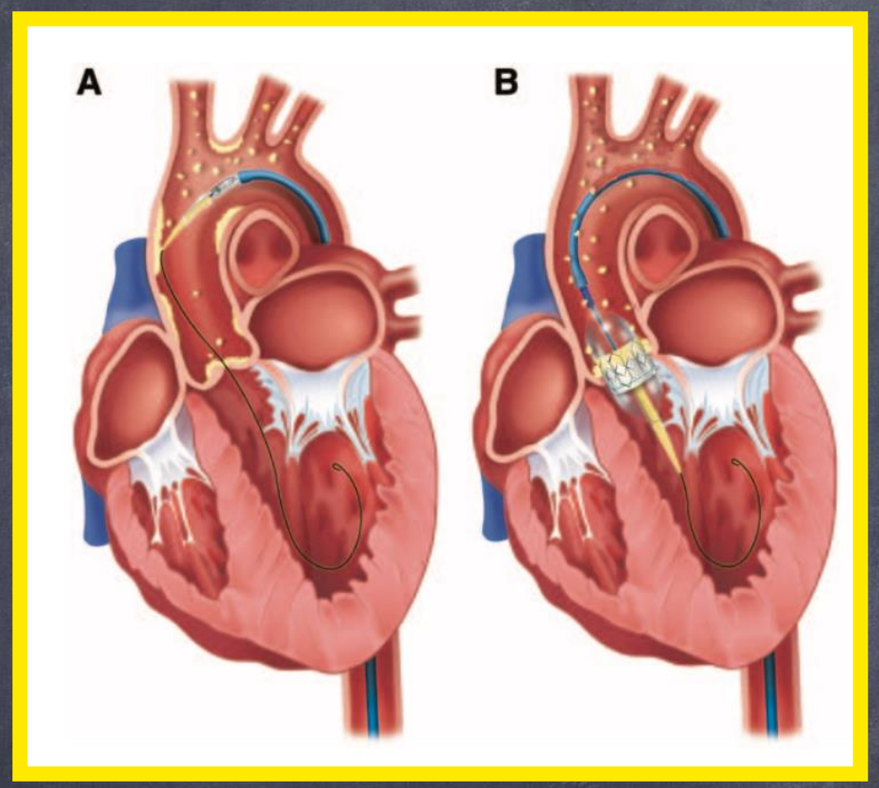
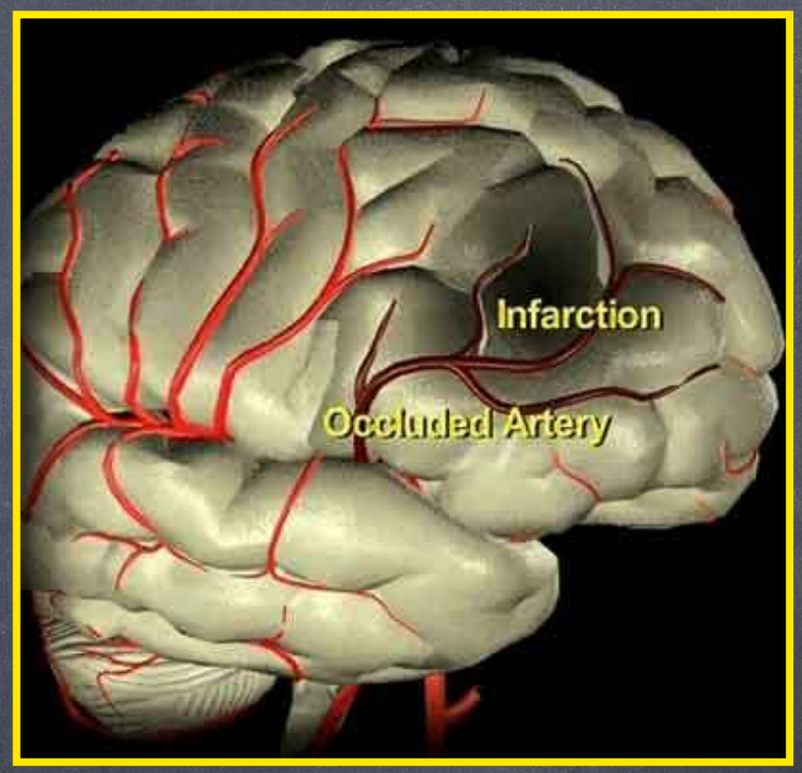
How To Manage Stroke After TAVR





Steve Ramee, MD

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New Orleans, LA

Disclosure

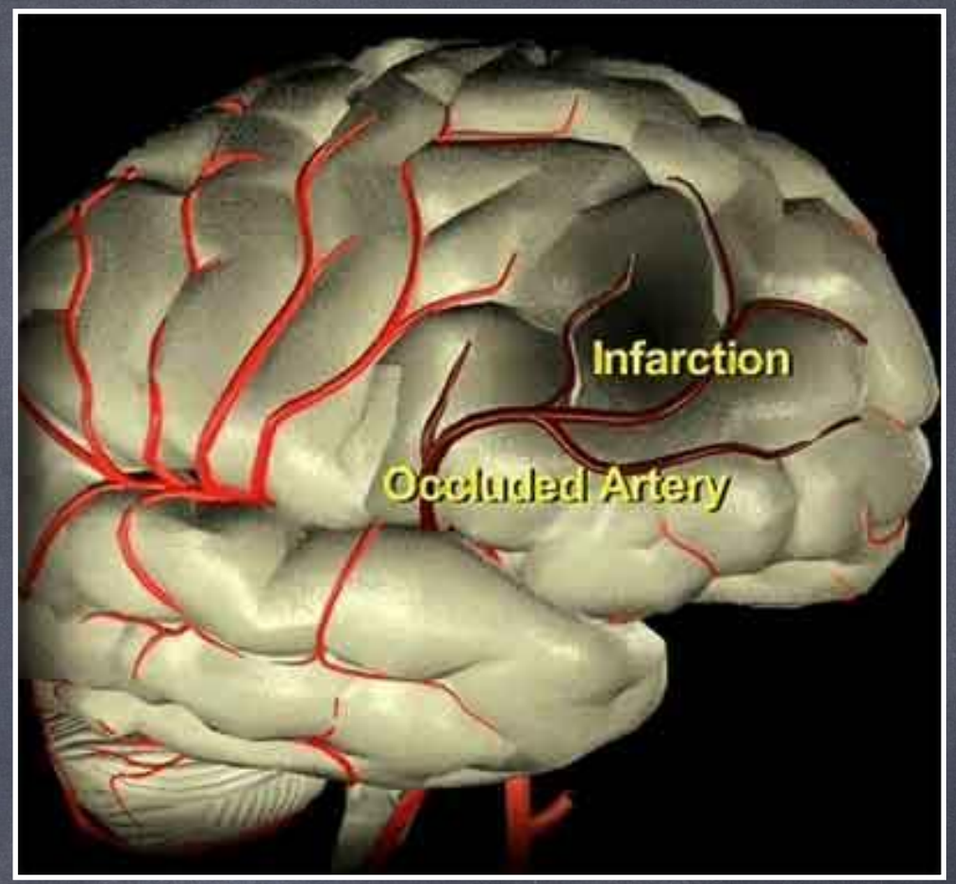
- Investor
  - Ocular Therapeutix, Northwind, Large Bore, The Stroke Project
- Advisory Board
  - Gardia Medical, Neurointerventions, The Stroke Project
- Honoraria
  - Edwards, Medtronic
- Clinical Research
  - Edwards, Abbott

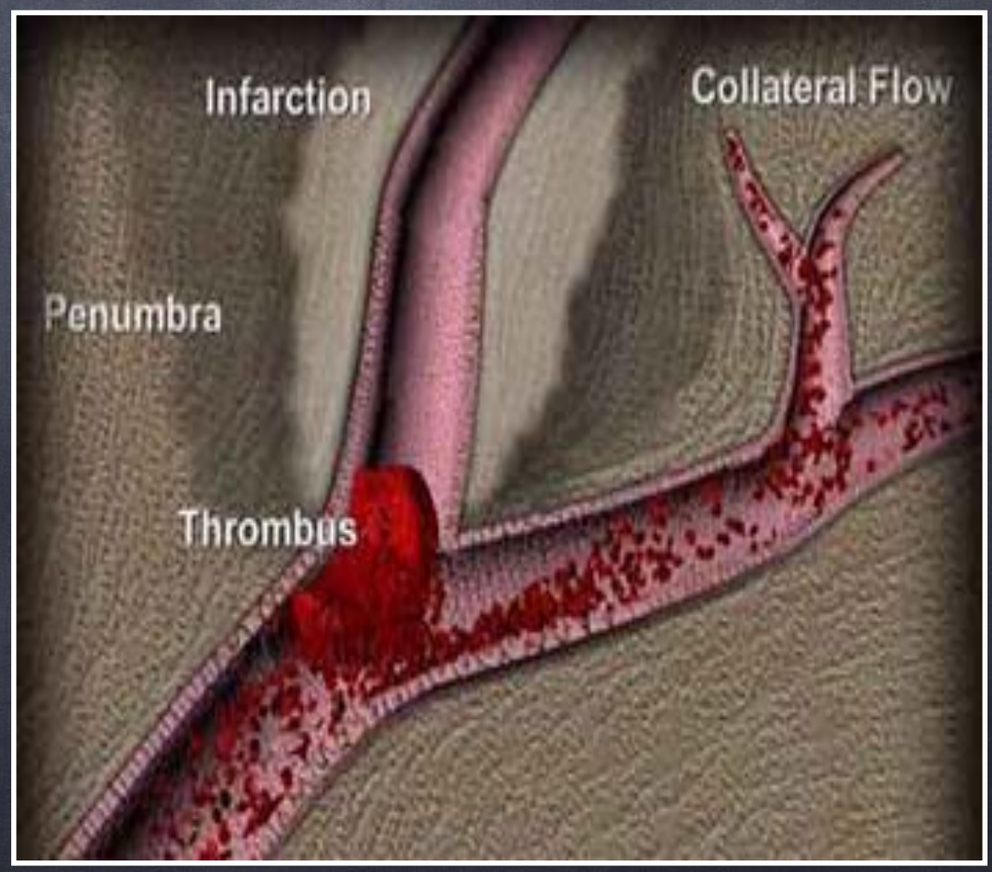
My Credentials

- Over 1000 TAVR's
- 30 years of coronary intervention
- 20 yrs of stroke intervention

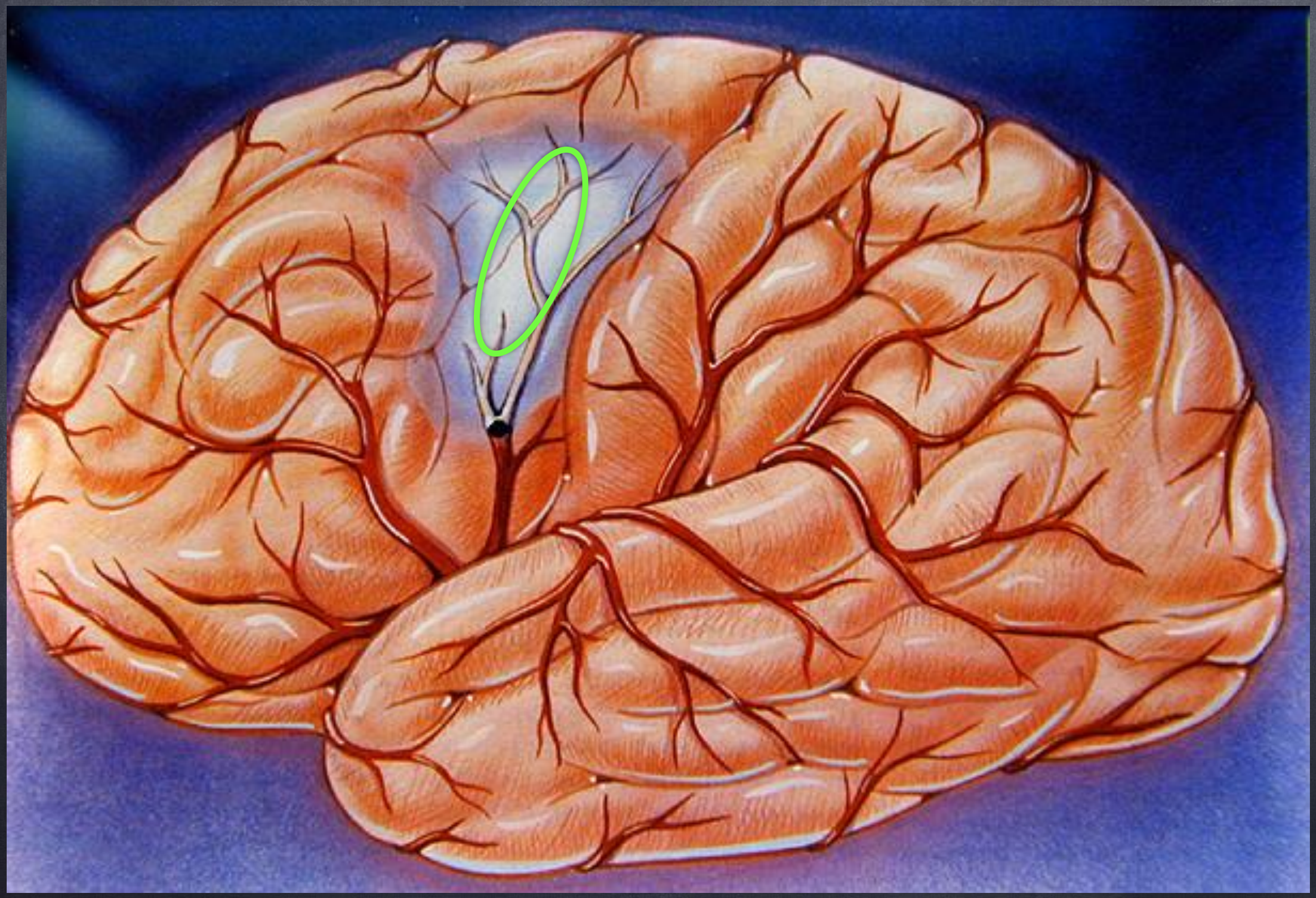
What causes ischemic stroke?

- *Different* than MI.
- Embolic occlusion rather than intracranial plaque rupture
- Extracranial sources in 85%:
  - Carotid plaque
  - Cardioembolic
    - Atrial appendage
    - LV thrombus
    - PFO
    - Surgical and endovascular procedures
  - Dissection





Ischemic Penumbra



Time is BRAIN!

Time Is Brain—Quantified

Jeffrey L. Saver, MD

Background and Purpose—The phrase "time is brain" emphasizes that human nervous tissue is rapidly lost as stroke progresses and emergent evaluation and therapy are required. Recent advances in quantitative neurostereology and stroke neuroimaging permit calculation of just how much brain is lost per unit time in acute ischemic stroke.

Methods—Systematic literature-review identified consensus estimates of number of neurons, synapses, and myelinated fibers in the human forebrain; volume of large vessel, supratentorial ischemic stroke; and interval from onset to completion of large vessel, supratentorial ischemic stroke.

Results—The typical final volume of large vessel, supratentorial ischemic stroke is 54 mL (varied in sensitivity analysis from 19 to 100 mL). The average duration of nonlacunar stroke evolution is 10 hours (range 6 to 18 hours), and the average number of neurons in the human forebrain is 22 billion. In patients experiencing a typical large vessel acute ischemic stroke, 120 million neurons, 830 billion synapses, and 714 km (447 miles) of myelinated fibers are lost each hour. In each minute, 1.9 million neurons, 14 billion synapses, and 12 km (7.5 miles) of myelinated fibers are destroyed. Compared with the normal rate of neuron loss in brain aging, the ischemic brain ages 3.6 years each hour without treatment. Altering single input variables in sensitivity analyses modestly affected the estimated point values but not order of magnitude.

Conclusions—Quantitative estimates of the pace of neural circuitry loss in human ischemic stroke emphasize the time urgency of stroke care. The typical patient loses 1.9 million neurons each minute in which stroke is untreated. (***Stroke.*** **2006;37:263-266.)**

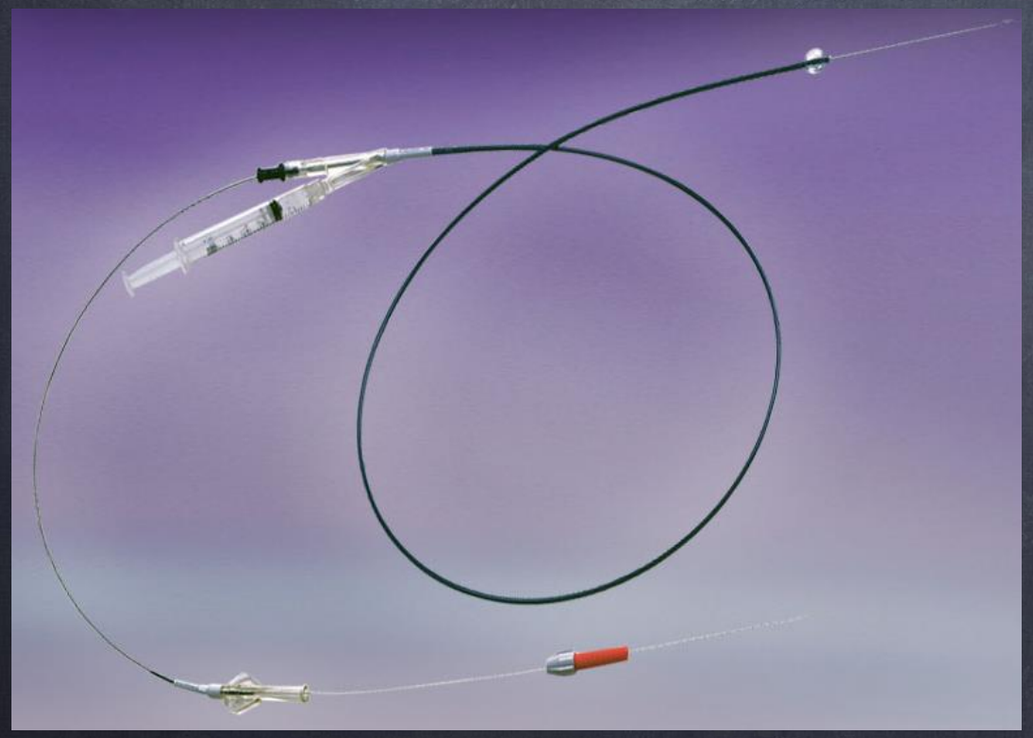
"The typical (stroke) patient loses 1.9 MILLION neurons each minute in which stroke is untreated."

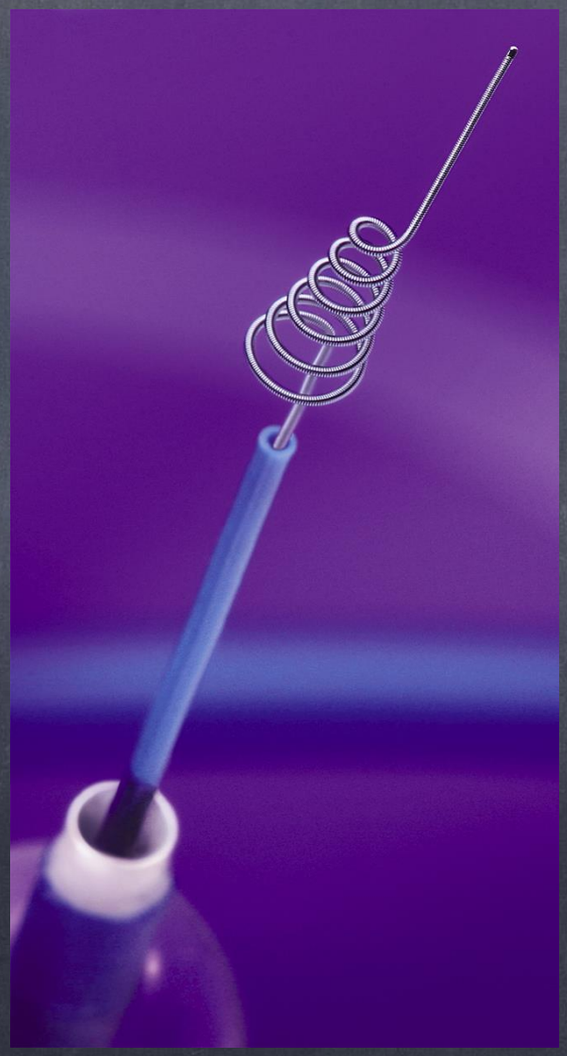
Catheter-based Approach to Stroke

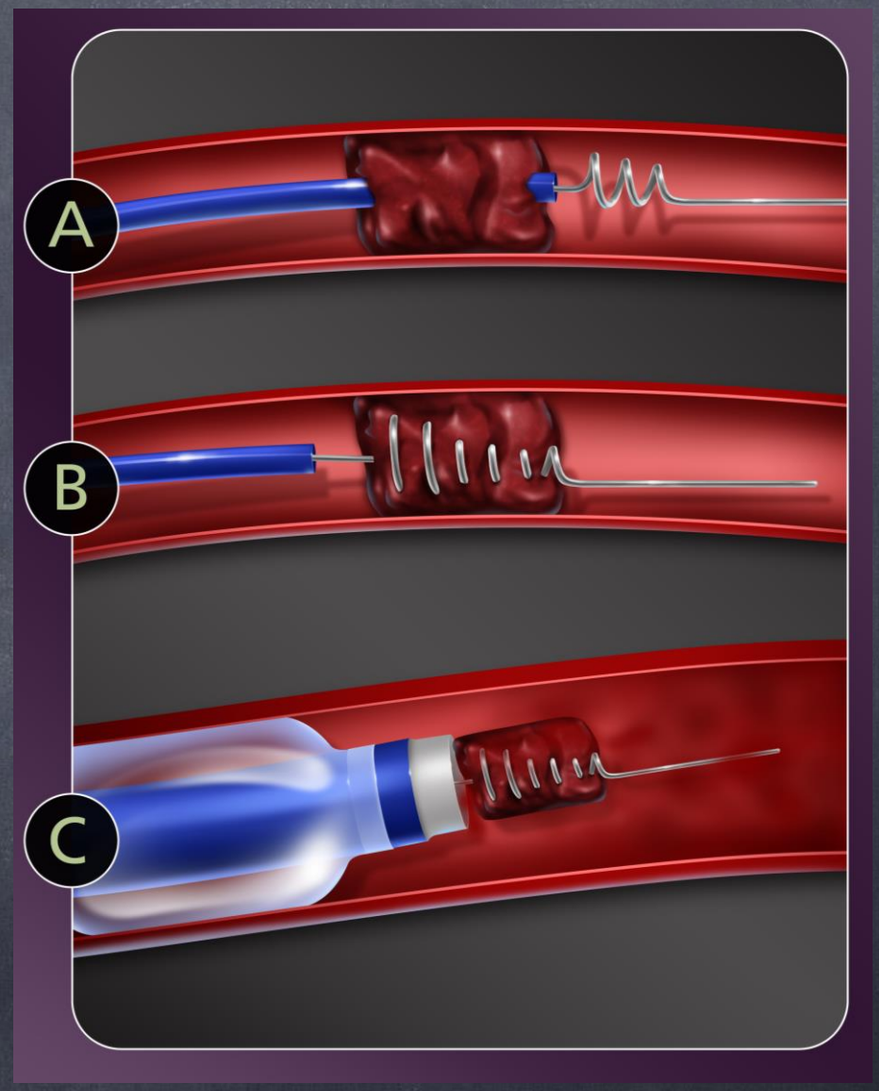
- Time is brain
- Target vessel angiography first
  - Other vessels only if dx is in question
- Cross lesion with hydrophilic wire
- If soft thrombus: Lysis, Stentriever.
  - Do NOT use lysis if time > 4-6hr or contraindications
- If hard thrombus: Merci, stentriever, stent
- Remember: Primum non-nocere!

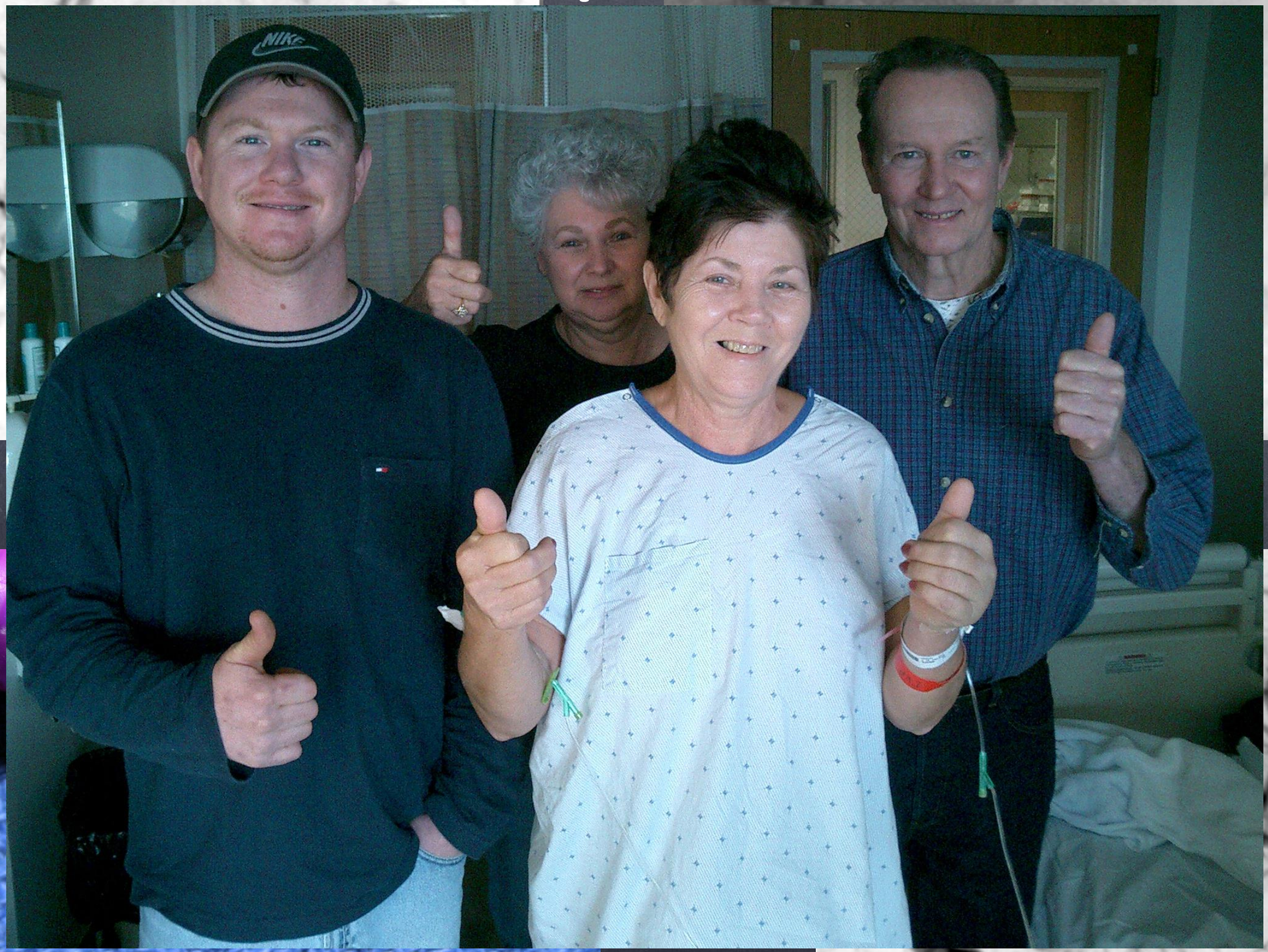
Merci® Retrieval System

- Retriever
- Microcatheter
- Balloon Guide Catheter

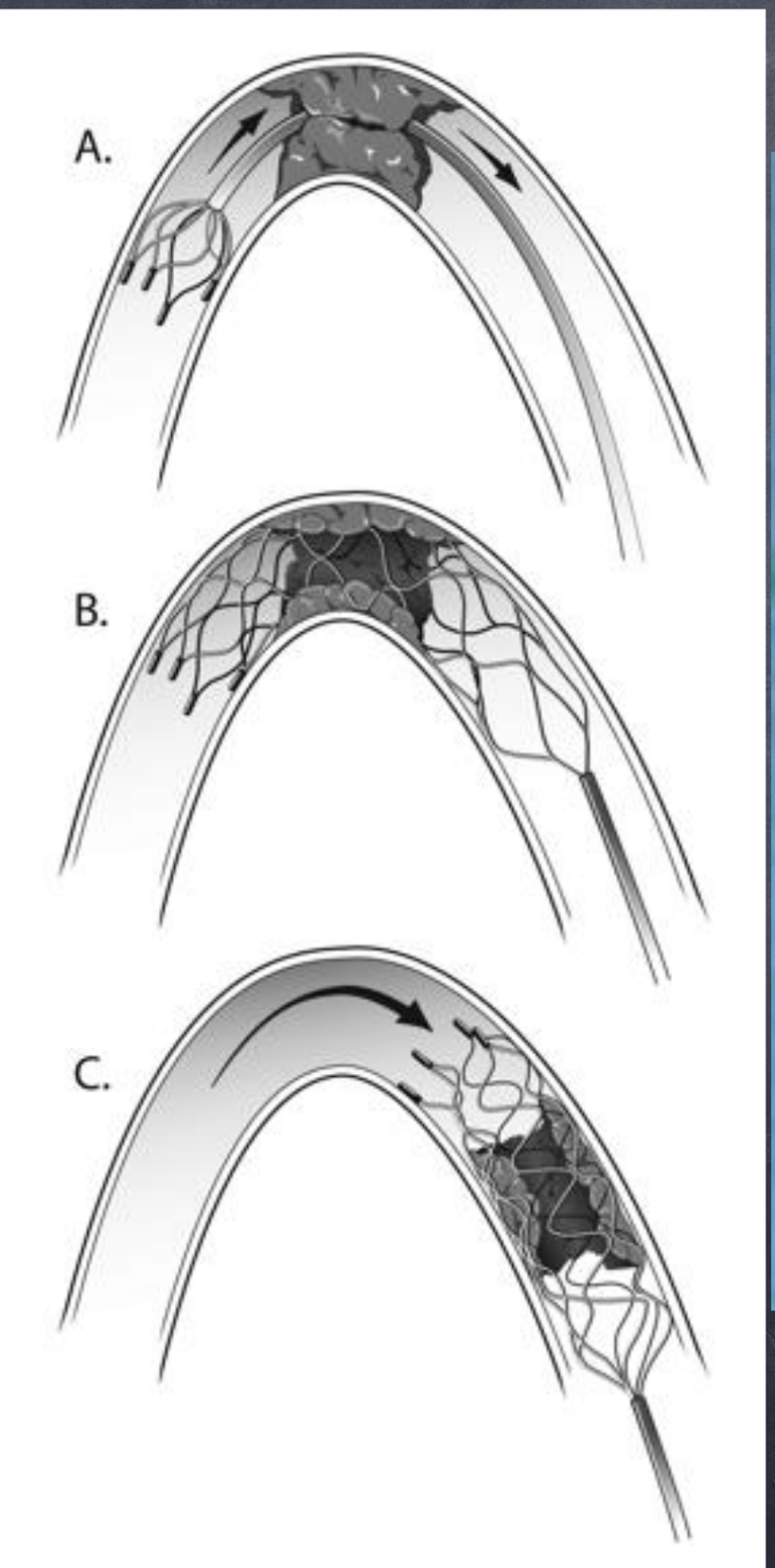


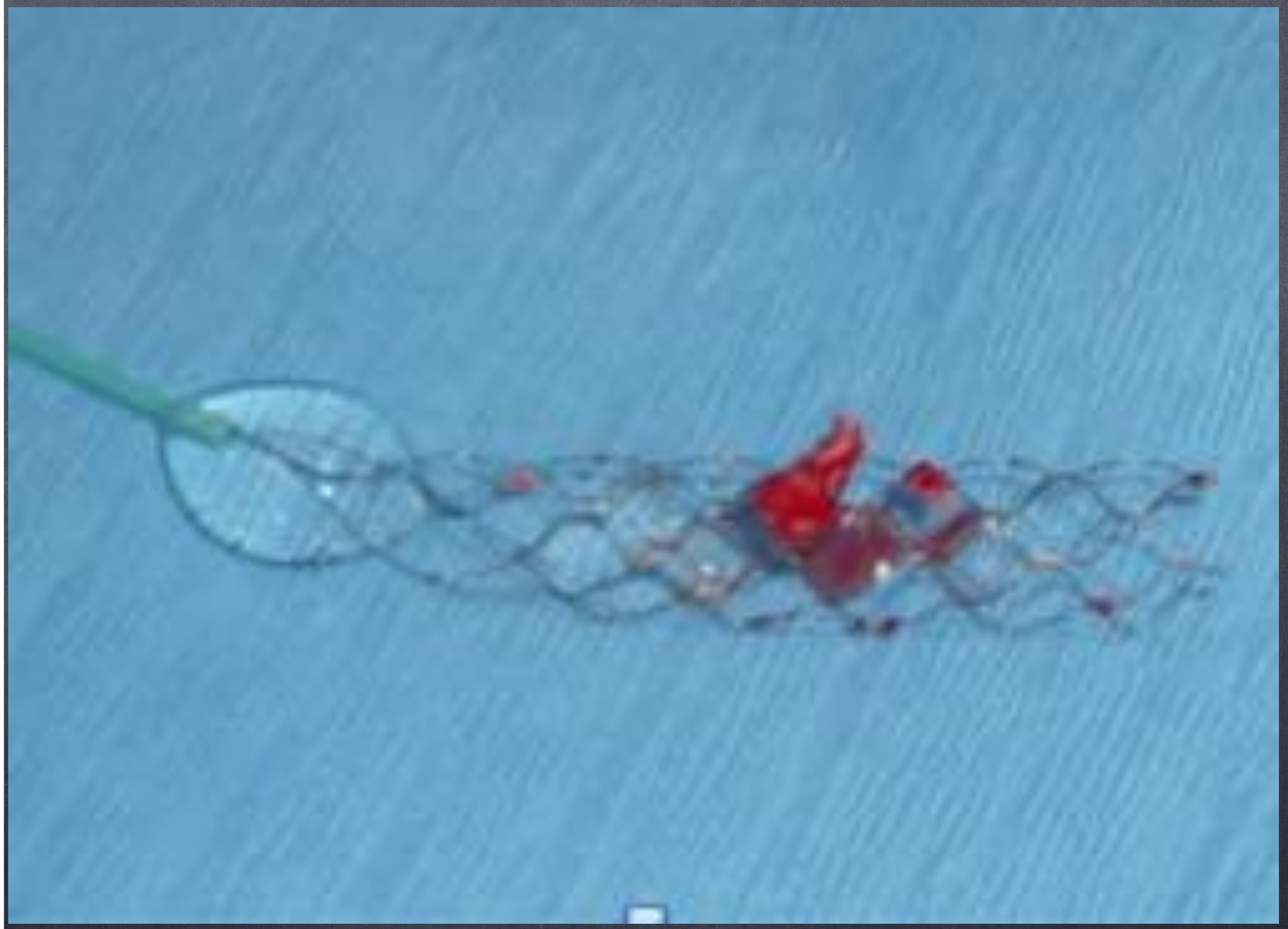





NIKE

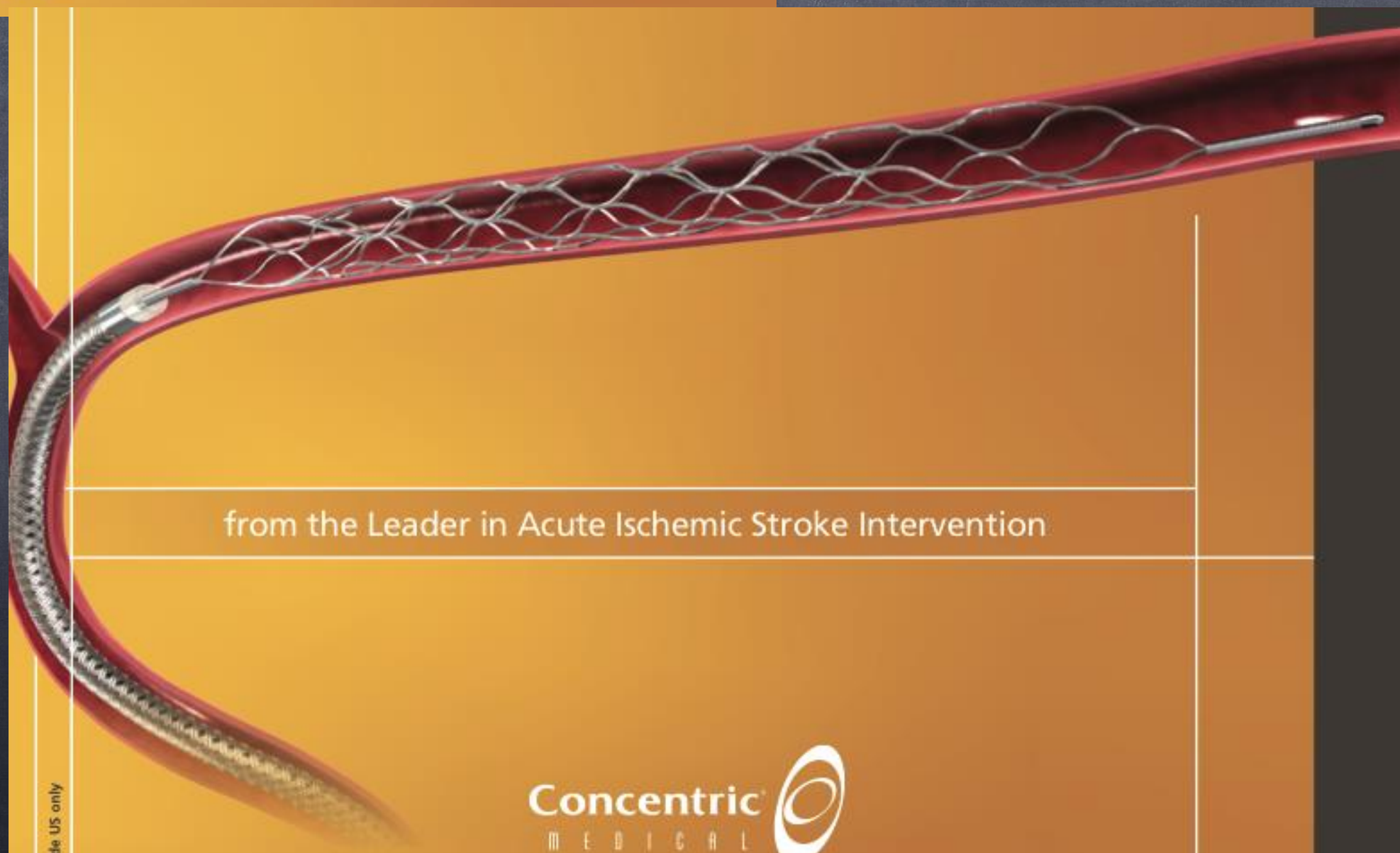
Solitaire Temporary Stent





TREVO™

The First Stentriever™ Designed and Built for Stroke



from the Leader in Acute Ischemic Stroke Intervention

Concentric® MEDICAL

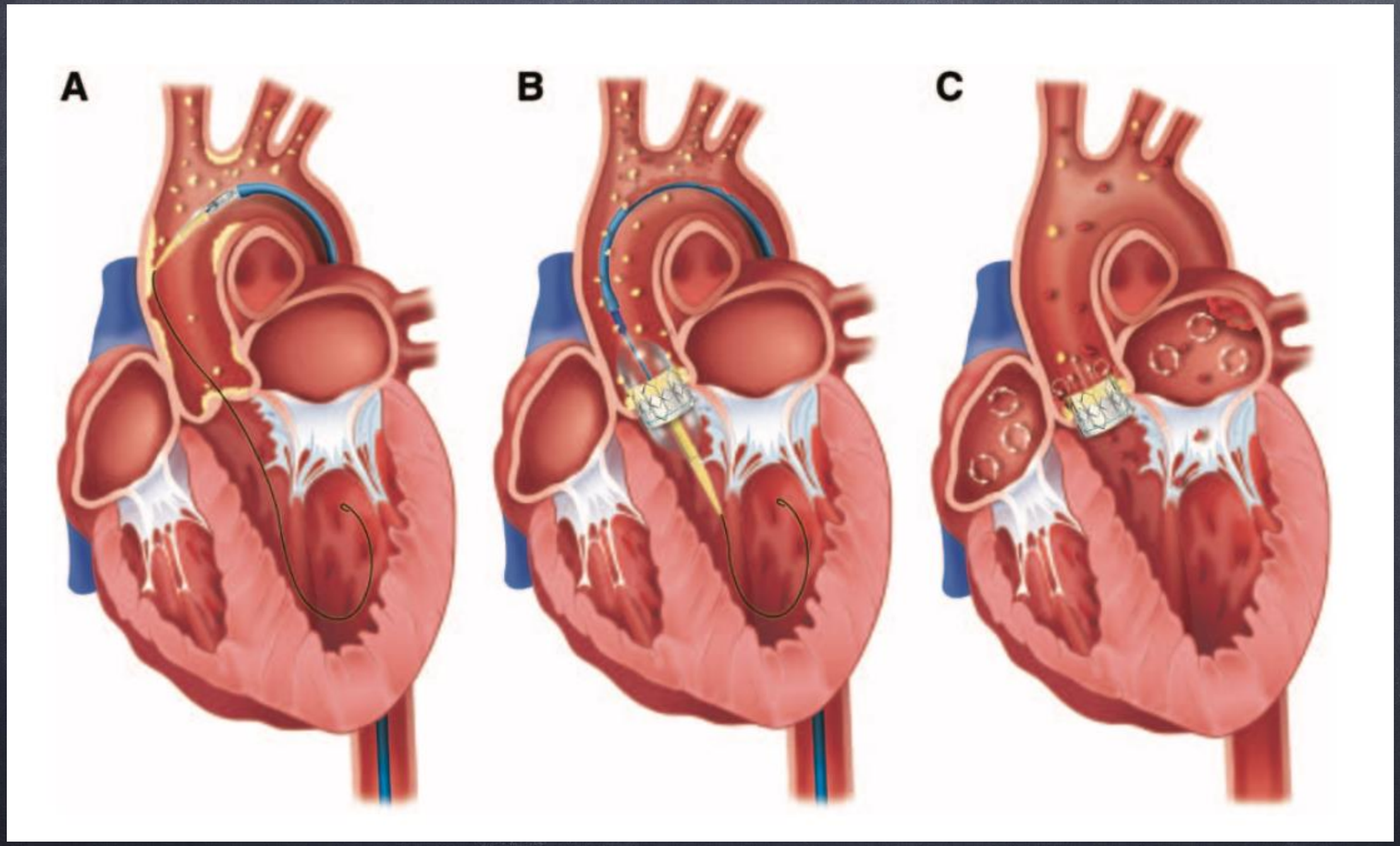
Rx only

Outside US only

Stroke after TAVR is a special situation

- The incidence of stroke after TAVR exceeds that of any other interventional procedure.
- The cause of the stroke is likely NOT clot, but atherosclerotic debris and not likely lyse-able or retrievable.
- TAVR patients cannot receive IV thrombolysis because of fresh access sites which could bleed.
- Patients are under anesthesia when the stroke occurs. May be hours before they regain consciousness and can be assessed for stroke which reduces the time available for stroke intervention.

Sources of Embolization with TAVR



Circulation. **2014;129:504-515.**

30d Incidence of Stroke after TAVR

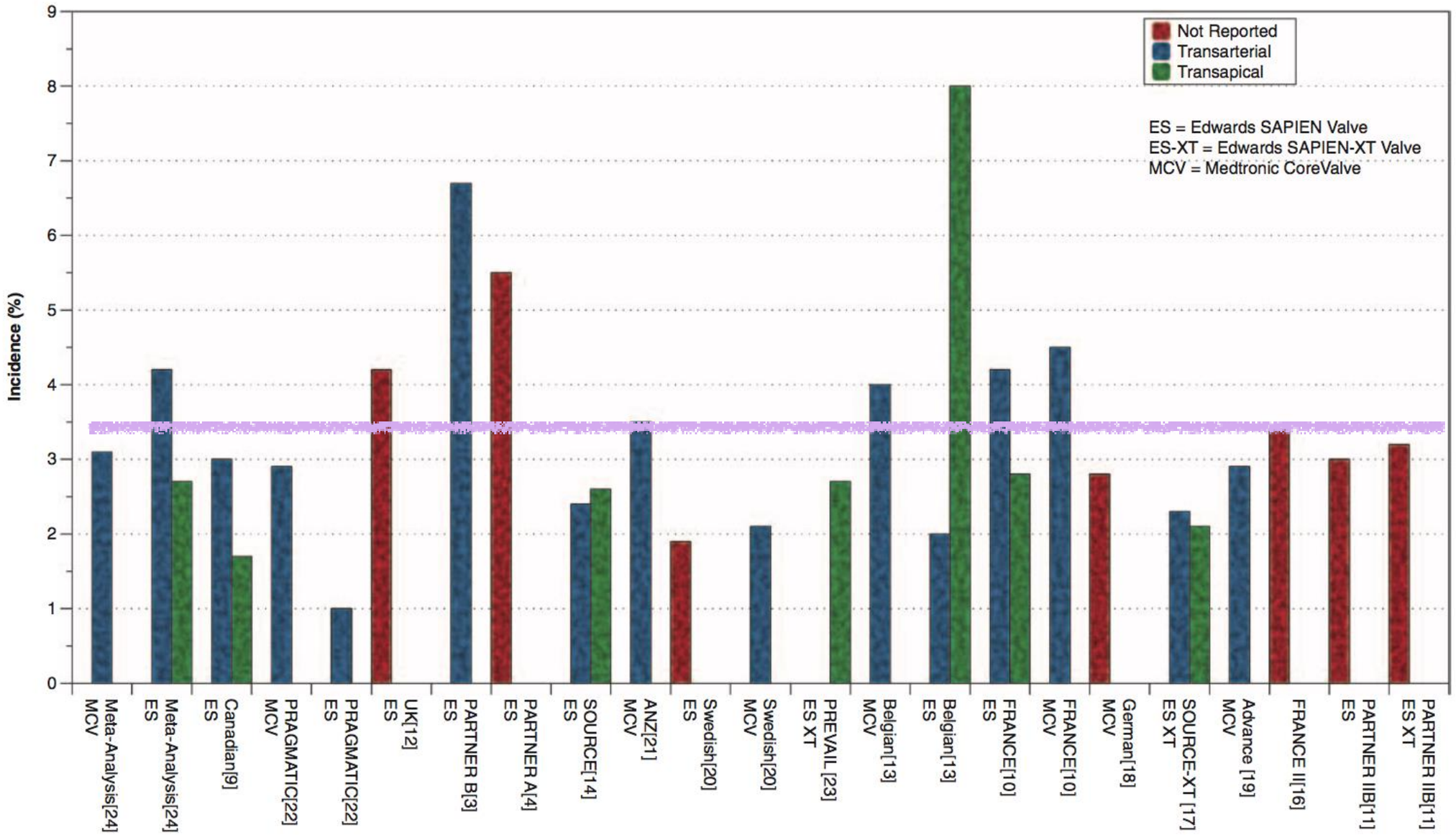


Figure 2. Thirty-day stroke incidence following TAVI. Studies arranged chronologically (from left to right) based on date of first patient recruitment. TAVI indicates transcatheter aortic valve implantation.

Circulation. **2014;129:504-515.**

DW-MRI lesions post TAVR

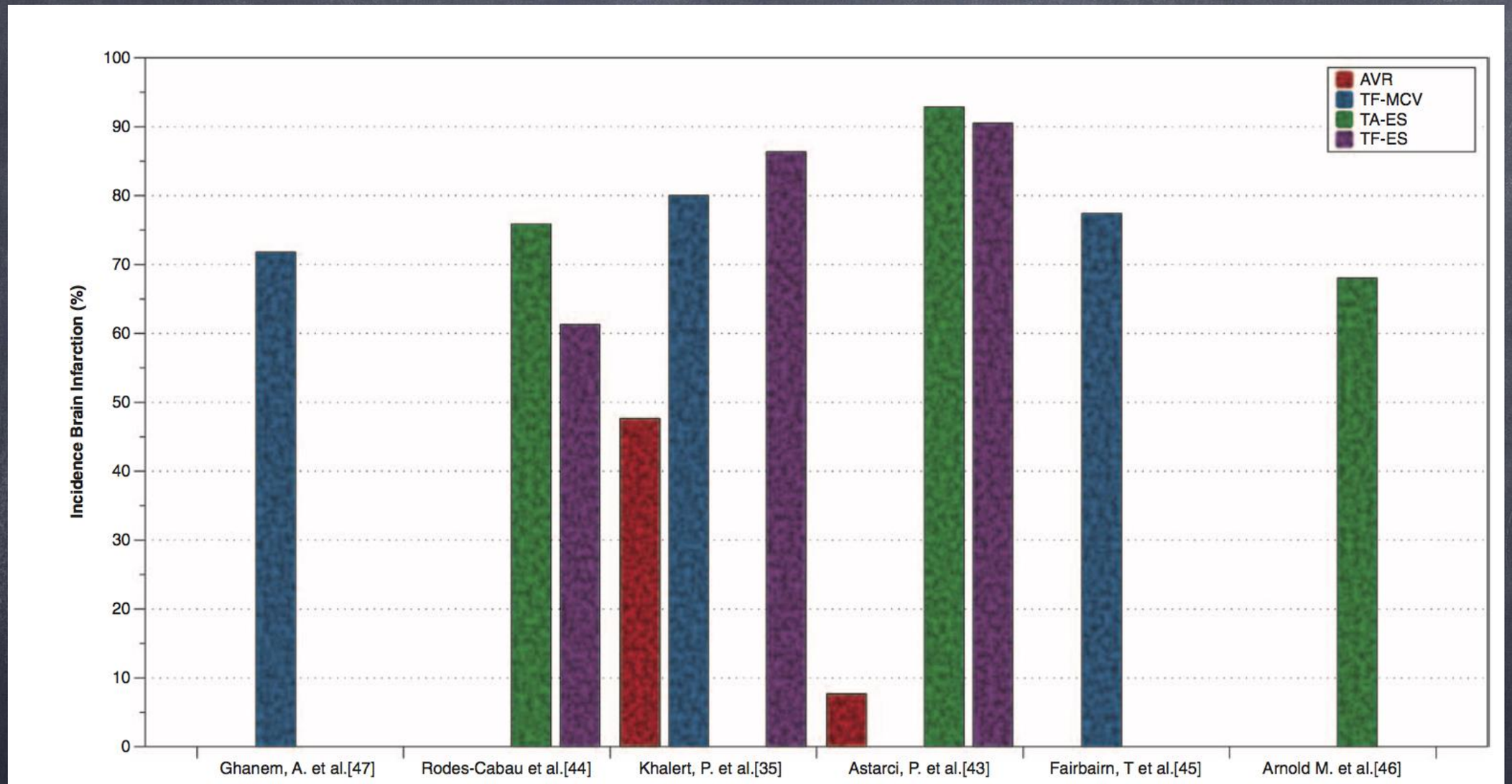


Figure 5. Silent cerebral ischemic lesions on DW-MRI post-TAVI. AVR indicates aortic valve replacement; DW-MRI, diffusion-weighted MRI; ES, Edwards SAPIEN valve; MCV, Medtronic CoreValve; TA, transapical; TAVI, transcatheter aortic valve implantation; and TF, transfemoral.

Circulation. **2014;129:504-515.**

Spectrum of Neurologic Injury in Stroke after TAVR

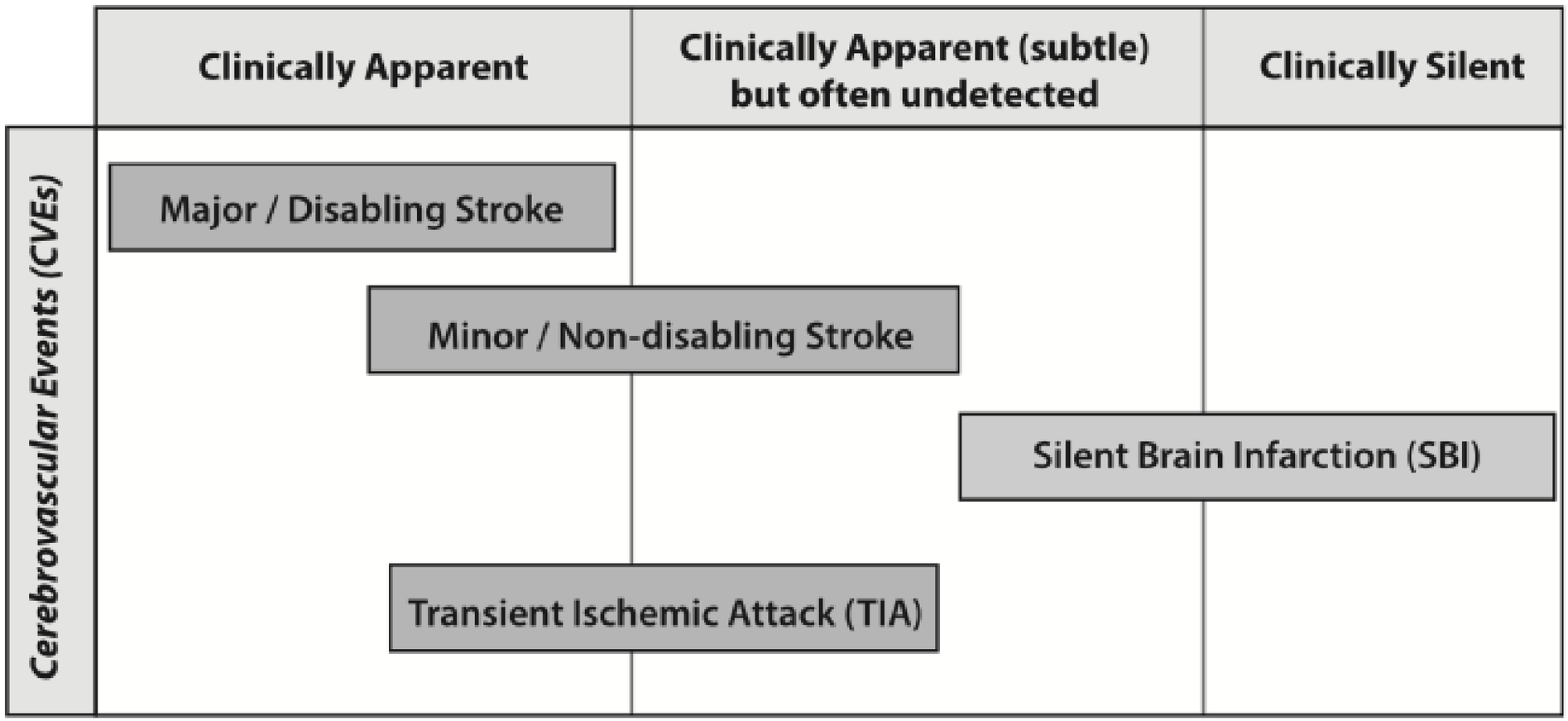


Figure 1. Spectrum of neurological injury in TAVI. TAVI indicates transcatheter aortic valve implantation.

Circulation**. 2014;129:504-515.**

Significance of Silent DW-MRI Events

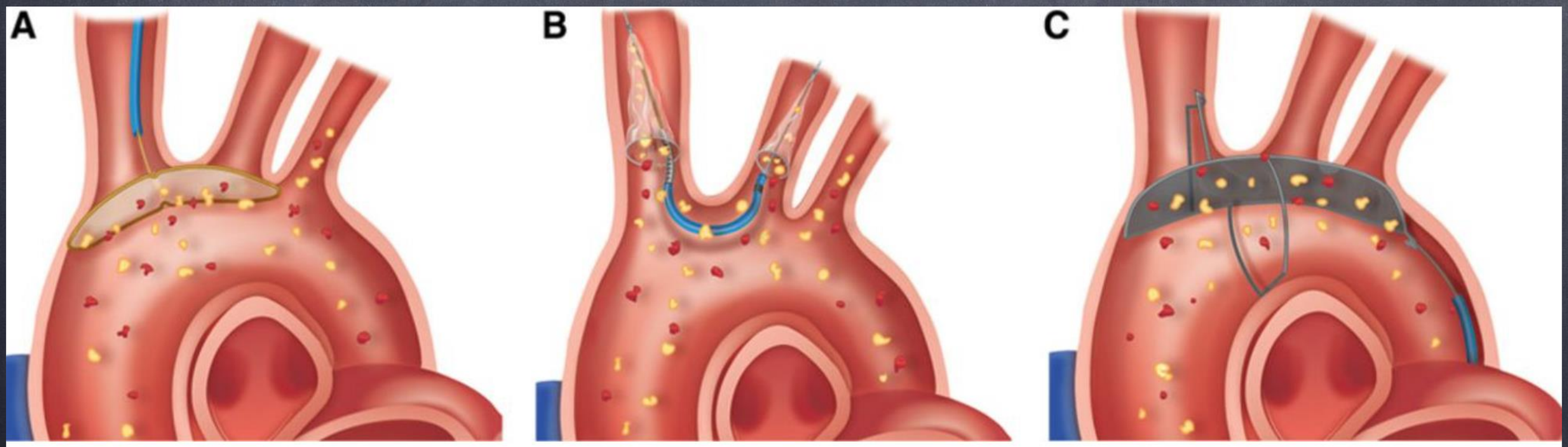
- No correlation with risk of symptomatic stroke post TAVR.
- Unknown significance of long term neuro-cognative decline.

When you recognize a stroke after TAVR

- Initiate a “stroke code”
- Stroke specialists will order imaging studies
  - CT perfusion
  - MRI/MRA
- Treatment will be directed by these studies.
- Often, conservative management will be the default therapy because of athero-embolic debris rather than clot.

When it comes to Stroke and TAVR

Embolic Protection Devices for TAVR

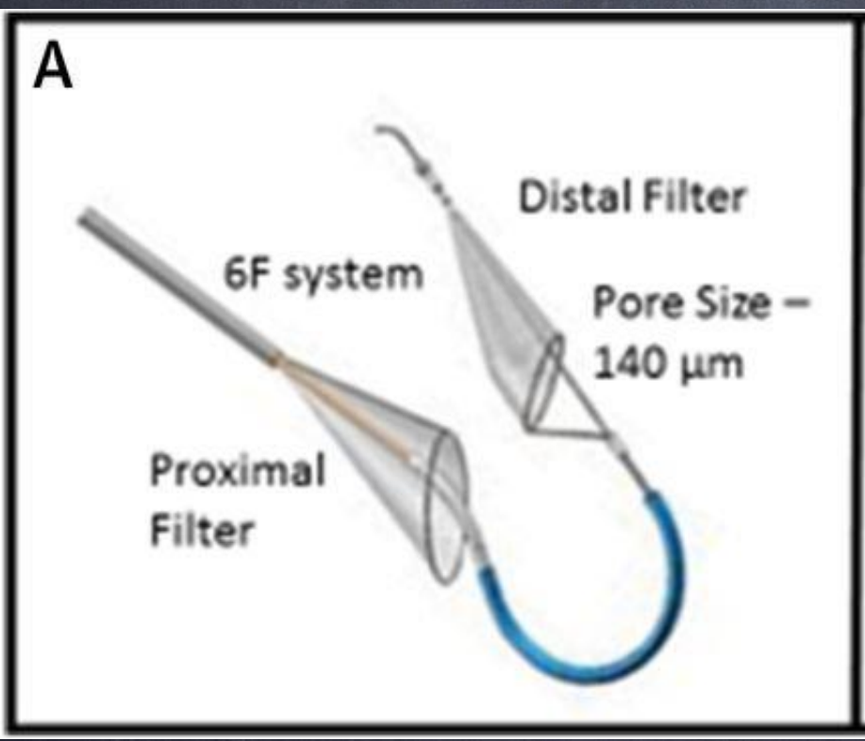


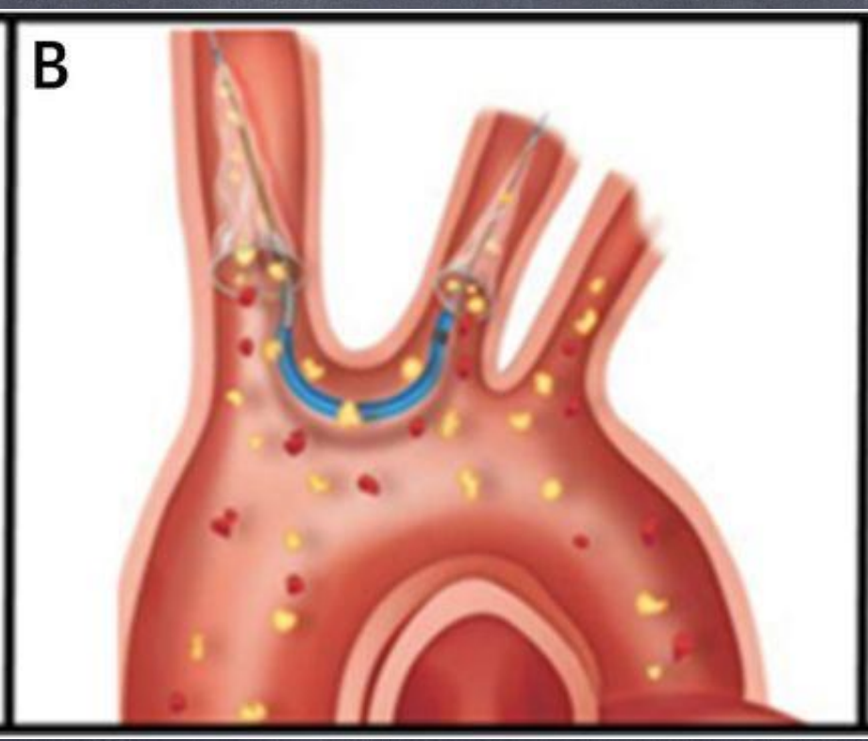
Edwards
Umbrella

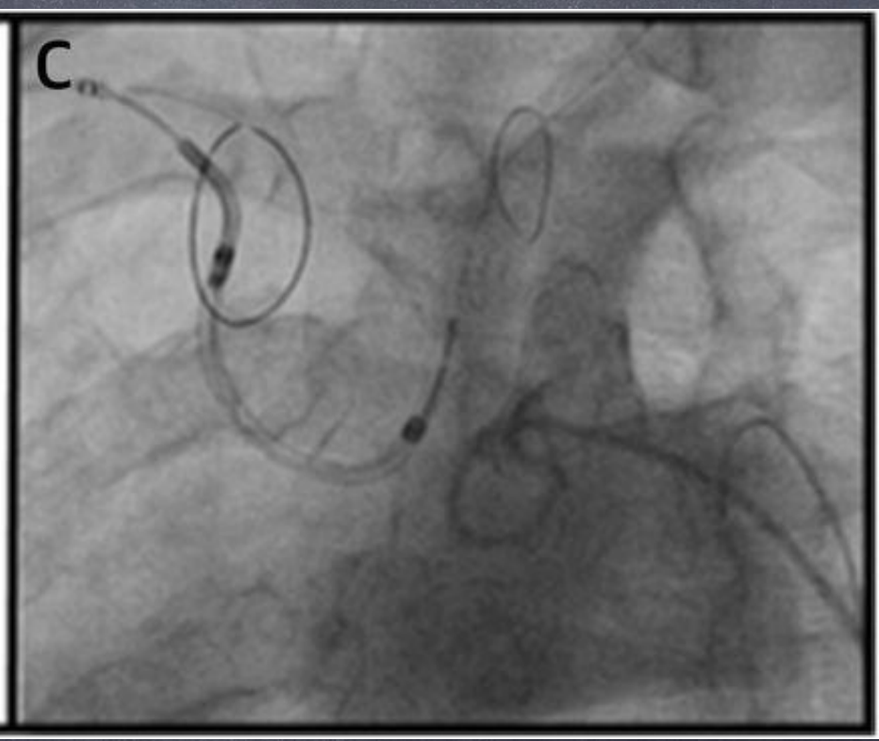
Claret
Montage 2

Keystone
TriGuard

Claret Device
Only FDA approved device for TAVR

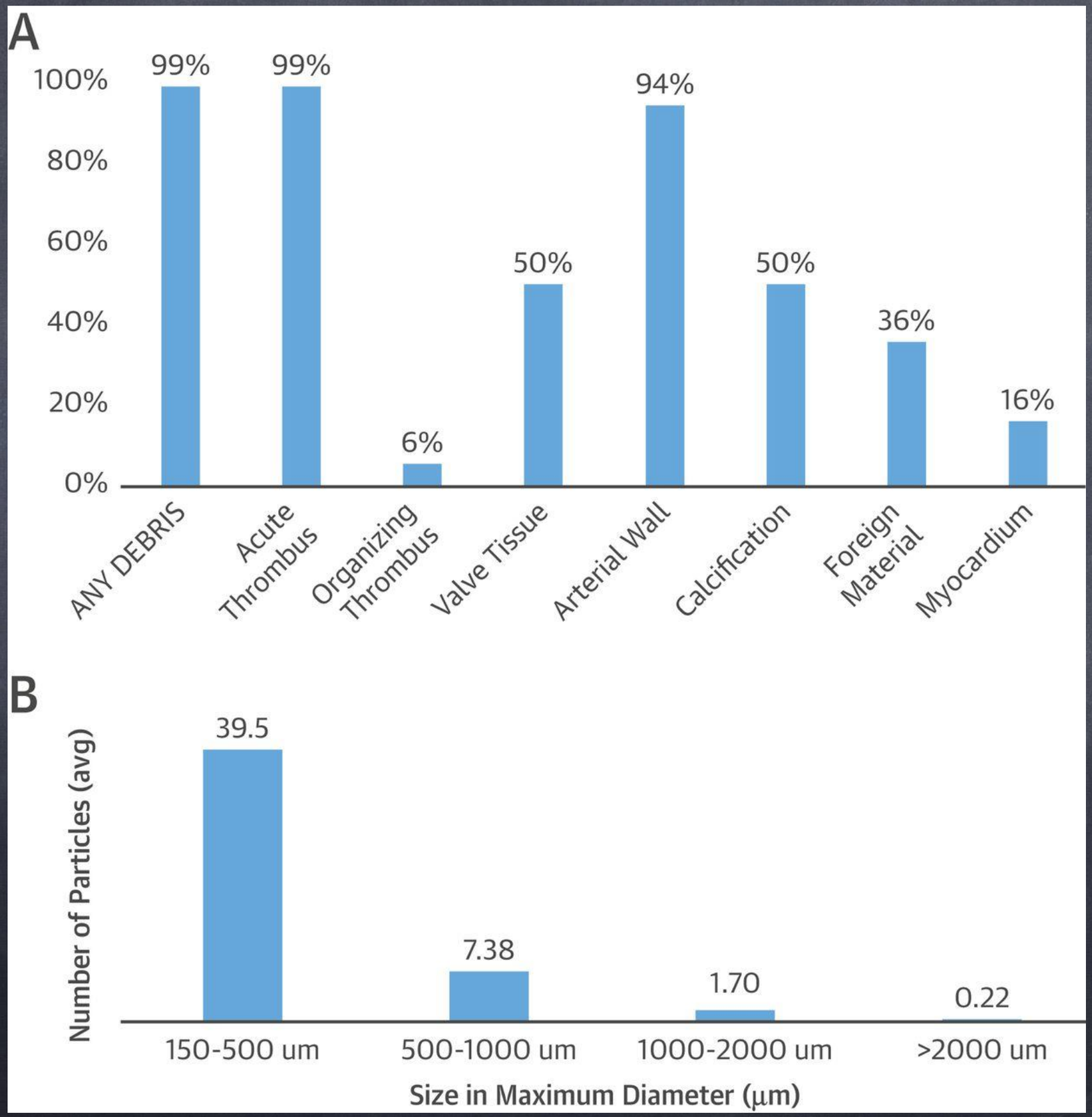






Reduced procedural stroke from 8.2% to 3%

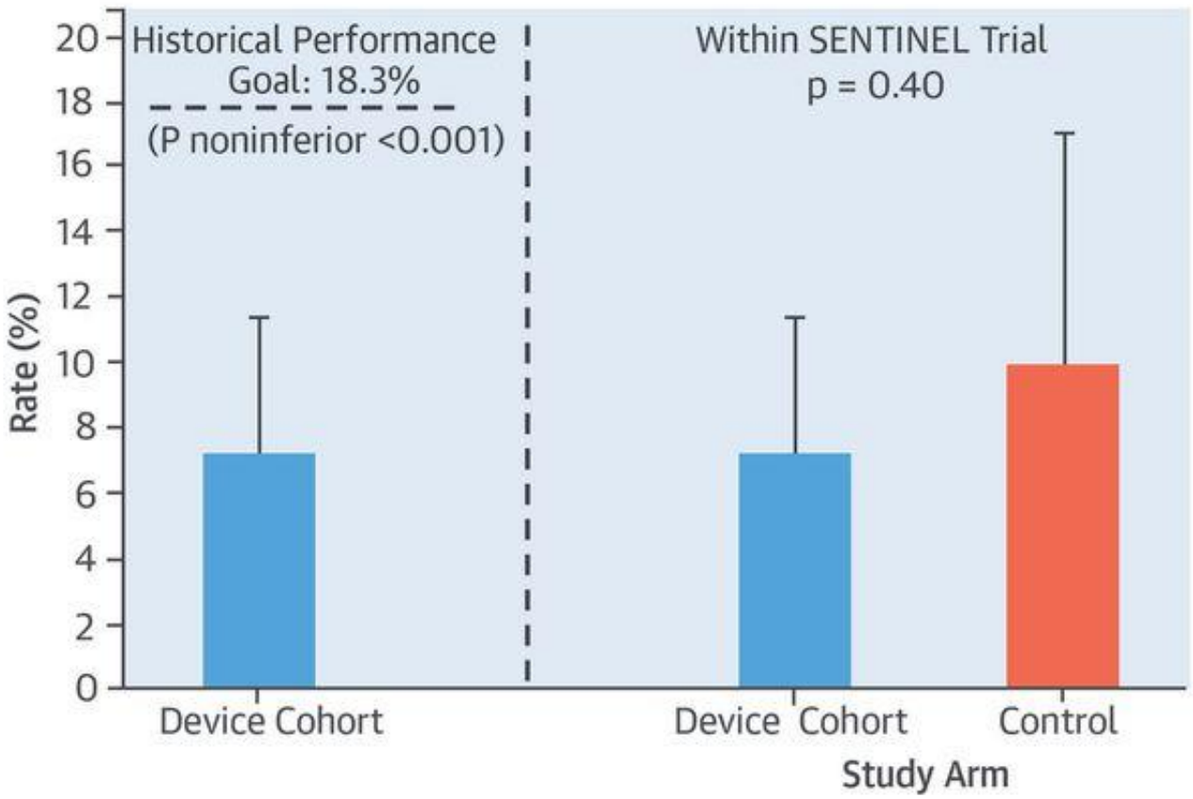
Debris Collection in SENTINEL



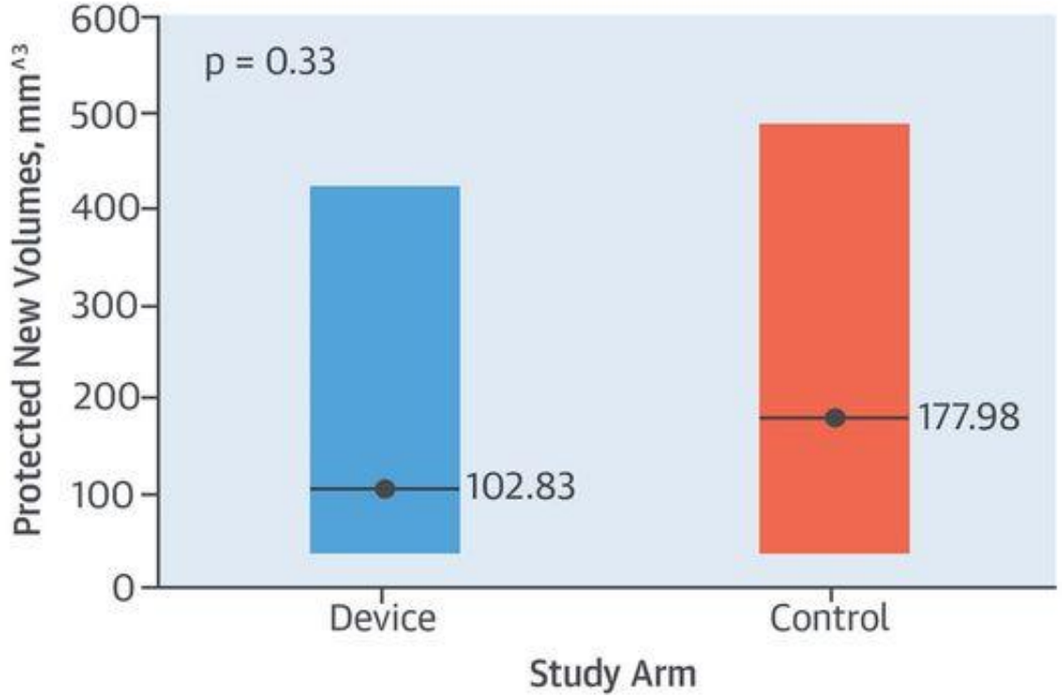
SENTINEL Trial with Claret Device

CENTRAL ILLUSTRATION: Primary Safety and Efficacy Endpoints

A. 30-day MACCE Rates



B. New Lesion Volume on MRI



Kapadia, S.R. et al. J Am Coll Cardiol. 2017;69(4):367-77.

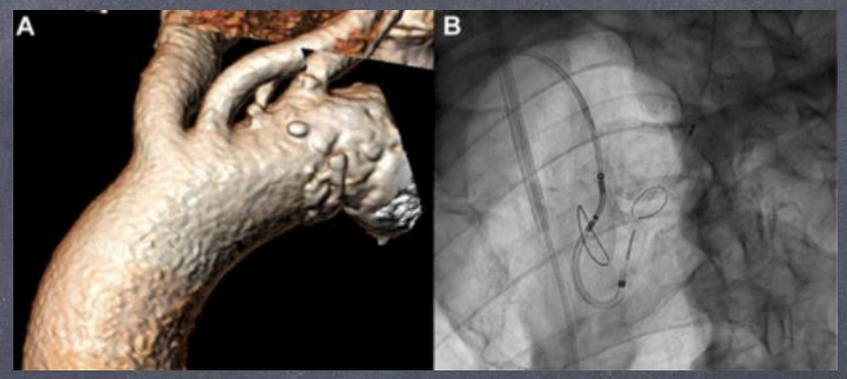
Improvement in Stroke-Free Survival post TAVR with Claret Device

JACC: Cardiovascular Interventions Sep 2017, 3303; DOI: 10.1016/j.jcin.2017.06.037

Table 3
Outcome: Propensity-Matched Population

	No Cerebral Embolic Protection (n = 280)	Cerebral Embolic Protection (n = 280)	OR (95% CI)	p Value
Mortality or stroke	19 (6.8)	6 (2.1)	0.30 (0.12–0.77)	0.01
Disabling and nondisabling stroke	13 (4.6)	4 (1.4)	0.29 (0.10–0.93)	0.03
Disabling	9 (3.2)	1 (0.4)	0.11 (0.01–0.86)	0.01
Nondisabling	4 (1.4)	3 (1.1)	0.75 (0.17–3.38)	0.70
Mortality	8 (2.9)	2 (0.7)	0.25 (0.05–1.20)	0.06
Acute kidney injury stage 2/3	4 (1.4)	3 (1.1)	0.64 (0.15–2.71)	0.54
Major vascular complications	10 (3.6)	5 (1.8)	0.64 (0.23–1.78)	0.19
Major bleeding	12 (4.3)	4 (1.4)	0.33 (0.11–1.05)	0.05
SENTINEL endpoint*	22 (7.9)	7 (2.1)	0.32 (0.14–0.77)	0.01

Values are n (%) unless otherwise indicated



Reduction of death or stroke from 6.8% to 2.1 % in a non-randomized Cohort.

J Am Coll Cardiol Intv 2017;

Ochsner Stroke Rate after TAVR 2015-2017

- Manual Bilateral carotid occlusion while passing TAVR device around the aortic arch and crossing valve.
  - No routine MRI or stroke neurologist
- Patients with TAVR 400
- TAVR Patient with Stroke 1
- Stroke rate 0.3%
  - Posterior Circulation yes
- Expected Post-TAVR stroke rate 6-8%

SUMMARY

- Stroke is serious complication of TAVR
- TAVR device manipulation causes embolic debris in every case which can cause stroke.
- Treating stroke after TAVR is not like treating usual embolic stroke so prevention is much better than treatment.
- Broad acceptance of embolic protection devices in TAVR awaits randomized trial data and reimbursement by CMS and insurers.
- Available information and common sense dictate that some form of embolic protection will become standard treatment in TAVR.