

# **The Evidence and Clinical Need Justifies the Widespread Use of Embolic Protection During TAVR**

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# Disclosure

- **Co PI for Sentinel Trial**

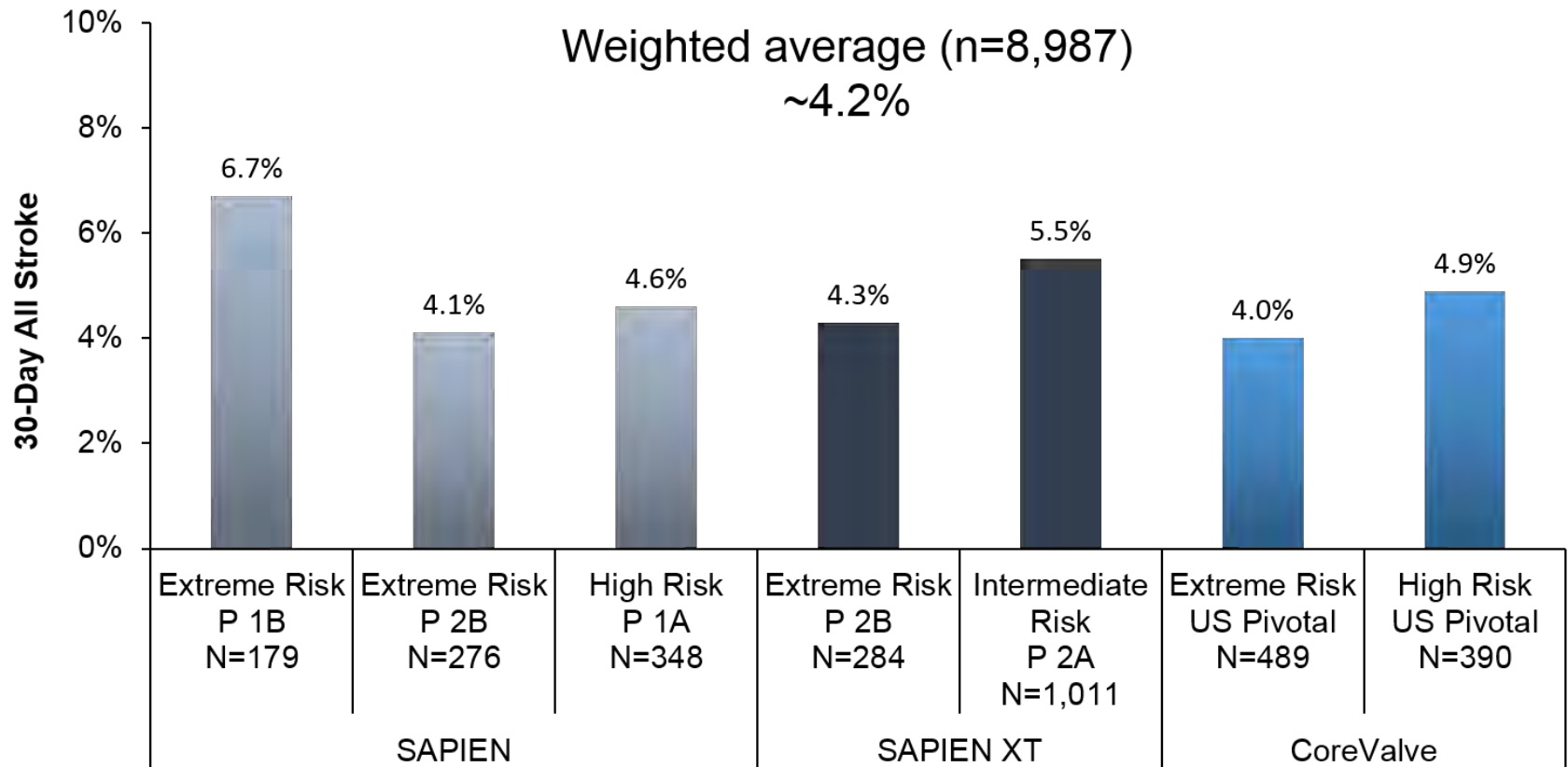
# Questions

- **Is Stroke a Problem with TAVR in 2017?**
- **How Common is Stroke in Comparison With SAVR?**
- **Does Cerebral Protection Work?**

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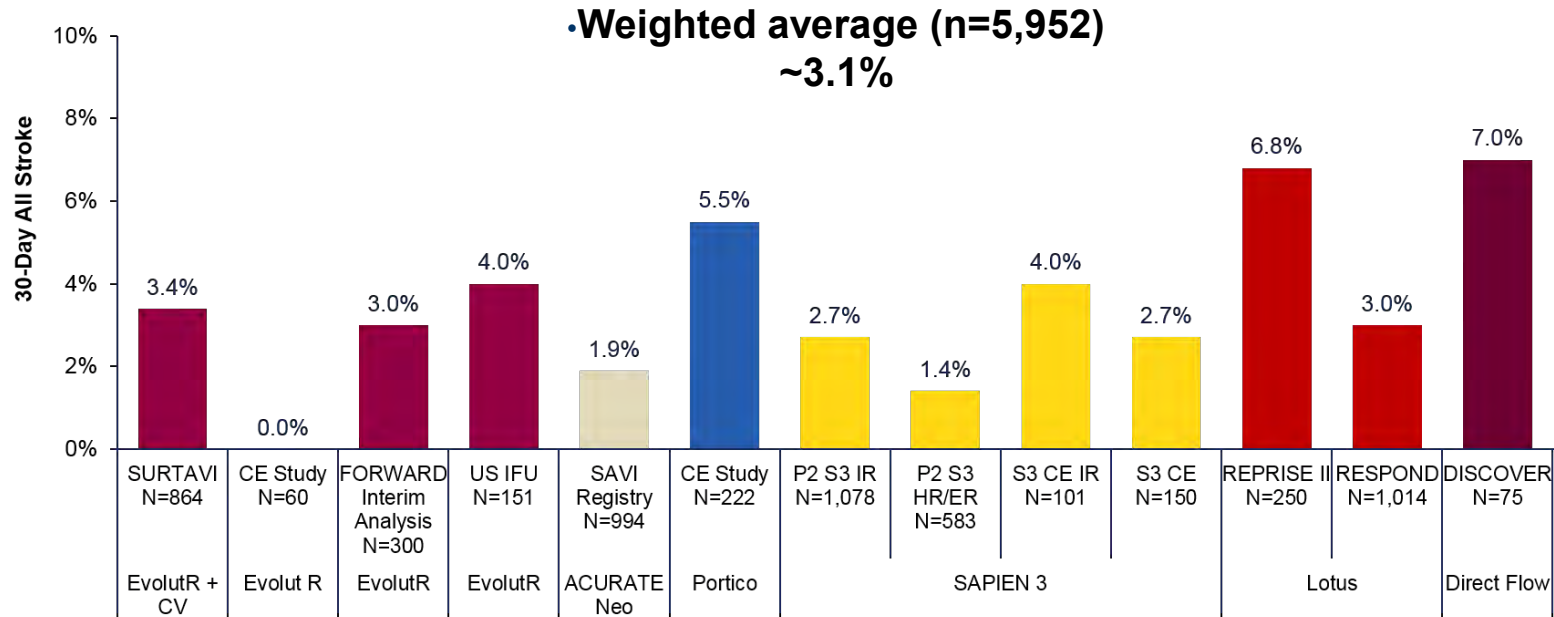
# Stroke Rates in Randomized Trials



<sup>1</sup>Leon, et al., *N Engl J Med* 2010;363:1597-1607; <sup>2</sup>Webb, et al., *J Am Coll Cardiol Interv* 2015;8:1797-806; <sup>3</sup>Smith, et al., *N Engl J Med* 2011;364:2187-98;

<sup>4</sup>Leon, et al., *N Engl J Med* 2016;374:1609-20; <sup>5</sup>Popma, et al., *J Am Coll Cardiol* 2014;63:1972-81; <sup>6</sup>Adams, et al., *N Engl J Med* 2014;370:1790-8;;

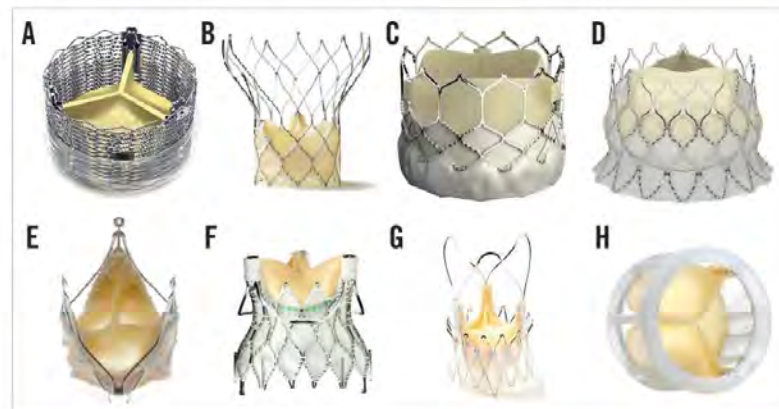
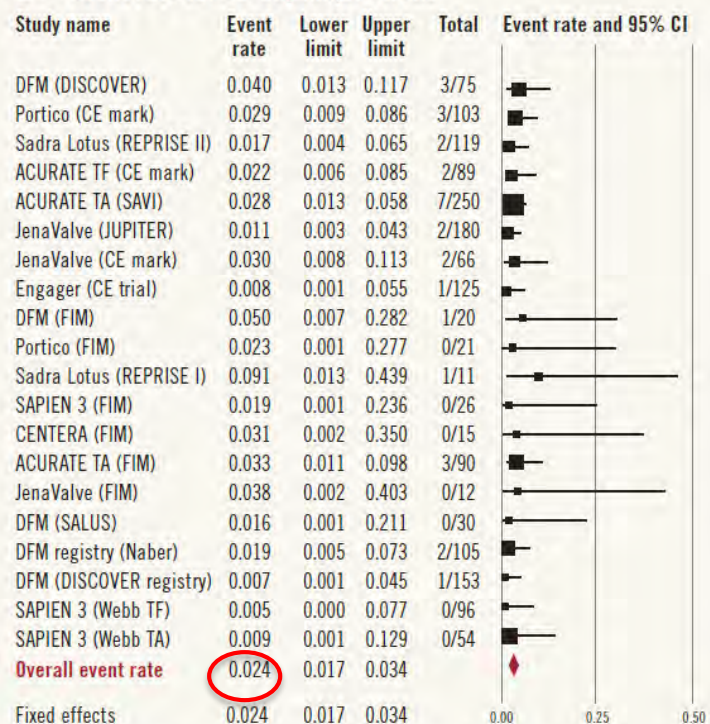
# Stroke Rates with Contemporary Devices



<sup>1</sup>Manoharan, et al., *J Am Coll Cardiol Interv* 2015; 8: 1359-67; <sup>2</sup>Moellman, et al., presented at PCR London Valves 2015; <sup>3</sup>Linke, et al., presented at PCR London Valves 2015; <sup>4</sup>Kodali, et al., *Eur Heart J* 2016; doi:10.1093/eurheartj/ehw112; <sup>5</sup>Vahanian, et al., presented at EuroPCR 2015; <sup>6</sup>Webb, et al. *J Am Coll Cardiol Interv* 2015; 8: 1797-806; <sup>7</sup>DeMarco, et al, presented at TCT 2015; <sup>8</sup>Meredith, et al., presented at PCR London Valves 2015; <sup>10</sup>Falk, et al., presented at EuroPCR 2016; <sup>11</sup>Kodali, presented at TCT 2016; Reardon, M  
Published in NEJM March 2017

# Stroke Risk With Second Generation TAVR valves

## B Event rate for 30-day major stroke

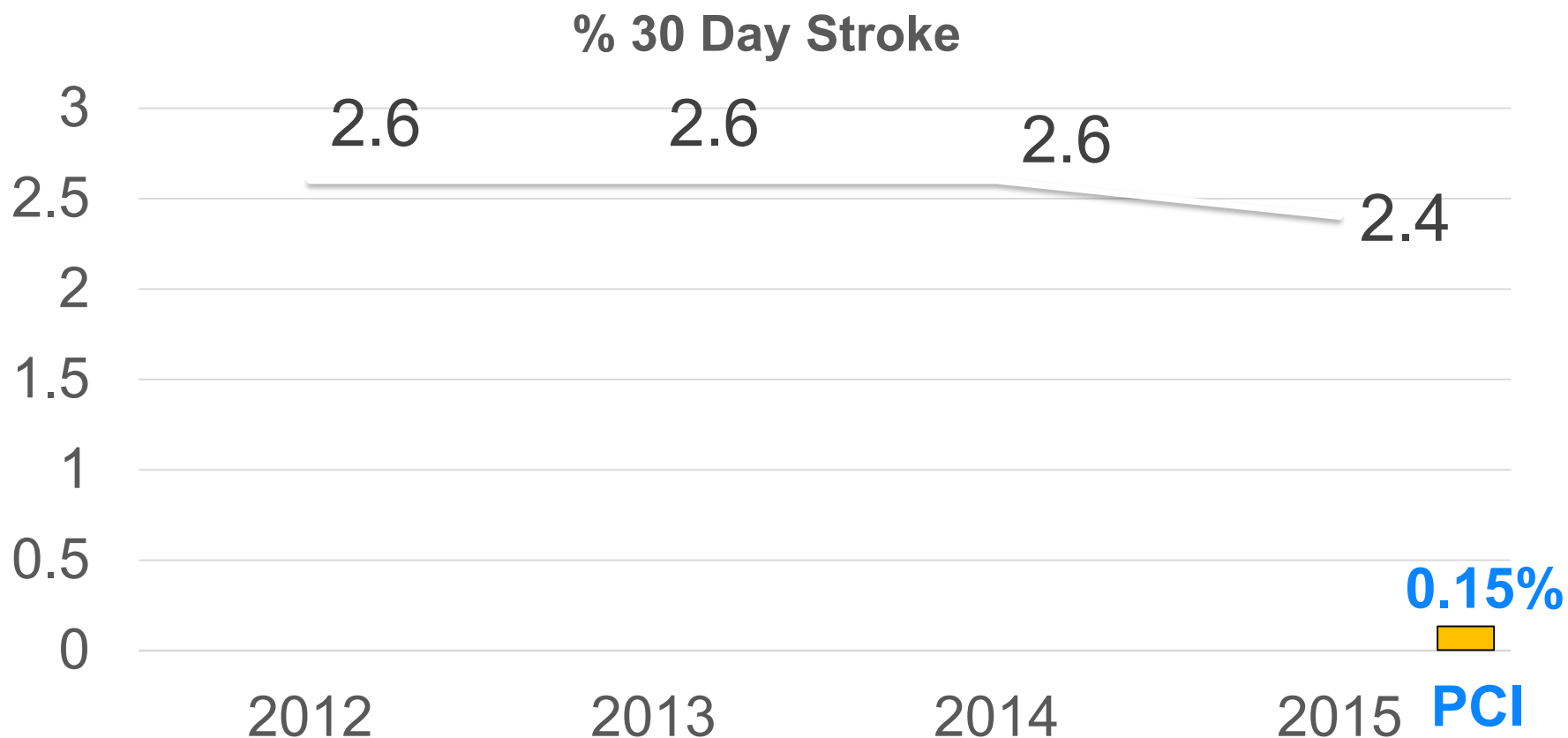


**Figure 7.** Second-generation transcatheter aortic valves. A) Sadra™ Lotus Medical valve (Boston Scientific SciMed Inc, Maple Grove, MN, USA); B) Portico® valve (St. Jude Medical); C) Edwards SAPIEN 3 valve (Edwards Lifesciences); D) Edwards CENTERA valve (Edwards Lifesciences); E) JenaValve (JenaValve Technology); F) Engager™ valve (Medtronic Inc.); G) Symetis ACURATE™ valve (Symetis SA); H) Direct Flow Medical® valve (Direct Flow Medical).

- **Meta-analysis of ~20 non-randomized, mostly FIM, valve-company sponsored studies**
- **2.4% major stroke at 30-days**

Athappan, et al. A systematic review on the safety of second-generation transcatheter aortic valves. *EuroIntervention* 2016; 11:1034-1043

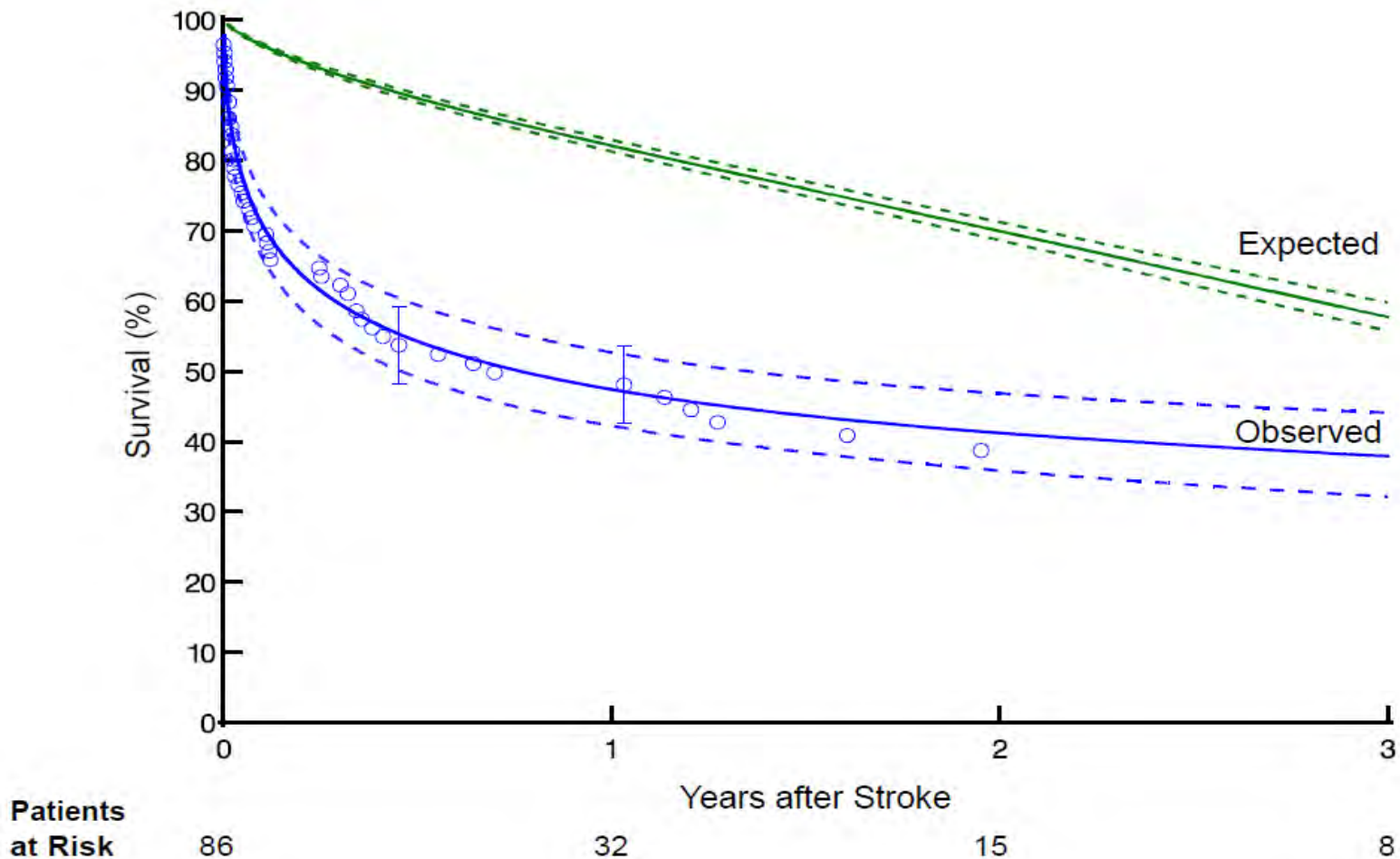
# TVT Stroke Rate





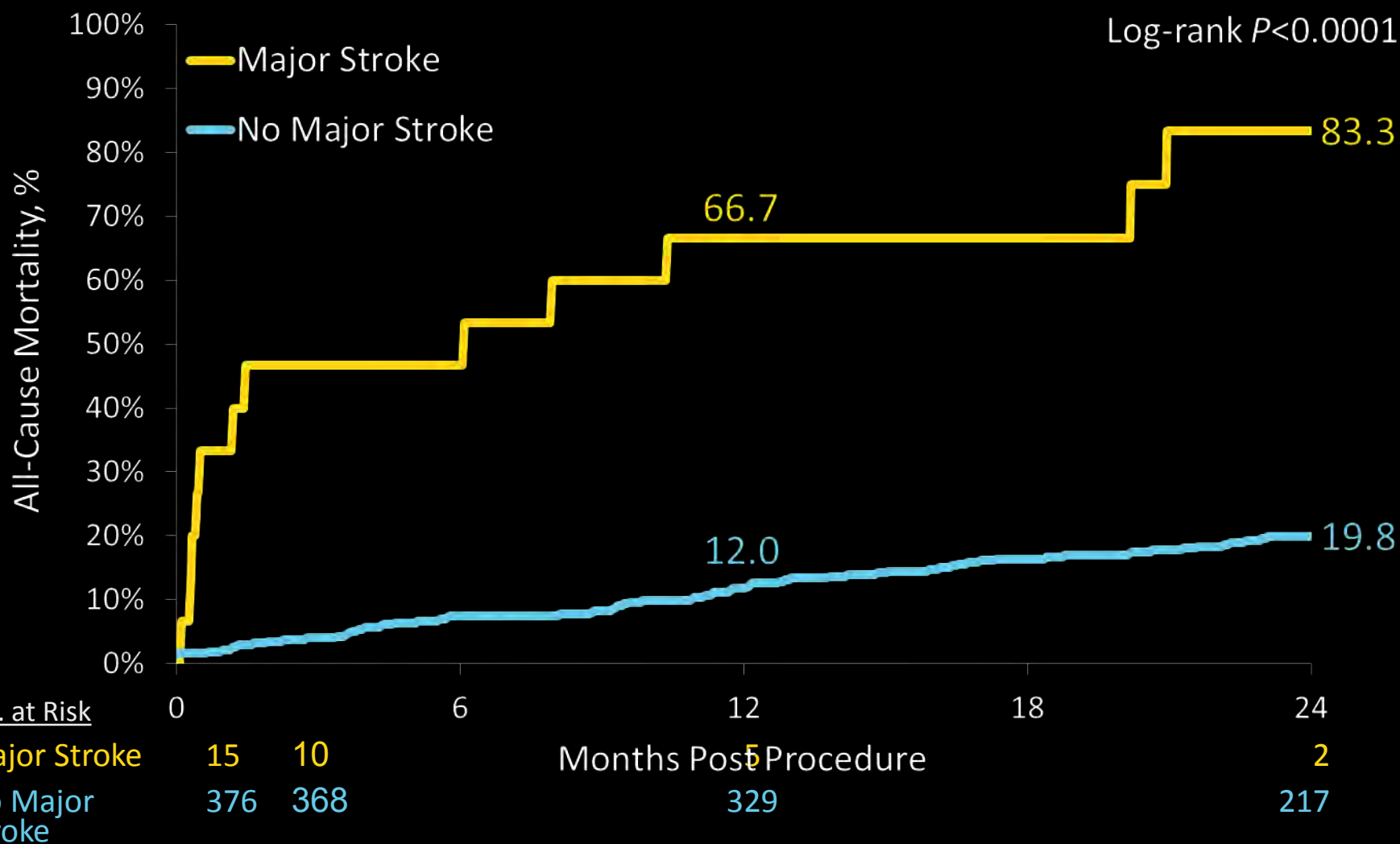
# Mortality After Stroke

## TF TAVR – PARTNER Trial



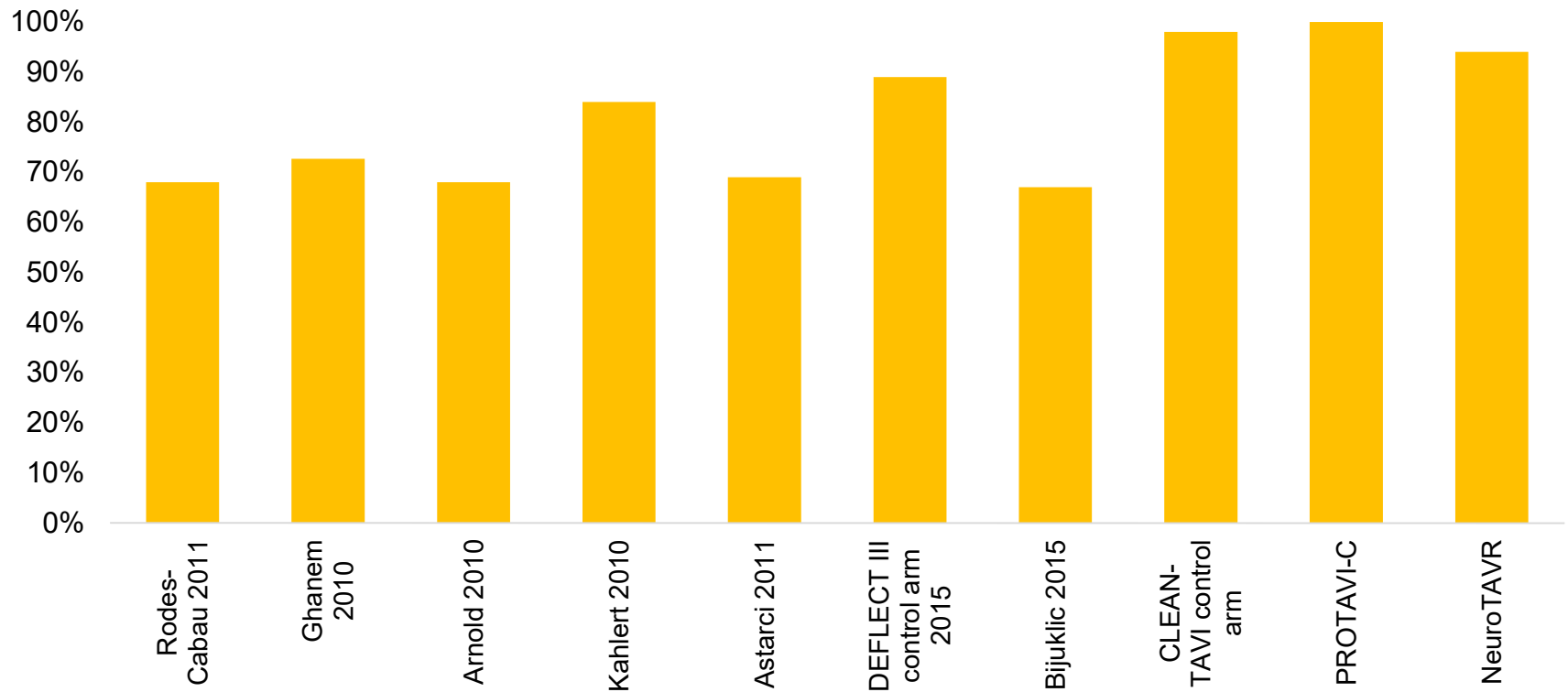
# Mortality after Stroke

## CoreValve High Risk Trial



# MRI Lesions After TAVR

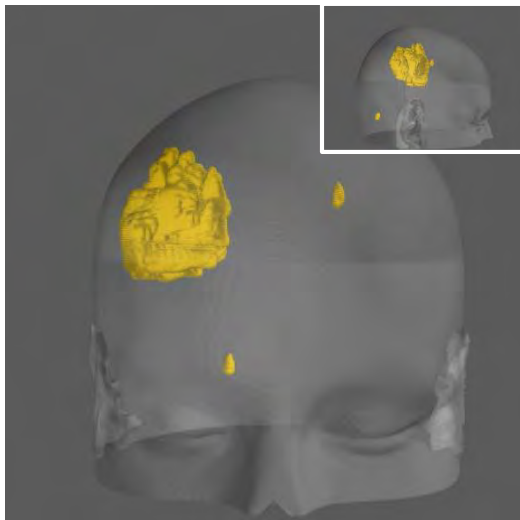
% of TAVI patients with new cerebral lesions on DW-MRI



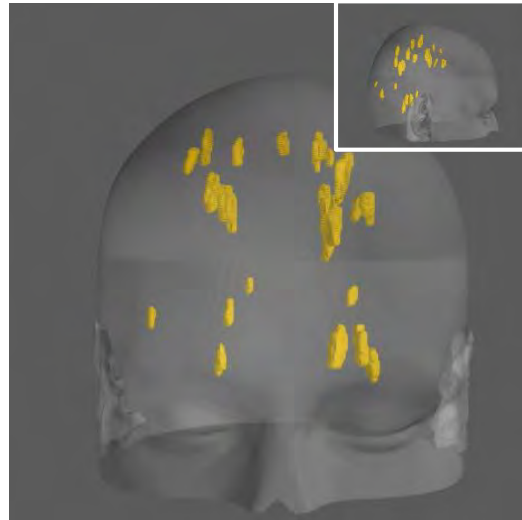
- 1. Rodes-Cabau, et al., JACC 2011; 57(1):18-28 ·4. Kahlert, et al., Circulation. 2010;121:870-878 ·7. Bijuklic, et al., JACC: CVI 2015 ·10. Lansky, et al. London Valves 2015
- 2. Ghanem, et al., JACC 2010; 55(14):1427-32 ·5. Astarci, et al., EJCTS 2011; 40:475-9 ·8. Linke, et al., TCT 2014 ·11. Sacco et al., Stroke 2013
- 3. Arnold, et al., JACC:CVI 2010; 3(11):1126-32 ·6. Lansky, et al., EHJ 2015; May 19 ·9. Vahanian, TCT 2014 ·12. Vermeer et al., Stroke 2003
- 13. Vermeer et al., New Engl J Med 2009

# Overt Stroke – Size, Number, LOCATION

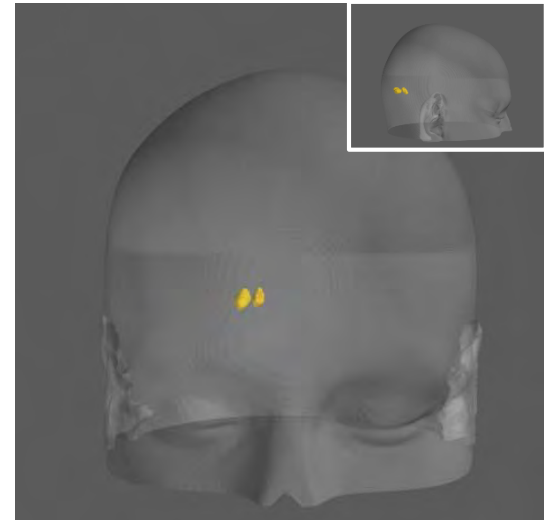
**Size**



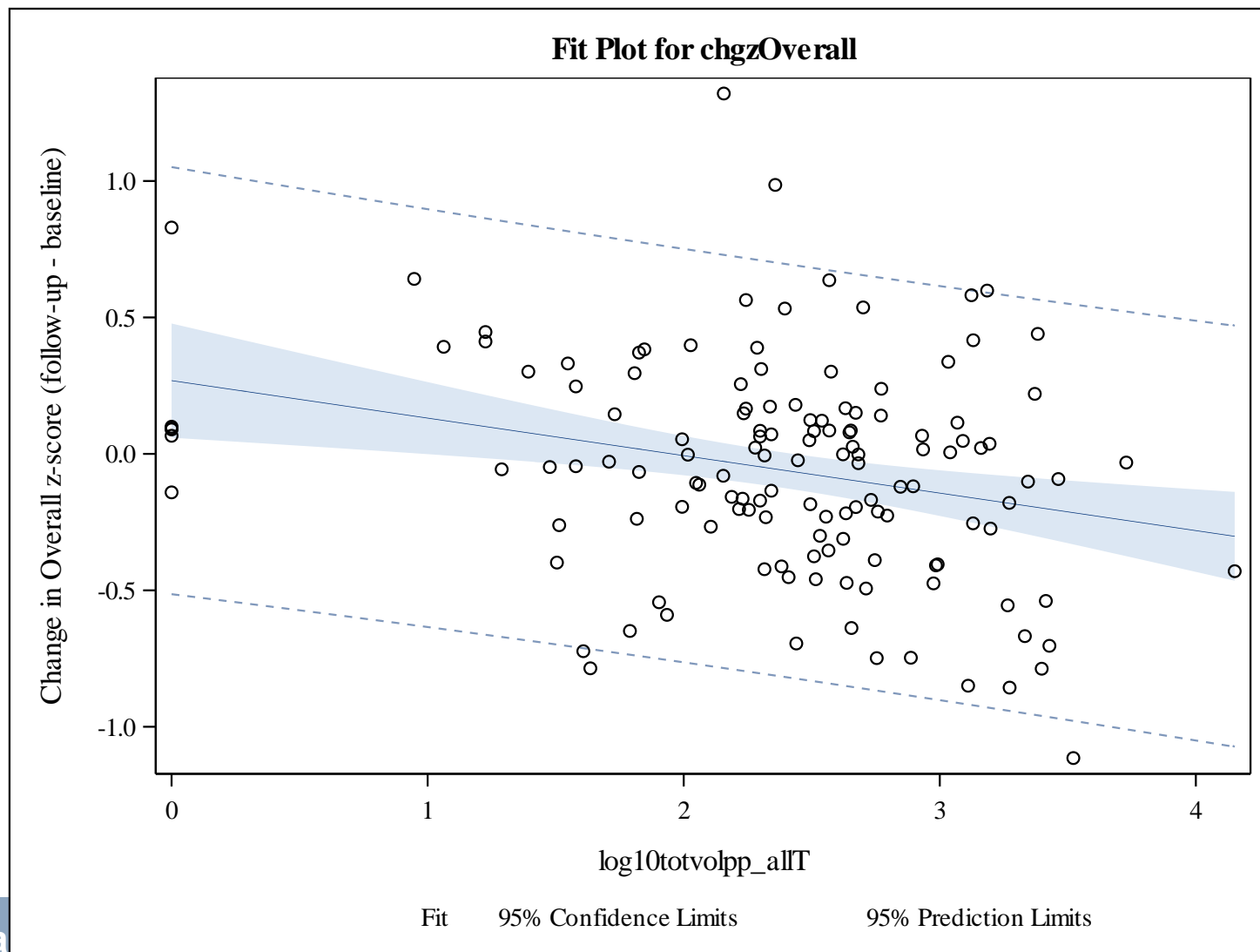
**Number**



**Location**



# Neurocognitive Changes and Lesions



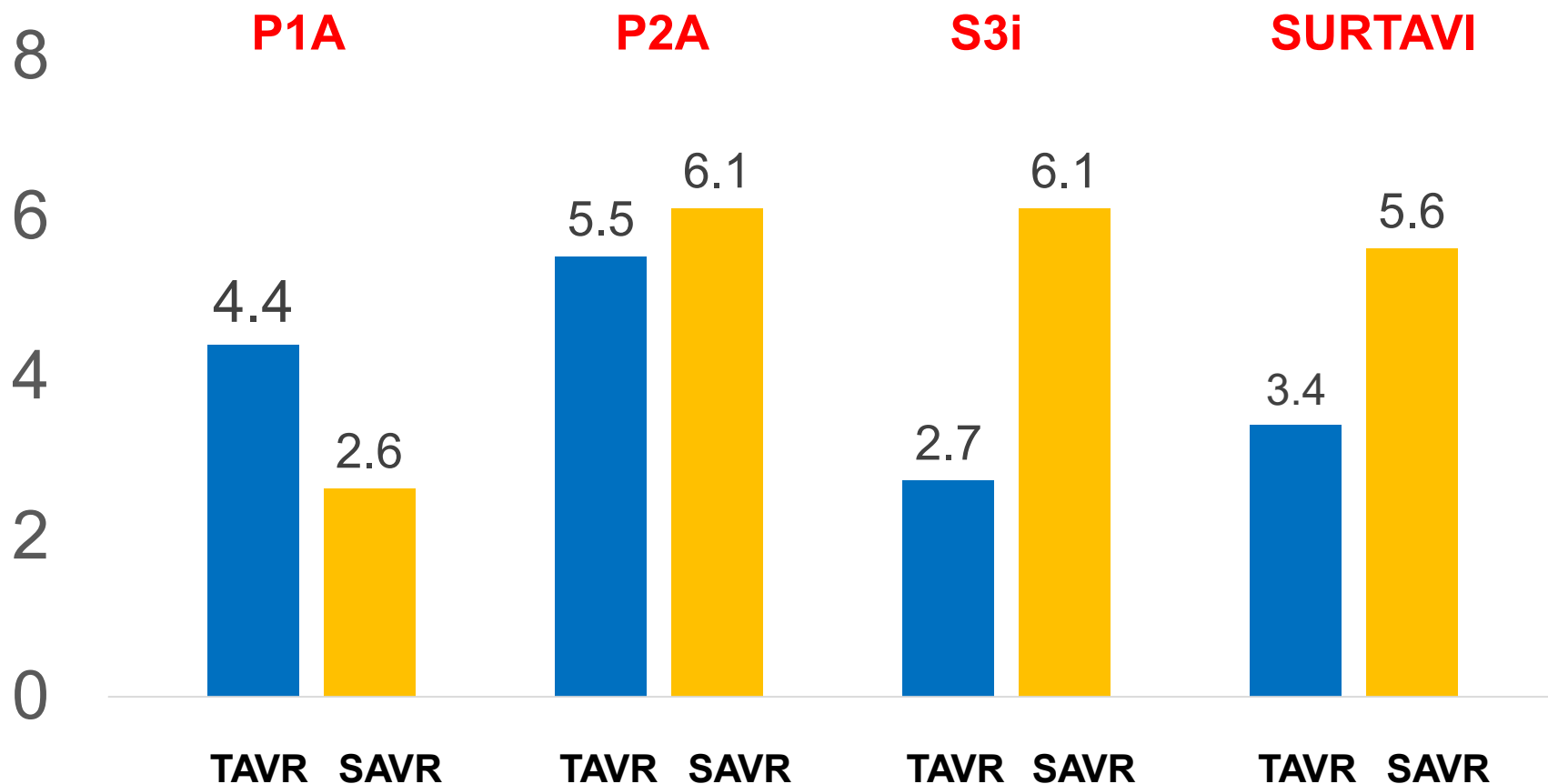
# Stroke Risk Summary

**Stroke risk is decreased compared to early feasibility trials (but not much) and is still a significant clinical problem**

# Questions

- **Is Stroke a Problem with TAVR in 2017?**
- **How Common is Stroke in Comparison With SAVR?**
- **Does Cerebral Protection Work?**

# Stroke : TAVR versus SAVR





# TAVR and SAVR Stroke

- **Risk of stroke with TAVR is not higher than risk of stroke with SAVR**

# Questions

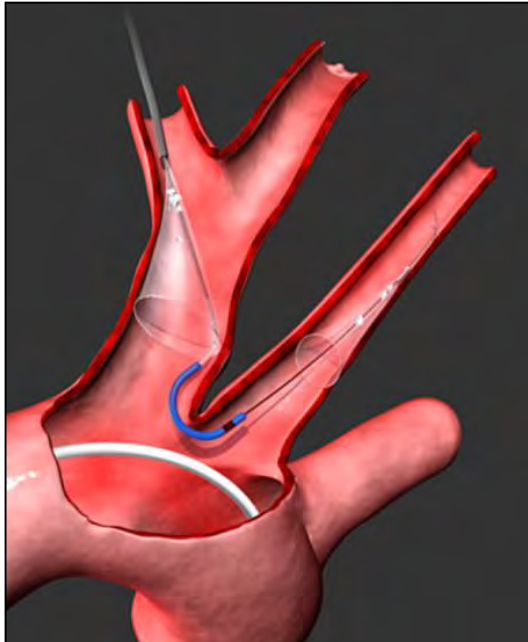
- **Is Stroke a Problem with TAVR in 2017?**
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# Cerebral Protection

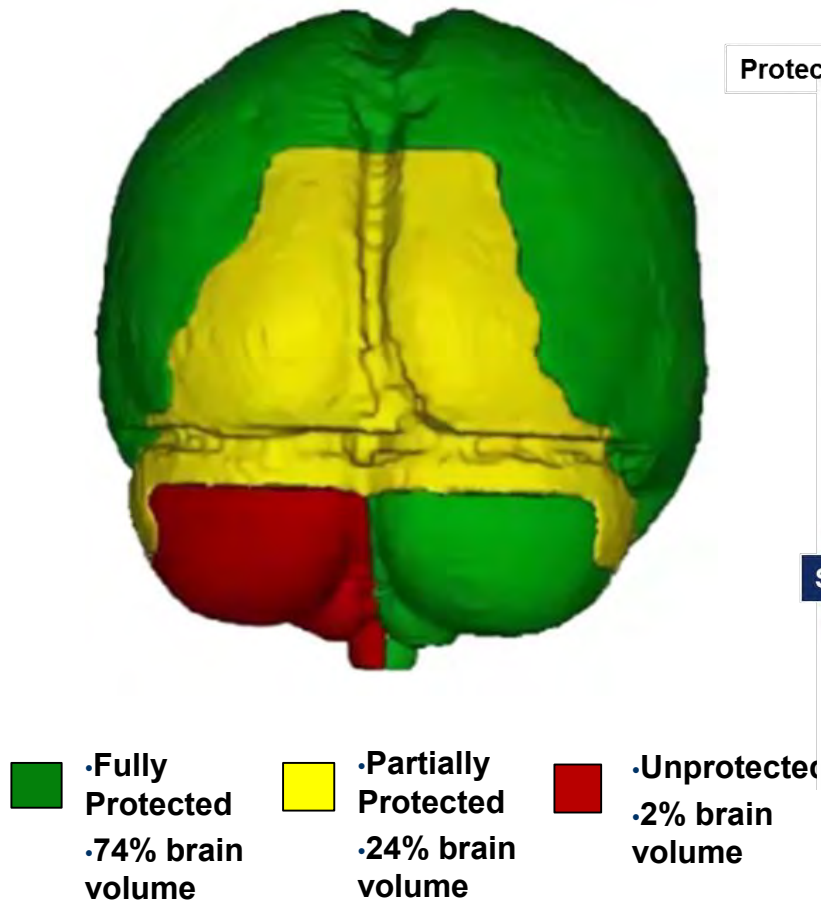
Company and Product	Claret Medical Sentinel 	Keystone TriGuard 	Edwards Embrella 	ICS Emblok 	Transverse Point-Guard 
<b>EU Status</b>	CE Mark 97% market share	CE Mark 3% market share	CE Mark <3% market share	FIM first clinical case March 15, 2017	Pre-clinical/prototype
<b>US Status</b>	IDE study completed Positive FDA Panel Feb 23, 2017	IDE trial underway	No IDE yet	No IDE yet	No IDE yet
<b>Access</b>	6 Fr Right Radial	9Fr TF	Right Radial	12Fr TF sheath	TF
<b>Debris</b>	Captures and removes	Deflects downstream	Deflects downstream	Captures and removes	Deflects downstream
<b>Placement and Interaction with TAVR devices</b>	Not in aortic arch	Sits in aortic arch. Devices must pass over and back across	Sits in aortic arch. Devices must pass over and back across	Sits in ascending aorta Devices must pass over and back across	Sits in aortic arch. Devices must pass over and back across

# Claret Medical™

## Sentinel™ Cerebral Protection System

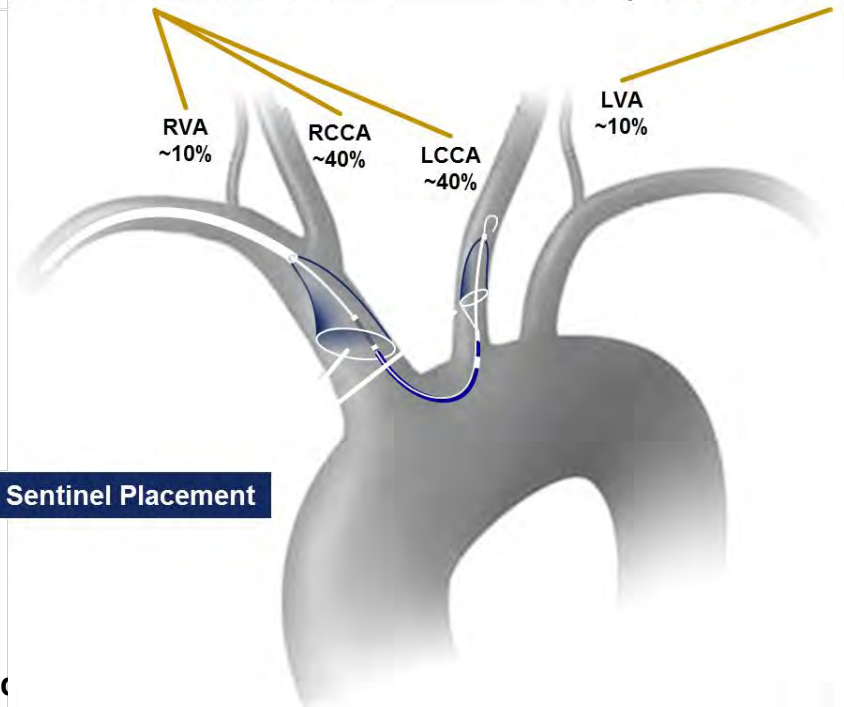


# Sentinel Filters Protection



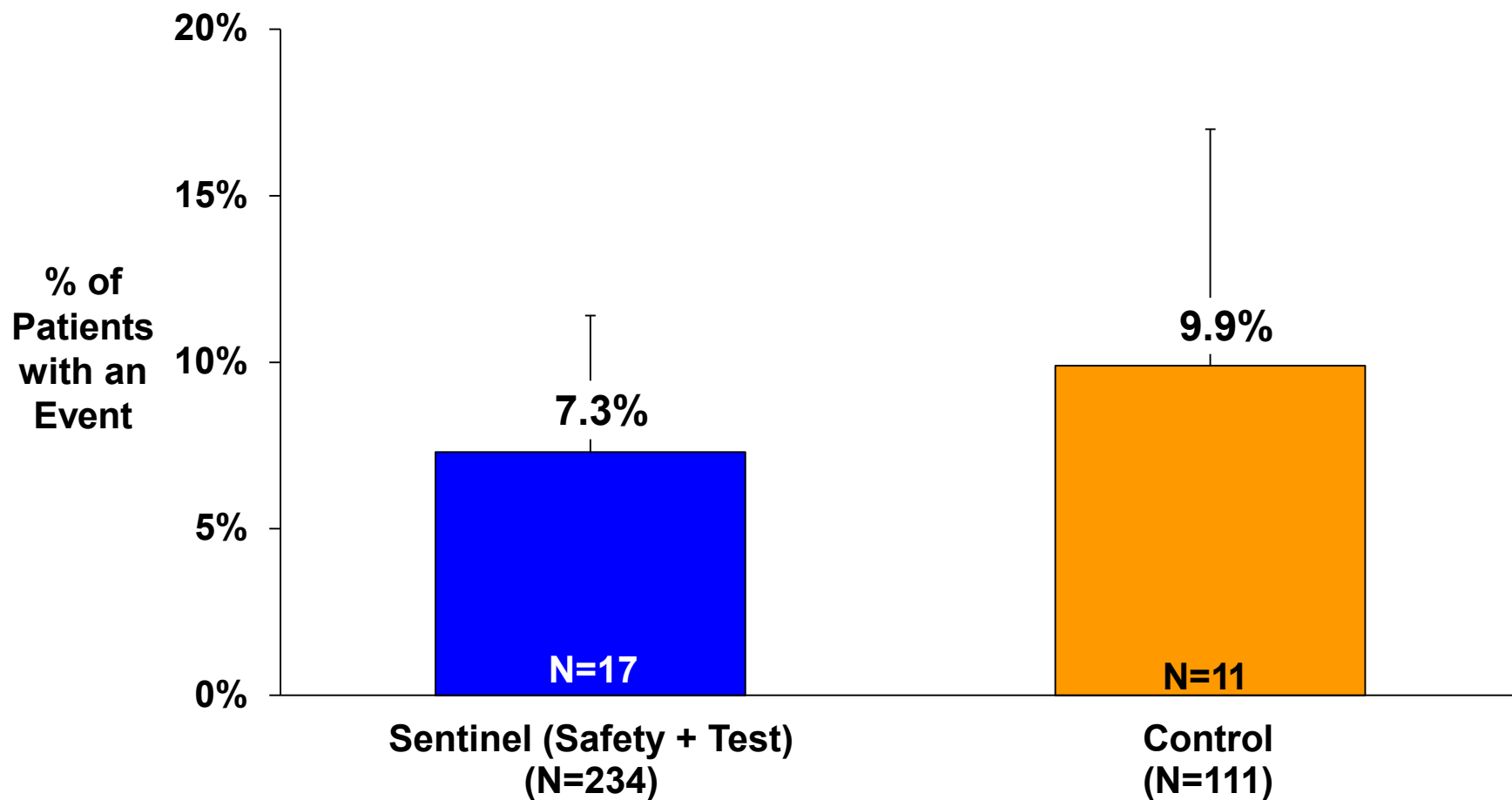
Protected blood flow to the brain

Unprotected blood flow to the brain

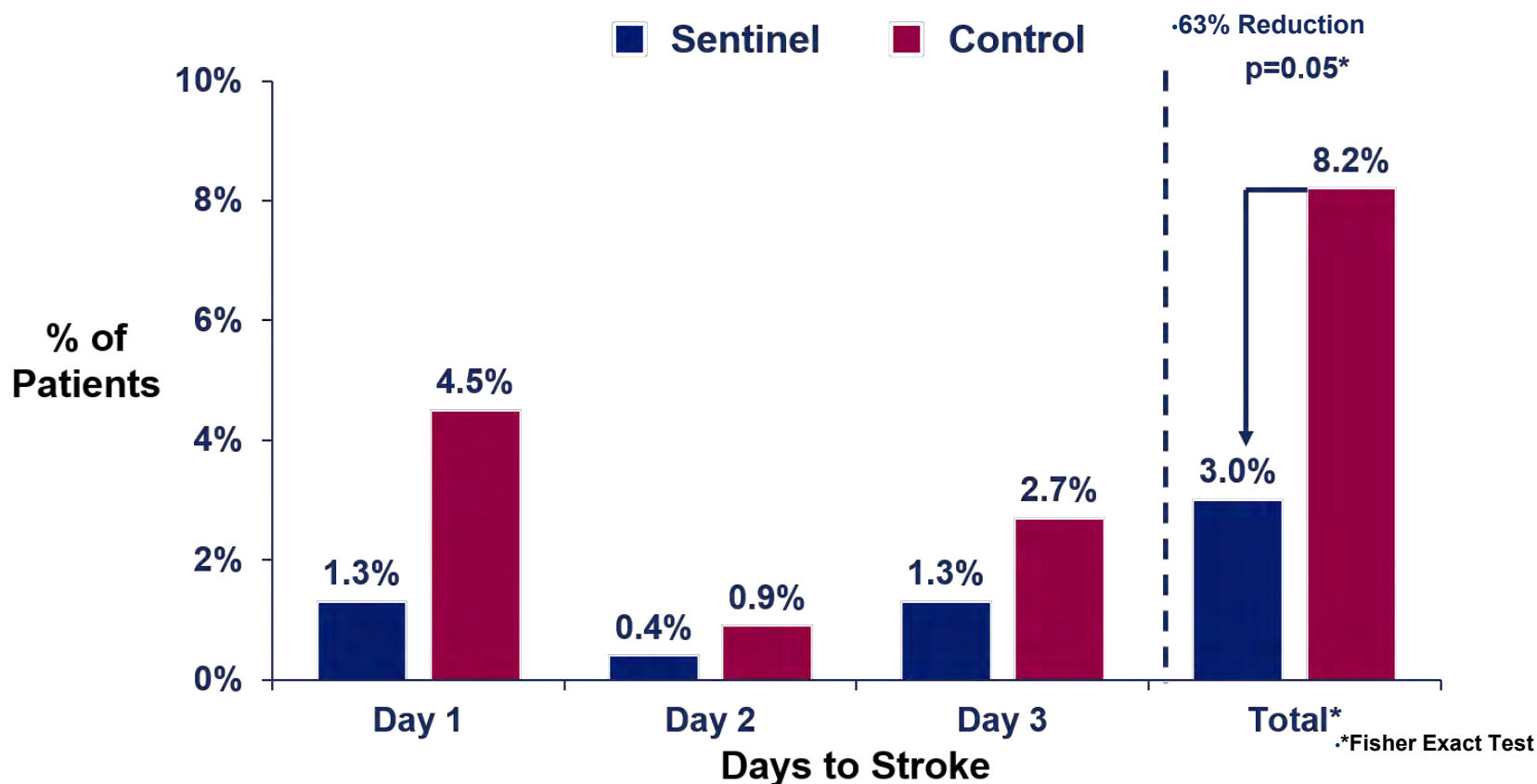


Zhao M, et al. Regional Cerebral Blood Flow Using Quantitative MR Angiography. *AJNR* 2007;28:1470-1473

# 30-Day MACCE Sentinel vs. Control (ITT)



# SENTINEL Study: Procedural Stroke



·95% of SENTINEL patients were evaluated by neurologists

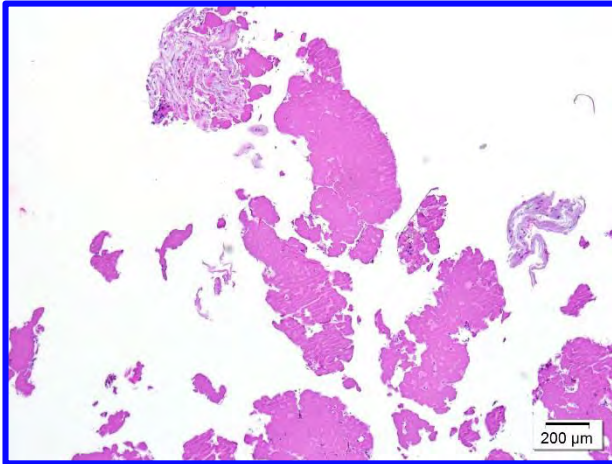
·Clinical Events Committee included 2 stroke neurologists

·SENTINEL trial. Data presented at Sentinel FDA Advisory Panel, February 23, 2017

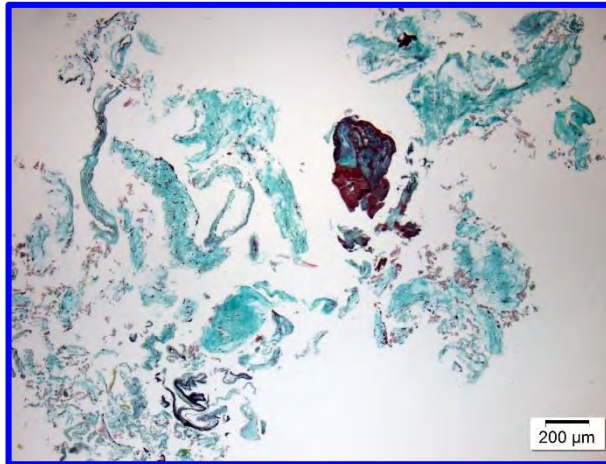


# Type of Tissue Identified

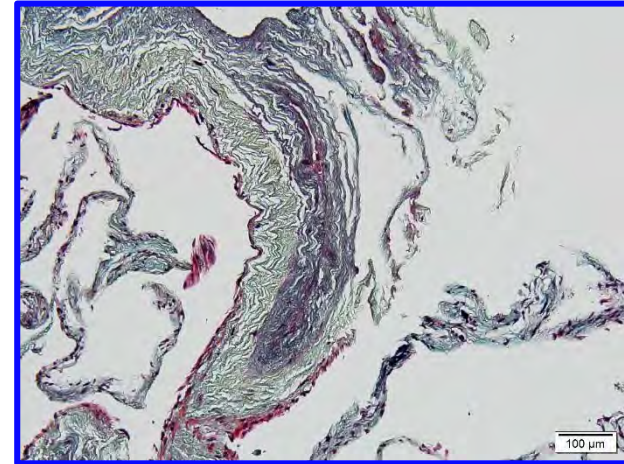
**Acute + organizing thrombus**



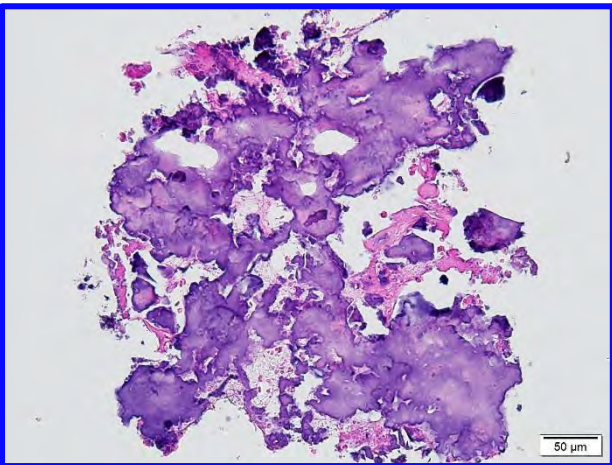
**Arterial wall + thrombus**



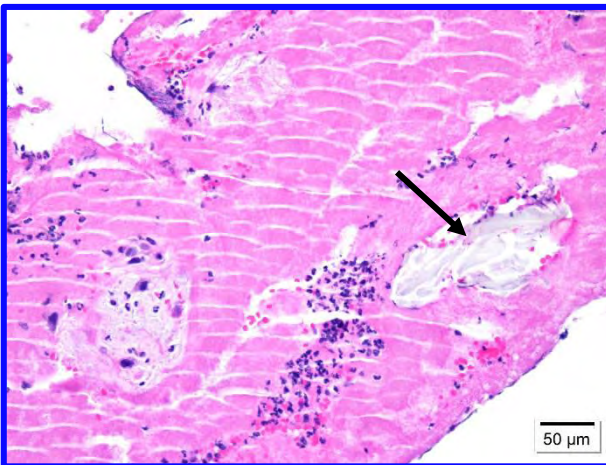
**Valve tissue**



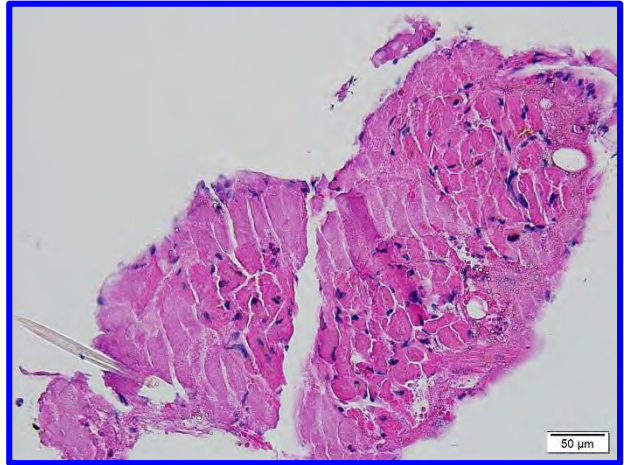
**Calcium nodules**



**Foreign material + thrombus**



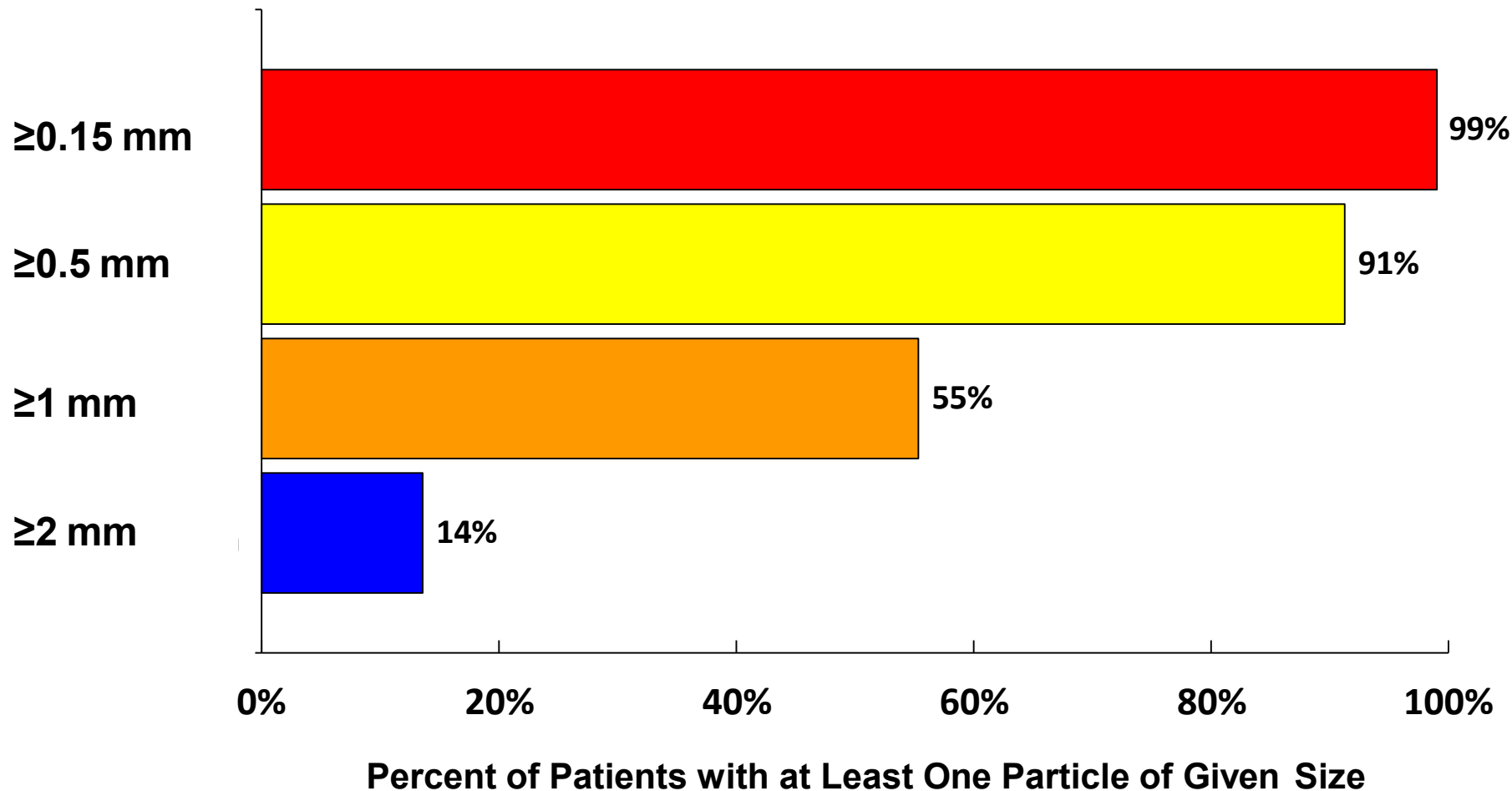
**Myocardium + thrombus**



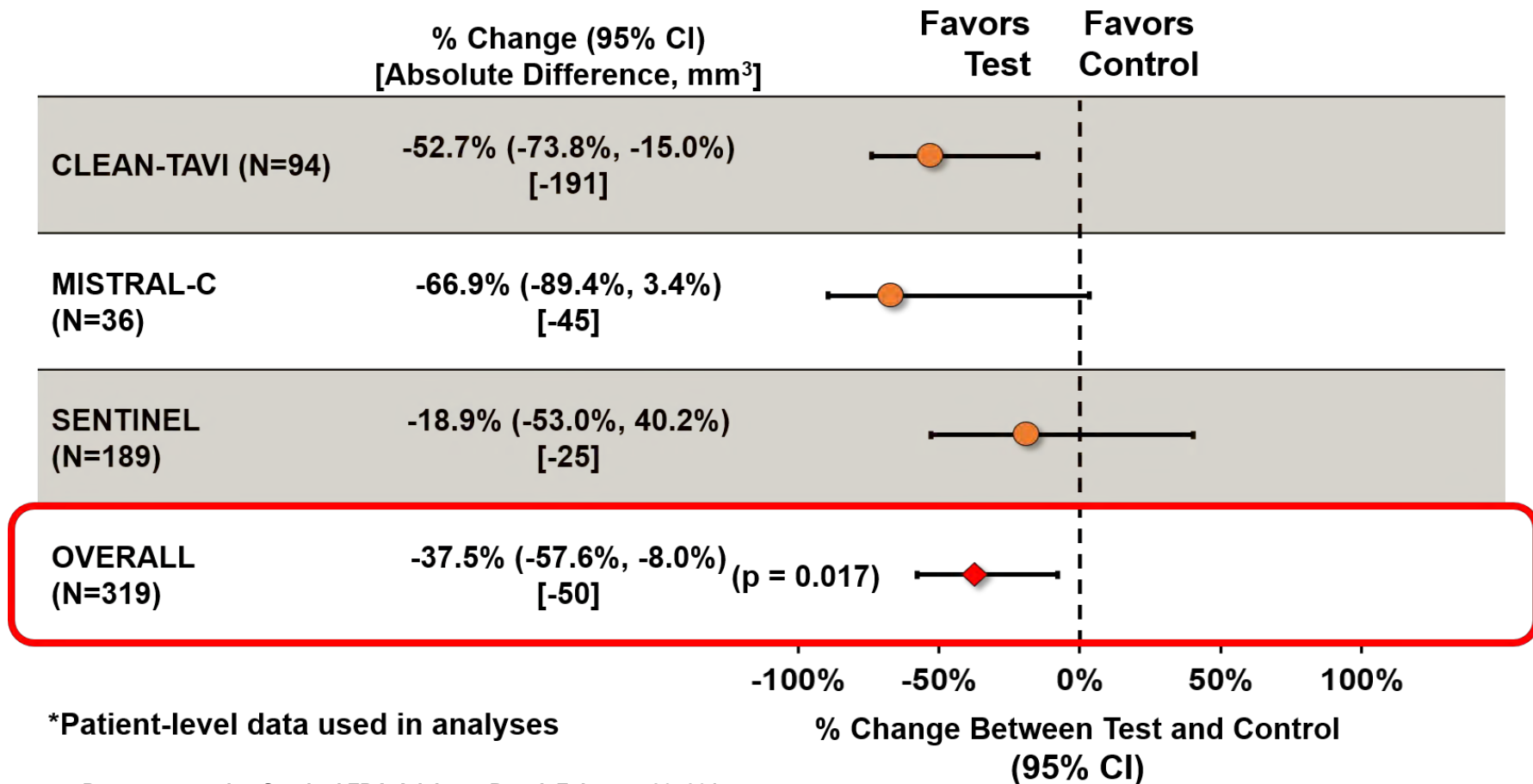


# Morphometric Analysis:

## Embolitic Material by Particle Size



# Patient Level Meta-analysis: CLARET Lesion Volume in Protected Territories

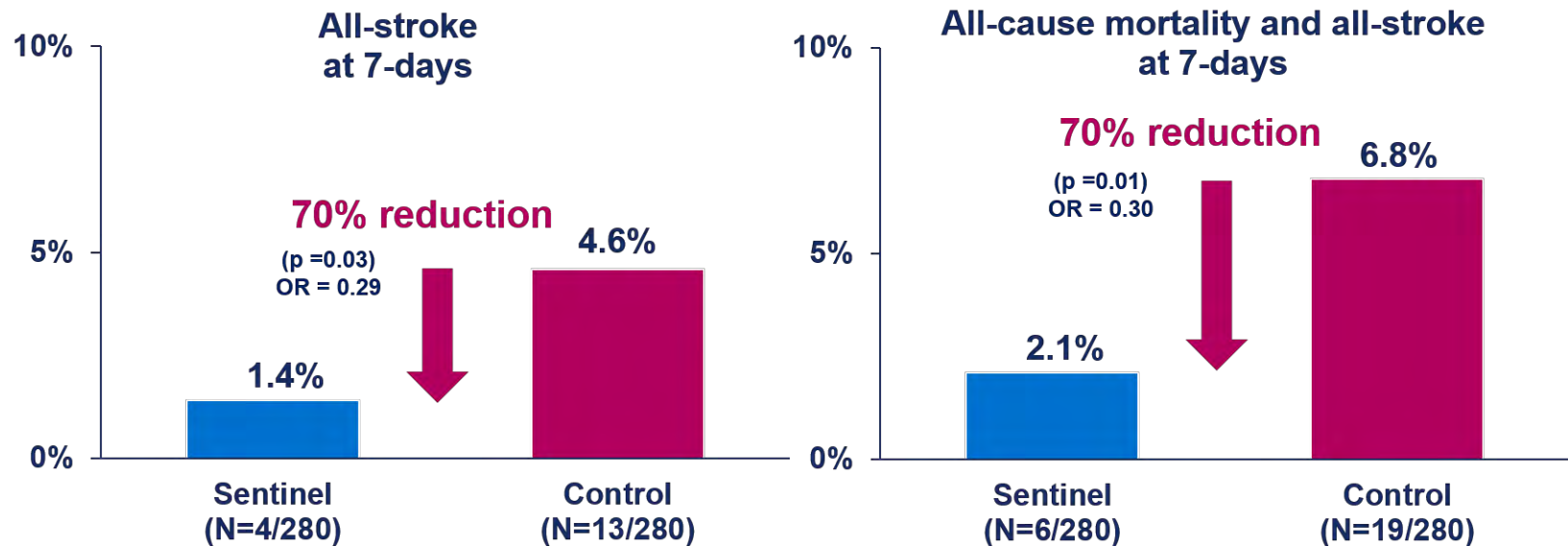


\*Patient-level data used in analyses

Data presented at Sentinel FDA Advisory Panel, February 23, 2017

# Ulm Sentinel study

- 802 all-comer consecutive TAVR patients at University of Ulm were prospectively enrolled
- A propensity-score analysis was done matching the 280 patients protected with Sentinel to 280 control patients



- In multivariable analysis, TAVR without cerebral emboli protection (p=0.044) was the only independent predictor for stroke at 7-days
- TAVR without cerebral emboli protection (p=0.028) and STS score (<8 vs. ≥8) (p=0.021) were the only independent predictors for mortality and stroke at 7-days



# Predictors of Stroke, Neuro events or MRI findings

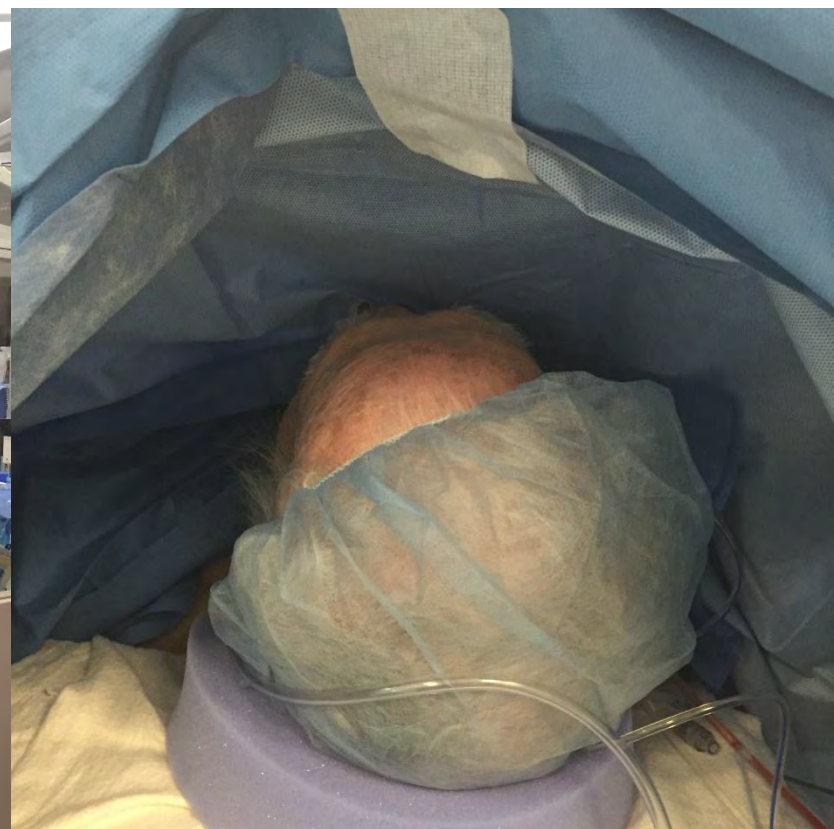
Author	N	Event rate	Approach	Clinical predictors	Anatomical predictors
Tay et al 2011	253	9%	TA/TF	H/O stroke/TIA	Carotid stenosis*
Nuis et al 2012	214	9%	TF	New onset AF	Baseline AR >3+
Amat Santos et al 2012	138	6.5%	TA/TF	New onset AF	None
Franco et al 2012	211	4.7%	TA/TF	None	Post-dilation
Miller et al 2012	344	9%	TA/TF	History of stroke Non TF-TAVR candidate	Smaller AVA
Cabau et al 2011	60	68% (MRI)	TA/TF	Male, History of CAD	Higher AVG
Fairbairn et al 2012	31	77% (MRI)	TF	Age	Aortic atheroma
Nombela-Franco et al 2012	1061	5.1%	TA/TF	Balloon postdilatation, valve dislodgement, New onset AF, PVD, Prior CVA	

# Summary

- **There is benefit of emboli prevention**
  - **Clinical benefit**
  - **“Covert” stroke benefit**
- **We can’t reliably identify patients at risk and 99% patients have embolic material in filter**
- **Device is safe**
- **Emboli prevention devices should be considered in all patients undergoing TAVR**

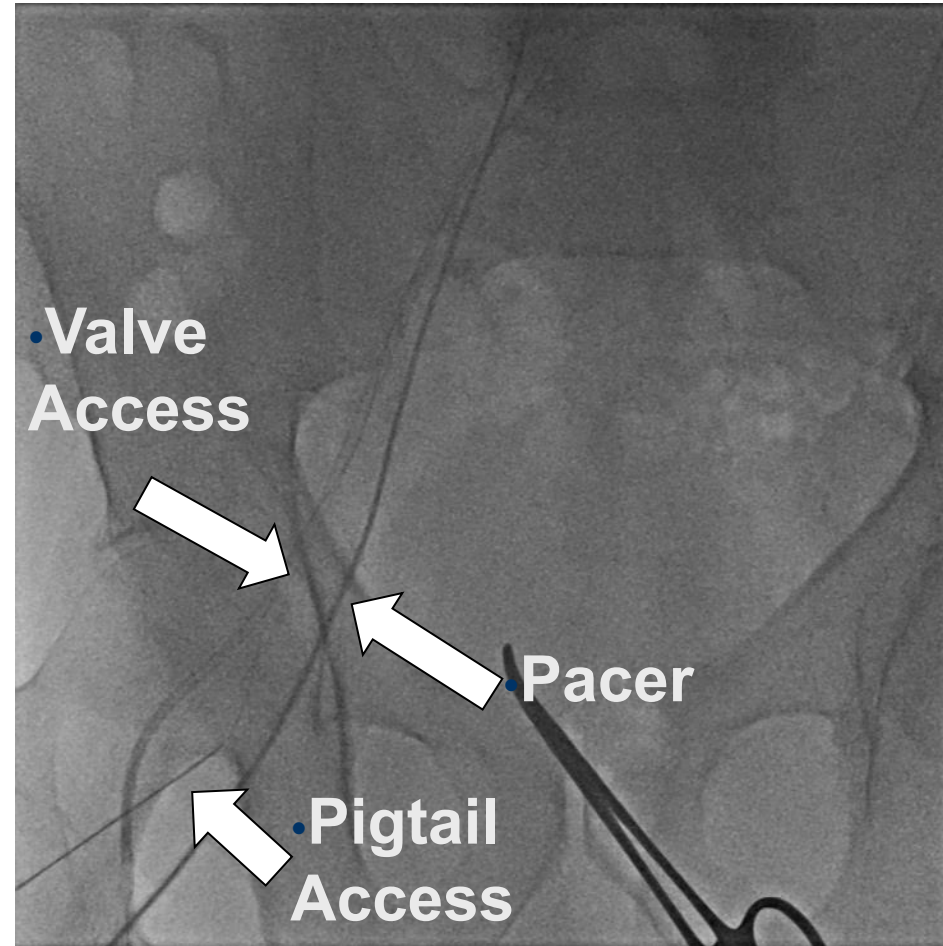
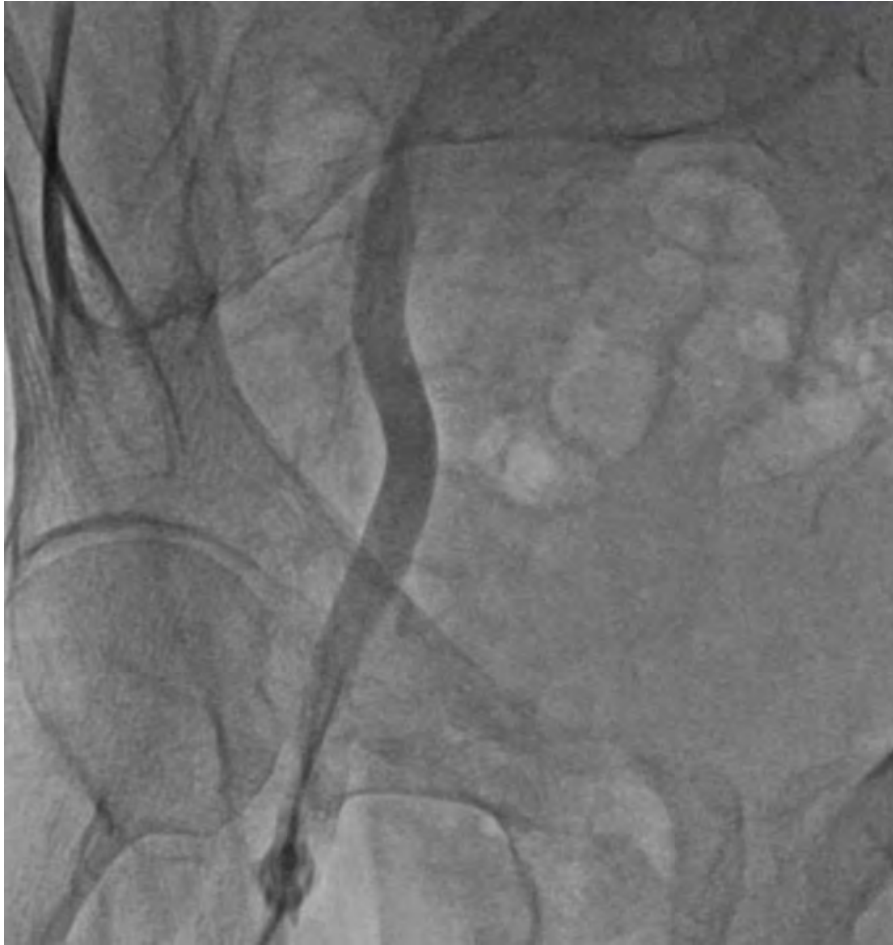
# TAVR in 2018

## Conscious sedation, TTE

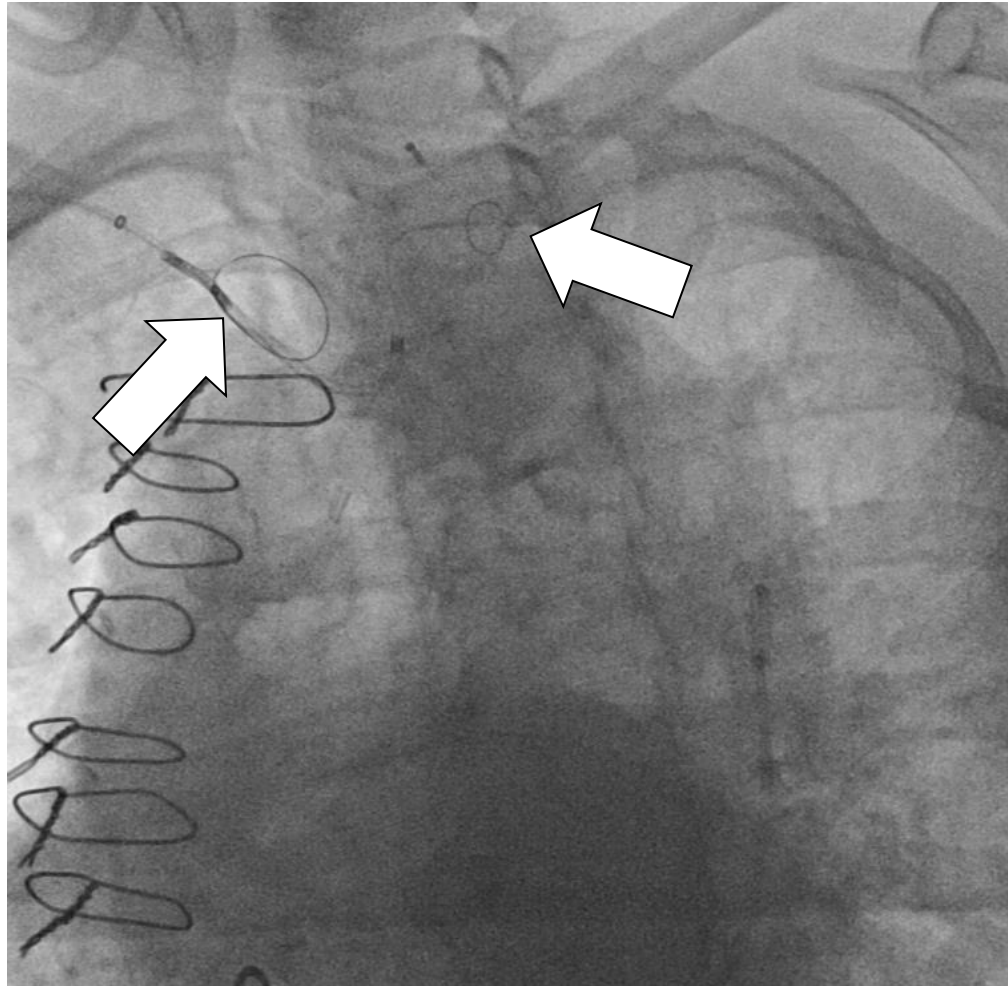




# One Perclose and Same Side Sheath

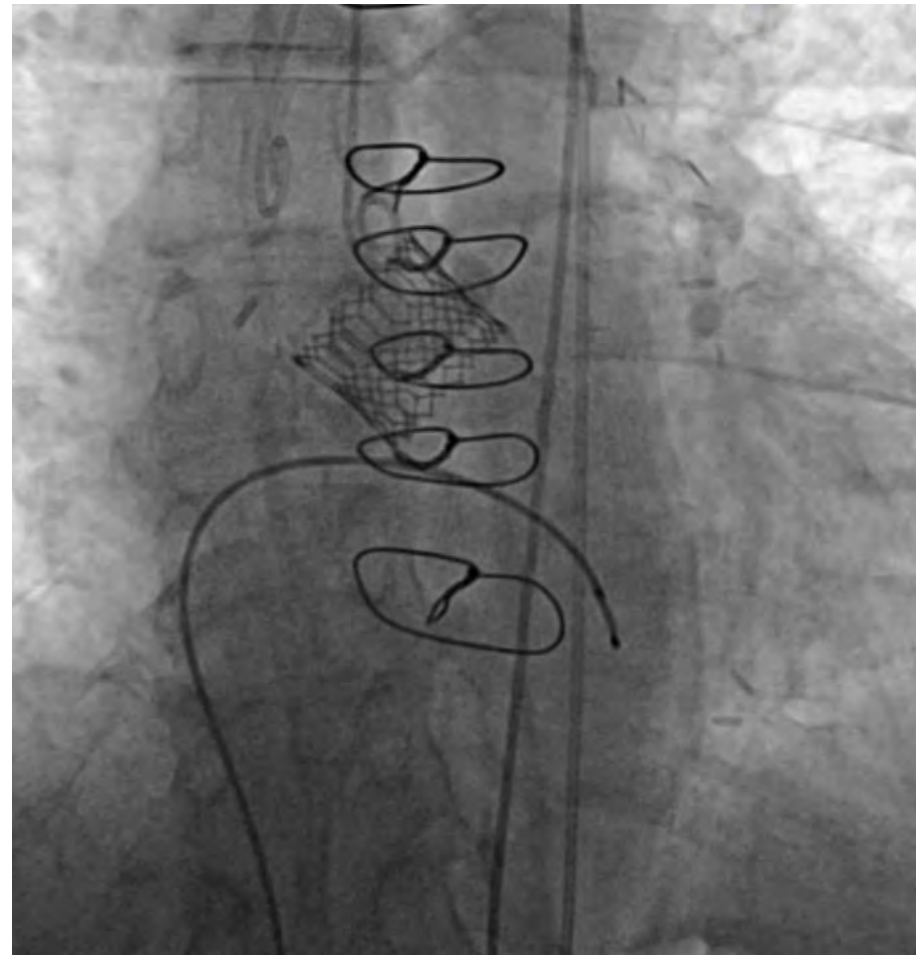
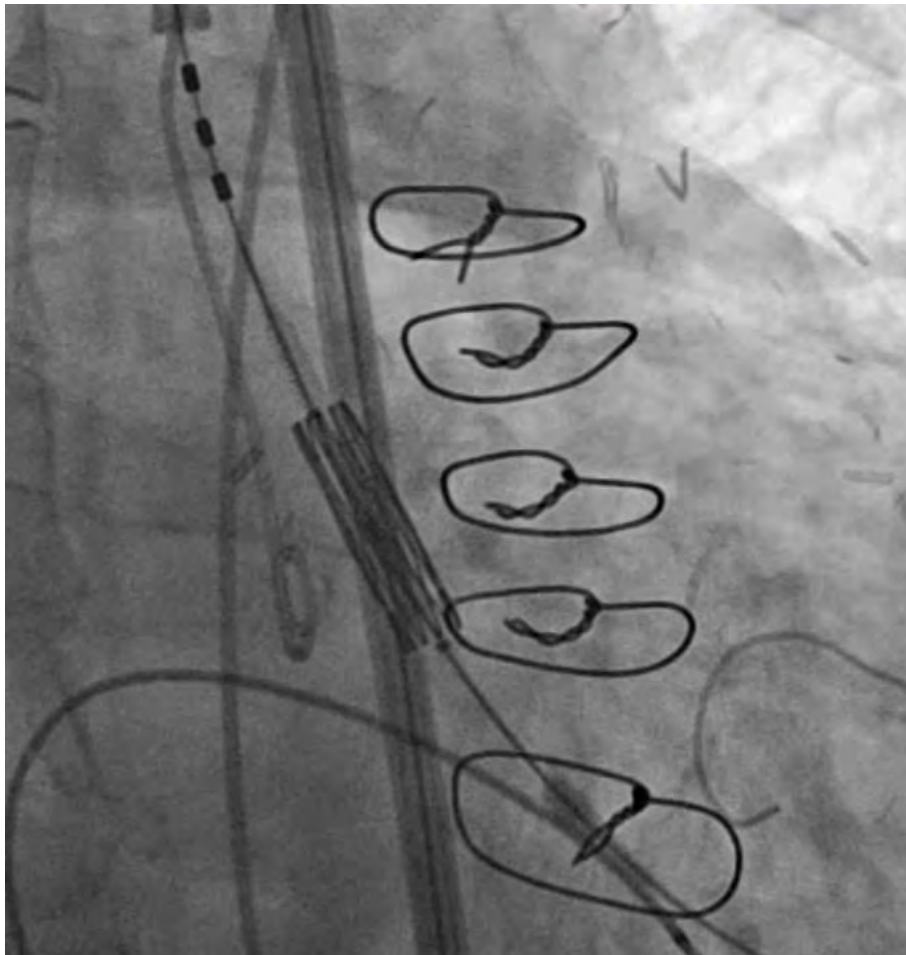


# Sentinel





# Valve Deployment



# Final Picture



# Procedural Log

08:47 "5 F Temporary Pacing wire inserted and advanced to RV.  
Position verified under fluoroscopy and connected to external  
device. Thresholds are checked. Settings remain at: Rate= 30  
BPM, MA= 20."  
08:57 Advancing Sentinel Filter system  
09:09 26 mm Sapien 3 Valve implanted paced @ 180 bpm  
09:13 Filter system removed  
09:15 Right femoral angiogram performed.

**8:47 to 9:15 = 28 minutes**

**Access, temp wire, Sentinel, Valve deployment  
Closure of groin**

**Fluorotime 11 minutes**

**Radiation 159 mGy**