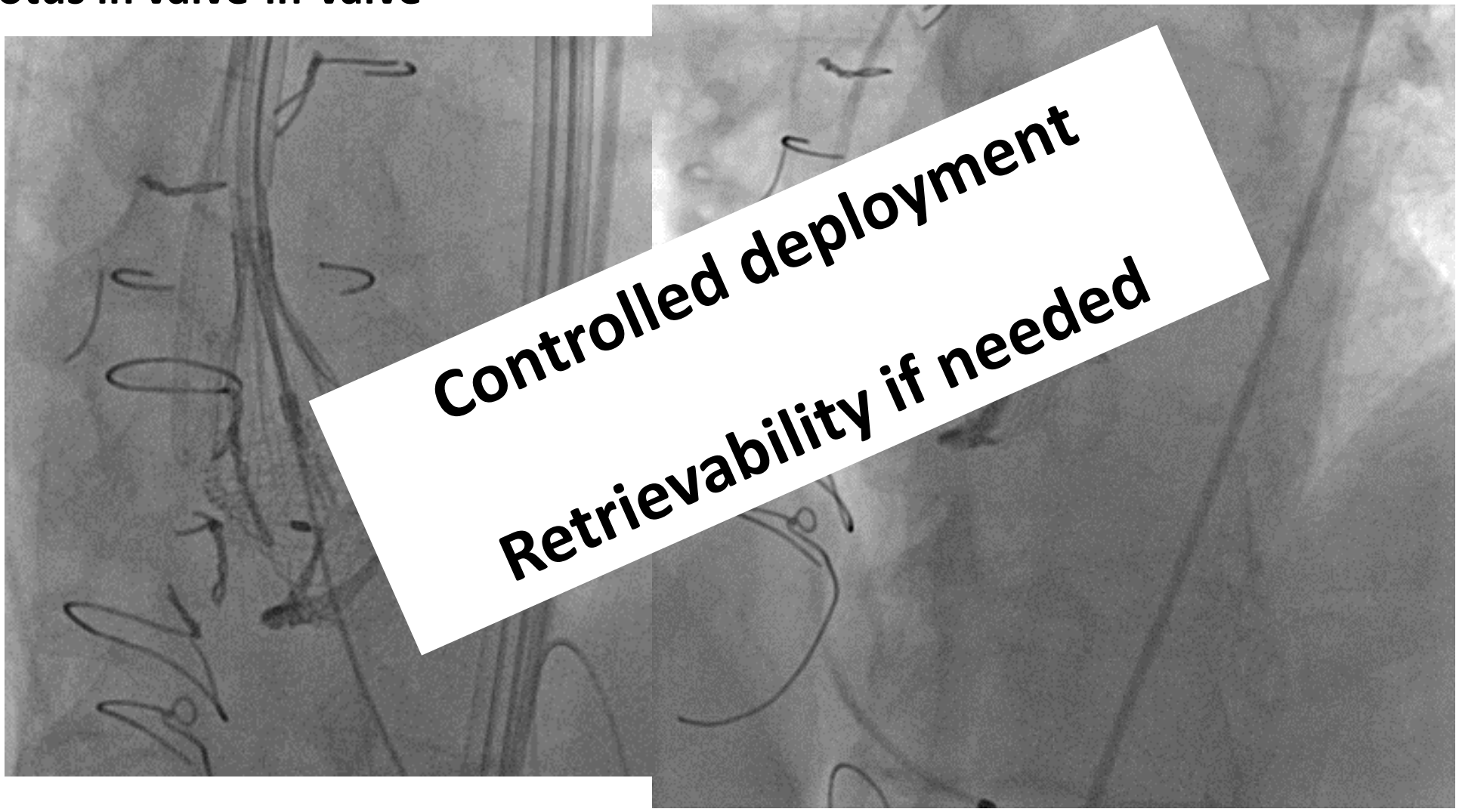
Lotus in valve-in-valve



LOTUS Clinical Program

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- REPRISE I
- REPRISE II/II EXT
- RESPOND
- LOTUS Edge Feasibility
- REPRISE Edge
- REPRISE III
- REPRISE JAPAN

Post Market Study
Safety & Performance, All Comers
N=1014, single arm
23, 25, & 27mm valve sizes
1^{o} Safety Endpoint: Mortality at 30 days & 1 year
Key Secondary Endpoint: PVL at hospital discharge & 1 year (Core Lab Adjudicated)

30d Results PCR 2016

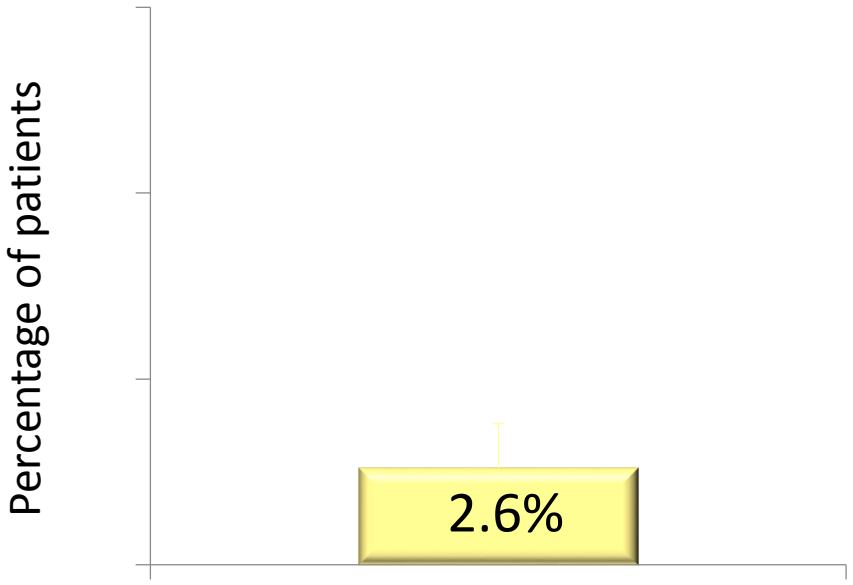
RESPOND Primary and Key Secondary Endpoints

Prospective, single-arm, multicenter, observational post-market study

All-Cause Mortality at 30 Days

Intent-to-treat population (N=1014)

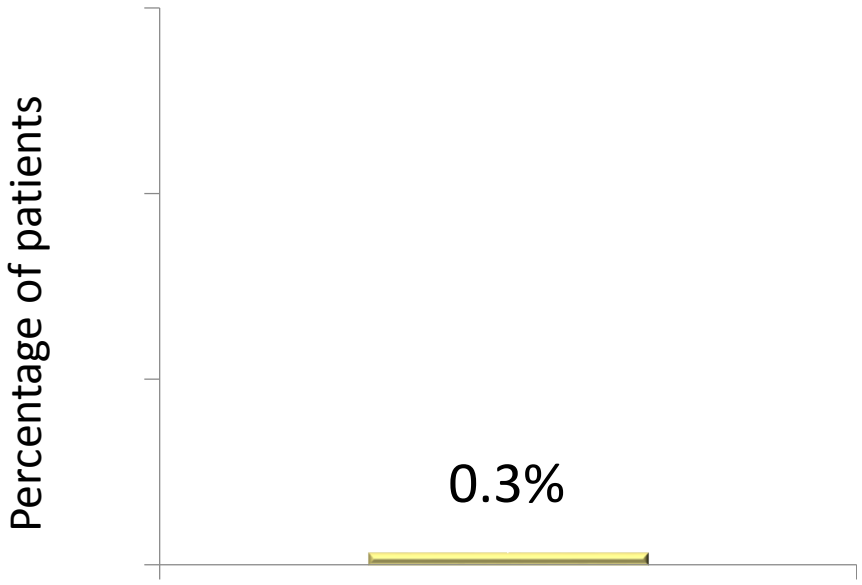
O:E Ratio = 0.43



2.6% is significantly below the performance goal of 14.0%* (P<0.001)

Moderate/Severe Paravalvular Regurgitation at Hospital Discharge

As-treated population (N=996)



0.3% is significantly below the performance goal of 16.5%† (P<0.001)

*Based on an expected rate of 10% (based on literature review) plus a test margin of 4%. †Based on an expected rate of 16.5% from the FRANCE 2 registry. *P* values are from the one-sample z test; 95% CI is from Clopper-Pearson Exact Method. Presented by Falk, PCR 2016.

RESPOND Safety Endpoints at 30 Days

As-treated population at 30 days (N=987)*

All-cause mortality	2.2%
Cardiovascular mortality	**2.0%**
All stroke	3.0%
Disabling stroke	**2.2%**
Life-threatening or disabling bleeding	2.2%
Myocardial infarction (>72h post-procedure)	0.3%
Acute kidney injury (Stage 2 or 3)	1.7%
Repeat procedure for valve-related dysfunction	0.1%
Valve- or CHF-related repeat hospitalization	1.2%
Prosthetic aortic valve thrombosis	0.4%
Newly implanted permanent pacemaker	**30.0%**
Pacemaker dependent at 30 days (Site-reported, n=107/296)	36.1%

REPRISE II Extension 30d Pacemaker Analysis (N=250)
Significant Multivariate Predictors of PPM for First Generation Lotus

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Newly implanted pacemaker through 30 days: 29.0% (72/248)

Variable	Odds Ratio	95% CI	*P* value
Baseline RBBB	12.70	4.45, 36.22	<0.001
LVOT area overstretch ≥10%	3.42	1.74, 6.74	<0.001
1st degree AV block	2.49	1.13, 5.47	0.02
LVOT total calcium volume, per 100 mm^3 increase	1.80	1.03, 3.14	0.04

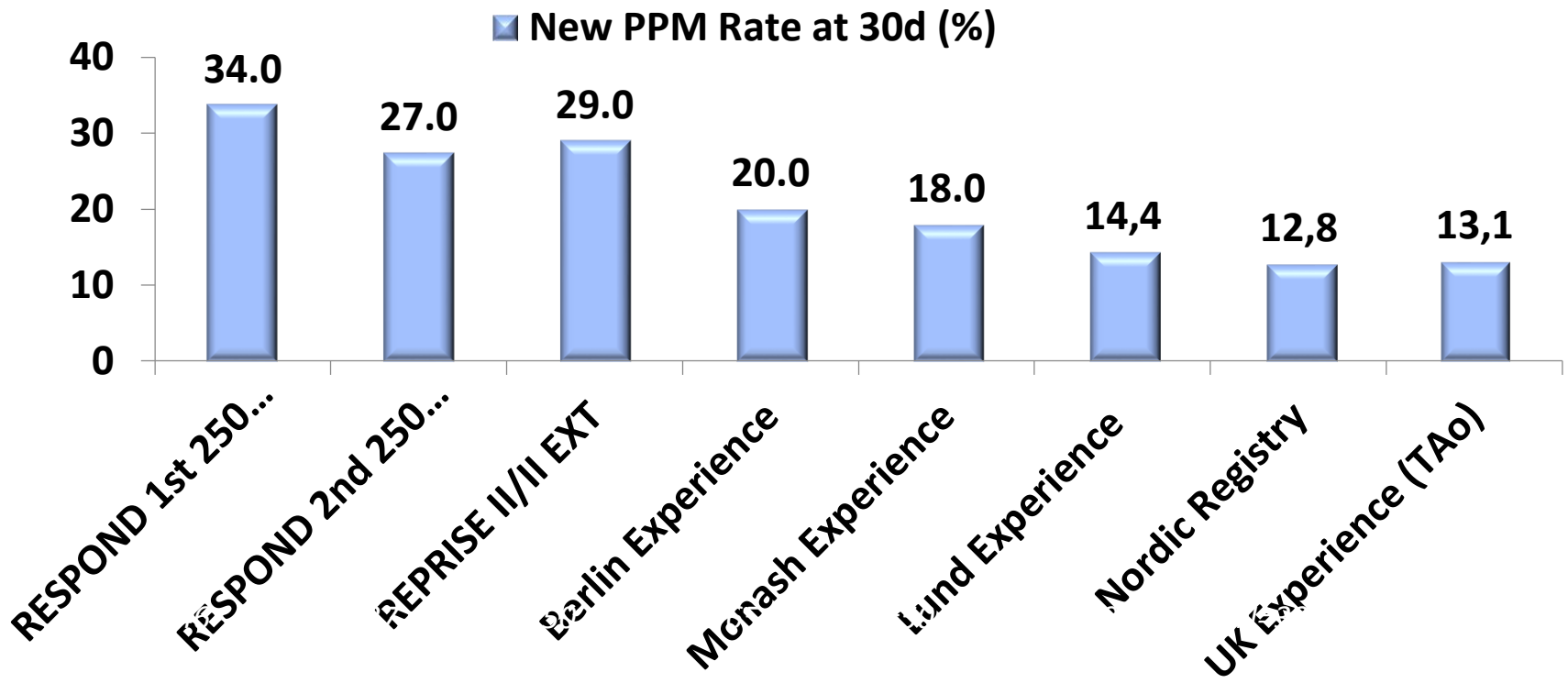
The need for a new pacemaker does not influence 30d or 1 year mortality[1*]

- One study has shown 30-day PPM as a protective factor for the occurrence of unexpected death but this largely remains unknown without further studies[2]

*Based on a 93 study non-overlapping meta-analysis including 37,836 patients reporting 30d PPM implantation rates post TAVI.

[1]Chakravarty, et al. *Circulation* 130.A19882 (2014). [2]Urena, et al. *Circulation* 129 (2014): 1233-1243.

How may technique/protocol impact PPM rate?
Recent experience from five studies with first generation Lotus

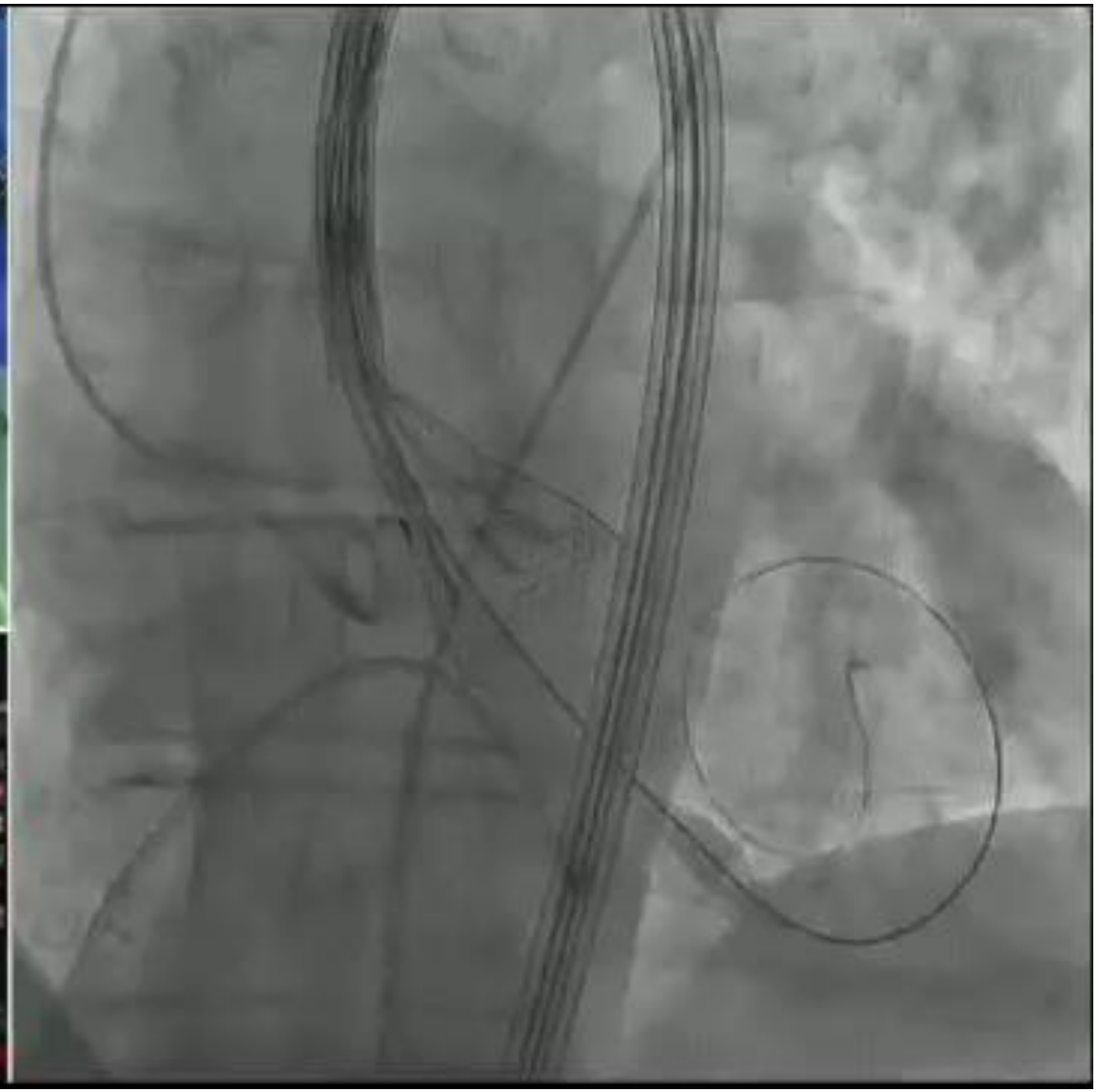


Possible contributors to reduction in PPM rate:

- Reduced valve interaction in LVOT during deployment
- Implant depth <4mm
- Sizing – Device/Annulus Ratio
- Use of alternate access (TAo)

RESPOND: Falk, PCR LV 2015. REPRISE II/II EXT: Meredith, PCR LV 2015. Berlin Experience: D'Ancona, TCT 2015. Monash Lotus Study: Gooley et al. J Am Cardiovasc Interv 2015;8:962-71 Lund Experience: Gotberg, TCT 2015. Nordic Registry: De Backer, et al. Int. Jour. of Card. 219 (2016) 92-97. TAo Experience: Bapat, TCT 2015. Results from different studies not directly comparable. Information provided for educational purpose only. Information not intended for use in France. CE mark received 2013. Information for the Lotus Valve System is for use in countries with applicable product registrations. Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

Lotus first generation

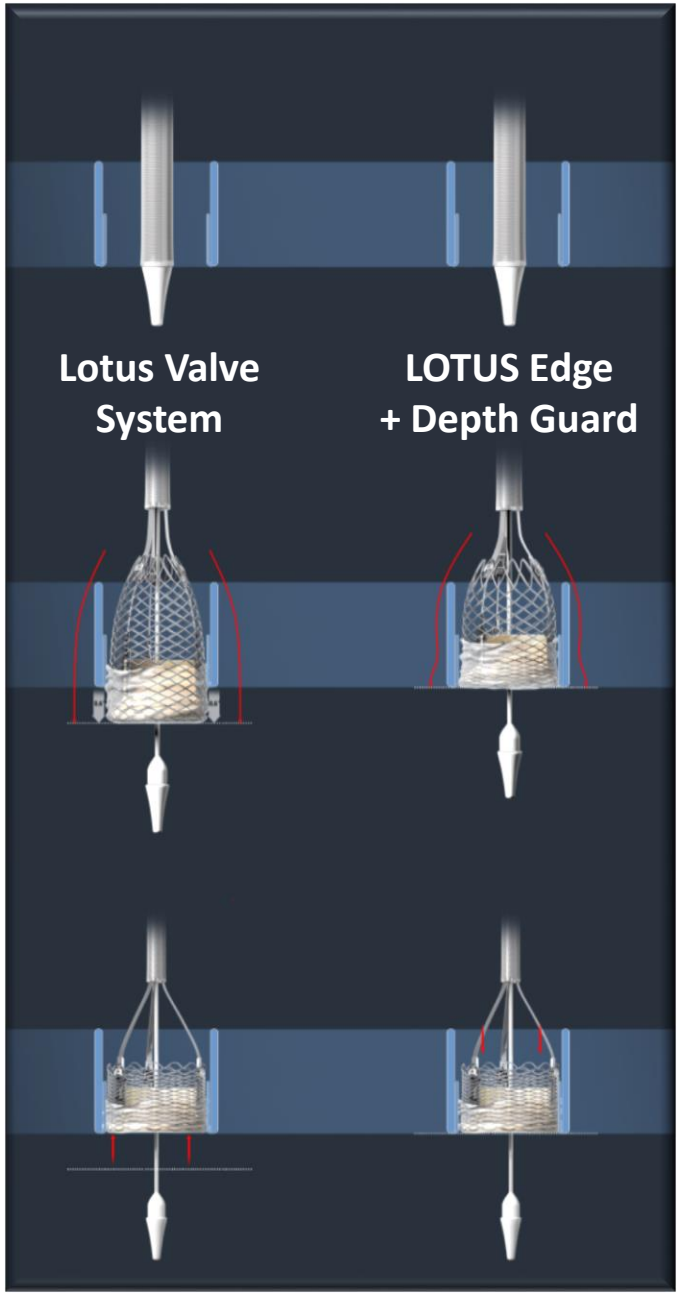


PPM 26%

Lotus with Depthguard technology

Optimizing Valve Deployment:

- Anchors early during deployment
- Minimizes depth of valve frame reducing LVOT interaction
- More predictable placement



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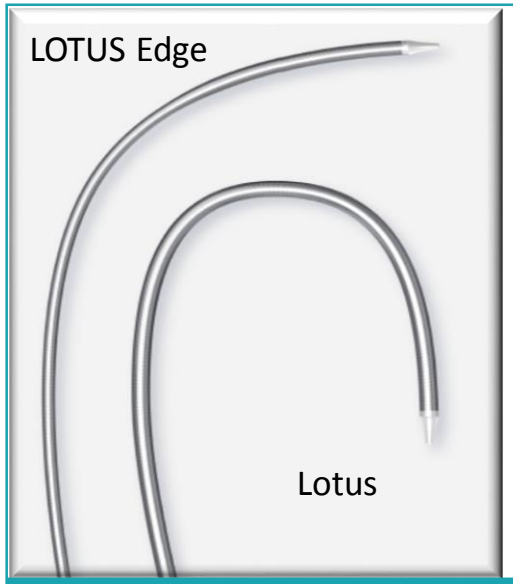
Lotus with Depthguard technology

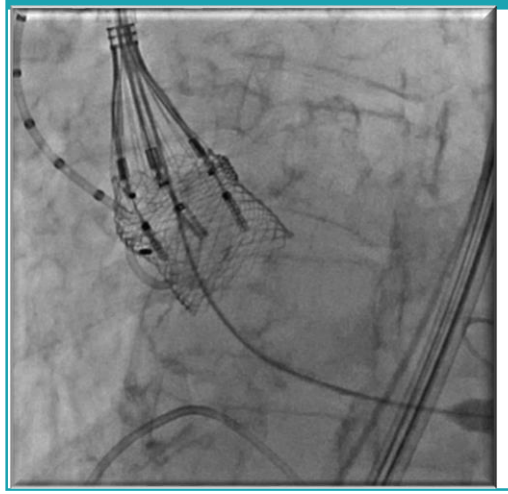
PPM 12%

Lotus Edge with Depthguard technology



LOTUS Edge Catheter

- Increased flexibility
- Exceptional coaxial alignment with optimized pre-shape curve
- Proximal catheter profile reduction (3F – 4F)



LOTUS Edge Valve Modifications

- One-view locking with RO markers
- Limited depth of implant with Depth Guard™ technology

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Conclusion

My experience with Lotus™ in real world patients

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- Various anatomies can be treated
  - Mechanical expansion and controlled deployment
  - Precise placement and coaxial alignment
- Extremely efficient for PVL prevention
- Improvement in PPM with DepthGuard

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Thank you