SNUH 분당서울대학교병원
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

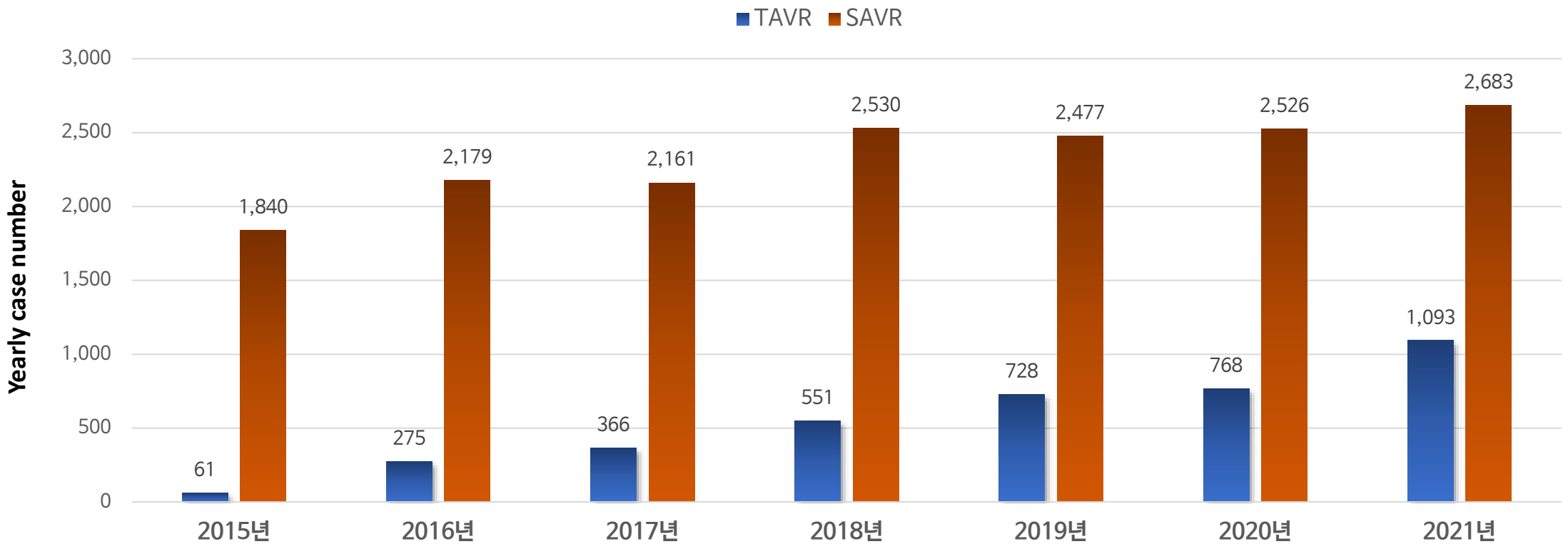
My Personal Experience with Sentinel Device

Sentinel cerebral protection system

Seoul National Univeristy Bundang Hospital

Si-Hyuck Kang, MD, PhD

TAVR/SAVR trends in Korea



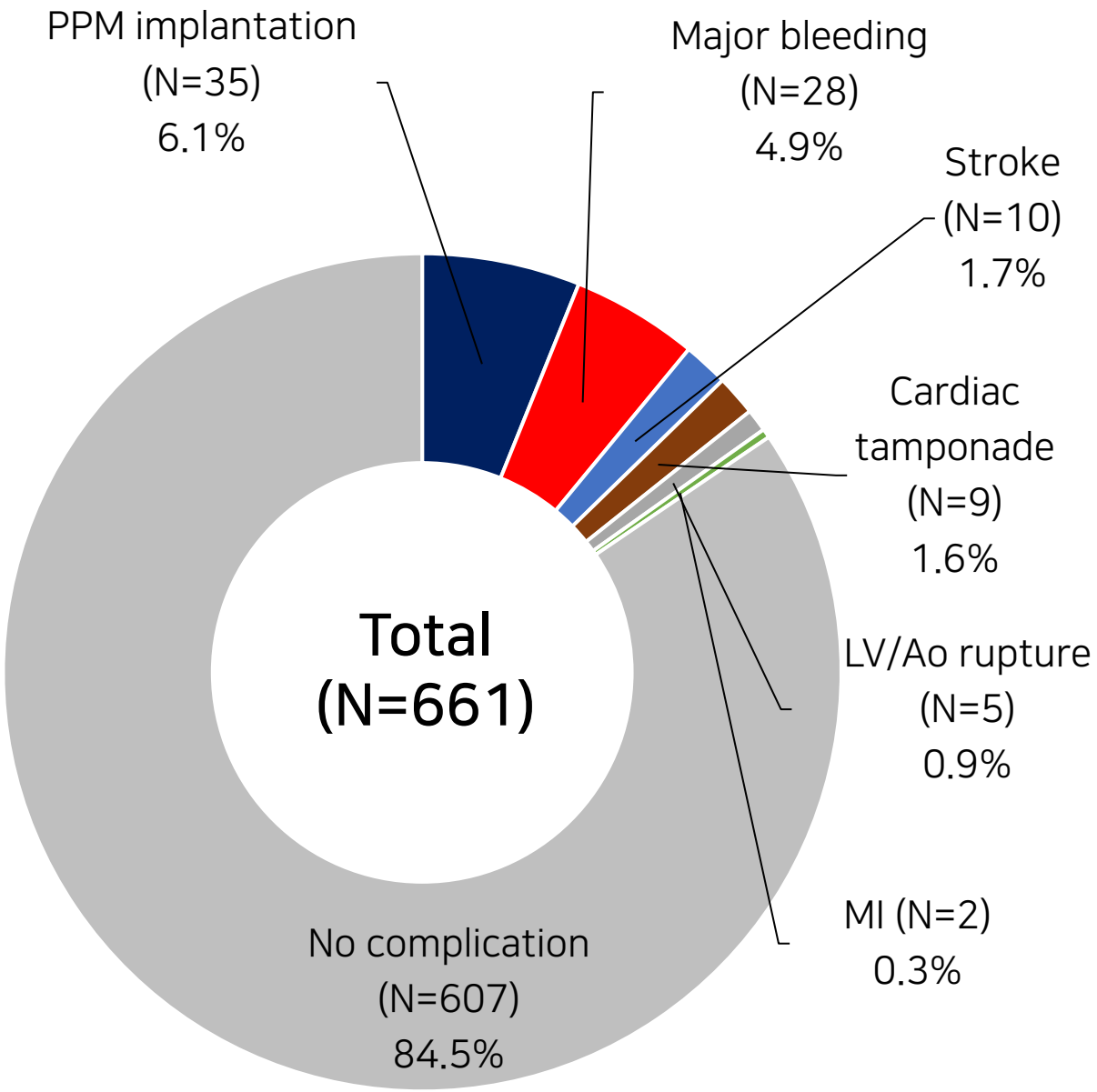
Source: HIRA healthcare big data Hub (2023)

SNUH 분당서울대학교병원

Complications after TAVR

K-TAVI registry

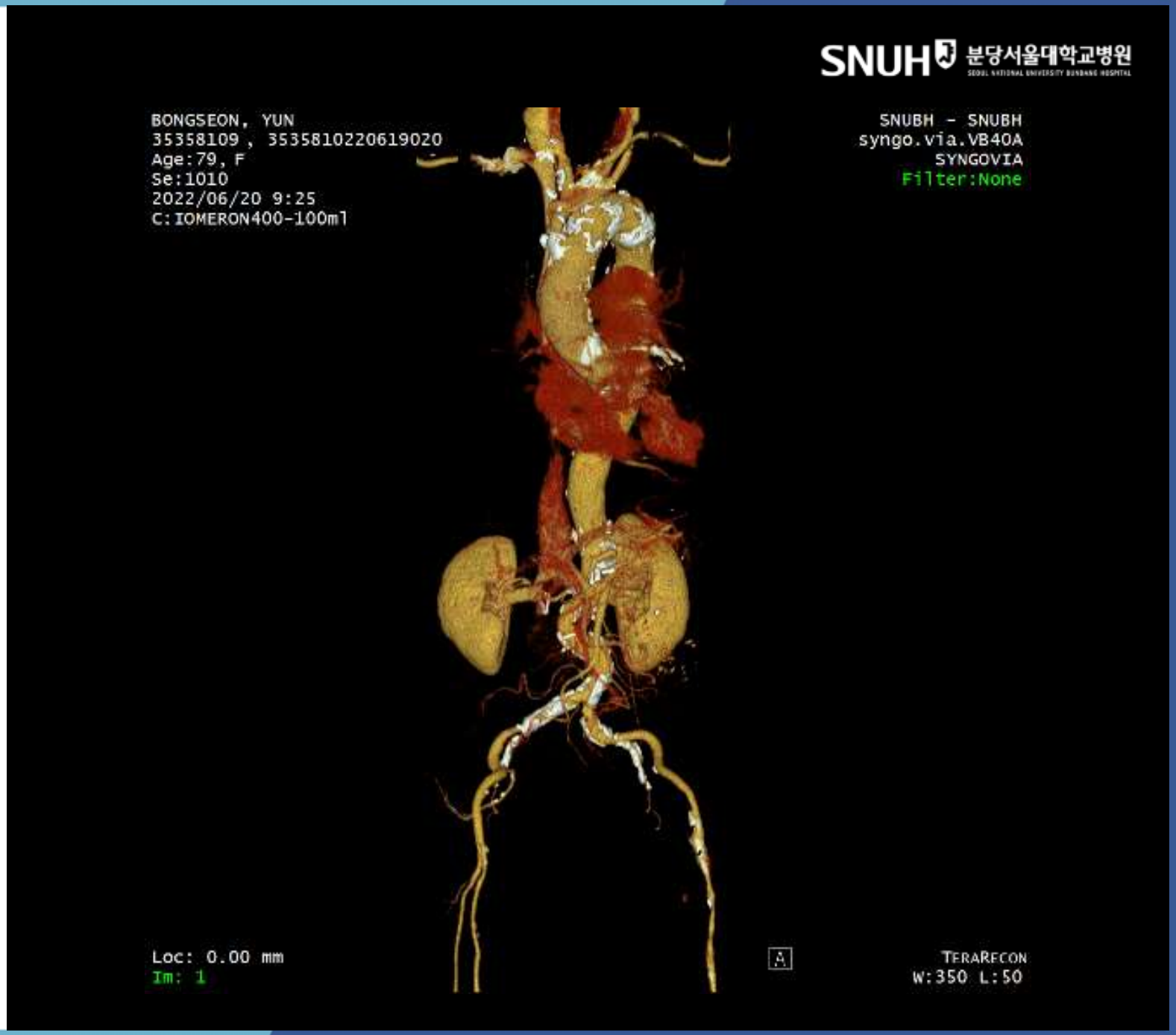
(Korean Transcatheter
Aortic Valve Implantation)



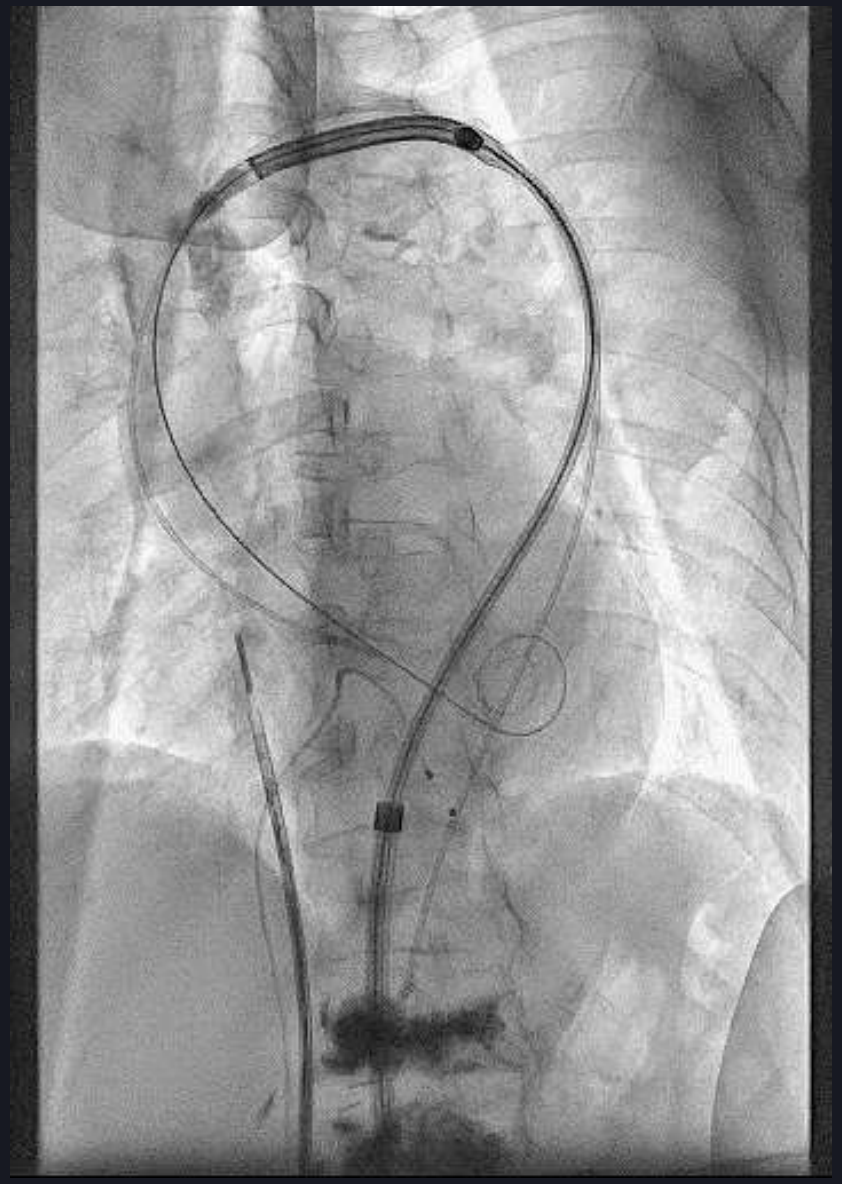
Yu CW et al. KCJ 2018

Case

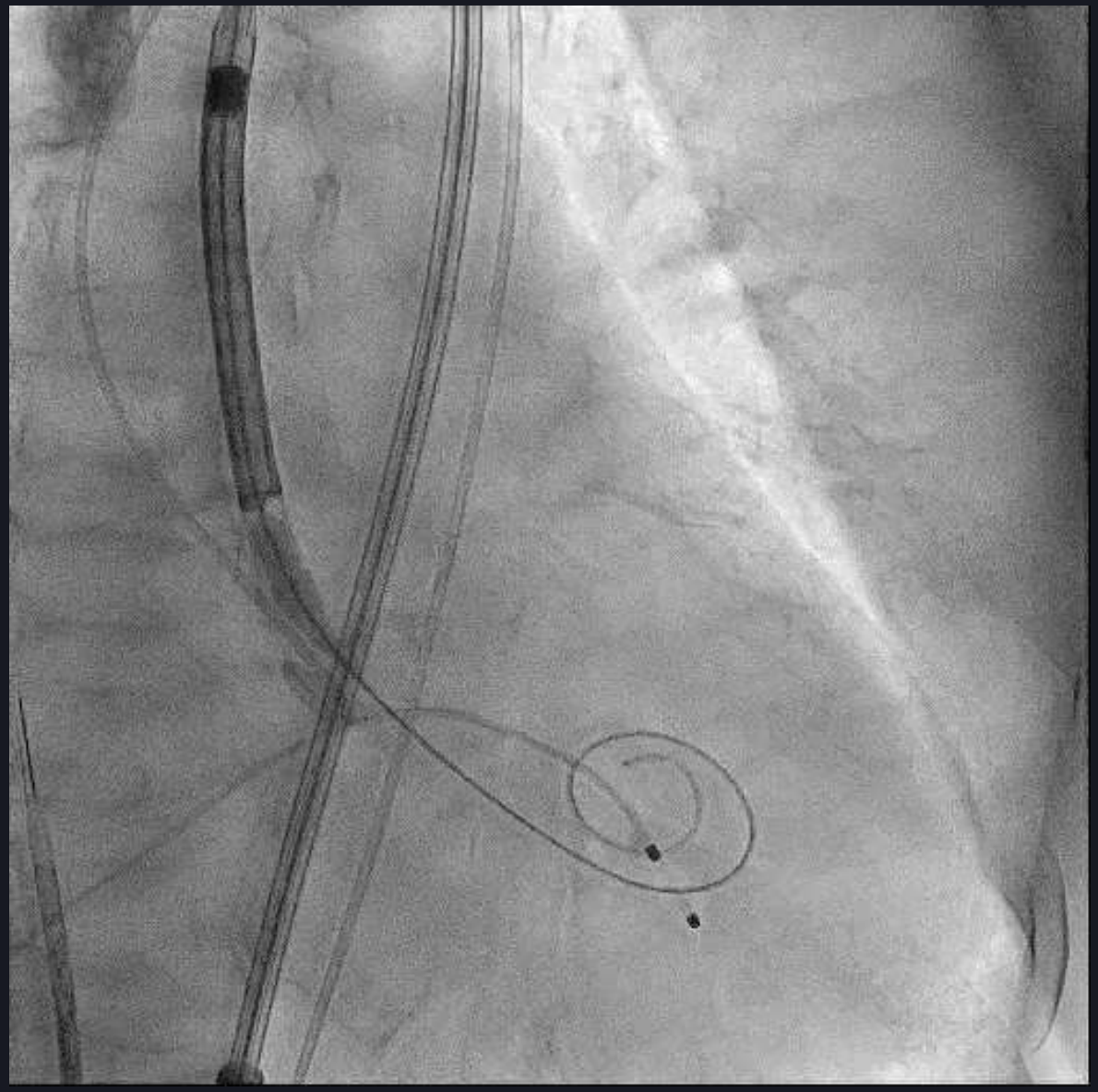
Stroke M/80



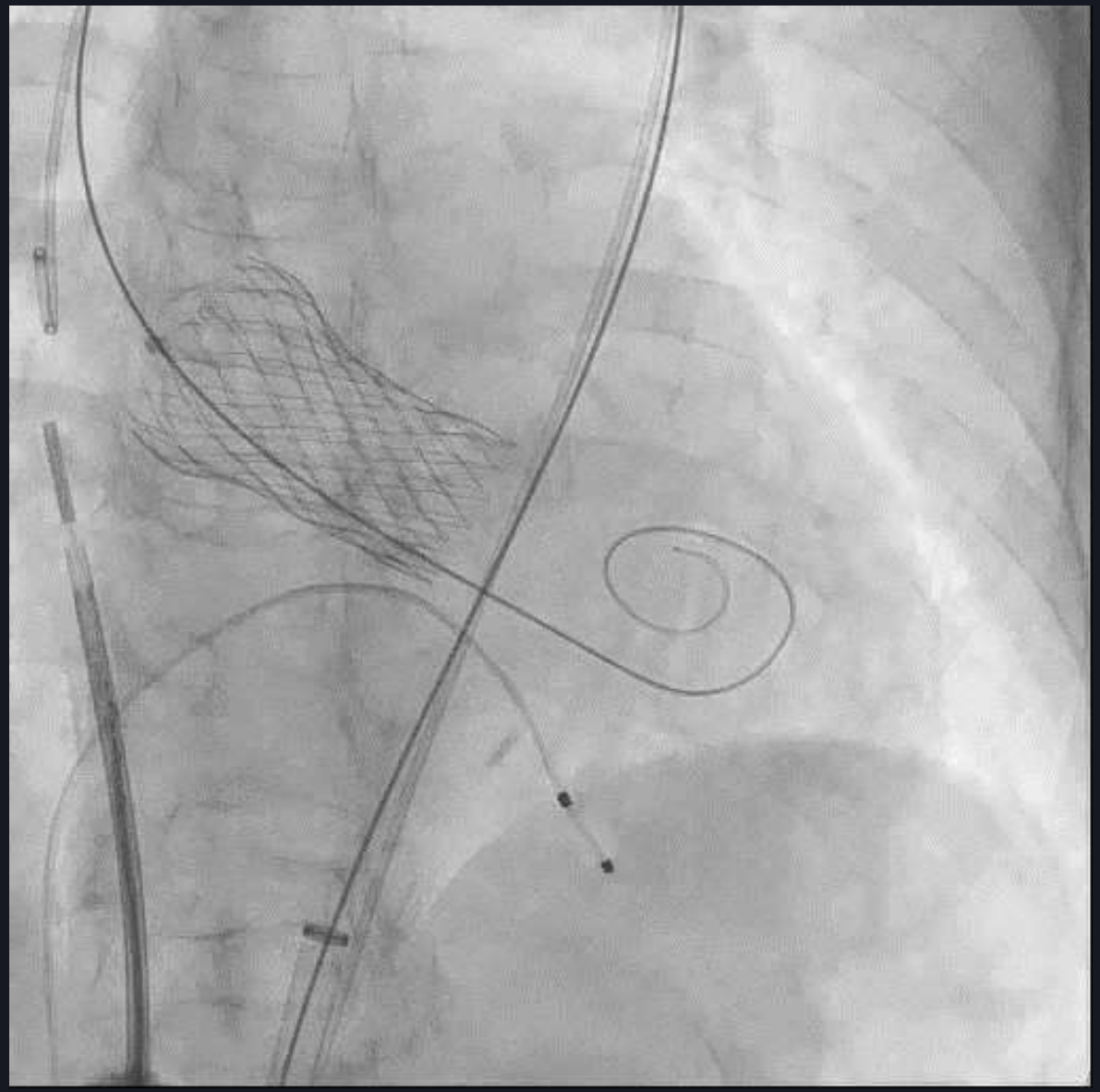
Device Advancement



Aortic valve crossing



Successful TAVR: Evolut Pro 29 mm



Hospital course

Post-TAVR 3D

Developed headache with dizziness and nausea

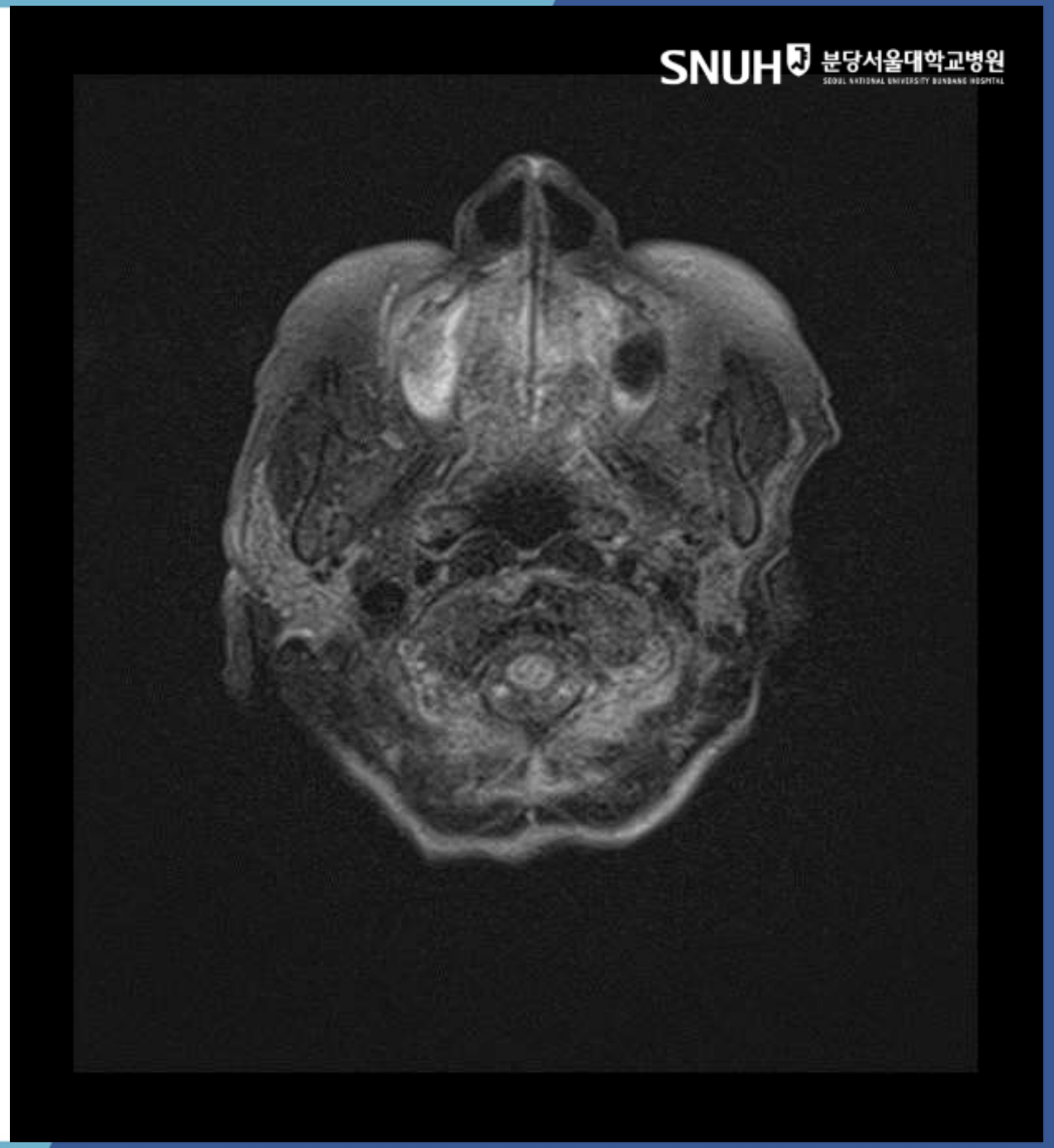
Right arm weakness picking up spoons

Disappeared within an hour

- Brain MRI: Multiple scattered probably acute embolic infarctions
- Holter: AF (-)

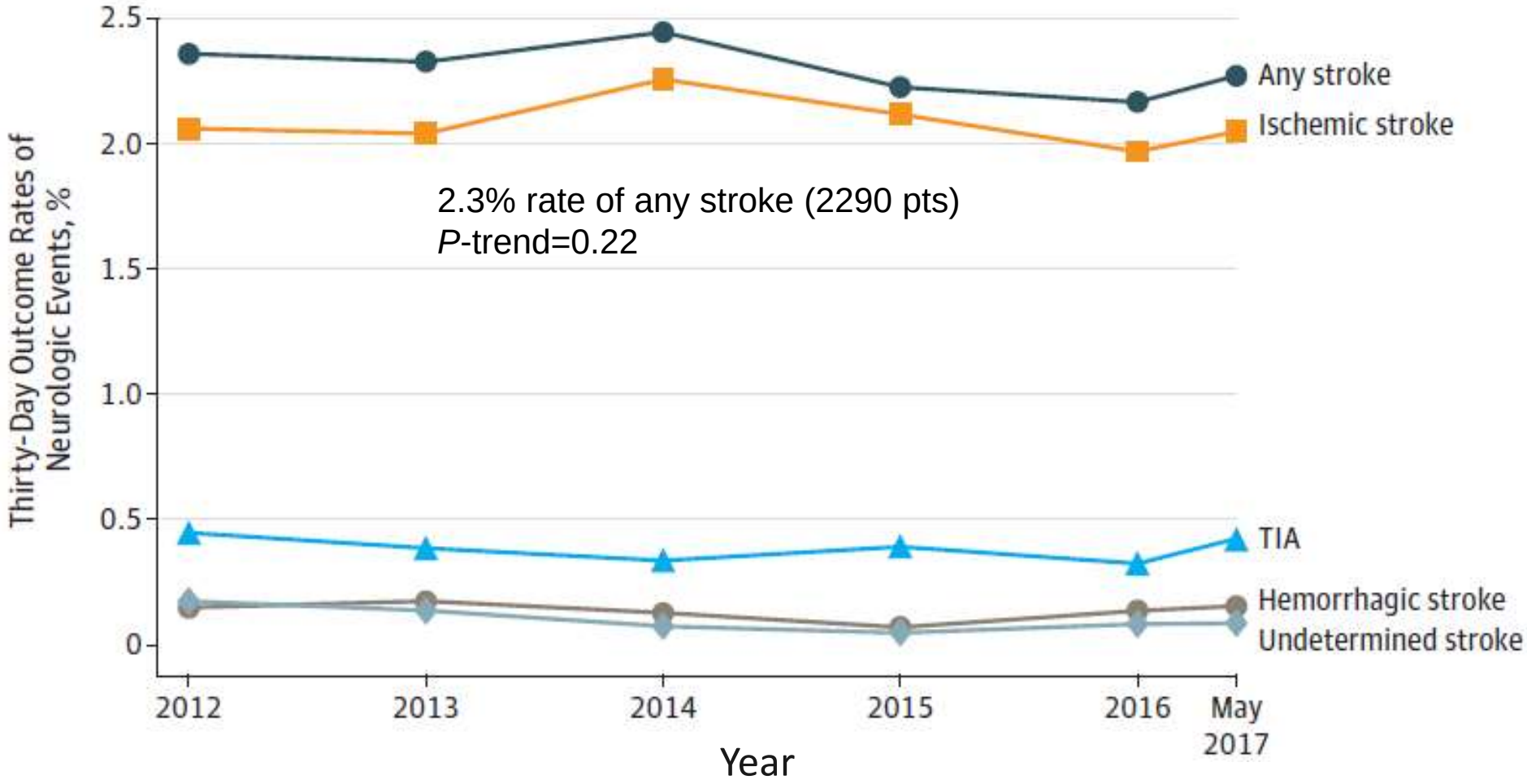
Post-TAVR 7D

- Discharged without neurologic deficit



Stroke Rate Over Time

2290 strokes at 30-days among N=101,430 patients who underwent TAVR at 521 US sites from 2011-2017.
STS/ACC TVT Registry



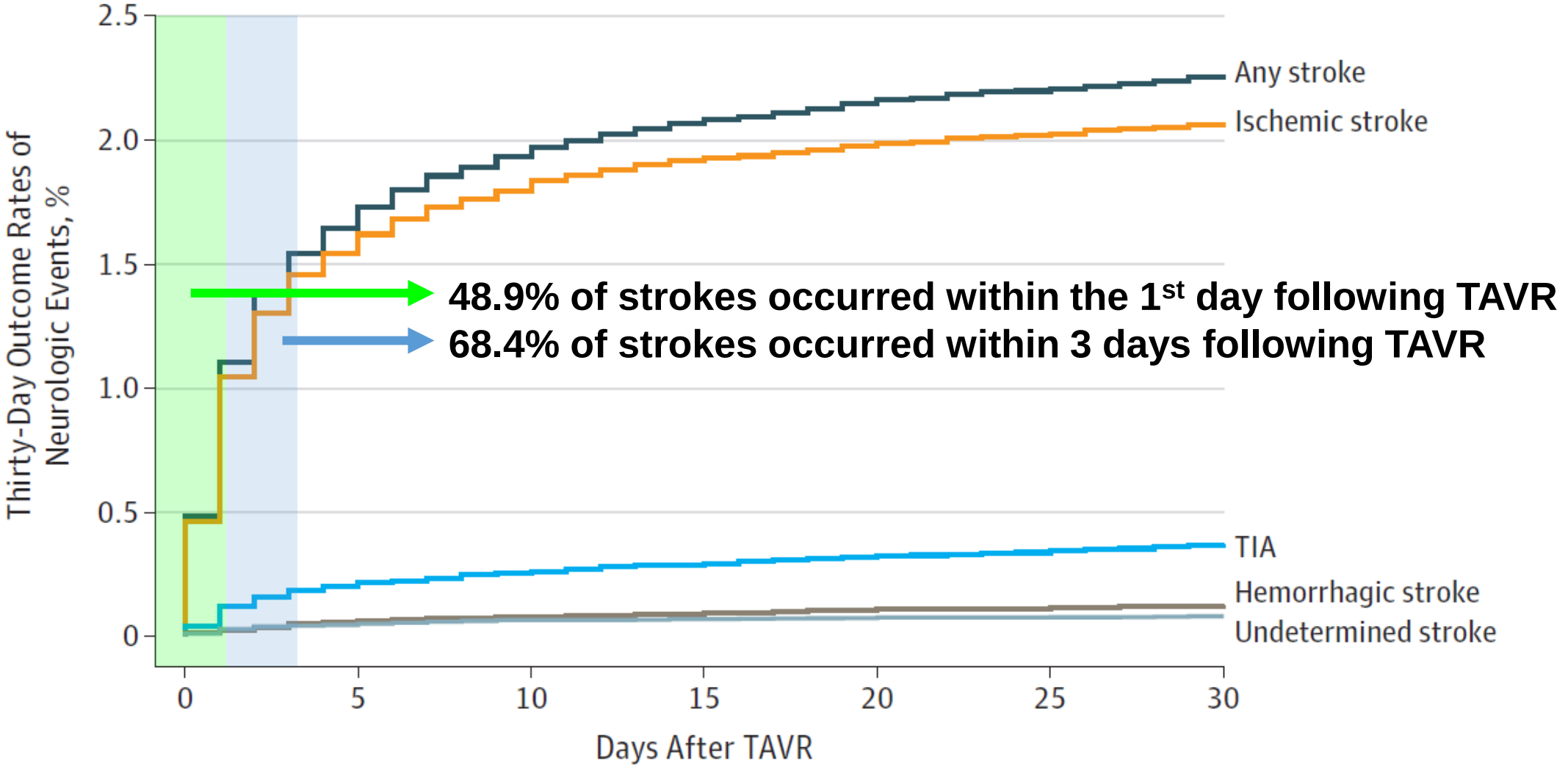
Despite newer-generation valve technology, real-world data demonstrates rate of stroke remains consistent over time.

Huded, C. et al. *JAMA*. 2019 Jun 18;321(23):2306-2315. doi: 10.1001/jama.2019.7525

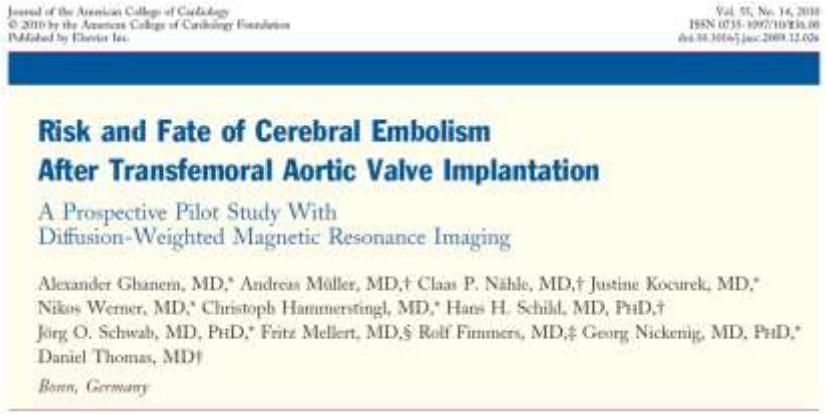
Stroke Timing Post-TAVR

Retrospective cohort study of N=101,430 patients from the STS/ACC TVT Registry (2011-2017) who underwent TAVR at 521 US hospitals

Majority of strokes within 30 days occurred within first 3 days following TAVR



Huded, C. et al. *JAMA*. 2019 Jun 18;321(23):2306-2315. doi: 10.1001/jama.2019.7525



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ISSN 0735-1097/10$36.00
doi:10.1016/j.jacc.2009.12.026

Risk and Fate of Cerebral Embolism After Transfemoral Aortic Valve Implantation

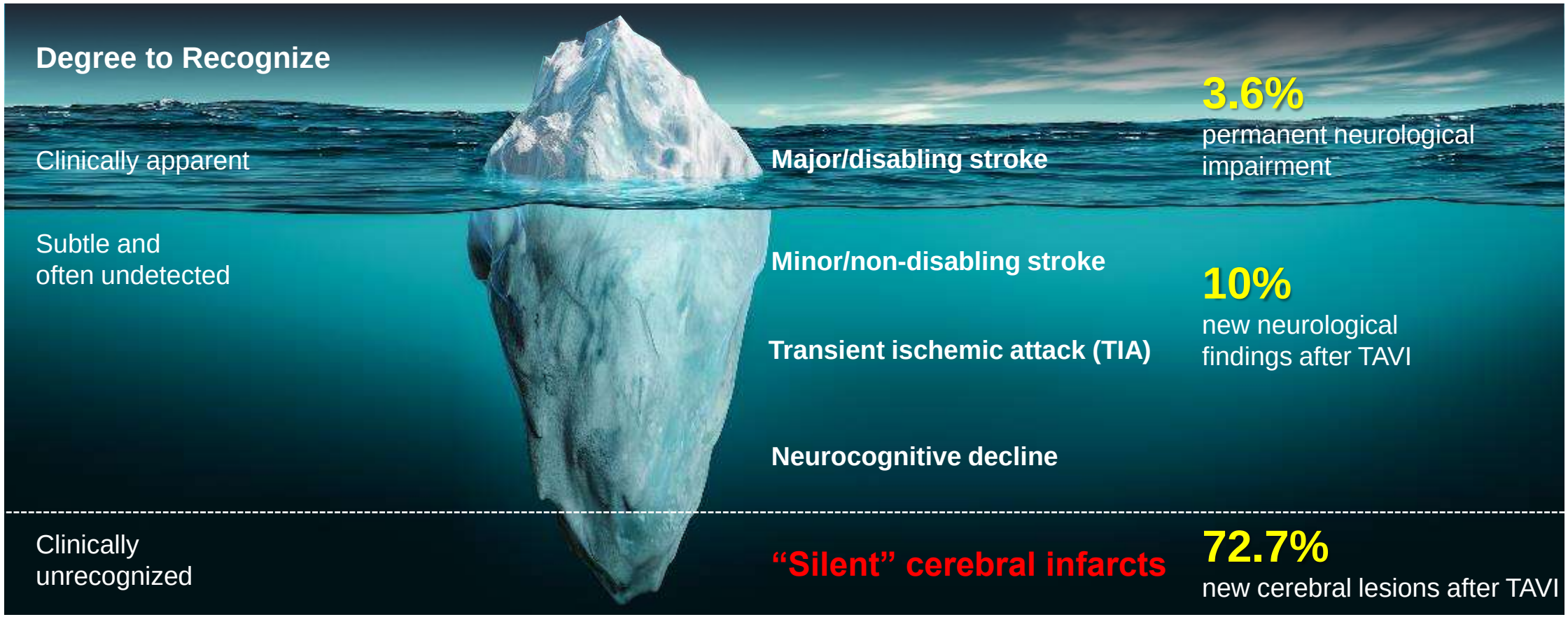
A Prospective Pilot Study With Diffusion-Weighted Magnetic Resonance Imaging

Alexander Ghanem, MD,* Andreas Müller, MD,† Claas P. Nähle, MD,† Justine Kocurek, MD,* Nikos Werner, MD,* Christoph Hammerstingl, MD,* Hans H. Schild, MD, PhD,† Jörg O. Schwab, MD, PhD,* Fritz Mellert, MD,§ Rolf Fimmers, MD,‡ Georg Nickenig, MD, PhD,* Daniel Thomas, MD†

Bonn, Germany

Single center prospective study

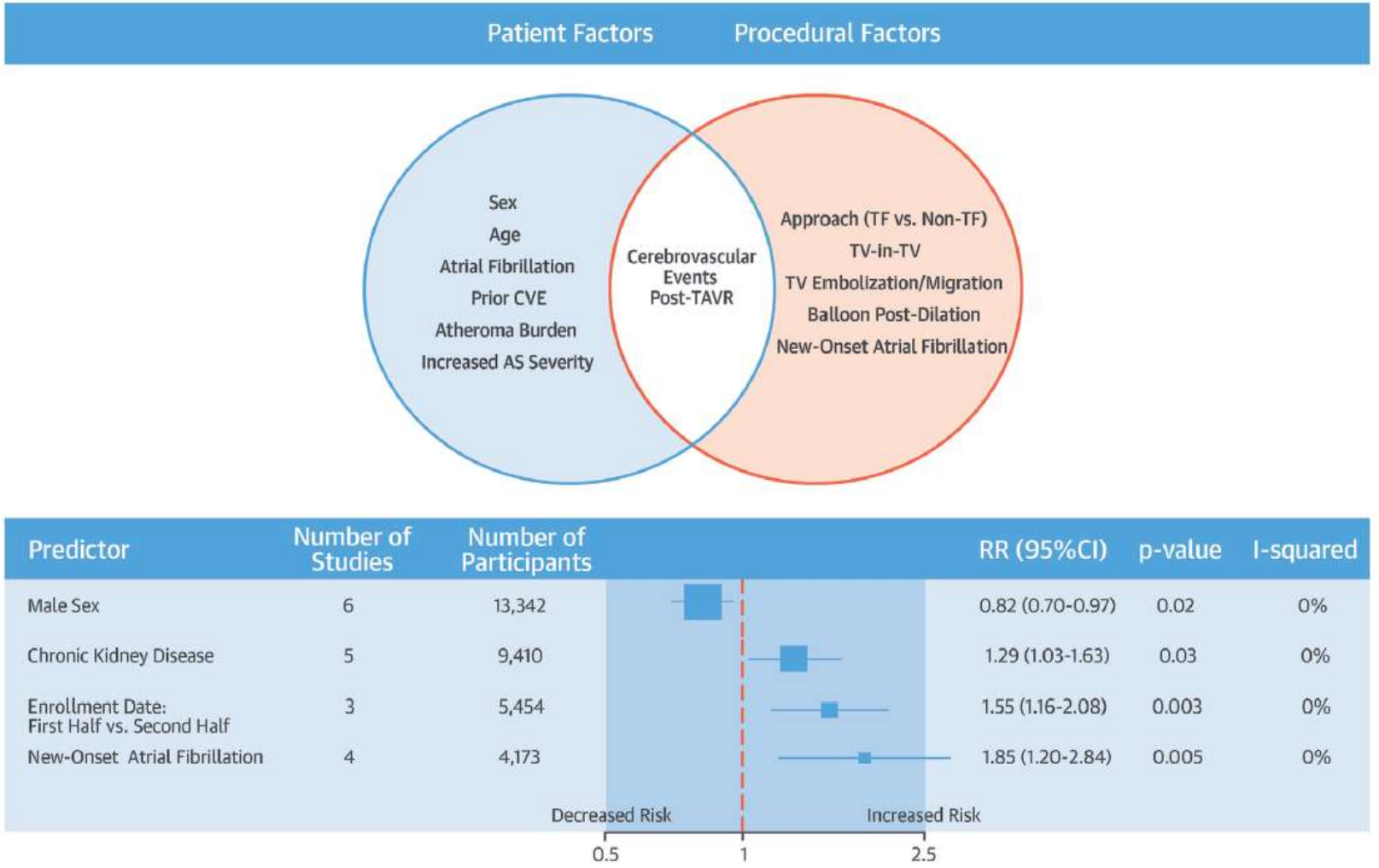
- 30 patients enrolled
- 22 completed the imaging protocol
  Cerebral DW-MRI before, directly, and 3 months after TAVI



Ghanem A et al. JACC 2010

Predictors of Stroke Post-TAVR in a Meta-Analysis

N=64 studies involving 72,813 patients (with 2,385 patients with a cardiovascular event within 30 days post-TAVR)



Predictor	Number of Studies	Number of Participants	RR (95%CI)	p-value	I-squared
Male Sex	6	13,342	0.82 (0.70-0.97)	0.02	0%
Chronic Kidney Disease	5	9,410	1.29 (1.03-1.63)	0.03	0%
Enrollment Date: First Half vs. Second Half	3	5,454	1.55 (1.16-2.08)	0.003	0%
New-Onset Atrial Fibrillation	4	4,173	1.85 (1.20-2.84)	0.005	0%

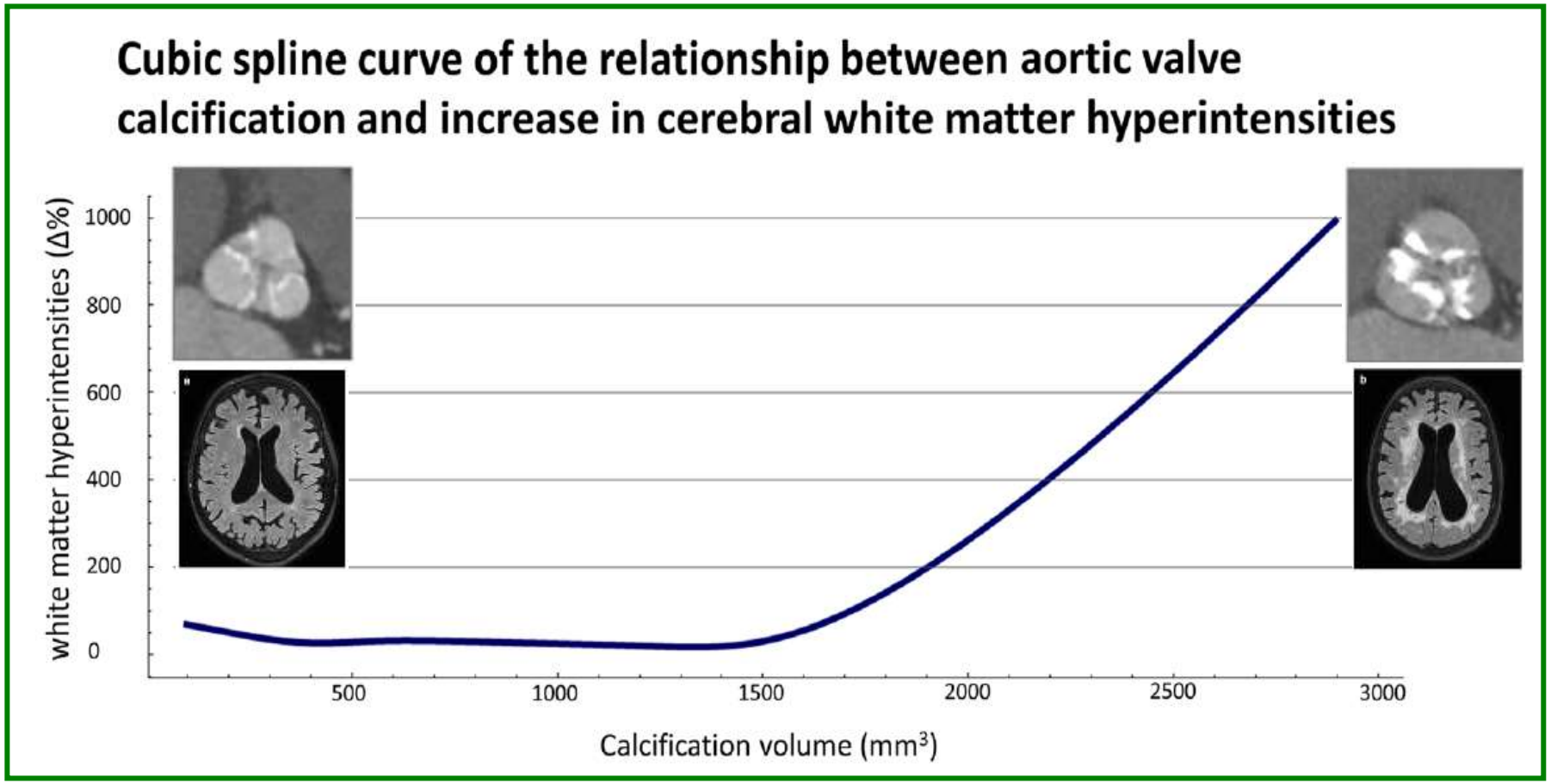
Valve type (balloon-expandable vs self-expanding) and approach (TF vs non-TF) did not predict cerebrovascular events.

Auffret, V. et al. *J Am Coll Cardiol* 2016;68:673–84.

Aortic Valve Calcification As A Predictor Of White Matter Hyperintensity Volume (WMHV)

Prospective, single center study of N=48 patients with severe AS who underwent TAVR (92% TF) with a Sapien 3™ (97%) in Amsterdam (Jun 2016-Nov 2017).

- **Aortic valve calcification** is associated with increase in WMHV ($p<0.001$), indicative of silent brain infarctions 3 months post-TAVR
- Calcification of the following did ***not predict*** relative increase in cerebral WMHV
  - **Aortic arch (*P*=0.42)**
  - **Landing zone (*P*=0.69)**
  - **Left ventricle (*P*=0.55)**

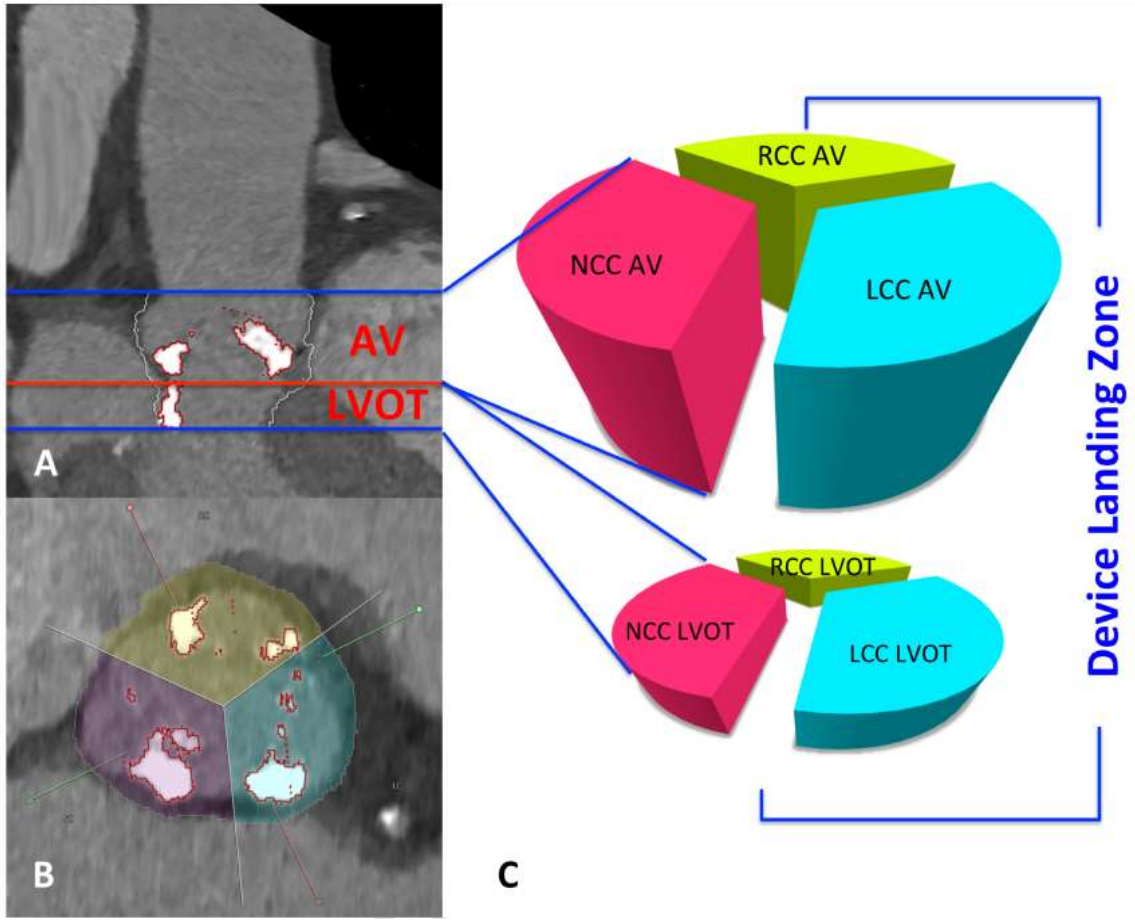


Final study population included N=36 TAVR patients, mean age 78.7 years, 61% female, median STS 2.8%. None of the patients experienced clinical overt stroke during the follow-up period, but in 72% of patients, white matter hyperintensity volume increased 27% (median) 3 months after TAVR.

Vlastra, W. et al. *Int J Cardiovasc Imaging*. 2019 Jul 16. doi: 10.1007/s10554-019-01663-0.

Aortic Valve Calcification As A Predictor of Stroke and Reduced Survival After TAVR

Retrospective analysis of pre-operative contrast enhanced MDCT scans of N=581 TAVR patients in Germany (between 2009-2017)



Calcium load in LVOT beneath the RCC significantly associated with <u>stroke</u>
(OR: 1.2; 95% CI: 1.03-1.3; *P*=0.0019)
and in-hospital mortality
(OR 1.1: 95% CI: 1.004-1.2; *P*=0.04)

Total calcium load in LVOT associated with in-hospital mortality
(OR 1.2; 95% CI: 1.01-1.4, *P*=0.03)
and 30-day mortality
(OR 1.2; 95% CI 1.02-1.43; *P*=0.029)

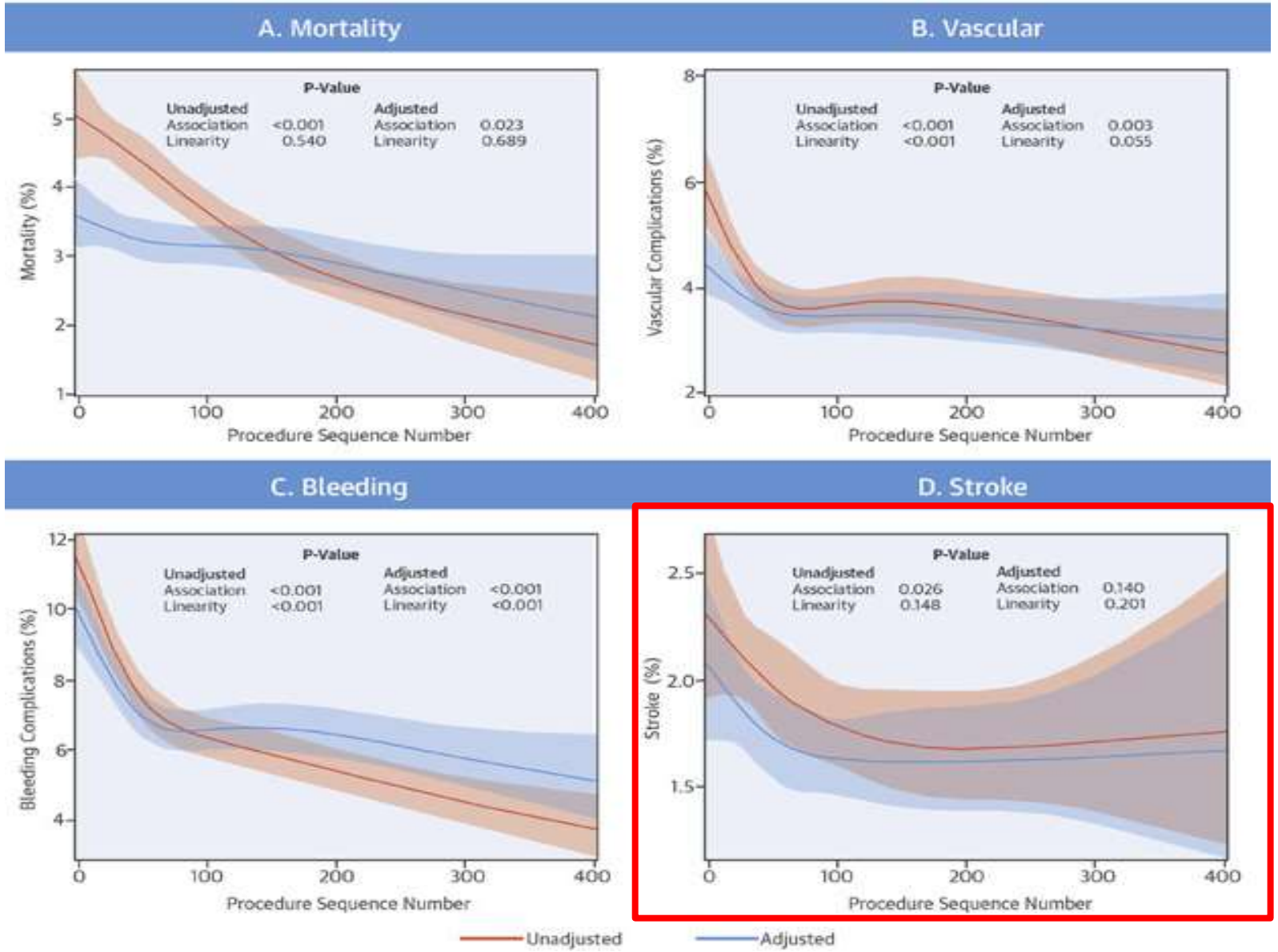
Implanted prostheses were: SAPIEN XT, SAPIEN 3, CoreValve, Evolut R, Engager, and ACURATE neo.
MDCT=multidetector computed tomography

Pollari, F. et al. *Journal of Cardiovascular Computed Tomograph* (2020), doi: https://doi.org/10.1016/j.jcct.2019.12.001

Assessing TAVR Outcomes Based on Site Experience

STS/ACC TVT Registry: N=42,988 TAVR procedures at 395 hospitals (between 2011-2015)

- Increasing site volume was associated with lower in-hospital risk-adjusted outcomes, including mortality, vascular complications, and bleeding **but was not associated with decreased stroke rate.**
- Stroke risk was independent of experience and operator volume.



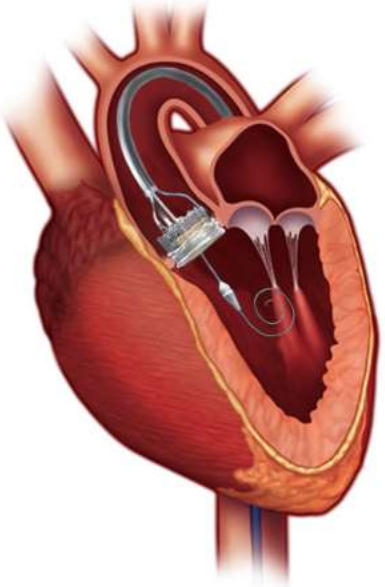
- Unadjusted (orange) and adjusted (blue) frequency of outcomes.
- The orange- and blue-colored bands represent 95% confidence intervals, which are broader for stroke due to low rate of site-reported stroke and the fewer hospital sites contributing cases.

Carroll JD, et al. Procedural Experience for Transcatheter Aortic Valve Replacement and Relation to Outcomes: The STS/ACC TVT Registry. J Am Coll Cardiol. 2017 Jul 4;70(1):29-41.

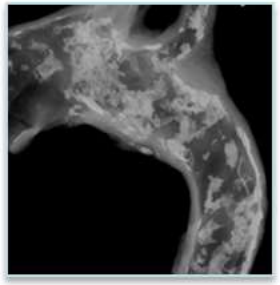
What Causes Stroke in TAVR?

ASCENDING ARCH
Arterial wall, calcific and atherosclerotic material

STENOTIC VALVE
Leaflet tissue, calcific deposits, acute thrombus



TRANSVERSE ARCH
Arterial wall, calcific and atherosclerotic material



TAVR DEVICES
Foreign material

NATIVE HEART
Myocardium

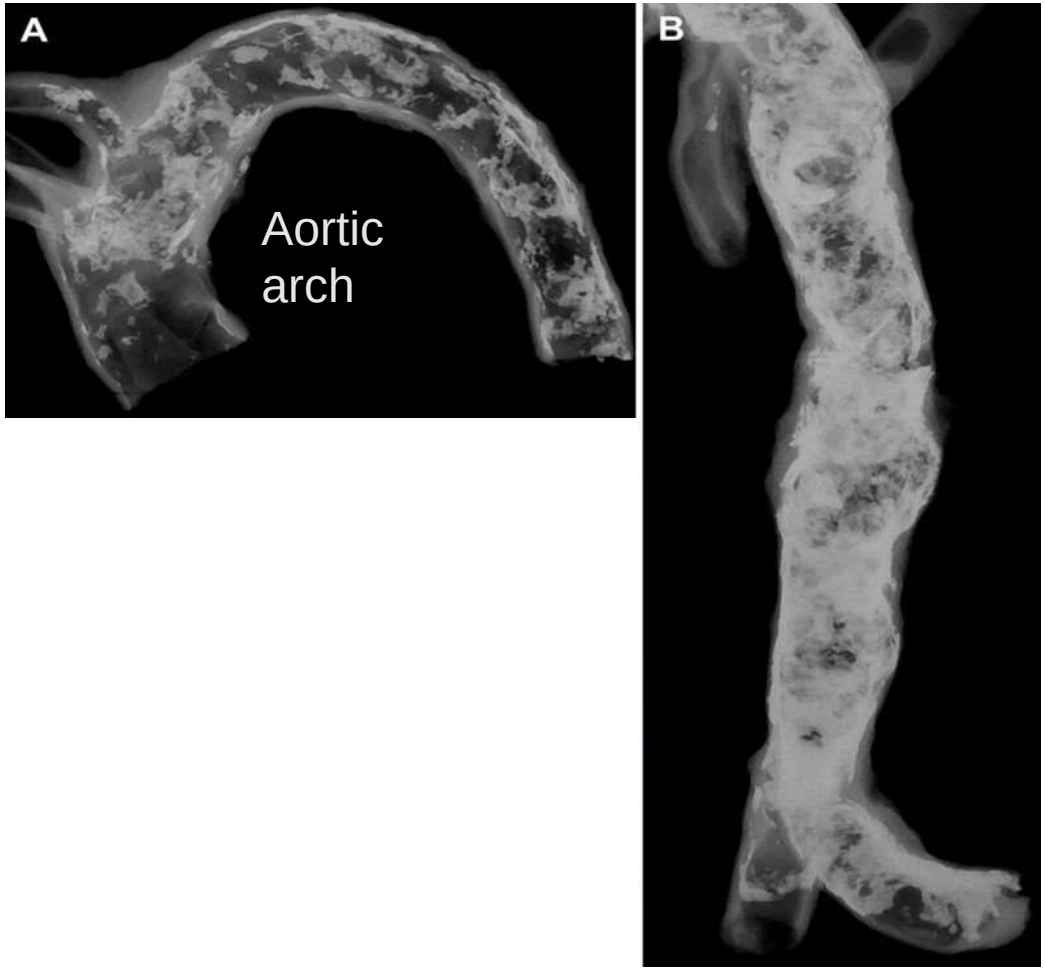
- Most strokes associated with TAVR are the result of embolization of debris during the procedure.
- Histopathology of filters used to catch debris have found acute and organizing thrombus, valve tissue, arterial wall, calcification, foreign material, and myocardium.

Kapadia, S. et al. JACC 2017;69(4): 367-77; Seeger, J. et al. JACC Cardiovasc Interv 2018;11(17):1683-1693.

Debris from – Hostile Arch

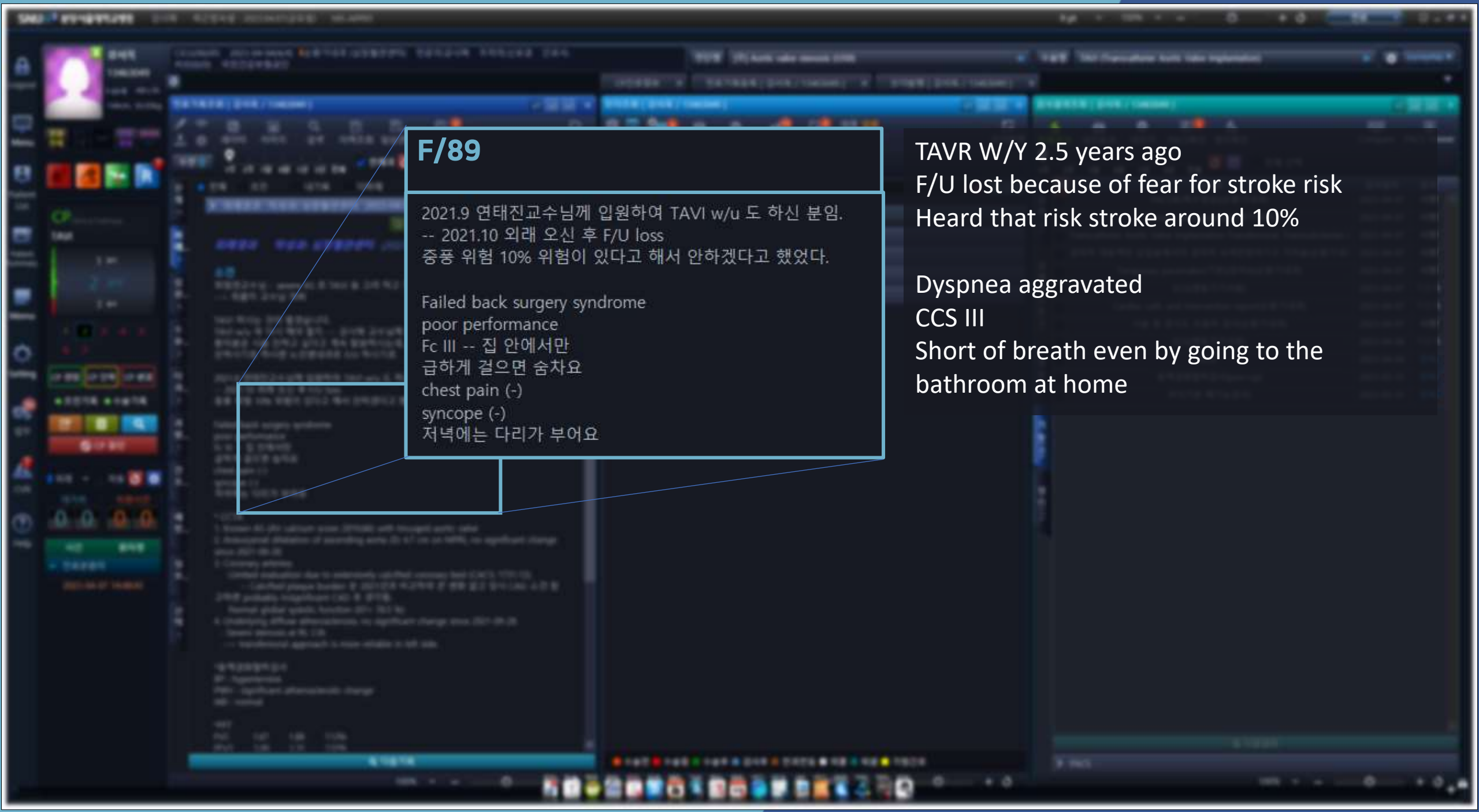
The luminal surface of aortas are often embologenic.

- 75% of arches seen in the SENTINEL™ IDE Trial were calcified, 43% had atheroma[1]
- In the SENTINEL™ IDE Trial, 50% of patients had calcium captured in filters and 94% had arterial wall tissue.[1]
- Arch atheroma is common in the aortic arch and susceptible to embolization during device manipulation in the arch.
- Patients with moderate or severe aortic stenosis are known to have more extensive atheroma than those with mild stenosis.[2]

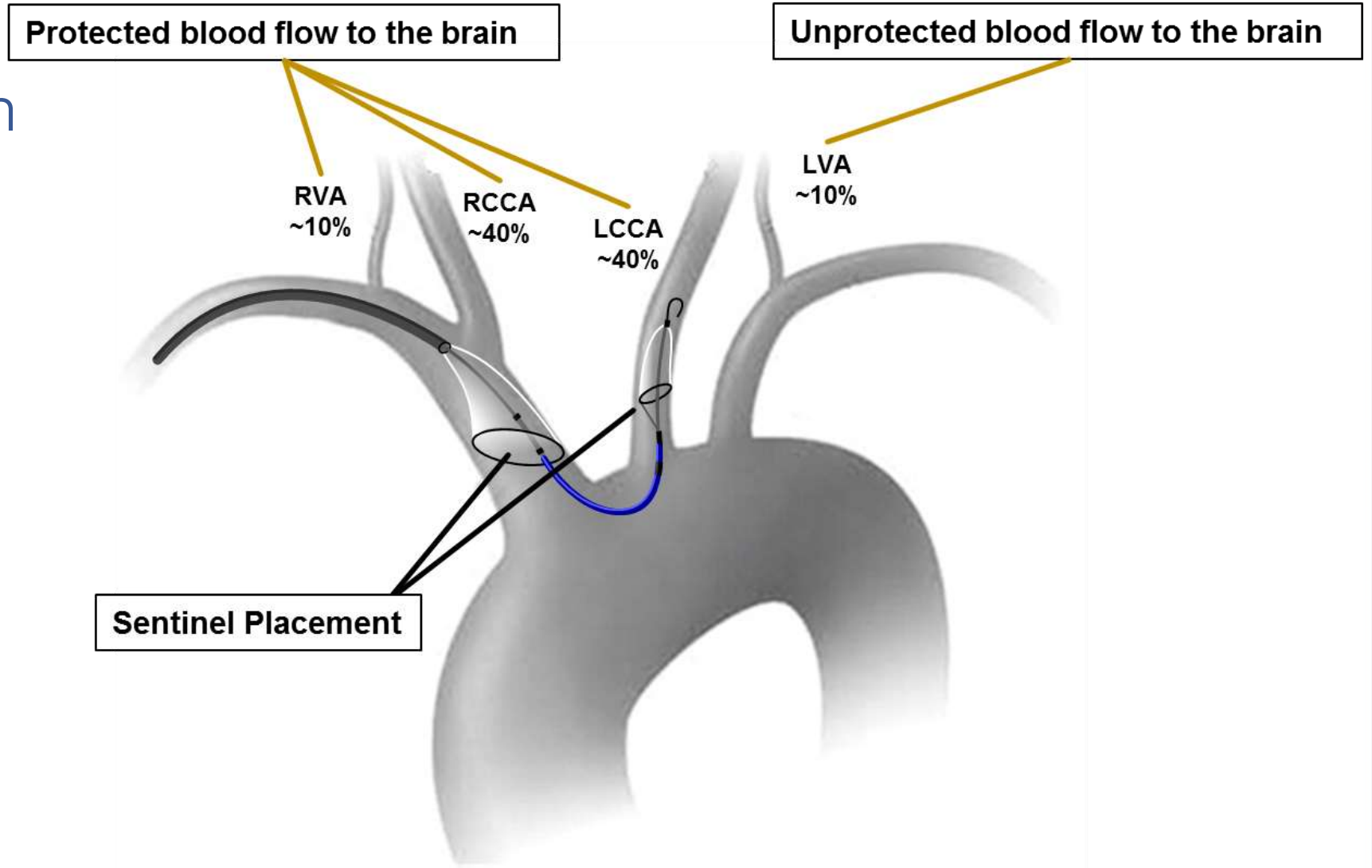


Thoracic and abdominal aorta with iliac bifurcation

[1]Data on file at Boston Scientific
[2]Vizzardi E et al. J Ultrasound Med 2015;34(1):105-10


F/89
2021.9 연태진교수님께 입원하여 TAVI w/u 도 하신 분임.
-- 2021.10 외래 오신 후 F/U loss
증풍 위험 10% 위험이 있다고 해서 안하겠다고 했었다.
Failed back surgery syndrome
poor performance
Fc III -- 집 안에서만
급하게 걸으면 숨차요
chest pain (-)
syncope (-)
저녁에는 다리가 부어요
TAVR W/Y 2.5 years ago
F/U lost because of fear for stroke risk
Heard that risk stroke around 10%
Dyspnea aggravated
CCS III
Short of breath even by going to the bathroom at home

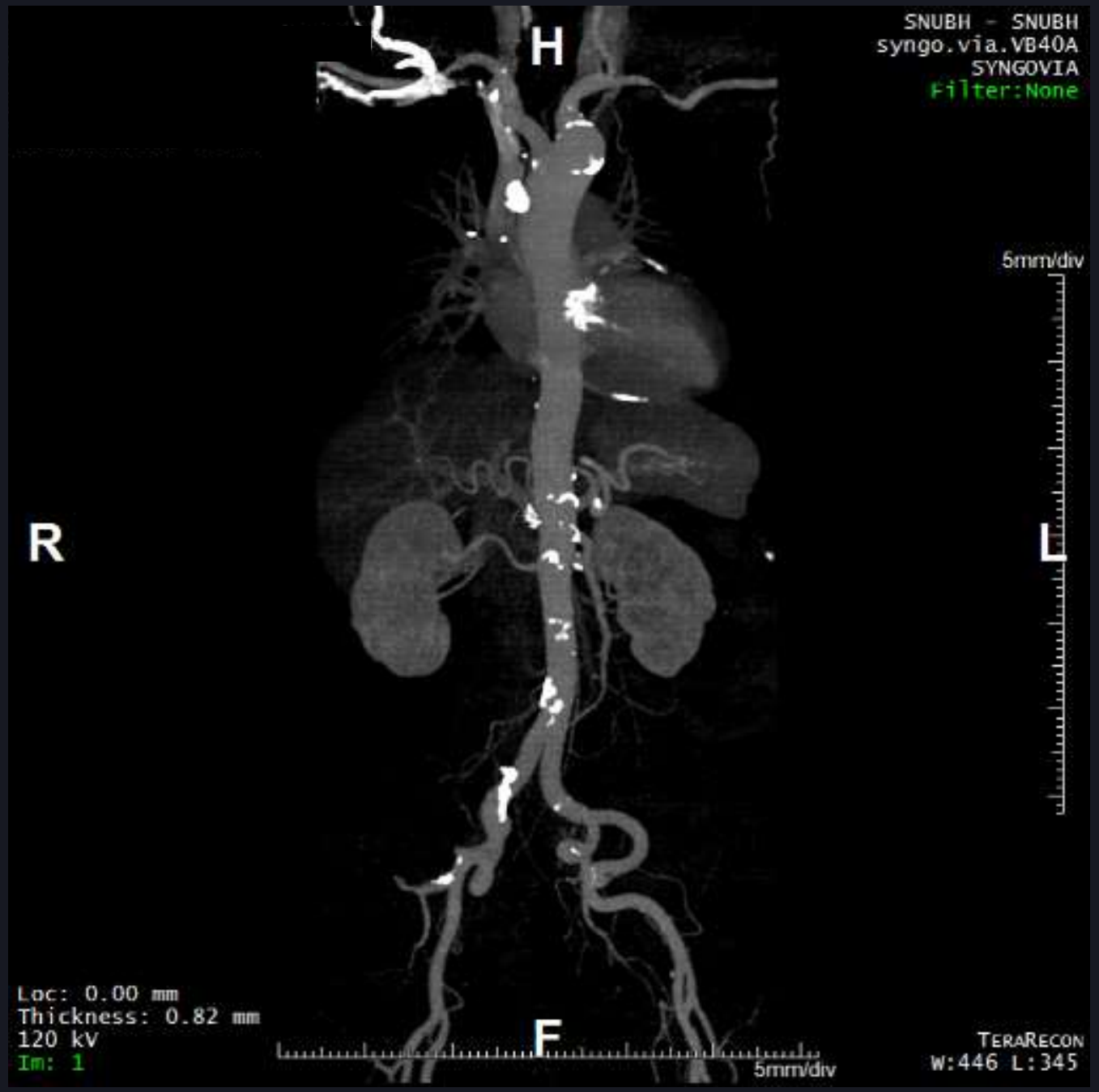
SENTINEL™
Cerebral Protection System (CPS)
Filters >90% of Blood Flow to Brain

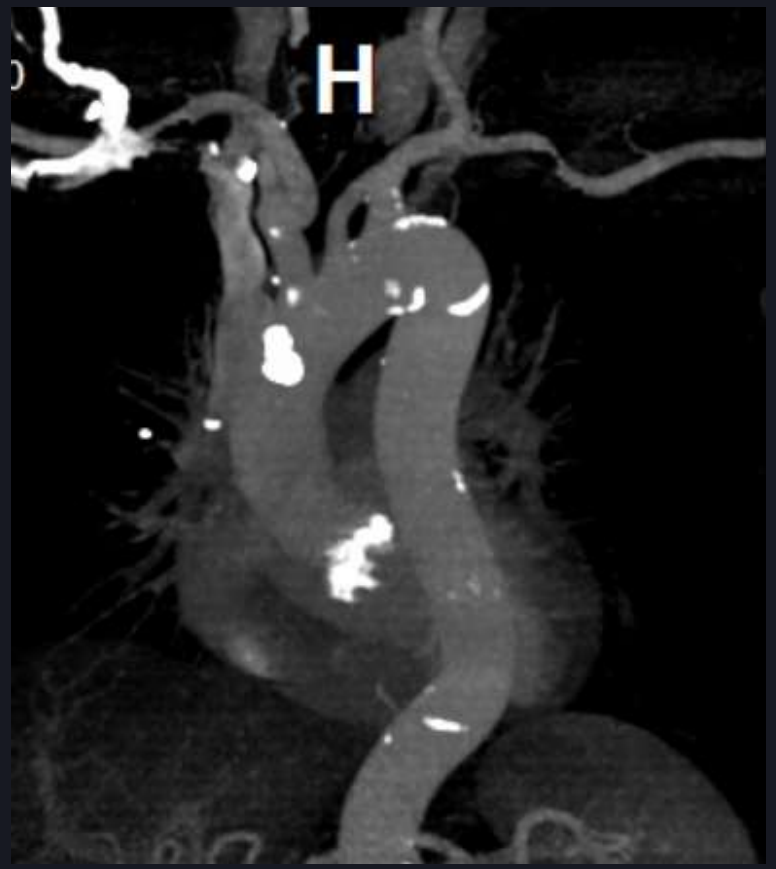


Zhao M, et al. *AJNR* 2007

SENTINEL™ Cerebral Protection System

- Two independent filters capture & remove embolic material
- Polyurethane filter, pore size = 140 µm
- Standard right trans-radial sheath access (6F)
- One size accommodates most vessel sizes; fits ~90% of anatomies
- Deflectable compound-curve catheter facilitates cannulation of LCC
- Minimal profile in aortic arch (little interaction with other devices)


SNUBH - SNUBH
syngo.via.VB40A
SYNGOVIA
Filter:None
H
5mm/div
R
L
F
5mm/div
Loc: 0.00 mm
Thickness: 0.82 mm
120 kV
Im: 1
TeraRecon
W:446 L:345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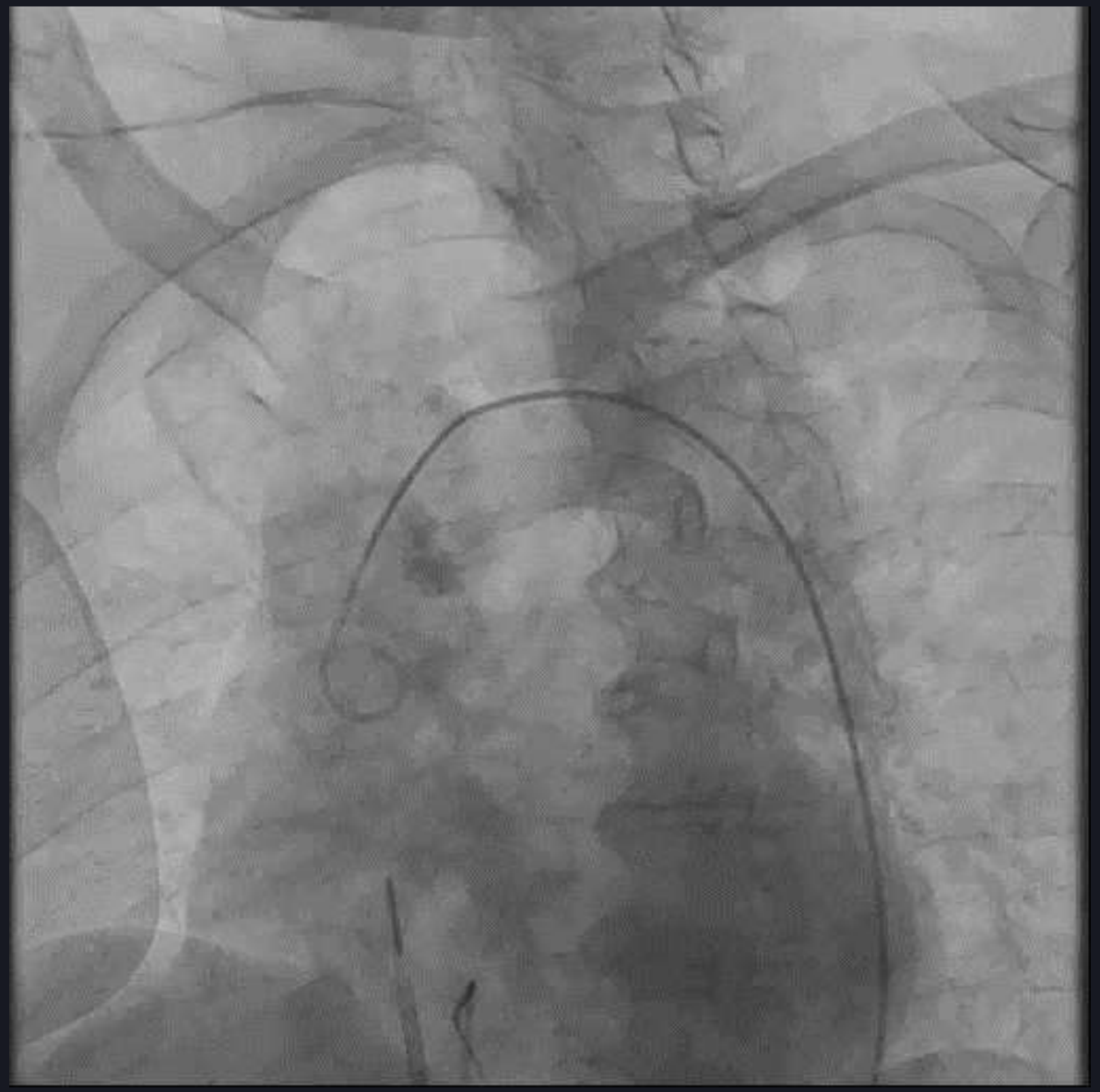
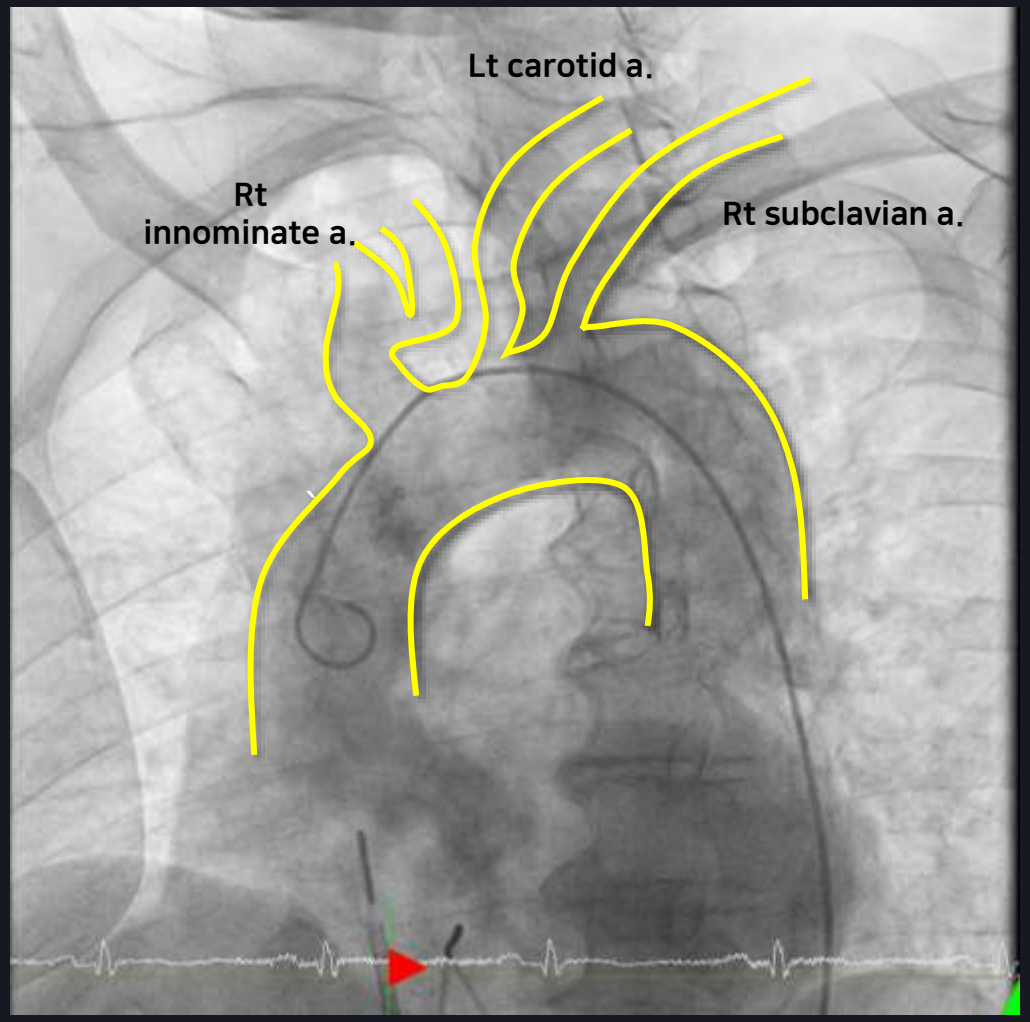
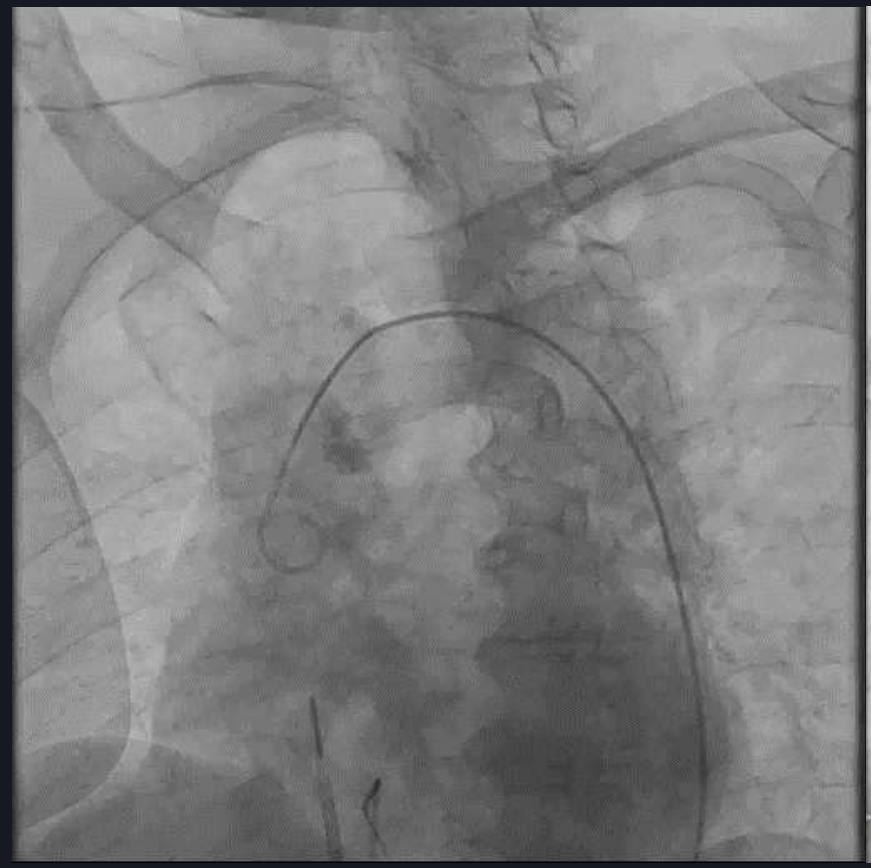
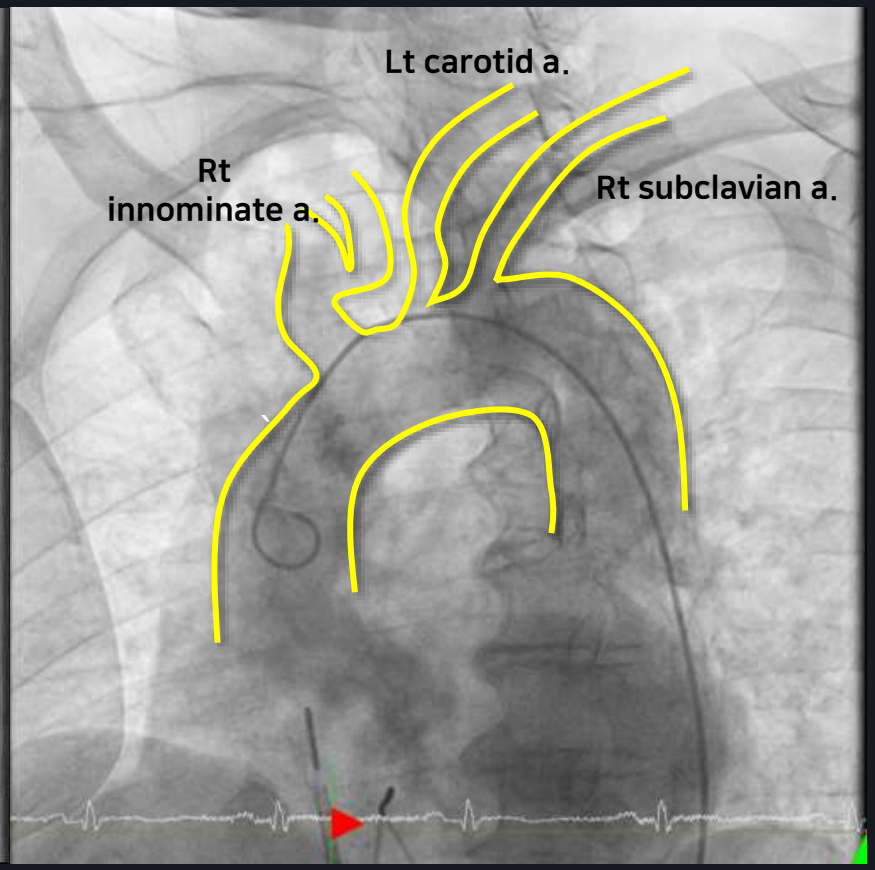


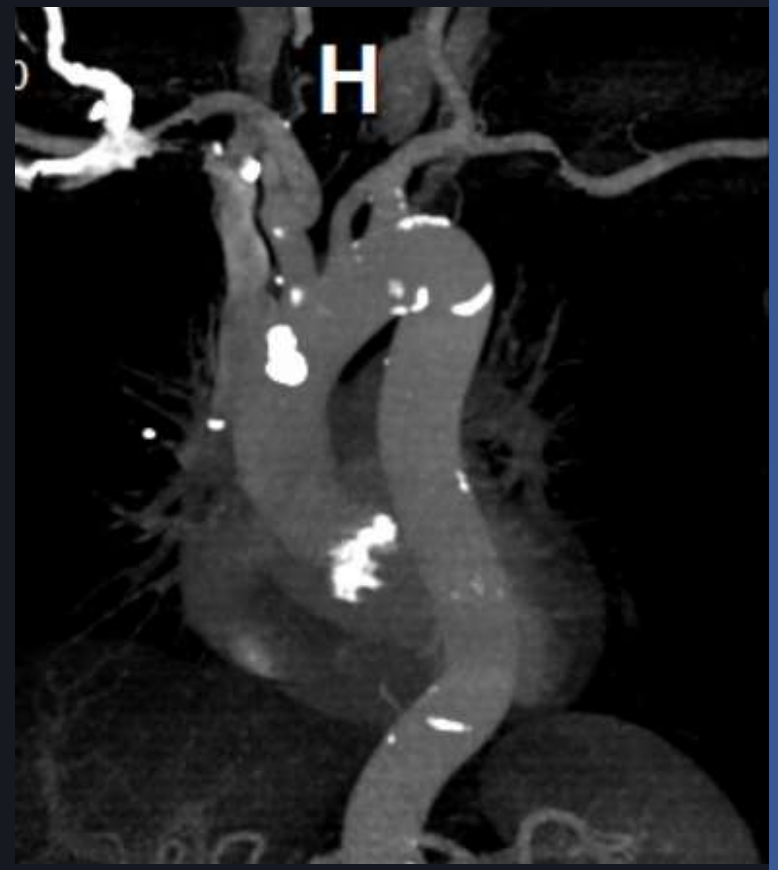
LAO 30’ ascending aortography



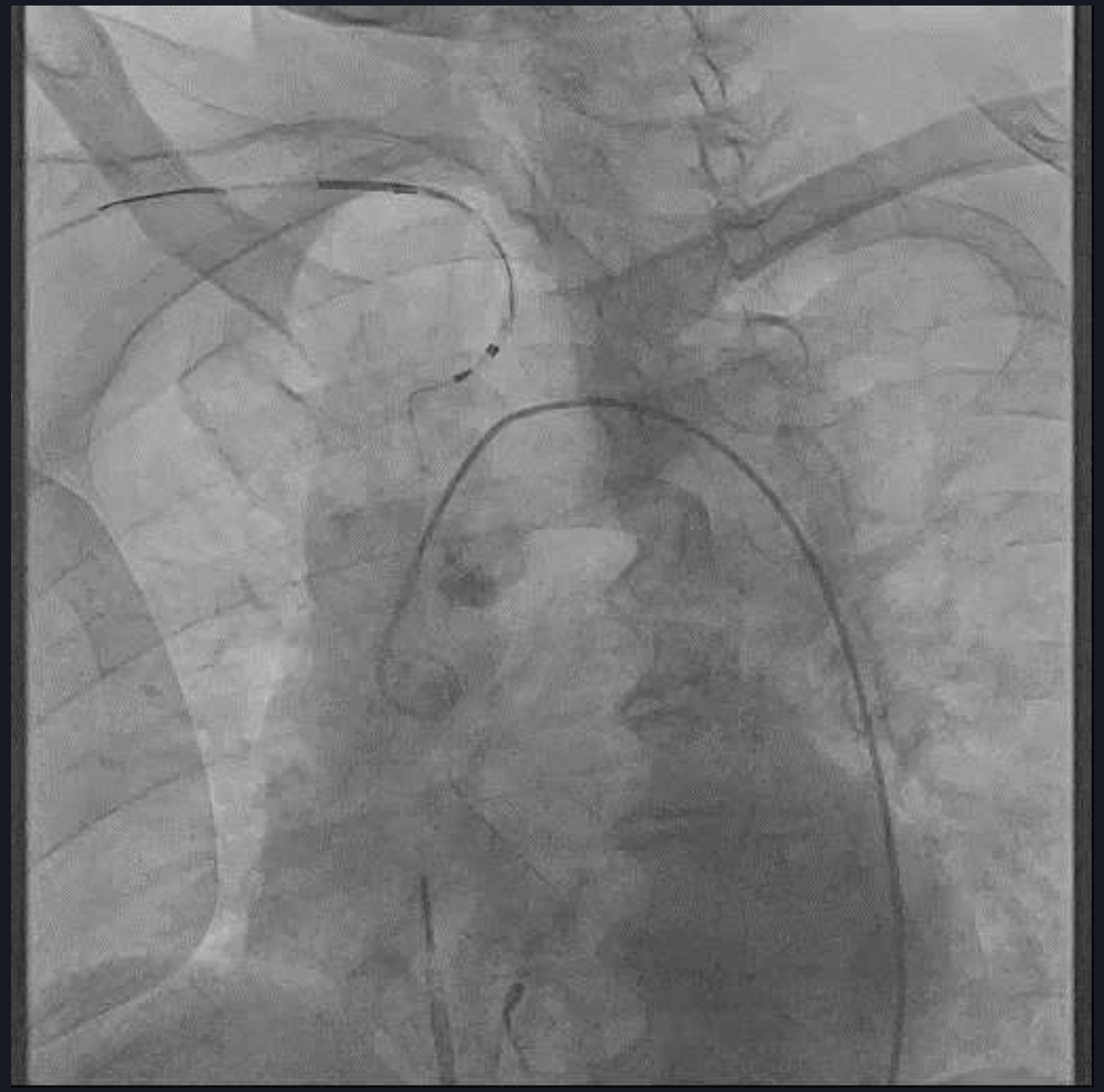
LAO 30’ ascending aortography



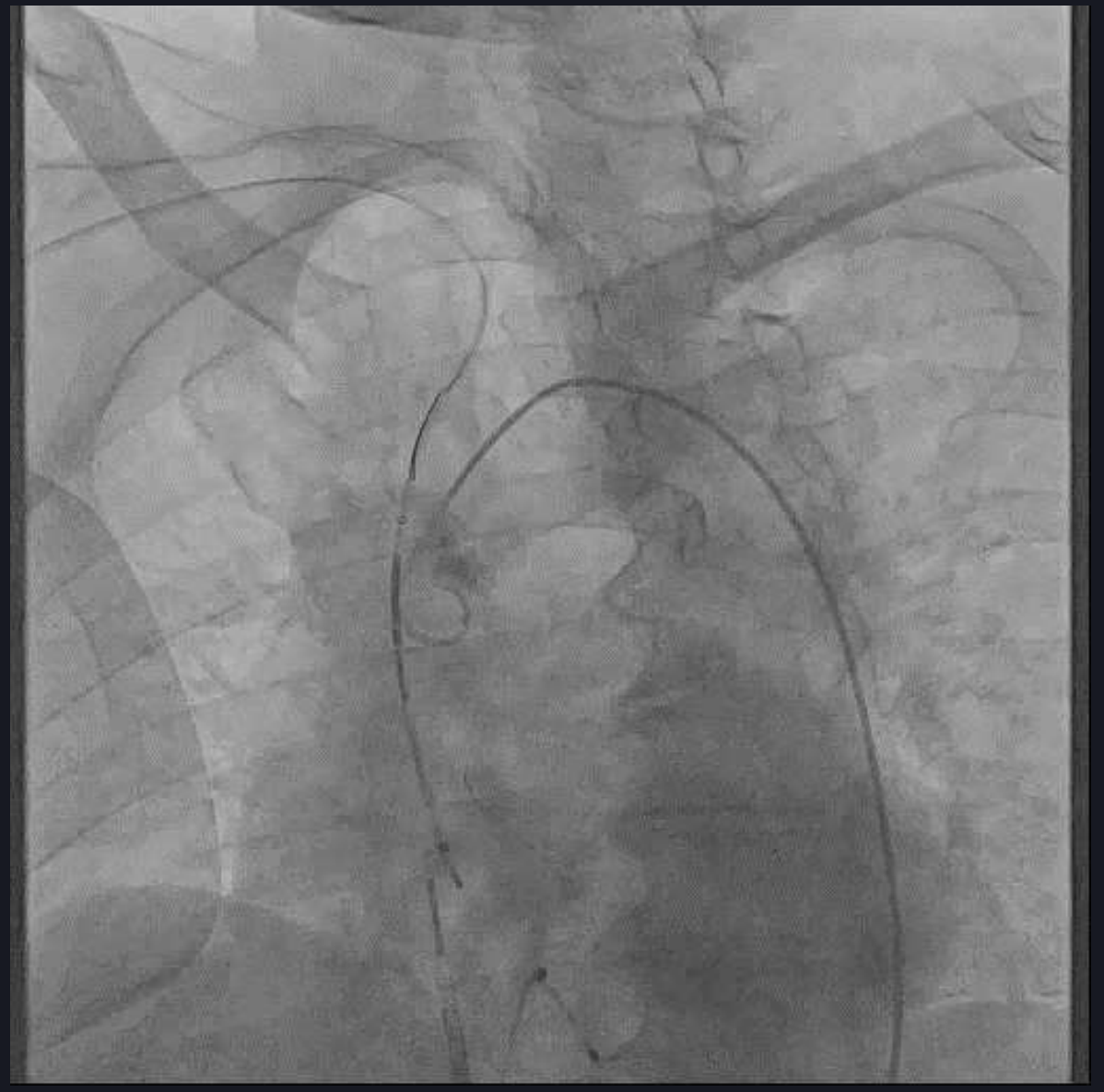




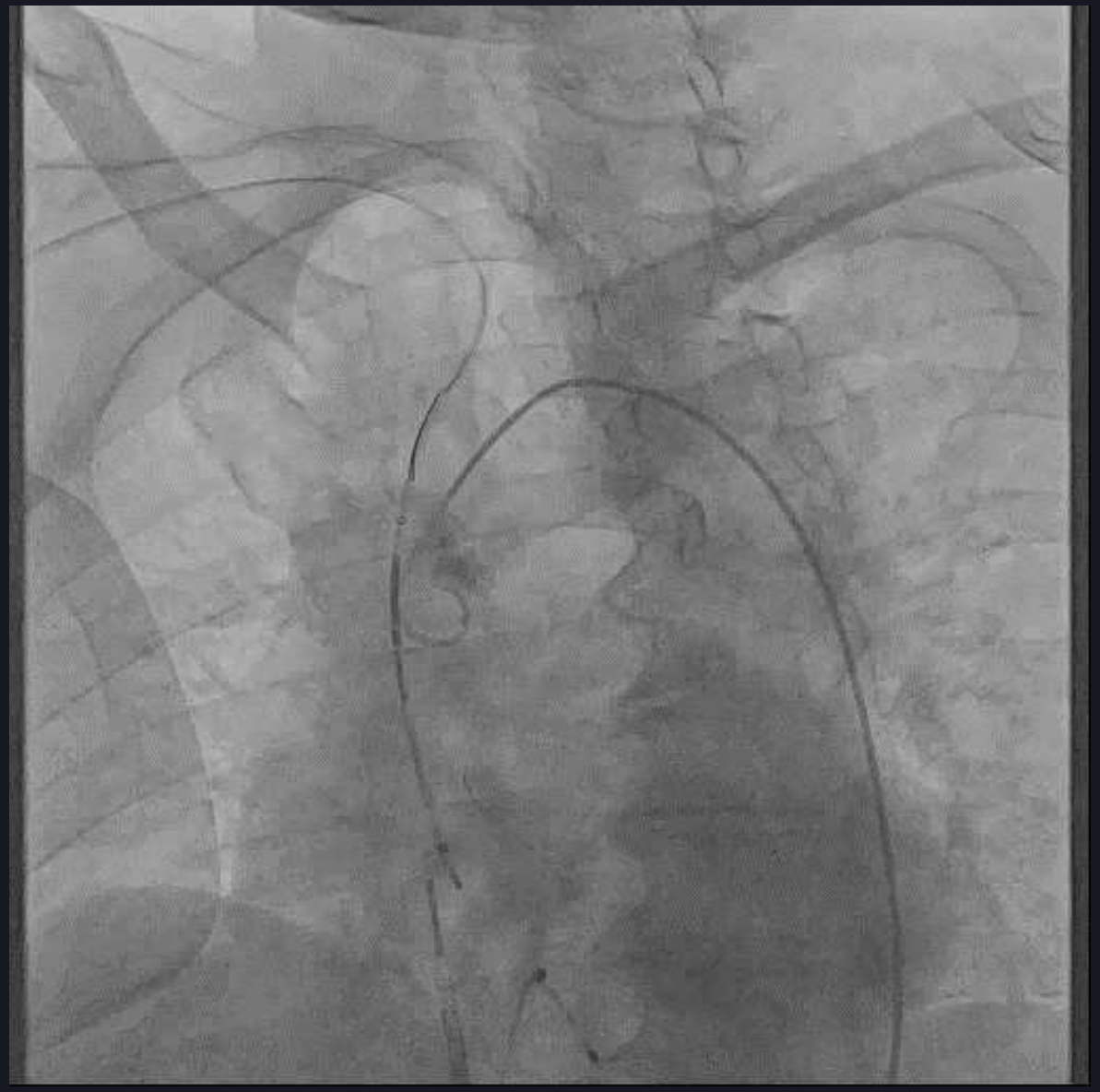
Device advance



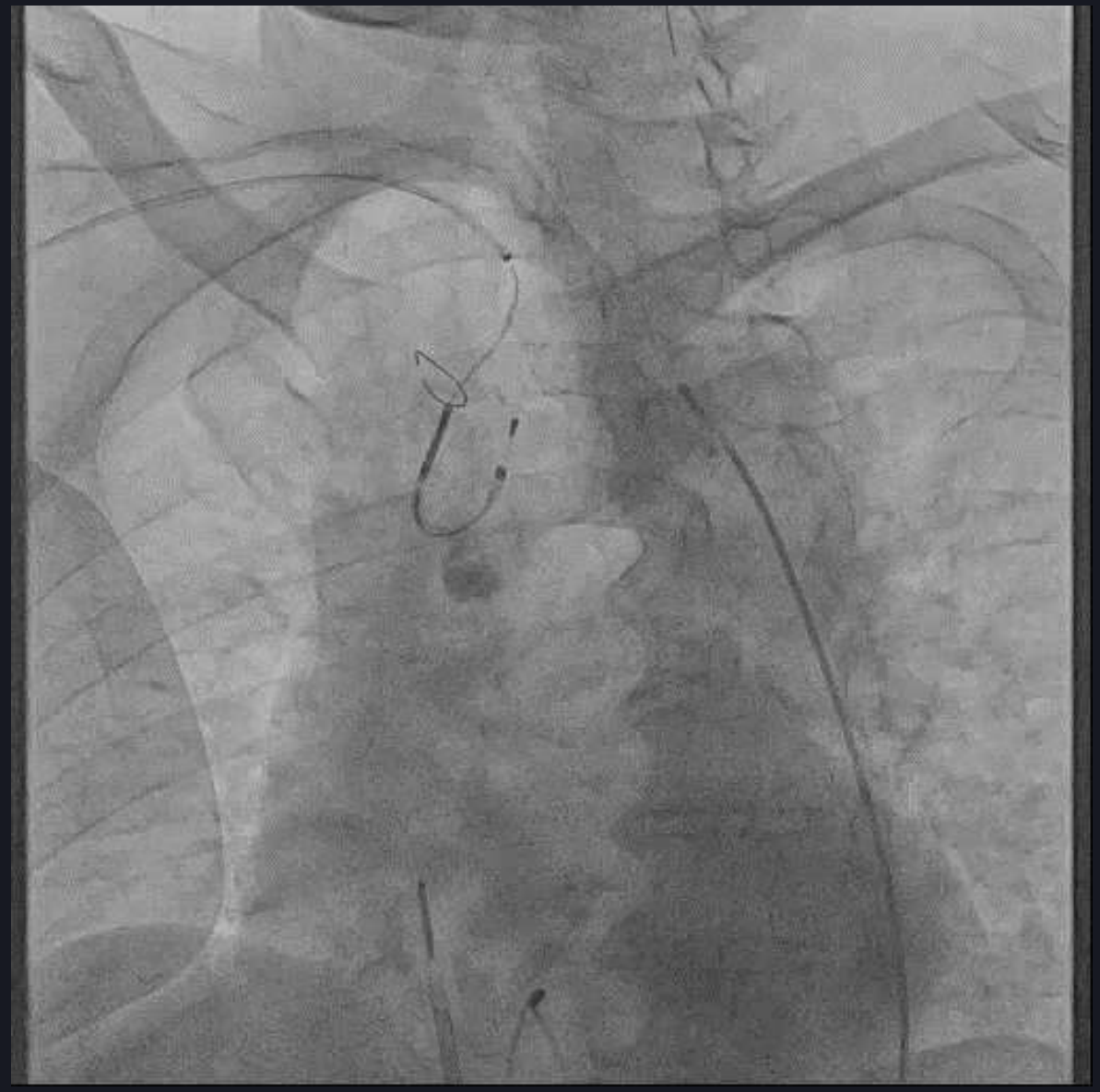
Proximal filter deployment



Proximal filter deployment



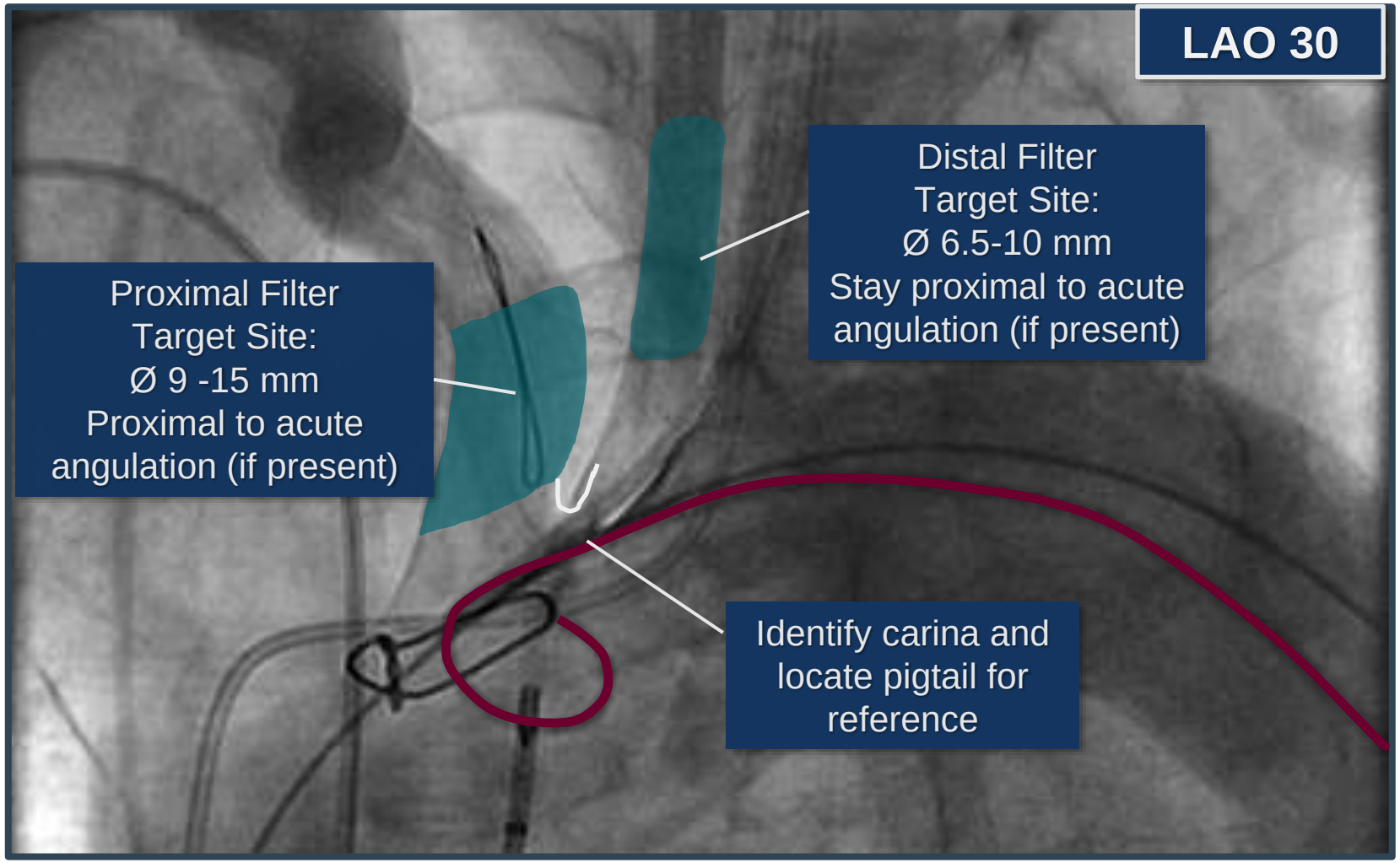
Left carotid artery selection



SENTINEL™ CPS Procedure – Device Deployment Target Zones

Never advance or withdraw SENTINEL CPS without proper fluoroscopic guidance or against resistance until cause is determined. Advancing with such resistance may lead to embolization of debris, and vessel and/or device damage

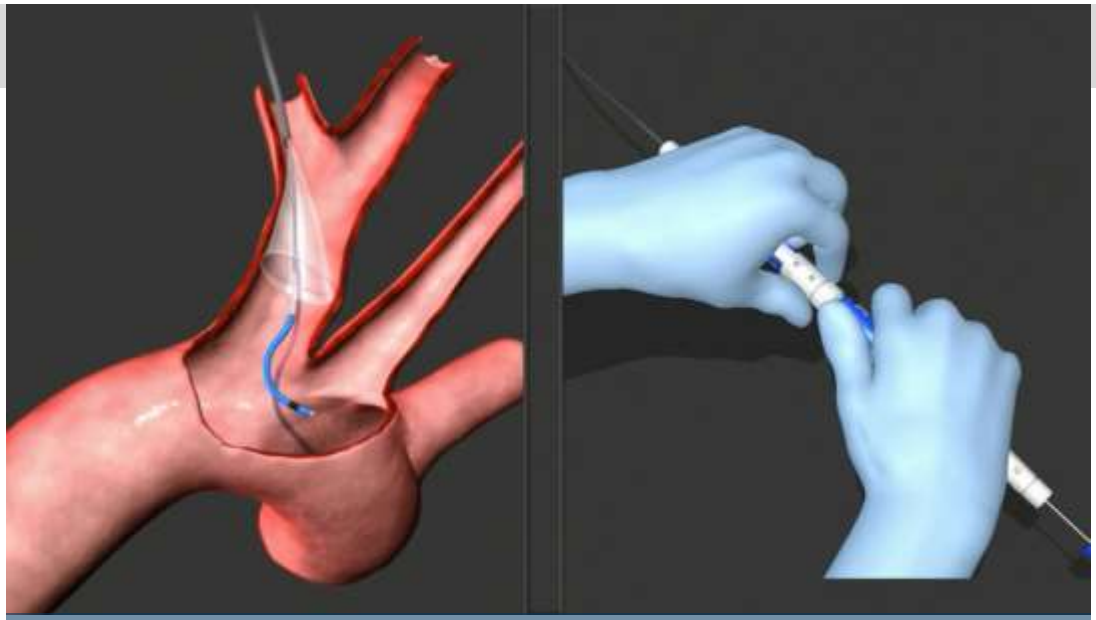
Targeted deployment zone:
1.5 - 2cm distal to ostium



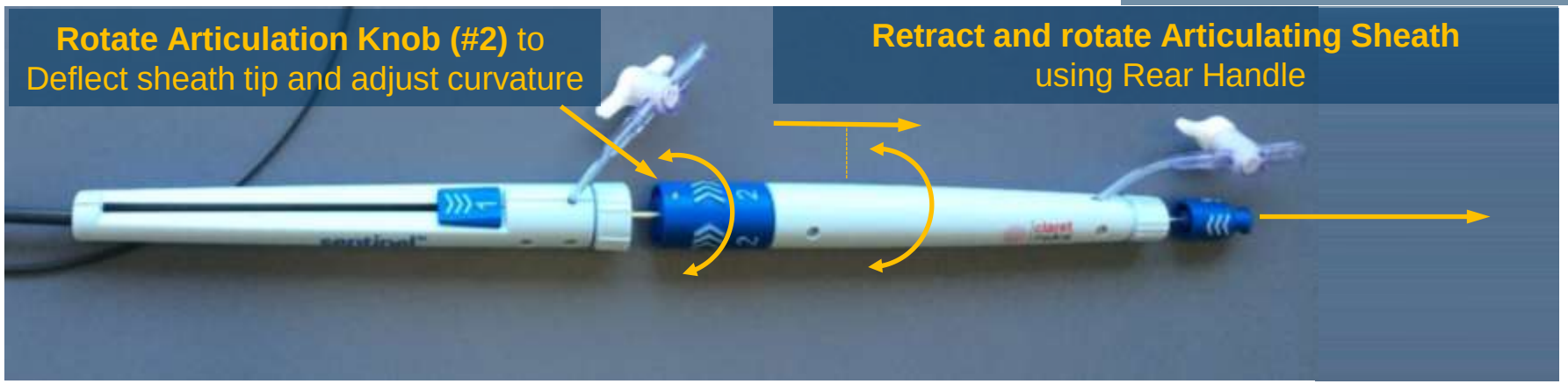
R_x Only. View the Sentinel IFU for clarification of any device usage details not found here.

SENTINEL™ CPS Procedure – Cannulating the Left Common Carotid (LCC)

Steps to cannulate the LCC:



To play video place cursor on image and click arrow

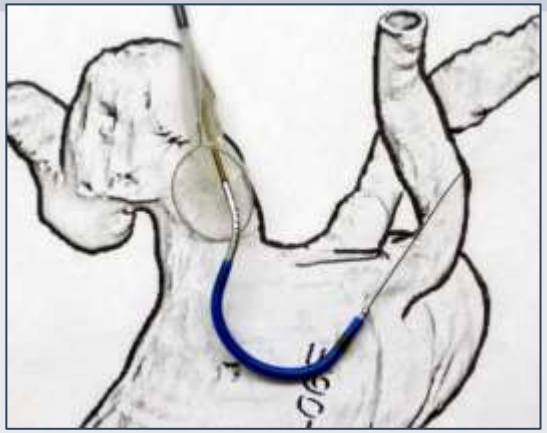


SENTINEL™ CPS Procedure – Cannulating the LCC Considerations

When cannulating the LCC, be aware of different approaches

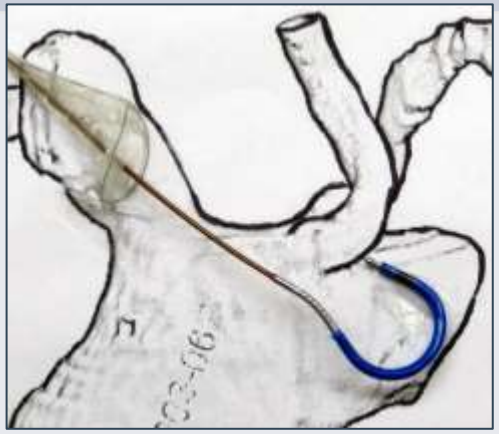
Retroflex

Ascending Aorta



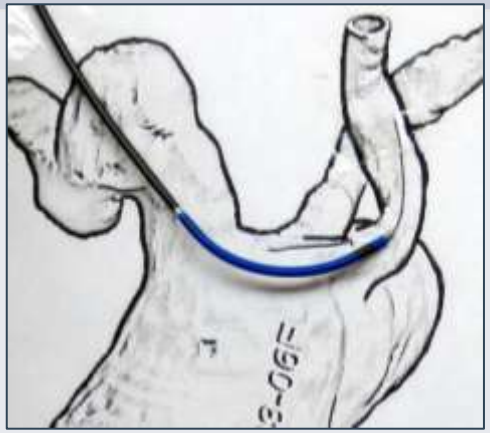
- **To direct wire into the LCC, after deploying proximal filter**, withdraw and articulate the Articulating Sheath (AS) back on itself, and manipulate in either ascending or descending aorta, depending on catheter and anatomy natural preference

Descending Aorta



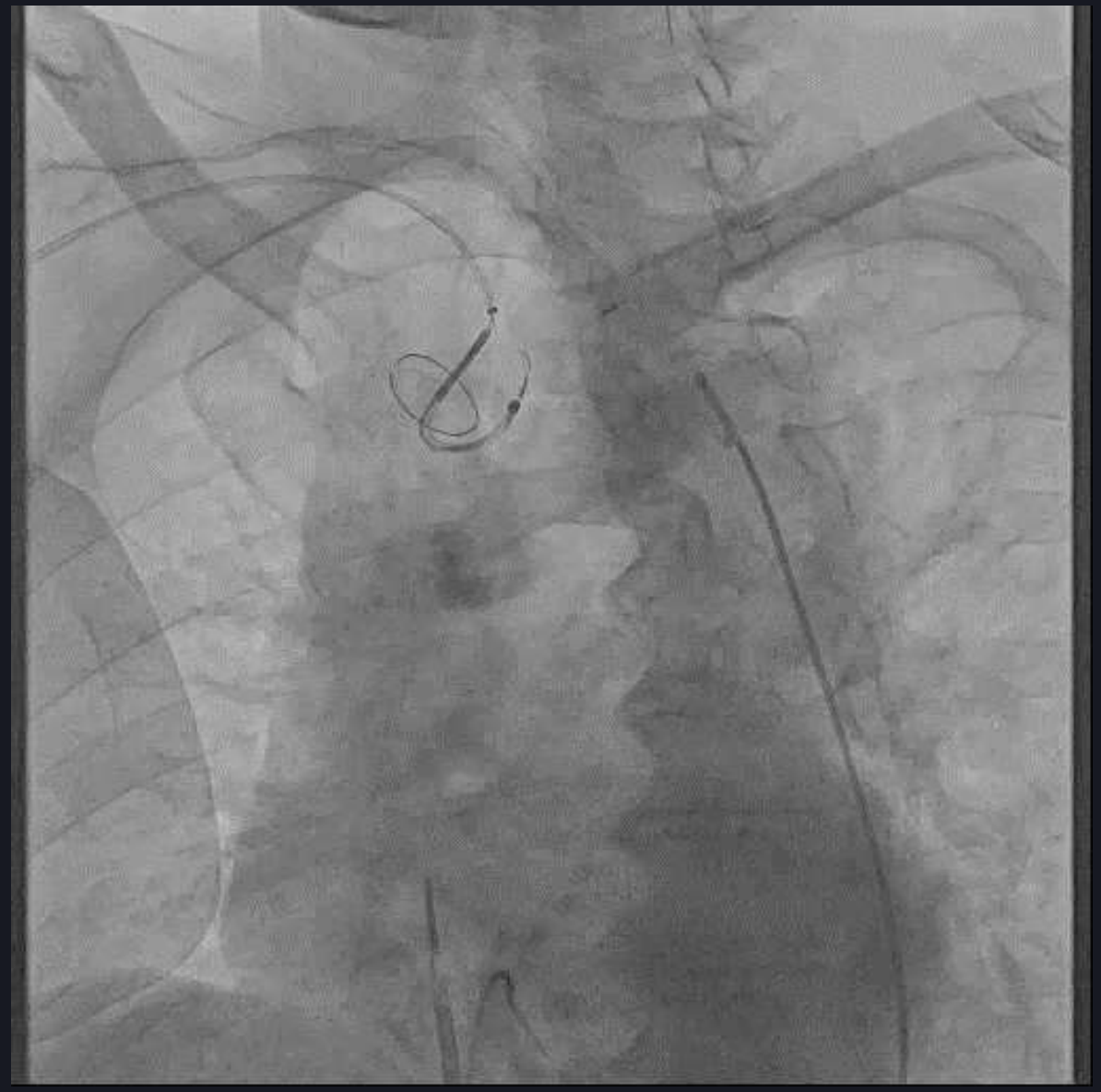
Direct

Direct into LCC

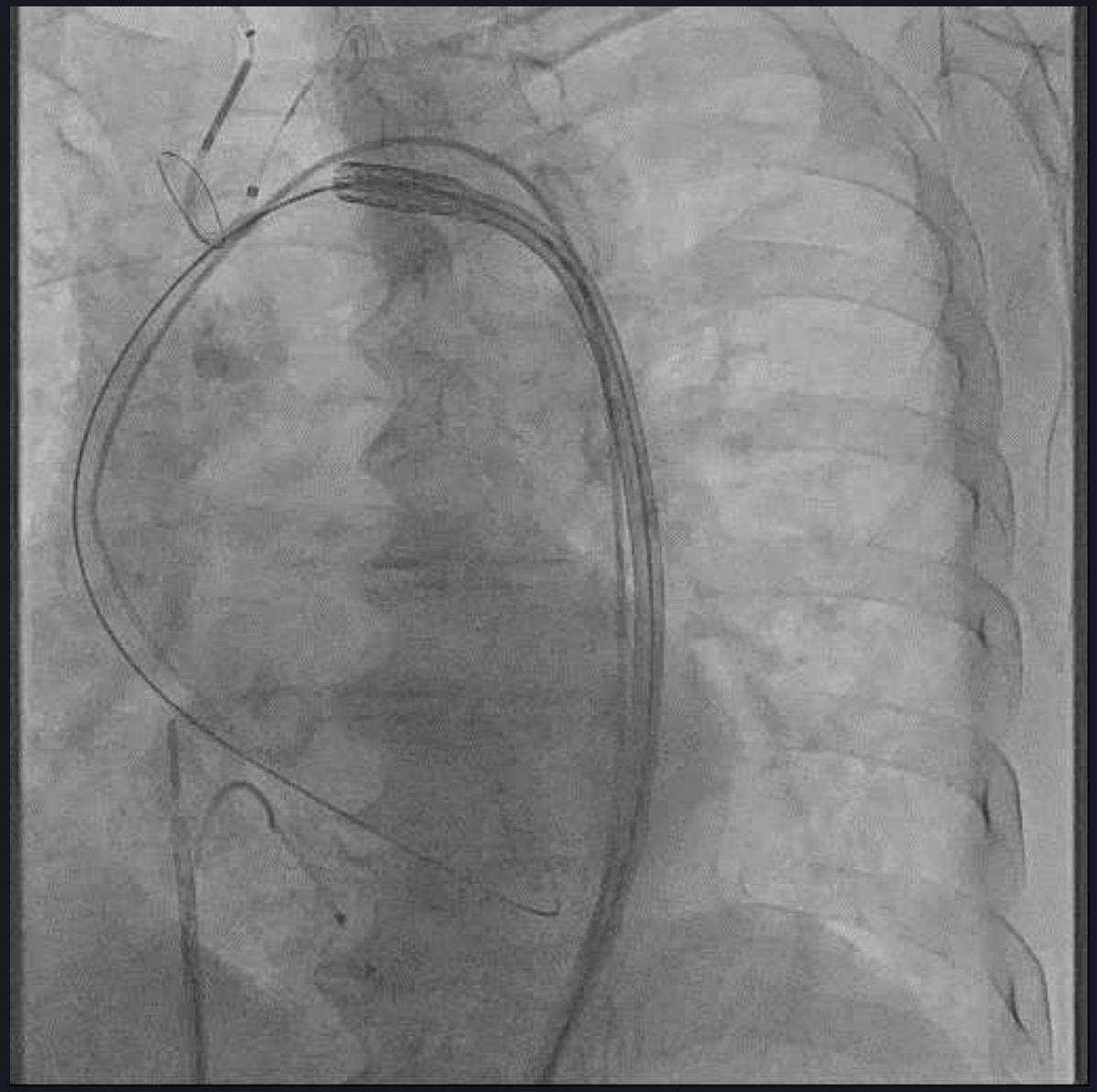


- **Often before deploying proximal filter,** interrogate with wire and cannulate LCC directly from brachio-cephalic without articulating AS

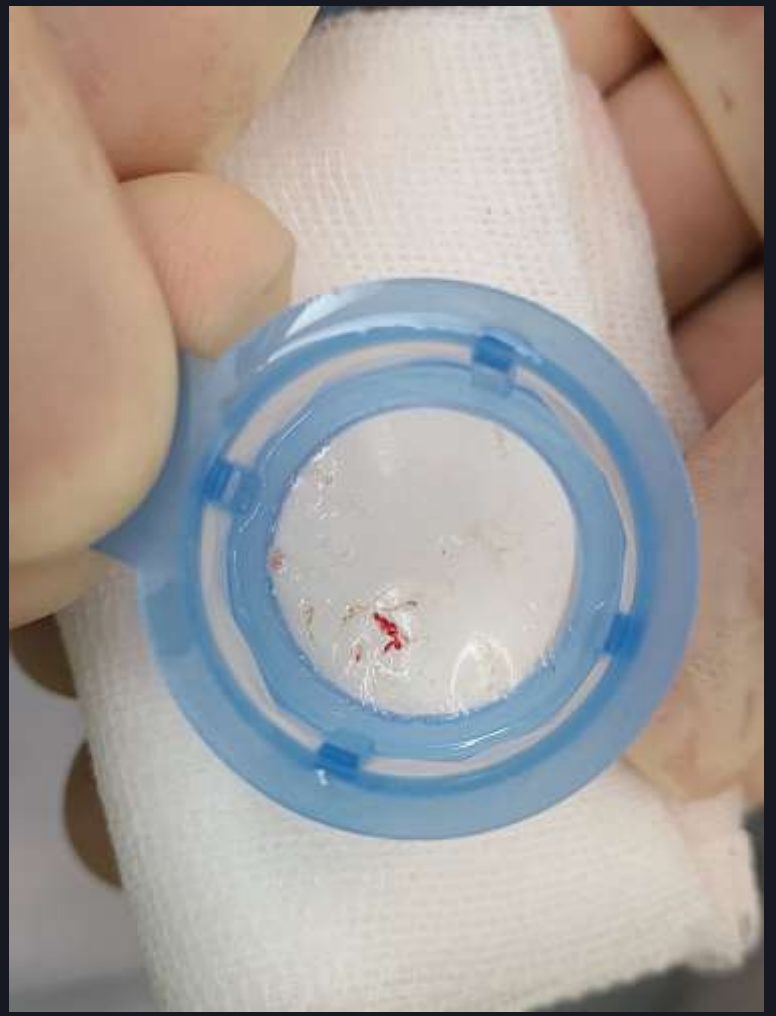
Distal filter deployment



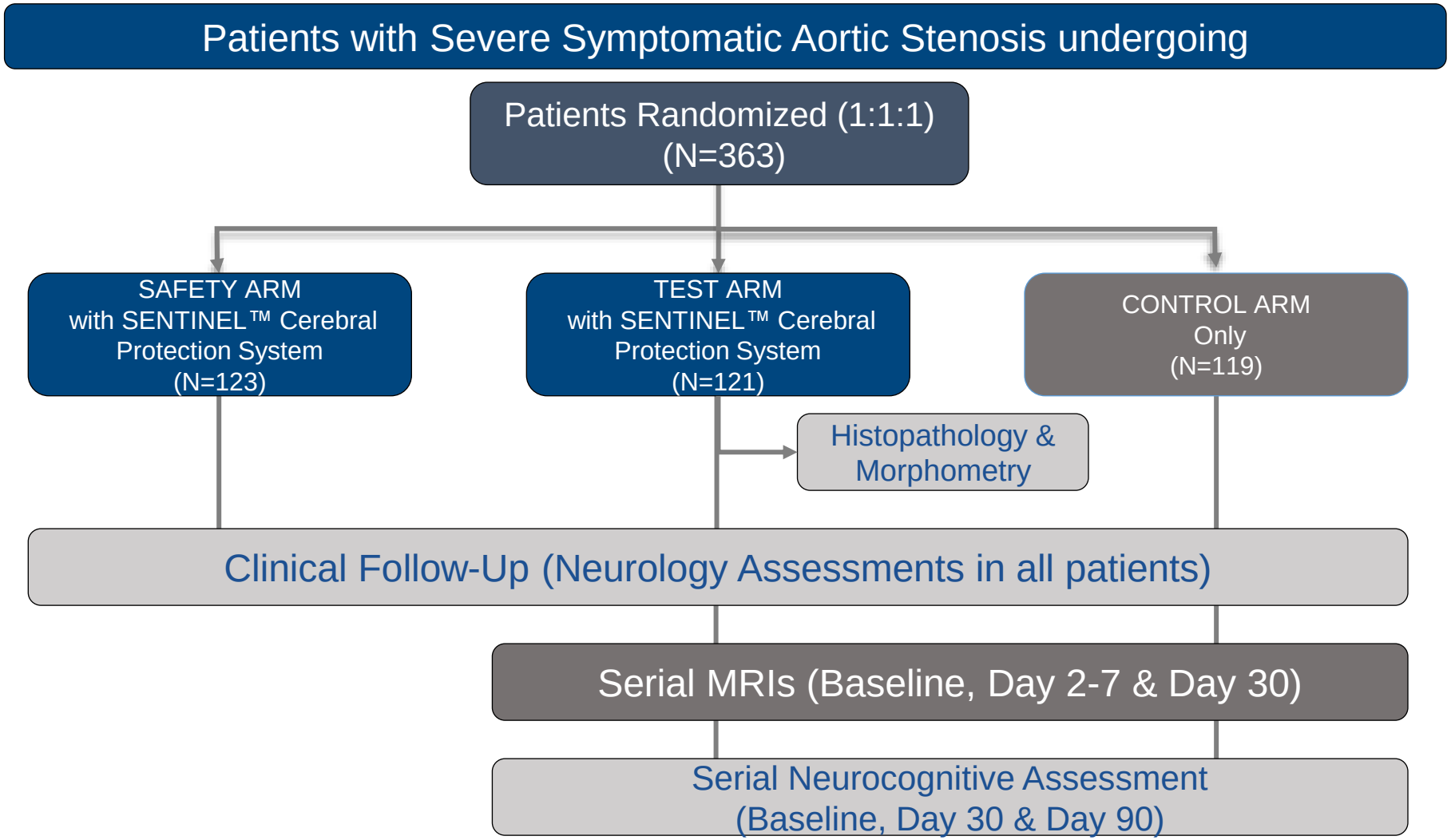
TAVR device advance



Embolic debris captured and removed



SENTINEL™ IDE Trial Design Overview



SENTINEL™ IDE Trial. Kapadia S, et al. *J Am Coll Cardiol* 2017;69:367–77

SENTINEL™ IDE Trial Study Endpoints

Safety Success Criteria

MACCE rate (derived from the Safety cohort (Safety Arm + Test Arm subjects) must be less than the pre-specified threshold of 18.3%.

Observational Success Criteria

To demonstrate the observed ratio of the median total new lesion volumes is ≥ 30% in favor of the Test Group having a lower median total new lesion volume in the protected territories as compared to the Control Group.

Efficacy Success Criteria

A significant difference ($p<0.05$) in the median total new lesion volume between the two randomized Imaging Arms where the *Test Group* has a lower median total new total lesion volume in the protected territories compared to the *Control Group*.

Kapadia S, et al. *J Am Coll Cardiol* 2017;69:367–77.

SENTINEL™ IDE Trial Primary Safety Endpoint: 30 Day MACCE

- SENTINEL™ IDE Trial 30-day MACCE rate directionally lower than Control Arm, driven by lower stroke rate

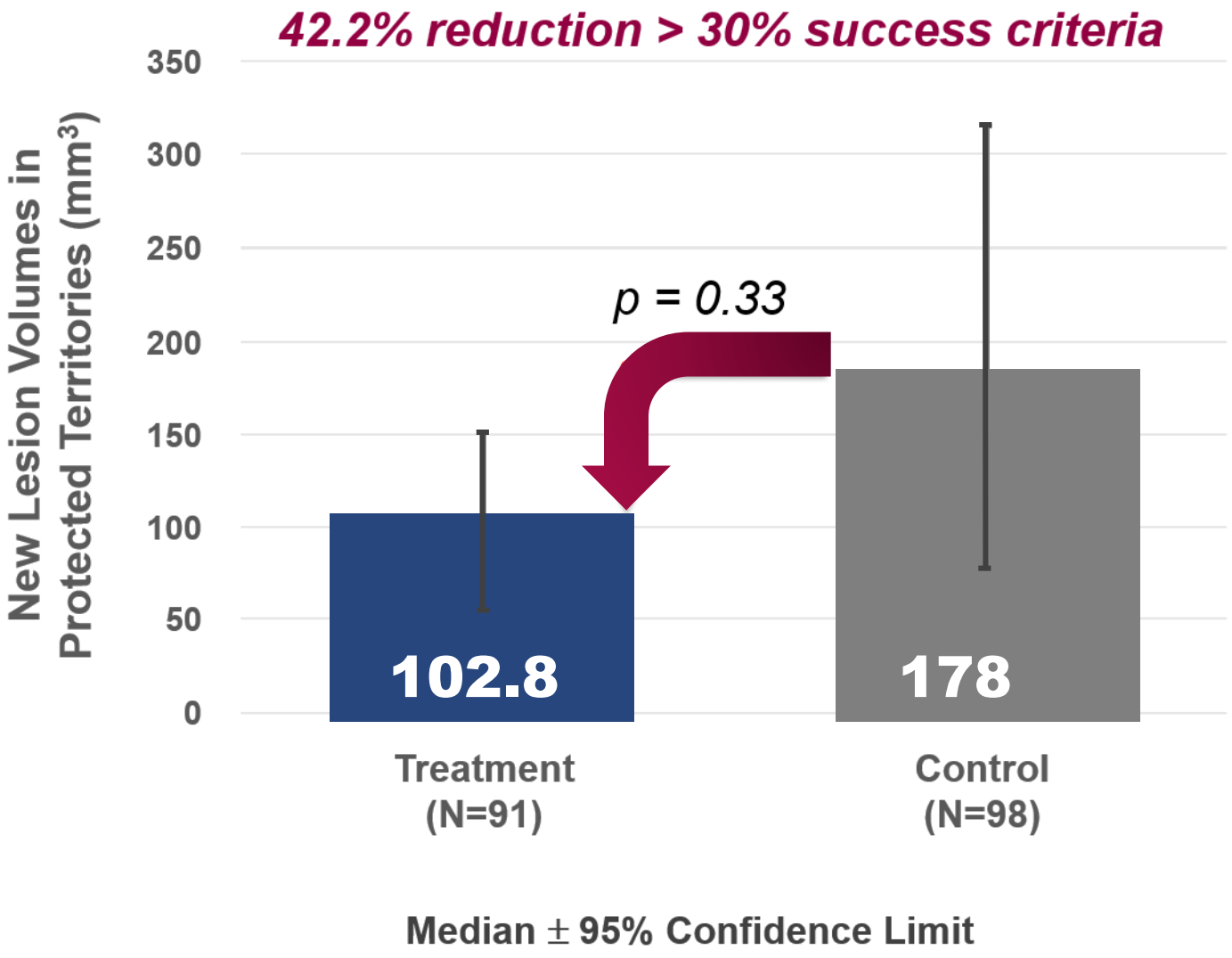
	SENTINEL™ Cerebral Protection System (Safety + Test) (N=234)		Without SENTINEL™ Cerebral Protection System (N=111)		
	N	%	N	%	P-value
Any MACCE† patients	17	**7.3**	11	**9.9**	0.40
Events					
Death (all-cause)	3	**1.3**	2	**1.8**	0.65
Stroke	13	**5.6**	10	**9.1**	0.25
Disabling	2	**0.9**	1	**0.9**	1.00
Non-disabling	11	**4.8**	9	**8.2**	0.22
AKI (Stage 3)	1	**0.4**	0	**0**	1.00
TIA	1	**0.4**	0	**0**	1.00
SENTINEL™-related complications[1]	1	**0.4**	N/A	**N/A**	N/A

[1]Late brachial artery pseudo-aneurysm treated with thrombin injection
†MACCE = major adverse cardiac and cerebrovascular events defined as Death (any cause), Stroke (any), Acute Kidney Injury (AKI, Stage 3).
Note: MACCE events adjudicated by independent Clinical Events Committee who were blinded to treatment arm

SENTINEL™ IDE Trial. Kapadia S, et al. *J Am Coll Cardiol* 2017;69:367–77

SENTINEL™ IDE Trial Primary Efficacy Endpoint

DW-MRI new lesion volume

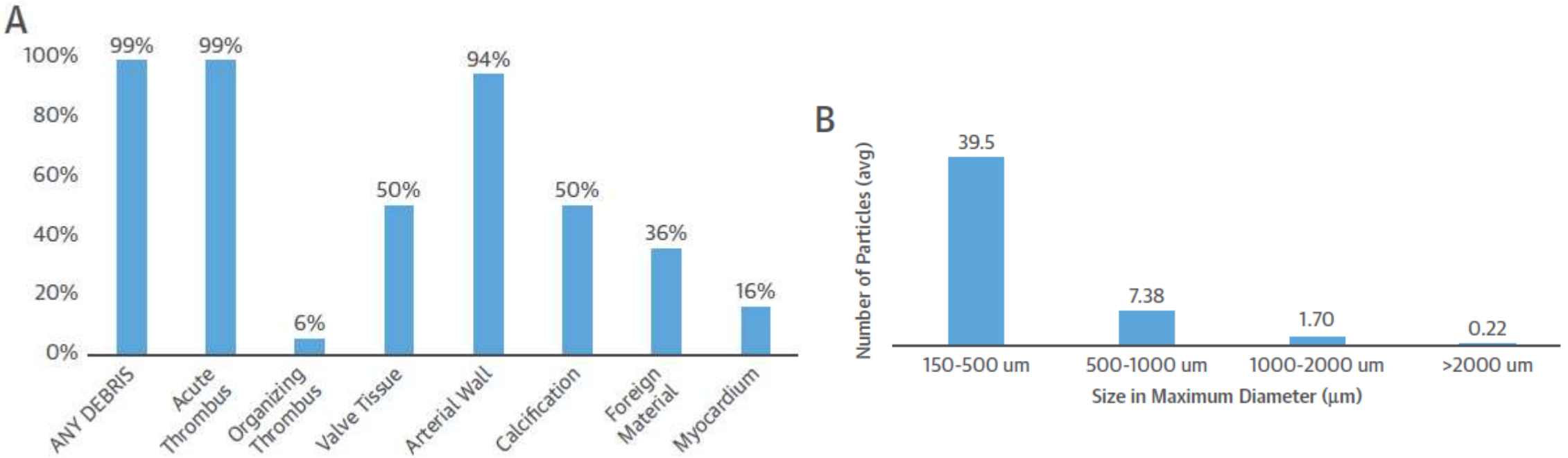


Kapadia S *et al.* JACC 2017;69:367–77

SENTINEL™ IDE Trial

Histopathologic Particulate Debris Analysis

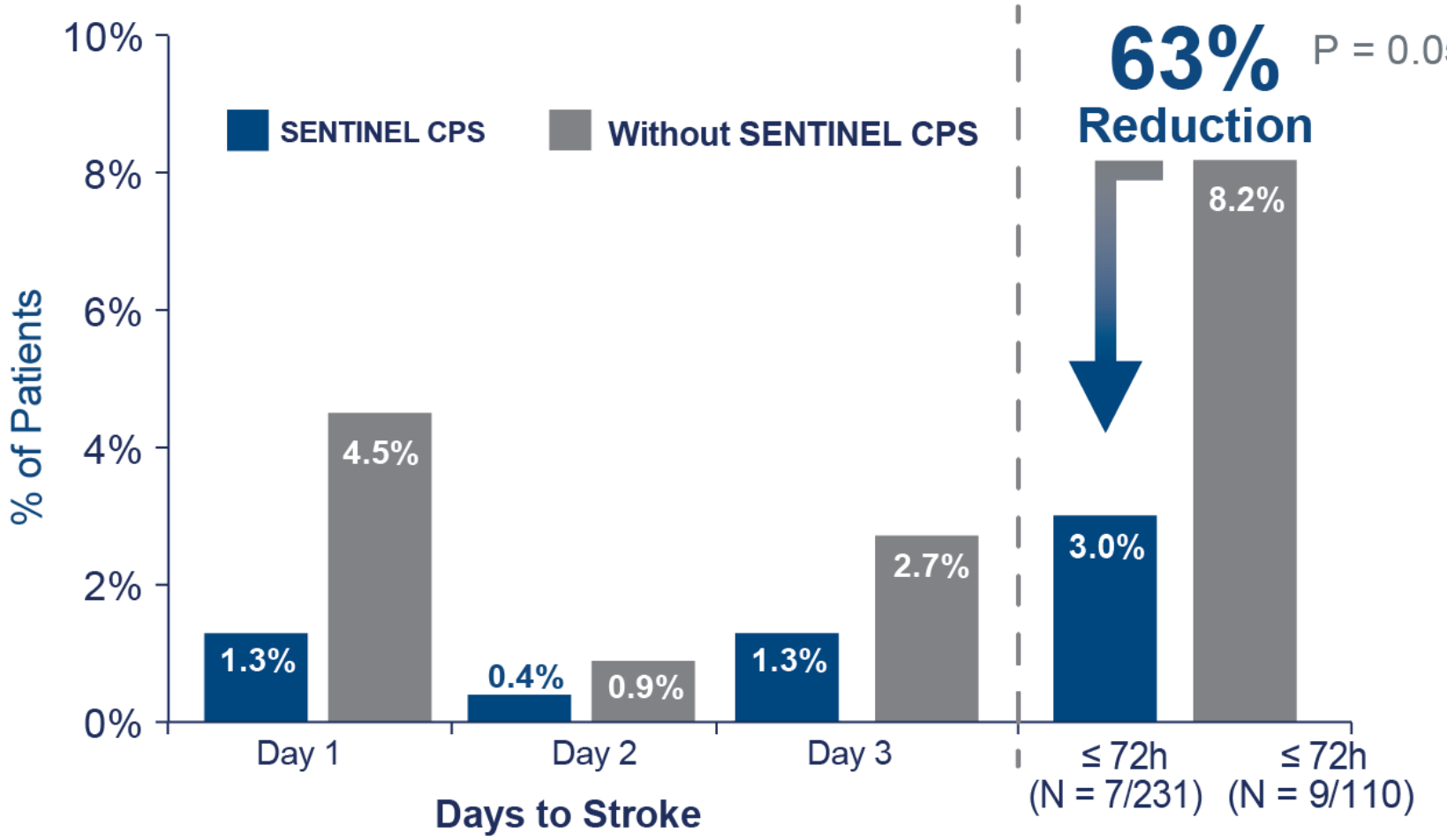
- Debris found within filters in 99% of patients
- Thrombus, calcification, valve tissue, artery wall, and foreign material



Kapadia S *et al.* JACC 2017;69:367–77

SENTINEL™ IDE Trial Peri-procedural (≤ 72 h) Stroke Reduction

➢ Statistically significant 63% peri-procedural (≤ 72 hours) stroke reduction with SENTINEL™ CPS.

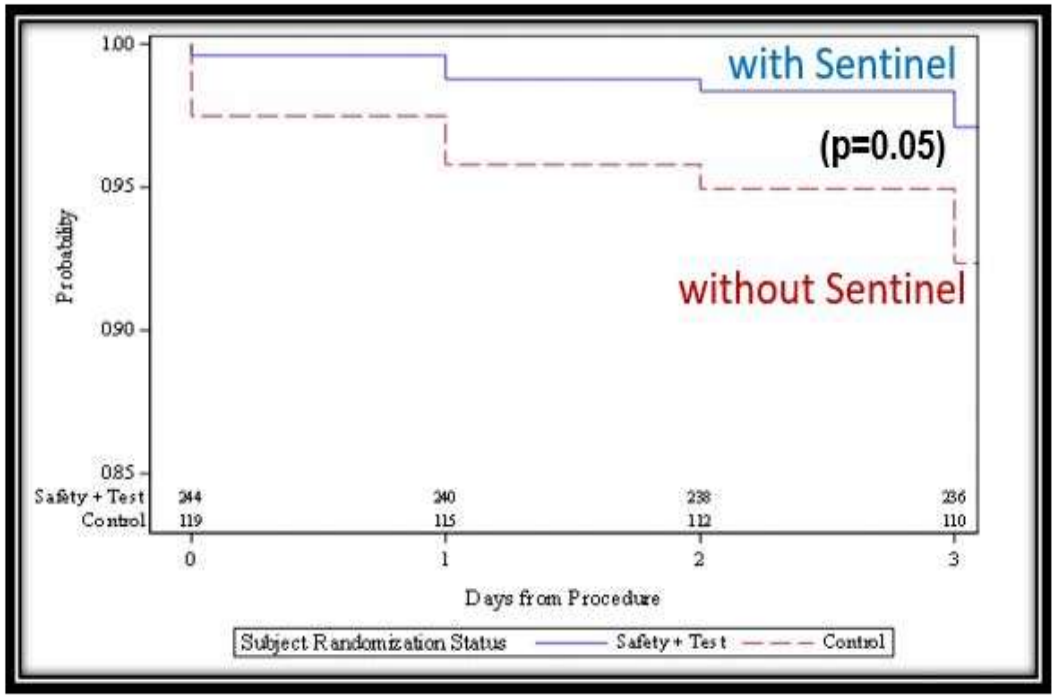


- 95% of SENTINEL™ CPS patients were evaluated by neurologists
- Clinical Events Committee included 2 stroke neurologists

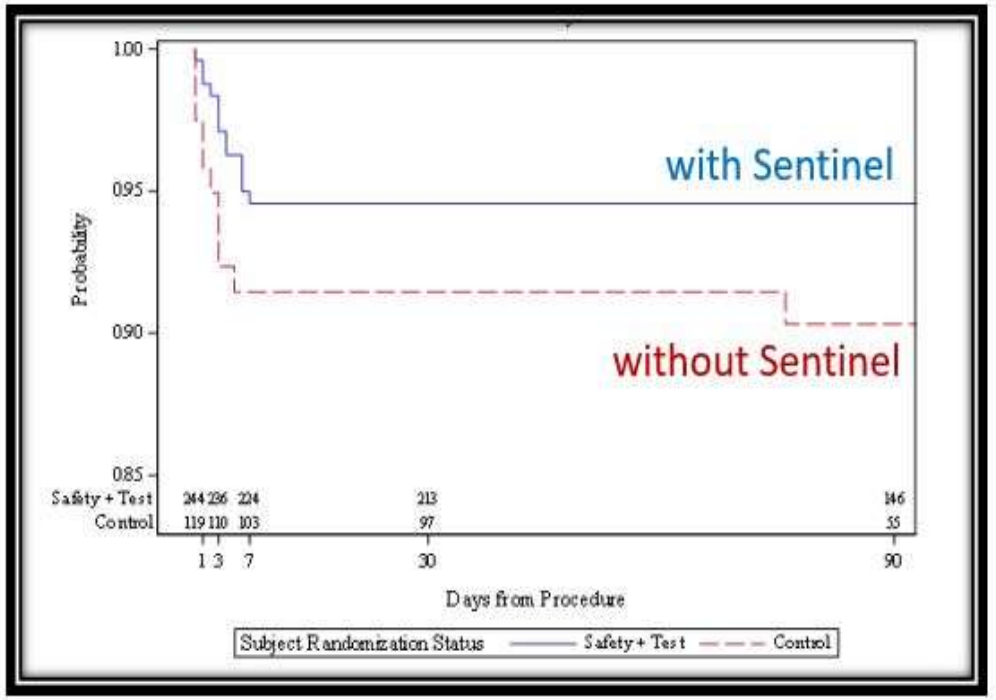
SENTINEL™ IDE Trial. Data presented at SENTINEL™ FDA Advisory Panel, February 23, 2017

SENTINEL™ IDE Trial: Freedom From Stroke – Kaplan-Meier Curves

- SENTINEL™ CPS provides a significant treatment effect during the critical peri-procedural (≤ 72 hours) period.
- The treatment effect is preserved through 90 days post-procedure.



Through 3 days post-procedure



Through 90 days post-procedure

Data on file from the SENTINEL™ IDE Trial.

NEWS • Daily News

FDA Clears Sentinel Cerebral Protection Device for Use During TAVR

The filter device becomes the first of its kind cleared for use in the United States during transcatheter aortic valve procedures.

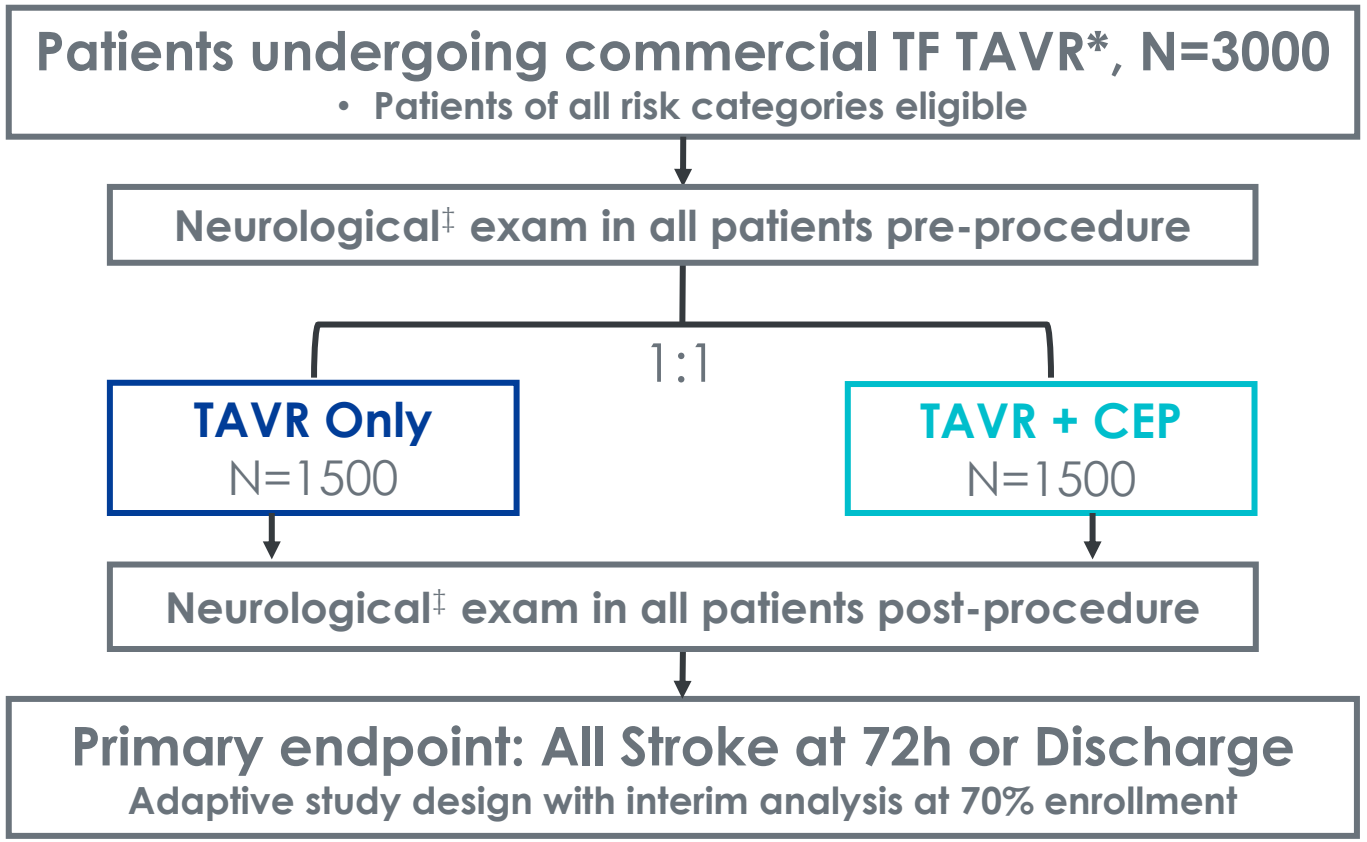
by Shelley Wood | JUNE 05, 2017

- …most panelists agreed that potential benefits of protection using the device outweigh any risks and said that despite the lack of clear clinical benefit —the SENTINEL trial did not meet its primary efficacy endpoint of significant reductions in new brain lesion volume on MRI—they themselves would want to have the device in place if they were undergoing TAVR
- “Intuitively, it seems like a very good thing to me that these [bits of] debris are taken out of the circulation pretty effectively by this filter and I think that’s a good thing” - FDA advisory panel member Jeffrey S. Borer, MD (SUNY Downstate Medical Center, New York, NY)

TCTMD daily news. Access on May 2023

PROTECTED TAVR Study Design

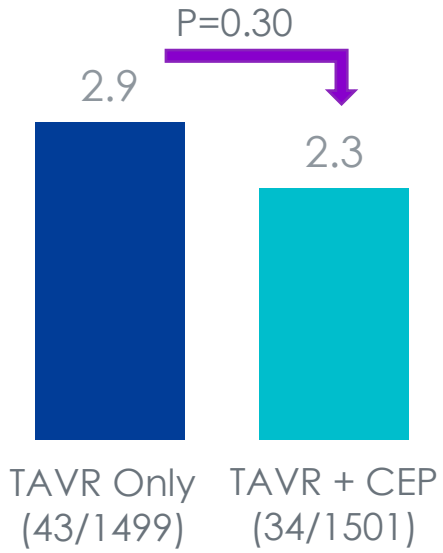
Prospective postmarket, multicenter, randomized, controlled trial
to investigate whether CEP reduces the risk of periprocedural stroke with TAVR



*Any commercially available TAVR device; ‡ Neurological examination at baseline, and post-procedure and through 72 hours after TAVR or discharge (whichever comes first), performed by a neurology professional (board certified/board eligible neurologist, neurology fellow, neurology physician assistant, or neurology nurse practitioner)

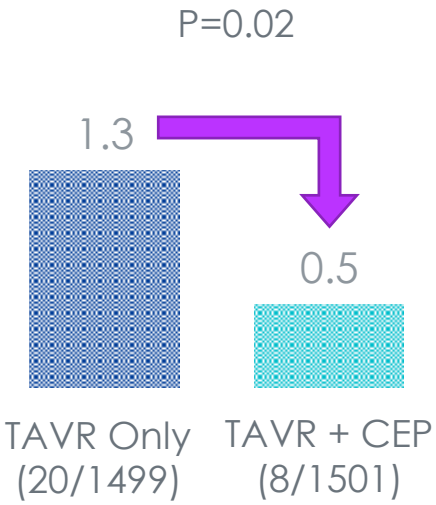
PROTECTED TAVR Results

Primary Endpoint: All Stroke



21%
relative risk reduction
in **All Stroke**
through 72 hours

Secondary Analysis: Disabling Stroke



60%
relative risk reduction
in **Disabling Stroke**
through 72 hours

- Largest randomized TAVR trial to date with 3,000 patients enrolled at more than 50 global sites
- Data demonstrated a non-significant but numerical trend toward a lower risk of stroke in patients treated with the SENTINEL device
- Secondary analysis of disabling stroke showed a statistical difference

Takeaways

- Stroke remains one of the major complications after TAVR. TAVR-related stroke is costly devastating
- SENTINEL is the only commercially approved cerebral embolic protection device for TAVR in the U.S
- Studies have shown that SENTINEL captures debris in 99% of patients in TAVR, while adding no additional risk to patients
- Fewer disabling strokes were observed with SENTINEL