Pacemaker rates Second generation TAVI Devices

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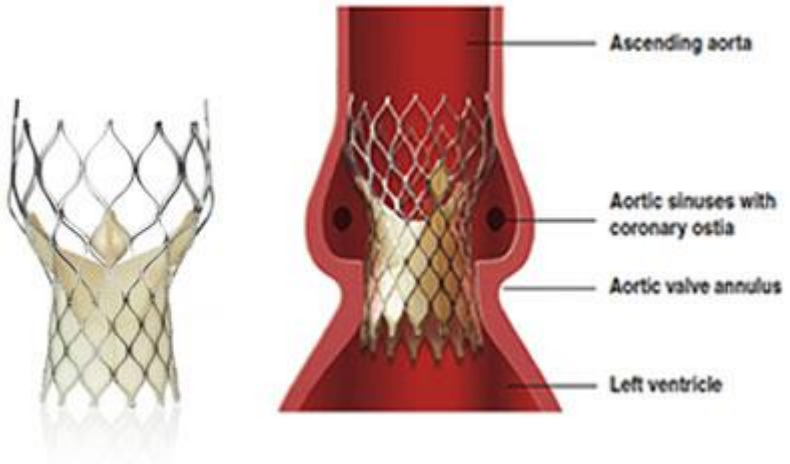
2015 JCR Joint meeting of Coronary Revascularization

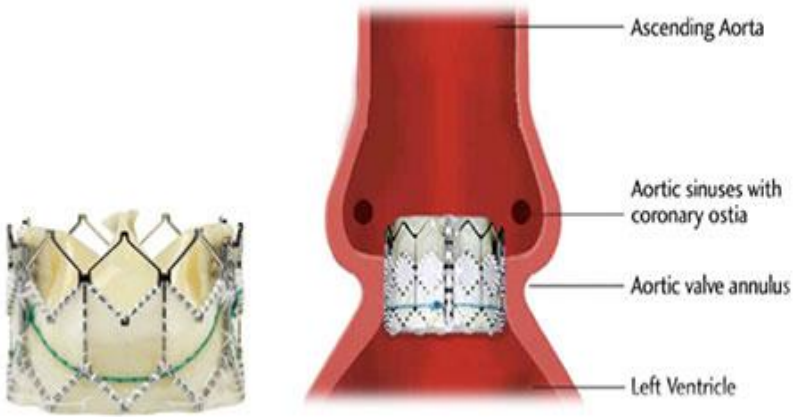
TAVI

„The future´s looking very positive for TAVI and it´s continued expansion into intermediate and low-risk cohorts“



- Next TAVI prosthesis generation
- Data from new trials

  Indication Expansion ?



TAVI

Disadvantages

Paravalvular leak

Vascular complications

Stroke rate

Pacemaker rates

Cardiac surgery

Reimbursement companies

„The future´s looking very positive for TAVI and it´s continued expansion into intermediate and low-risk cohorts“

Second Generation TAVI Devices

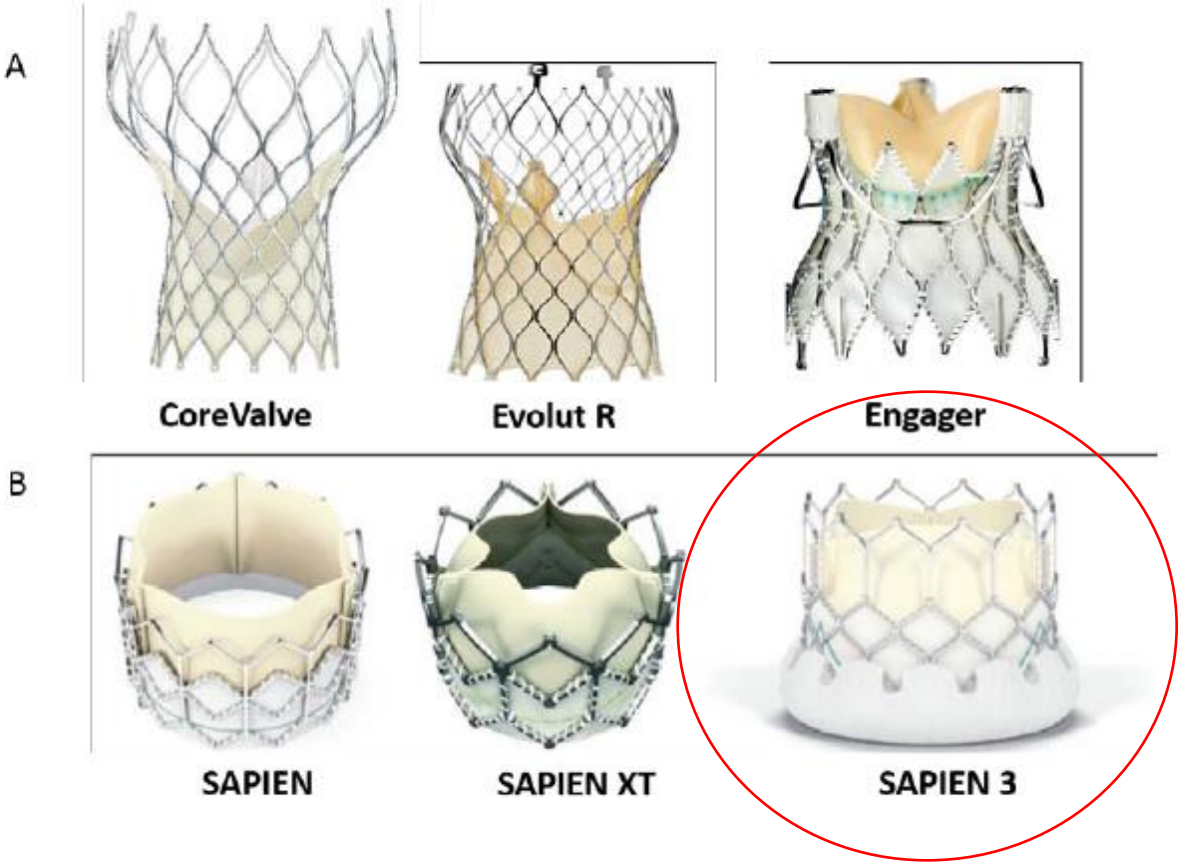
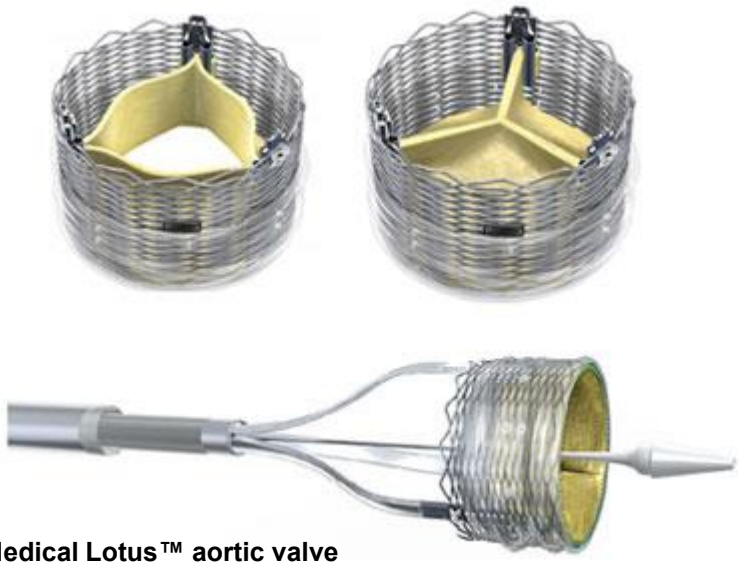


Figure 2. Evolution of (A) CoreValve and (B) SAPIEN devices.

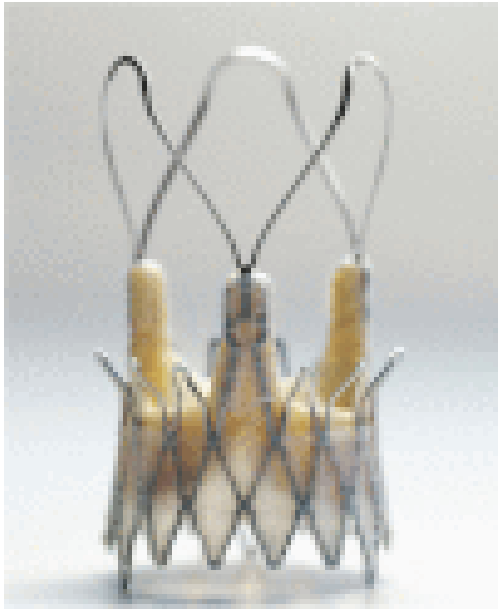
Sheat

14-18 F

Second Generation TAVI Devices



Sadra Medical Lotus™ aortic valve



Symetis Acurate TA™ Aortic Bioprosthesis.

Direct Flow Medical aortic valve

St. Jude Medical Portico

Next generation TAVI Devices

Boston Lotus:
- bovine
- retractable
- „adaptive seal“ skirt
- 18 F sheat
- without BVP

Direct Flow:
- bovine
- retractable
- Polyester Ring
- 18 F sheat
- Balloonvalvuloplasty

Symmetris:
- porcine
- self-expandable Nitrinolring
- Dacron Skirt
- 18 F sheat
- Balloonvalvuloplasty

St Jude Portico:
- bovine
- self-expandable Nitrinolring
- 18 F Schleuse
- Ballonvalvuloplasty

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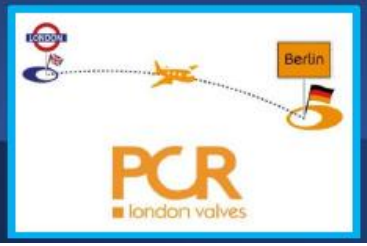
TAVI Moving Into Younger Patients: *Have We Overcome the Durability Concern?*

Martin B. Leon, MD

Columbia University Medical Center
Cardiovascular Research Foundation
New York City



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Who are Younger Patients Considered for TAVI?

- "Younger" = 60-80 yo
- Generally lower surgical risk patients with few co-morbidities (intermediate or low risk categories)
- Must be good candidates for TAVI – favorable anatomic considerations
- Usually are good candidates for minimalist procedural and early discharge strategies

M. Leon, TCT 2015

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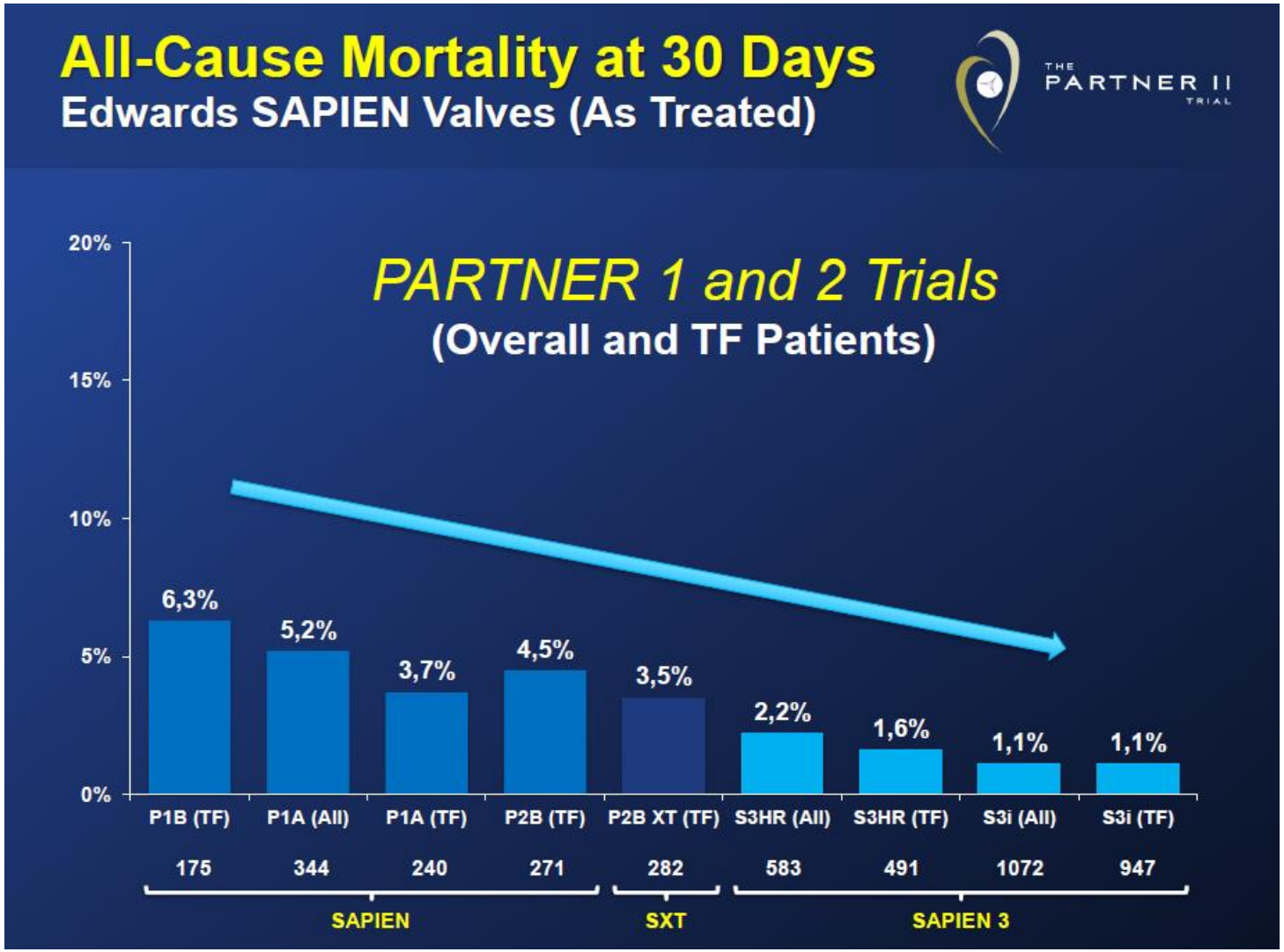
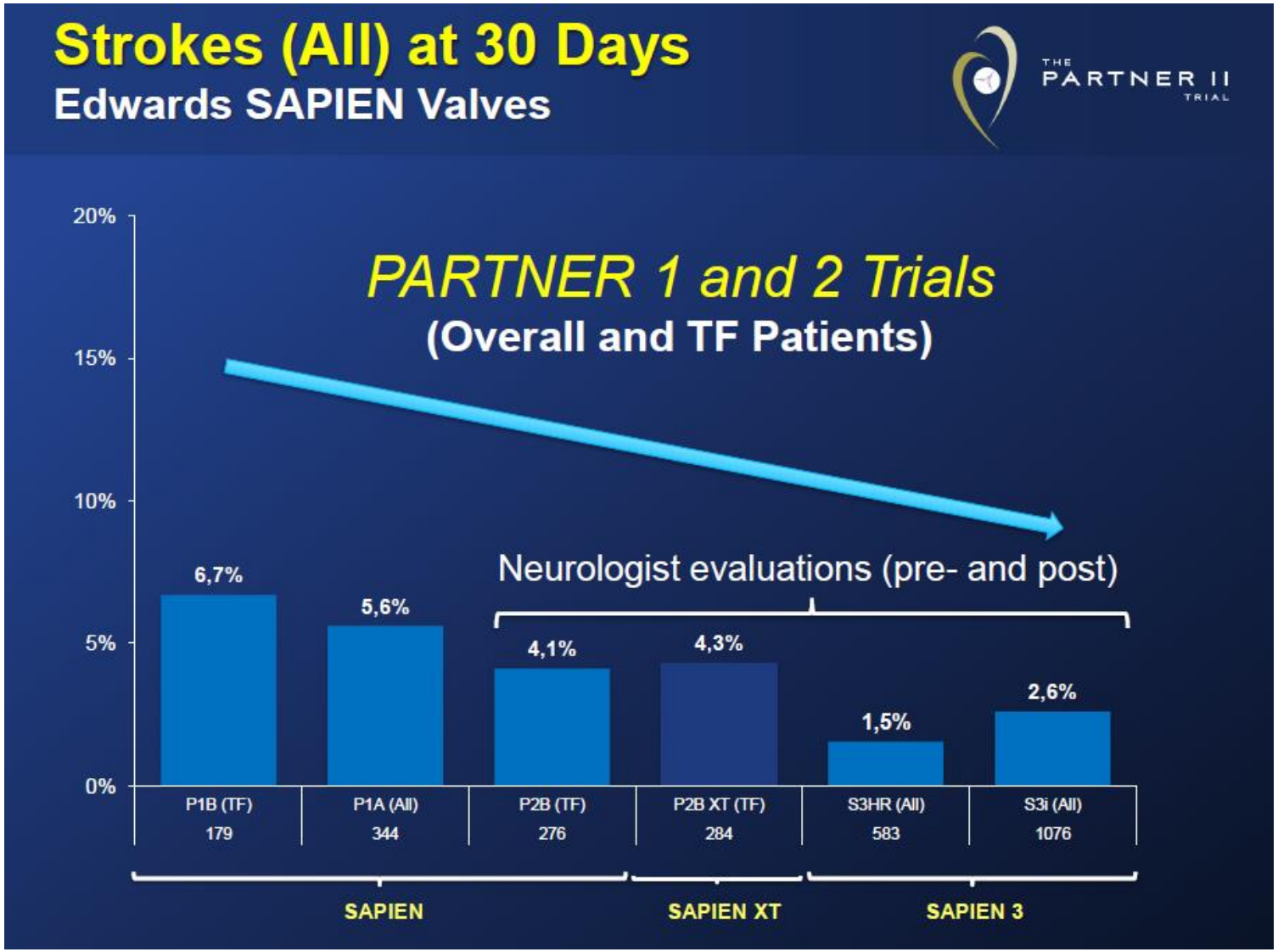
Requirements to Treat Younger Patients with TAVI

- Major endpoints (mortality and stroke) = surgery
- Low frequency of important other endpoints – vascular events, bleeding, AKI, and PVR
- Without "troubling" other complications – new onset AF, new pacemakers, coronary occlusions, or annulus rupture
- Generalizable and user-friendly to operators with rapid ambulation and short duration hospital stay
- *Bioprosthetic valve durability = (or close to) surgery*

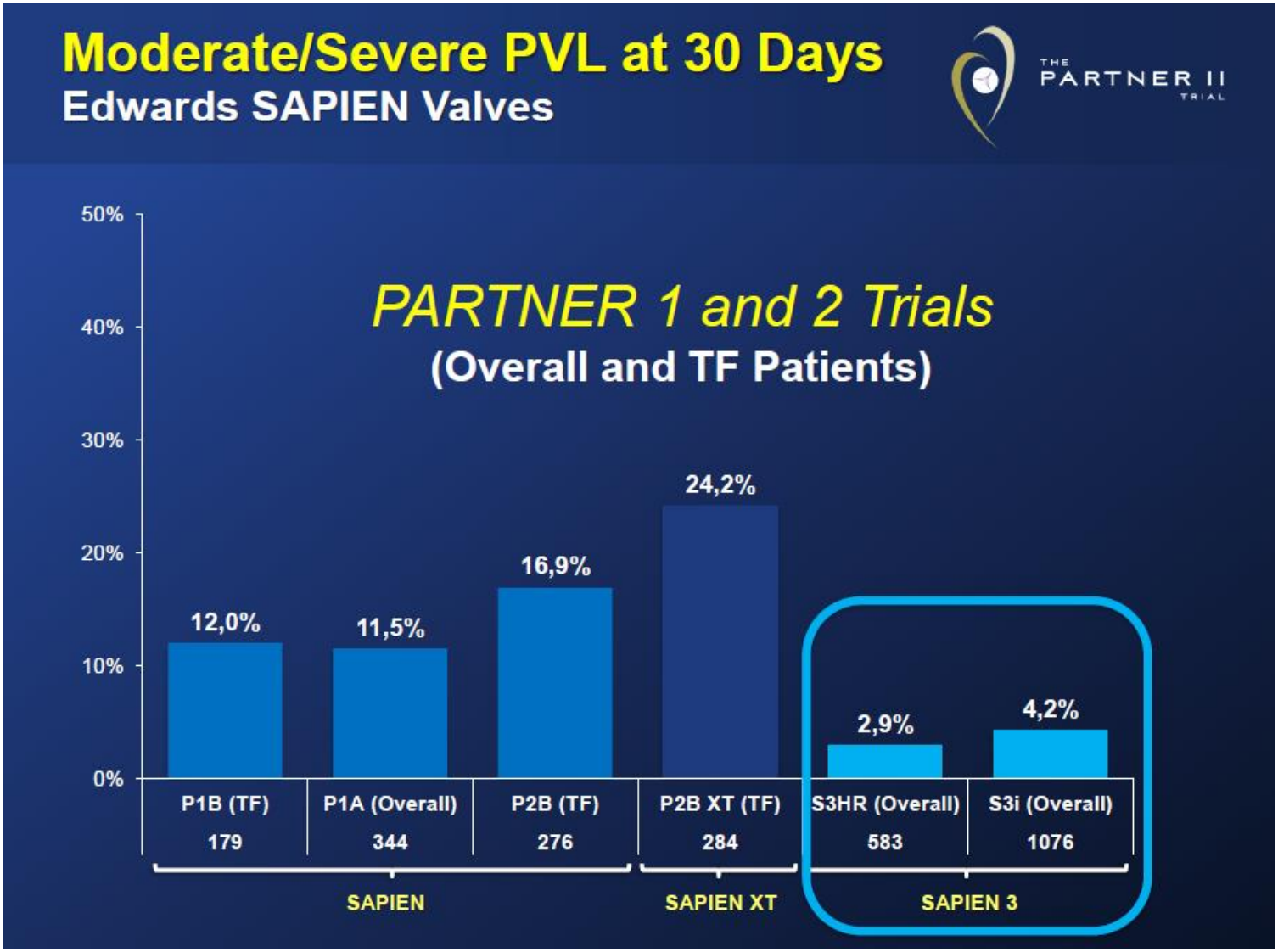
M.Leon, TCT 2015


All-Cause Mortality at 30 Days
Edwards SAPIEN Valves (As Treated)
THE PARTNER II TRIAL
PARTNER 1 and 2 Trials
(Overall and TF Patients)
20%
15%
10%
5%
0%
6,3%
5,2%
3,7%
4,5%
3,5%
2,2%
1,6%
1,1%
1,1%
P1B (TF)
P1A (All)
P1A (TF)
P2B (TF)
P2B XT (TF)
S3HR (All)
S3HR (TF)
S3i (All)
S3i (TF)
175
344
240
271
282
583
491
1072
947
SAPIEN
SXT
SAPIEN 3


Strokes (All) at 30 Days
Edwards SAPIEN Valves
THE PARTNER II TRIAL
PARTNER 1 and 2 Trials
(Overall and TF Patients)
Neurologist evaluations (pre- and post)
20%
15%
10%
5%
0%
6,7%
5,6%
4,1%
4,3%
1,5%
2,6%
P1B (TF) 179
P1A (All) 344
P2B (TF) 276
P2B XT (TF) 284
S3HR (All) 583
S3i (All) 1076
SAPIEN
SAPIEN XT
SAPIEN 3

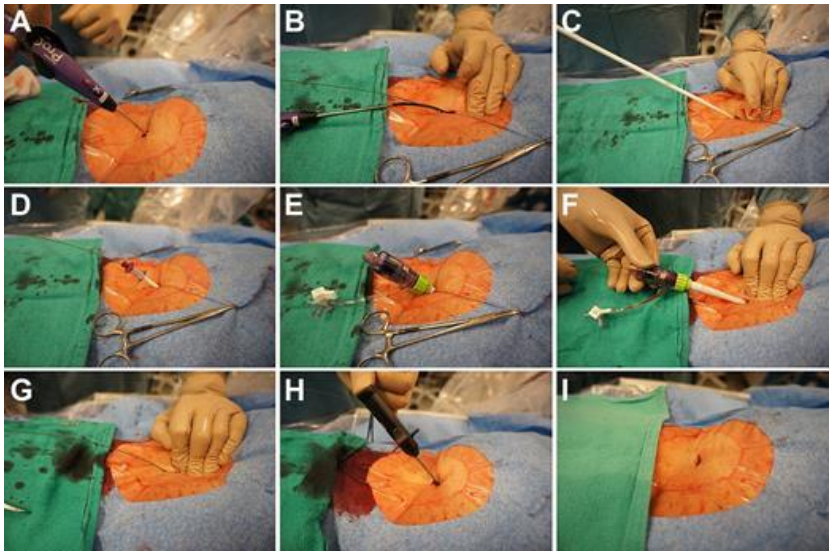
Moderate/Severe PVL at 30 Days
Edwards SAPIEN Valves

THE PARTNER II TRIAL

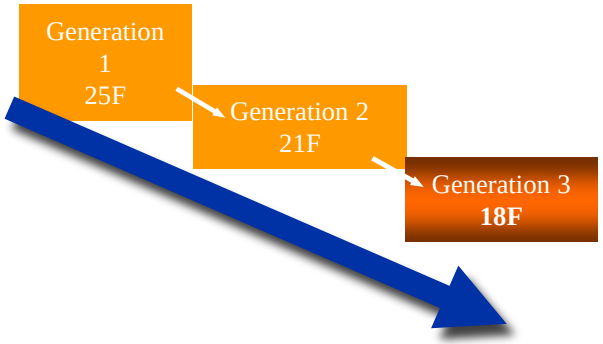


Bleeding

- Improved imaging
- Lower sheat Size
- Transfemoral access
- PreClose technique



CoreValve Self-Expanding ReValving™ System
Technological Progress



Major bleeding	13.5%	8.0%	2.3%

TAVI-Procedures

New prothesis Generation

Disadvantages

Paravalvular Leak √

Vascular Complications √

Stroke √

Permanent Pacemaker ?

Permanent Pacemaker Implantation

- Atrioventricular conduction disturbances, with or without the need for permanent pacemaker (PPM) implantation, are one of the most common adverse events after TAVI.

- Among transcatheter heart valves (THV), rates of conduction abnormalities vary from less than 10 % to more than 50 %.

- Although generally considered as a minor complication, PPM may have a profound impact on prognosis and quality of life after TAVI.

- The debate about predictors for pacemaker implantation and their impact on outcome after TAVI is still ongoing.

Predictors of PPM Implantation

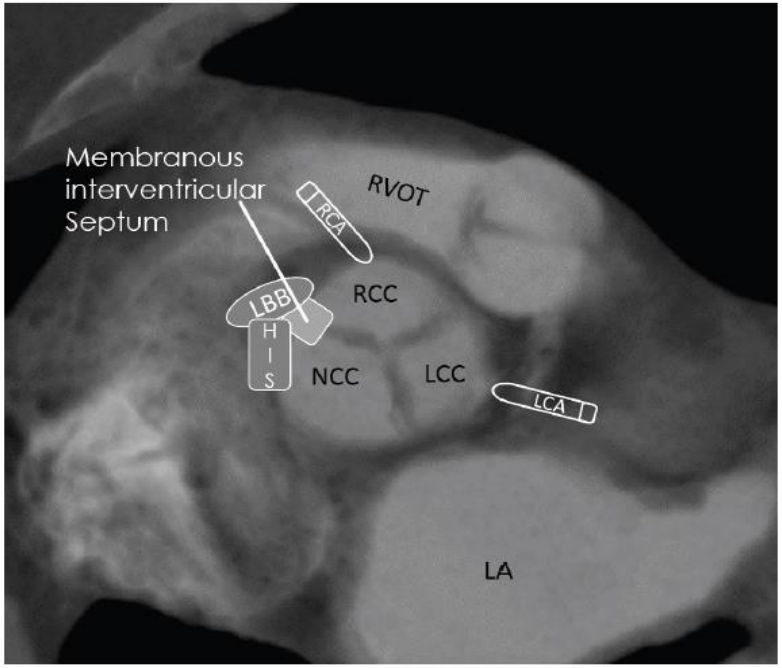
Pre-existing Conduction Abnormalities and Anatomical Conditions
Patients undergoing TAVI have similar rates of pre-existing conduction disease as SAVR patients, which are described at 40–50 % in both surgical and transcatheter populations

Left bundle-branch block (LBBB)
Increased interventricular septal diameter (>17mm)
Increased non-coronary aortic cusp thickness (>17mm)
In an early study with self-expanding Medtronic CoreValve Prosthesis (MCP, Medtronic, Minneapolis, Minnesota), left bundle-branch block (LBBB) at baseline, increased interventricular septal diameter (>17 mm) and increased non-coronary aortic cusp thickness (>8 mm) were highly predictive for PPM

Predictors of PPM Implantation

Predicting post-TAVI PPM
Most significant predictors of PPM

Right bundle-branch block (RBBB) at baseline
Baseline AV-Block
Small left-ventricular outflow tract diameter
left axis deviation
significant mitral annular calcification
lower post-implant valve area



Meta-analysis
The strongest predisposing conduction disturbances for PPM:

RBBB (n=2158; risk ratio (RR): 2.89 (CI: 2.36–2.54), p<0.01),
Baseline AV block (n=1381; RR: 1.52 (CI: 1.15–2.01), p<0.01),
left anterior hemiblock (n=1065; RR: 1.62 (CI: 1.17–2.25), p<0.01)

Siontis et al. J Am Coll Cardiol 2014;64(2):129–140.

Predictors of PPM Implantation

Prothesis Type	Implantation rate (day 30)
Edwards SAPIEN and SAPIEN XT	**5–14.2 %**
Edwards SAPIEN 3 THV20	**13.3 %**
More liberal Pacemaker implantation strategy after MCP TAVR	
Medtronic Corevalve	**24 %** FRANCE-2 [French Aortic National CoreValve and Edwards] registry
	33 % UK CoreValve registry)
Low incidence of permanent pacemaker	
Medtronic Corevalve	**13.3 %** ADVANCE II, PCR 2014
MCP was deployed according to Best recommendation practice (implantation depths <6 mm).	
CoreValve Extreme Risk pivotal trial	**21.6 %**

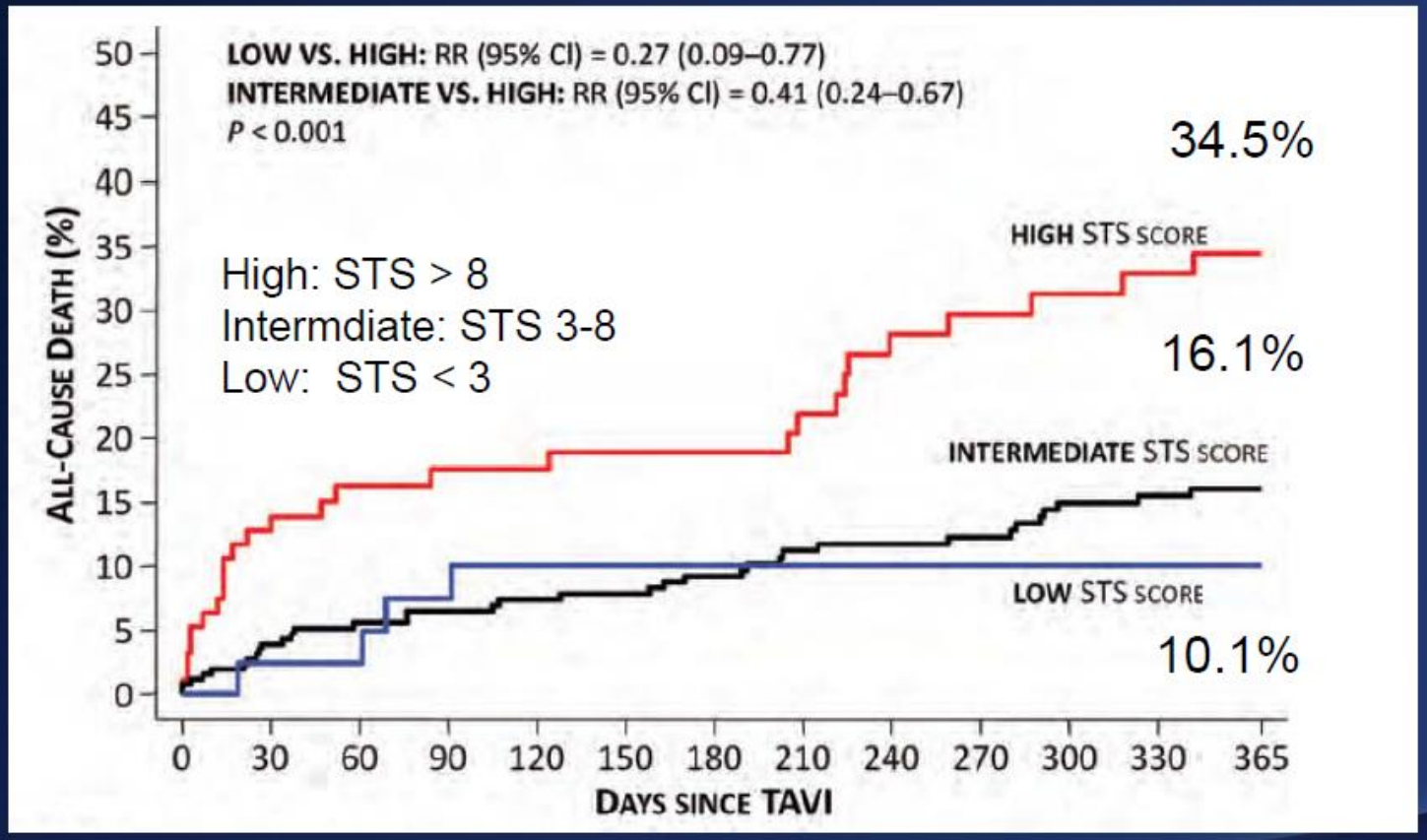
Predictors of PPM Implantation

Prothesis Type	Implantation rate (day 30)	
Next generation devices		
Direct Flow	**17 %**	**DISCOVER (100 patients)**
Boston LOTUS	**28 %**	**REPRISE II (120 patients)**
Medtronic Engager	**26 %**	**Multicentre European pivotal trial (TA)**
Jena Valve	**26 %**	

Predictors of PPM Implantation

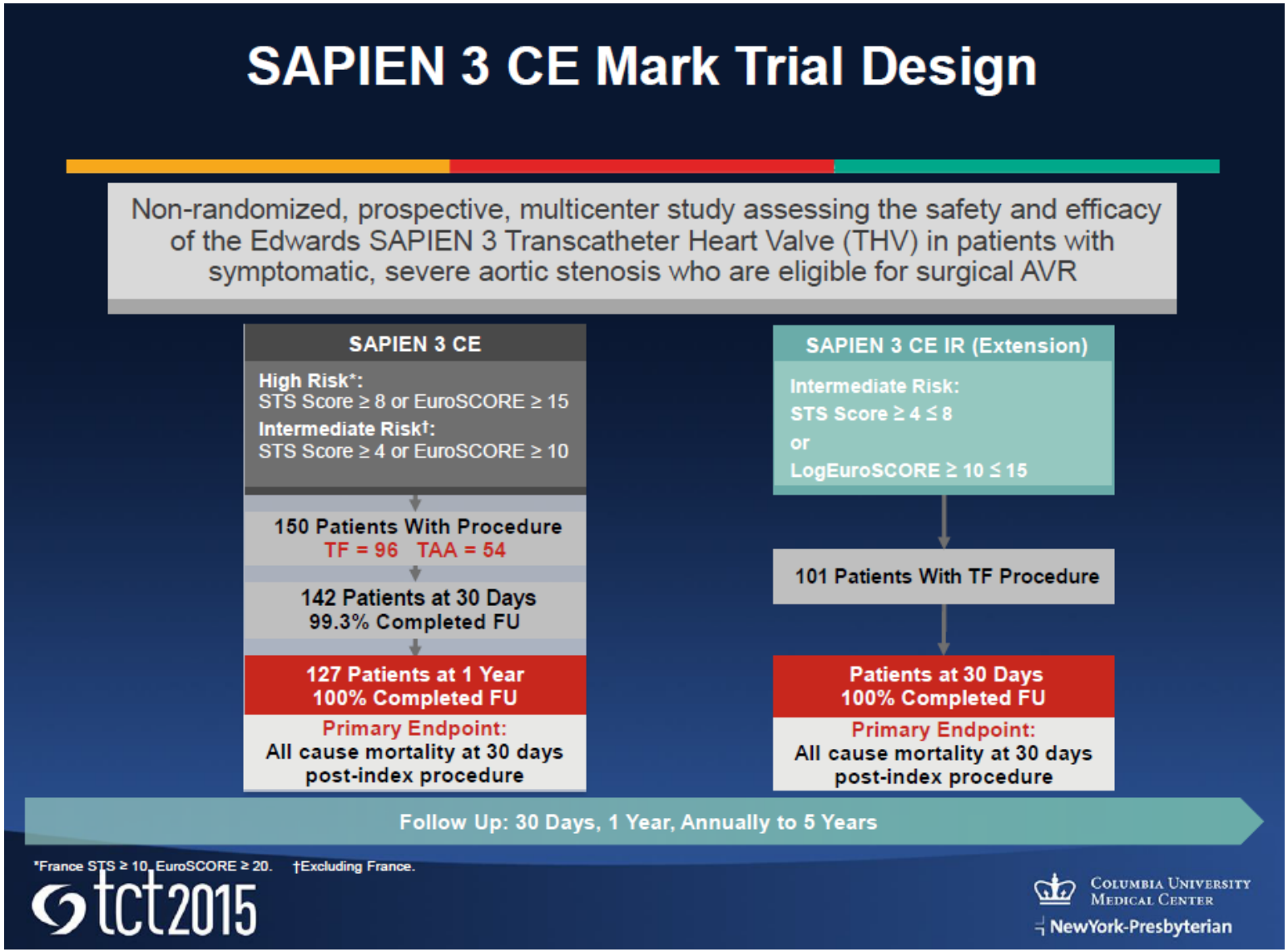
Bern Low-Intermediate Risk

Very low one year mortality in intermediate STS patients



Wenaweser et al European Heart Journal (2013) 34, 1894–1905

Predictors of PPM Implantation



Predictors of PPM Implantation

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SAPIEN 3 CE IR
Clinical Outcomes at 30 Days

Clinical Outcome	N = 101 KM Event Rate (%) 30 Days
Major Vascular Complications	2%
Life-Threatening Bleeding	2%
Myocardial Infarction	0%
Acute Kidney Injury	2%
New-Onset Atrial Fibrillation	6.9%
New Permanent Pacemaker	4%
Valve Thrombosis	0%
CHF/Worsening CHF	0%
SVD Requiring Repeat Procedure	0%

VI, valve implant = all enrolled patients who received a SAPIEN 3 implant, and retained the valve upon leaving the cath lab.

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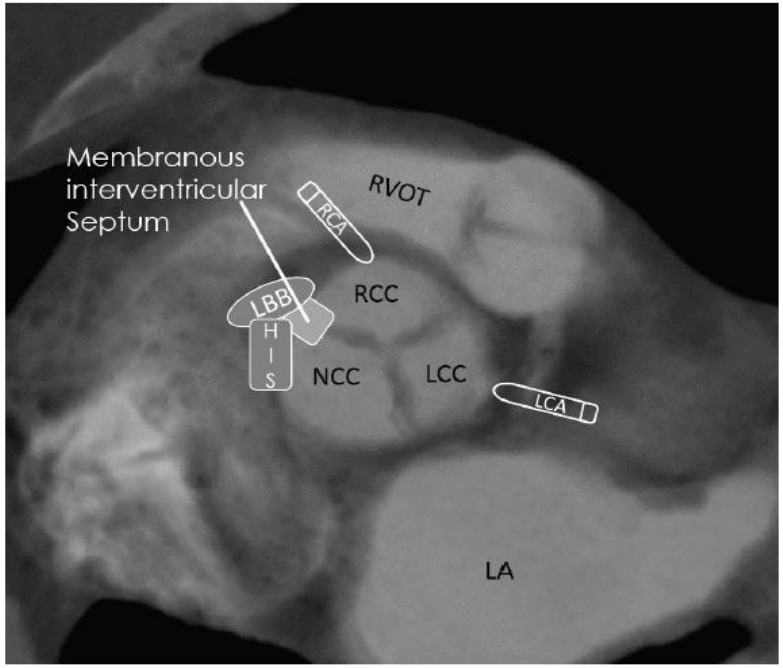
Predictors of PPM Implantation

Pre- and Post-dilatation and Prosthesis Sizing



- Close relationship of the conduction to the aortic annulus
- Mechanical interaction between the stent frame of the transcatheter valve prosthesis and the left bundle-branch
- Impact of valvuloplasty balloon catheter size on the need for PPM
  - Cohort of 237 patients without prior pacemaker, who underwent TAVI with the MCP
  - The overall incidence of PPM was 21.1 %
  - Significantly higher when a 25 mm balloon was used (27.1 %) than when a 23 mm or smaller balloon was used (15.4 %) for the balloon valvuloplasty (BAV)

Lange et al. EuroIntervention 2014;9(10):1151–57

Predictors of PPM Implantation

Pre- and Post-dilatation and Prosthesis Sizing

•Pacemaker rates after TAVI may be reduced by using undersized BAV balloons or even avoidance of pre-dilation

•Two randomised studies are currently ongoing to investigate direct TAVR without pre-dilatation with the MCP

SIMPLIFY TAVI Trial; NCT01539746

ESV EASE-IT Trial; NCT02127580

•The degree of prosthesis oversizing may lead to a higher incidence of PPM implantation

Predictors of PPM Implantation

- Persistence of conduction disturbances and high-degree AV block over time seems to differ between valves
- Self-expanding prostheses may lead to delayed injuries of the conduction system
- Proportion of AV conduction disturbances after intervention has been shown to recover over time at three months of follow-up
- Only 40 % of the PPM patients for high-degree AVB still had an AVB underlying their paced rhythm.
- **Low sample size of these studies**
- **Data in relation to the appropriate time point of pacemaker implantation are rare**
- **There is no explicit data for the best time point for PPM implantation**

Predictors of PPM Implantation

Implantation Depths and Approach

•Mean implantation depth: CoreValve prosthesis implantation depth is a predictor for PPM.

•The deeper the CoreValve frame protrudes into the left ventricular outflow tract, the more likely the patient is to develop an LBBB

•Cutoff of 6.0 mm as an independent predictor of the development of a high-degree AV block and the requirement for permanent pacing

Guetta et al Am J Cardiol 2011;108(11):1600–5.

•Implantation of balloon-expandable transfemoral prothesis with increased implantation depth is associated with clinically significant new conduction disturbances and permanent pacemaker implantation

Binder RK et al. JACC Cardiovasc Interv 2013;6(5):462–68.

Repositionable Percutaneous Aortic Valve Replacement: 30-Day Outcomes in 250 High Surgical Risk Patients in the REPRISE II Extended Trial Cohort

Ian T. Meredith AM
MonashHeart, Clayton, Victoria, Australia

Nicolas Dumonteil, Daniel J. Blackman, Didier Tchétché, Darren Walters,
David Hildick-Smith, Ganesh Manoharan, Jan Harnek, Stephen Worthley,
Gilles Rioufol, Thierry Lefèvre, Thomas Modine, Nicolas Van Mieghem,
Dominic J. Allocco, Keith D. Dawkins

on behalf of the REPRISE II Investigators

REPRISE II

OBJECTIVE

- Evaluate safety & performance of the Lotus Valve System for TAVI in symptomatic patients with severe calcific aortic stenosis considered
  high risk for surgical valve replacement

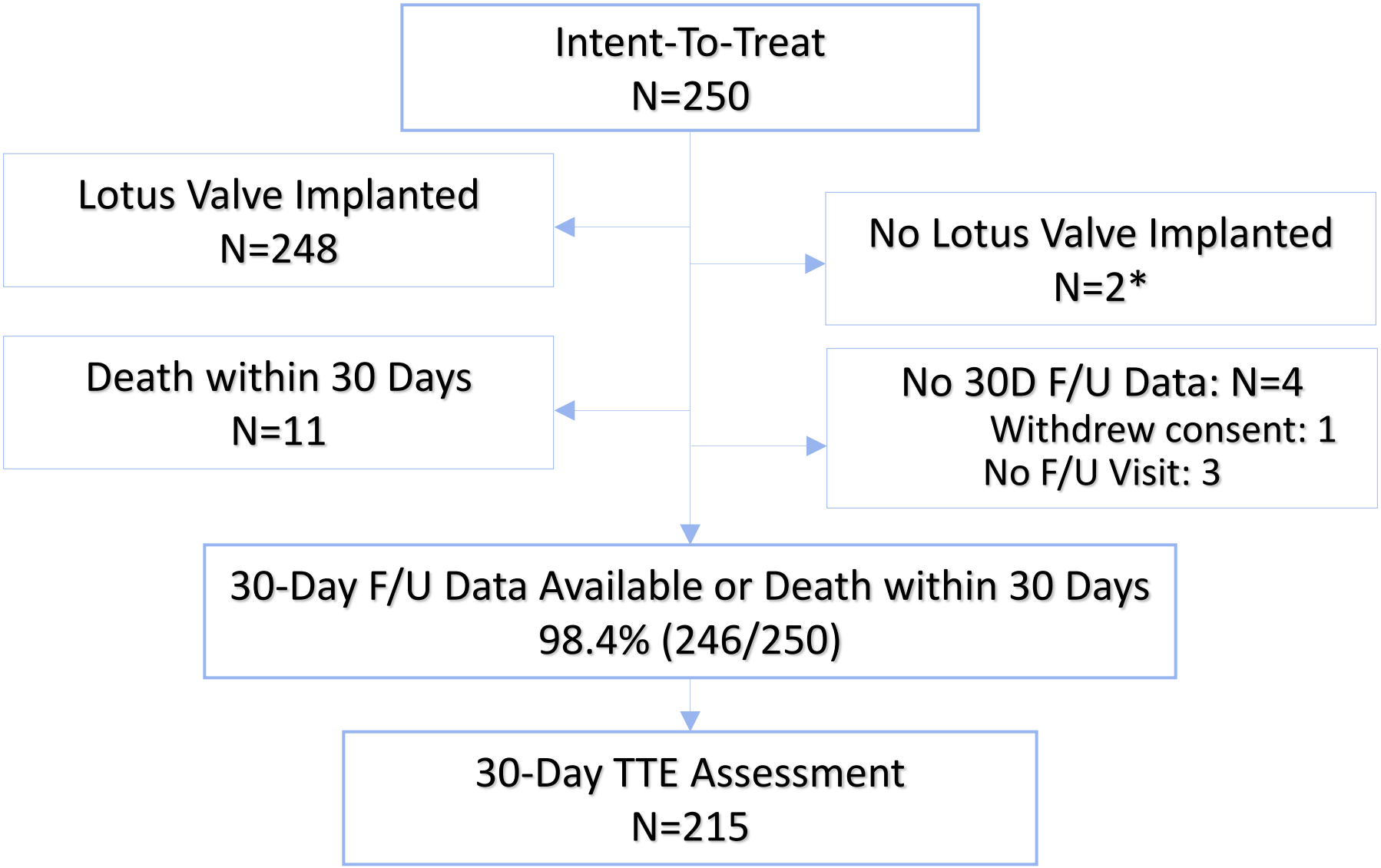
DESIGN

- Prospective; single-arm; multicentre
- Available valve sizes: 23mm & 27mm
- F/U at 7 days/discharge, 30 days, 3 & 6 months, annually 1–5 years

INDEPENDENT DATA ASSESSMENTS

- Clinical Events Committee
- Core Labs: Angiography, ECG, Echocardiography, Pathology

Study Flow – REPRISE II with Extended Cohort



Baseline Characteristics
REPRISE II with Extended Cohort (N=250)

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Comorbidities & Baseline Scores

Age (Years)	84.0 ± 5.2 (250)	**NYHA Class III or IV**	77.2% (193)
Gender (Female)	52.4% (131)	**euroSCORE 2011 (%)**	6.4 ± 6.2 (250)
Diabetes, treated	24.0% (60)	**STS Score (v 2.73; %)**	6.5 ± 4.2 (250)
Atrial fibrillation	37.2% (93)	**STS Plus Score (%)**	10.6 ± 7.7 (250)

Echocardiographic Measurements*

AVA (cm^2)	0.7 ± 0.2 (197)	**LVEF (%)**	53.1 ± 10.5 (126)
MR (mod/severe)	10.6% (24)	**Mean gradient (mmHg)**	45.2 ± 13.6 (212)
AR (mod/severe)	13.3% (29)	**Peak gradient (mmHg)**	74.7 ± 21.1 (212)

Frailty Indices		**Threshold**
5 Meter gait speed (sec)	8.6 ± 5.2 (236)	> 6
Max grip strength average (kg)	21.1 ± 11.5 (246)	≤ 18
Katz Index	5.7 ± 0.8 (247)	< 6
Mini-Cognitive Assessment for Dementia	3.5 ± 1.4 (244)	< 4

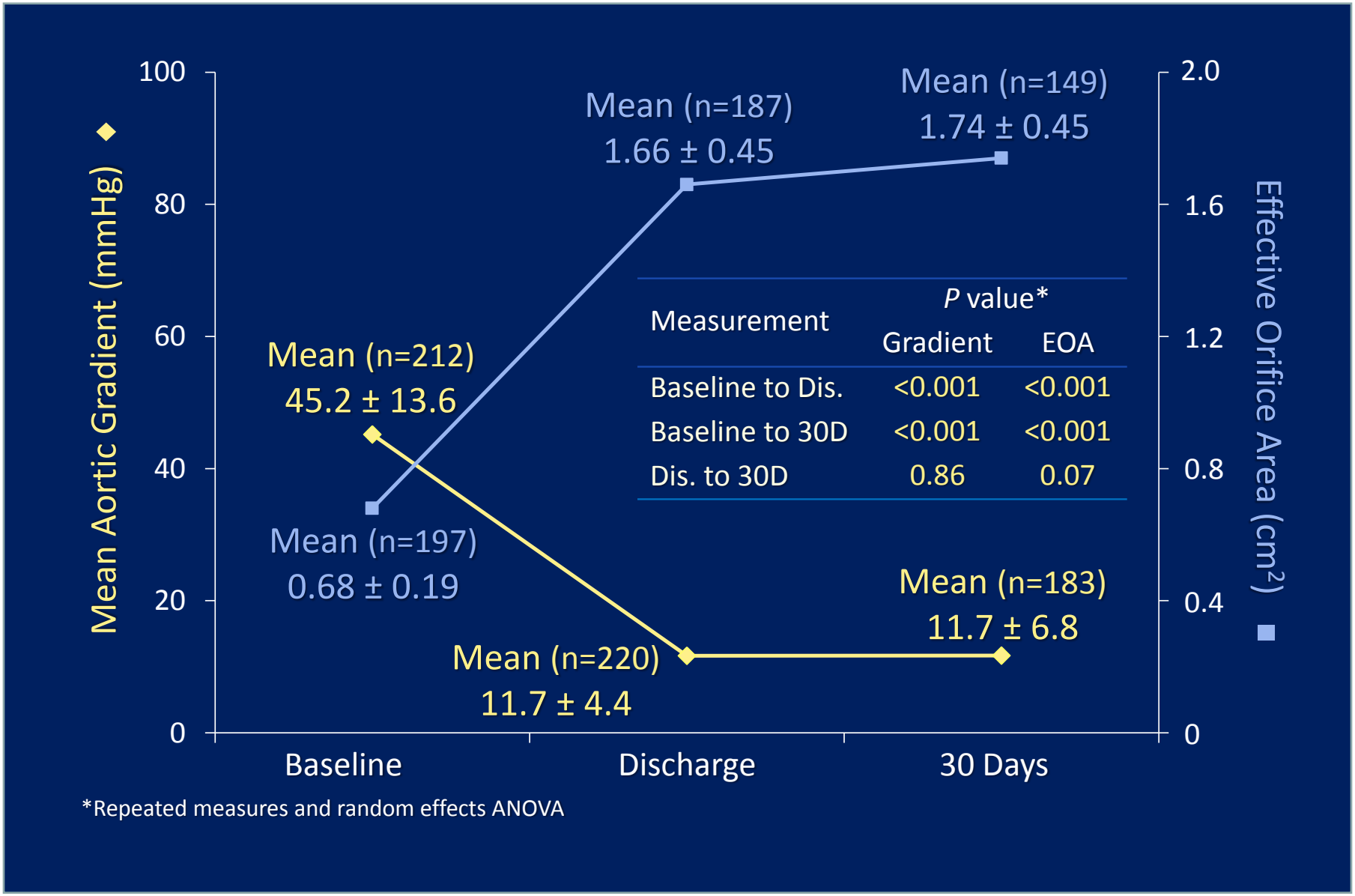
Device Performance
REPRISE II with Extended Cohort (N=250)

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%

Device Success – VARC 2 Metrics
REPRISE II with Extended Cohort (N=250)

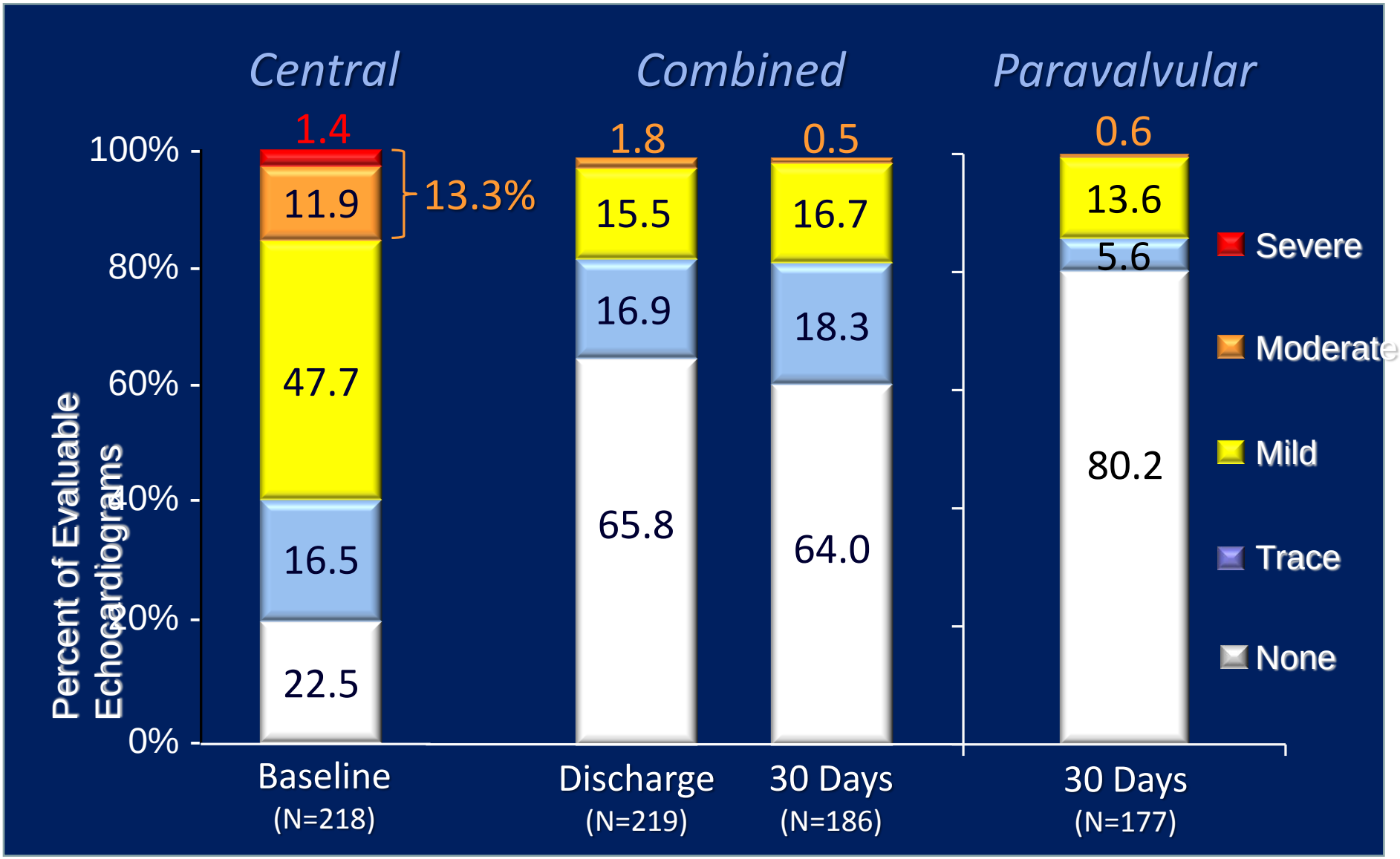
No procedural mortality	98.4% (246/250)
Correct positioning of one valve in proper location	99.2% (248/250)
Mean aortic valve gradient <20 mmHg	95.0% (209/220)
Peak velocity <3 m/s	94.6% (209/221)
No moderate/severe prosthetic valve regurgitation	98.2% (215/219)

Mean Aortic Gradient & EOA
REPRISE II with Extended Cohort (N=250)



Aortic Regurgitation – Core Lab Adjudication

REPRISE II with Extended Cohort (N=250)



Safety: Death & Stroke at 30 Days
REPRISE II with Extended Cohort (N=250)

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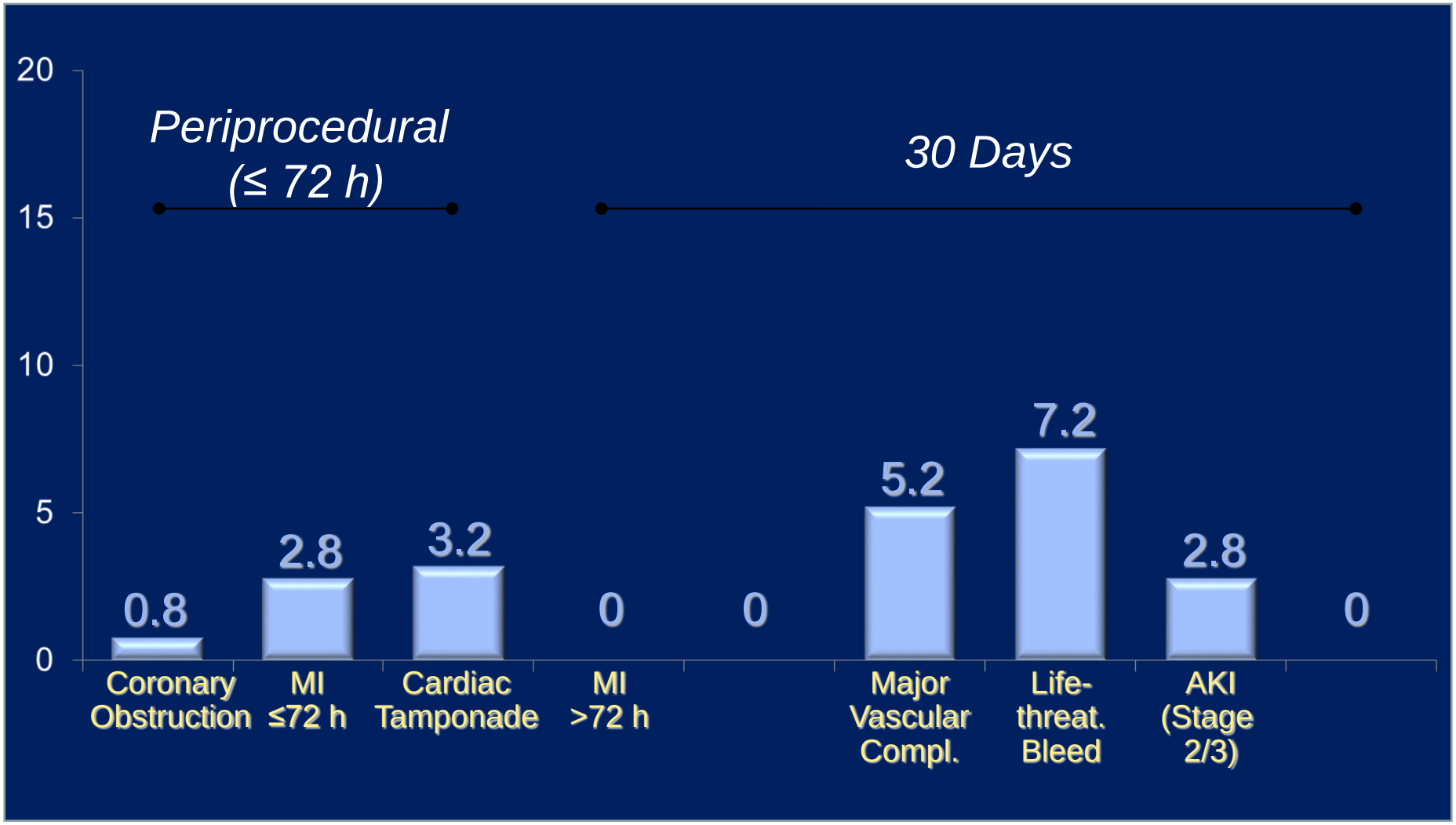
Event	*Patients (N=249*)*
All-cause mortality	4.4% (11)
Cardiovascular mortality	4.0% (10)
Disabling stroke†	3.2% (8)
Non-disabling stroke†	3.6% (9)
All-cause mortality & disabling stroke	6.8% (17)

* **One patient withdrew consent**

† **All REPRISE II patients (n=120) were assessed by a neurologist before and after TAVI**

Additional VARC 2 Safety Endpoints
REPRISE II with Extended Cohort (N=250)

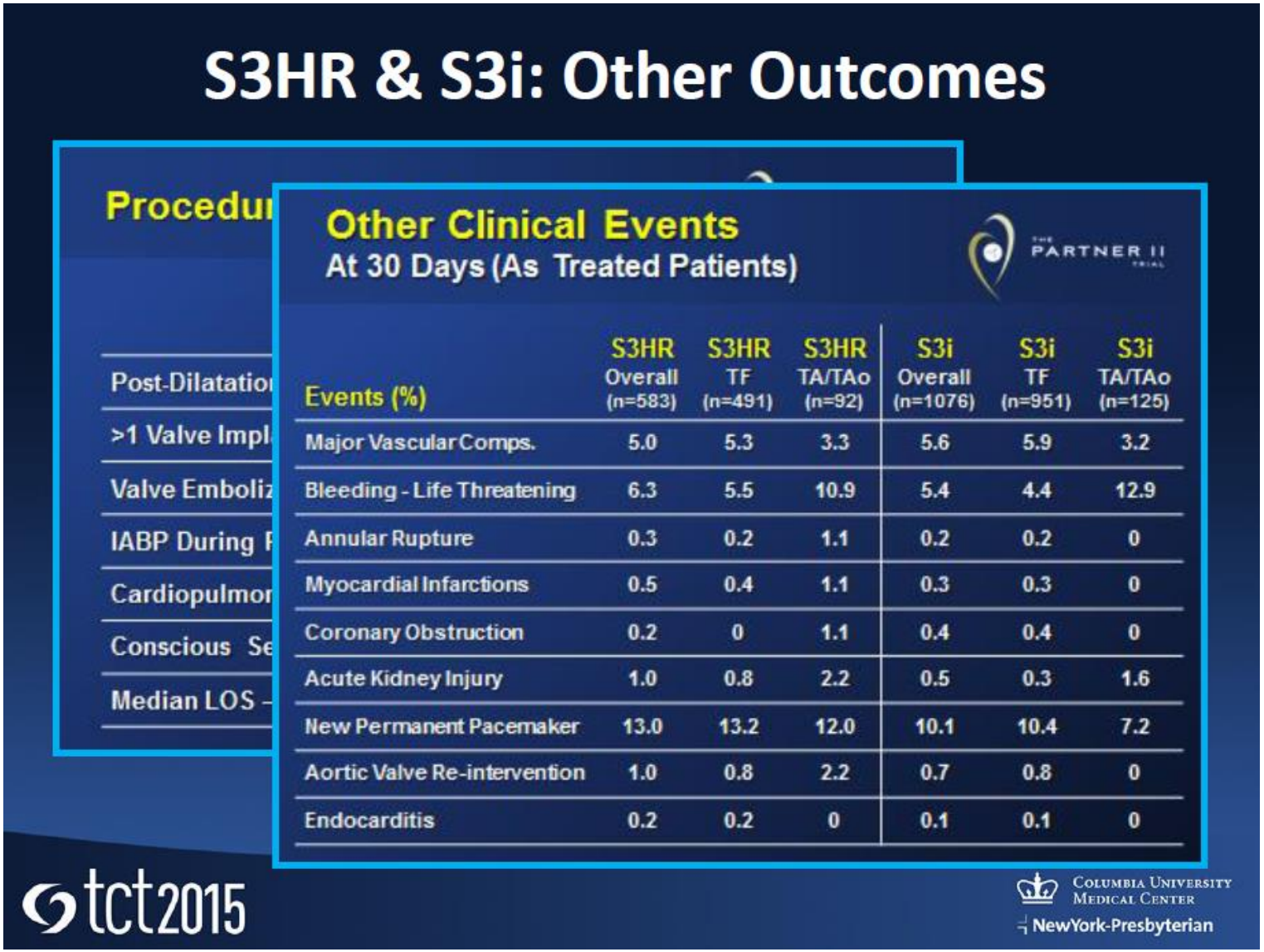


Pacemaker Implantation
REPRISE II with Extended Cohort (N=250)

Variable	*Patients*
Newly implanted pacemaker	28.9% (72/249)
Baseline RBBB	27.8% (20/72)
New conduction disturbance post valvuloplasty	34.7% (25/72)
LVOT overstretch ≥10%	61.1% (44/72)
Annulus overstretch ≥10%	34.7% (25/72)

Indication		Indication	
3rd deg. AV block	59	LBBB & 1st deg. AV block	3
Atrial fibrillation & bradycardia	4	LBBB & 2nd deg. AV block (Type 1)	1
Trifascicular block	1	LBBB, EP study showing severe infranodal disease	3
New LBBB, symptomatic bradycardia	1		

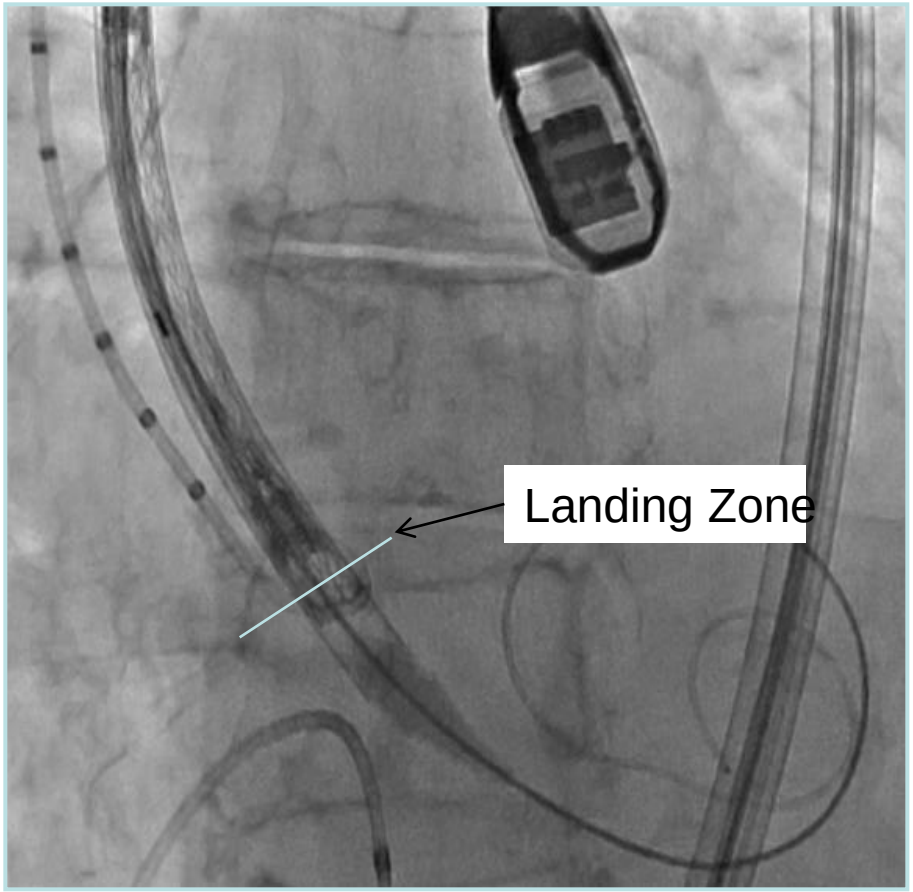
Pacemaker Rates Sapiens 3



Events (%)	S3HR Overall (n=583)	S3HR TF (n=491)	S3HR TA/TAo (n=92)	S3i Overall (n=1076)	S3i TF (n=951)	S3i TA/TAo (n=125)
Major Vascular Comps.	5.0	5.3	3.3	5.6	5.9	3.2
Bleeding - Life Threatening	6.3	5.5	10.9	5.4	4.4	12.9
Annular Rupture	0.3	0.2	1.1	0.2	0.2	0
Myocardial Infarctions	0.5	0.4	1.1	0.3	0.3	0
Coronary Obstruction	0.2	0	1.1	0.4	0.4	0
Acute Kidney Injury	1.0	0.8	2.2	0.5	0.3	1.6
New Permanent Pacemaker	13.0	13.2	12.0	10.1	10.4	7.2
Aortic Valve Re-intervention	1.0	0.8	2.2	0.7	0.8	0
Endocarditis	0.2	0.2	0	0.1	0.1	0

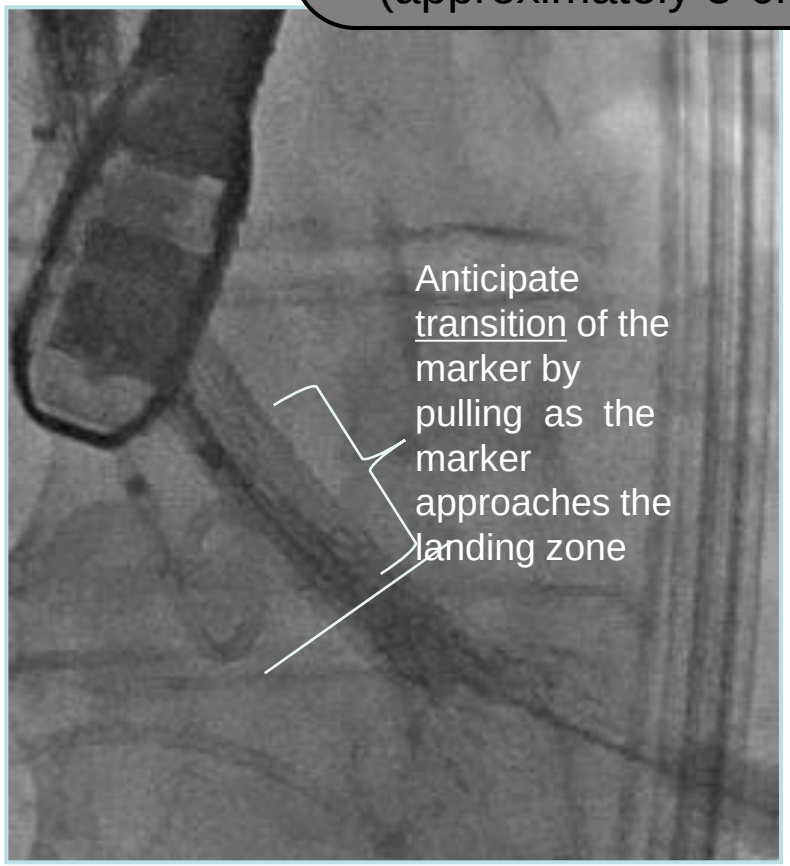
Lotus Valve Implantation

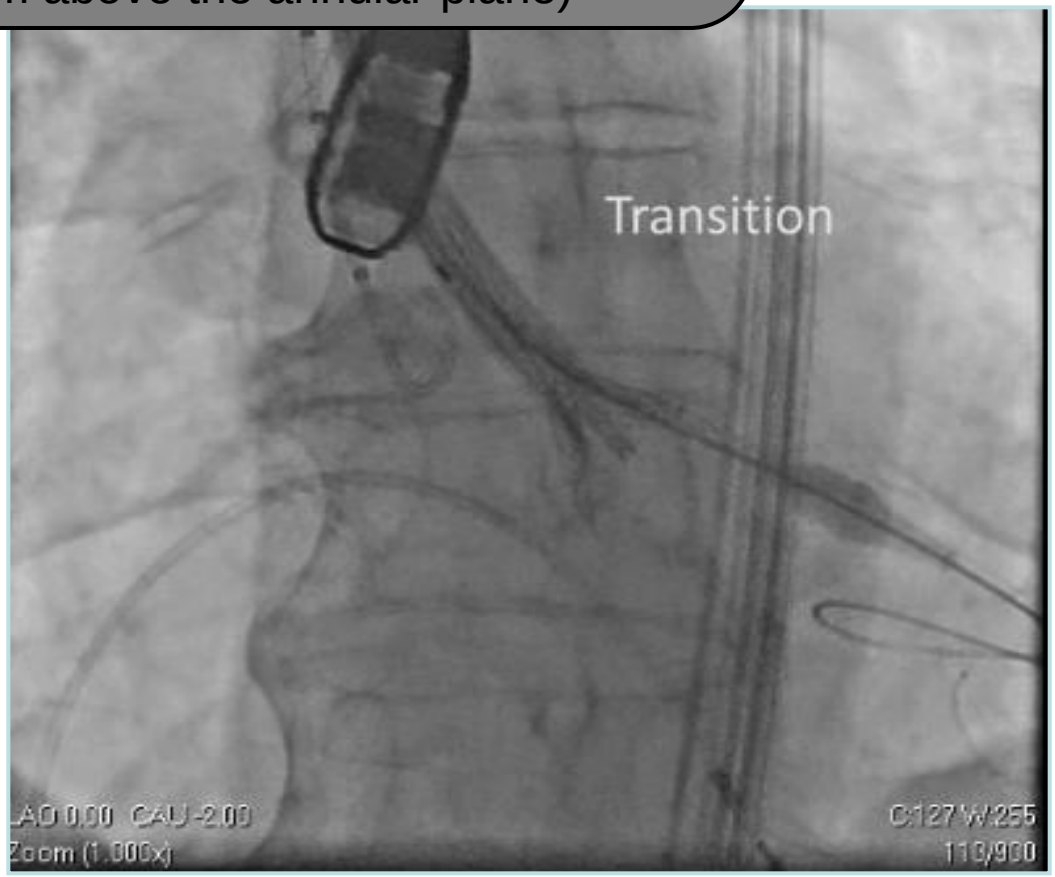
- Slowly start CCW rotation to unsheath the valve
- Target the landing zone with the radiopaque marker about 5-6mm above the annulus (center of pigtail)



Transition to Expansion

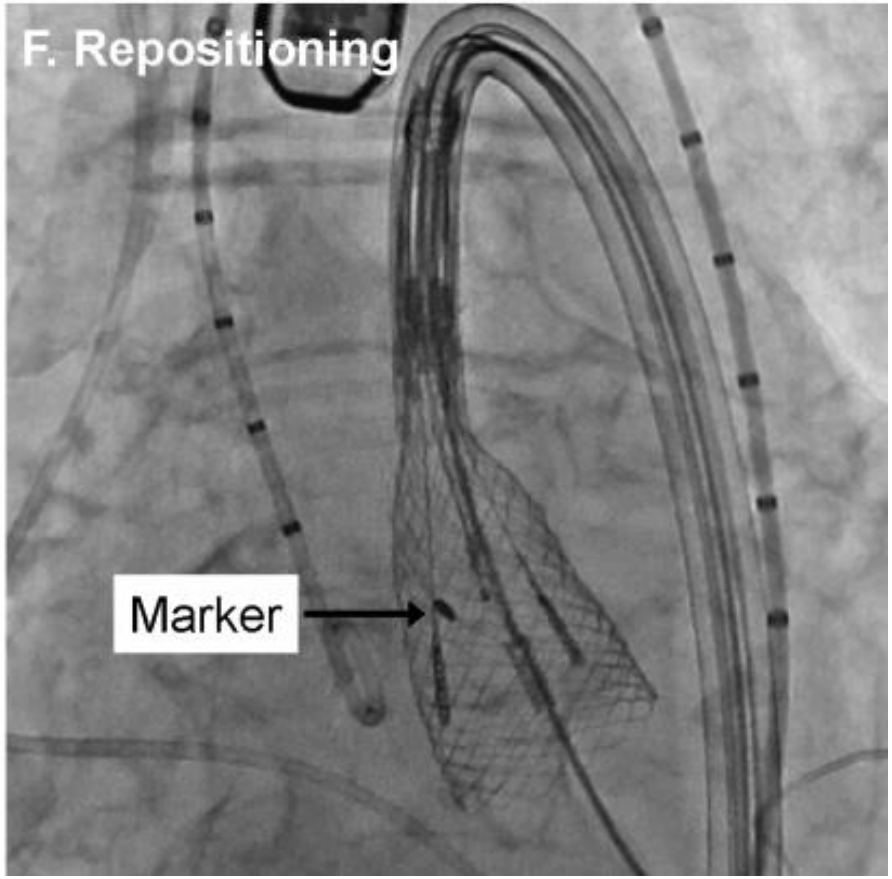
- Anticipate the “Transition” phase – when the marker is close to the top of the pigtail
  - “Transition” by applying slight backward tension, while continuing to unsheath the valve
- Allow the marker to land at the “Landing Zone” (approximately 5-6mm above the annular plane)





Lotus Valve Implantation

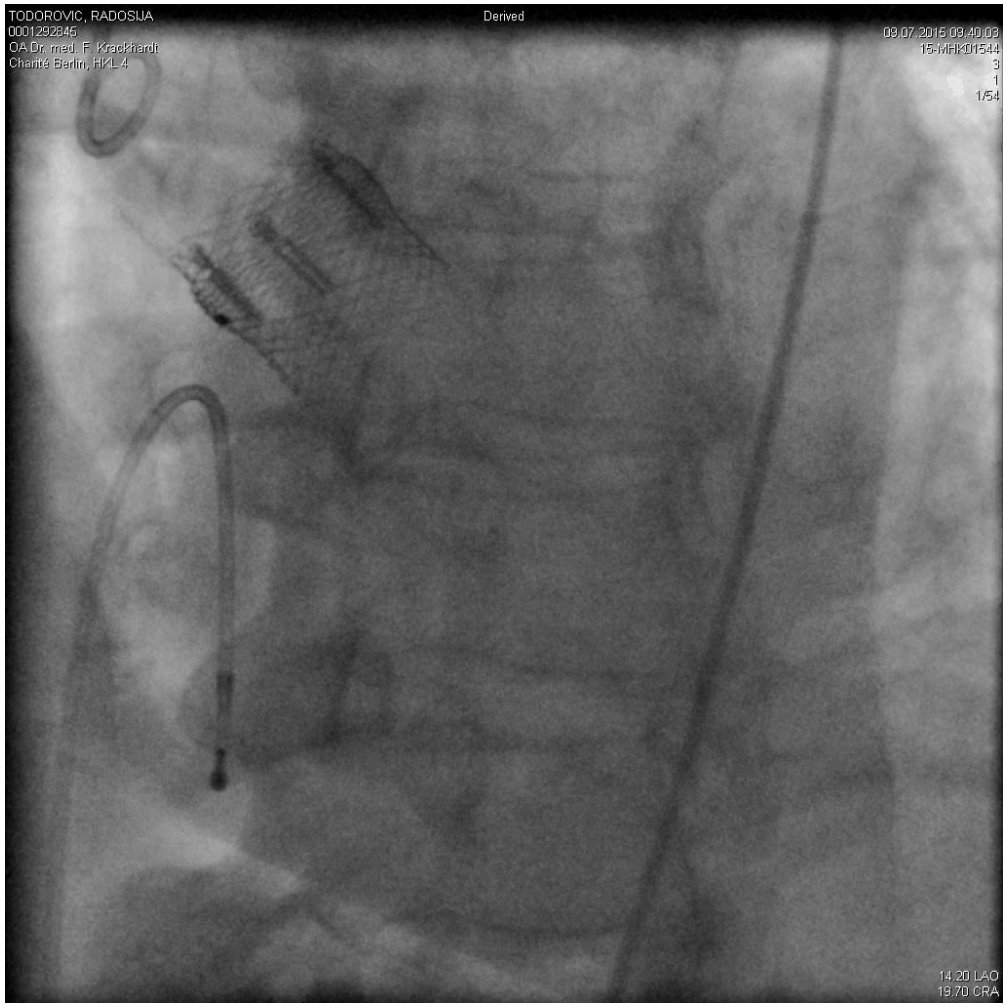
Check position and consider resheathing to reposition

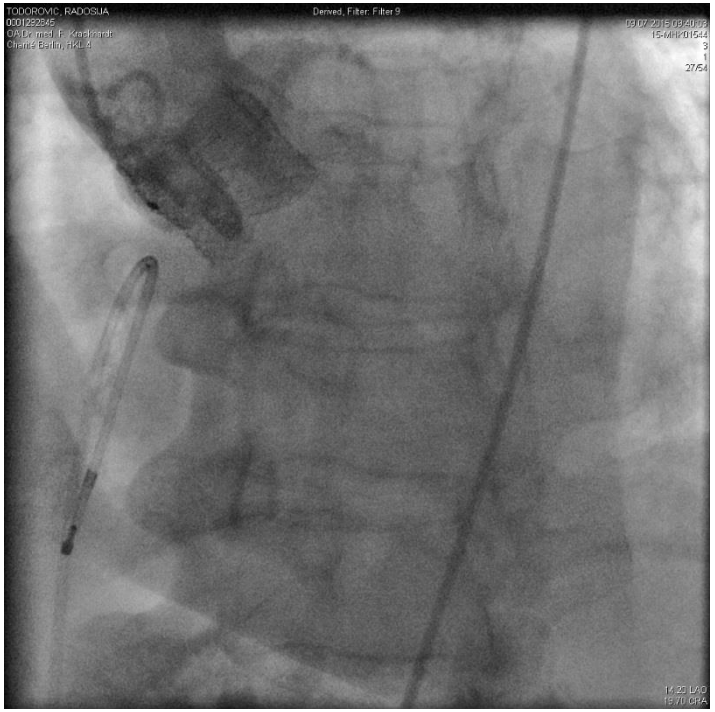


Check valve (marker) position and only use resheathing to reposition

- Minor resheathing is best way to fine tune and reposition
- Can be done at any stage
- The earlier the better

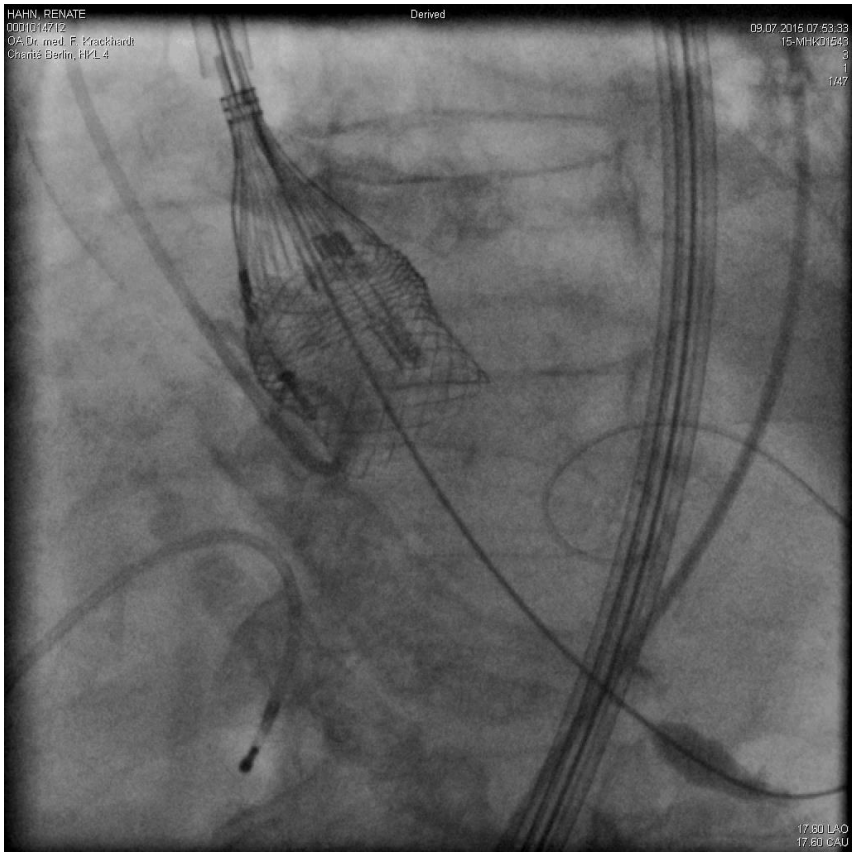
Lotus Valve Implantation

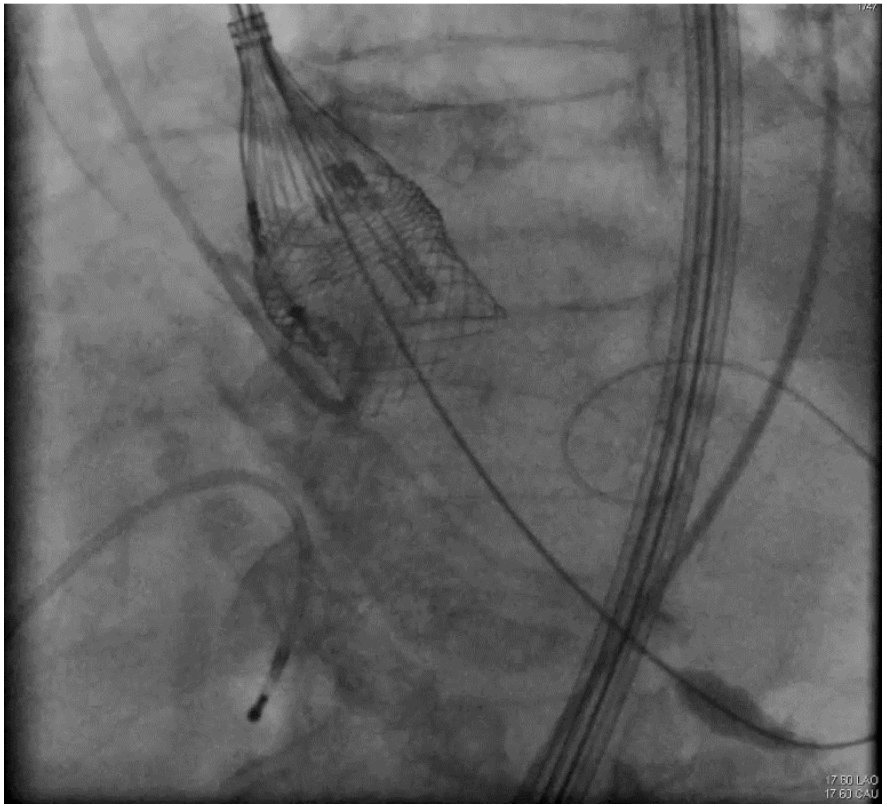




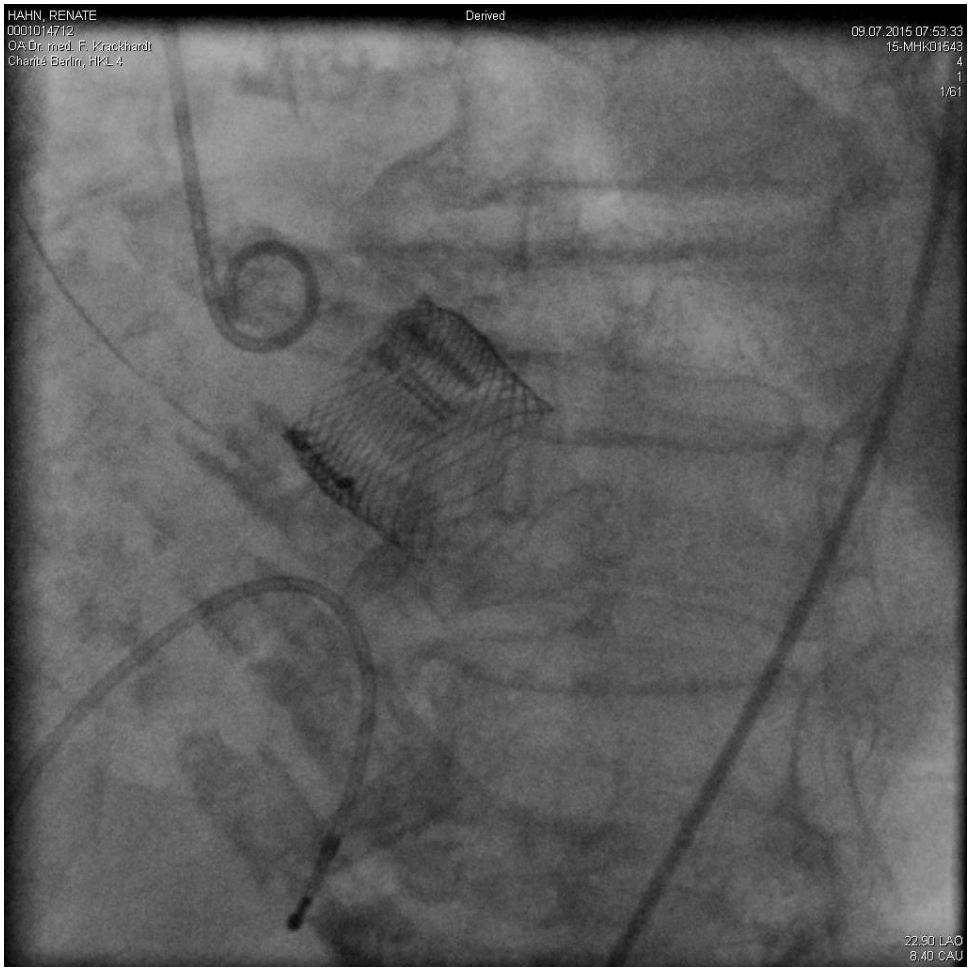
Lotus valve 23 mm

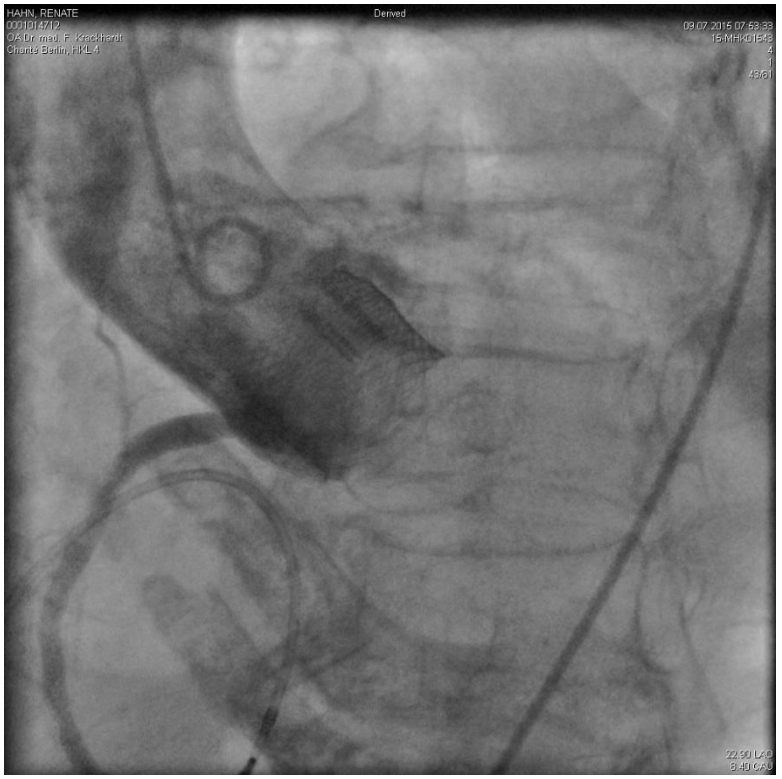
Lotus Valve Implantation





Lotus Valve Implantation





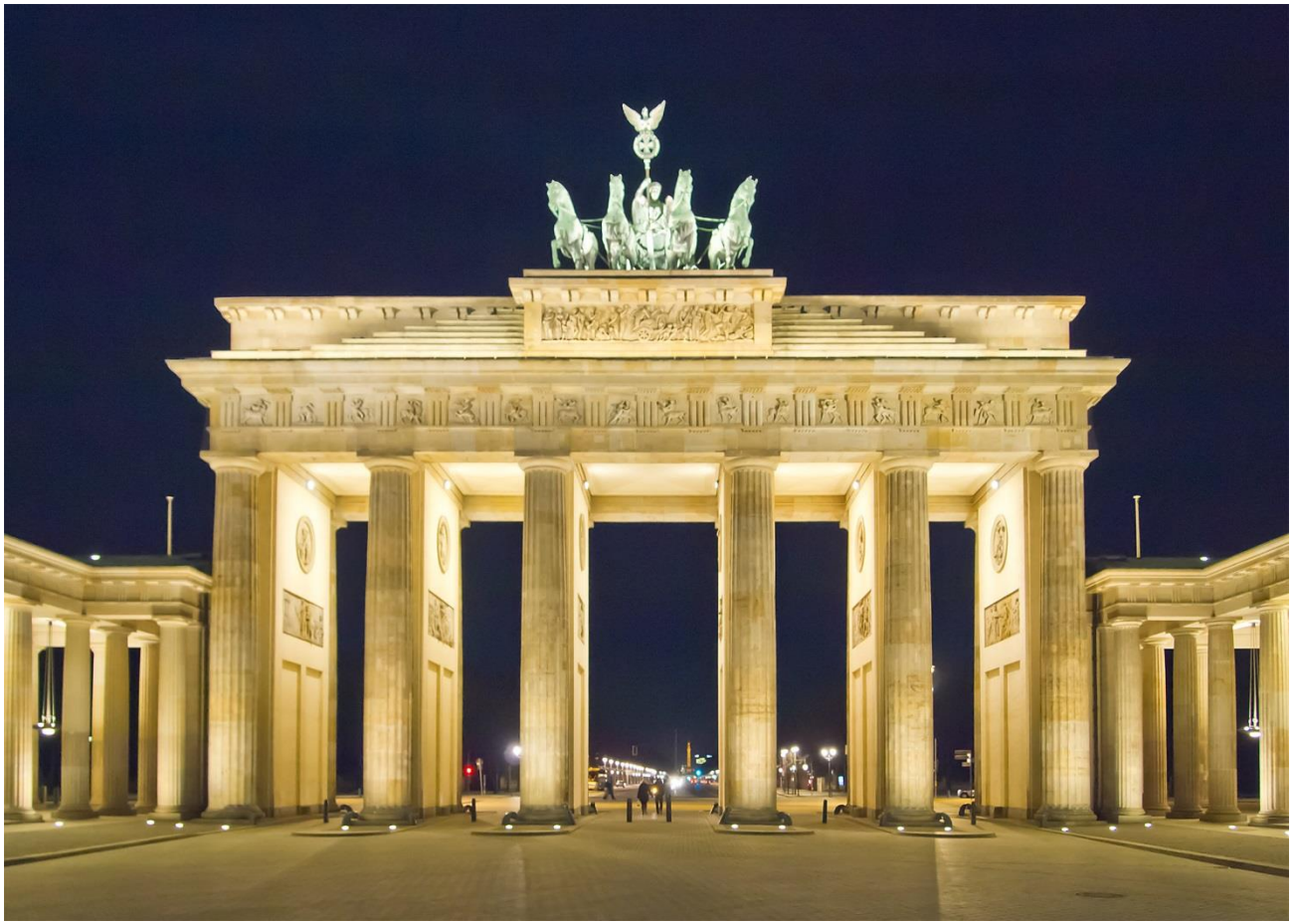
Lotus valve 25 mm

Lotus Valve Implantation Data CVK Berlin

Lotus Valve 23-29 mm		
n=25, 2014		
Periprocedural success	25/25	100 %
Permanent Pacemaker	1/25	4 %
Minor Bleeding	1/25	4 %
30-days Mortality	1/25	4 %
Minor Stroke	1/25	4 %

Conclusion

- TAVI remains associated with potential procedure-related complications
- New LBBB and the need for PPM implantation are the most frequent adverse events after TAVI.
- The incidence of significant conduction disturbances is dependent on TAVI Prosthesis.
- PPM rates has decreased as a result of improved implantation techniques.
- In addition, next-generation devices with reduced interaction with the LVOT might further decrease conduction disturbances after TAVI
- Minimising PPM rate is important, especially as TAVI technology could be increasingly applied to younger and healthier patients.



Thank you very much !