Strokes and Paravalvular Regurgitation – Will New TAVR Systems or Accessory Devices Make a Difference?

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Stroke

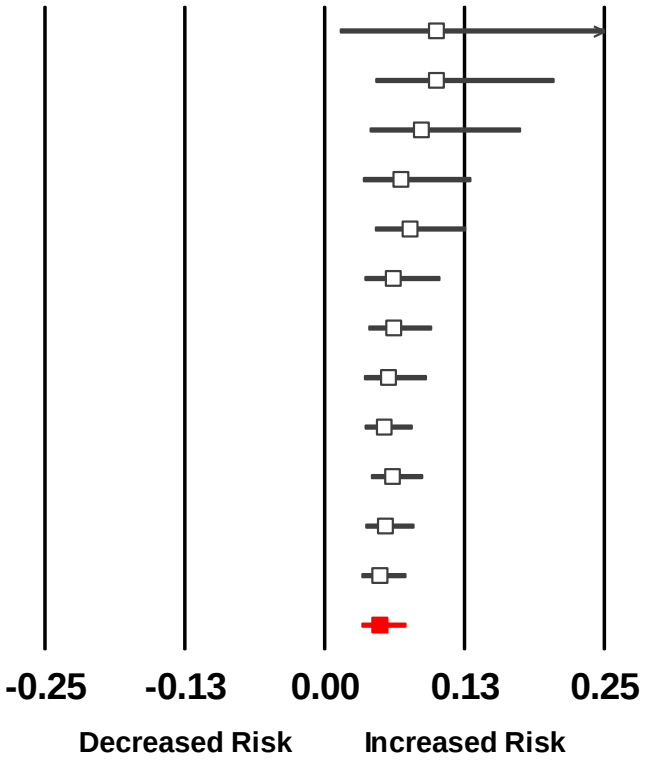
- **Stroke risk is decreasing compared to feasibility trials but is stable since**
- **Timing of stroke**
  - **Procedural versus non procedural**
- **Predictors of stroke after TAVR**
  - **Procedural**
  - **Non procedural**

Stroke : Feasibility Trials

Study name	Cumulative statistics					
	Point	Lower limit	Upper limit	Z-Value	p-Value	Total
24 F	0.100	0.014	0.467	-2.084	0.037	1 / 10
21 F	0.100	0.046	0.205	-5.106	0.000	6 / 60
Walther***	0.087	0.041	0.175	-5.721	0.000	6 / 90
Walther **	0.068	0.034	0.131	-7.108	0.000	8 / 149
REVIVAL	0.076	0.045	0.126	-8.765	0.000	13 / 204
REVIVE 2	0.061	0.036	0.103	-9.466	0.000	16 / 310
REVIVAL 2	0.062	0.039	0.096	-11.244	0.000	18 / 350
Walther*	0.057	0.035	0.091	-10.909	0.000	18 / 400
Vancouver Exp	0.053	0.036	0.078	-13.662	0.000	25 / 568
18 F	0.061	0.042	0.088	-13.517	0.000	37 / 694
PARTNER EU	0.054	0.037	0.080	-13.533	0.000	40 / 824
Traverce	0.049	0.033	0.073	-13.969	0.000	44 / 992
	0.049	0.033	0.073	-13.969	0.000	

4.9%

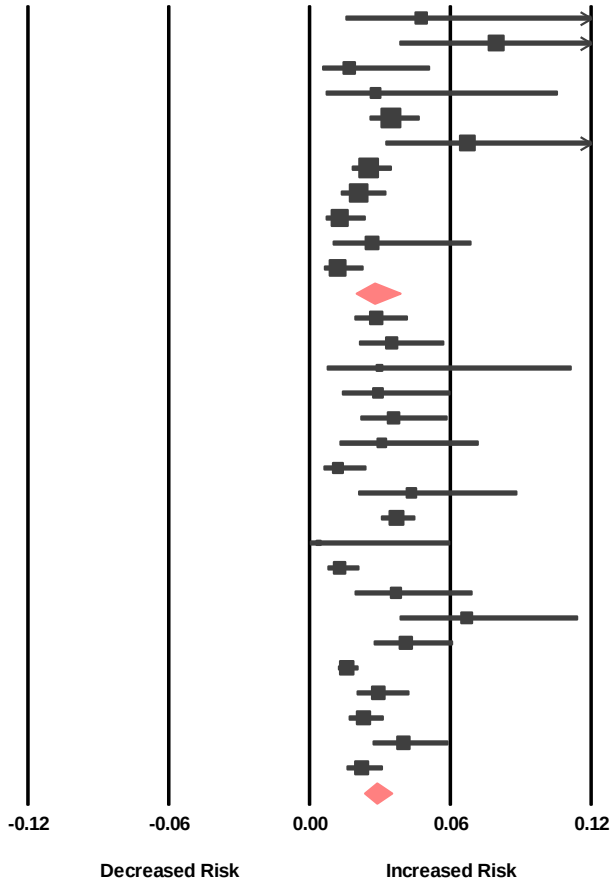
Cumulative event rate (95% CI)



Athappan et al, JACC 2014

In hospital or 30 day stroke TA versus TF (Major Registries)

Group by Subgroup within study	Study name	Subgroup within study		Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total
TA	ANZ Source	TA		0.048	0.015	0.138	-5.064	0.000	3 / 63
TA	Belgium	TA		0.080	0.038	0.158	-6.215	0.000	7 / 88
TA	Canada	TA		0.017	0.005	0.051	-6.973	0.000	3 / 177
TA	France	TA		0.028	0.007	0.106	-4.937	0.000	2 / 71
TA	GARY	TA		0.035	0.026	0.047	-20.919	0.000	41 / 1181
TA	PARTNER I cohort A	TA		0.067	0.032	0.135	-6.717	0.000	7 / 104
TA	SOURCE Registry	TA		0.025	0.018	0.035	-21.343	0.000	35 / 1387
TA	SOURCE XT	TA		0.021	0.013	0.033	-16.576	0.000	19 / 906
TA	I-TA Registry	TA		0.013	0.007	0.024	-13.623	0.000	10 / 774
TA	PREVAIL TA	TA		0.027	0.010	0.069	-7.098	0.000	4 / 150
TA	EORP/TCVT	TA		0.012	0.006	0.023	-13.149	0.000	9 / 749
TA			2.8%	0.028	0.020	0.039	-20.357	0.000	
TF	ADVANCE	TF		0.028	0.019	0.042	-17.402	0.000	25 / 879
TF	ANZ CoreValve	TF		0.035	0.021	0.057	-12.613	0.000	15 / 428
TF	ANZ Source	TF		0.030	0.007	0.112	-4.849	0.000	2 / 67
TF	Belgium	TF		0.029	0.014	0.060	-9.137	0.000	7 / 240
TF	Brazil	TF		0.036	0.022	0.059	-12.515	0.000	15 / 418
TF	Canada	TF		0.031	0.013	0.072	-7.587	0.000	5 / 162
TF	Italian CoreValve Registry	TF		0.012	0.006	0.024	-12.367	0.000	8 / 659
TF	France	TF		0.043	0.021	0.088	-7.998	0.000	7 / 161
TF	GARY	TF		0.037	0.031	0.045	-31.948	0.000	100 / 2694
TF	Greece	TF		0.004	0.000	0.060	-3.905	0.000	0 / 126
TF	Ibero-American Registry	TF		0.013	0.008	0.021	-16.715	0.000	15 / 1170
TF	PARTNER I cohort A	TF		0.037	0.019	0.069	-9.605	0.000	9 / 244
TF	PARTNER I cohort B	TF		0.067	0.038	0.114	-8.810	0.000	12 / 179
TF	PARTNER II	TF		0.041	0.027	0.061	-14.796	0.000	23 / 560
TF	EORP/TCVT	TF		0.016	0.012	0.021	-30.059	0.000	54 / 3390
TF	SOURCE Registry	TF		0.029	0.020	0.042	-17.911	0.000	27 / 920
TF	SOURCE XT	TF		0.023	0.017	0.031	-23.135	0.000	39 / 1694
TF	U.K TAVI	TF		0.040	0.027	0.059	-15.246	0.000	24 / 599
TF	18F EE Registry	TF		0.022	0.016	0.031	-21.487	0.000	33 / 1483
TF			2.9%	0.029	0.023	0.035	-33.155	0.000	



Athappan et al, JACC 2014

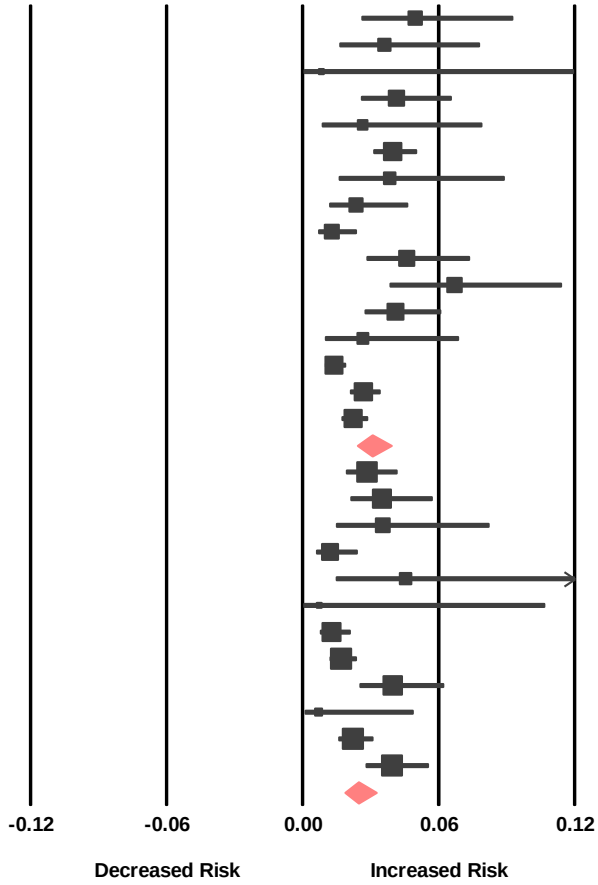
In Hospital or 30 Day Stroke ES versus MC – Major Registires

Group by Subgroup within study	Study name	Subgroup within study	Event rate	Lower limit	Upper limit	Z-Value	Total
ES	Belgium	ES	0.050	0.026	0.093	-8.628	9 / 181
ES	France	ES	0.036	0.016	0.078	-7.896	6 / 166
ES	Greece	ES	0.008	0.001	0.120	-3.365	0 / 59
ES	U.K TAVI	ES	0.041	0.026	0.066	-12.678	17 / 410
ES	Asia TAVI	ES	0.027	0.009	0.079	-6.155	3 / 113
ES	FRANCE 2	ES	0.040	0.031	0.050	-25.15365	/ 1634
ES	ANZ Source	ES	0.038	0.016	0.089	-7.058	5 / 130
ES	Canada	ES	0.024	0.012	0.046	-10.404	8 / 339
ES	I-TA Registry	ES	0.013	0.007	0.024	-13.623	10 / 774
ES	PARTNER I cohort A	ES	0.046	0.028	0.074	-11.848	16 / 348
ES	PARTNER I cohort B	ES	0.067	0.038	0.114	-8.810	12 / 179
ES	PARTNER II	ES	0.041	0.027	0.061	-14.796	23 / 560
ES	PREVAIL TA	ES	0.027	0.010	0.069	-7.098	4 / 150
ES	EORP/TCVT	ES	0.014	0.010	0.019	-25.42736	/ 2604
ES	SOURCE Registry	ES	0.027	0.021	0.034	-27.88062	/ 2307
ES	SOURCE XT	ES	0.022	0.017	0.029	-28.46758	/ 2600
ES			0.031	0.024	0.039	-27.136	
MC	ADVANCE	MC	0.028	0.019	0.042	-17.402	25 / 879
MC	ANZ CoreValve	MC	0.035	0.021	0.057	-12.613	15 / 428
MC	Belgium	MC	0.035	0.015	0.082	-7.254	5 / 141
MC	Italian CoreValve Registry	MC	0.012	0.006	0.024	-12.367	8 / 659
MC	France	MC	0.045	0.015	0.132	-5.152	3 / 66
MC	Greece	MC	0.007	0.000	0.107	-3.456	0 / 67
MC	Ibero-American Registry	MC	0.013	0.008	0.021	-16.71515	/ 1170
MC	EORP/TCVT	MC	0.017	0.012	0.024	-23.11533	/ 1943
MC	U.K TAVI	MC	0.040	0.025	0.062	-13.231	18 / 452
MC	Asia TAVI	MC	0.007	0.001	0.049	-4.917	1 / 140
MC	18F EE Registry	MC	0.022	0.016	0.031	-21.48733	/ 1483
MC	FRANCE 2	MC	0.039	0.028	0.056	-17.415	31 / 785
MC			0.025	0.019	0.032	-25.270	

3.1%

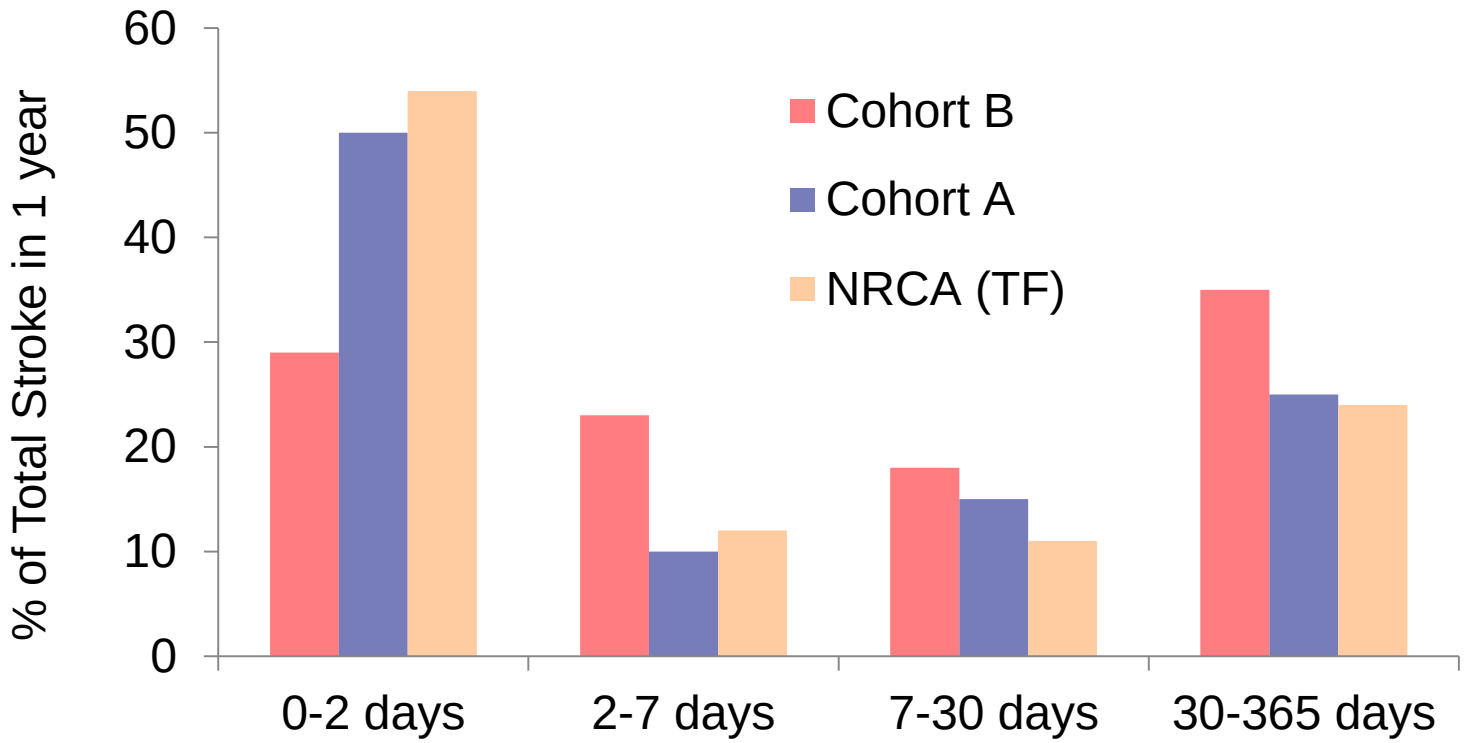
2.5%

Event rate and 95% CI



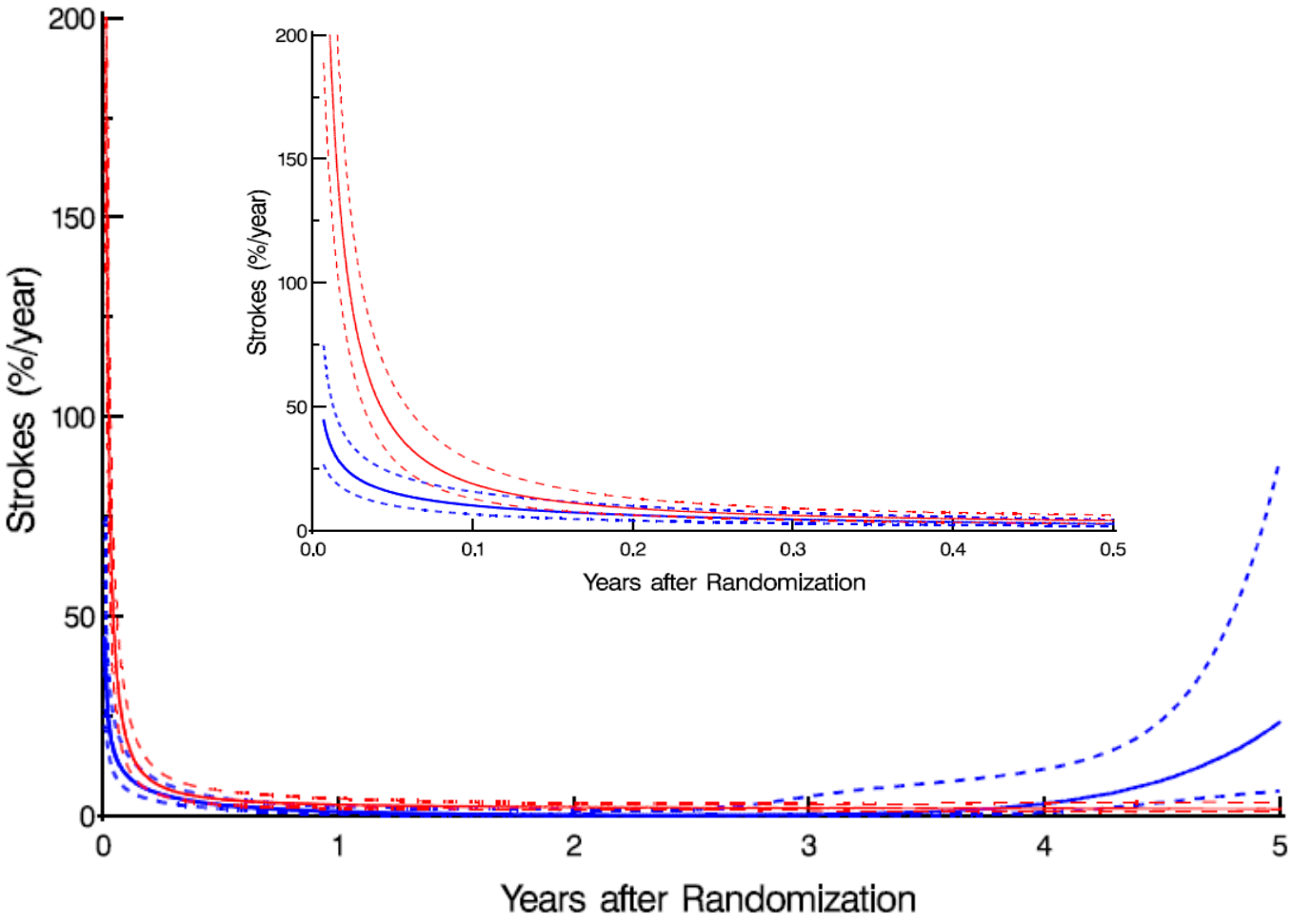
Athappan et al, JACC 2014

Stroke Timing within 1 year

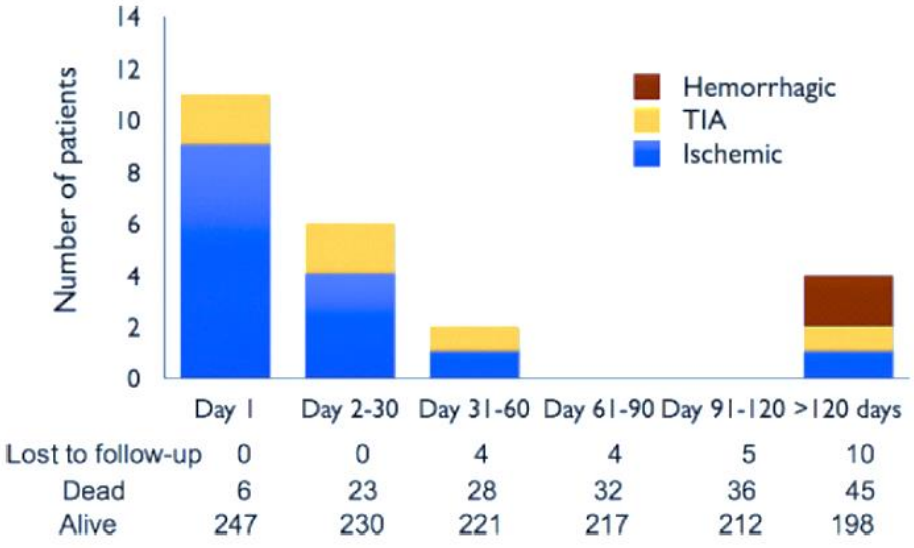


Leon et al, NEJM
Smith et al, NEJM
Kodali et al, ACC 2013

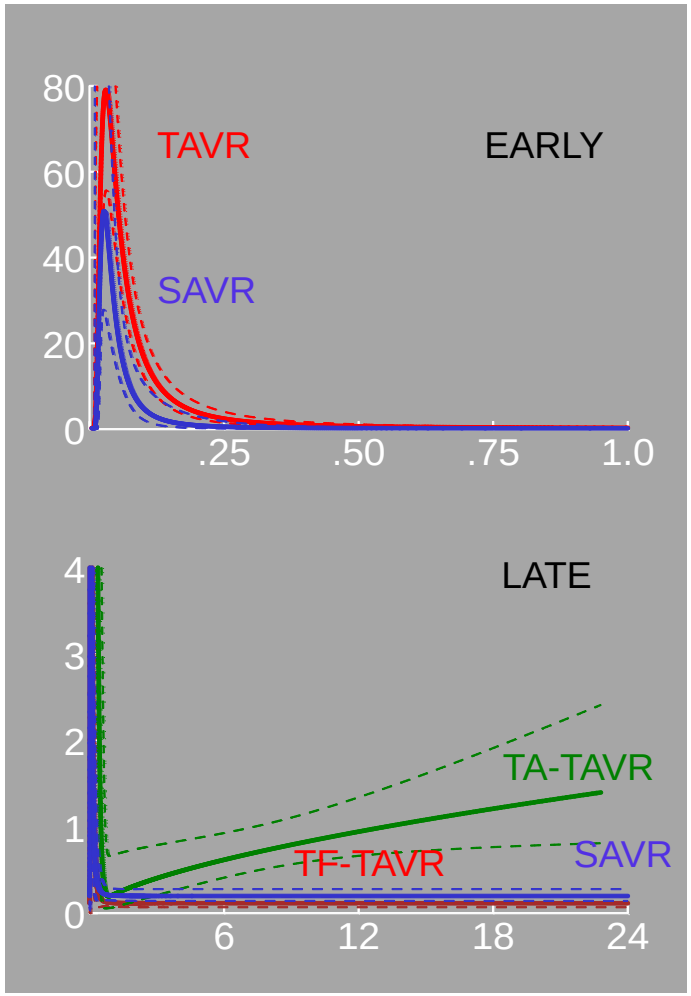
Stroke Analysis : Timing PARTNER 1B Instantaneous Risk of Stroke



Timing of Neurological Event
Emboli Prevention versus Pharmacotherapy



Tay et al, J Am Coll Cardiol Intv 2011;4:1290 –7



Miller et al, 2012;143:832-43

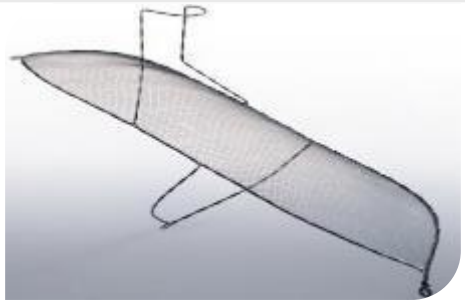
Stroke Prevention Measures

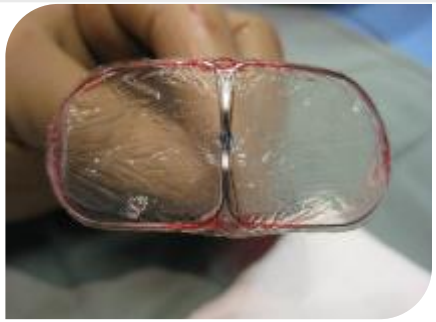
- Carotid pressure at the time of advancing the sheath
- Careful manipulations
- Minimize post-dilations
- ? Pretreat carotid disease

- Emboli prevention devices
  - Claret device
    - CLEAN TAVI
    - Sentinel Trial
  - Embrella Device – ProTAVI
  - TriGaurd – DEFLECT 1

Emboli Protection Devices

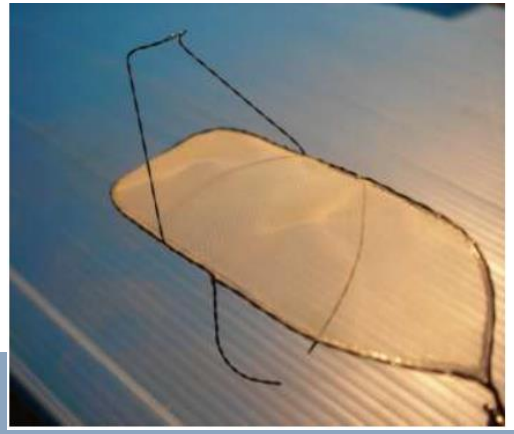
TriGuard Cerebral Protection Device	Edwards Embrella Embolic Deflector	Claret Sentinel Cerebral Protection System
Deflector	Deflector	**Filter capture**
9F (femoral)	6F (radial)	**6F (radial)**
240 micron pore size	100 micron pore size	**140 micron pore size**
Aortic arch position	Aortic arch position	**Brachiocephalic and LCC**
CE Marked	CE Marked	**CE Marked and Commercialized**

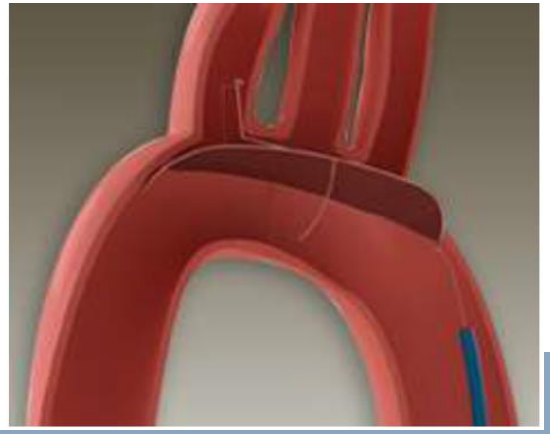




TriGuard - DEFLECT 1

Parameter	DEFLECT-I N=20	Historical Data N=150
Proportion of Patients with New Lesions	70%	76%
Number of New Lesions	5.1 (0 - 28)	4.4 (0 -39)
Average New Lesion Volume	0.12 (0 - 0.39) cm^3	0.34 cm^3
Max Single New Lesion Volume	0.39 cm^3	6.45 cm^3
Total New Lesion Volume	0.70 (0 – 3.94) cm^3	1.64 (0 – 70.3) cm^3





PROTAVI-C

euro PCR 2013

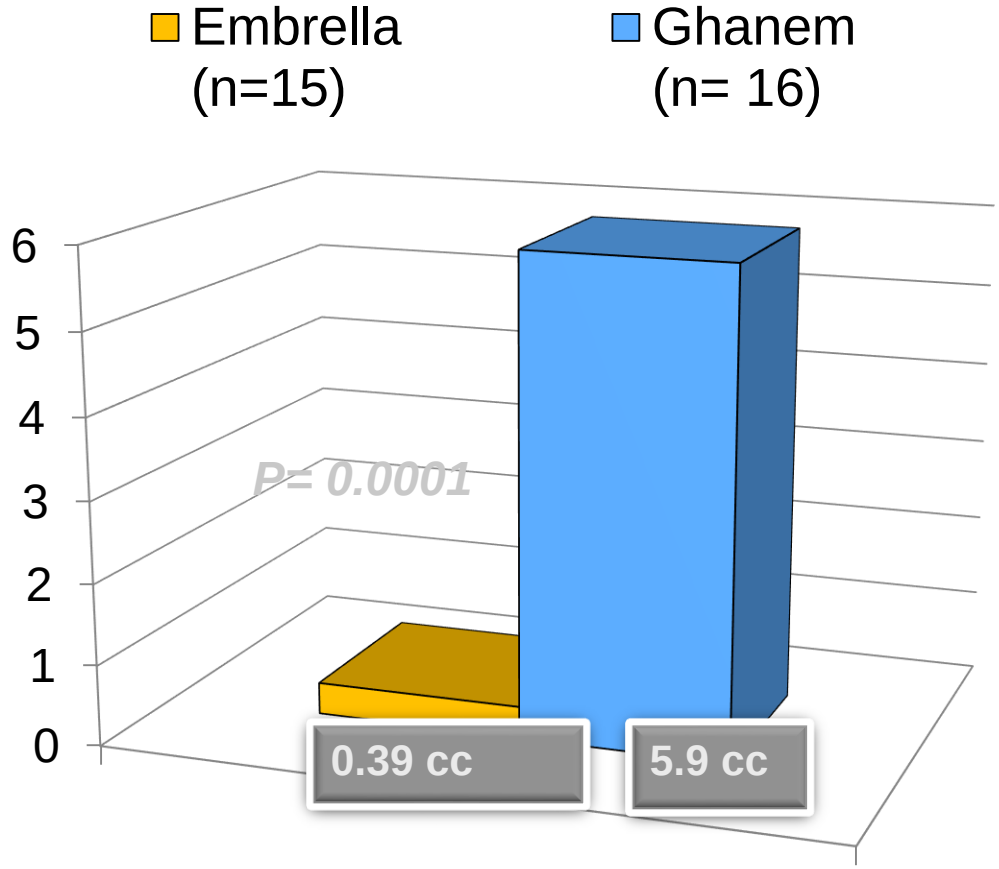
DW-MRI Data

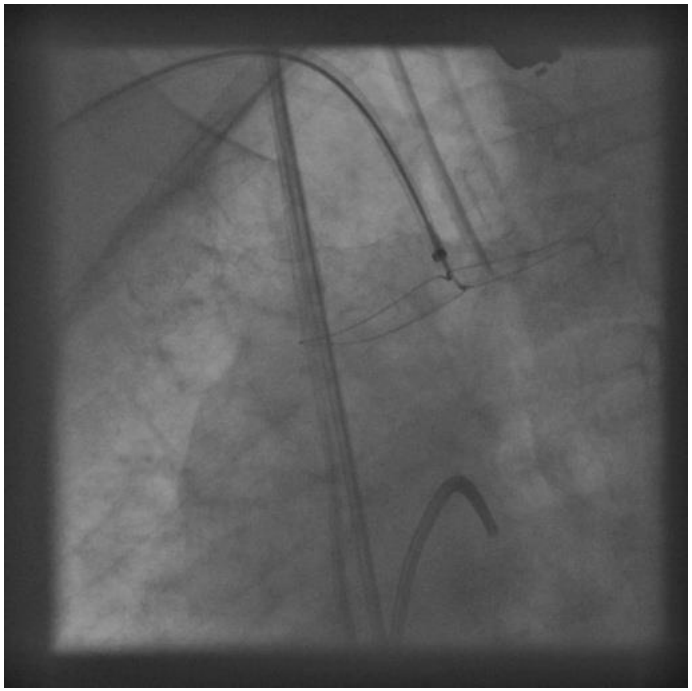
	Roll-In (n=9)	Treatment TAVI + Embrella (n=24)	P Value
Time from TAVI procedure, days, median (min, max)	3 (1,7)	3 (1-7)	NA
Patients with new Lesions	9/9 (100%)	24/24 (100%)	NA
Total No. of lesions, n			
Anterior cerebral artery	1 (11%)	6 (25%)	0.642
Medial cerebral artery	9 (100%)	20 (83%)	0.555
Posterior cerebral artery	6 (67%)	16 (67%)	>.999
Cerebellum	8 (89%)	15 (63%)	0.217
Border zone	0	2 (8%)	>.999
Patients with single lesions	0	4 (17%)	>.999
Patients with multiple lesions	9 (100%)	20	0.555
Lesions per patient, median (min, max)	9 (2, 21)	7 (1, 70)	0.361
Lesion volume (mm^3), median (min, max)	69.4 (25.0, 210.6)	40.0 (10.8, 196.7)	0.897

PROTAVI-C

Presented by Dr. Rodes-Cabau

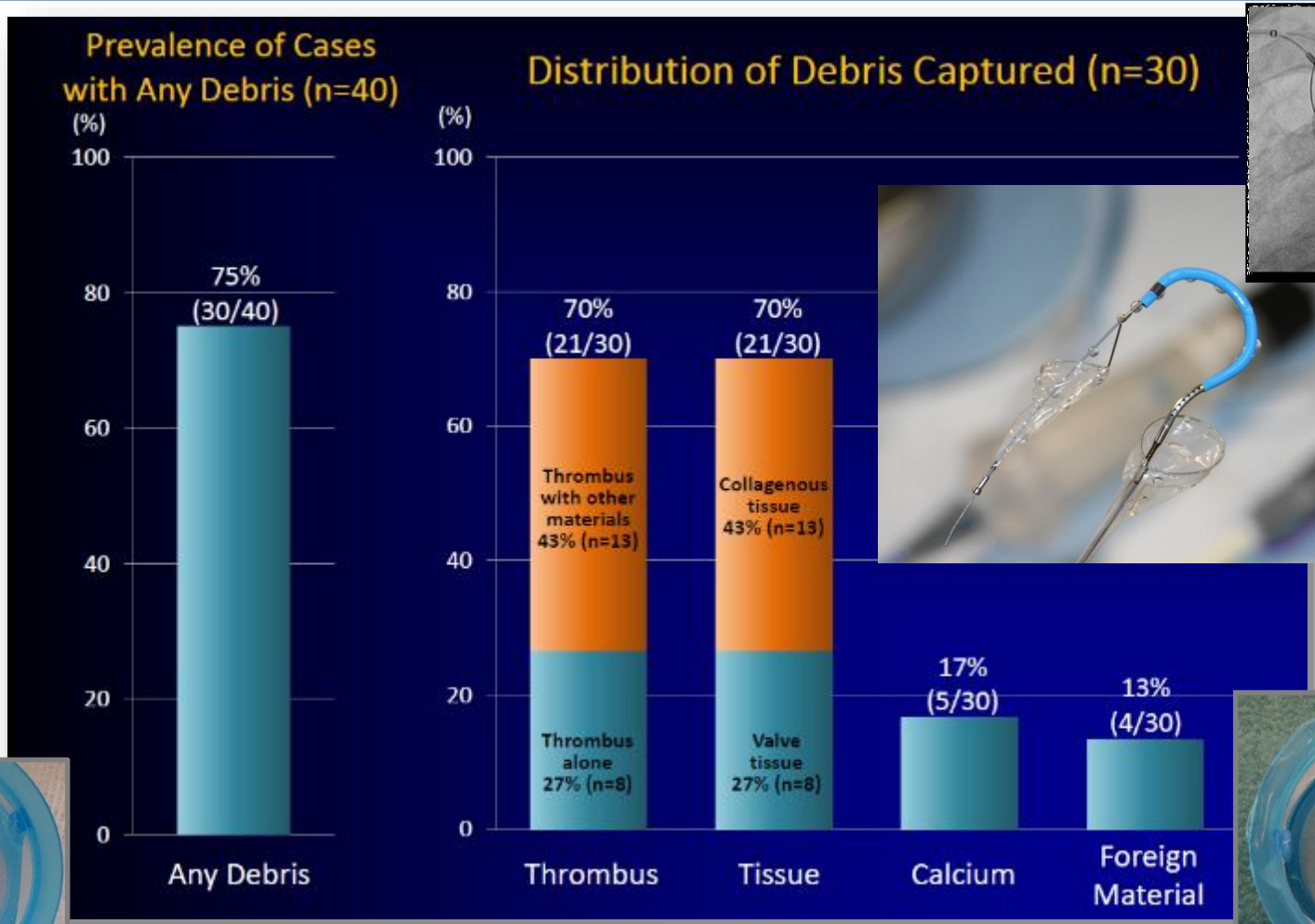
Average Volume (cc) of Lesions/Subject

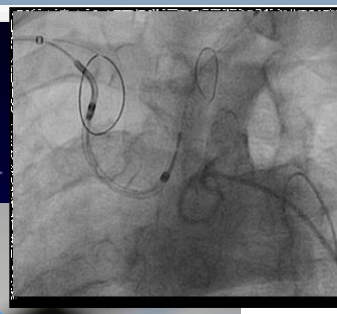


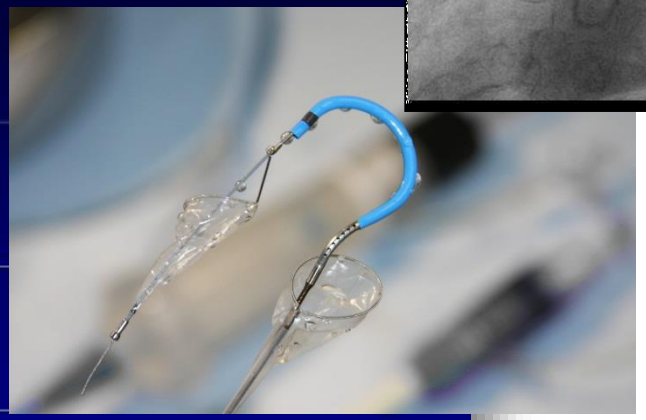


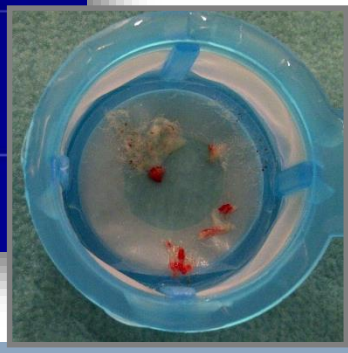
- Ghanem et al, J Am Coll Cardiol 2010;55:1427–32 (TF TAVI)
- Embrella Subjects: 1 BAV, 14 TF TAVI

Histopathology - Claret Debris Capture



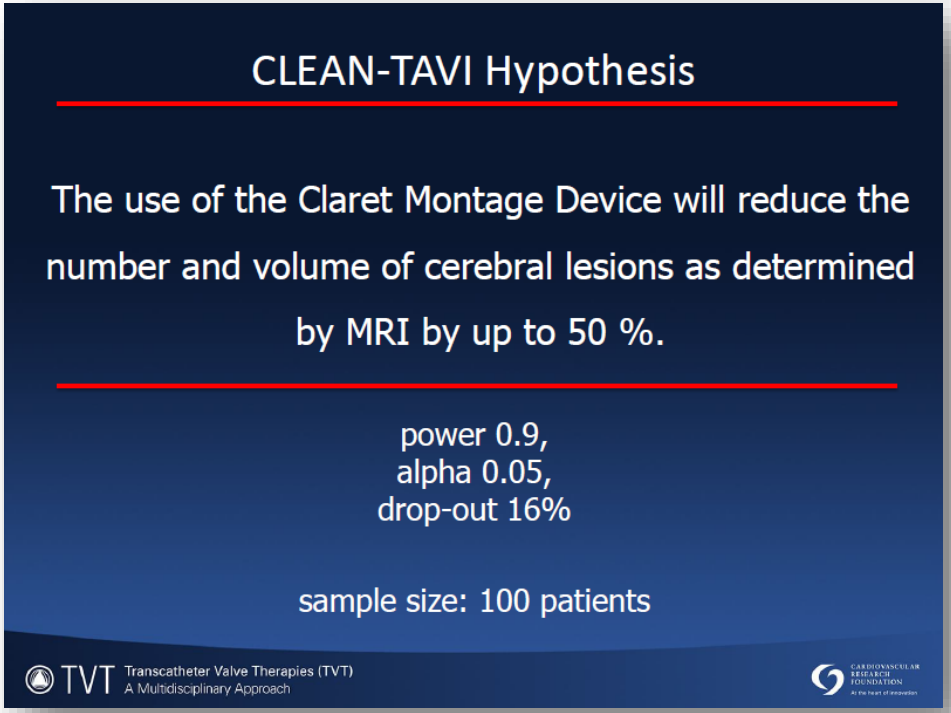


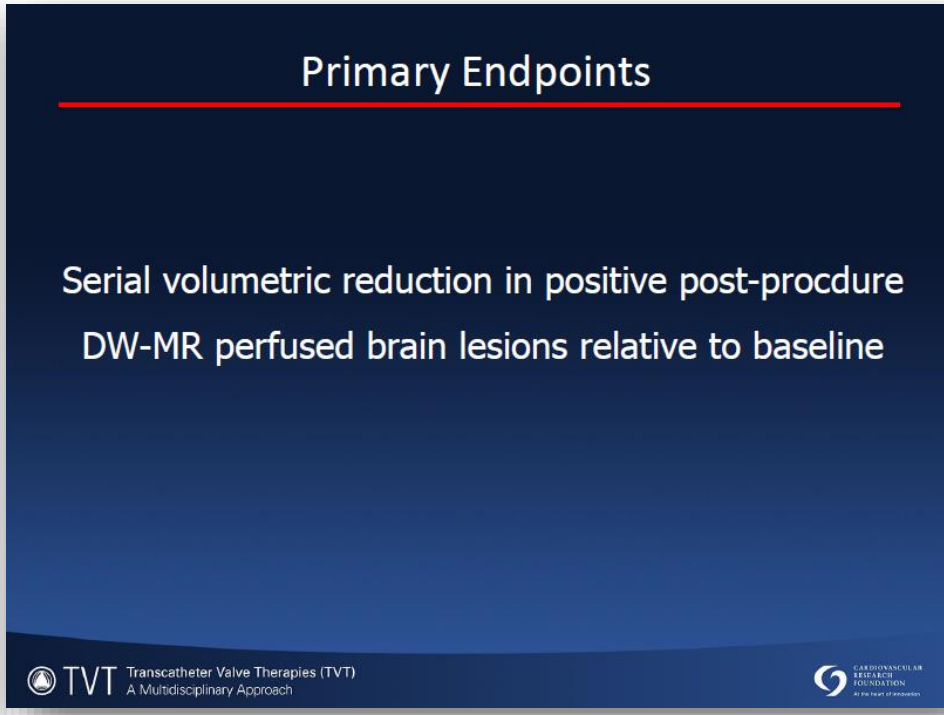




Van Mieghem et al, Circulation 2013;127:2194-2201
Debris analysis by Dr. Renu Virmani, CVPath Institute of Histopathology

Clean-TAVI Study

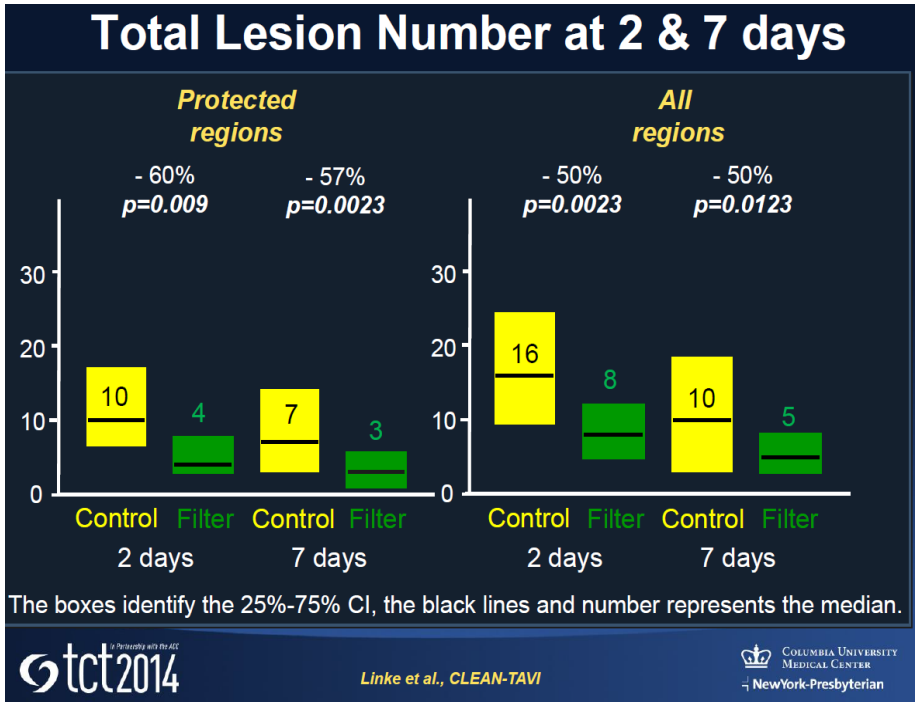


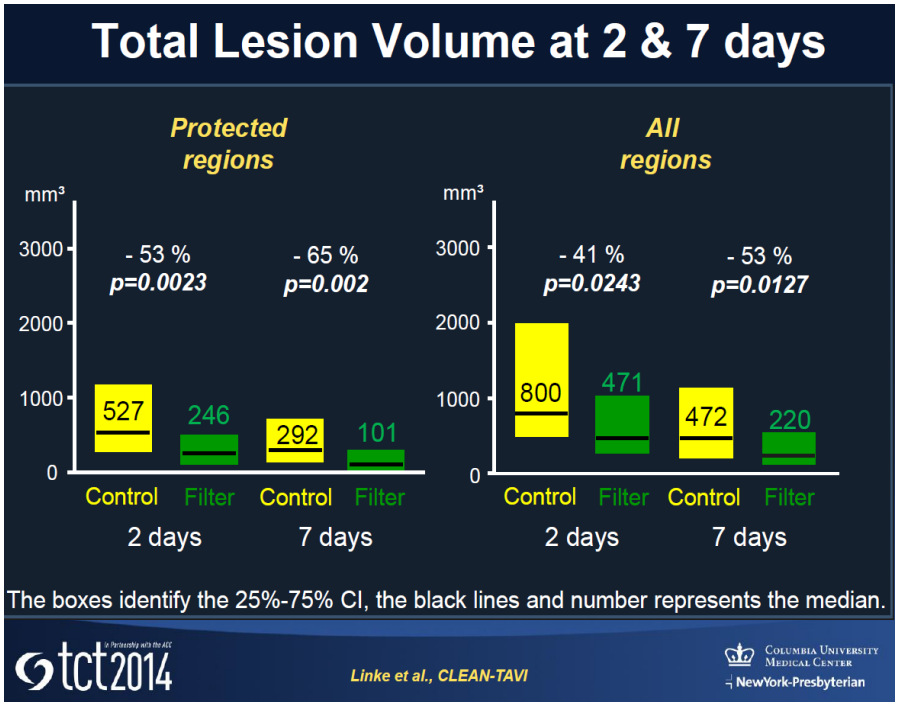


- ***Statistically-powered: 100 patients randomized 1:1***
- ***Serial 3 Tesla MRI: Baseline, 2-days, 7-days, 1-month & 1-year***
- ***Medtronic CoreValve used exclusively***
- ***Presented at TCT on Saturday 13th 11am LBCT session***
- ***Data Showed decrease in volume, number of emboli with decrease in ataxia.***

Courtesy of Prof Axel Linke, MD

CLEAN TAVI data





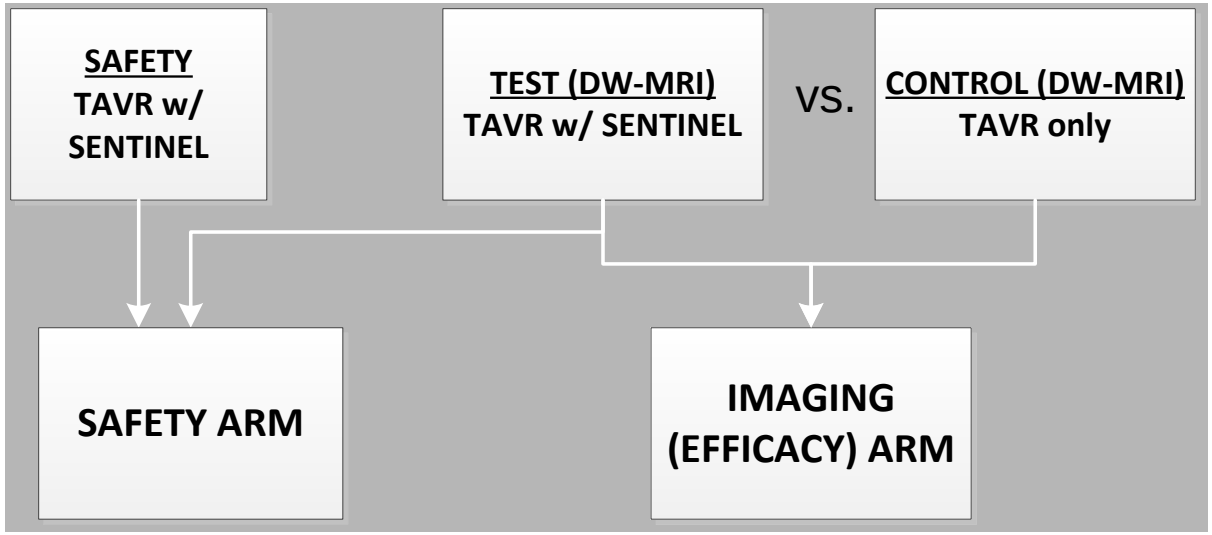
Presented by Linke 2014

US IDE Sentinel Study Summary

- **Title**
  - **Cerebral Protection in Transcatheter Aortic Valve Replacement Th SENTINEL Study**
- **Study Objective**
  - **Assess the safety and efficacy of the Claret Medical Sentinel Cerebral Protection System for embolic protection during Transcatheter Aortic Valve Replacement (TAVR) compared to TAVI standard of care (without embolic protection)**
- **Study Population**
  - **Subjects with severe symptomatic calcified native aortic valve stenosis who meet the commercially approved indications for TAVR with the Edwards SAPIEN THV or XT (if approved)**
- **Number of Centers**
  - **Up to 15 clinical study centers**

IDE Study Design - Overview

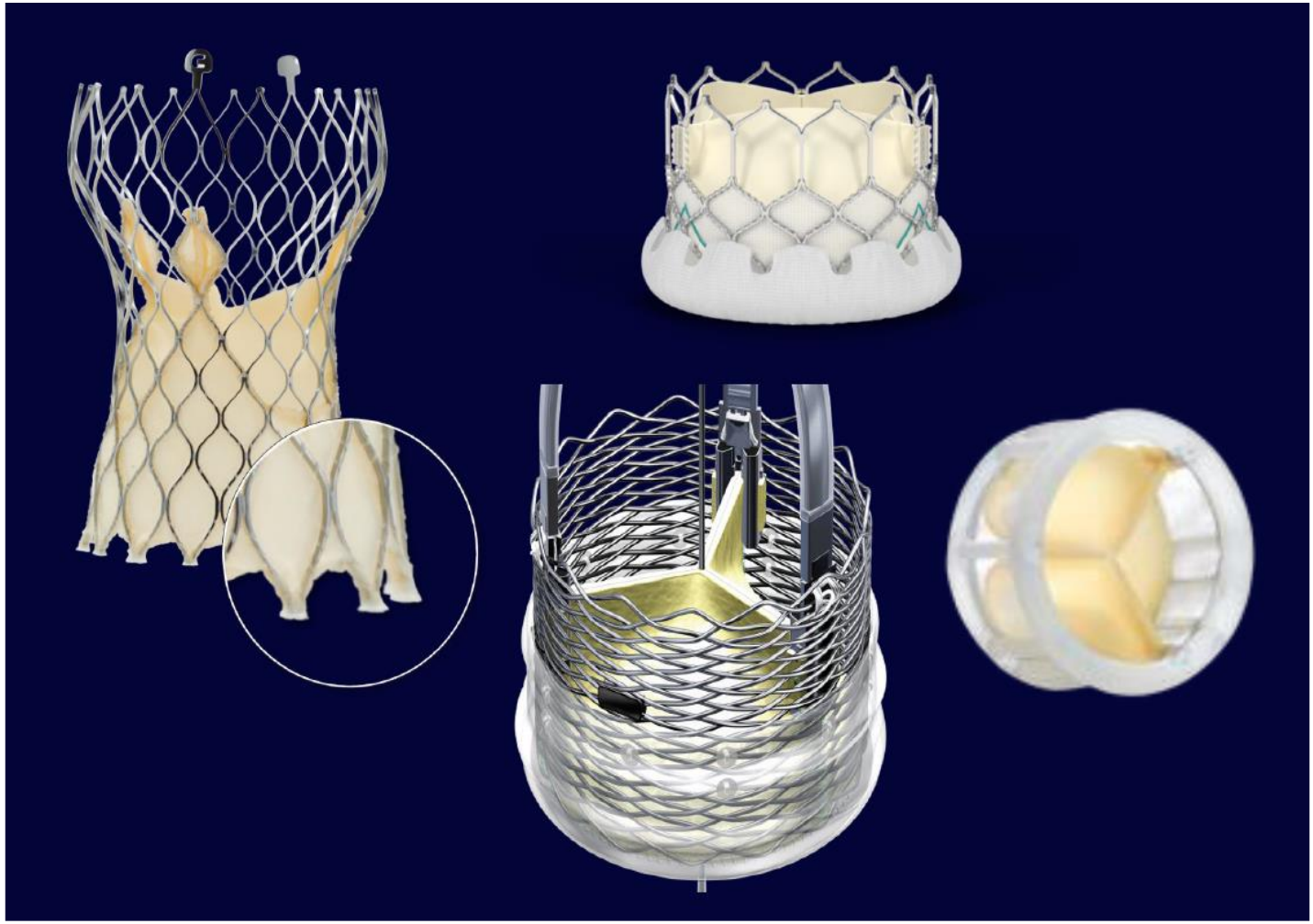
- Prospective, multicenter, blinded, randomized controlled trial
- 284 subjects randomized into a three-arm study
- Enrollment at up to 15 centers in the United States



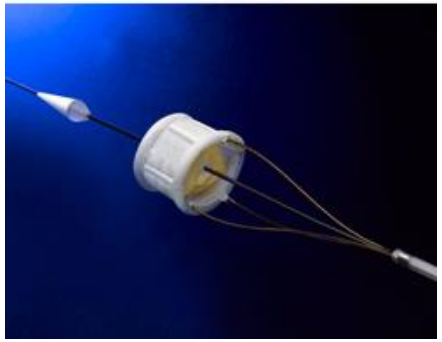
Implication

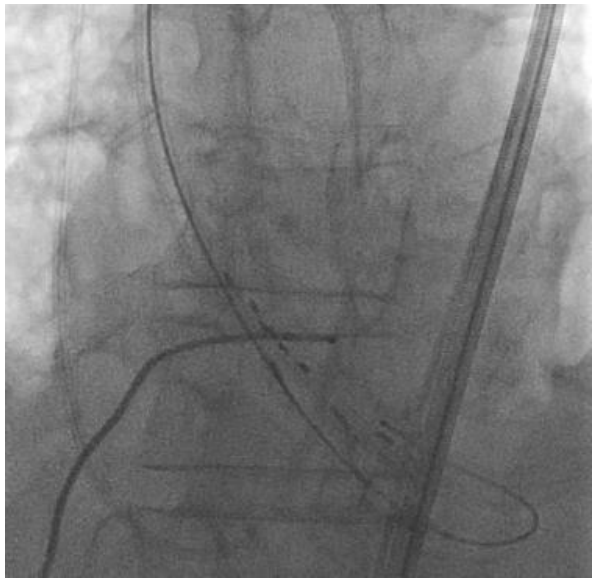
- Stroke prevention will help to move to lower risk patients
- It may be an advantage rather than disadvantage for TAVR compared to SAVR (similar to PCI compared to CABG)

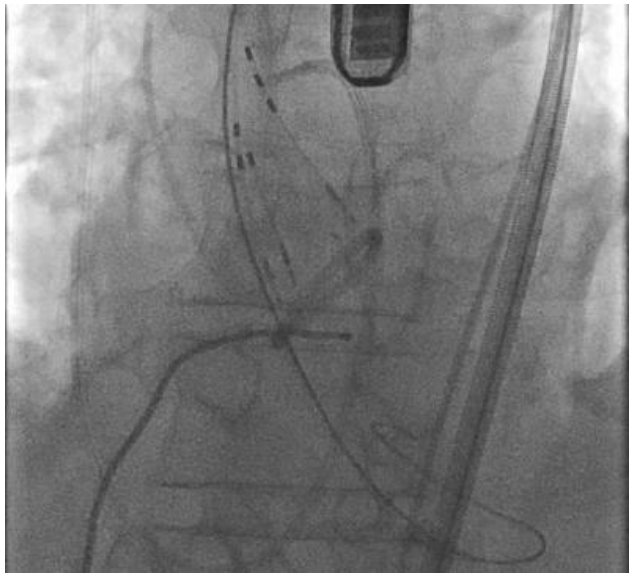
Newer Valves

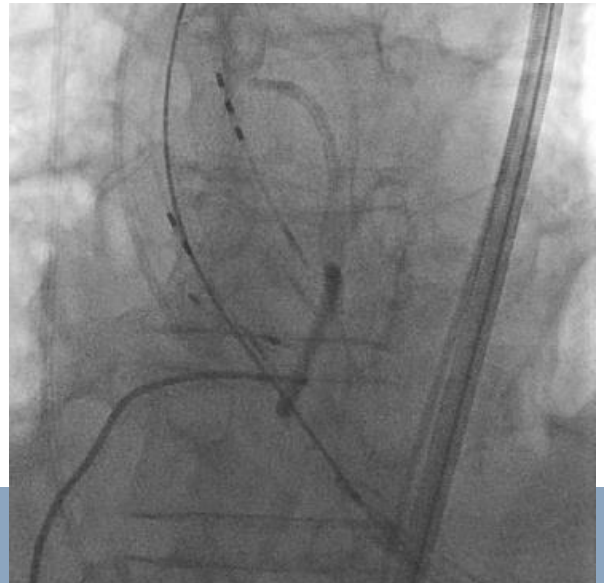


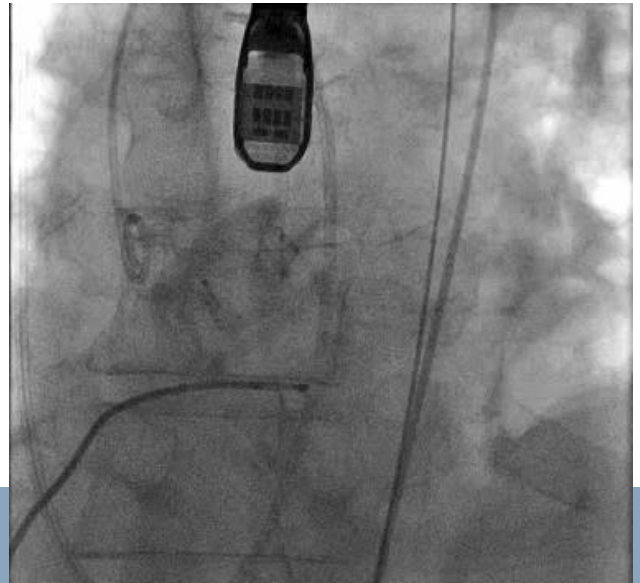
Newer Valve Design – Direct Flow









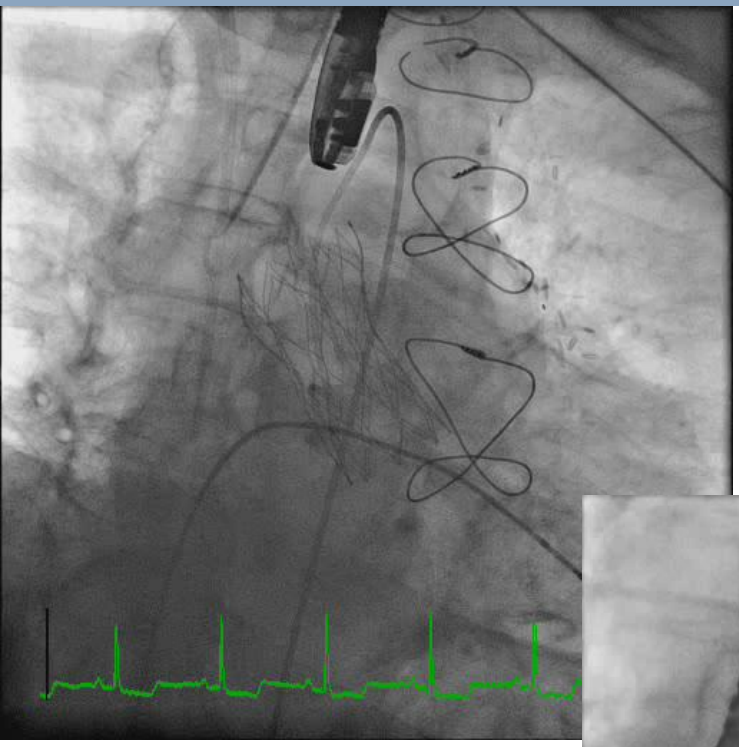


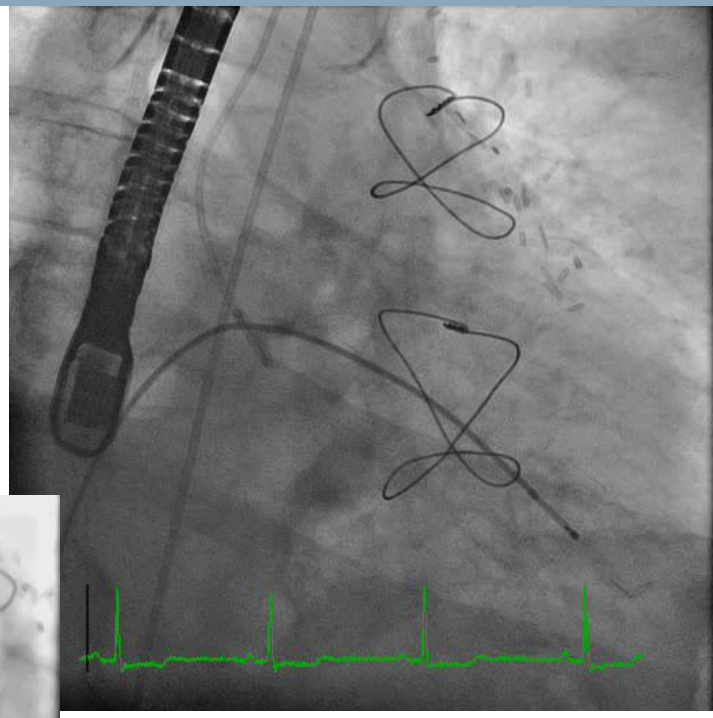
Portico Sealing Cuff

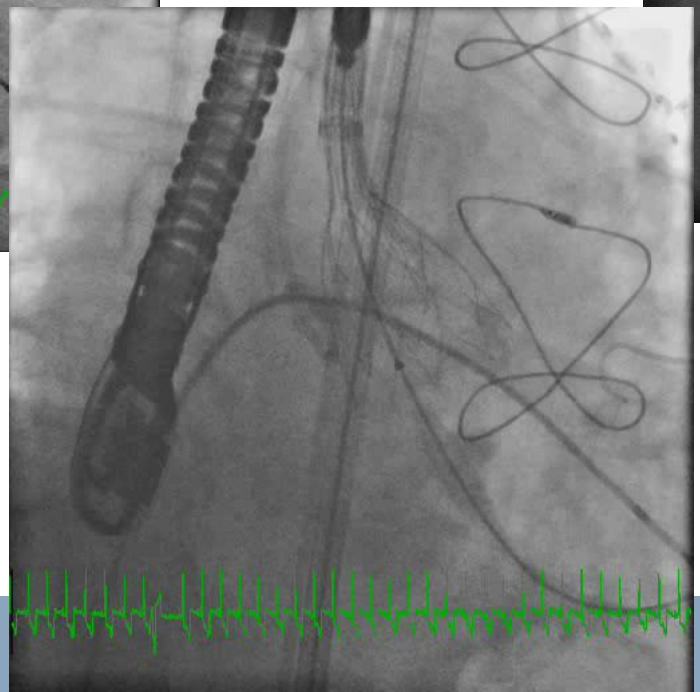
- **Conforms to native anatomy for sealing**
- **Designed for sub-annular sealing of 1 – 9 mm**

Sealing Cuff

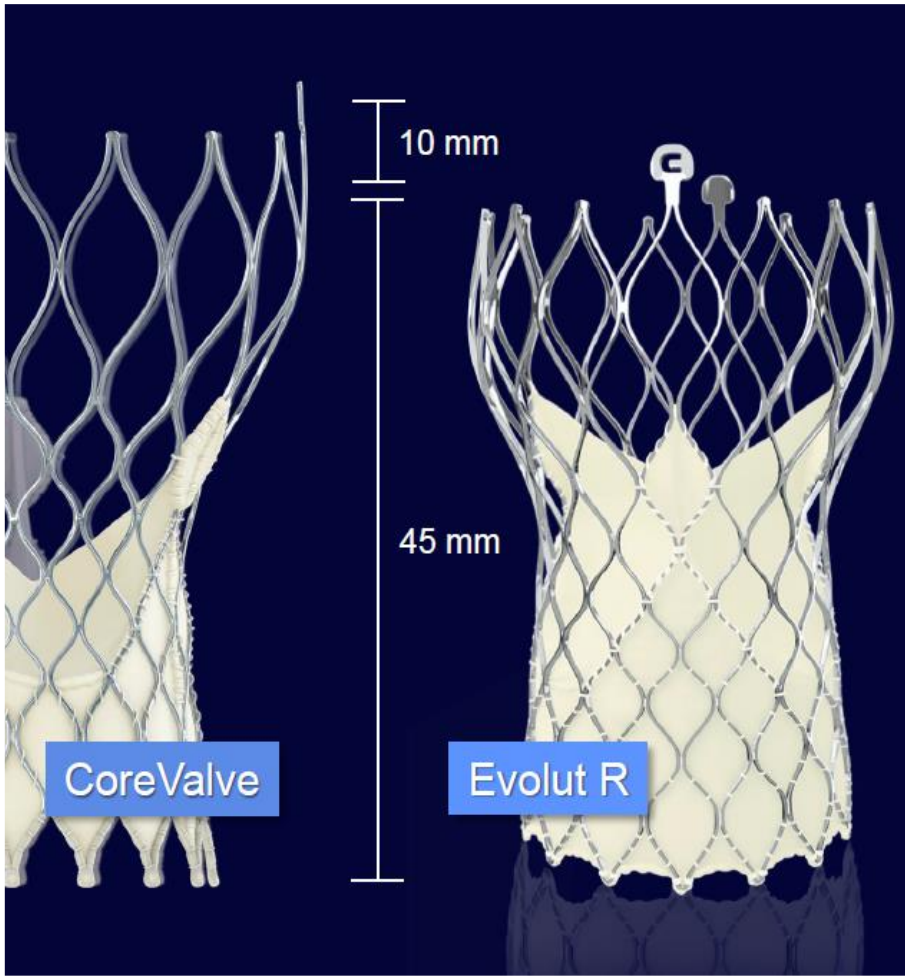
PORTICO Case







EVOLUTE R



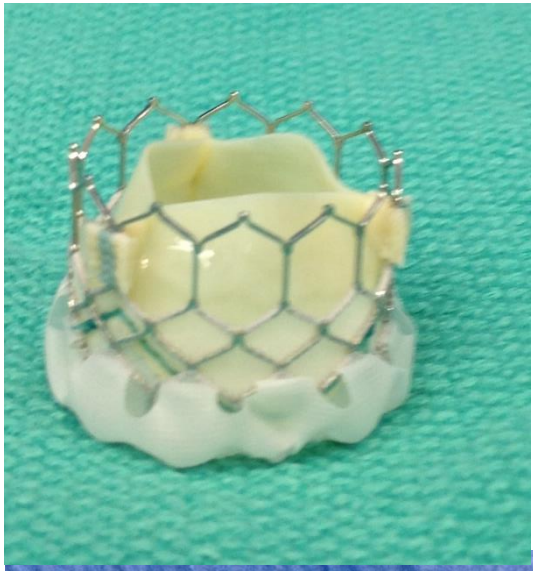
Redesigned Outflow

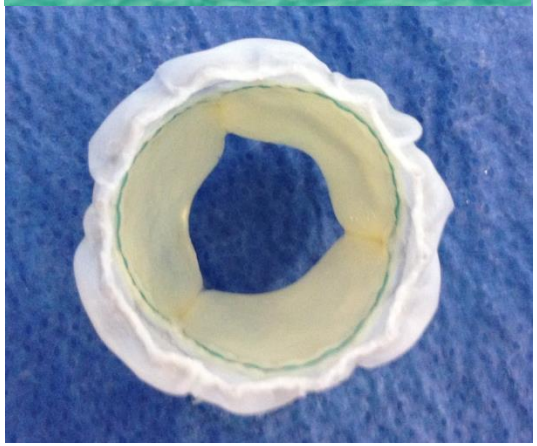
- Reduced height, reshaped for improved fit, especially in angulated anatomy

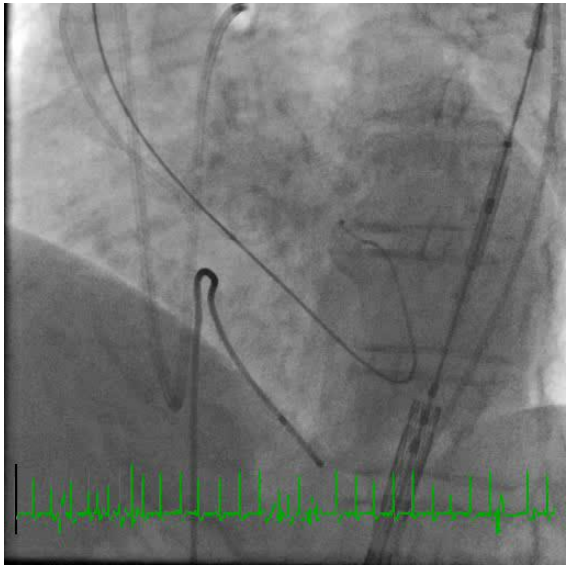
Enhanced sealing

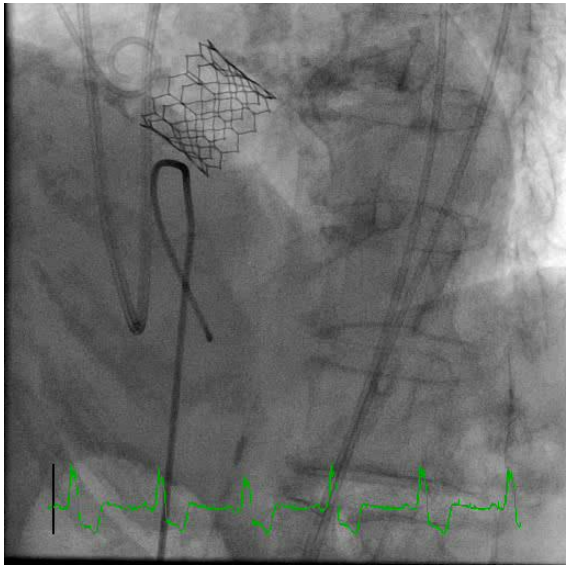
- Optimized cover index (sizing), consistent radial force
- Extended skirt (1mm)

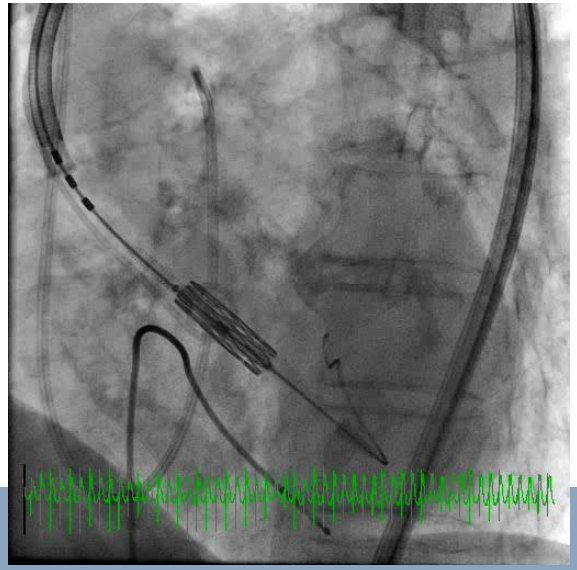
Newer Valve Designs - S3

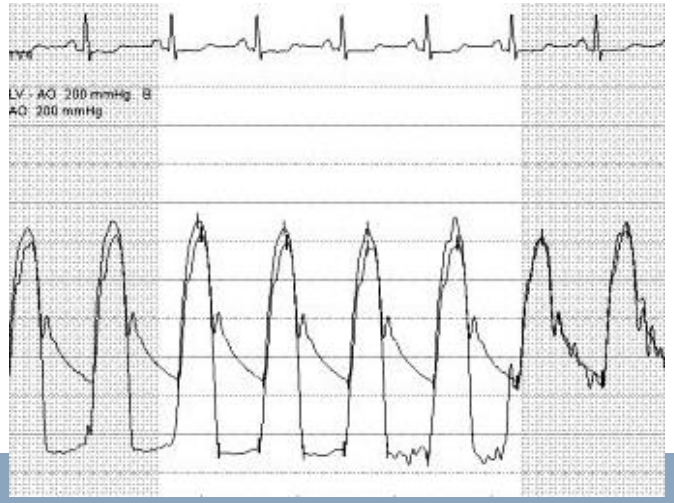




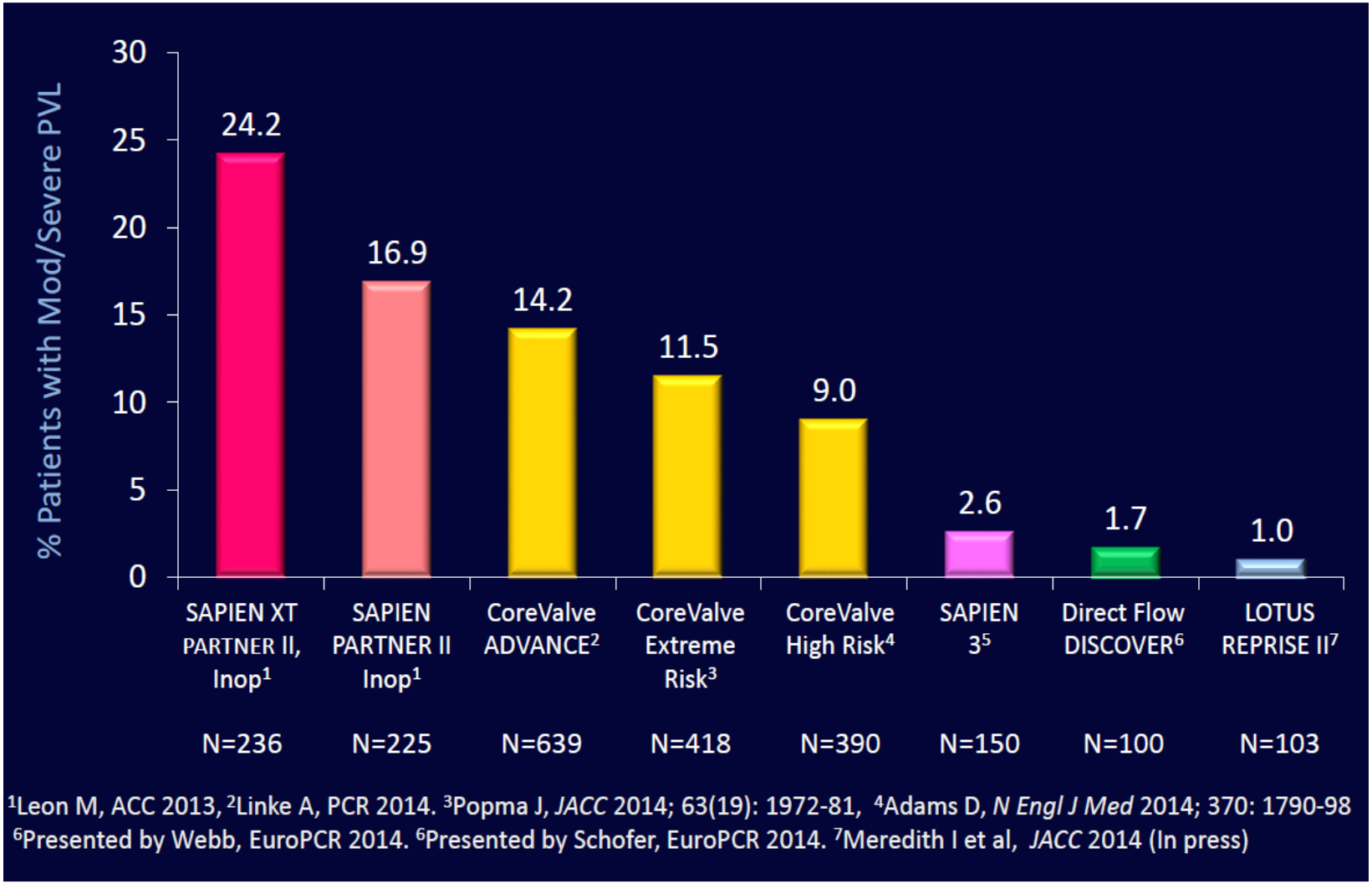








Paravalvular Leak
Echo Core Lab Adjudication



[1]Leon M, ACC 2013, [2]Linke A, PCR 2014. [3]Popma J, *JACC* 2014; 63(19): 1972-81, [4]Adams D, *N Engl J Med* 2014; 370: 1790-98
[6]Presented by Webb, EuroPCR 2014. [6]Presented by Schofer, EuroPCR 2014. [7]Meredith I et al, *JACC* 2014 (In press)

Adapted from Dr. Meredith

Summary

- **PVL is almost solved!**
- **Strokes will be solved soon!**

- **Will not have anything to talk about!**