TAVI in Korea,
How to Avoid Conduction Disturbance after CoreValve

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Current Status of TAVI in Asia

Feb 2010 to July 2013

	Total 672	Edwards 304	CoreValve 368
Asan Medical Center	87	36	51
Yonsei University	29		29
Seoul National University	23	3	20
Sam Sung Medical Center	10	10	
Catholic Medical Center	7	7	
Korea (23%)	156	56	100
Chiam, Tay, Singapore	130	100	30
Lee, Lan, Hong Kong	52	2	50
Paul Kao, Chang, Taiwan	52	12	40
Philippine	22		22
Thailand	36	20	16
Japan	165	100	65
China	35	10	25
Malaysia	24	4	20

Baseline Characteristics

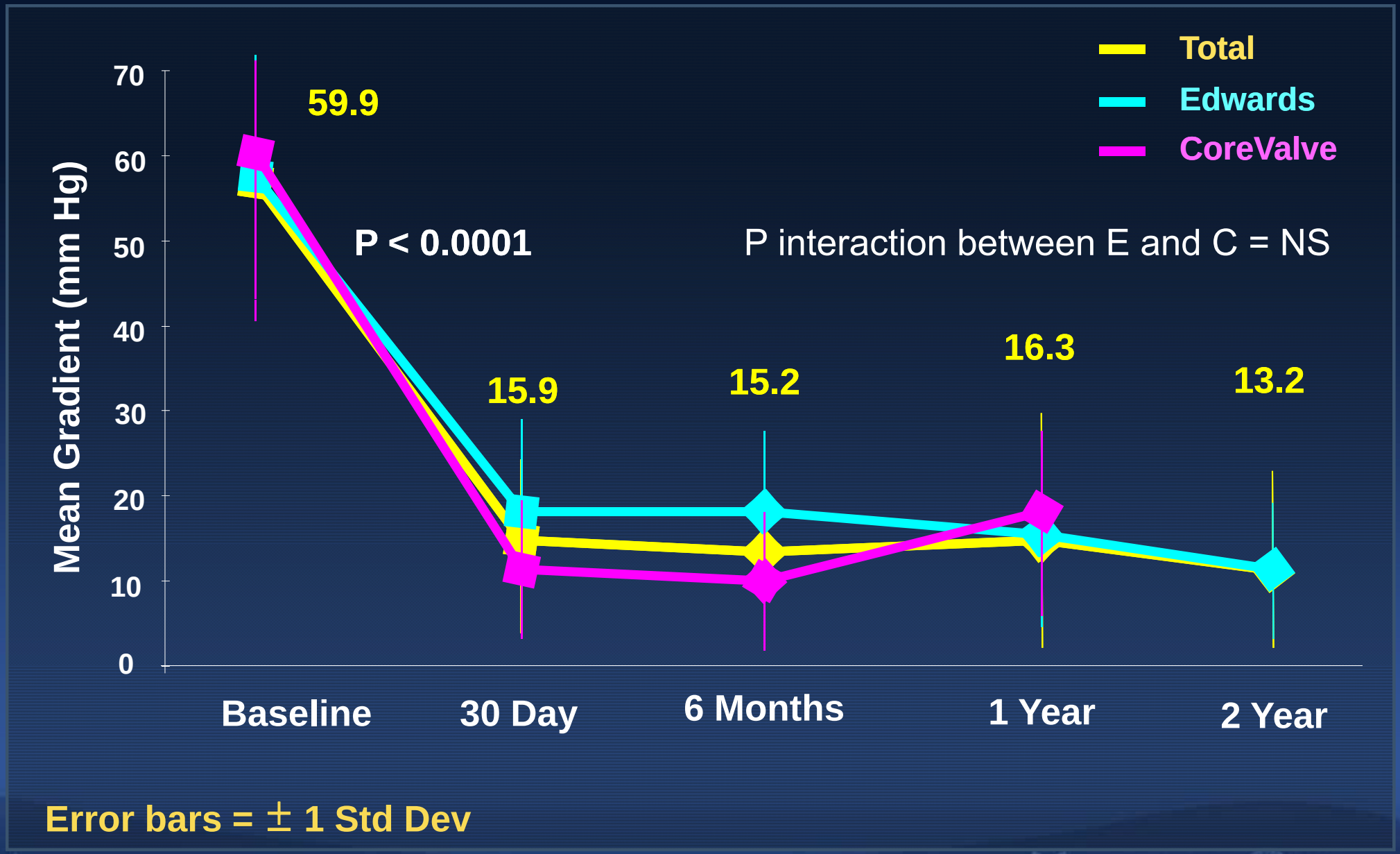
	KOREA			FRENCH 2			PARTNER		SOURCE		ADVANCE
Design	Registry			Registry			RCT		Registry		Registry
Treament	Total	Edw	Core	Total	Edw	Core	Edw(B)	Edw(A)	Edw (I)	Edw (II)	Core
No.	132	35	97	3195	2107	1043	179	348	1038	1269	162
Age, yr	78.9	76.6	81.2	82.7	82.3	82.5	83.1	83.6	81.2	81.1	81
Male, %	44	36.7	51.3	51	46.6	48.5	45.8	57.8	44.5	41.3	49.4
STS score	-	-	-	64	58	-	11.2	11.8	-	-	-
EuroSCORE,%	22.1	24.9	19.2	21.9	22.2	24.7	26.4	29.3	27.6	25	19.2
NYHA, III,IV,%	89.8	100	79.5	75.9	75.5	76.1	92.2	94.3	-	-	79.6
CAD, %	45.5	53.3	37.6	47.9	48.7	46.9	67.6	74.9	-	-	57.6
Prior MI, %	14.1	1.3	12.8	16.4	17	15.0	18.6	26.8	-	-	16
Prior CABG, %	5.5	3.3	7.7	18.2	18.2	18.1	37.4	42.6	-	-	21.4
Prior Stroke, %	1.3	3.3	0	10	10	10	27.4	29.3	5.5	6.1	-
Prior PCI, %	37.2	36.7	37.6	-	-	-	30.5	34	-	-	31.1
Prior BAV, %	-	-	-	-	-	-	16.2	13.4	-	-	-

N Engl J Med. 2010;363, N Engl J Med. 2011;364 3, N Engl J Med. 2012;366, TCT 2010 presentation, J Am Coll Cardiol . 2010;55:1080

TAVI Korea, Results
Echocardiographic Findings

	Baseline (N=130)	Immediate (N=124)	1 month (N=70)	6 months (N=32)	1-2 year (N=20)
LVEF, %	58±11.2	63.6±7.6	62.2±7.7	61.5±7.7	63.1±3.8
AV area, cm2	0.64±0.19	1.45±0.33	NA	NA	NA
Mean PG, mmHg	58.1±18.6	14.9±3.3	15.9±7.3	15.2±7.0	16.3±6.3
Peak PG, mmHg	100.5±31.5	28.9±7.8	29.3±11.2	29.4±13.0	30.8±10.8
Mod-sev AR	8 (8.3%)	5 (6.5%)	0	0	0
Paravalvular leak	NA	Mild-Mod	Mild-Mod	Mild	Mild
Mod-sev MR	3 (3.1%)	2	1	1	1
Mod-sev pul HTN	9 (9.3%)	3	2	0	0

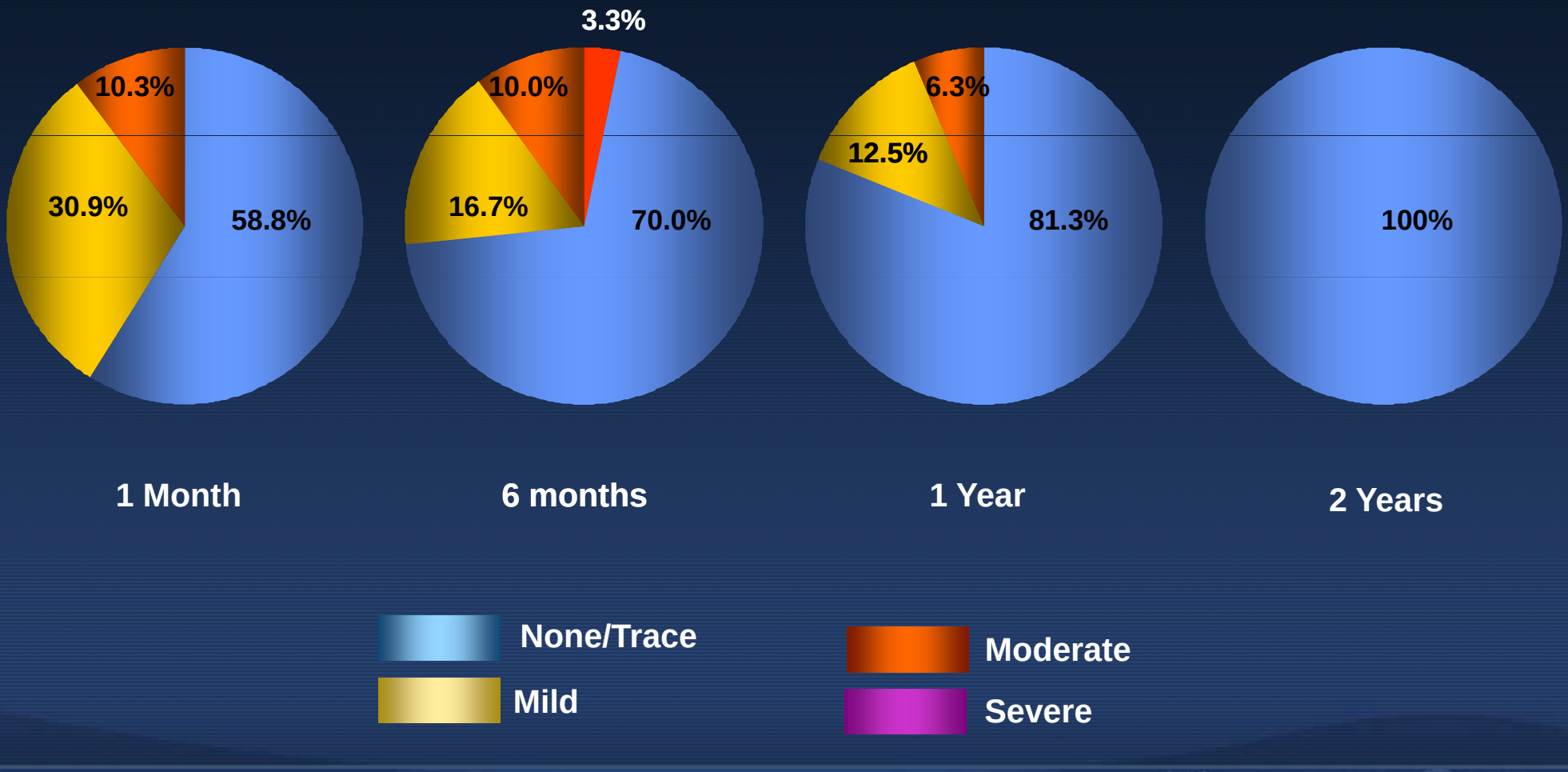
Mean Gradients Over Time



Paravalvular Regurgitation

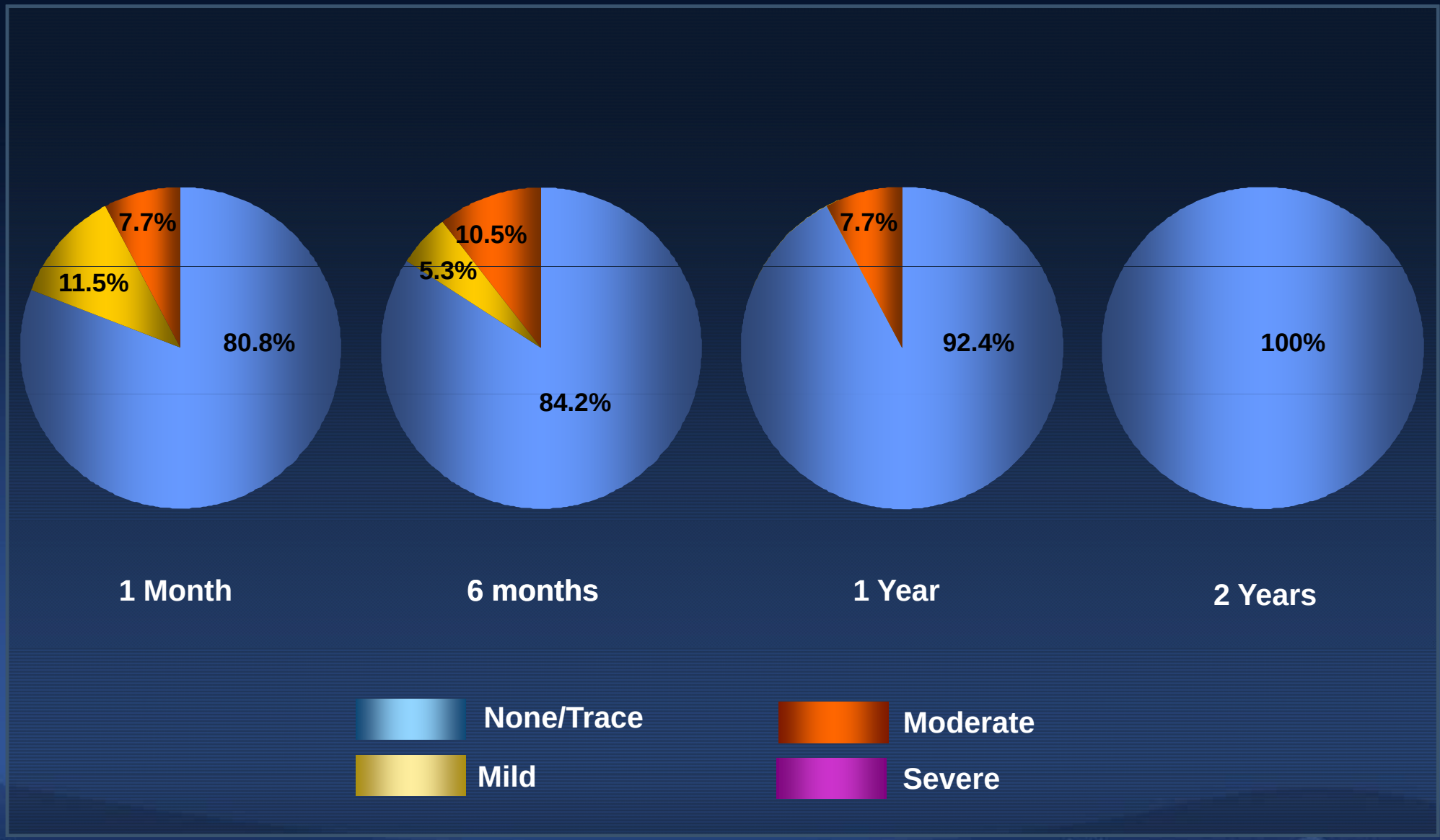
Total Registry

Decrease in Amounts Over Time !



Paravalvular Regurgitation

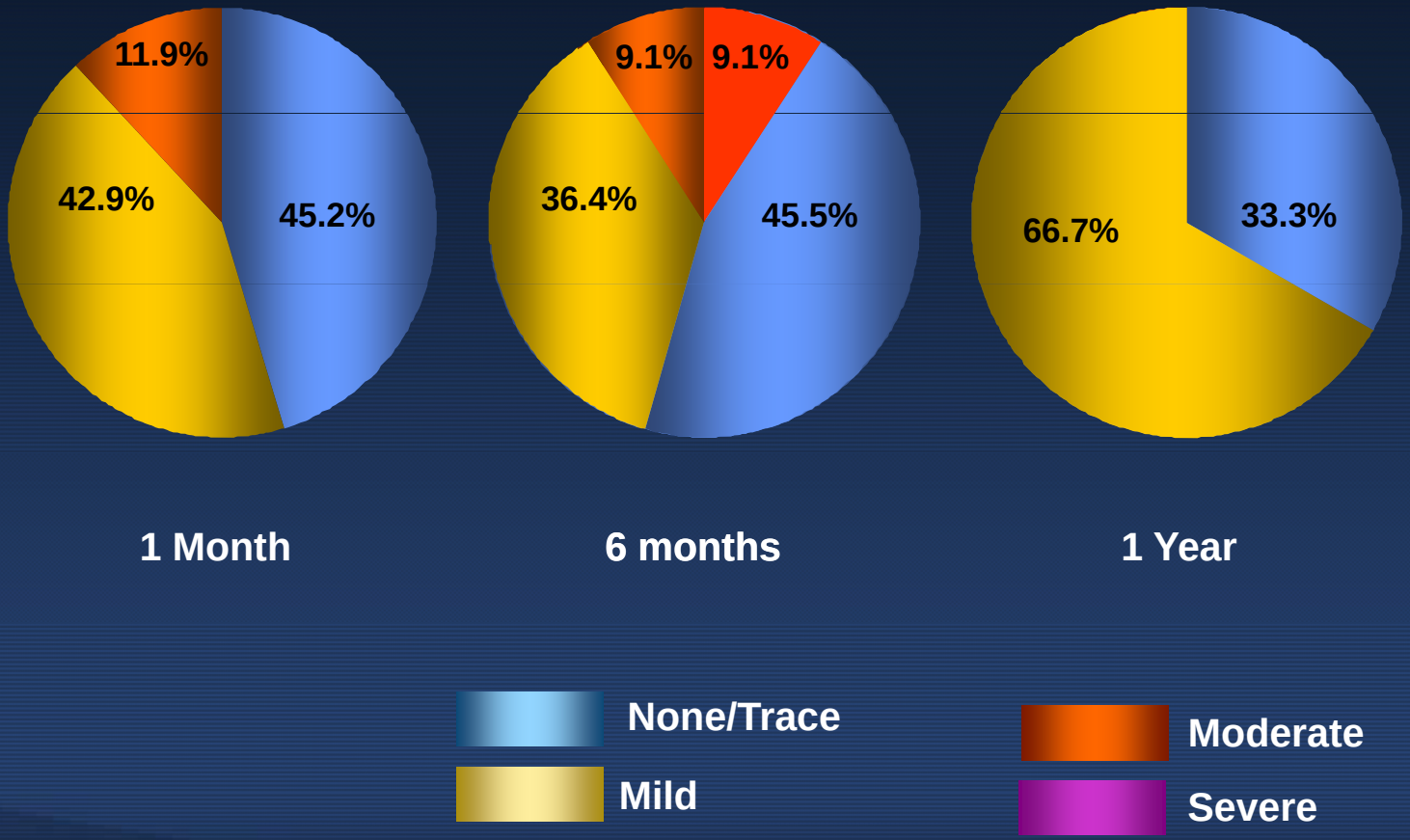
Edwards Valve



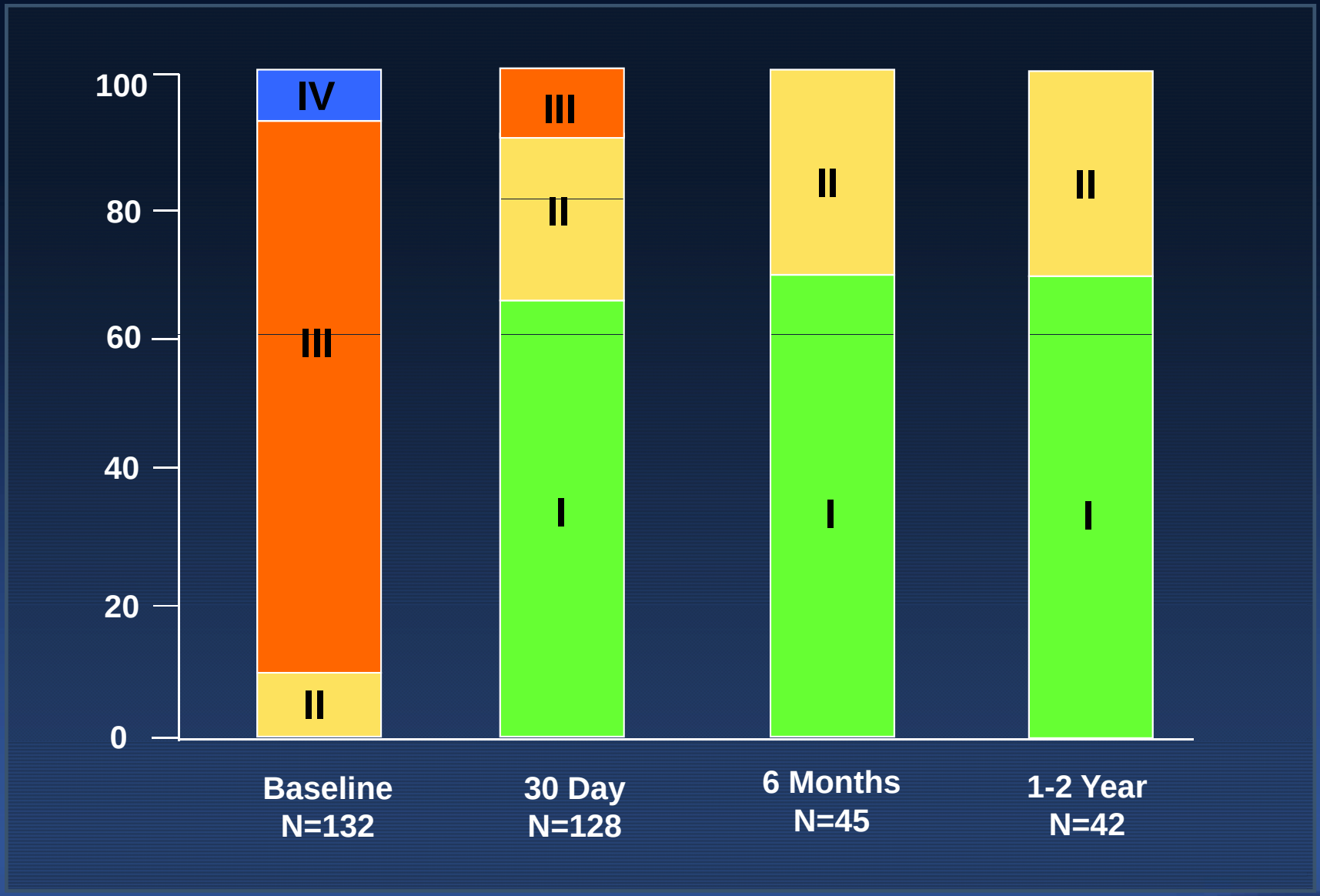
Paravalvular Regurgitation

CoreValve

Higher Frequency of PVL, but Not Significant !



Subjective Symptom: NYHA



Procedural Results

	Total (n=132)	Edward (n=35)	CoreValve (n=97)
Valve Size,mm			
23		22	0
26		12	44
29		0	42
31		0	11
Transfemoral	125 (94.7%)	32	93
Surgical Closure	6	4	2
Percutaneous	119	28	79
Transapical	3 (2.3%)	3	0
Direct Aortic	3 (2.3%)	0	3
Subclavian	1	0	1

In-Hospital, 30 days

	Total (n=132)	Edward (n=35)	CoreValve (n=97)
Procedural Success	130 (98.5%)	34 (97.2%)	96 (99%)
Mortality	2 (1.5%)	1 (2.9%)	1 (1.0%)
Cardiovascular Death	2 (1.5%)	1 (2.9%)	1 (1.0%)
Major or Minor Stoke	1 (0.8%)	1 (2.9%)	0
Permanent Pacemaker	17 (12.9%)	0	17 (17.5%)
Vascular Complication	2 (1.5%)	2	0
Access site	1	1 (RF1)	0
Iliac Perforation	1	1	0

1 Year Outcomes
(8 months to 1.4 yrs)

	Total	Edwards CoreValve
No.	132	35	97
All Death at 1 year	6/132 (4.6%)	1/35 (2.9%)	5/97 (5.2%)
Cardiovascular	1	0	1
Sepsis	1	0	1
Readmission	6 (4.6%)	1	5
Mitral valve endocarditis	1	0	1
Heart failure exacerbation	1	0	1
Aspiration pneumonia	3	1	2

VARC Meta-Analysis (16 studies; 3,519 patients) vs. TAVI Korea

Endpoints	Pooled Estimates (%)	KOREA
Log Euroscore	22.8	22.1
Age, yrs	81.5	81.2
Female	52.0	56
NYHA 3 or 4	82.0	89.8
AVA, cm2	0.61	0.64
Mean gradient, mmHg	47.6	58.1

J Am Coll Cardiol 2012;59:2297-306

VARC Meta-Analysis (16 studies; 3,519 patients) vs. TAVI Korea

Endpoints (%)	Pooled Estimates	KOREA
Mortality		
All at 30 days	7.8	1.5
CV at 30 days	5.6	1.5
All at 1 year	22.1	4.6
CV at 1 year	14.4	0.8
Stroke		
Major at 30 days	3.2	0.8
Perm Pacemaker at 30 days		
CoreValve	28.9	17.5
Vascular Cx at 30 days	18.8	1.5

J Am Coll Cardiol 2012;59:2297-306

Lessons
from Korean Experiences

1. TAVI provides favorable short and longer term (1yr) clinical outcomes from 3 center registry.
2. TAVI showed definite objective and subjective improvement in hemodynamics and symptoms.
3. This results would be concordant in survival benefit as accumulation of experiences.
4. We need a prospective cohort registry in Korea.

Efficacy Concerns
Sapien vs. Core

Sapien vs. Core : France-2

Characteristic	SAPIEN (N=2107)	Core (N=1043)
Age, yr	82.9 ± 7.2	82.3 ± 7.2
Male sex %	46.6	60.0
STS score %	15.6 ± 12.4	14.2 ± 11.2
Logistic EuroSCORE %	22.2 ± 14.3	21.3 ± 14.3
NYHA class III or IV %	75.5	76.1
Clinical history %		
CAD	48.7	46.2
Previous MI	17.0	15.4
Previous CABG	18.2	18.3
Cerebrovascular disease	10.0	9.9
PVD	21.8	18.6
COPD	25.3	26.2
Atrial fibrillation	25.2	29.6
Permanent pacemaker	13.5	15.5
Pulmonary hypertension	19.8	19.2
Mean Pr gradient (mmHg)	48.6 ± 16.5	47.1 ± 16.4

Gilard M et al. N Engl J Med 2012;366:1705-15.

Outcomes : France-2

%	Total N = 3195	Sapien N= 2107	Core N=1043
Procedural success	96.9	97.0	97.6
Hospital stay, days	11.1 ± 8.0	10.9 ± 7.5	11.3 ± 8.9
Total deaths			
30 days	9.7	9.6	9.4
1 year	24.0	24.0	23.7
Cardiac deaths at 1 yr	14.3	14.2	14.3
Implanting two devices	2.3	1.4	3.5
Conversion to surgery	0.4	0.4	0.4

Gilard M et al. N Engl J Med. 2012;366:1705

Major Complications : France-2

%	Total N = 3195	Sapien N= 2107	Core N=1043
Major Vascular complications	4.7	2.7	4.5
Myocardial Infarction	1.2	0.8	0.8
New Pacemaker	15.6	11.5	**24.2**
Bleeding (+ tamponade)	13.1	11.4	8.8
AR ≥ grade 2 at *30 days*	16.5	14.1	**21.5**
Stroke	4.1	3.8	4.3
Major	2.3	1.9	2.6

Gilard M et al. N Engl J Med. 2012;366:1705

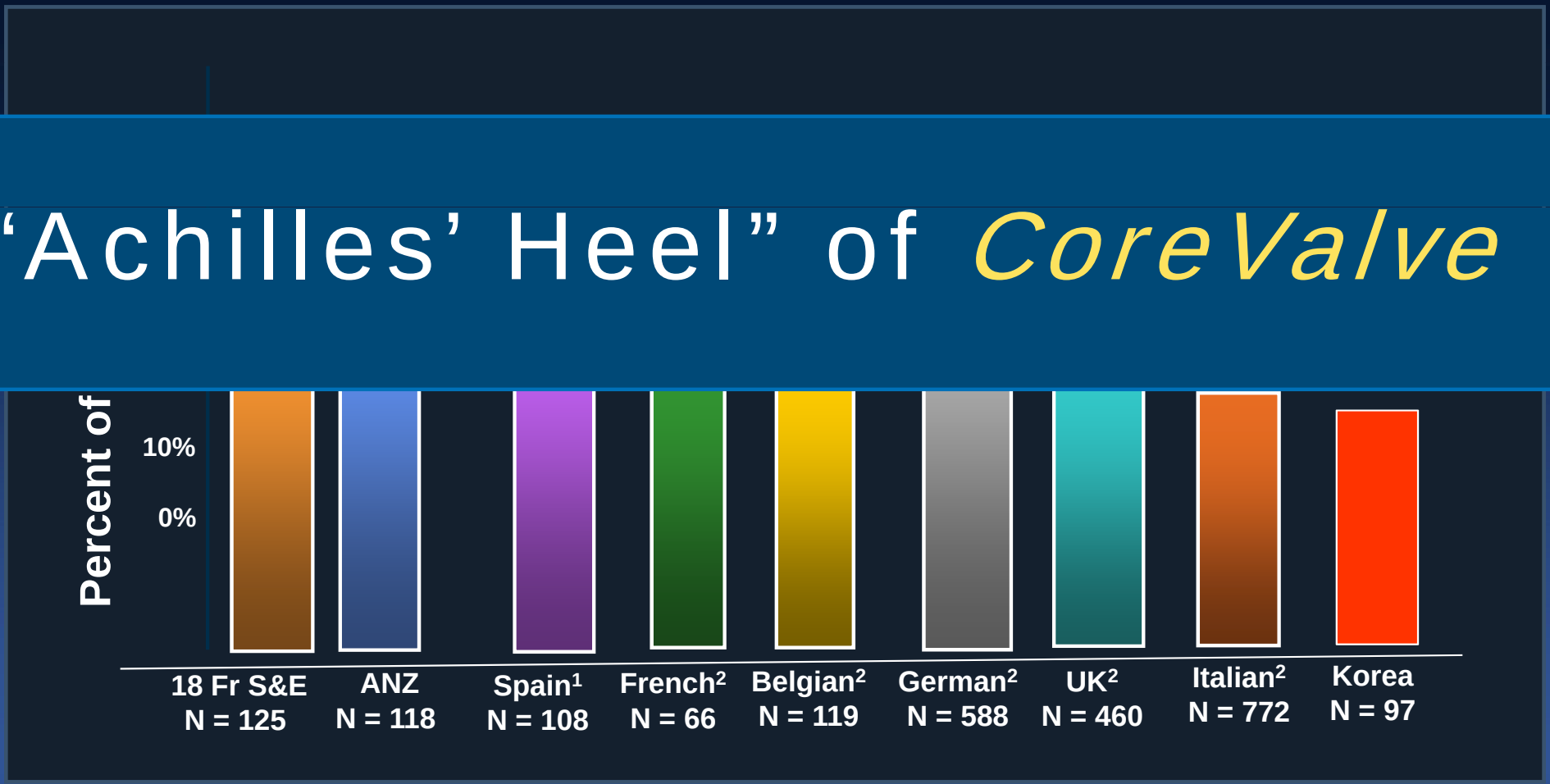
Valve Performance - VARC Meta-Analysis
(16 studies; 3,519 patients)

Endpoint	*Pooled Estimate (%)*	*[95% CI]*
MI (peri-procedural)	1.1	[0.2, 2.0]
Valve performance at 30 days		
AVA ≤ 1.2 cm^2	4.8	[3.0, 6.6]
Mean gradient ≥ 20 mmHg	1.0	[0.0, 2.1]
AR ≥ moderate (PVL)	7.4	[4.6, 10.2]
Valve-in-valve	2.3	[1.3, 4.5]
Valve embolization	1.7	[0.2, 3.3]
Perm Pacemaker at 30 days		
Edwards	4.9	[3.9, 6.2]
Corevalve	28.9	[23.0, 36.0]

Généreux P et al. J Am Coll Cardiol 2012;59:2317

CoreValve Pacemaker Implantation

"Achilles' Heel" of *CoreValve*



1. Avanzas P, et al; Rev Esp Cardiol. 2010;63:141-148
2. TAVI Facts, Figures and National Registries. EuroPCR 2010

Known Predictors for PPM in CoreValve

81/270 pts (33%) permanent PM within 30 days; Median time = 4 days
Baseline ECG: RBBB 65.2%, LBBB 43.8%, and normal QRS 27.6%

1. Peri-procedural AVB (OR 6.29, P<0.001),
2. Balloon pre-dilatation (OR 2.68, P<0.001),
3. Prolonged QRS duration (baseline) (OR 3.45, P=0.02)
4. Large CV prosthesis (29mm) (OR 2.50, P=0.019)
5. IV septum diameter (OR 1.18, P=0.025),
6. Depth of implantation (too low & deep),
7. Calcification several small sized of articles

J Cardiovasc Electoro 2011 (32 articles, 5258 pts analysis)
Khawaja et al. Circulation 2011;123:951-60 (270 pts analysis)

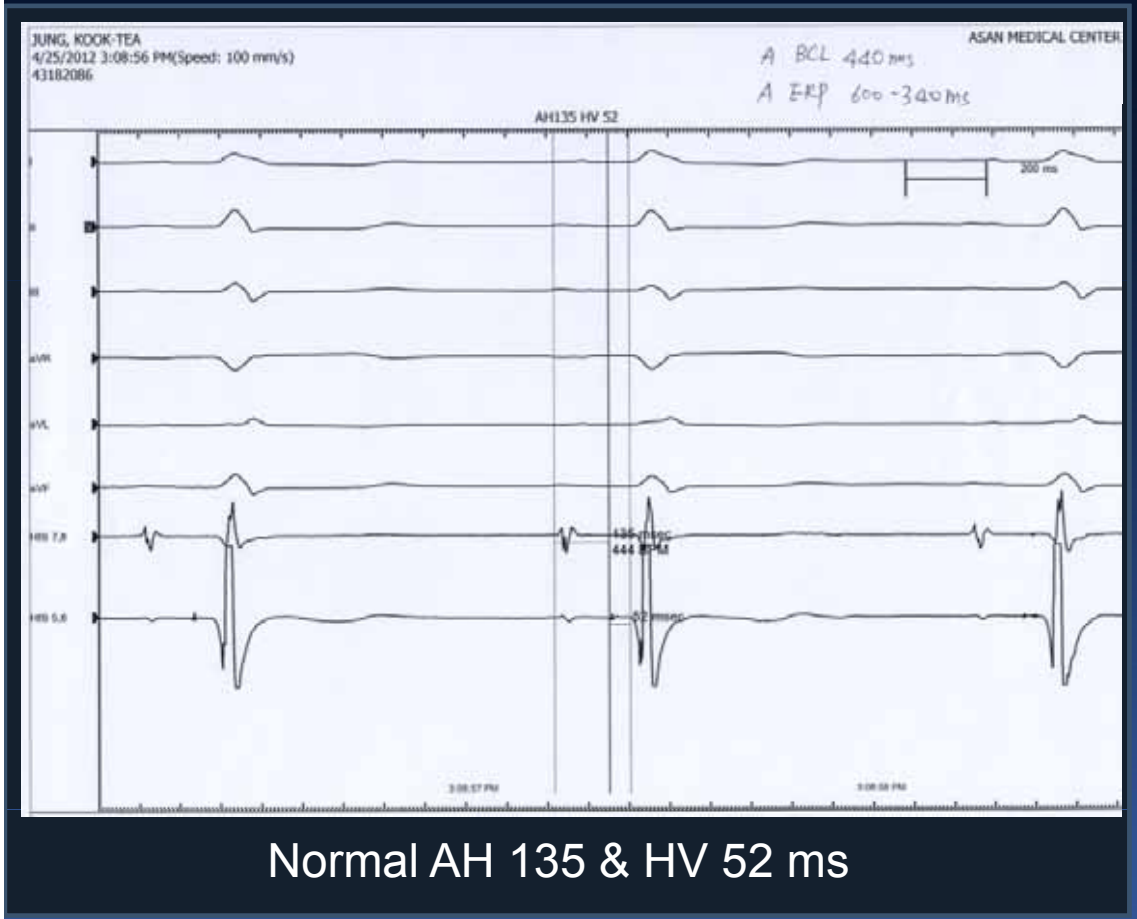
Permanent Pacemaker Predictor
Analysis from Multicenter Registry for CoreValve in Asia

1. 117 patients (81.2 ± 5.1 years) from 6 centers,
2. 23 patients (19.7%) required PPM, within a median time-to-insertion of 7 days (interquartile range, 5–13 days).
3. QCA analysis, CT diameter, CT perimeter Anaysis in All Patients.

Clinical & Procedural Characteristics

	PPM (+) N=17	PPM (-) N=80	P
Age, yr	83.2±4.2	80.1±4.8	0.08
Male, %	4 (23.5%)	33 (41.3%)	0.48
Euroscore, %	18.9±9.4	19.5±11.5	0.69
NYHA,III,IV, %	13 (76.5%)	63 (78.8%)	0.43
LV EF, %	62.2±4.0	59.5±12.3	0.52
CAD, %	4 (23.5%)	35 (43.8%)	0.09
Prior MI, %	0	0	-
Prior CABG, %	0	3 (3.8%)	1.00
Prior PCI, %	4 (23.5%)	28 (35.1%)	0.69
Prio BAV, %	0	0	-
Prior stroke	0	0	-
Time to PPM implant, day	4.2±3.2	-	-

His-Bundle Electrogram Immediate After CoreValve



Normal AH 135 & HV 52 ms

Cosecutive 19 pts, Same day

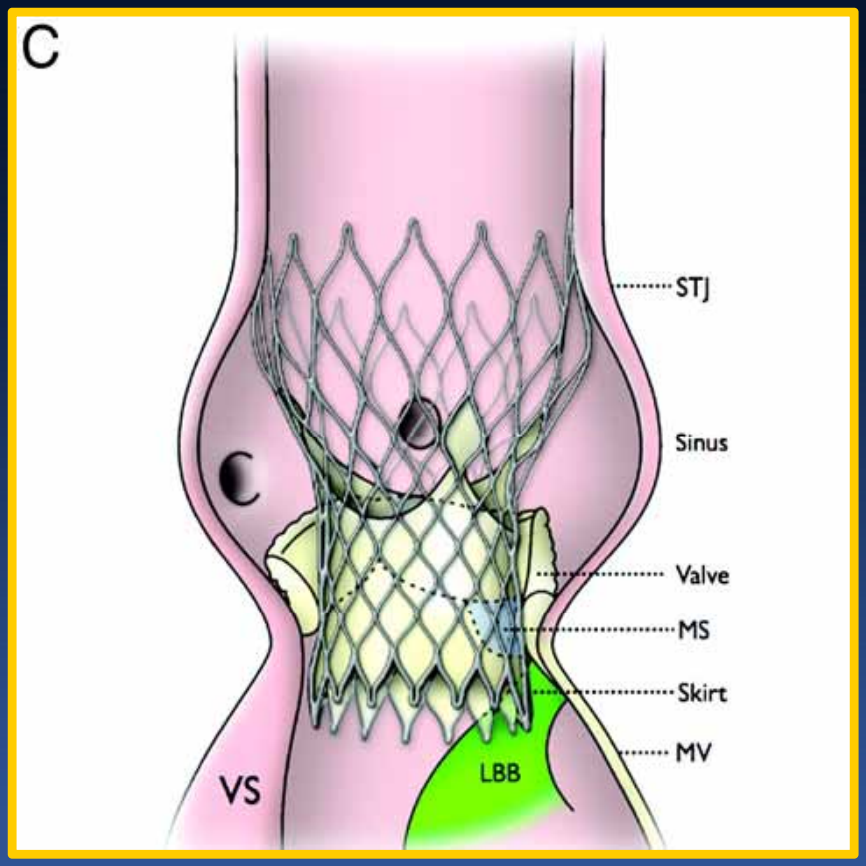
Average, (ms)
AH 130±4.2 (Normal 50-120)
HV 40±6.2 (Normal 35-55)

All patients showed normal His-bundle electrogram immediately after the procedure.

Complete AV Block After CoreValve

"Delayed Injury" ?

Suggest !
Delayed Stretching Injury,



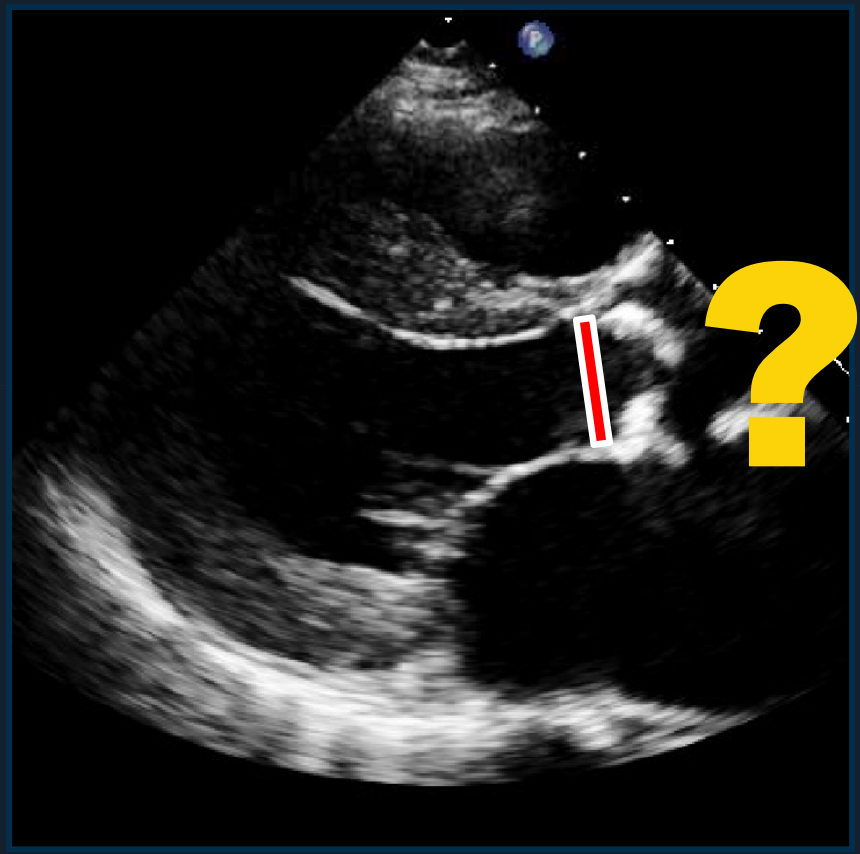
Gradual Stretching of Annulus can make acute and chronic inflammation and related tissue edema including conduction system over time,

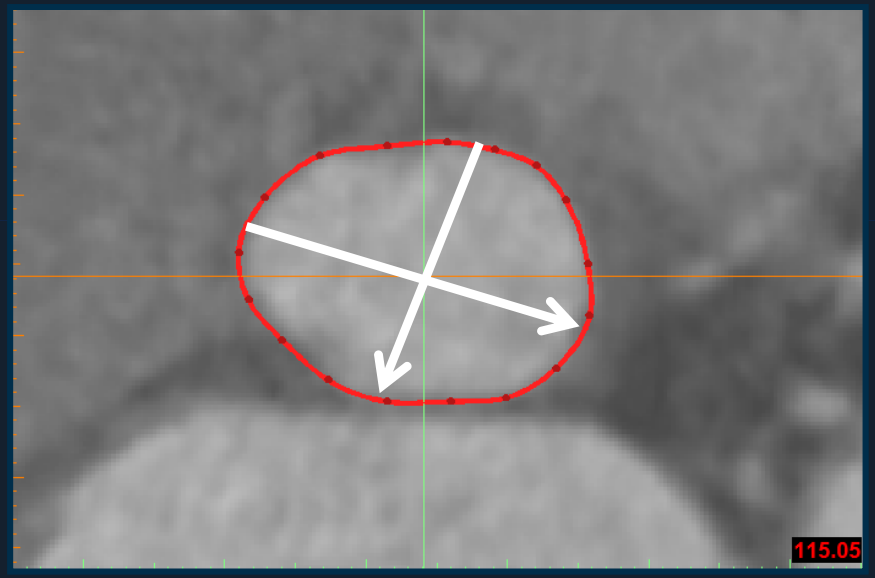
Therefore, the ratio of Annulus Stretching would be important to induce CAVB.

Which One Do You Use
For the Sizing of Device ?

1. **TEE Diameter**
2. **CT Diameter**
3. **CT Perimeter**
4. **CT Area**

A Limitation of TEE

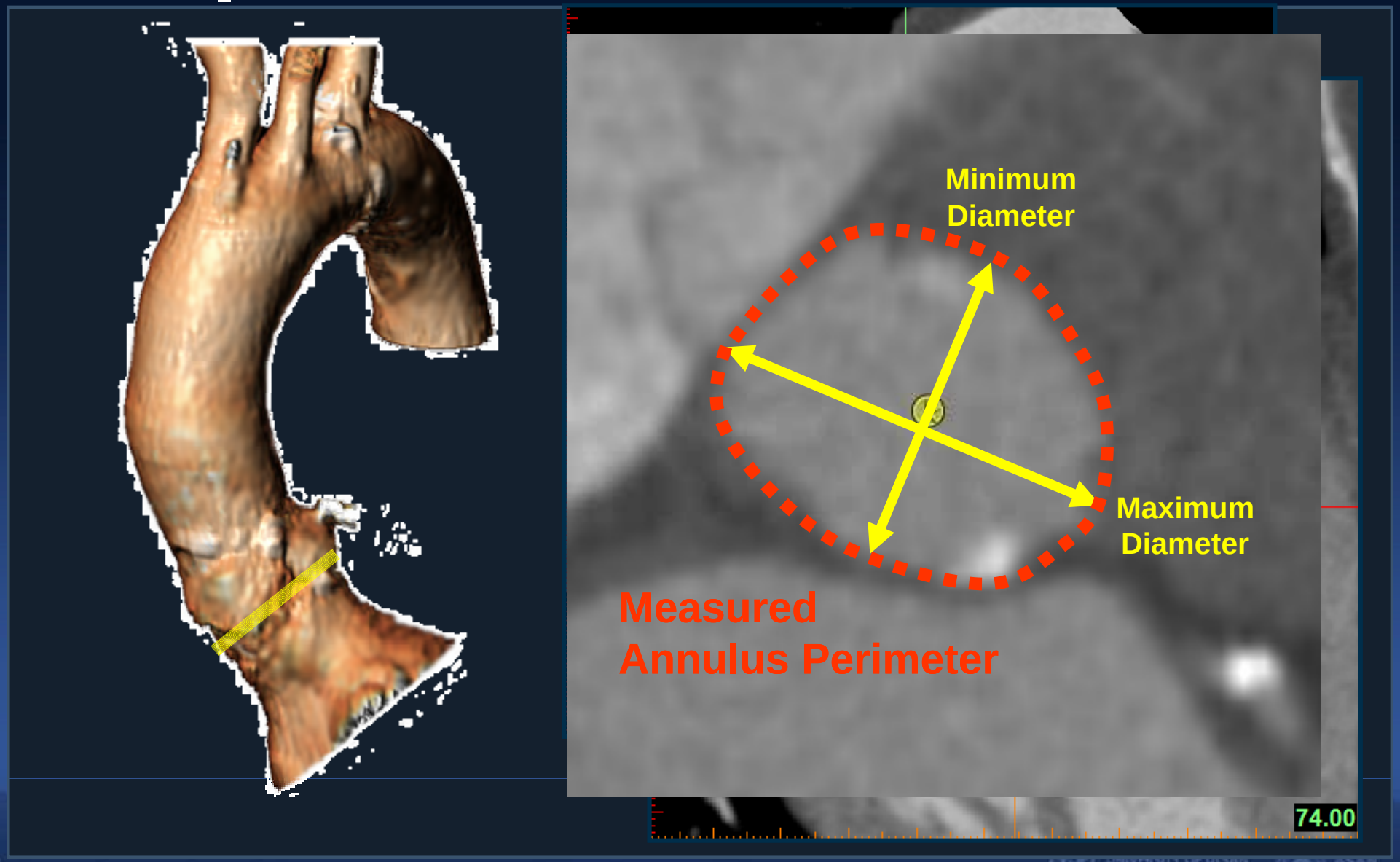




A true diameter may not be measured by TEE due to the various imaging plane. The annulus is not ALWAYS circular in geometry.

Piazza N, et al. *Circ Cardiovasc Intervent*. 2008;1:74.

CT Parameters (Diameter, Perimeter, Area)



Why Perimeter ?

Reliability Comparison

TEE vs. CT Diameter vs. CT Perimeter

(N=30, Preliminary AMC Data)

TEE Diameter	20.4±1.6					
CT Diameter	3-Chamber	Coronal	*Basal Mean*	*Area-derived*	*Rule of sine*	CT Perimeter
(mm)	20.3±2.1	22.5±1.9	22.6±2.0	22.6±2.0	24.5±2.7	
Inter-Reader Reliability By ICC	0.51 (0.40-0.62)	0.75 (0.63-0.80)	0.80 (0.70-0.85)	0.81 (0.71-0.89)	0.81 (0.72-0.88)	0.86 (0.79-0.92)
Intra-Reader Reliability by ICC (1)	0.72 (0.47-0.88)	0.89 (0.76-0.94)	0.94 (0.84-0.96)	0.95 (0.88-0.98)	0.94 (0.85-0.97)	0.97 (0.93-0.98)
(2)	0.51 (0.40-0.62)	0.93 (0.84-0.97)	0.95 (0.88-0.97)	0.96 (0.89-0.99)	0.93 (0.83-0.96)	0.95 (0.86-0.98)

ICC ; Intraclass correlation coefficient

Reliability Comparison

TEE vs. CT Diameter vs. CT Perimeter

(N=30, Preliminary AMC Data)

1. CT diameter of annulus are usually larger than TEE measurements.
2. CT perimeter measurements are most reproducible and reliable.

Device Sizing for CoreValve
Using CT Perimeter

Diameter Range (mm)	Device Size (*perimeter, mm)	Annulus Size (Perimeter, mm)
18 - 20	**23 (72.2)**	**Measured Annulus Perimeter**
20 - 23	**26 (81.6)**	
23 - 27	**29 (91.1)**	
26 - 29	**31 (97.3)**	

(*Calculated Perimeter)

Stretching Index

$$\frac{\text{Device Perimeter (Calculated)}}{\text{Annulus Perimeter}}$$

Predictors for Permanent Pacemaker -Multivariable Analysis-

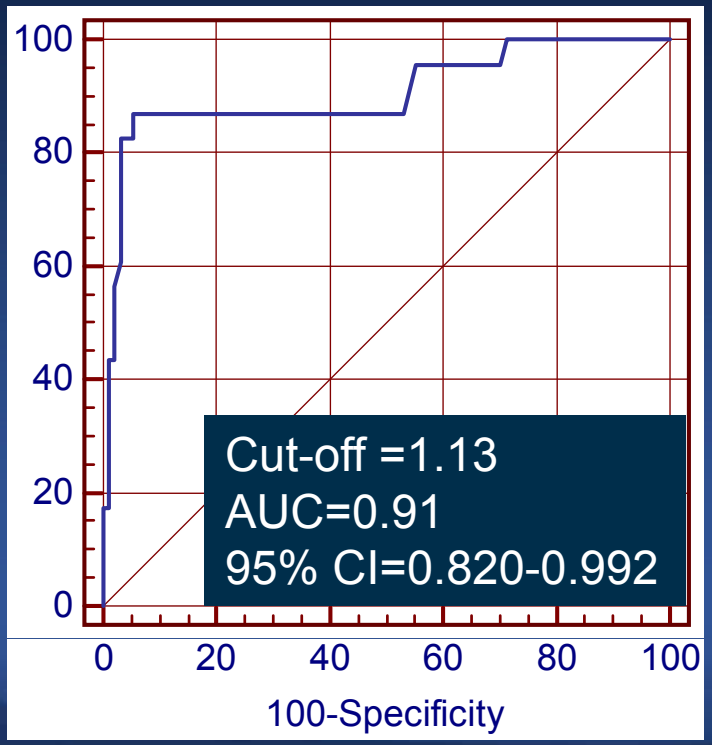
Endpoints (%)	Odd Ratio	95% CI	P
Age	1.09	0.99-1.20	0.07
Male	0.67	0.27-1.70	0.41
Large THV (29, 31)	1.79	0.69-4.64	0.23
PR interval, base	1.00	0.99-1.10	0.59
QRS duration, base	5.88	0.59-58.1	0.13
RBBB, base	2.89	0.92-9.09	0.07
LBBB, base	-	-	-
Septum Thickness	1.09	0.84-1.41	0.52
Block during implant	3.56	1.08-11.6	0.33
Pre-, Postdilation	1.67	0.38-7.29	0.50

Predictors for Permanent Pacemaker -Multivariable Analysis-

Endpoints (%)	Odd Ratio	95% CI	P
Stretching Index with CT perimeter	1.54	1.24-1.94	<0.0001
Implanted depth	1.26	1.03-1.54	0.02
Stretching Index with CT diameter	1.07	0.91-1.27	0.40
Calcium, agstone	1.00	0.99-1.00	0.63
Aortoseptal angle	0.98	0.92-1.04	0.43

Stretching Index Cut-Off for Permanent Pacemaker

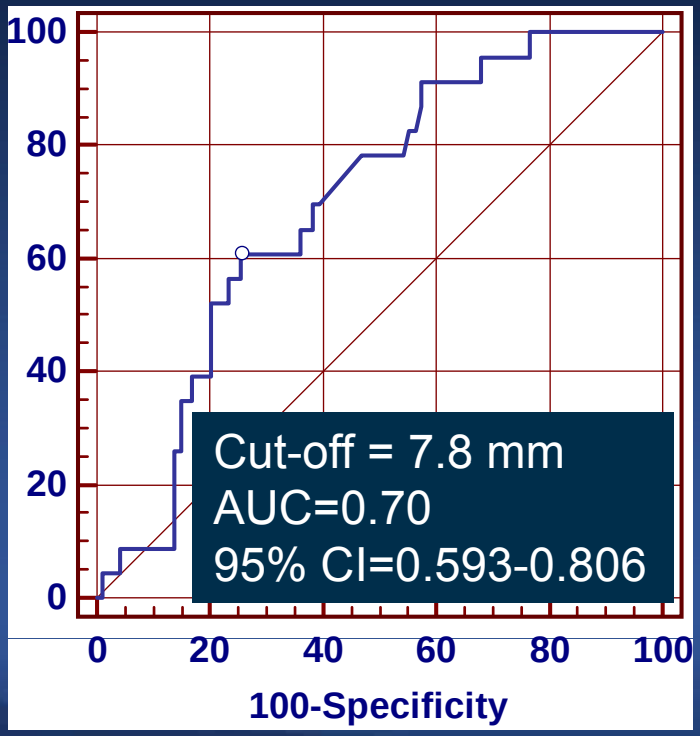
$$\frac{\text{Device Perimeter}}{\text{Annulus Perimeter}} > 1.13$$



Sensitivity 86.96%
Specificity 94.68%
PPV 80%
NPV 96.74%
Accuracy 93.2%

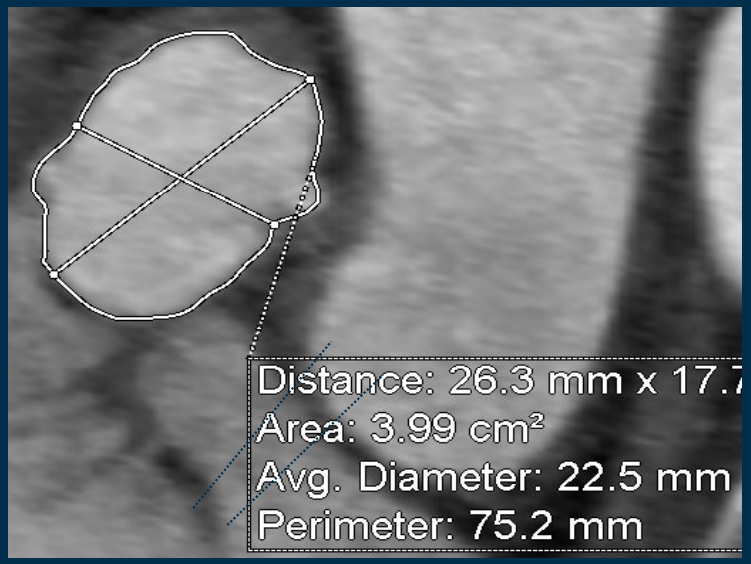
Implanted Depth Cut-Off for Permanent Pacemaker

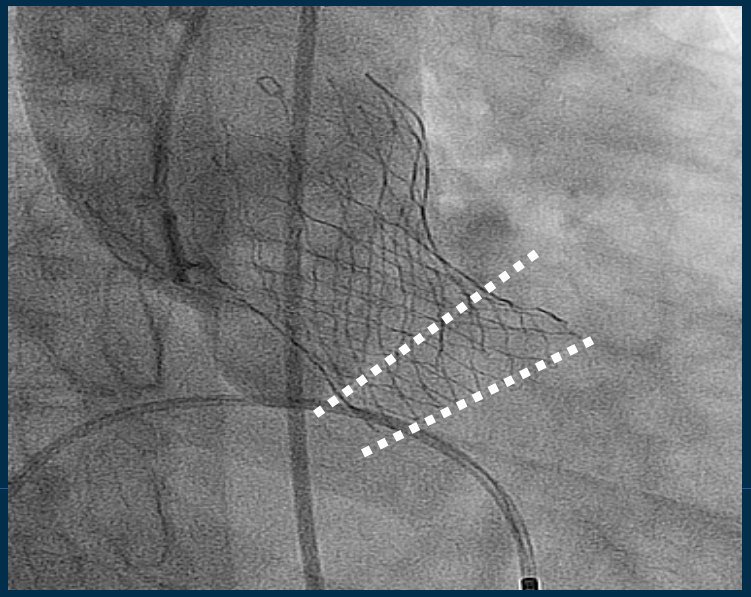
Implanted Depth > 7.8 mm



Sensitivity 60.87%
Specificity 74.47%
PPV 35.14%
NPV 87.5%
Accuracy 70.94%

Device 26 mm,
No Permanent Pacemaker





1. Stretching Index

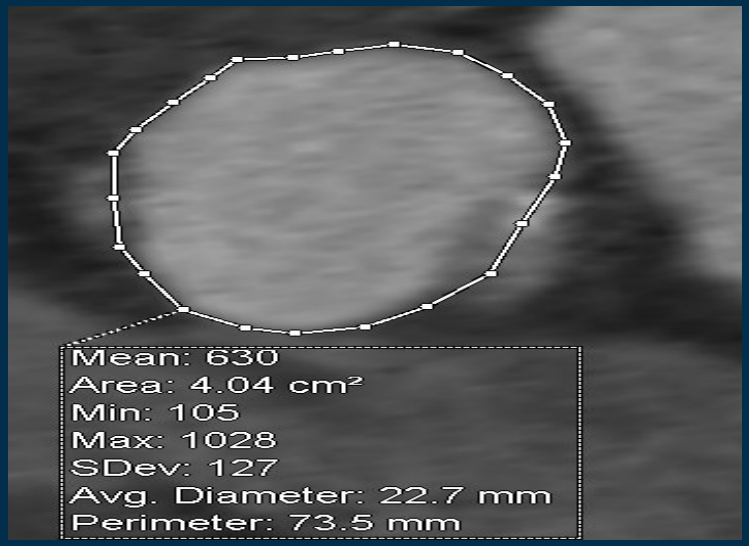
$$\frac{\text{Device Perimeter } 81.6 \text{ mm}}{\text{Annulus Perimeter } 75.2 \text{ mm}} = 1.09$$

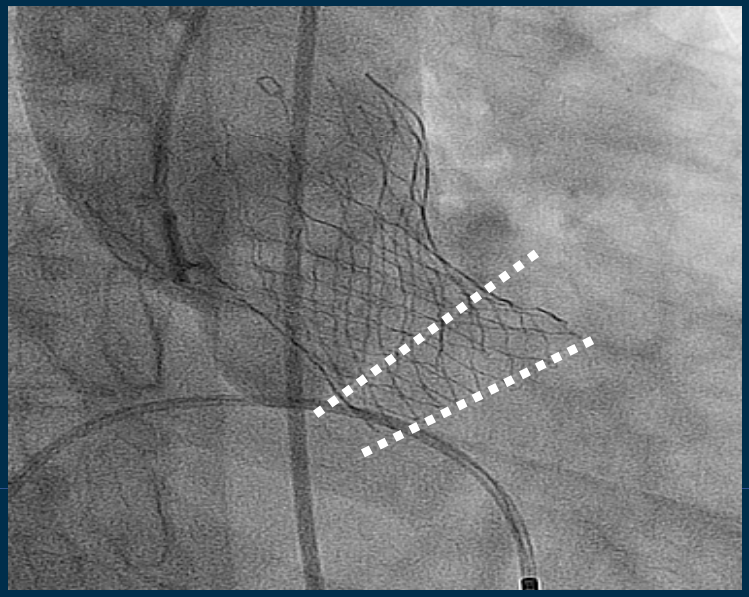
2. Implanted Depth of Device :

NCC 5.5mm

LCC 9.6mm

Device 29 mm, Permanent Pacemaker



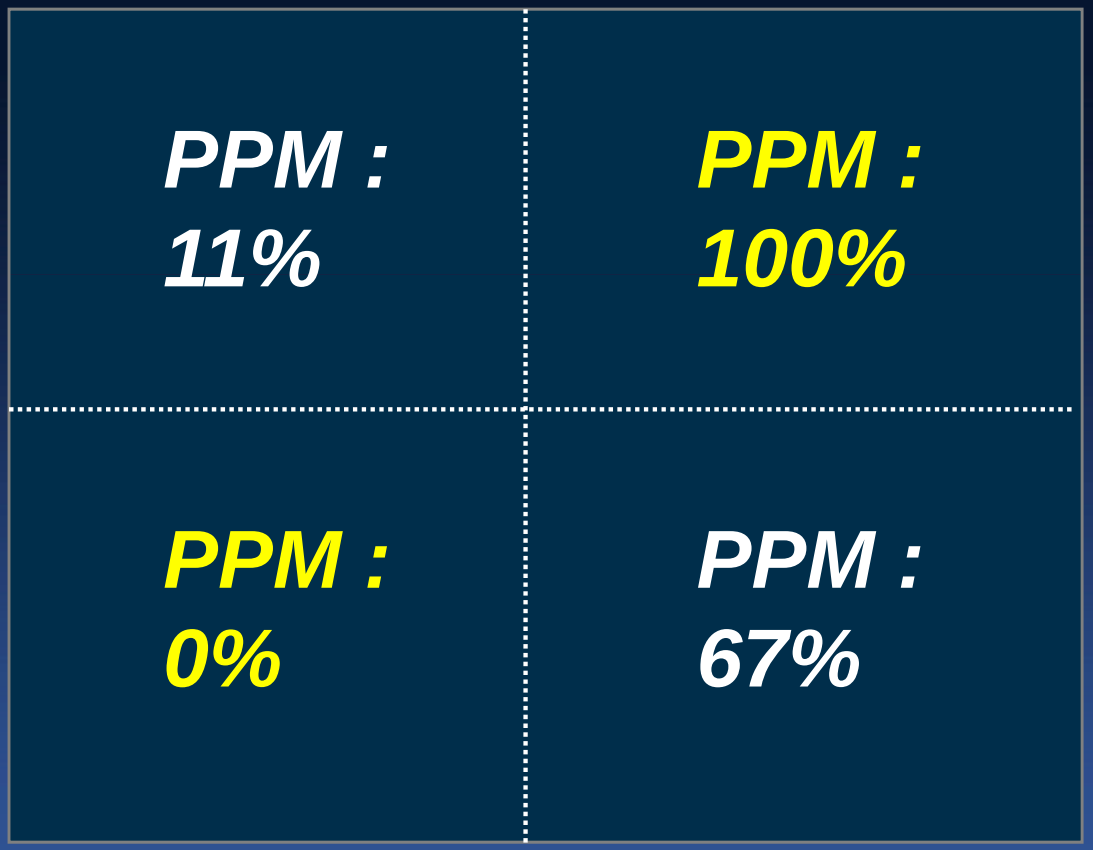


1. Stretching Index

$$\frac{\text{Device Perimeter } 91.9 \text{ mm}}{\text{Annulus Perimeter } 73.5 \text{ mm}} = 1.24$$

2. Implanted Depth of Device :
   - NCC 13 mm
   - LCC 12.7 mm

Combined Criteria Of Depth and Stretching Index



Logistic regression p<0.0001, AUC 0.97, 95% CI=0.94-0.99

Remember !!
Rule of 1.13 and 7.8

Appropriate Size of Device Selection
(CT perimeter Stretching Index < 1.13)
And Shallow Implantation (Depth < 7.8 mm),
Can Avoid Permanent Pacemaker Insertion
after CoreValve.


Thank You !!
summitMD.com

Decrease Vascular Complications with Experiences and Device Developments

Edwards Cases	RF I or III N=9	NovaFlex N=27
Procedural success	8 (88.9%)	27 (100%)
Mortality	0	0
Stroke	0	1 (4.8%)
Permanent pacemaker	0	0
Vascular complication		
Access site	1 (11.1%)	0
Iliac artery perforation	1 (11.1%)	0
Device embolization	2 (22.2%)	1 (3.7%)

AMC Edward Registry