



Endovascular Therapy for Acute Ischemic Stroke

The new Standard of care for acute large vessel occlusion

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Stroke and Interventional Neurologist



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Presenter Disclosure Information

FINANCIAL DISCLOSURE:

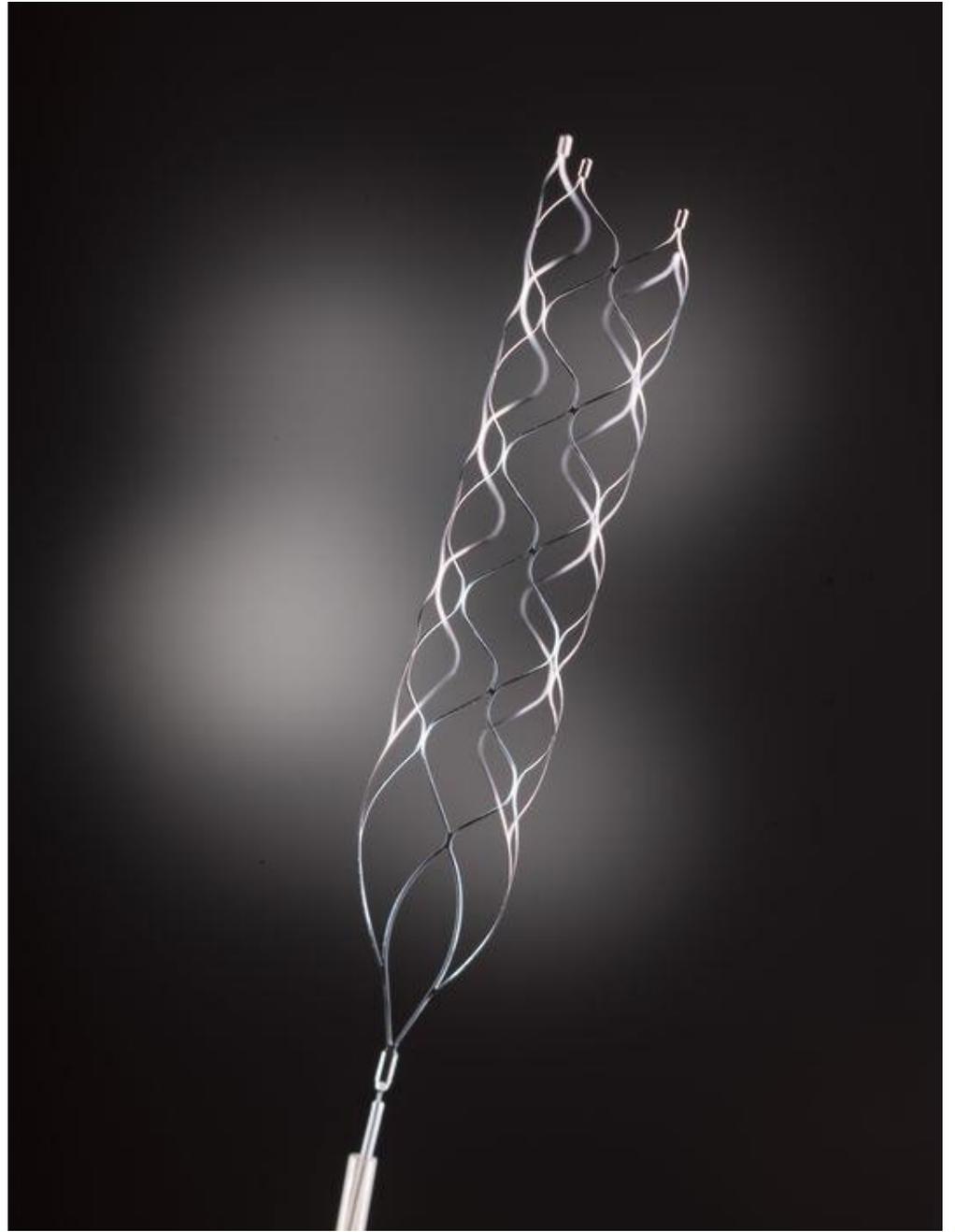
- No relevant financial relationship exists



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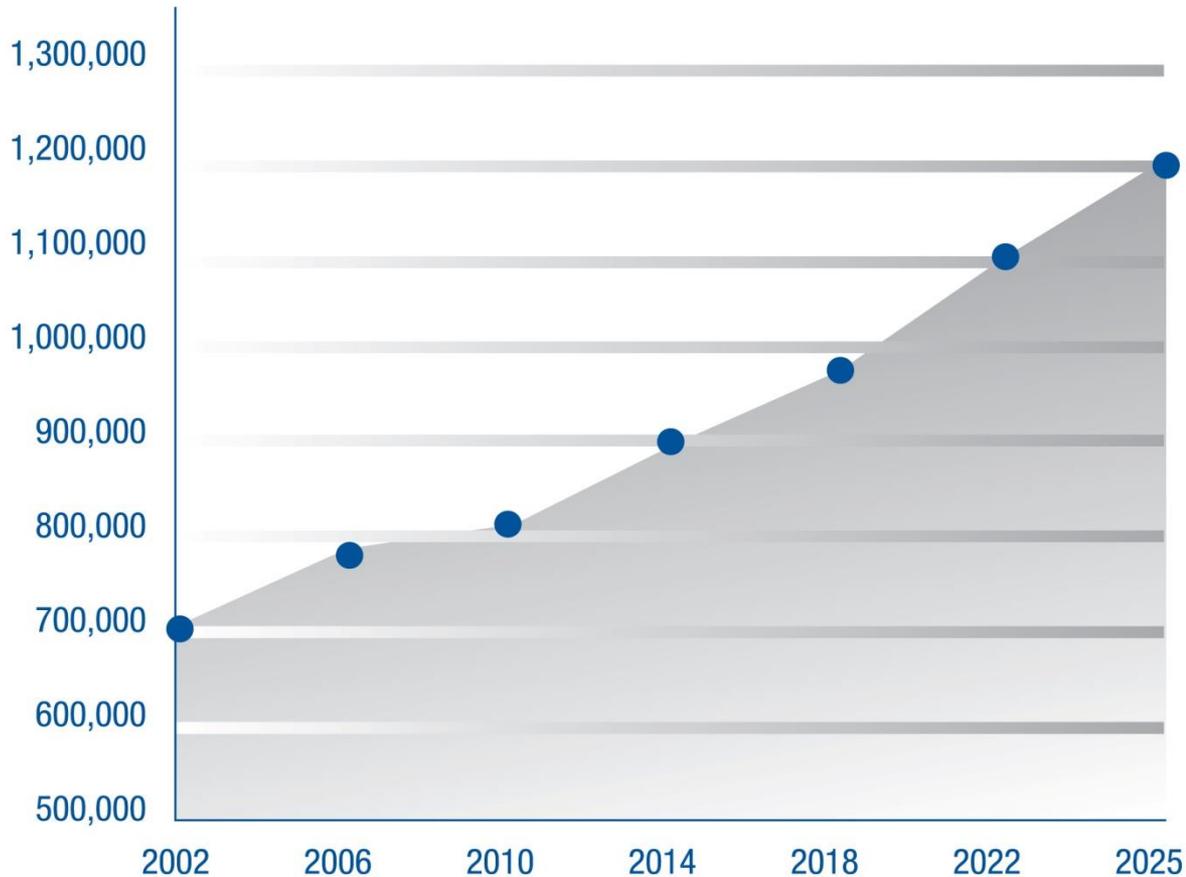
2015



Public Health Impact of Stroke

- Estimated 700,000 strokes occur each year.
- Every 45 seconds, someone in the U.S. has a stroke.
- Stroke is 4th leading cause of death
- **Stroke is leading cause of long-term care disability.**
- 5 million Americans currently living with effects of stroke.
- AHA stroke calculated costs ~ \$58 billion in 2006.
- The cost of stroke will double by 2030





Projected number of strokes in US: 2002 - 2025

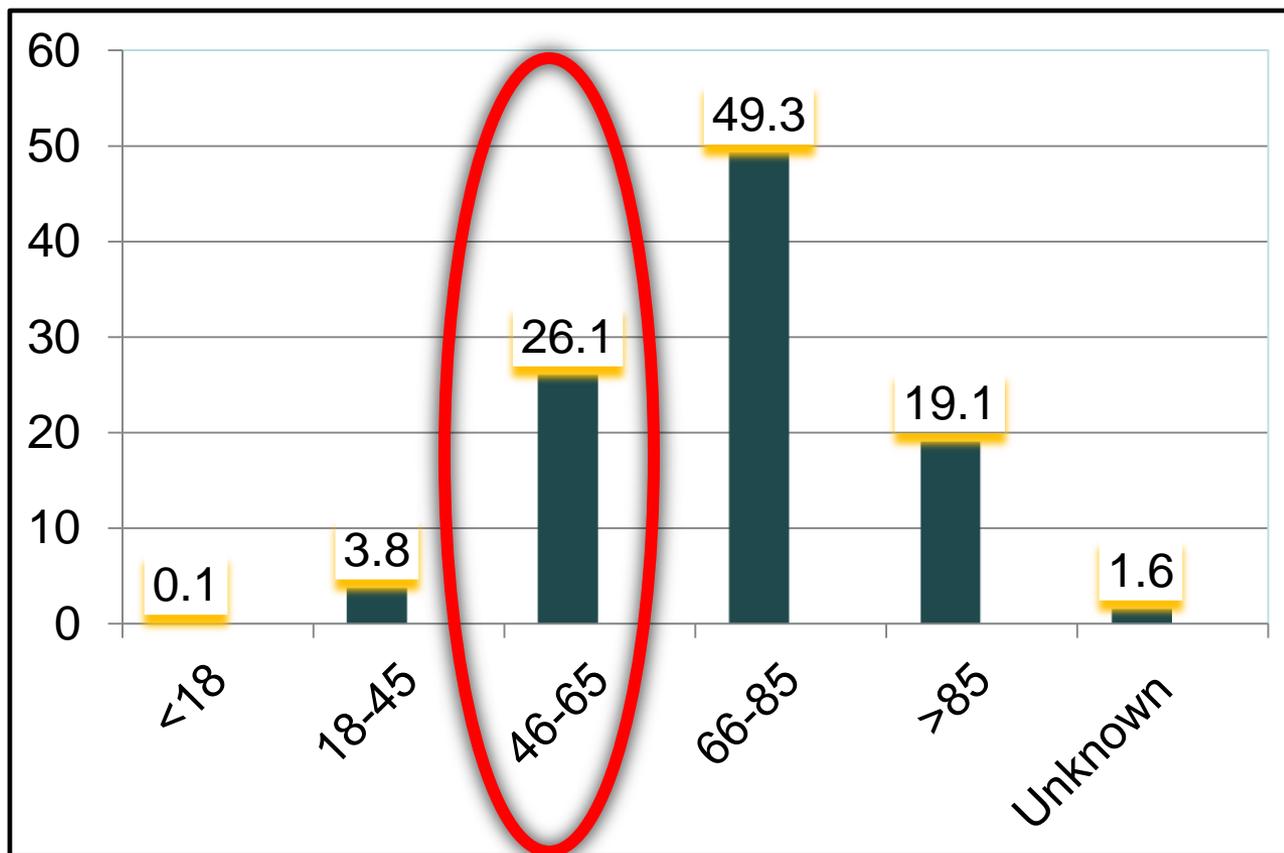
Stroke by age group



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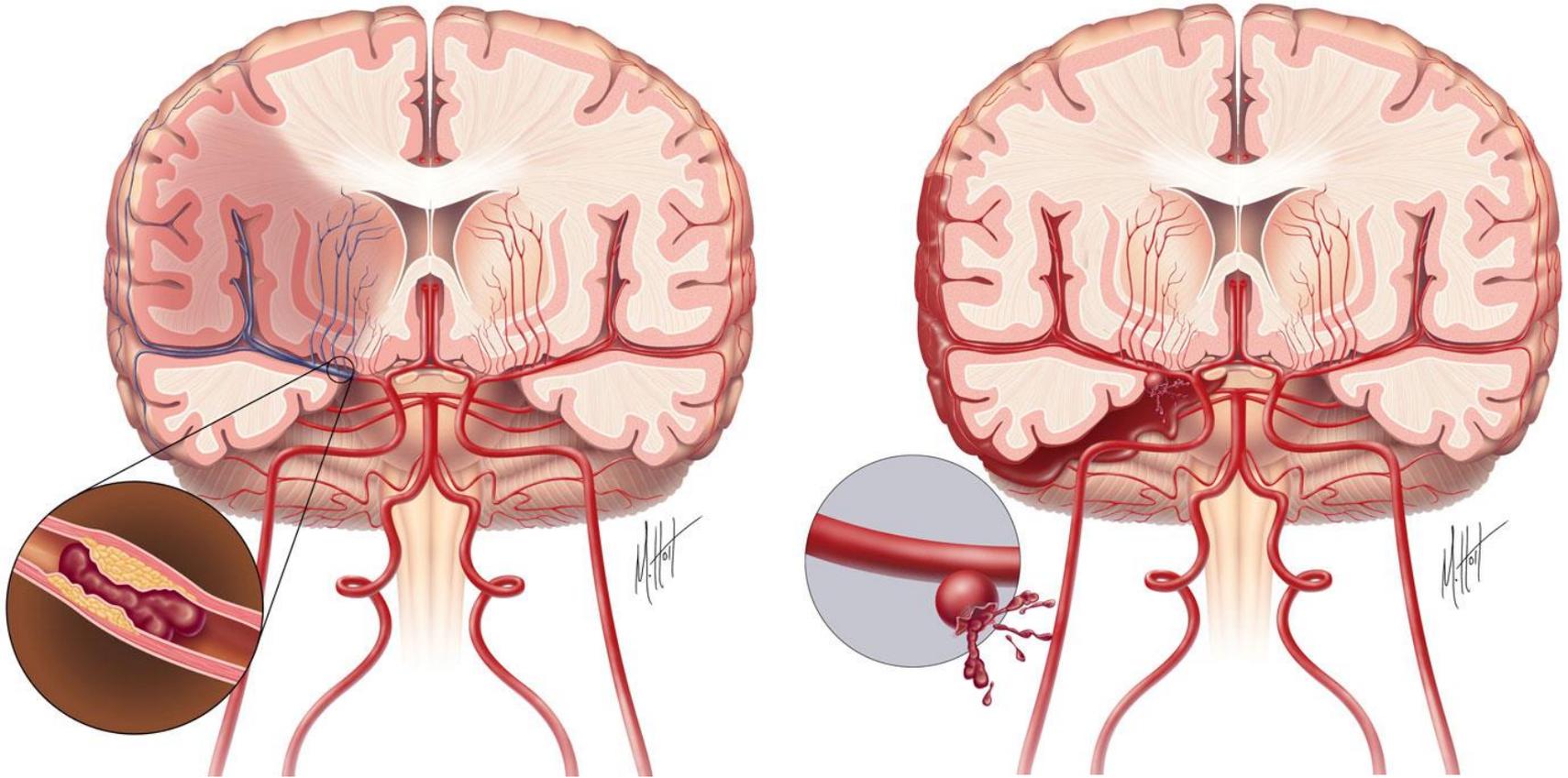
North Dakota State Stroke registry



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Types of stroke



Types of stroke

Ischemic stroke (Blockage)

Caused by blockage of a blood vessel in the brain

80%

Hemorrhagic stroke (Bleeding)

Caused by burst or a leaking blood vessel in the brain

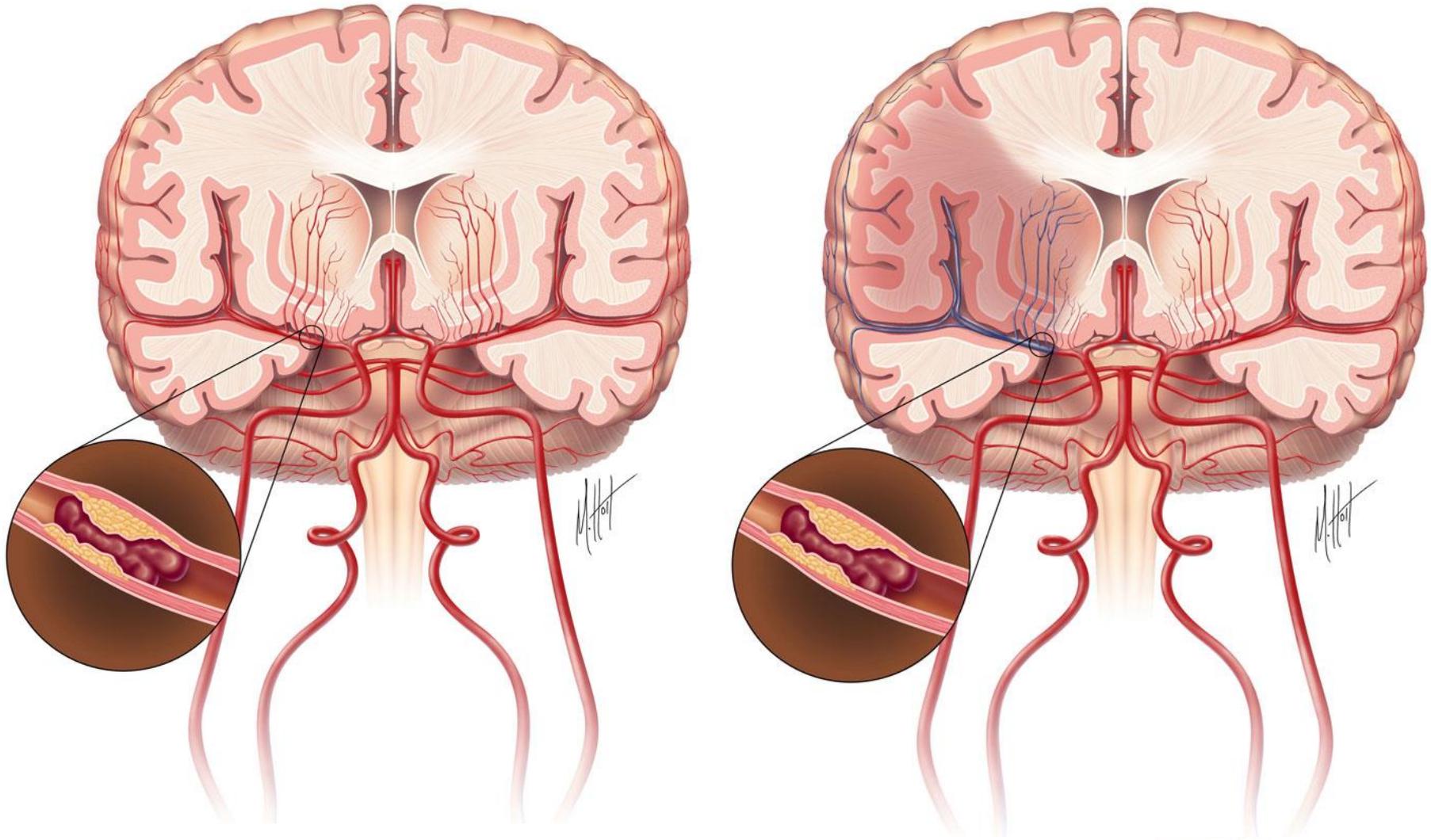
20%



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Ischemic stroke



Warning Signs of Stroke



**LOSS OF SPEECH
OR COMPREHENSION**

NUMBNESS ON

NUMBNESS ON

ONE SIDE



UNSTEADY GAIT



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PATHOPHYSIOLOGY



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ACUTE STROKE

CBF *

- 55 cc/100 gm/min → Normal flow
- 20 cc/100 gm/min → Reversible symptoms
- <10 cc/100 gm/min → Irreversible damage



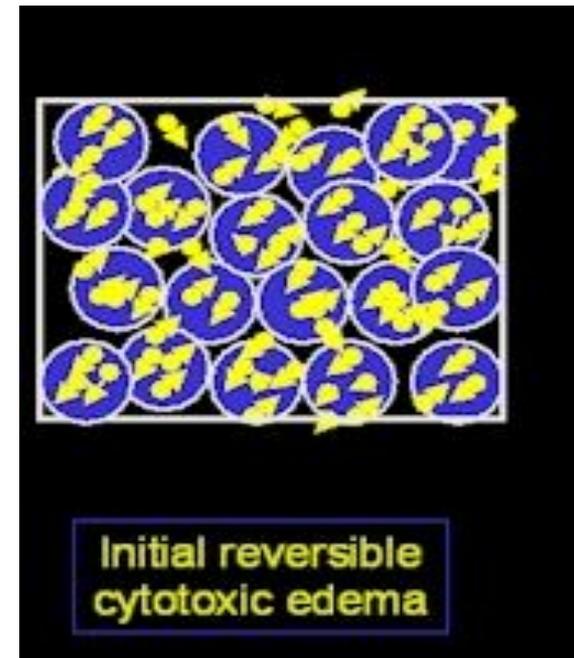
* Walters, FJM. 1998. "Intracranial Pressure and Cerebral Blood Flow." Physiology. Issue 8, Article 4. Accessed January 4, 2007



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STROKE PATHOPHYSIOLOGY (REVERSIBLE INJURY)

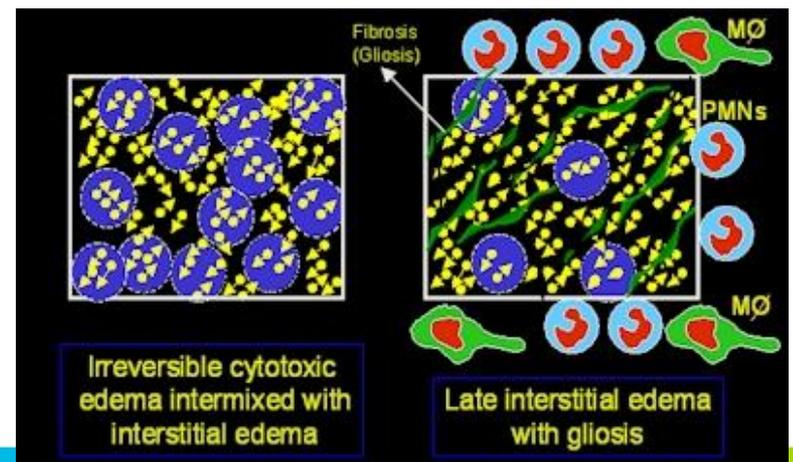
- Hemodynamic derangement → low O₂ to neurons
- Failure of aerobic respiration and Na/K pump dysfunction
- Cytotoxic edema- Na and H₂O flow into cell (cell dysfunction, not destruction)



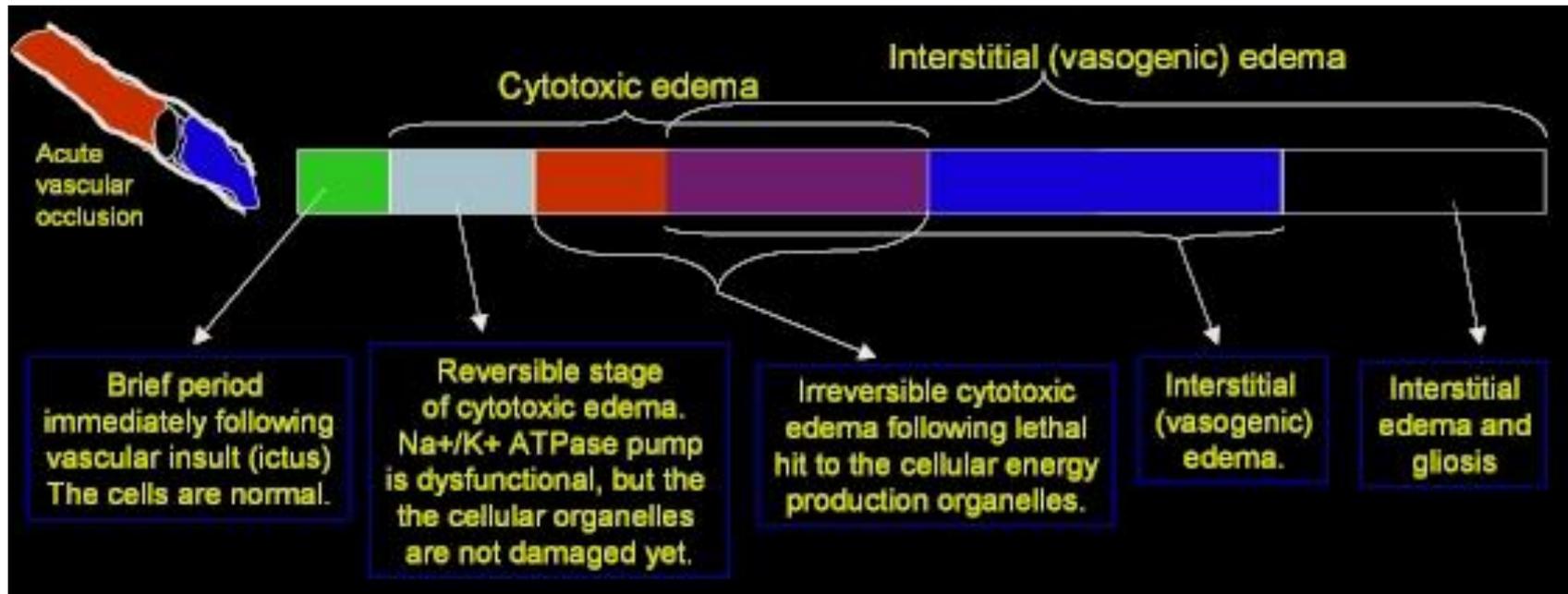
STROKE PATHOPHYSIOLOGY (IRREVERSIBLE INJURY)

- Ca into cell (Beginning of Irreversible cell injury) → Self-destructive lysosomal enzymes, and apoptotic mechanisms
- 3-4 hrs post ischemia, BBB compromised and plasma proteins released into extracellular spaces → Vasogenic edema
- Cytokines and increased expression of adhesion molecules → phagocytosis and gliosis (new fibrotic tissue)

Radaideh, et al. Neurographics. Correlating the Basic Chronological Pathophysiologic Neuronal Changes in Response to Ischemia with Multisequence MRI Imaging. Vol. 2, Issue 2, Article 1



PATHOLOGICAL CHANGES WITH TIME



ACUTE STROKE

CBF *

- 55 cc/100 gm/min → Normal flow
- 20 cc/100 gm/min → Reversible symptoms
- <10 cc/100 gm/min → Irreversible damage

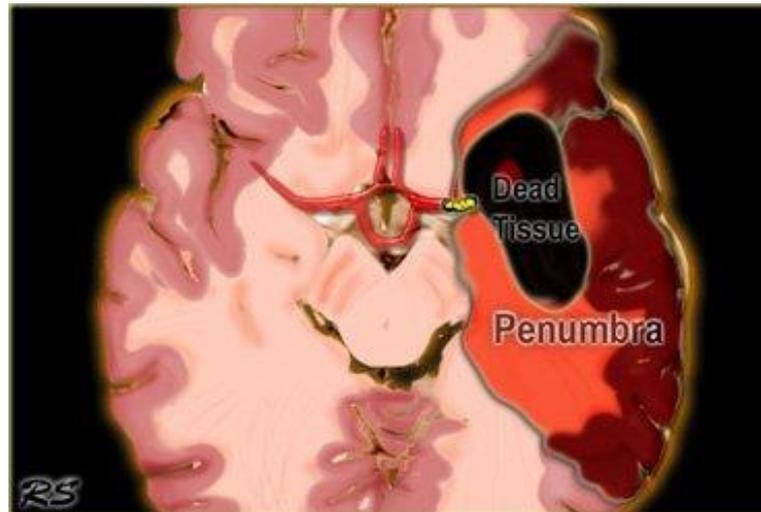


* Walters, FJM. 1998. "Intracranial Pressure and Cerebral Blood Flow." Physiology. Issue 8, Article 4. Accessed January 4, 2007



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ISCHEMIC PENUMBRA

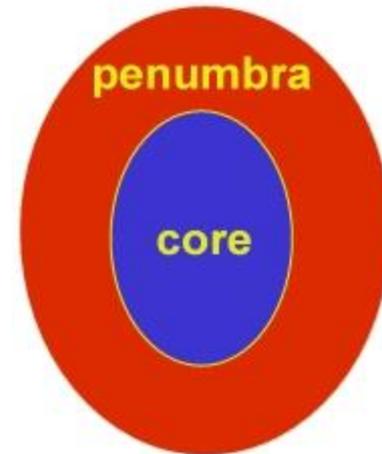
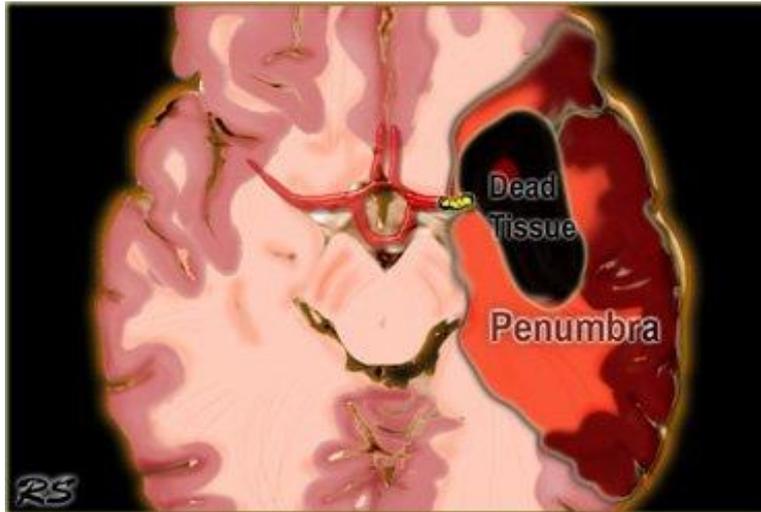


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ISCHEMIC PENUMBRA

Described in 1981*

“ischemic tissue potentially destined for infarction but not yet irreversibly injured and the target of acute therapies.”**



*Astrup J, Siesjo BK, Symon L: Thresholds in cerebral ischemia – the ischemic penumbra. *Stroke* 1981; 12: 723–725.

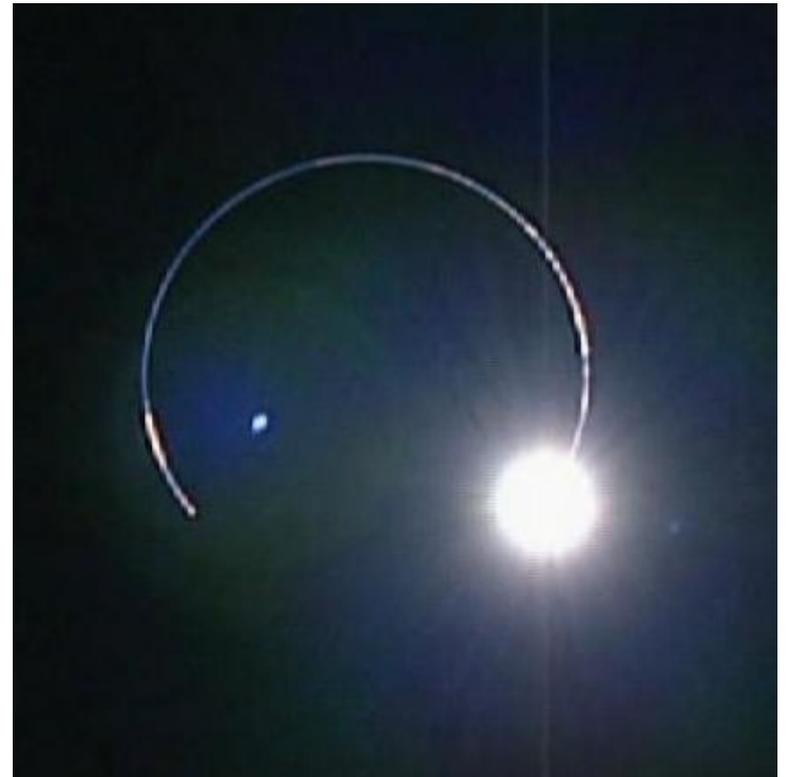
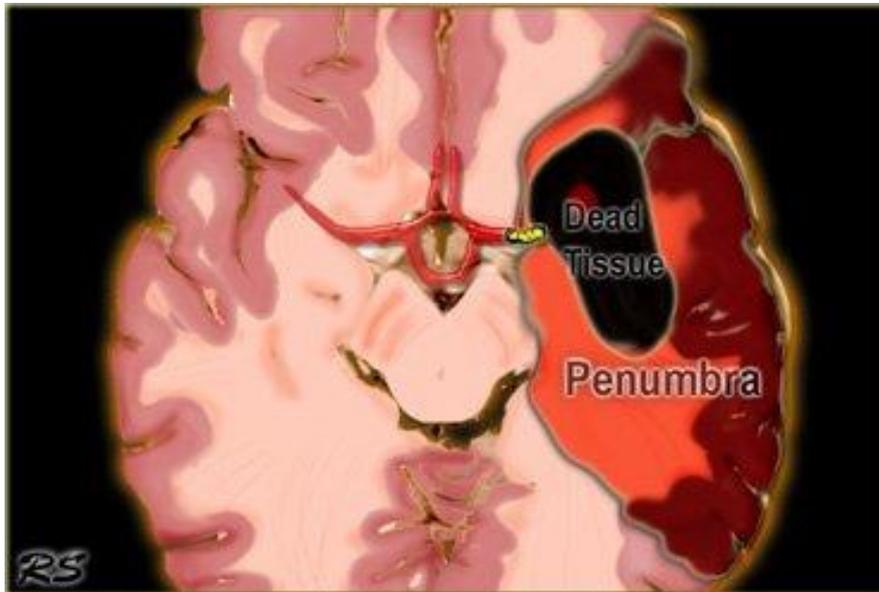
**Fisher M. Characterizing the target of acute stroke treatment. *Stroke*.1997;28:866–872.



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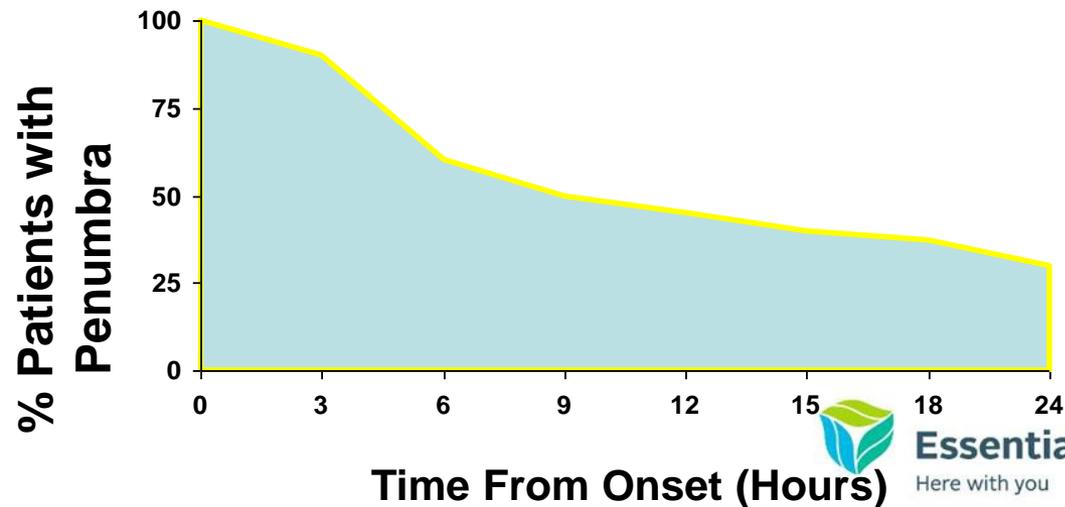
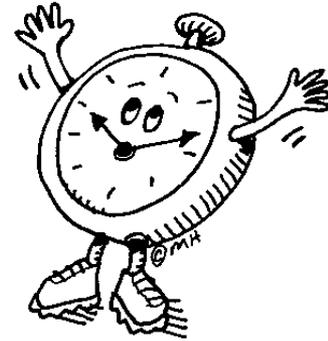
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PENUMBRA



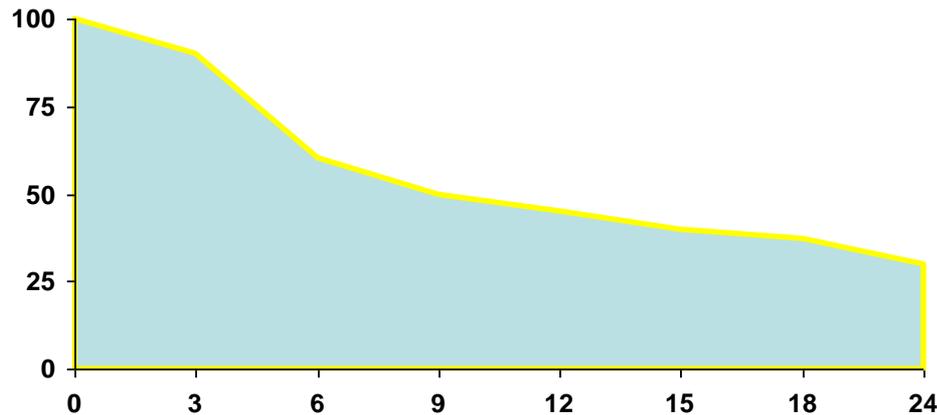
DETERMINING FACTORS

- The duration of ischemia (“time is brain”)
- The availability of collateral circulation
- The magnitude and rapidity of the reduction of flow



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PENUMBRA IS THE TARGET OF ACUTE STROKE THERAPY

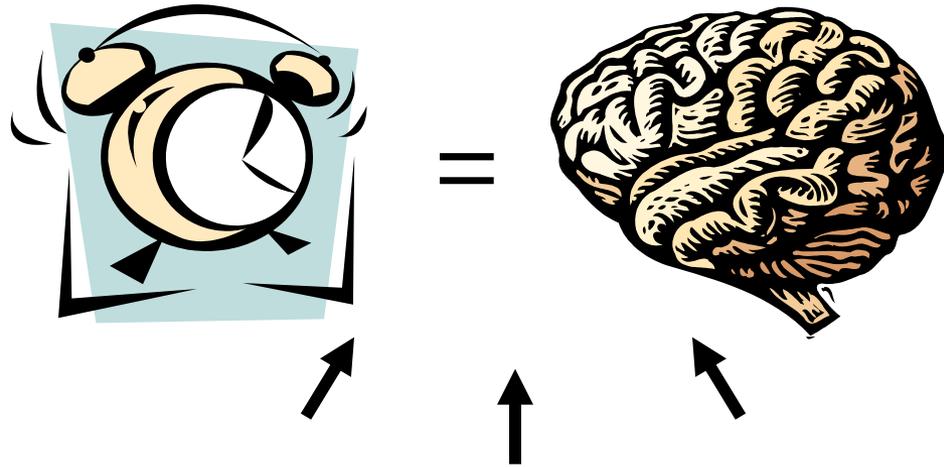


- The goal of acute stroke therapy is to save the penumbra

PATIENT SELECTION

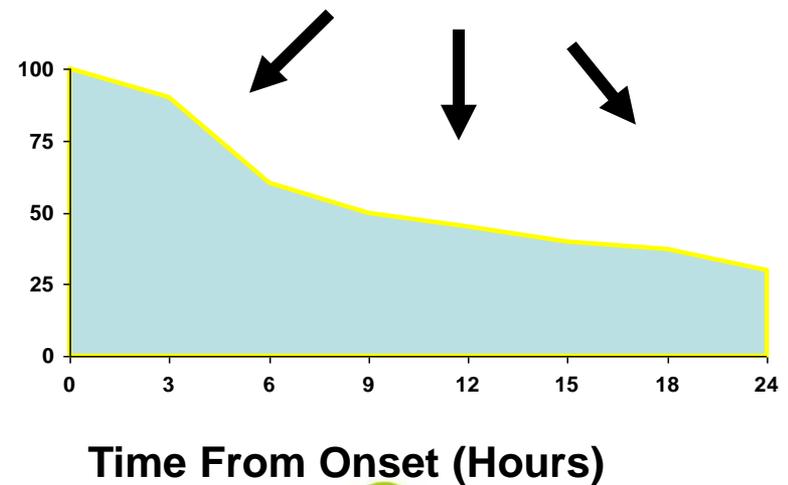
< 3 Hrs

> 3 Hrs

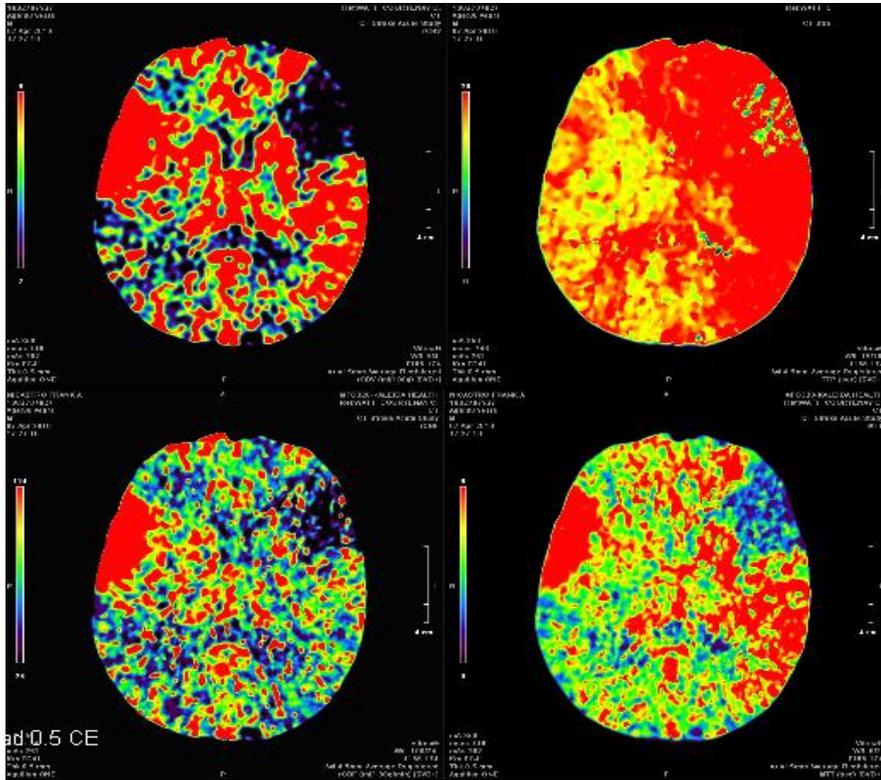


Early time is surrogate marker for penumbra

% Patients with Penumbra



CTP: EXAMPLES



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HOW TO USE THIS KNOWLEDGE?



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STRATEGIES OF ACUTE STROKE THERAPIES

1- Restore the Flow

- Revascularization

- Blood pressure
- Avoid any increase in ICP

2- Neuroprotection

- Avoid hyperglycemia/hypoglycemia
- Avoid and treat fever
- Neuroprotectants (NXY-059, Indomethacin, Mg, hypothermia...)



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REVASCULARIZATION TECHNIQUES



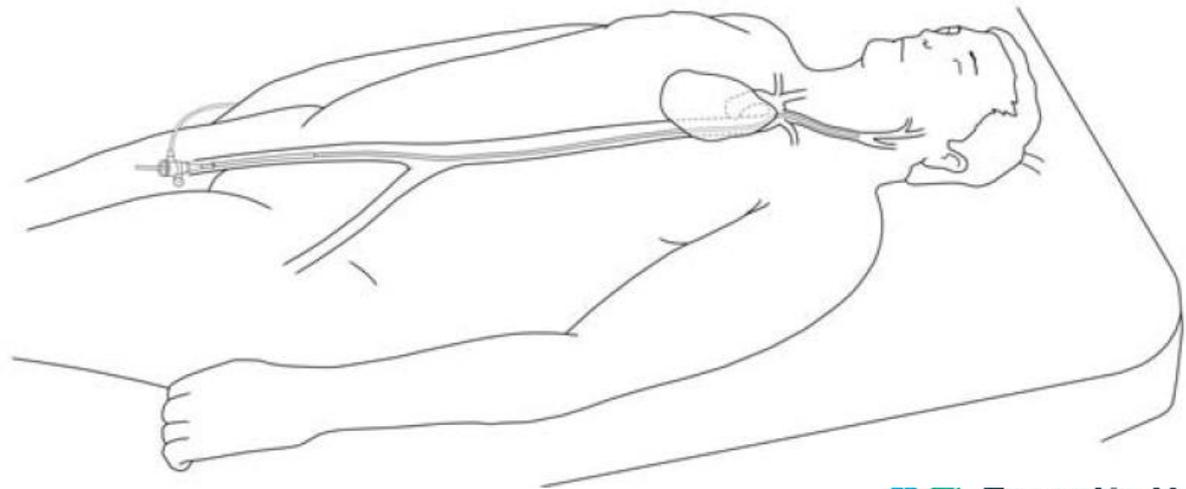
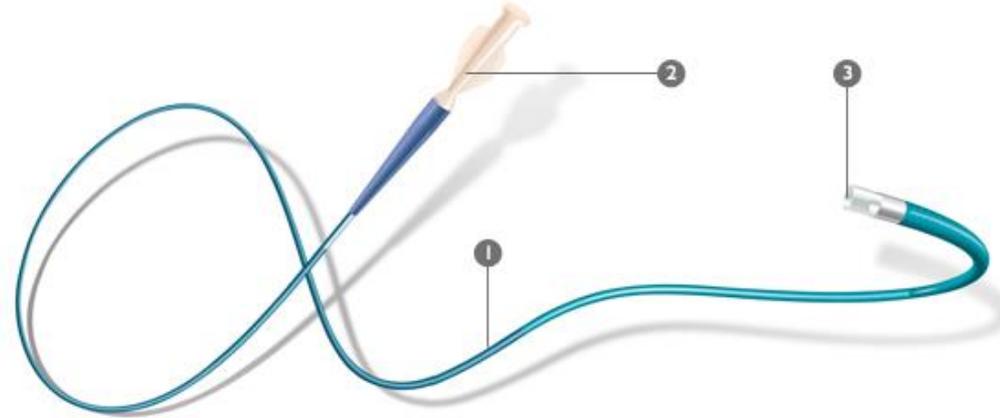
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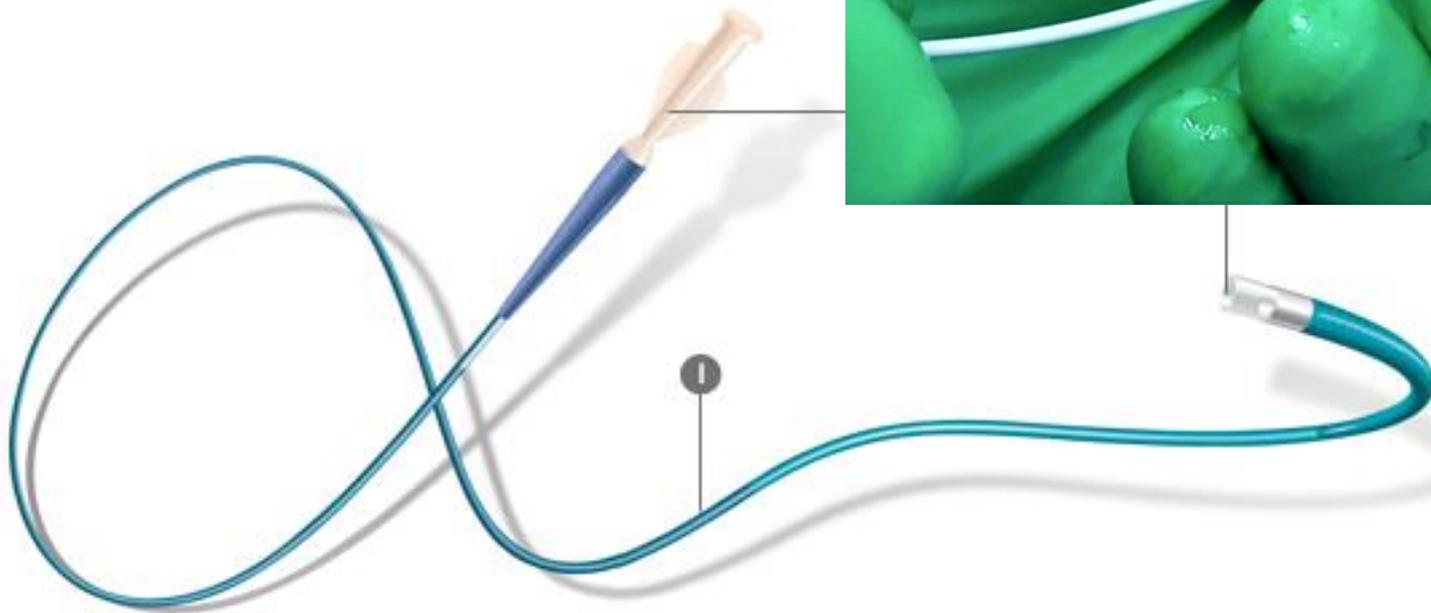
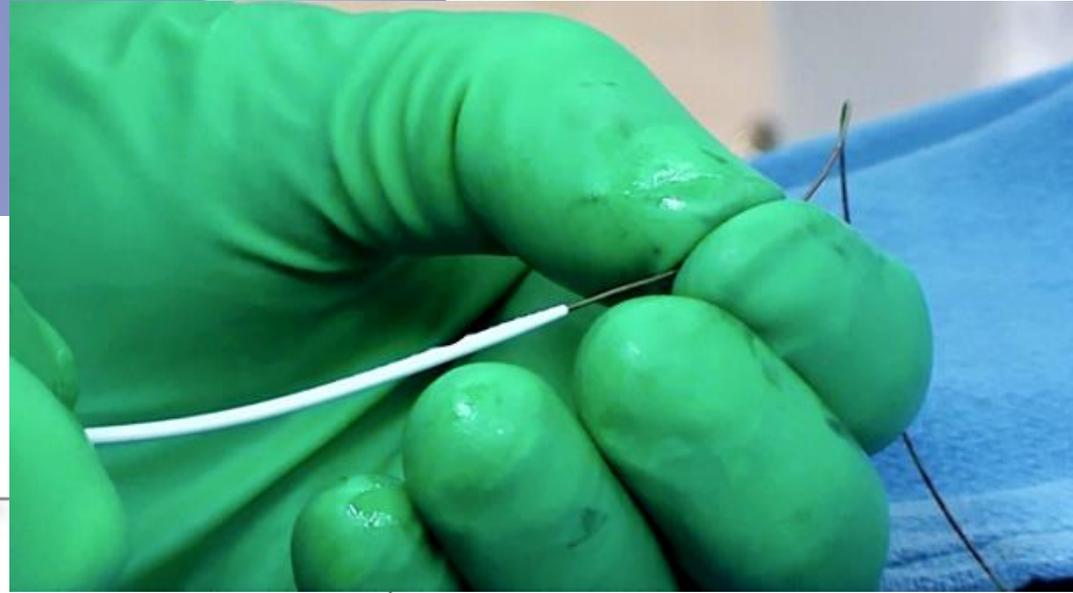
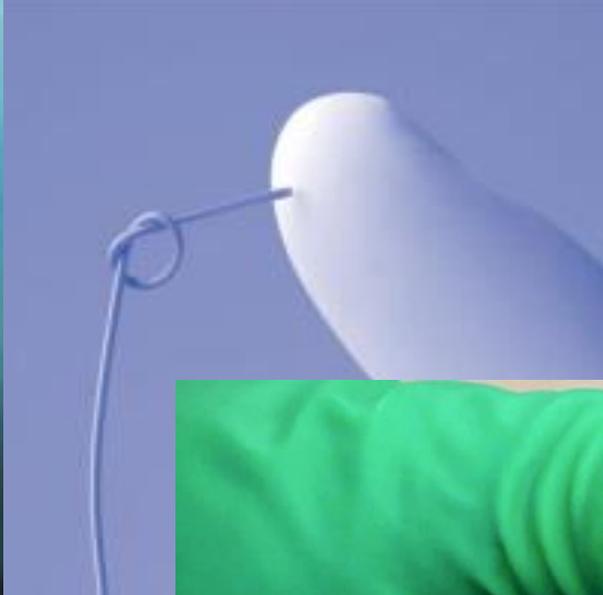
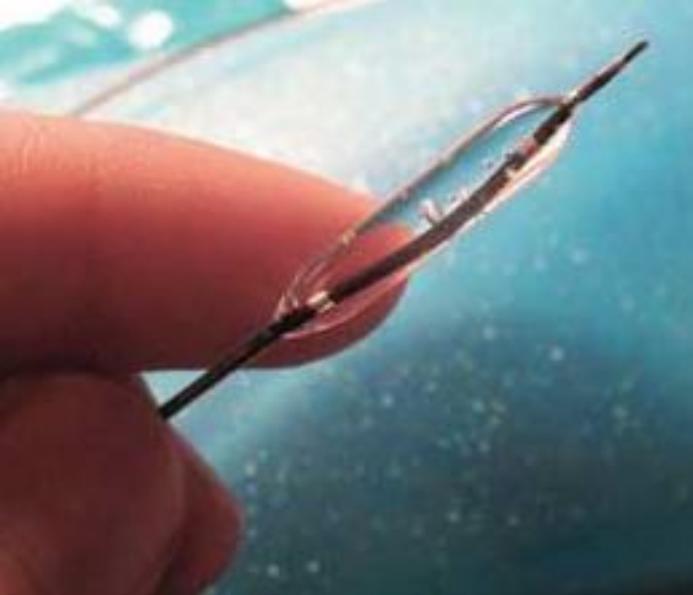
IV Thrombolytics (clot busting medications)

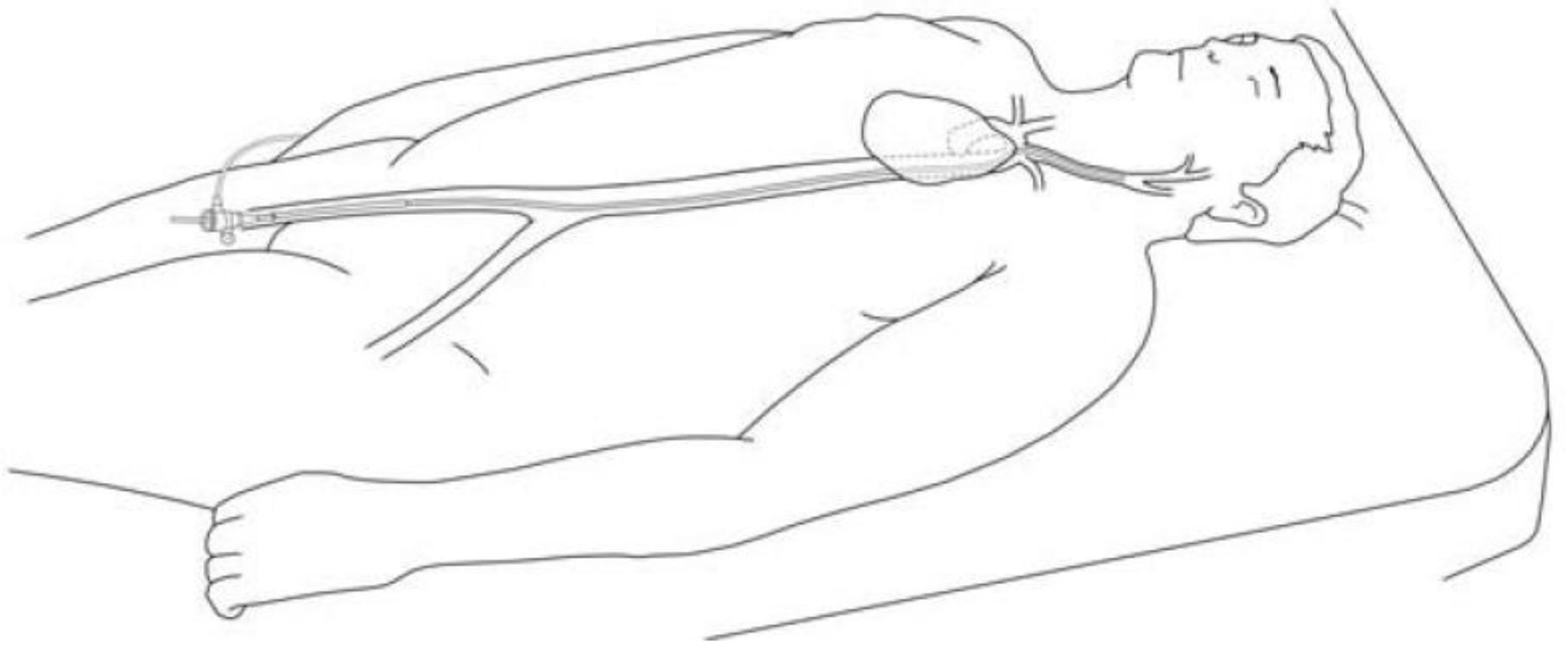
- FDA approved in 1995
- Standard of care for ischemic stroke for patients presenting within 3 hours of acute ischemic stroke
- Can be used up to 4.5 hours in certain patients.
- Within 90 minutes, Odd ratio for improvement
OR = 4.43 (patient is 4 times more likely to improve)



Interventional Therapy (Endovascular)





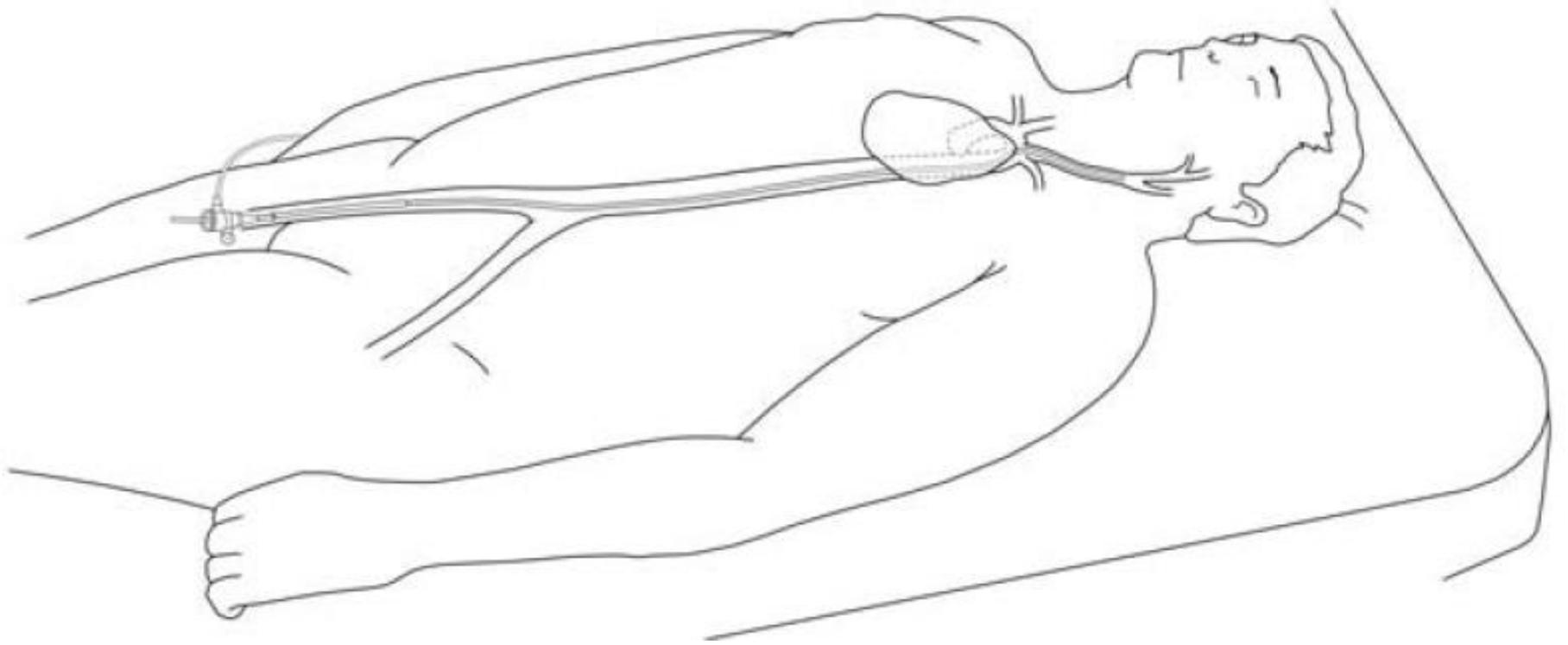


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Angiography suite

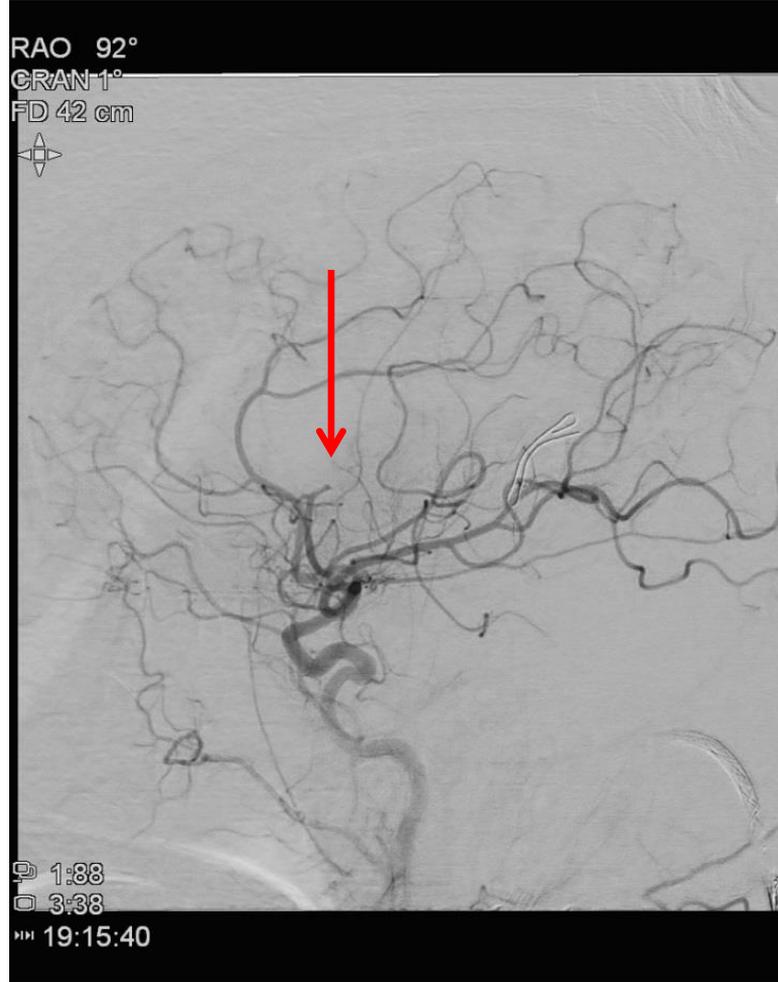




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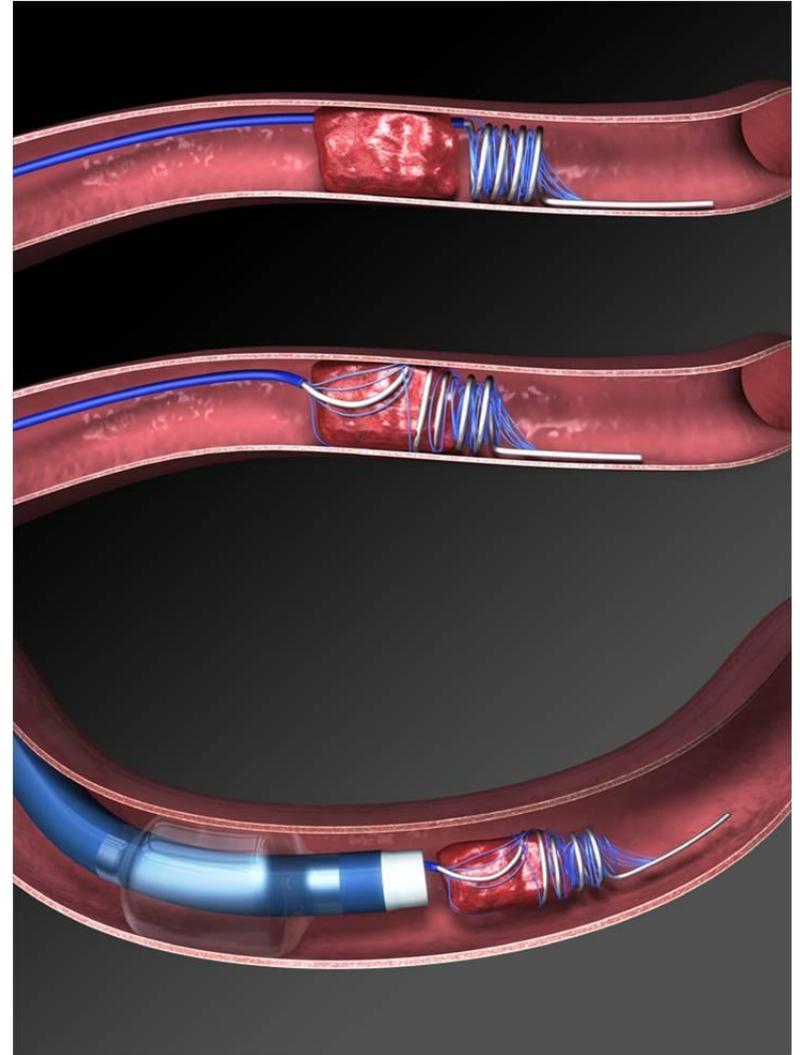
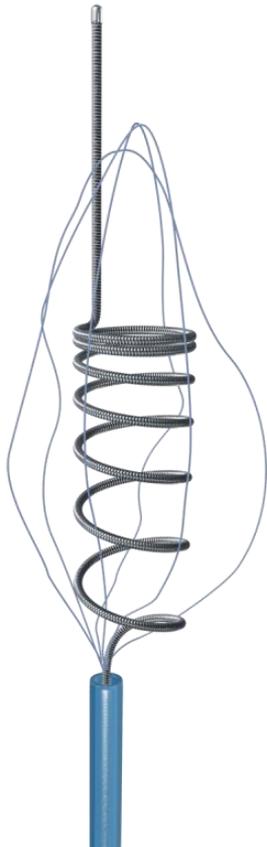
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Thrombolysis



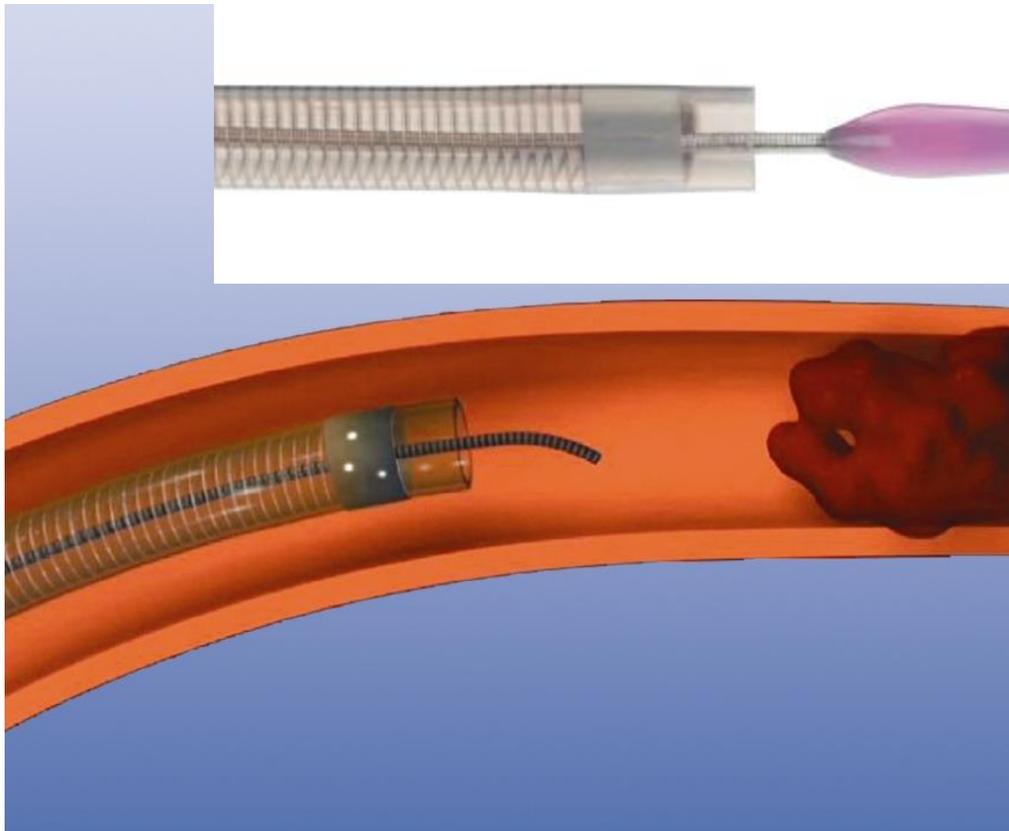
Endovascular therapies for acute ischemic stroke

- **Mechanical Thrombectomy**
 - Merci



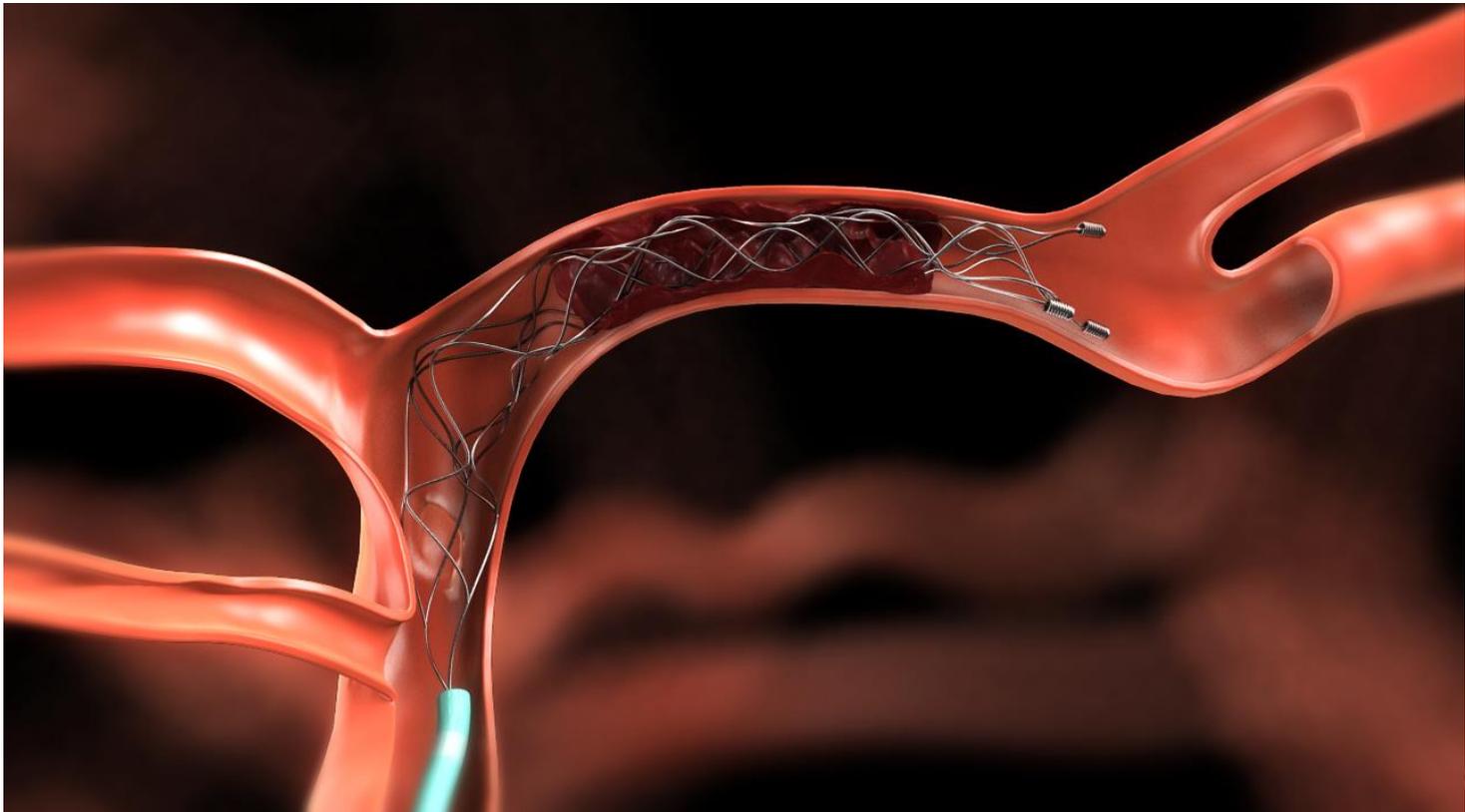
Endovascular therapies for acute ischemic stroke

- **Mechanical Thromboaspiration**
 - Penumbra aspiration system

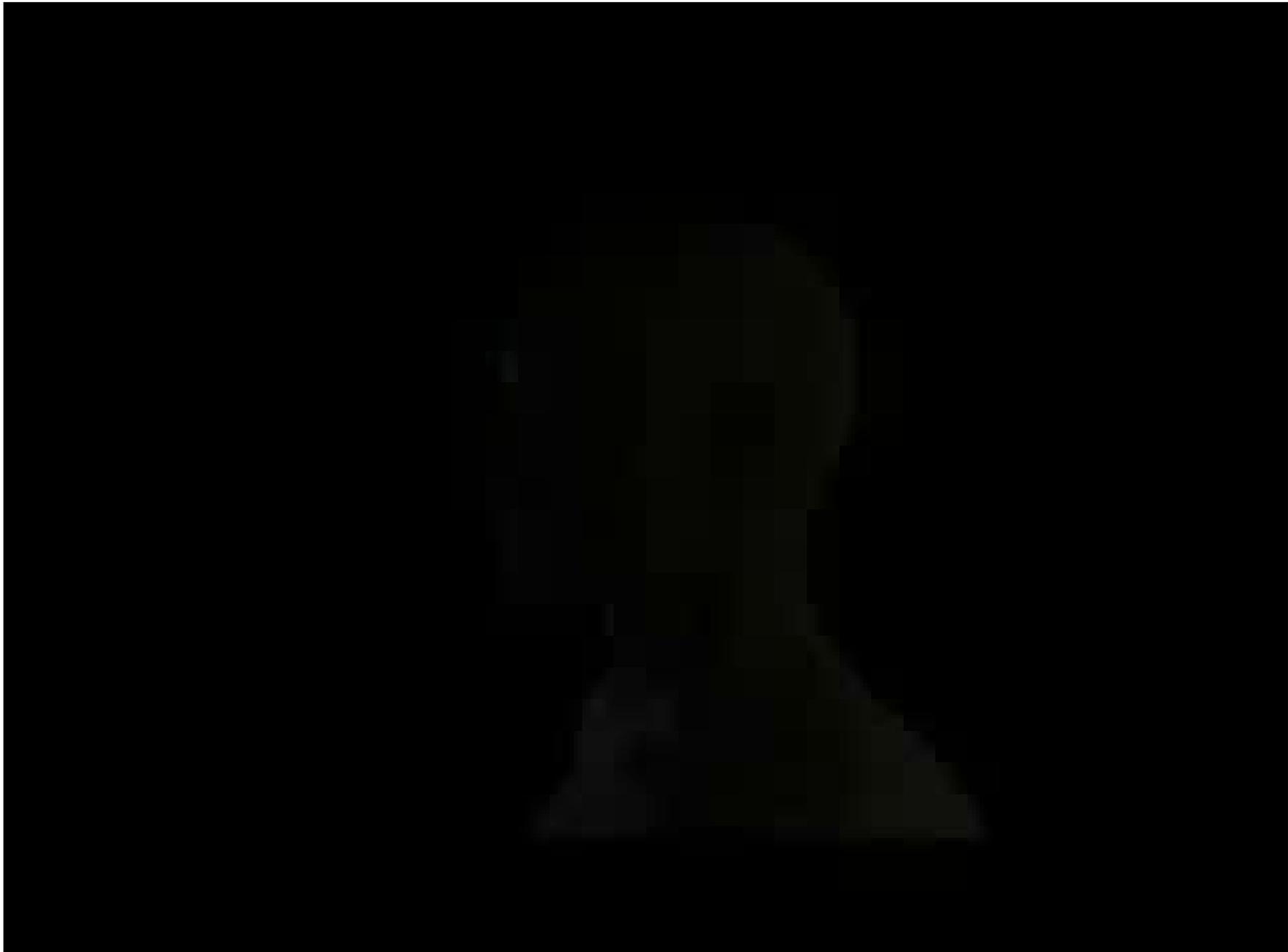


Endovascular therapies for acute ischemic stroke

- **Mechanical Thrombectomy**
 - Solitaire FR







Acute Stroke Case

- 52 yo M h/o high cholesterol
- 2 weeks of severe coughing
- Presented with a left middle cerebral artery (MCA) stroke syndrome.
- NIHSS 19.
- Unknown onset. Last known well 4.5 hours.

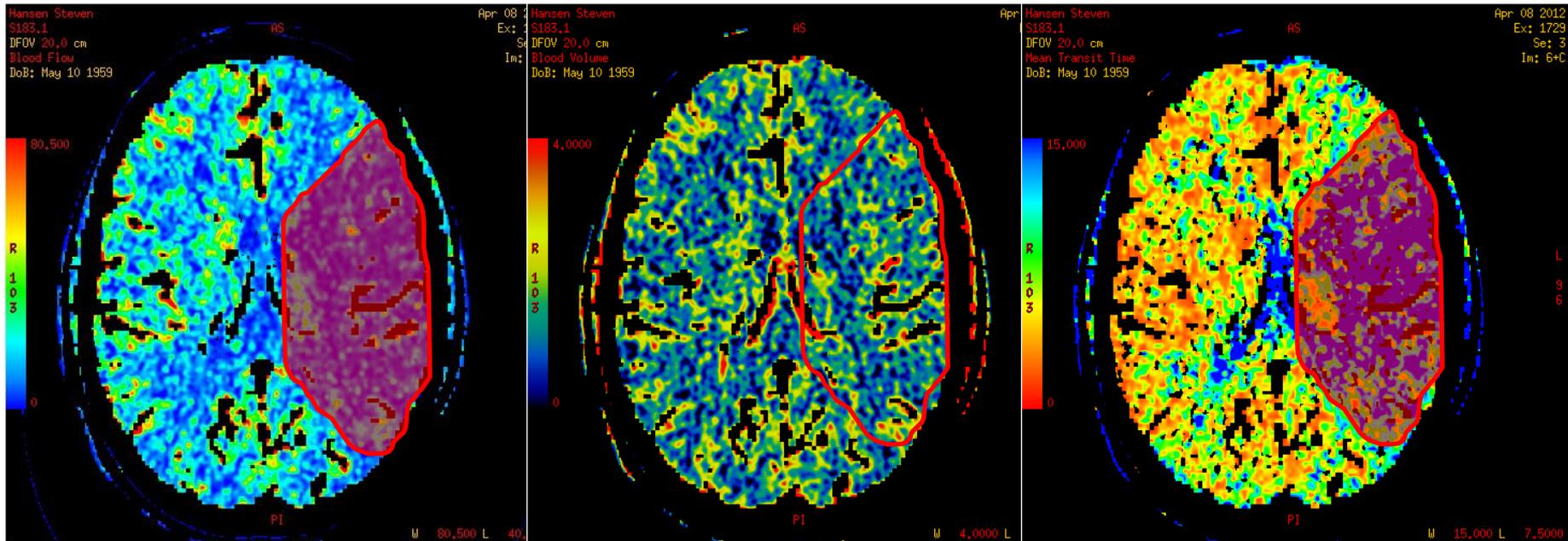


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Acute Stroke Case

- CT perfusion scan demonstrates penumbra, suspected region of salvageable tissue.



Acute Stroke Case



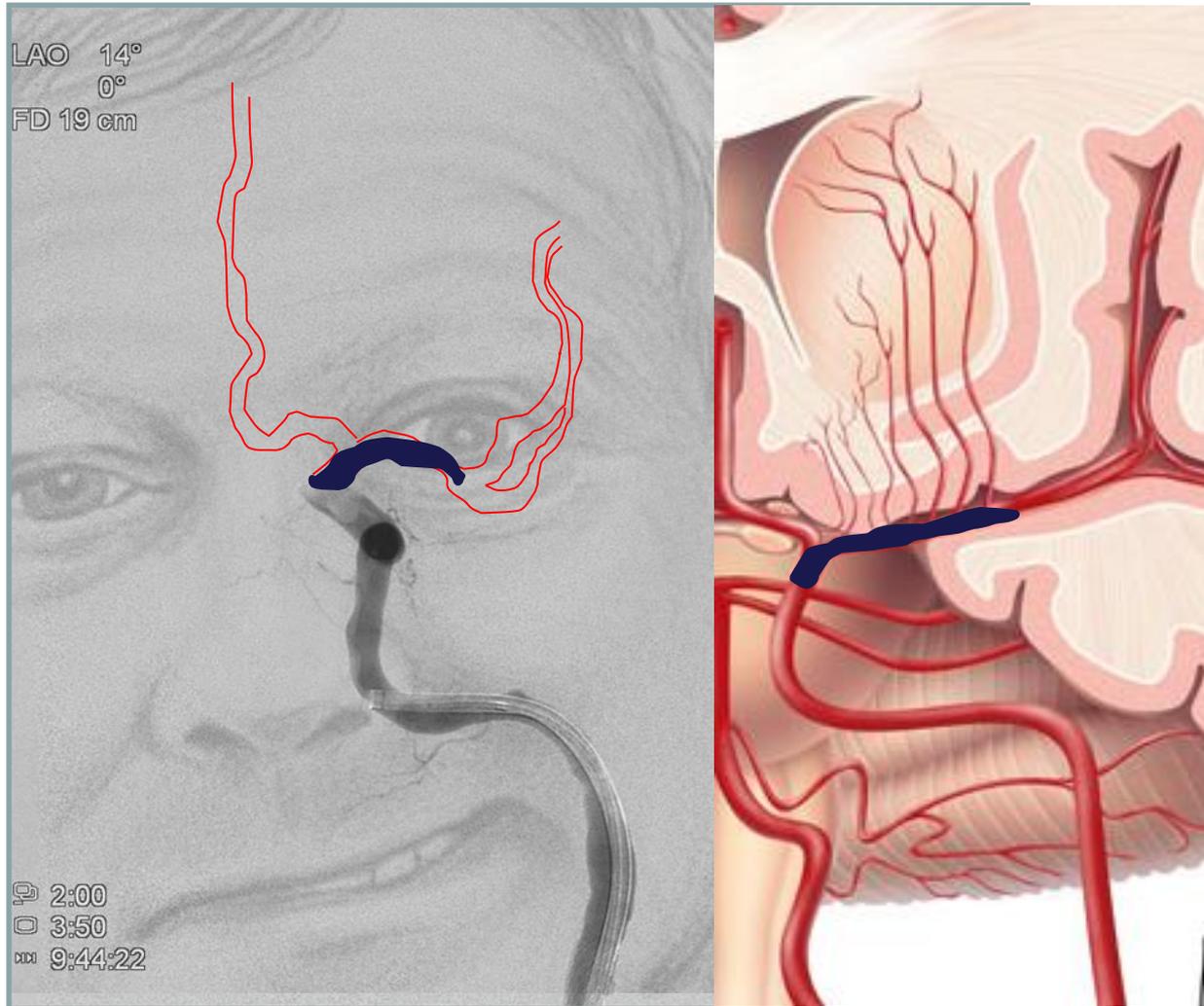
Dense left MCA sign



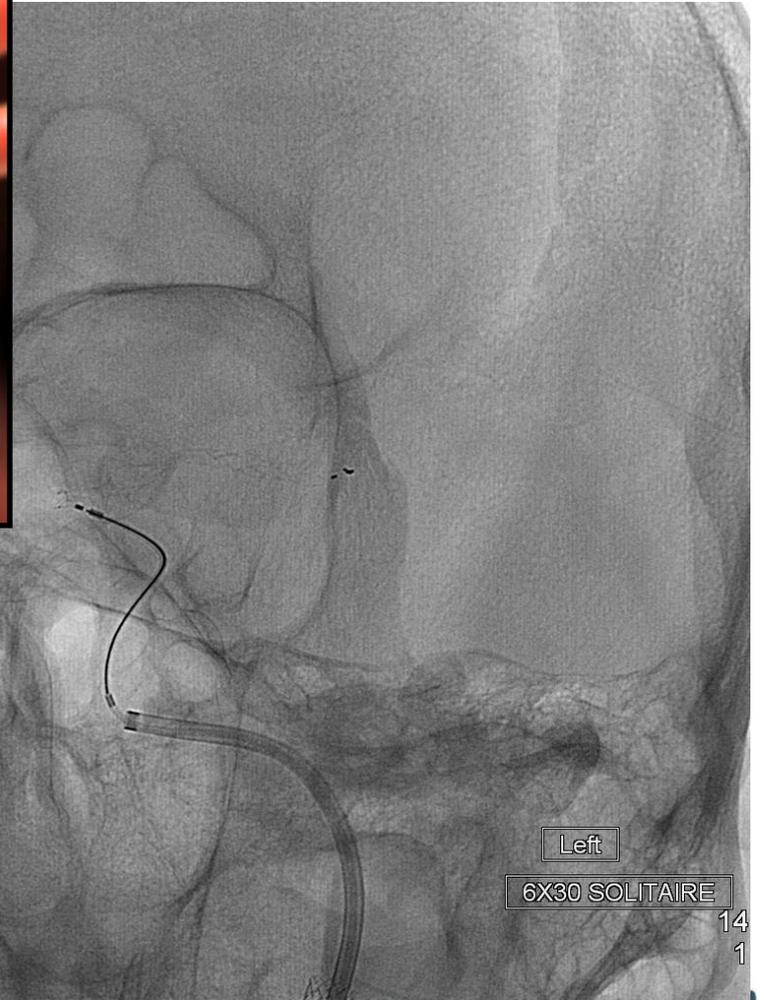
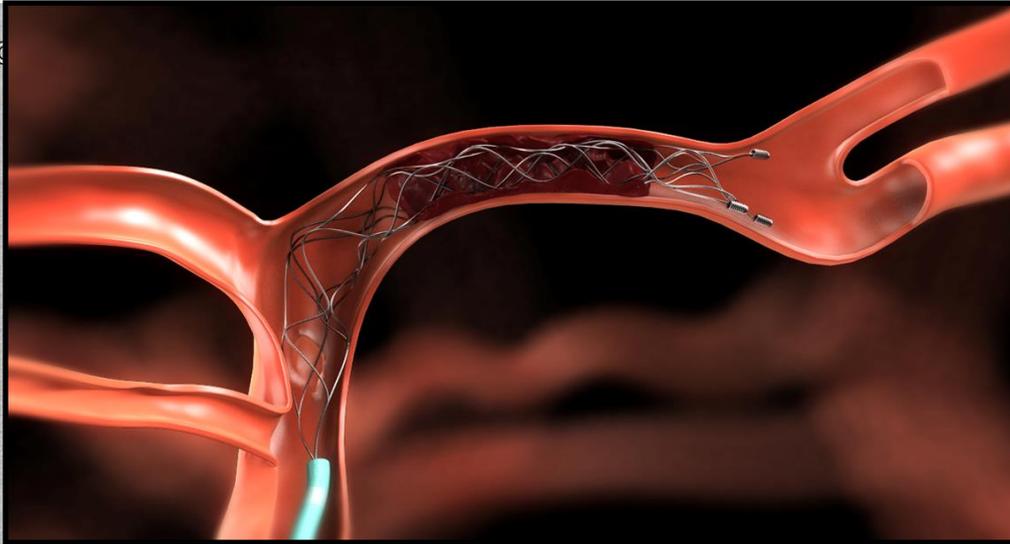
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Acute Stroke Case



Acute Stroke Case



LAC
FD

🗣️ 2:00
🕒 3:50
🕒 9:44:22

🕒 0:00
🕒 10:00:27

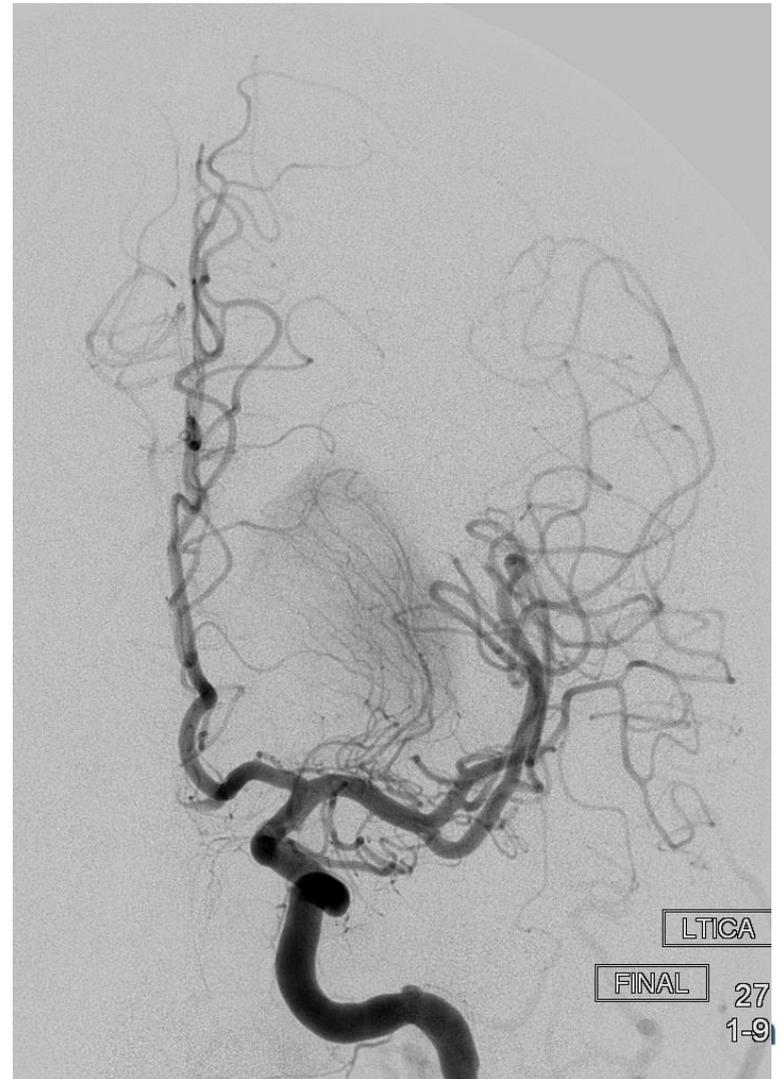
Left
6X30 SOLITAIRE

14
1

Acute Stroke Case



Acute Stroke Case



Acute Stroke Case

- The following morning patient had improved to minimal aphasia, dysarthria, and right arm pronator drift.
- NIHSS = 3



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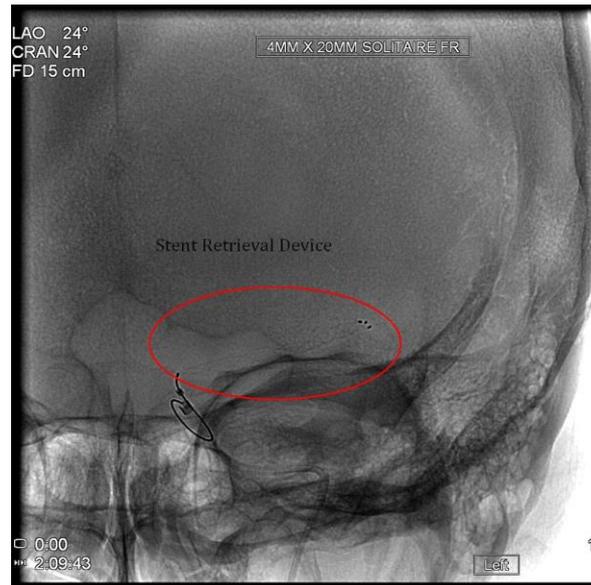
Endovascular therapy for acute ischemic stroke

53 year-female presented to Essentia Health-Fargo emergency room with severe acute ischemic stroke, severe aphasia and right sided hemiplegia, NIHSS 22 (severely disabled with inability to speak or move her right arm and leg)

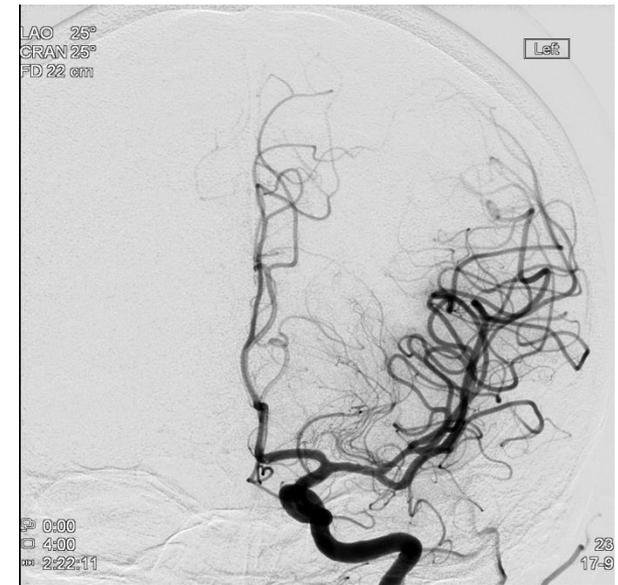
Received IV tPA (clot busting treatment) and endovascular therapy (using catheter techniques)



Angiogram showing left Middle Cerebral Artery (MCA) occlusion



Stent retrieval Device deployed in the left MCA.



Complete recanalization of the left Middle Cerebral artery

Patient was completely back to normal with very mild right arm weakness when she was discharged from the hospital with NIHSS of 1.



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Latest Stroke Trials

- MR CLEAN
- ESCAPE
- EXTEND-IA
- SWIFT PRIME
- REVASCAT



MR CLEAN

- Results of the **M**ulticenter *R*andomized **C**linical trial of **E**ndovascular treatment for **A**cute ischemic stroke in the **N**etherlands



Design

- Multicenter (16 Centers in Netherlands)
 - Prospective, randomized trial, open label treatment
 - Blinded assessment of functional outcome at 90 days
 - Blinded assessment of neuro-imaging at baseline and follow-up
- Blinded, web-based, 1:1 randomization
 - Intra-arterial treatment (IA thrombolysis, mechanical treatment or both) plus usual care (could include IV tPA)
 - Usual care alone (control group)



Design

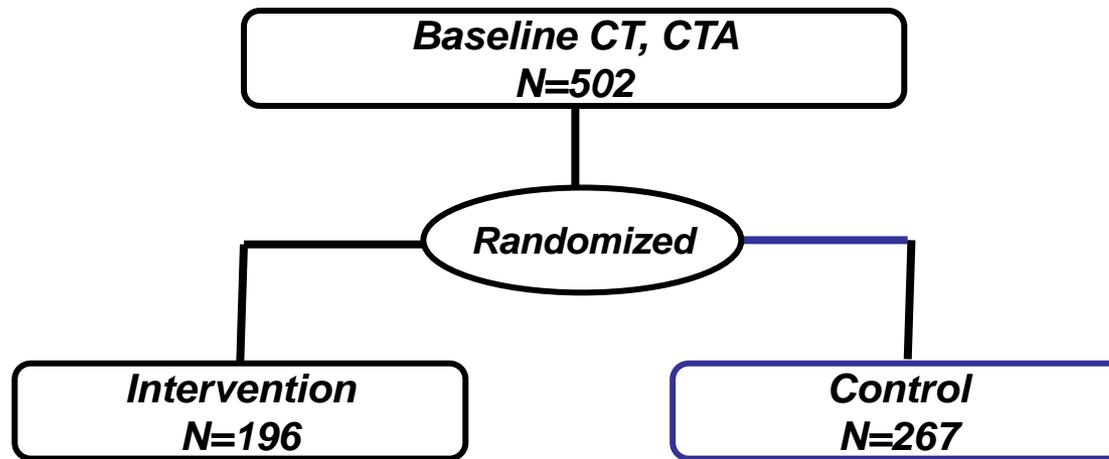
- Inclusion Criteria
 - Acute ischemic stroke, Age ≥ 18 , NIHSS ≥ 2
 - Intracranial anterior circulation occlusion (confirmed by CTA)
 - Initiation of IA treatment within 6 hours from onset



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Patients were randomized 1:1



Received Therapy

*Actual IA Therapy
was performed in 196
of 233 pts

End of Follow Up



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Results

- Main device: Stent retriever
- NIHSS average at presentation
 - Intra-arterial: 17
 - Control: 18
- Vessel involved
 - M1 in > 60%
 - Distal ICA > 25%

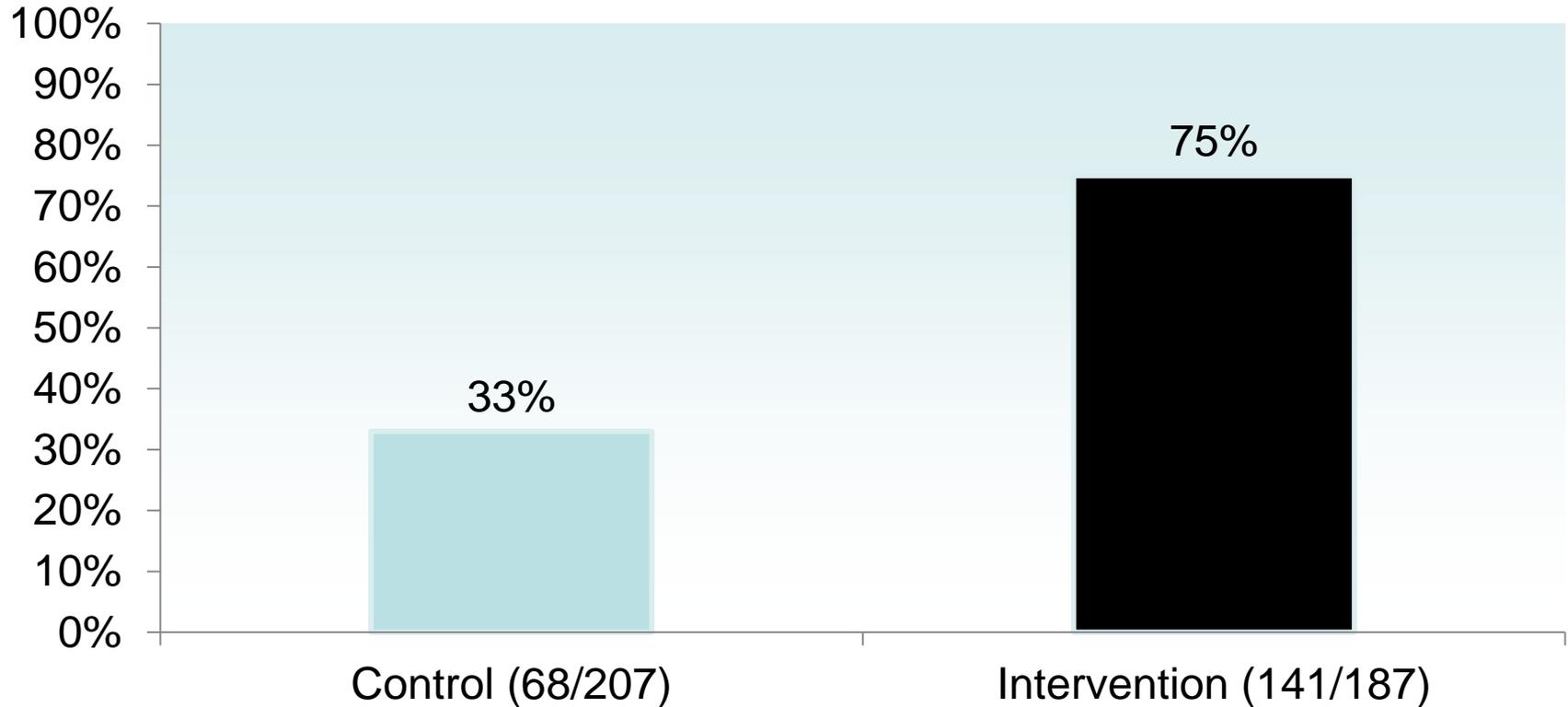


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Vessel recanalization

Recanalization on CTA after 24 Hours



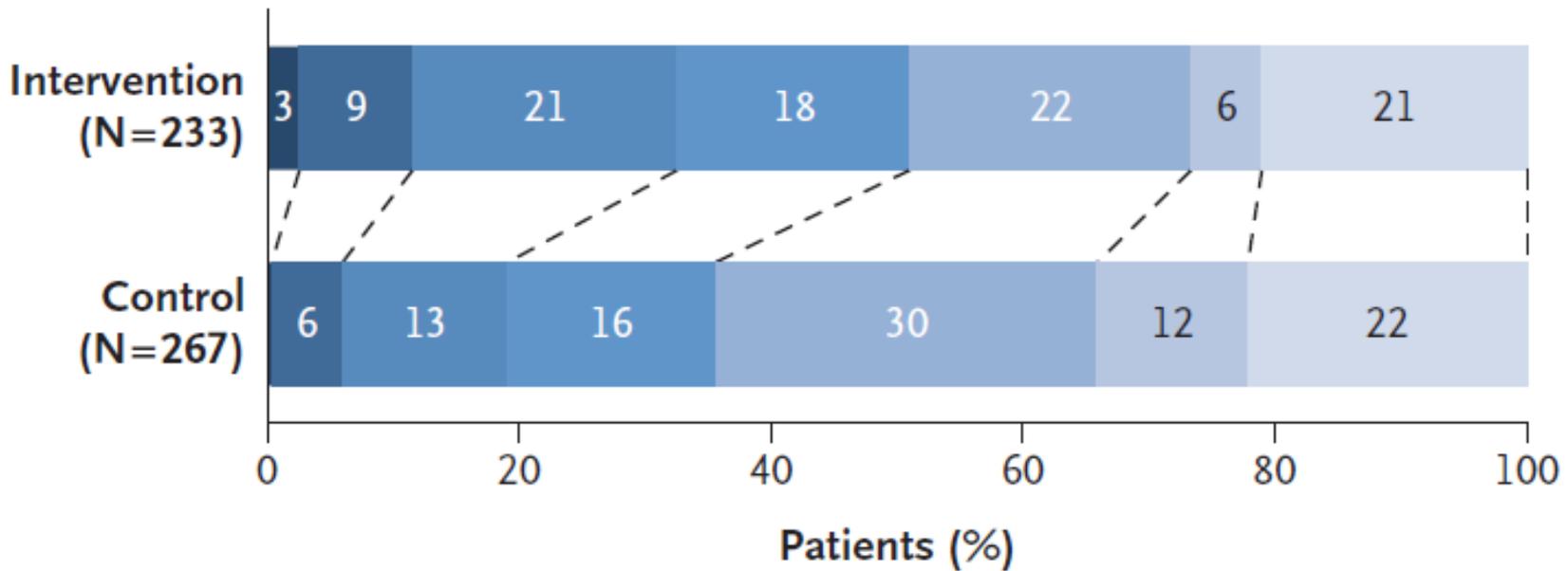
* Slide courtesy of Stryker 2015

Historical Approach to Dichotomized Modified Rankin Scale Evaluation

0	1	2	3	4	5	6
No symptoms	No significant disability	Slight disability	Moderate disability	Moderately severe disability	Severe disability	Dead
	Able to carry out all usual activities, despite some symptoms	Able to look after own affairs without assistance, but unable to carry out all previous activities	Requires some help, but able to walk unassisted	Unable to attend to own bodily needs without assistance, and unable to walk unassisted	Requires constant nursing care and attention, bedridden, incontinent	
SUCCESS			FAILURE			



Results



Conclusion

- In patients with acute ischemic stroke caused by a proximal intracranial arterial occlusion of the anterior circulation, intraarterial treatment administered within 6 hours after stroke onset was effective and safe
- This treatment leads to a clinically significant increase in the functional independence in daily life by 3 months, without an increase in mortality



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ESCAPE

- Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times



Design

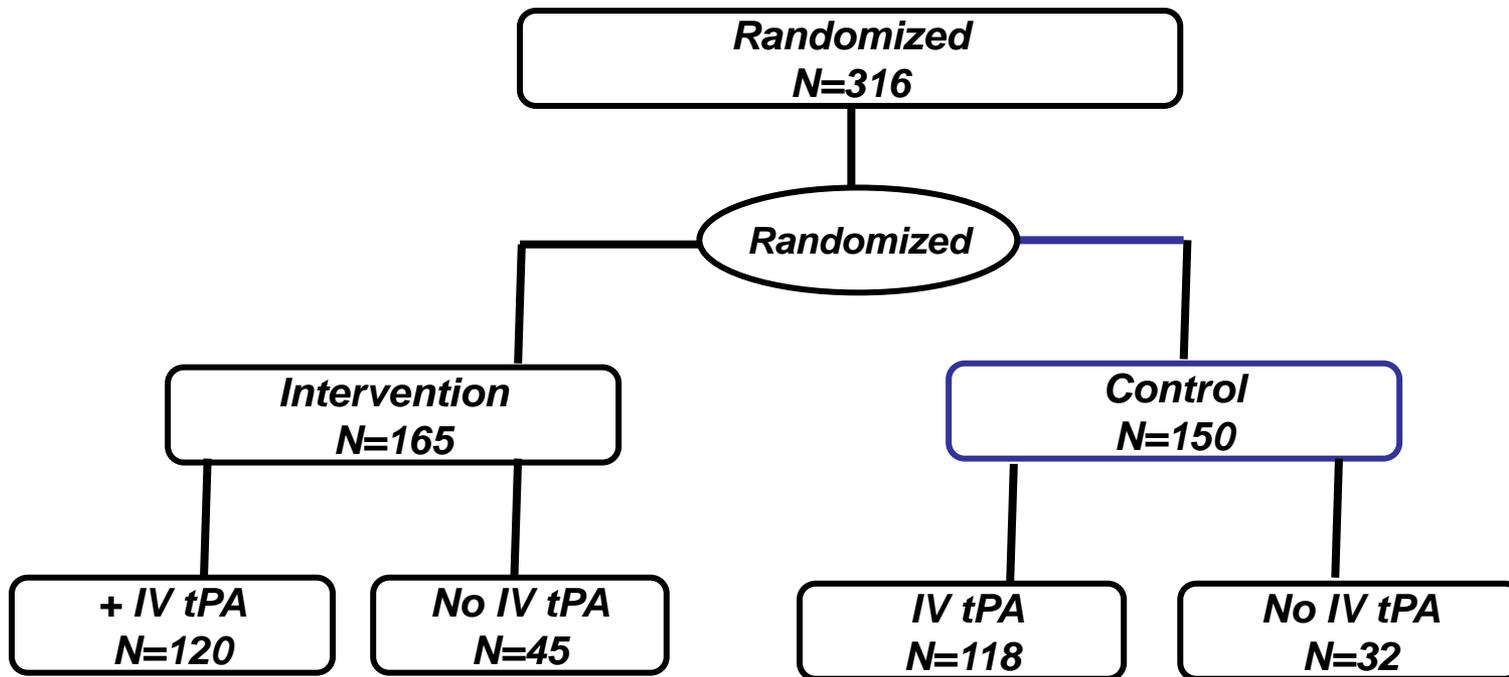
- **Methods:**
 - 22 centers in Canada, US, Korea, UK and Ireland
 - Randomized, open-label with blinded outcome evaluation, parallel group trial
 - *Intervention:* Endovascular mechanical thrombolysis with an approved approach/device (use of retrievable stents and balloon guide catheters recommended)
 - *Control:* Guideline-based standard of care (IV tPA if <4.5 hrs / stroke unit care)



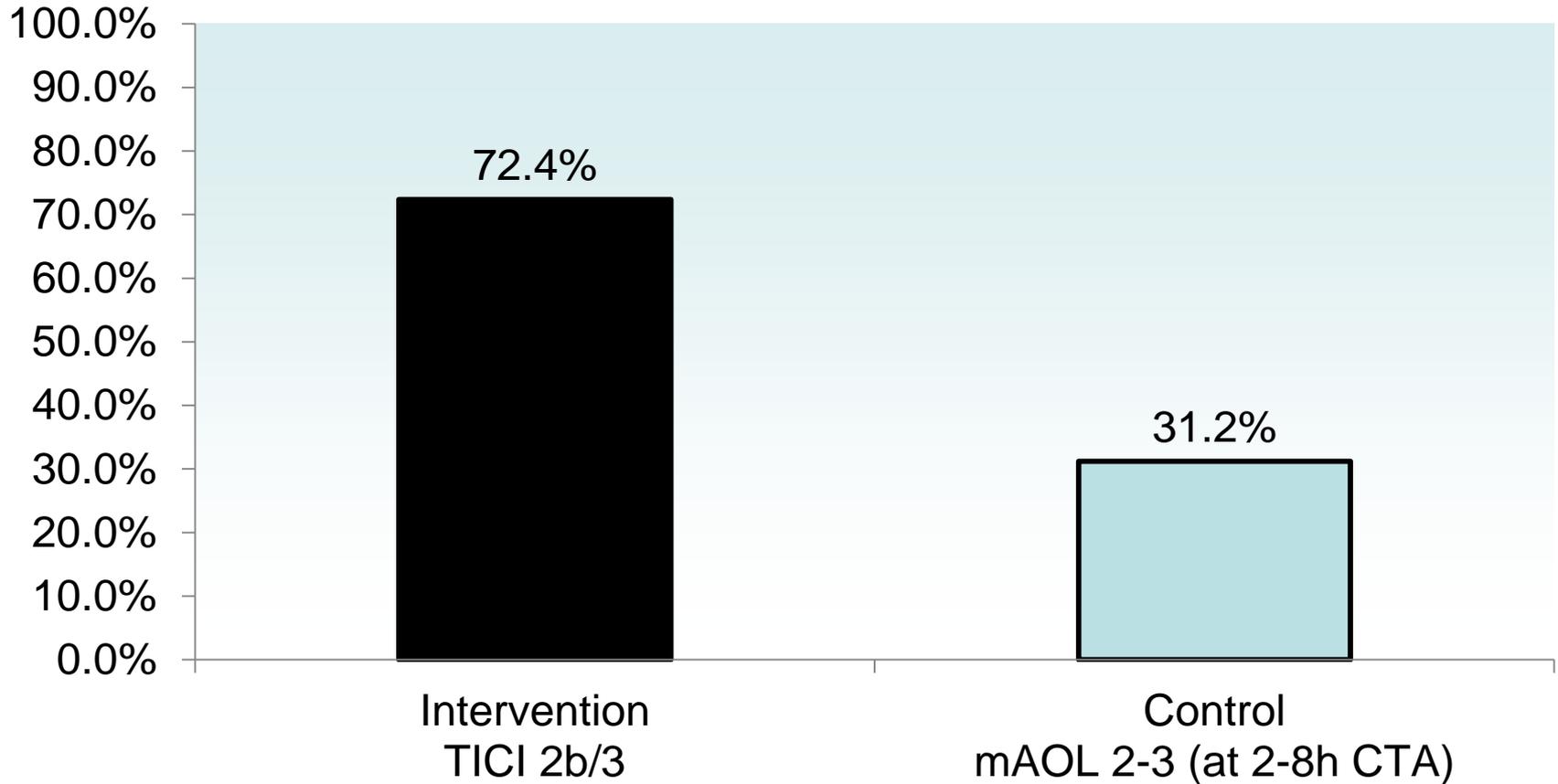
Inclusion Criteria

- Acute ischemic stroke
- Age \geq 18 years
- Last-seen-well time to randomization < 12 hours
- ASPECTS >5
- Baseline NIHSS >5 at time of randomization
- Good functional status: pre-stroke modified Barthel Index \geq 95, not living in a nursing home; fully independent
- Confirmed symptomatic intracranial occlusion based on CTA in anterior anatomy (Carotid T/L, M1, 2 or more M2's not including the anterior temporal artery)
- Moderate to good collaterals on CTA
- Endovascular treatment can be initiated within 60 minutes of baseline NCCT with target CT to first recanalization of 90 minutes

Patients were randomized 1:1



Revascularization



* Slide courtesy of Stryker 2015

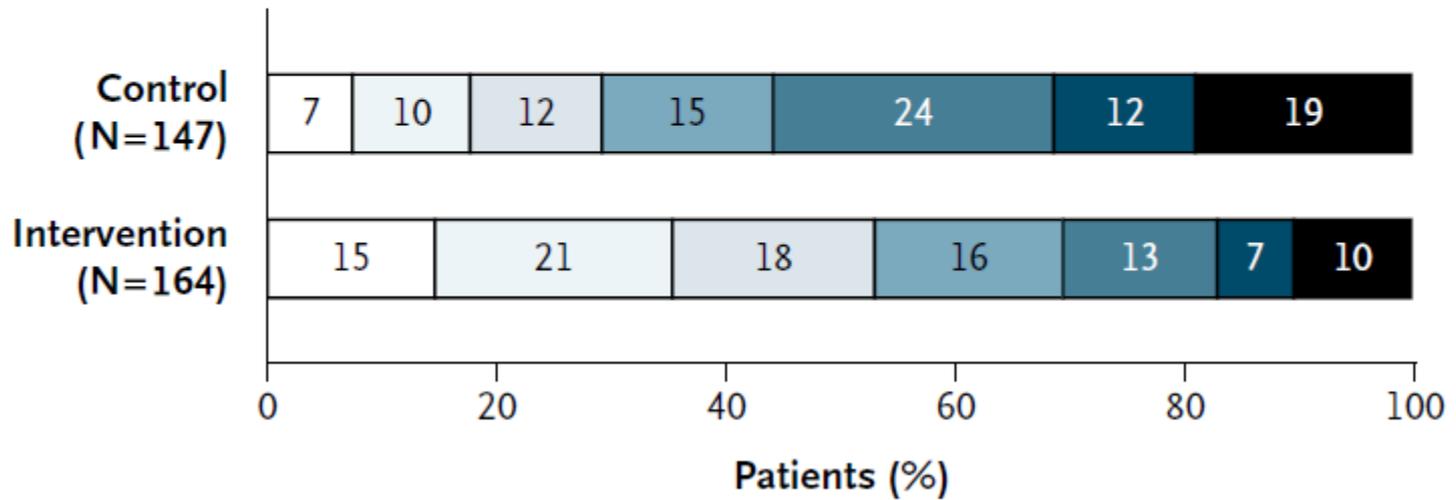


Results

Modified Rankin Scale Score



A Overall



Conclusions

- Endovascular thrombectomy is a safe, highly effective procedure that saves lives and dramatically reduces disability WHEN:
 - Patients are carefully selected by imaging to identify proximal occlusions and exclude large core and exclude patients with absent collaterals

SWIFT PRIME

- Solitaire FR With the Intention For Thrombectomy as PRIMary Endovascular treatment for acute ischemic stroke

Results of the SWIFT PRIME Trial were presented by Dr. Jeffery Saver and Dr. Michael D. Hill at the International Stroke Conference in Nashville, TN on Wednesday, February 11, 2015.



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Design

- Methods:
 - Randomized, open-label with blinded outcome evaluation, parallel group trial
 - *Intervention*: IV tPA with Solitaire FR Device
 - *Control*: IV tPA alone
 - 39 enrolling sites in the USA and Europe



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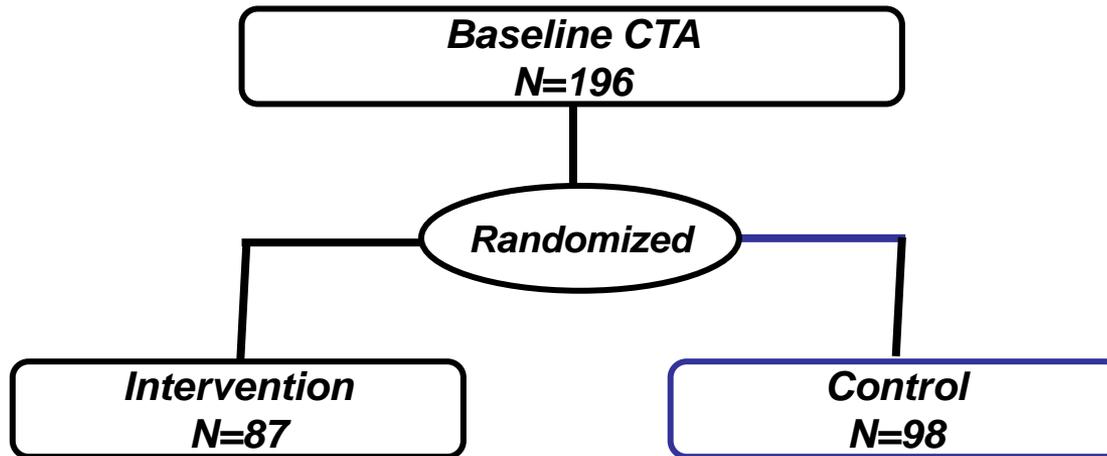
Inclusion Criteria

- Acute ischemic stroke
- Age 18-80
- Pre-stroke mRS ≤ 1
- ASPECTS ≤ 6
- Baseline NIHSS 8-29 at time of randomization
- Initiation of IV tPA within 4.5 hours of onset of stroke
- CTA or MRA confirmation of large vessel occlusion in ICA, M1 segment of MCA or carotid terminus
- Endovascular treatment can be initiated within 6 hours of onset of stroke symptoms and within 90 minutes from CTA/MRA to groin puncture



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Patients/Randomization



Received Therapy

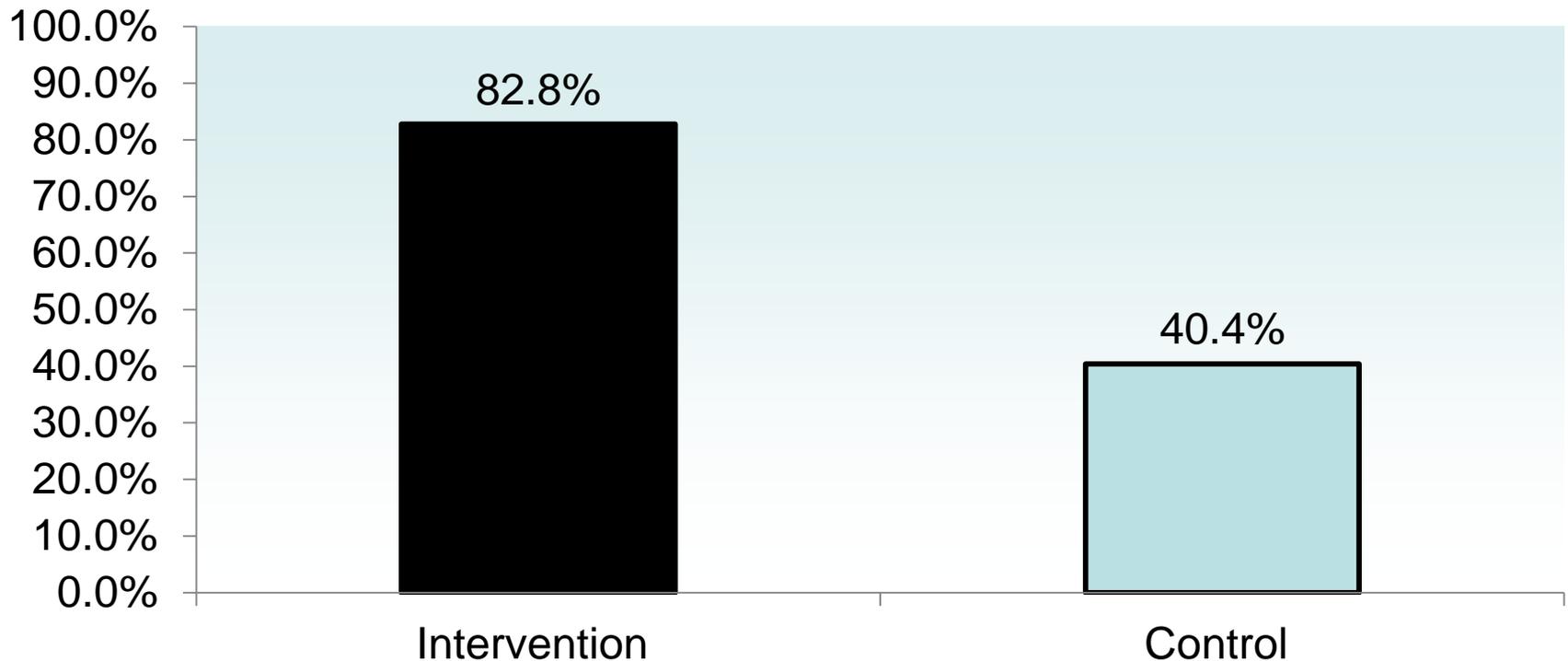
Modified Intention
to Treat



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Successful Reperfusion* ($\geq 90\%$ reperfusion) at 27 hours

OR: 7.11 (95% CI: 3.03 to 16.70)



* Slide courtesy of Stryker 2015

*Reperfusion measured by reperfusion ratio assessed by core lab: reperfusion volume at 27 hrs + hypoperfusion lesion volume (Tmax > 0s) at baseline



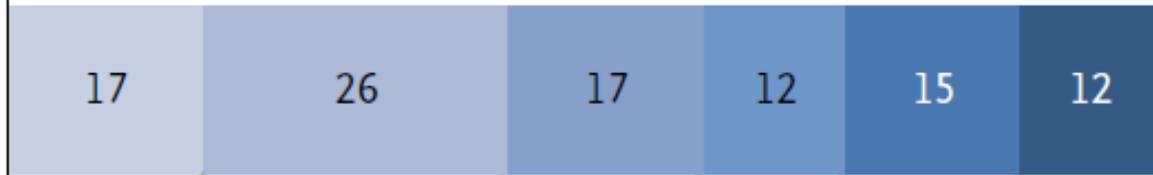
Results of the SWIFT PRIME Trial were presented by Dr. Jeffery Saver at the International Stroke Conference in Nashville, TN on Wednesday, February 11, 2015.

Result

Score on Modified Rankin Scale

No symptoms ← → Death
■ 0 ■ 1 ■ 2 ■ 3 ■ 4 ■ 5 or 6

Stent Retriever +
Intravenous t-PA
(N=98)



Intravenous t-PA
(N=93)



Conclusions

- In AIS patients with confirmed large vessel anterior circulation occlusions treated with IV tPA, rapid treatment with the Solitaire stent retriever lessens post-stroke disability over the entire outcome range and increases the proportion of patients who are alive and independent 3 months after stroke
- For every two and a half patients treated, one more patient has a better disability outcome
- For every four patients treated, one more patient is independent at long term follow up



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EXTEND-IA

- A randomized controlled trial of endovascular thrombectomy after standard dose intravenous t-PA within 4.5 hours of stroke onset utilizing dual target imaging selection



Rational and Methods

- Rational:
 - To select patients with the best chance of benefit from reperfusion (“Dual Target”)
 - Proven major vessel occlusion **AND**
 - Salvageable tissue with ischemic core <70mL (CT perfusion)
 - Treat as fast as possible (no waiting to assess tPA “failure”)
 - Use the most effective device (stent retriever)
- Methods:
 - Randomized, open-label with blinded endpoint (PROBE) design
 - *Intervention*: **Stent Retriever** (Solitaire FR) + IV tPA
 - *Control*: IV tPA



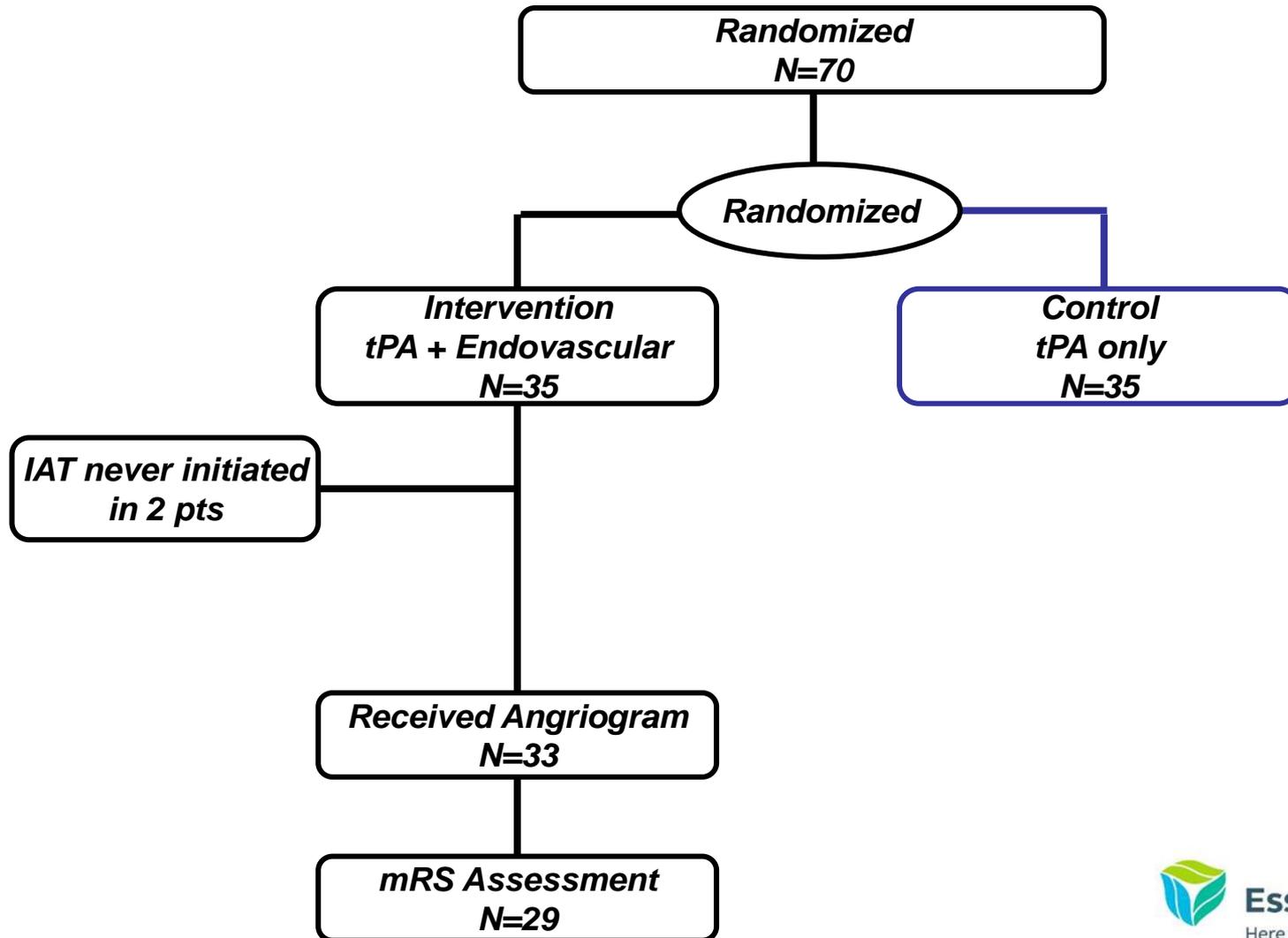
Inclusion Criteria

- Acute ischemic stroke
- Age \geq 18 years
- Pre-stroke mRS 0-1
- Intra-arterial clot retrieval treatment can commence (groin puncture) within 6 hours of stroke onset.
- Imaging inclusion criteria. Dual target:
 - CTA reveals large artery occlusion in anterior anatomy (ICA, M1 or M2)
AND
 - Mismatch - Using CT or MRI with a Tmax >6 second delay perfusion volume and either CT-rCBF or DWI infarct core volume.
 - Mismatch ratio of greater than 1.2 and
 - Absolute mismatch volume of greater than 10ml and
 - Infarct core lesion volume of less than 70mL



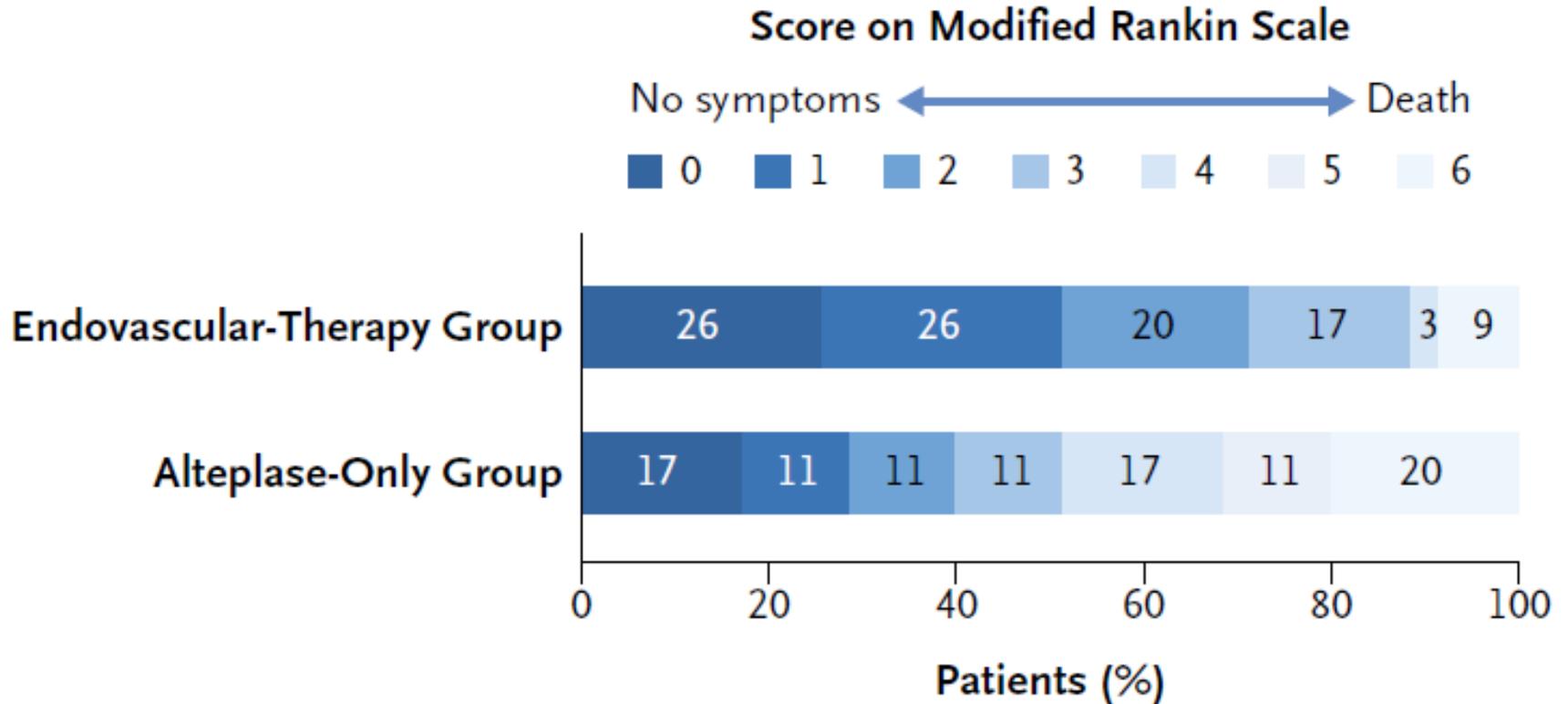
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Patients/Randomization



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Results



Conclusions

- Early mechanical stent thrombectomy after tPA using Solitaire FR led to faster and more complete reperfusion
- In this population selected for vessel occlusion and salvageable tissue this translated to:
 - Improved early neurological recovery
 - Improved functional outcome at 3 months
 - No safety concerns
- **tPA + mechanical stent thrombectomy should be the new standard of care**



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Trials Summary

Trial	Imaging Required to Confirm Occlusion Prior to Randomization?	Device(s) Used in Intervention Arm	TICI 2b/3 Revascularization Rate in the Intervention Arm	mRS 0-2		
				Intervention Arm	Control Arm	Odds Ratio (95% CI)
IMS III	No	IA Lytic (138), Merci Retriever® (95), EKOS (22), Penumbra (54), Solitaire FR (5)	38% ICA 44% M1 44% M2 23% multi M2	40.8% (N=415)	38.7% (N=214)	0.02 (-0.06 to 0.09)
MR RESCUE	No	Merci Retriever®, EKOS, IA Lytic, Penumbra	24% pen (n=34) 27% nonp (n=30)	21% pen (n=34) 17% nonp (n=30)	26% pen (n=34) 10% nonp (n=20)	NS
MR CLEAN	Yes	97% Stent Retrievers, 2% other Mechanical	58.7% (N=196)	33% (N=233)	19% (N=267)	2.16 (1.39-3.38)
ESCAPE	Yes	86% Stent Retriever	72.4% (n=156)	53.0% (n=164)	29.3% (n=147)	1.8 (1.4-2.4)
SWIFT PRIME	Yes	100% Stent Retriever	88.0% (n=83)	60.2% (n=98)	35.5% (n=93)	2.75 (1.53,4.95)
EXTEND-IA	Yes	100% Stent Retriever	86.2% (n=29)	71% (n=35)	40% (n=35)	4.2 (1.3-13)

* Slide courtesy of Stryker 2015

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Stroke and Neurovascular Program

3 Years Outcome Data



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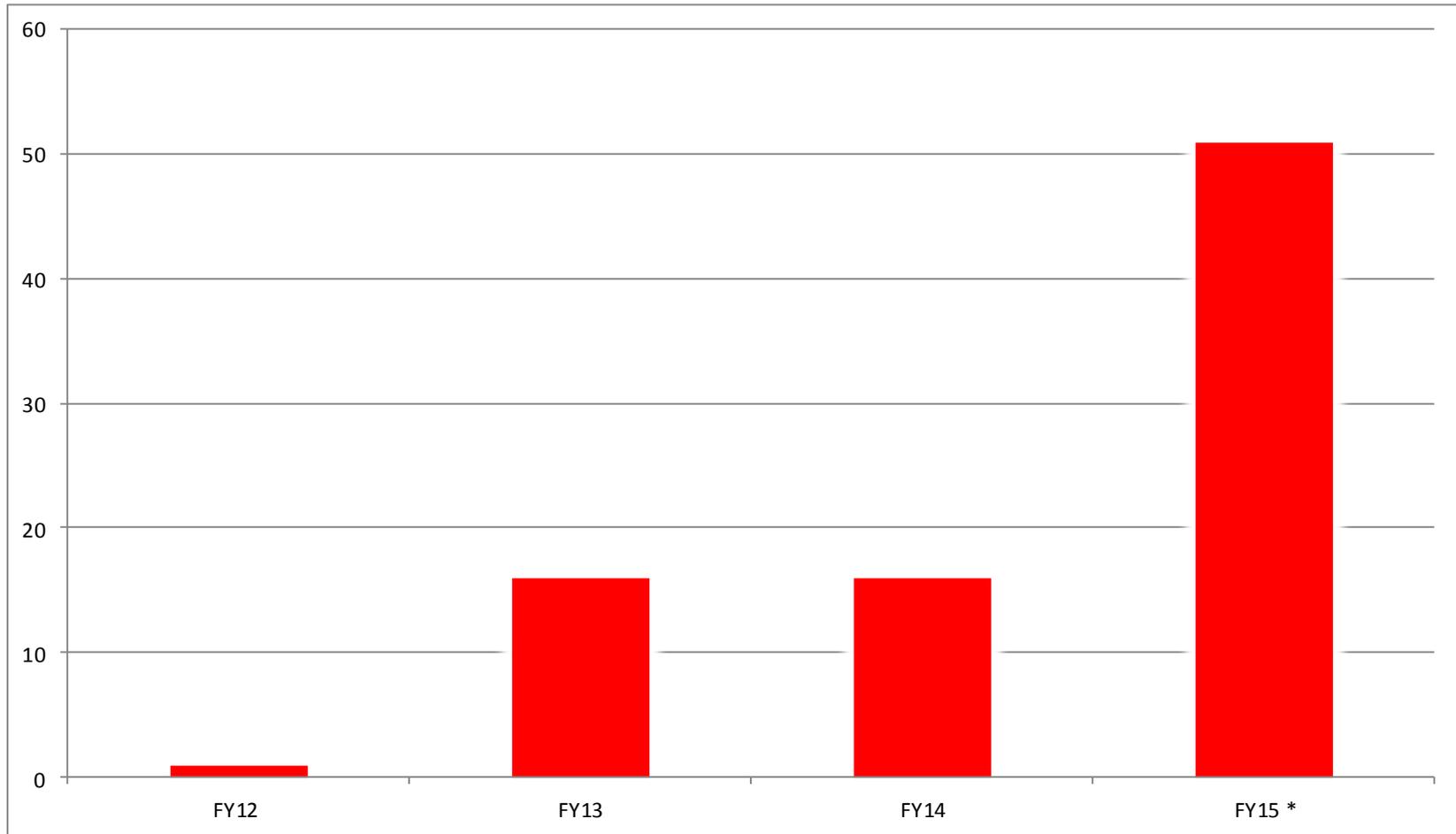


IV tPA by year

- FY13: 16
- FY14: 16
- FY15: 43



IV tPA by year

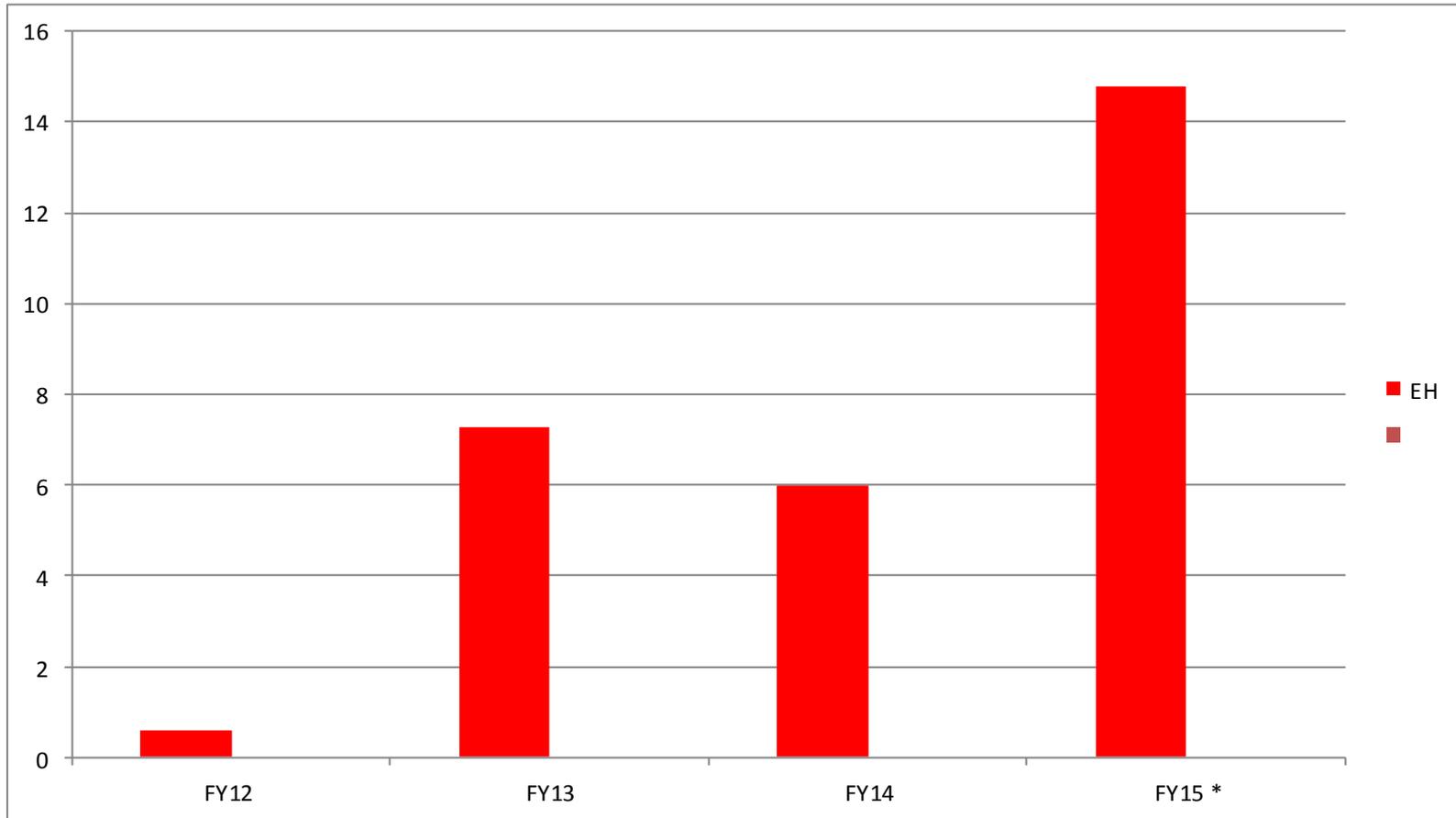


* Projected number for 2015



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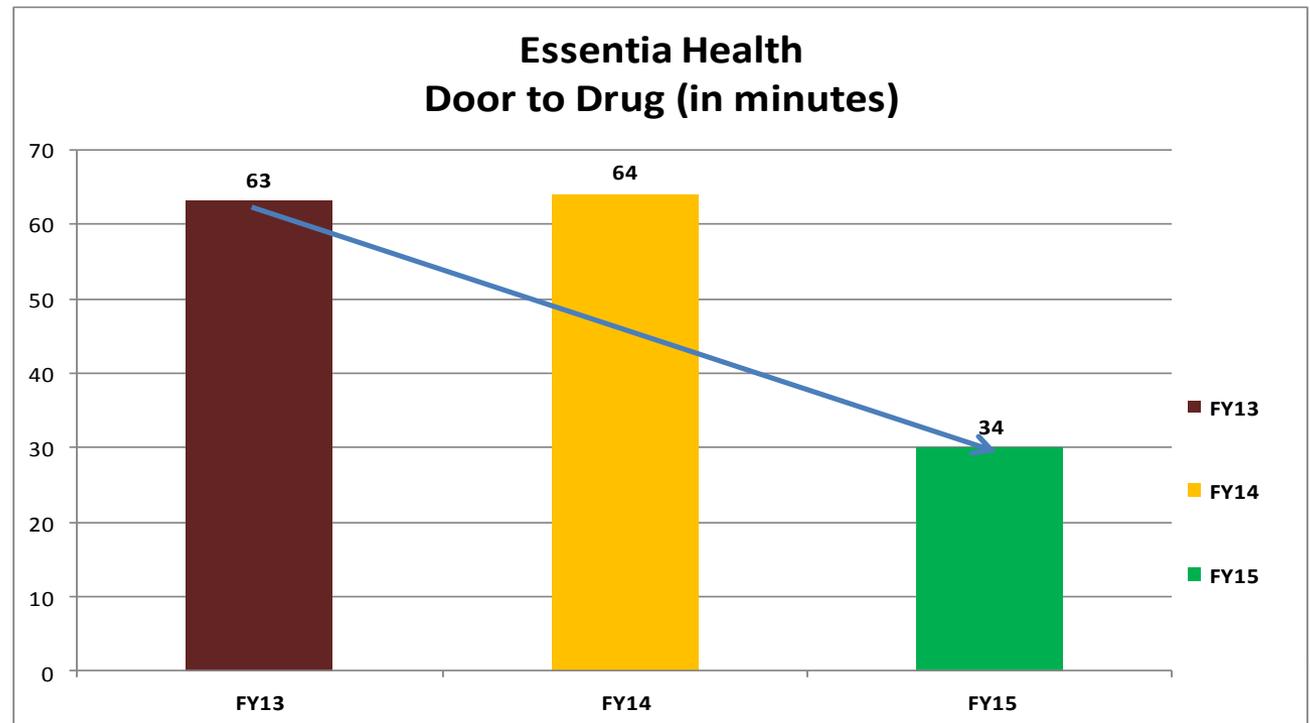
IV tPA by year and percentage



* Projected number for 2015

tPA times (Mean)

- FY13: 63 minutes
- FY14: 64 minutes
- FY15: 34 minutes



Our Center Experience

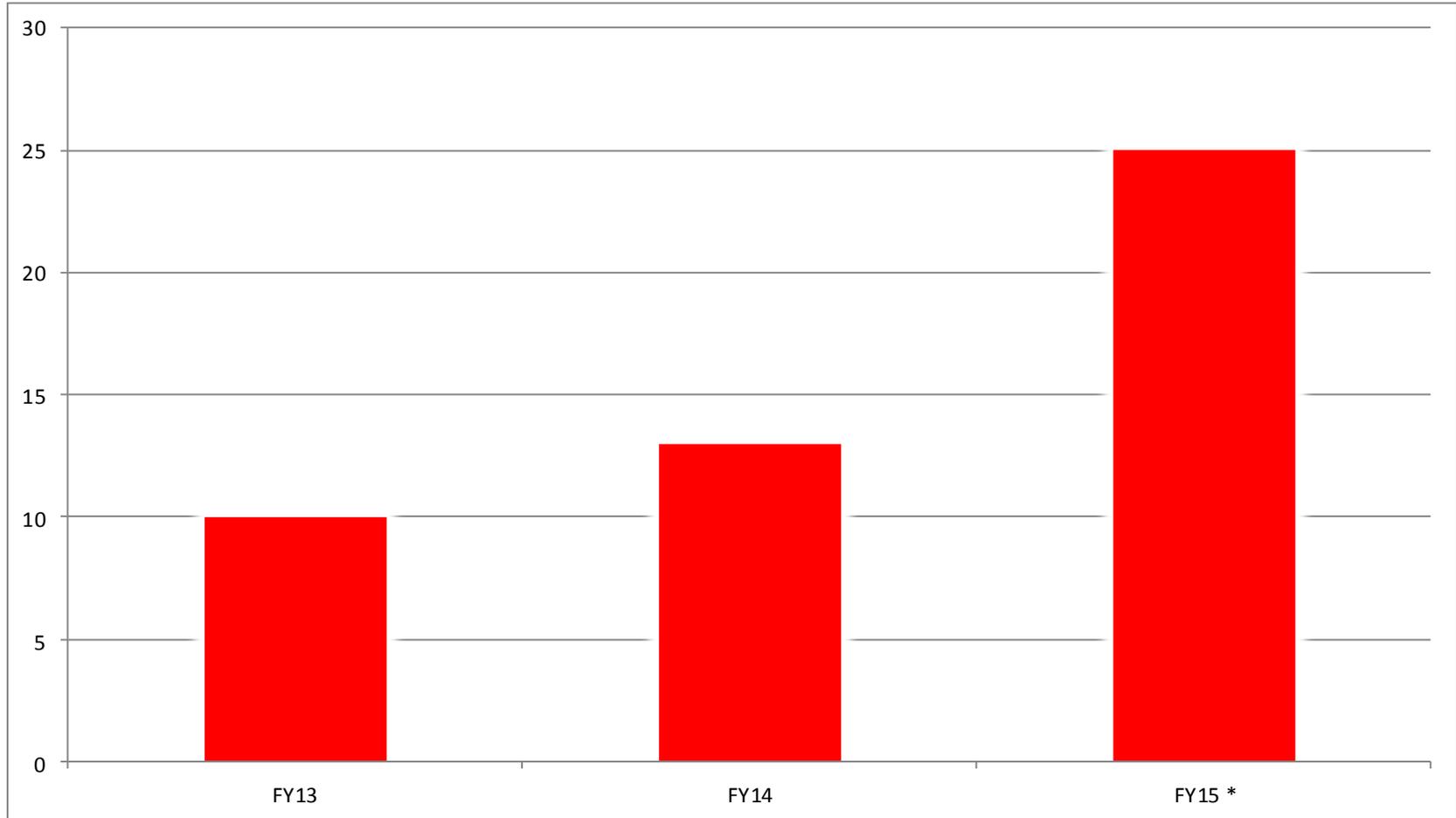
- 2012-Current
- 48 Endovascular intervention
- 9.9% of stroke patient received IA therapy



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IA Therapy by year

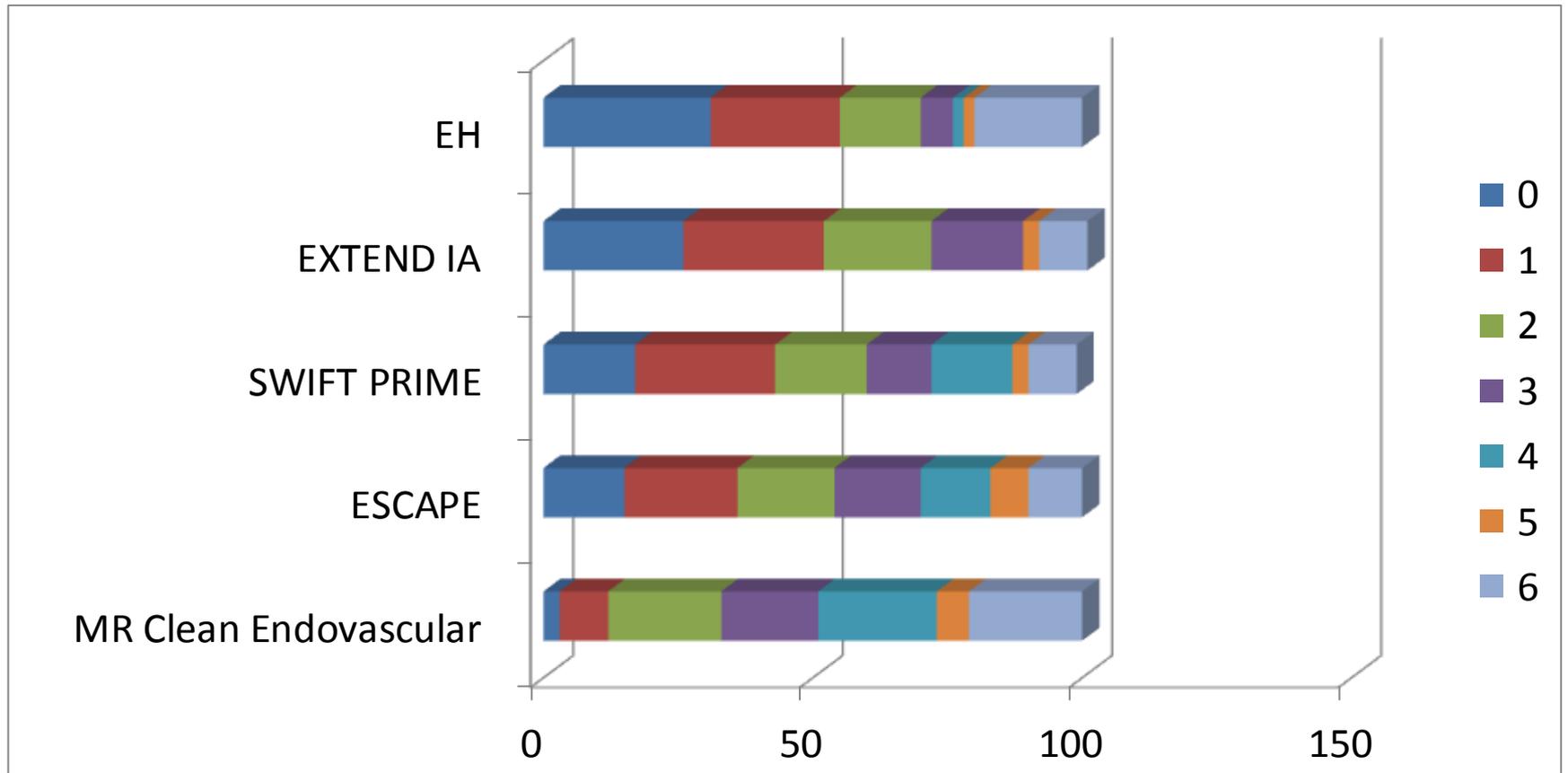


* Projected number for 2015



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Endovascular therapy outcome by MRs



Thank you



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