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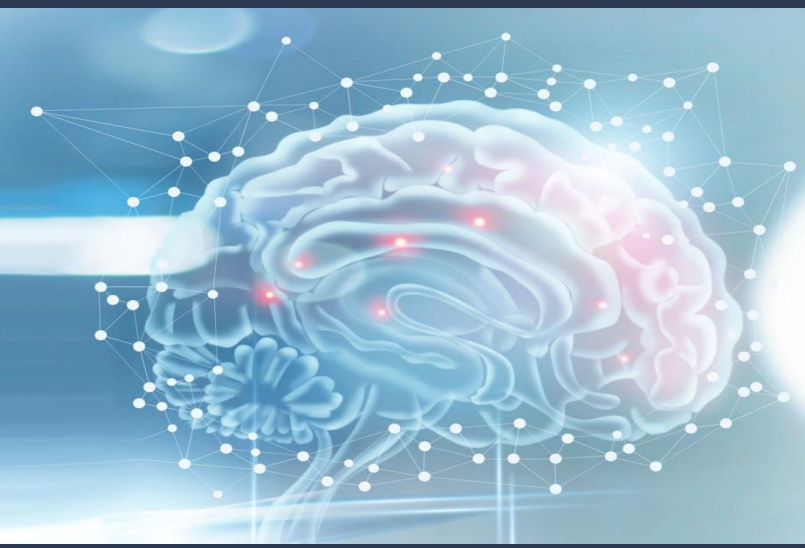
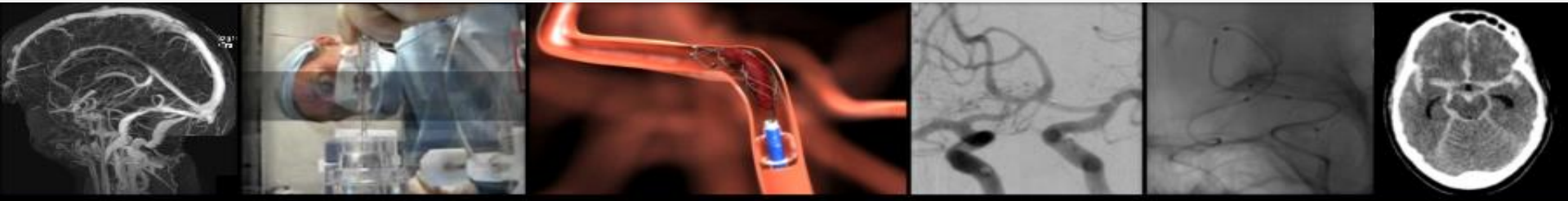


Ischemic Stroke Secondary to Large Vessel Occlusion: Where are We Today?

Donald Frei, M.D.

Director, Neuro-interventional Surgery

Swedish Medical Center



Disclosures

- Consultant/speakers bureau
  - Genentech, Penumbra, Stryker
- Research support
  - Cerenovus, Medtronic, Microvention, Penumbra, Stryker
- Stock ownership
  - Penumbra

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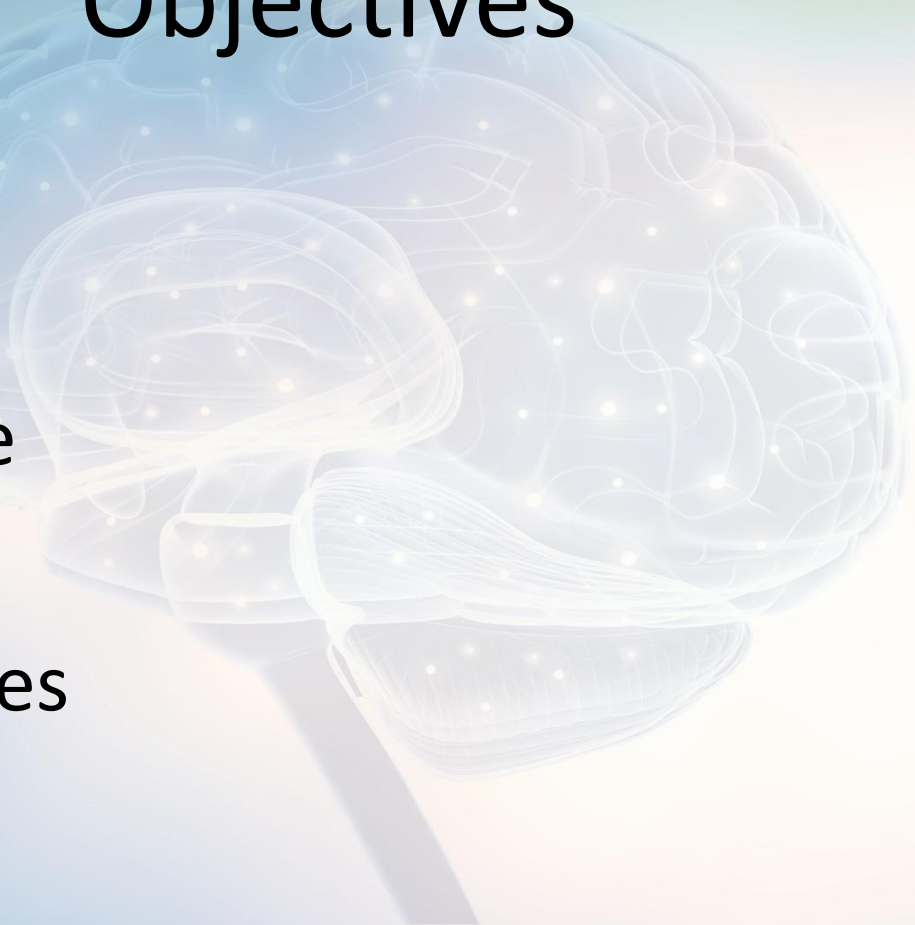
Objectives

- The problem
- The options
- The evidence
- The solution
- The challenges



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The Problem

Stroke: The sudden death of brain cells due to lack of oxygen, caused by blockage of blood flow or rupture of an artery to the brain.

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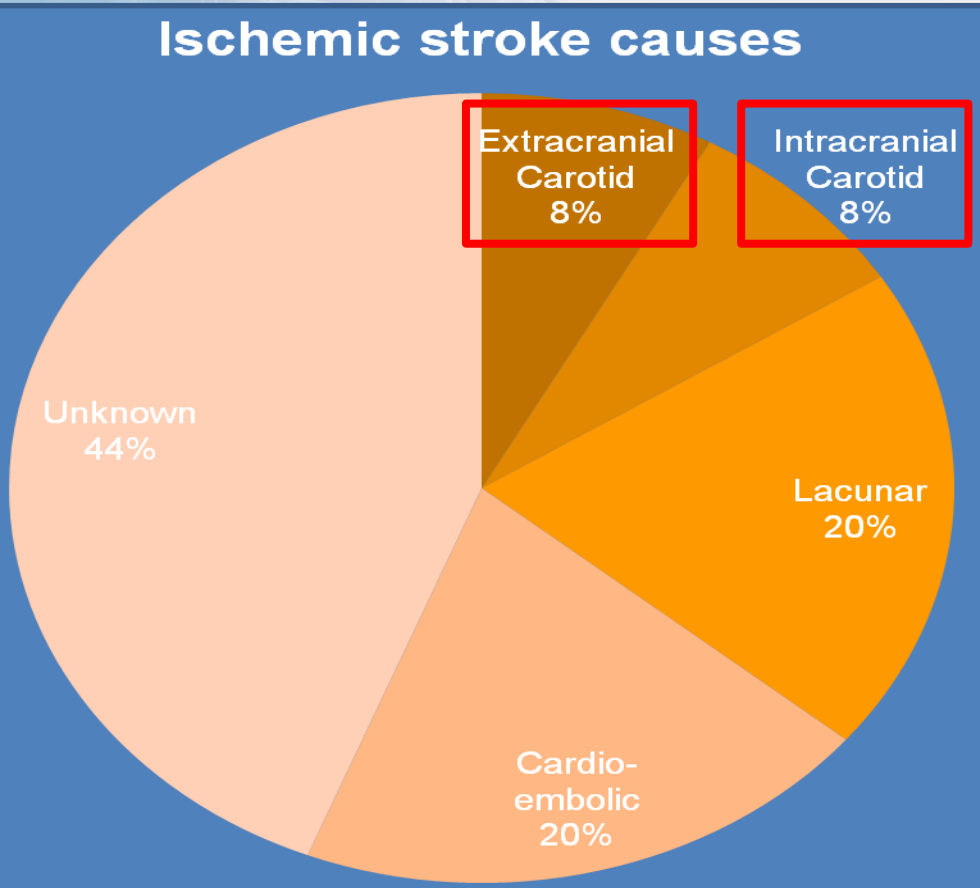
Stroke

Hemorrhagic: 13%

Ischemic: 87%

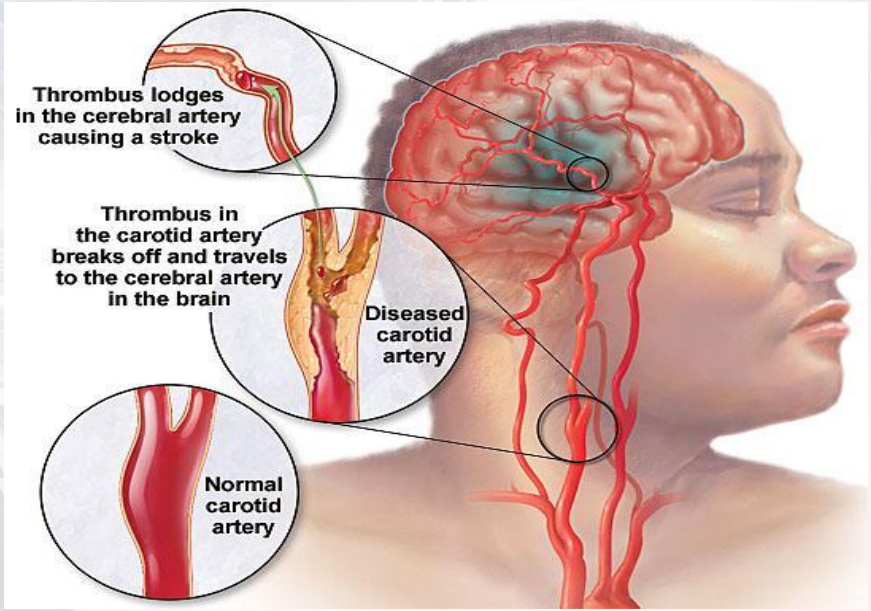
Stroke Etiology



Source: Mackey WC. CHAPTER 92 – Cerebrovascular Disease : General Considerations. Rutherford's Vascular Surgery. 7th Edition. 2010.

Ischemic Stroke

- Stroke affects >800,000 people in US each year
- It is the 4th leading cause of death in North America
  - >150,000 deaths in US/year
- Morbidity
  - 15-30% permanently disabled
- Economic
  - 2012 direct and indirect cost of stroke: $45.5 billion



https://www.cdc.gov/stroke/

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Time is Brain

	Neurons Lost	Synapses Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	36 yrs
Per Hour	120 million	830 billion	3.6 yrs
Per Minute	1.9 million	14 billion	3.1 weeks
Per Second	32,000	230 million	8.7 hrs

(Total number of neurons in the average human brain is 130 billion)

Stroke 2006;37:263-266

LVO Background - USA

Table 5: J.P. Morgan US Stroke Market Model

	2014	2015E	2016E	2017E	2018E	2019E	2020E
US Stroke Patients	795,000	818,850	843,416	868,718	894,780	921,623	949,272
% Ischemic	87%	87%	87%	87%	87%	87%	87%
US Ischemic Stroke Patients	691,650	712,400	733,771	755,785	778,458	801,812	825,866
% Large Vessel Strokes	43%	43%	43%	43%	43%	43%	43%
US Large Vessel Strokes	297,410	306,332	315,522	324,987	334,737	344,779	355,122
% Treatable with Salvageable Tissue	50%	50%	50%	50%	50%	50%	50%
US Ischemic Stroke Patients with ELVO	148,705	153,166	157,761	162,494	167,369	172,390	177,561
% of US Ischemic ELVO Patients Treated	7.9%	11.5%	13.8%	17.3%	21.0%	25.0%	28.5%
US Ischemic ELVO Patients Treated	**11,750**	**17,616**	**21,695**	**28,033**	**35,150**	**43,100**	**50,608**

Thrombectomy - 100% increase, 2014 -> 2016, but
We only treated < 20% of eligible patients in 2016

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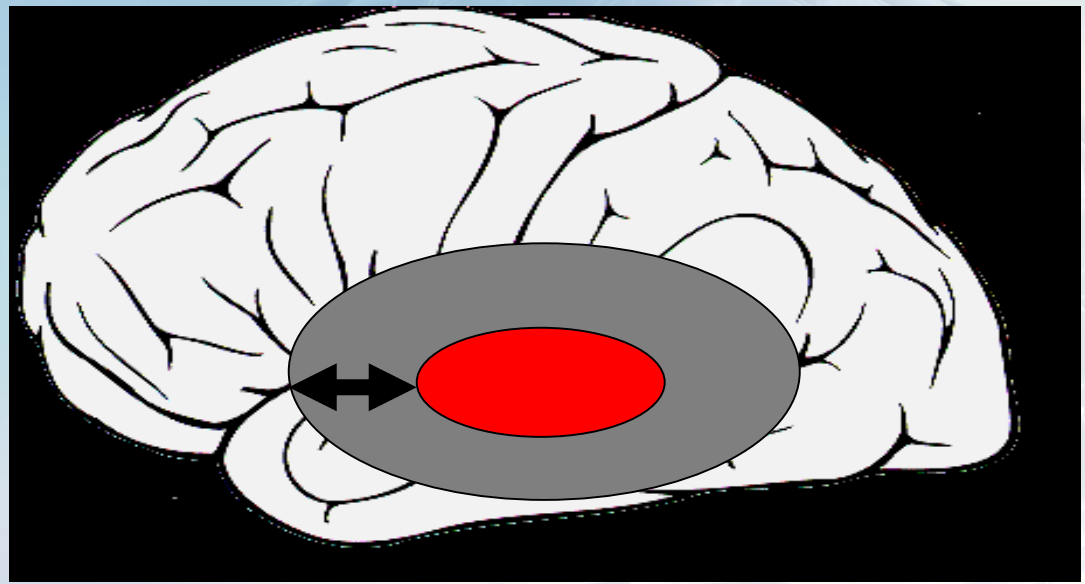
Mismatch: Penumbra



MRI/CT Abnormality: Bioenergetic Compromise = Core

Perfusion Abnormality: Hemodynamic Compromise = Ischemic

Diffusion/Perfusion Mismatch = Penumbra

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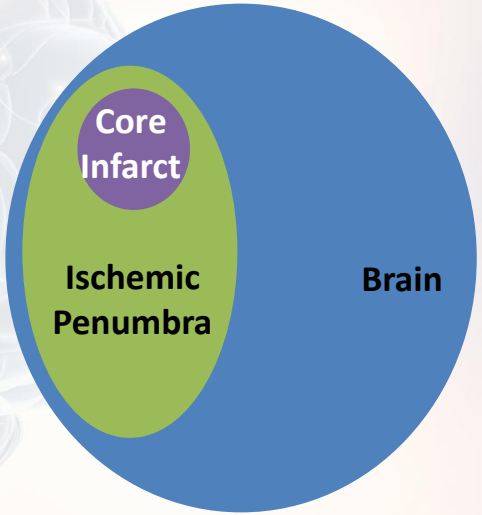
Why is Time Important?

- The area peripheral to a core infarct where metabolism is active but blood flow is diminished is called the **ischemic penumbra**
  - This is salvageable tissue that is at risk for infarction.

- The penumbra lies in a 'no-man's land' between a zone of low blood flow that is < 25 ml/100 mg brain tissue/min and a zone where brain tissue is undergoing necrosis/death, flow of < 8-10 ml/100 mg/min[1]

- Without restoration of blood flow/oxygen, the ischemic penumbra will convert to ischemic core or tissue death

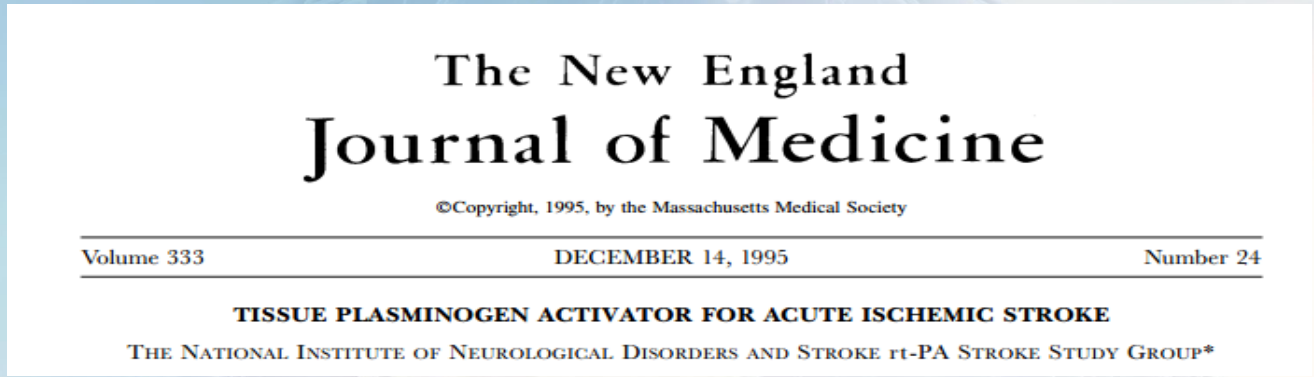


1- http://medical-dictionary.thefreedictionary.com/ischemic+penumbra

The Options

- Medical supportive care
- Intravenous t-PA
  - Clot busting medicine
  - < 3 hours from symptom onset
- Thrombectomy
  - Endovascular clot removal
  - Appropriate for LVO (large vessel occlusion)
  - < 24 hours from symptom onset based upon advanced imaging based patient selection

Intravenous Recombinant Tissue Plasminogen Activator



The New England
Journal of Medicine

Volume 333 DECEMBER 14, 1995 Number 24

TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE rt-PA STROKE STUDY GROUP*

- 333 patients, Published December 1995.
- Compared with patients given placebo vs. patients treated with t-PA **within 3 hours**
- Patients treated with t-PA were at least **30 percent more likely** to have minimal or no disability at three months.

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Options for Patients Experiencing an Ischemic Stroke

IV tPA

Gold-standard in ischemic stroke care. Drug is designed to break apart the clot.

Bridging Therapy

Endovascular Clot Removal

Mechanical disruption or removal of the clot using standard endovascular approaches

Medical Management

Monitor vitals and provide secondary stroke prevention. Patient is send to rehab or a nursing facility when stable.

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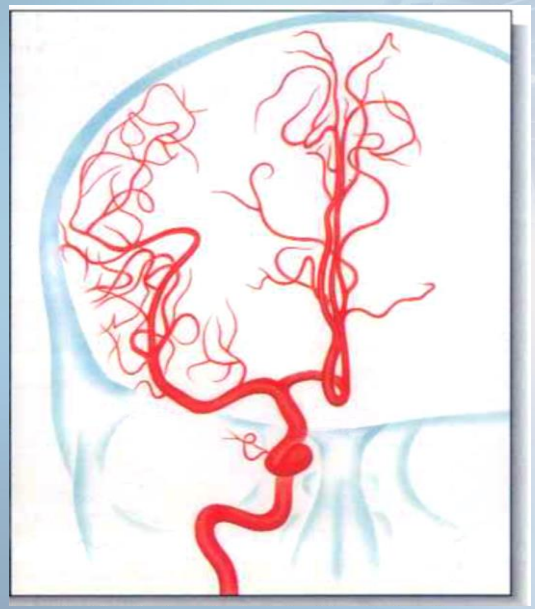
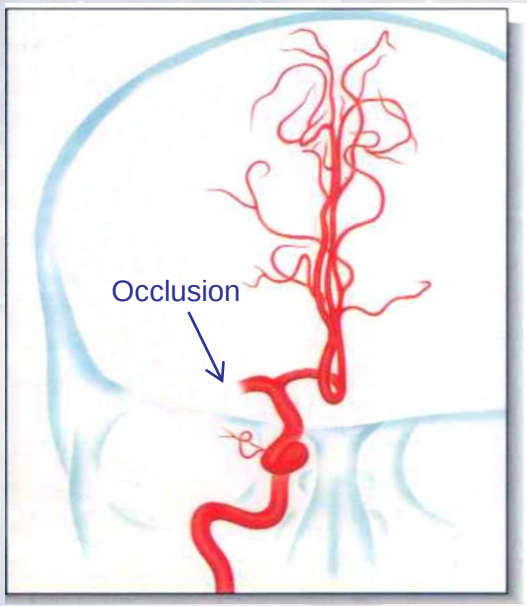
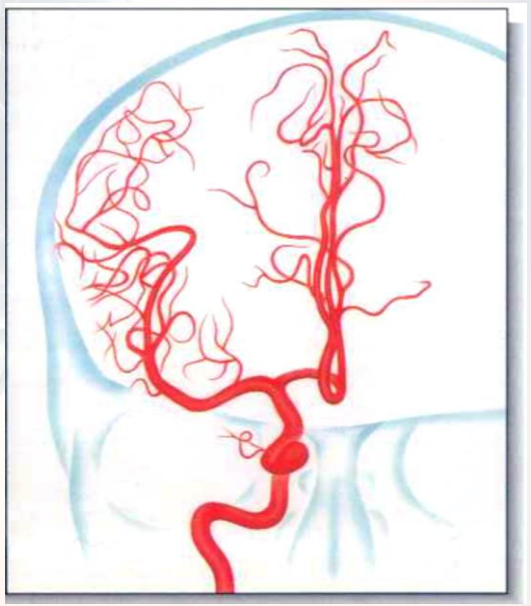
Thrombectomy Goals

Normal → Occlusive clot → Thrombectomy → Normal

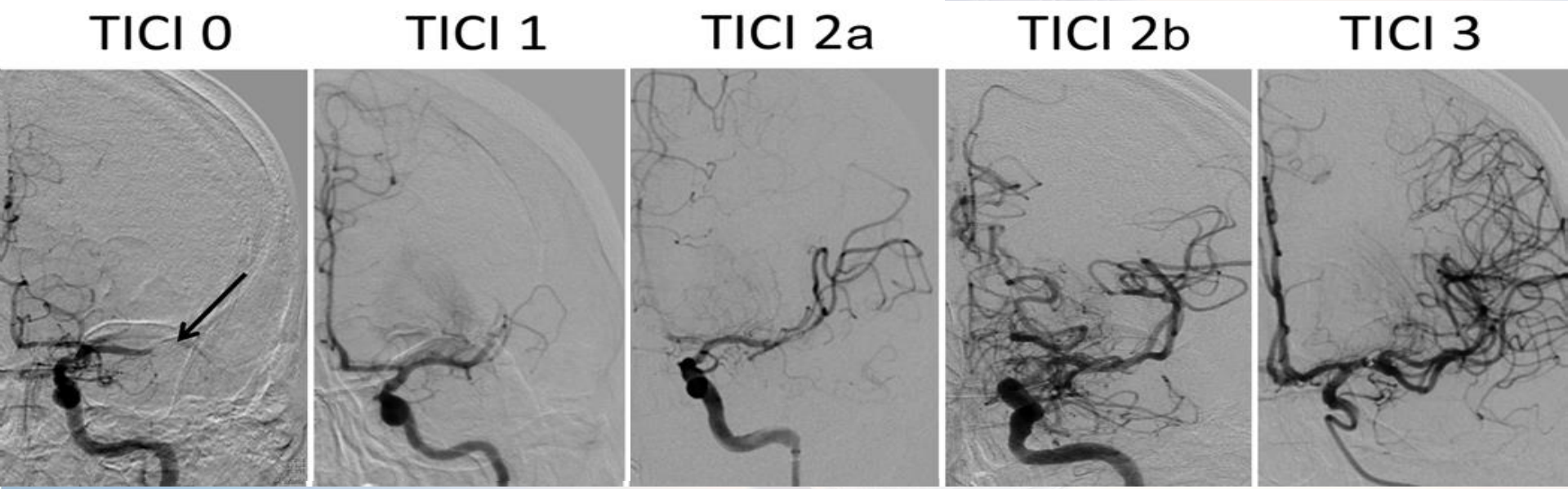






TICI Score

Thrombolysis in Cerebral Infarction Score



TICI 0	TICI 1	TICI 2a	TICI 2b	TICI 3
No perfusion	**Limited Perfusion**	**< 50% vascular territory**	**≥ 50% vascular territory**	**Full Perfusion**

Mokin et al; Neurosurg Focus *2014*

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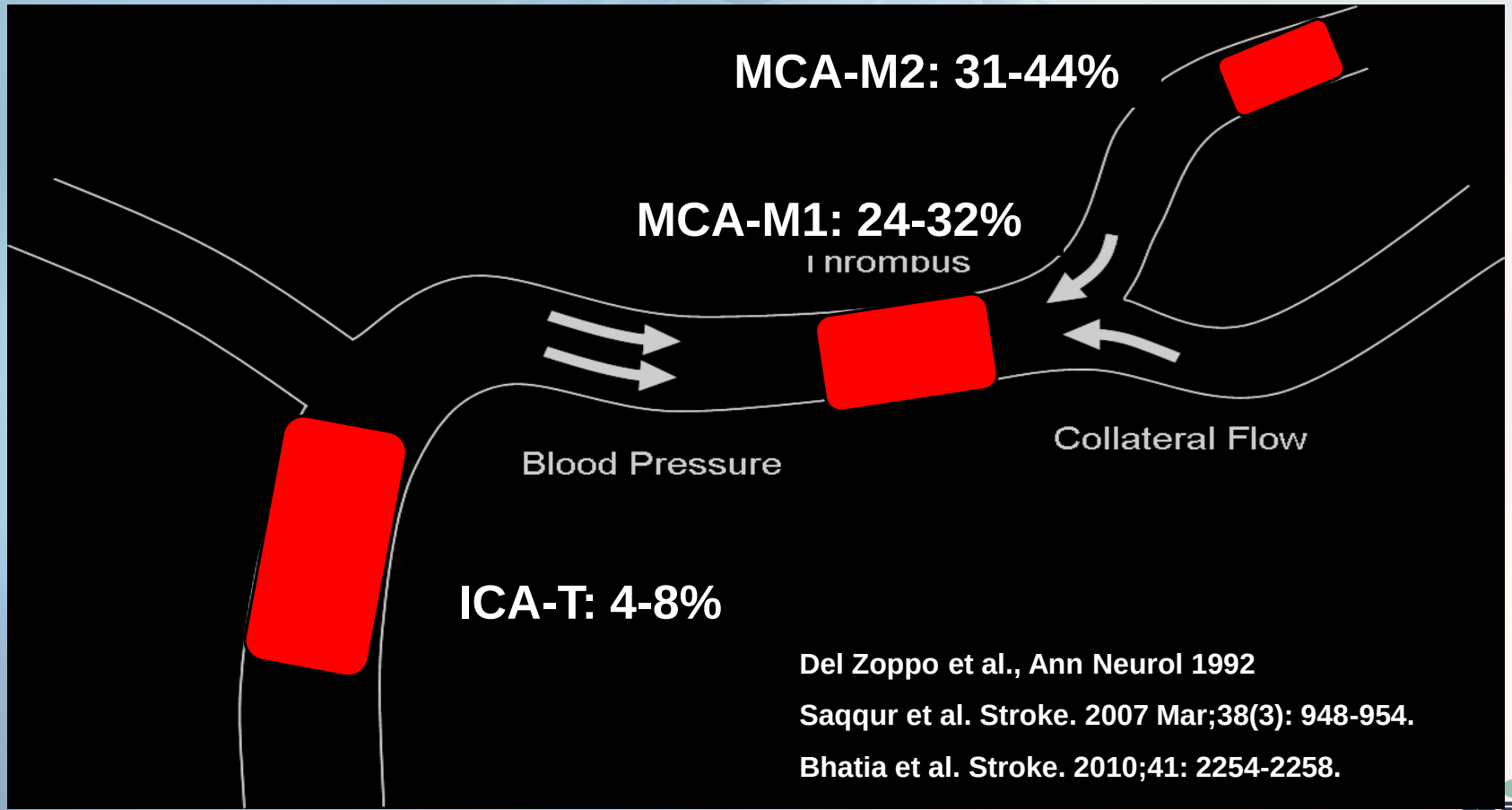
Reperfusion with IV rt-PA



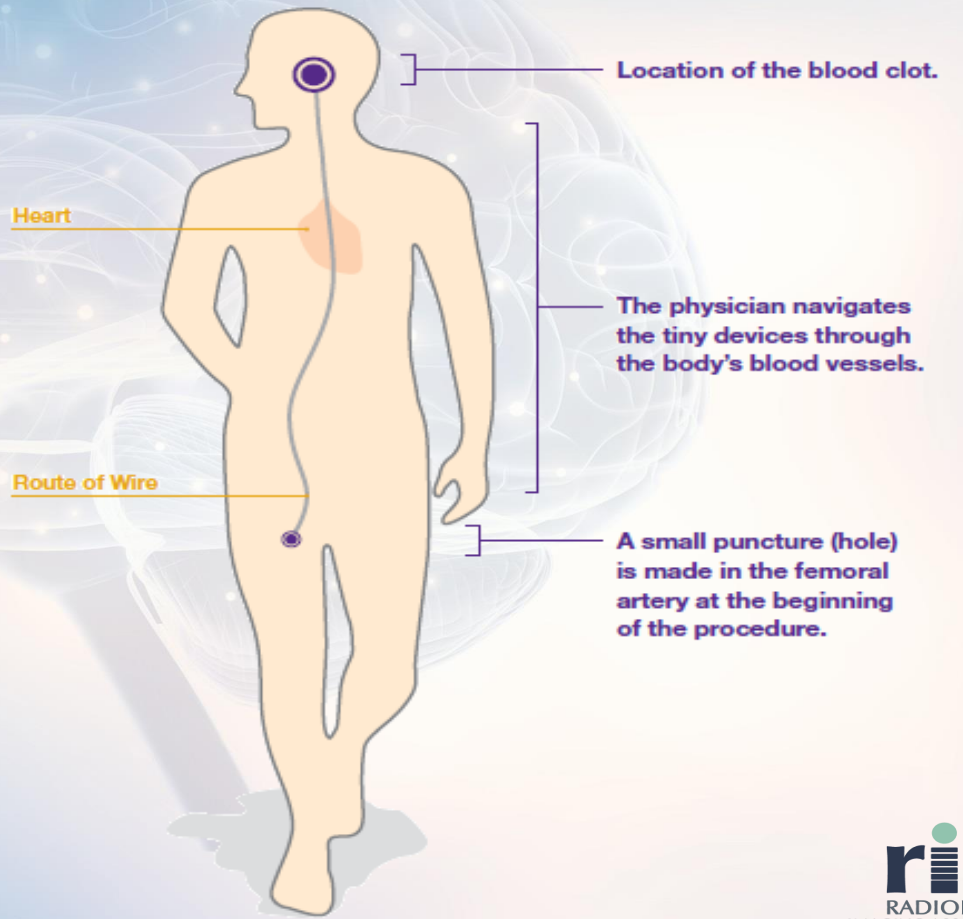
Del Zoppo et al., Ann Neurol 1992

Saqqur et al. Stroke. 2007 Mar;38(3): 948-954.

Bhatia et al. Stroke. 2010;41: 2254-2258.

Endovascular Clot Removal

Endovascular clot removal is a type of minimally invasive surgery that allows the physician to access various parts of the body, including the brain, through the body's major blood vessels.



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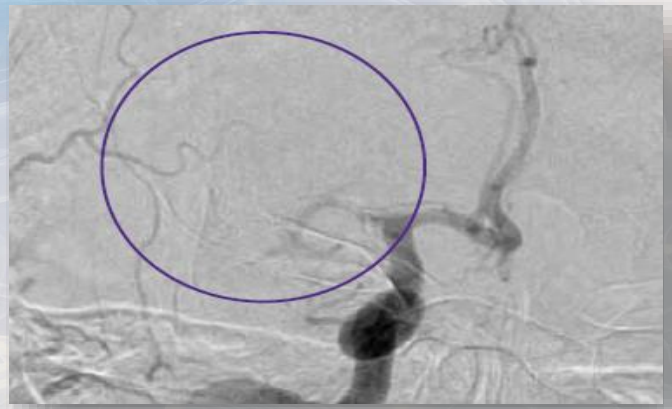
Goal of Ischemic Stroke Treatment

To open the blocked blood vessel, thereby restoring oxygen and nutrients to the affected territories in the brain



Before Intervention
The blood vessels in the circle are not visible because a blood clot is blocking blood flow to those vessels.

After Successful Intervention
Once the blood clot is removed, the blood vessels fill with blood and are visible again.

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Buying Time: Assessing collateral status

ORIGINAL RESEARCH

Journal of NEUROINTERVENTIONAL SURGERY

CT perfusion-guided patient selection for endovascular recanalization in acute ischemic stroke: a multicenter study

Aquilla S Turk,[1] Jordan Asher Magarick,[2] Don Frei,[3] Kyle Michael Fargen,[4] Imran Chaudry,[1] Christine A Holmstedt,[2] Joyce Nicholas,[2] J Mocco,[5] Raymond D Turner,[2] Daniel Huddle,[3] David Loy,[3] Richard Bellon,[3] Gwendolyn Dooley,[3] Robert Adams,[2] Michelle Whaley,[3] Chris Fanale,[3] Edward Jauch[2]

- Three medical centers retrospectively assessed stroke patients with a NIHSS of ≥8, regardless of time from symptom onset, who had CT perfusion maps that defined salvageable penumbra and underwent intra-arterial revascularization.
- Patients were divided into two groups for analysis: ≤8 h and >8 h from symptom onset to endovascular procedure.

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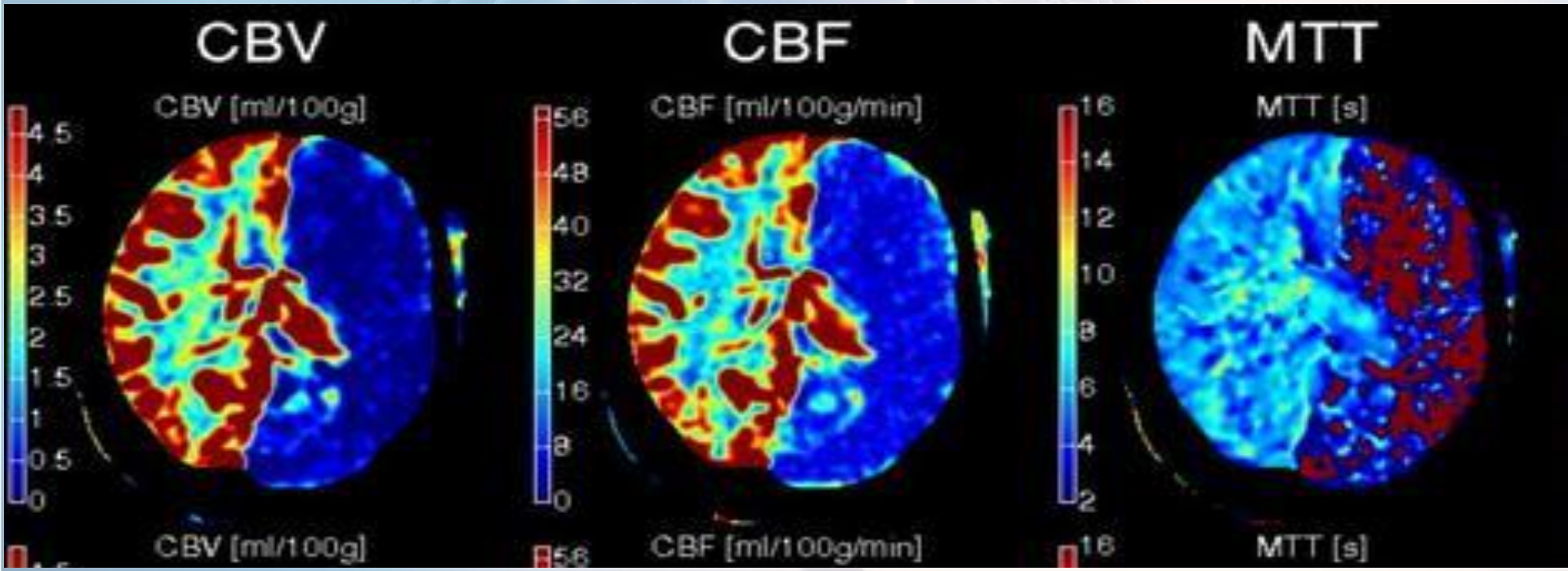
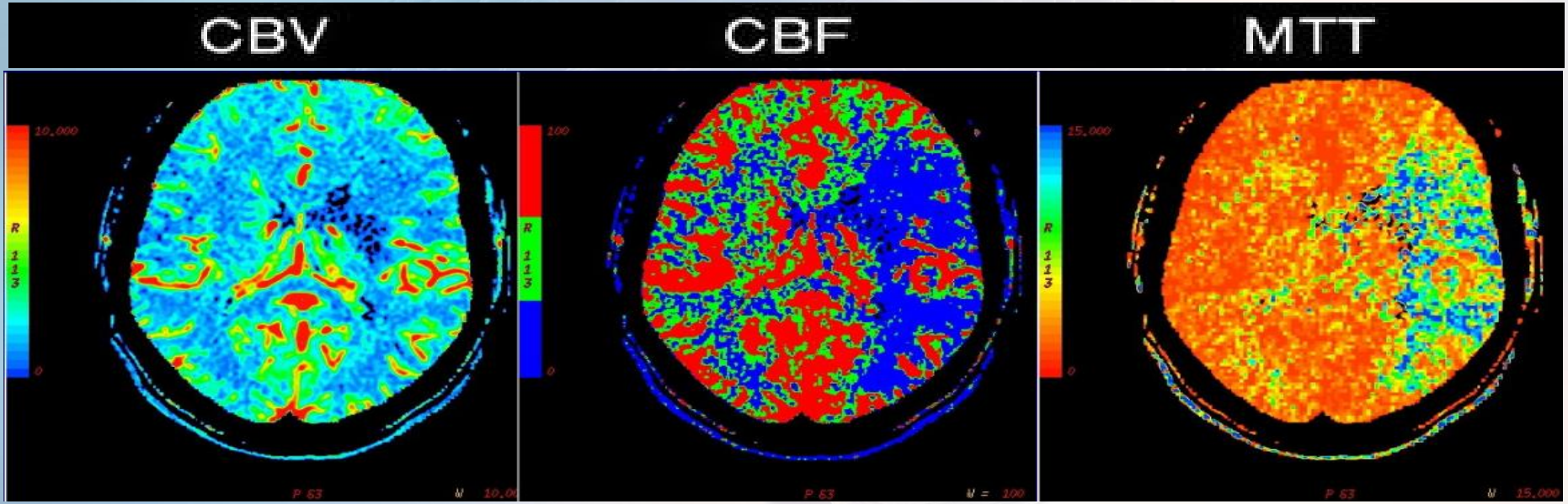
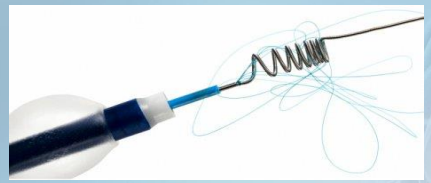
CT Perfusion: Completed Infarct

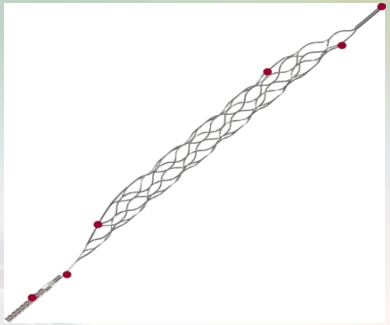


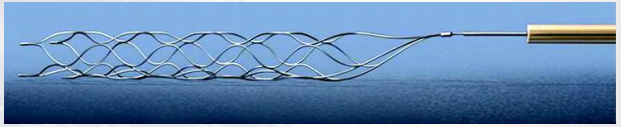
CT Perfusion: Salvageable Penumbra

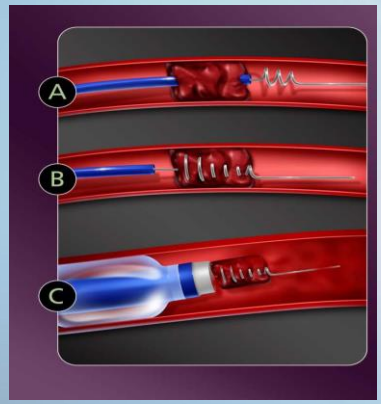


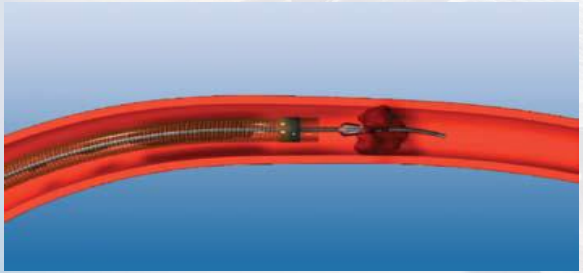
Thrombectomy Devices

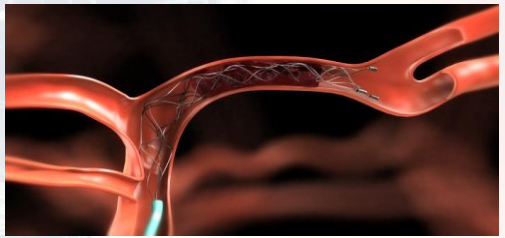


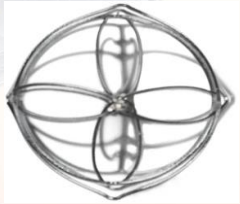


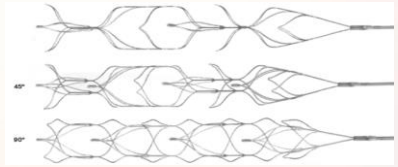












MERCI Retriever

Aspiration

Stentriever

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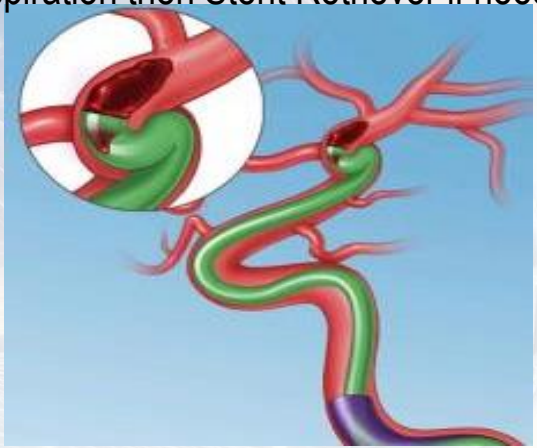
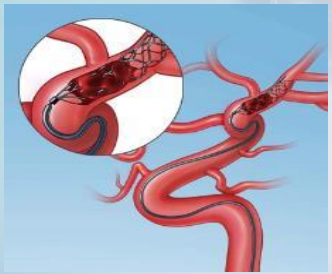
Rapid Evolution of Thrombectomy Approaches

Aspiration then Stent Retriever if needed



Aspiration & Stent Retriever

Stent Retriever



ACE™ 64

ACE™ and ADAPT

5MAX™ Solumbra

Solitaire, Trevo

Merci®

2007 2008 2009 2010 2011 2012 2013 2014 2015

Improvements Continue

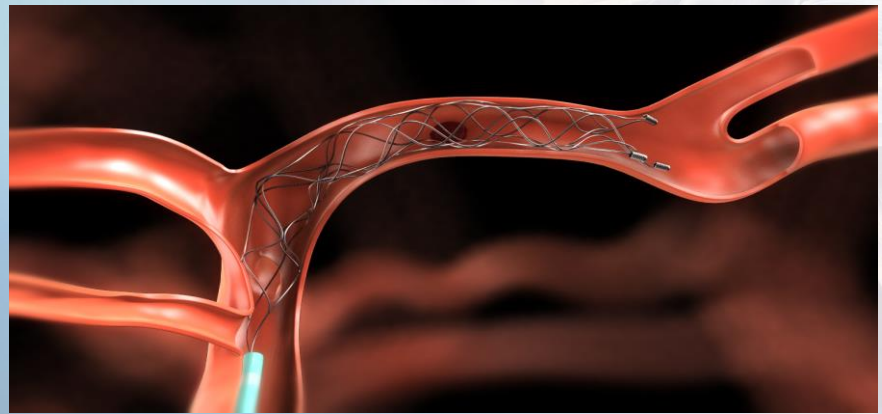
Original Penumbra System®

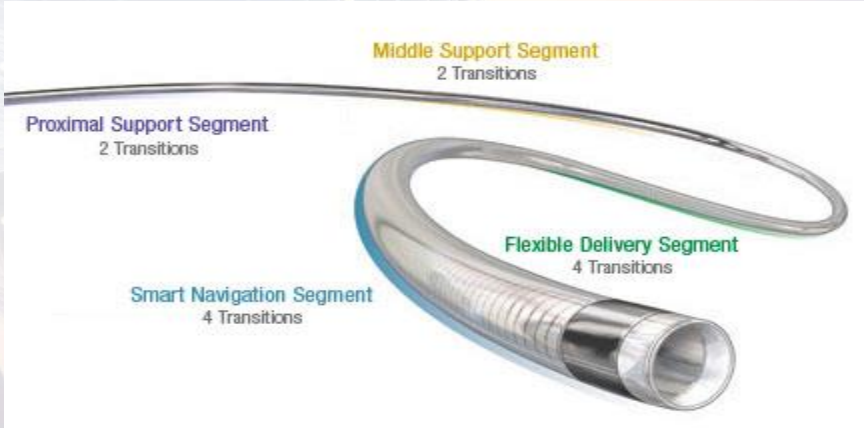
7 Trials Support Mechanical Thrombectomy

Improvements in Technology

Arrival of stentrievers and larger/more navigable aspiration catheters

- Easier to use
- More predictable outcomes
- Faster vessel recanalization



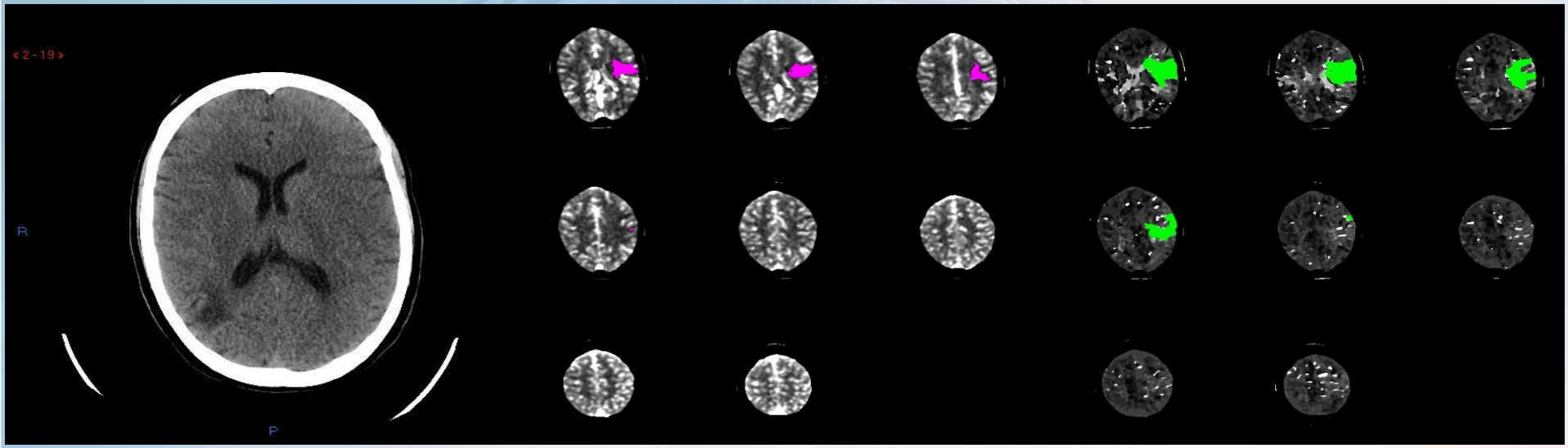


Images from; www.stryker.com, www.ev3.net, and www.penumbrainc.com

Stroke Case: Pre-Procedure

32 year old smoker, hypertension. Prior episodes of slurred speech but never sought medical attention. Witnessed onset of aphasia, Right hemiplegia and left gaze preference. Pre treatment NIHSS=20. IV tPA given

Stroke Case: Imaging



CT Scan RAPID analysis demonstrates a small area of infarct and a large area of hypoperfusion. There is also an old stroke on the contralateral (right) side.

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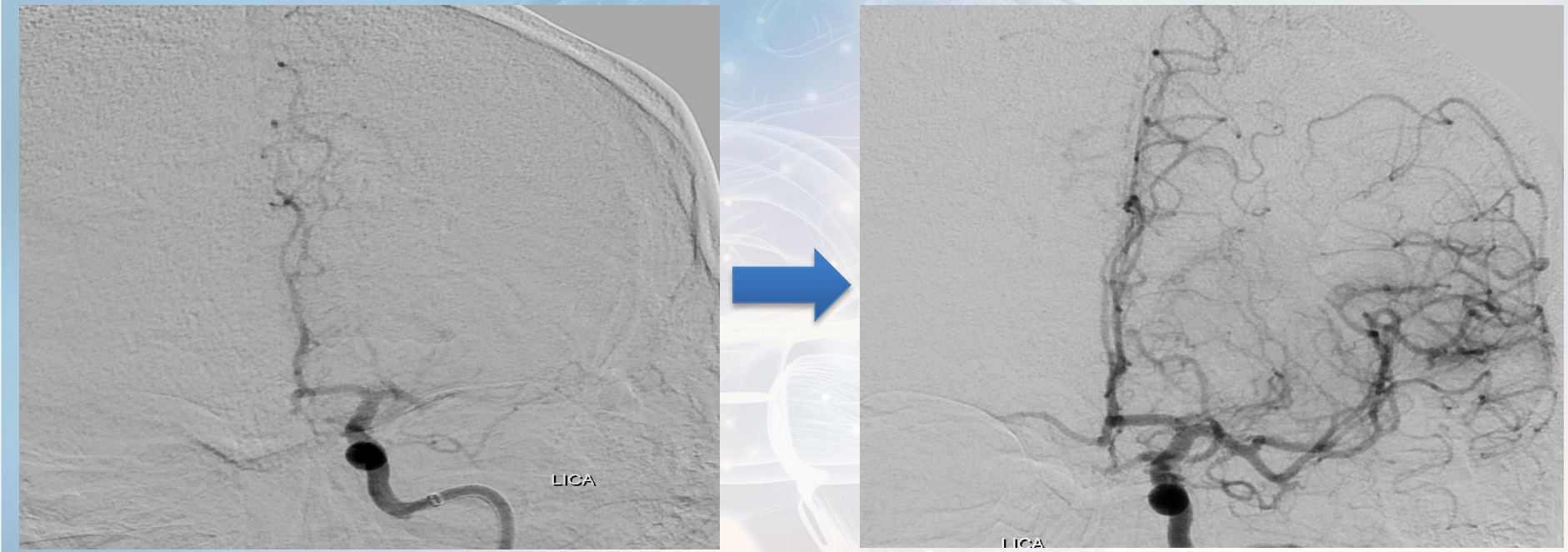
Stroke Case: Angiography

Initial angiography confirms large vessel occlusion (left M1 segment)

Stroke Case



ADAPT direct aspiration technique. Puncture to recanalization 14 minutes. Repeat angiography demonstrates complete recanalization

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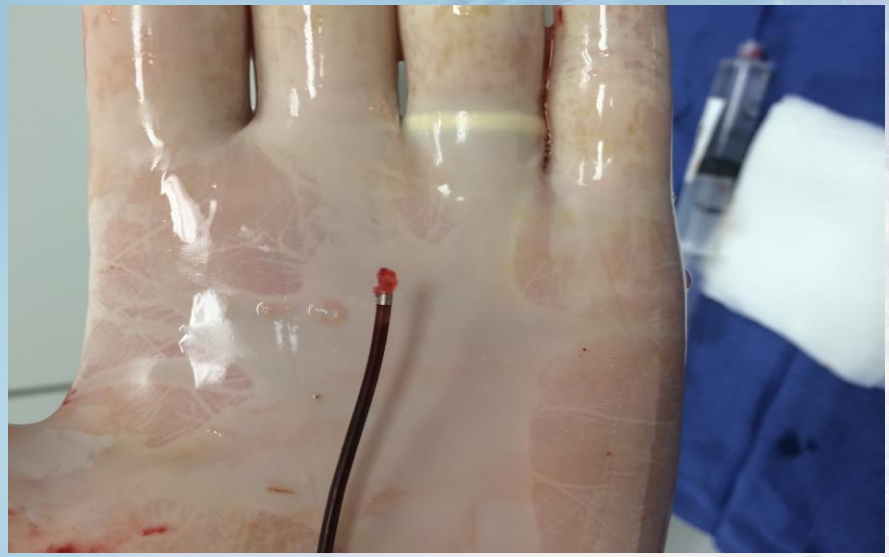
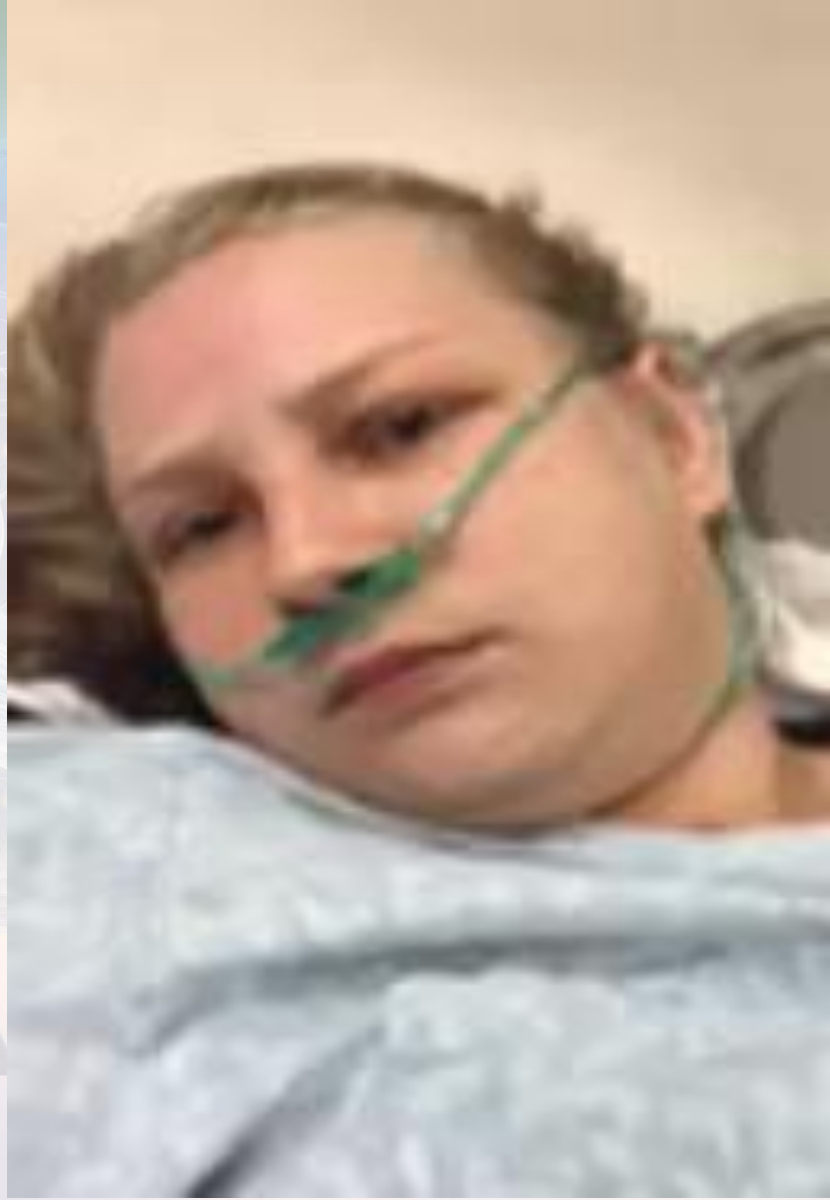
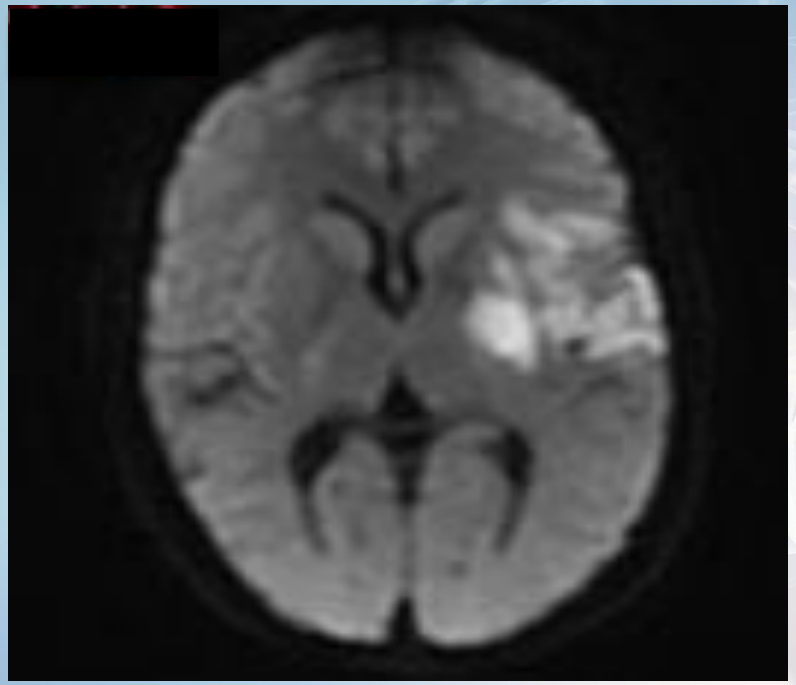
5 Min Post-Procedure



Puncture to recanalization: 14mins.
24 hour NIHSS=1



24h Post-Procedure



90 day follow up neurologically intact; mRS=0

The Evidence

- IV t-PA has been approved for treatment of acute ischemic stroke since 1996.
- It has to be administered within 3 hours of symptom onset
  - Up to 4.5 hours based upon recent European trials
- Evidence for endovascular treatment
  - 2015
  - 2018

New England Journal of Medicine 2015: Clear and Convincing Data

- Since January 1st of 2015, FIVE major prospective, randomized controlled trials have been published **comparing mechanical thrombectomy to best medical management**:
  - MR CLEAN
  - ESCAPE
  - EXTEND-IA
  - SWIFT PRIME
  - REVASCAT

A Multicenter Randomized CLinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands (MR CLEAN)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 1, 2015 VOL. 372 NO. 1

A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

O.A. Berkhemer, P.S.S. Fransen, D. Beumer, L.A. van den Berg, H.F. Lingsma, A.J. Yoo, W.J. Schonewille, J.A. Vos, P.J. Nederkoorn, M.J.H. Wermer, M.A.A. van Walderveen, J. Staals, J. Hofmeijer, J.A. van Oostayen, G.J. Lycklama à Nijeholt, J. Boiten, P.A. Brouwer, B.J. Emmer, S.F. de Bruijn, L.C. van Dijk, L.J. Kappelle, R.H. Lo, E.J. van Dijk, J. de Vries, P.L.M. de Kort, W.J.J. van Rooij, J.S.P. van den Berg, B.A.A.M. van Hasselt, L.A.M. Aerden, R.J. Dallinga, M.C. Visser, J.C.J. Bot, P.C. Vroomen, O. Eshghi, T.H.C.M.L. Schreuder, R.J.J. Heijboer, K. Keizer, A.V. Tielbeek, H.M. den Hertog, D.G. Gerrits, R.M. van den Berg-Vos, G.B. Karas, E.W. Steyerberg, H.Z. Flach, H.A. Marquering, M.E.S. Sprengers, S.F.M. Jenniskens, L.F.M. Beenen, R. van den Berg, P.J. Koudstaal, W.H. van Zwam, Y.B.W.E.M. Roos, A. van der Lugt, R.J. van Oostenbrugge, C.B.L.M. Majoie, and D.W.J. Dippel, for the MR CLEAN Investigators*

- Sites: 16 centers in Netherlands
- Patients: 500
  - 233 randomized to IA thrombectomy
  - 267 randomized to medical management
- Age 18+
- Included mild-severe stroke severity
- Time: Treatment initiated within 6 hrs

- Primary Outcome: mRS at 90 days
- Treatment in IA arm: No requirement, but retrievable stent in majority

Berkhemer et al; *NEJM*, 2015

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A Multicenter Randomized CLinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands (MR CLEAN)

Good Outcome (mRS 0-2):
33% in IA thrombectomy group
19% in medical group

Conclusion:
Significantly better outcomes with thrombectomy compared to medical management

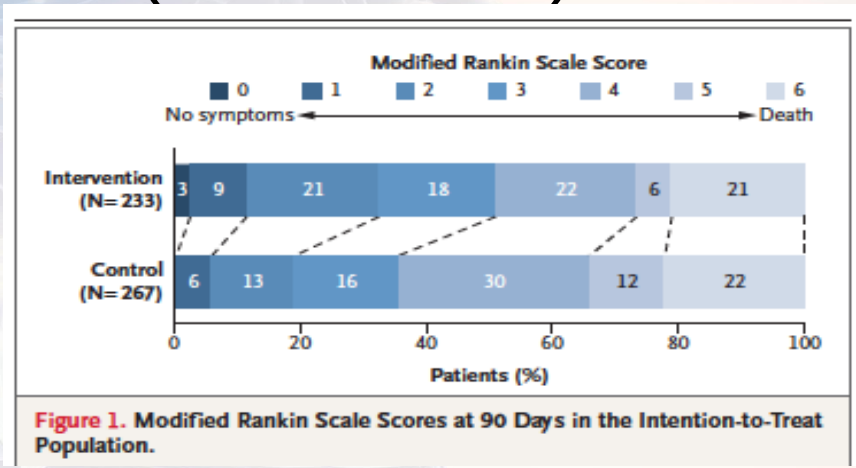

Figure 1. Modified Rankin Scale Scores at 90 Days in the Intention-to-Treat Population.

Table 2. Primary and Secondary Outcomes and Treatment Effects.*

Outcome	Intervention (N=233)	Control (N=267)	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)†
Primary outcome: modified Rankin scale score at 90 days — median (interquartile range)	3 (2 to 5)	4 (3 to 5)	Common odds ratio	1.66 (1.21 to 2.28)	1.67 (1.21 to 2.30)
Secondary outcomes					
Clinical outcomes					
Modified Rankin score of 0 or 1 at 90 days — no. (%)	27 (11.6)	16 (6.0)	Odds ratio	2.06 (1.08 to 3.92)	2.07 (1.07 to 4.02)
Modified Rankin score of 0–2 at 90 days — no. (%)	76 (32.6)	51 (19.1)	Odds ratio	2.05 (1.36 to 3.09)	2.16 (1.39 to 3.38)

Berkhemer et al*; NEJM*, 2015

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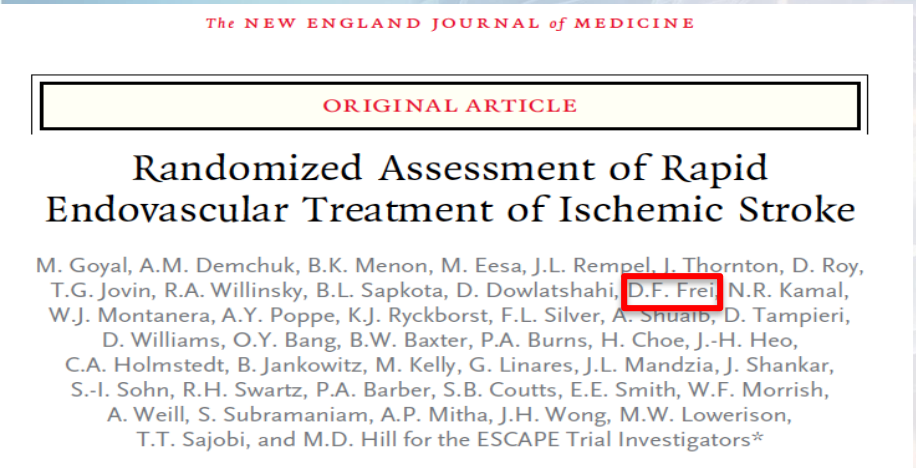
Endovascular Treatment for Small Core and Proximal Occlusion Ischemic StrokE (ESCAPE)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

M. Goyal, A.M. Demchuk, B.K. Menon, M. Eesa, J.L. Rempel, J. Thornton, D. Roy, T.G. Jovin, R.A. Willinsky, B.L. Sapkota, D. Dowlatshahi, D.F. Frei, N.R. Kamal, W.J. Montanera, A.Y. Poppe, K.J. Ryckborst, F.L. Silver, A. Shuaib, D. Tampieri, D. Williams, O.Y. Bang, B.W. Baxter, P.A. Burns, H. Choe, J.-H. Heo, C.A. Holmstedt, B. Jankowitz, M. Kelly, G. Linares, J.L. Mandzia, J. Shankar, S.-I. Sohn, R.H. Swartz, P.A. Barber, S.B. Coutts, E.E. Smith, W.F. Morrish, A. Weill, S. Subramaniam, A.P. Mitha, J.H. Wong, M.W. Lowerison, T.T. Sajobi, and M.D. Hill for the ESCAPE Trial Investigators*

- Sites: 22 centers mostly in N America
- Patients: 315 (halted early due to efficacy)
  - 165 randomized to IA thrombectomy
  - 150 randomized to medical
- Age 18+
- Included mild-severe strokes
- Time: Treatment within 12 hours of onset

- Primary Outcome: mRS at 90 days
- Treatment in IA arm: Retrievable stent

Goyal et al; *NEJM*, 2015

ria
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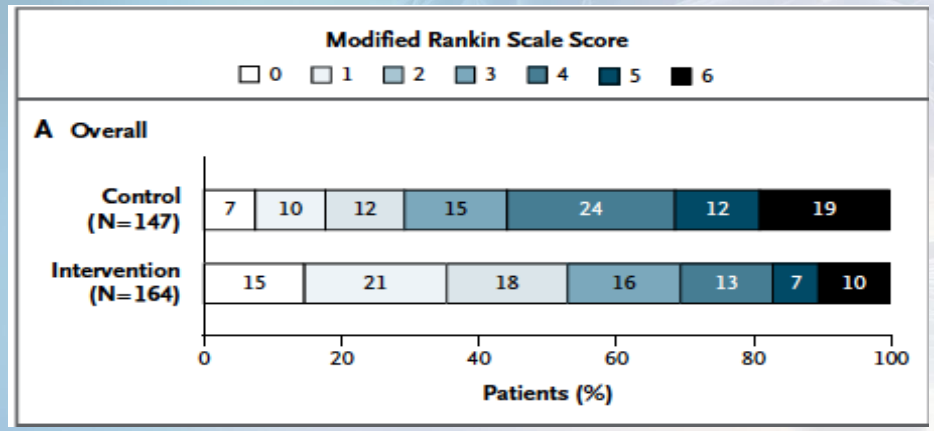
Endovascular Treatment for Small Core and Proximal Occlusion Ischemic StrokE (ESCAPE)



Good Outcome (mRS 0-2):
53% in IA thrombectomy group
29% in medical group

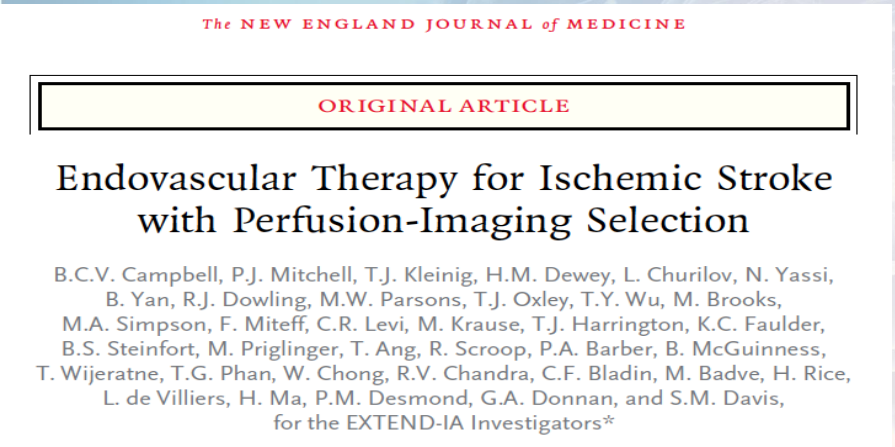
Conclusion:
Significantly better outcomes with thrombectomy compared to medical management

Table 2. Primary and Secondary Efficacy Outcomes.

Outcome	Intervention (N=165)	Control (N=150)	Difference (95% CI)*	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)†
Primary outcome: modified Rankin score at 90 days‡				Common odds ratio	2.6 (1.7–3.8)	3.1 (2.0–4.7)
Modified Rankin score of 0–2 at 90 days — no./total no. (%)§	87/164 (53.0)	43/147 (29.3)	23.8 (13.2–34.4)	Rate ratio	1.8 (1.4–2.4)	1.7 (1.3–2.2)

Goyal et al; *NEJM*, 2015

Extending the Time for Thrombolysis in Emergency Neurological Deficits – Intra-Arterial (EXTEND-IA)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

B.C.V. Campbell, P.J. Mitchell, T.J. Kleinig, H.M. Dewey, L. Churilov, N. Yassi, B. Yan, R.J. Dowling, M.W. Parsons, T.J. Oxley, T.Y. Wu, M. Brooks, M.A. Simpson, F. Miteff, C.R. Levi, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfort, M. Priglinger, T. Ang, R. Scroop, P.A. Barber, B. McGuinness, T. Wijeratne, T.G. Phan, W. Chong, R.V. Chandra, C.F. Bladin, M. Badve, H. Rice, L. de Villiers, H. Ma, P.M. Desmond, G.A. Donnan, and S.M. Davis, for the EXTEND-IA Investigators*

- Sites: 10 centers mostly in Australia and New Zealand
- Patients: 70 (halted early due to efficacy)
  - 35 randomized to IA thrombectomy
  - 35 randomized to medical
- Age 18+
- Included mild-severe strokes
- Time: Within 6 hours of onset

- Primary Outcomes:
  1. Reperfusion at 24 hours (% reduction in perfusion-lesion volume)
  2. Decrease in NIHSS of 8 or more points at 3 days, or NIHSS of 0 or 1 at 3 days
- Treatment in IA arm: retrievable stent

Campbell et al*; NEJM*, 2015

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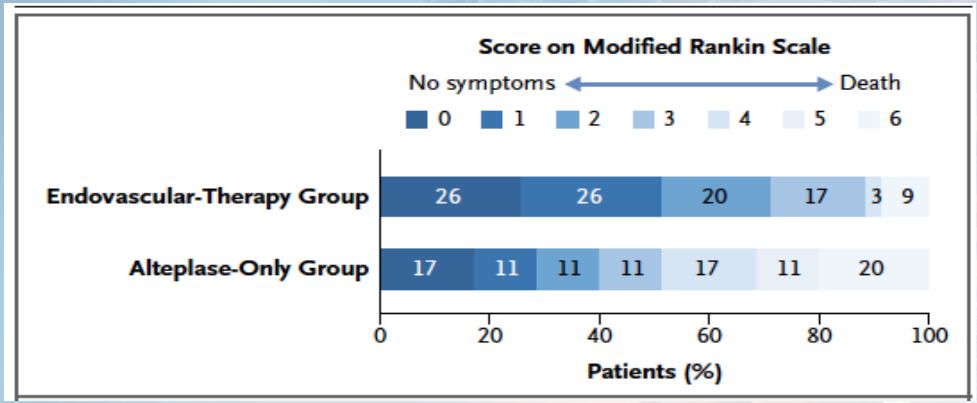
Extending the Time for Thrombolysis in Emergency Neurological Deficits – Intra-Arterial (EXTEND-IA)



Good Outcome (mRS 0-2):

71% in IA thrombectomy group

40% in medical group

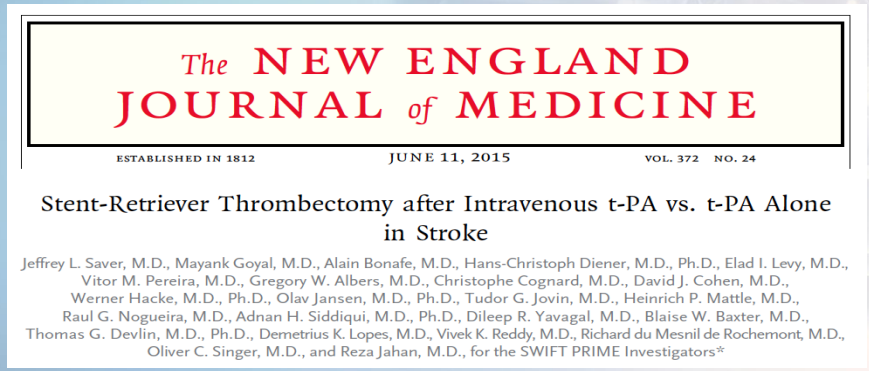
Conclusion:

Significantly better outcomes with thrombectomy compared to medical management

Outcome	Alteplase-Only Group (N=35)	Endovascular-Therapy Group (N=35)	Effect Size (95% CI)†			
			Adjusted	P Value	Unadjusted	P Value
Primary outcomes						
Median reperfusion at 24 hr (IQR) — (%)‡	37 (–0.5 to 96)	100 (100 to 100)	4.7 (2.5 to 9.0)	<0.001	4.9 (2.5 to 9.5)	<0.001
Early neurologic improvement — no. (%)§	13 (37)	28 (80)	6.0 (2.0 to 18.0)	0.002	6.8 (2.3 to 20)	<0.001
Secondary outcomes						
Score on the modified Rankin scale at 90 days¶						
Median score (IQR) on ordinal analysis	3 (1 to 5)	1 (0 to 3)	2.0	0.02	2.1 (1.2 to 3.8)	0.006
Independent outcome — no. (%)	14 (40)	25 (71)	4.2 (1.4 to 12)	0.01	3.8 (1.4 to 10.0)	0.009
Excellent outcome — no. (%)	10 (29)	18 (51)	2.4 (0.87 to 6.6)	0.09	2.6 (1.0 to 7.1)	0.05

Campbell et al; *NEJM*, 2015

Solitaire With the Intention For Thrombectomy as PRIMary Endovascular treatment (SWIFT PRIME)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 11, 2015 VOL. 372 NO. 24

Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke

Jeffrey L. Saver, M.D., Mayank Goyal, M.D., Alain Bonafe, M.D., Hans-Christoph Diener, M.D., Ph.D., Elad I. Levy, M.D., Vitor M. Pereira, M.D., Gregory W. Albers, M.D., Christophe Cognard, M.D., David J. Cohen, M.D., Werner Hacke, M.D., Ph.D., Olav Jansen, M.D., Ph.D., Tudor G. Jovin, M.D., Heinrich P. Mattle, M.D., Raul G. Nogueira, M.D., Adnan H. Siddiqui, M.D., Ph.D., Dileep R. Yavagal, M.D., Blaise W. Baxter, M.D., Thomas G. Devlin, M.D., Ph.D., Demetrius K. Lopes, M.D., Vivek K. Reddy, M.D., Richard du Mesnil de Rochemont, M.D., Oliver C. Singer, M.D., and Reza Jahan, M.D., for the SWIFT PRIME Investigators*

- Sites: 39 centers mostly in US and Europe
- Patients: 196 (halted early due to efficacy)
  - 98 randomized to IA thrombectomy
  - 98 randomized to medical
- Age 18-80
- Included moderate-severe strokes
- Time: Within 6 hours of onset and within 1.5 hours of imaging

- Primary Outcome: mRS at 90 days
- Treatment in IA arm: retrievable stent

Saver et al; *NEJM*, 2015

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Solitaire With the Intention For Thrombectomy as PRIMary Endovascular treatment (SWIFT PRIME)

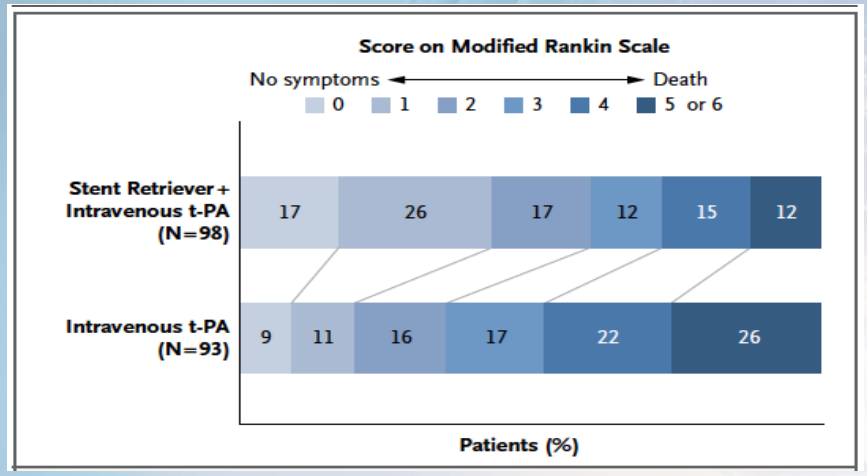

Table 2. Primary and Secondary Outcomes.*

Outcome	Intravenous t-PA Alone (N=98)	Stent Retriever plus Intravenous t-PA (N=98)	Risk Ratio (95% CI)	P Value
Primary outcome: score on modified Rankin scale at 90 days†				<0.001
No. of patients with data	93	98		
Median score	3	2		
Interquartile range	2–5	1–4		
Secondary outcomes				
Clinical efficacy outcome				
Functional independence at 90 days — no./total no. (%)‡	33/93 (35)	59/98 (60)	1.70 (1.23–2.33)	<0.001

Good Outcome (mRS 0-2):
60% in IA thrombectomy group
35% in medical group

Conclusion:
Significantly better outcomes with thrombectomy compared to medical management

Saver et al; *NEJM*, 2015

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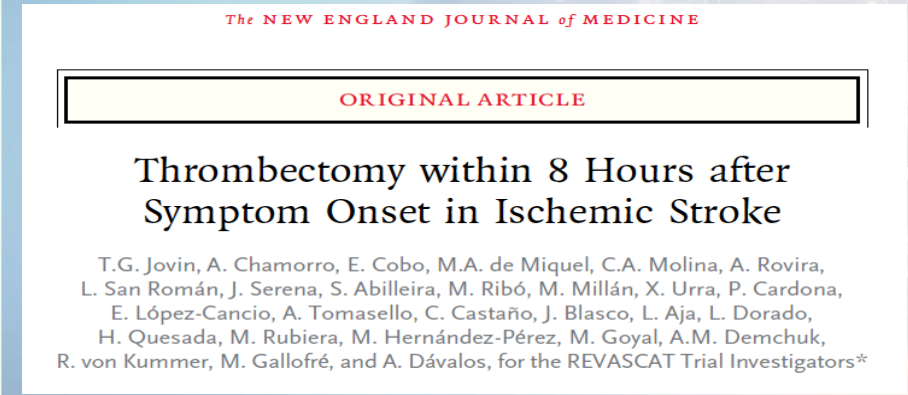
Endovascular Revascularization With Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 Hours (REVASCAT)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

T.G. Jovin, A. Chamorro, E. Cobo, M.A. de Miquel, C.A. Molina, A. Rovira, L. San Román, J. Serena, S. Abilleira, M. Ribó, M. Millán, X. Urra, P. Cardona, E. López-Cancio, A. Tomasello, C. Castaño, J. Blasco, L. Aja, L. Dorado, H. Quesada, M. Rubiera, M. Hernández-Pérez, M. Goyal, A.M. Demchuk, R. von Kummer, M. Gallofré, and A. Dávalos, for the REVASCAT Trial Investigators*

- Sites: 4 centers in Spain
- Patients: 206
  - 103 randomized to IA thrombectomy
  - 103 randomized to medical
- Age 18-85
- Included mild-severe strokes
- Time: Within 8 hours of onset

- Primary Outcome: mRS at 90 days
- Treatment in IA arm: retrievable stent

Jovin et al; *NEJM*, 2015

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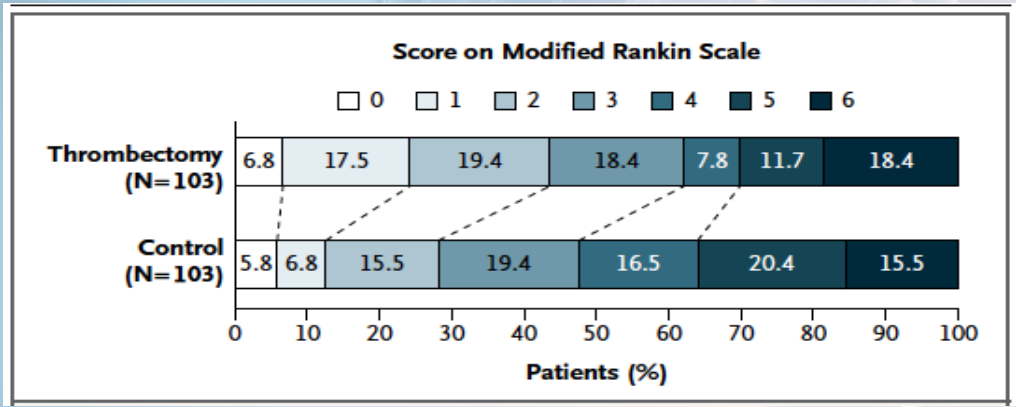
Endovascular Revascularization With Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 Hours (REVASCAT)



Good Outcome (mRS 0-2):
44% in IA thrombectomy group
28% in medical group

Conclusion:
Significantly better outcomes with thrombectomy compared to medical management

Table 2. Primary and Secondary Clinical and Imaging Outcomes.*

Outcome	Thrombectomy (N=103)	Control (N=103)	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)
Primary outcome: score on modified Rankin scale at 90 days	NA	NA	Common odds ratio	1.7 (1.04 to 2.7)	1.7 (1.05 to 2.8)
Secondary outcome					
Score of 0 to 2 on modified Rankin scale at 90 days — no. (%)†	45 (43.7)	29 (28.2)	Odds ratio	2.0 (1.1 to 3.5)	2.1 (1.1 to 4.0)

Jovin et al; *NEJM*, 2015

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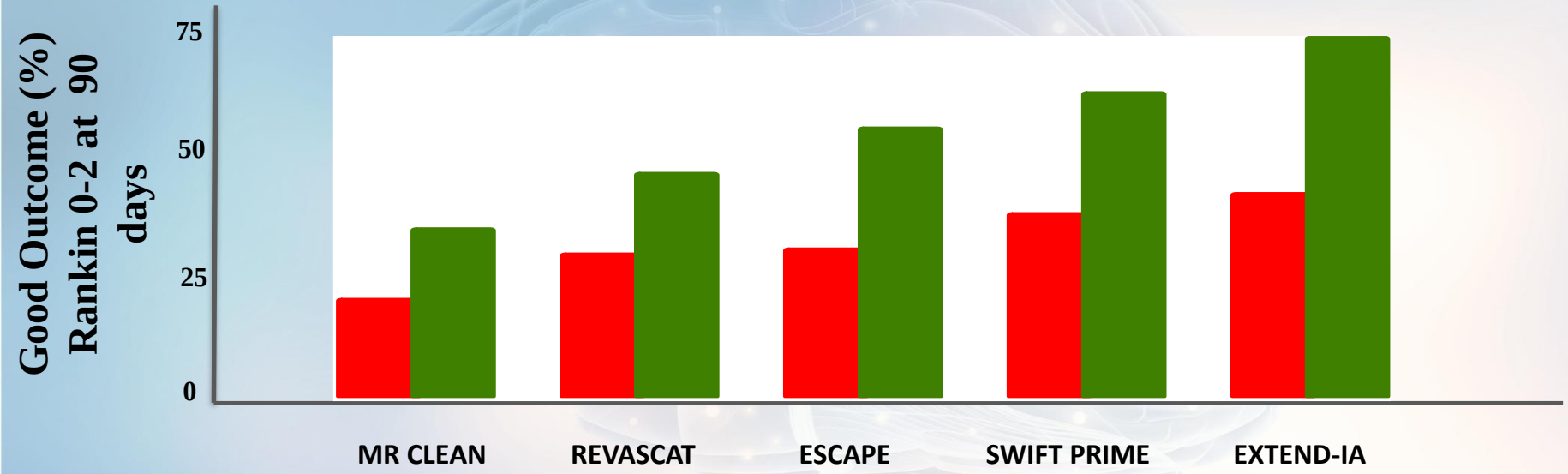
Endovascular Stroke Trials



	MR CLEAN	REVASCAT	ESCAPE	SWIFT PRIME	EXTEND-IA
	P<0.5	P<0.05	P<0.001	P<0.001	P<0.01
MT	33%	44%	53%	60%	71%
Control	19%	28%	29%	36%	40%

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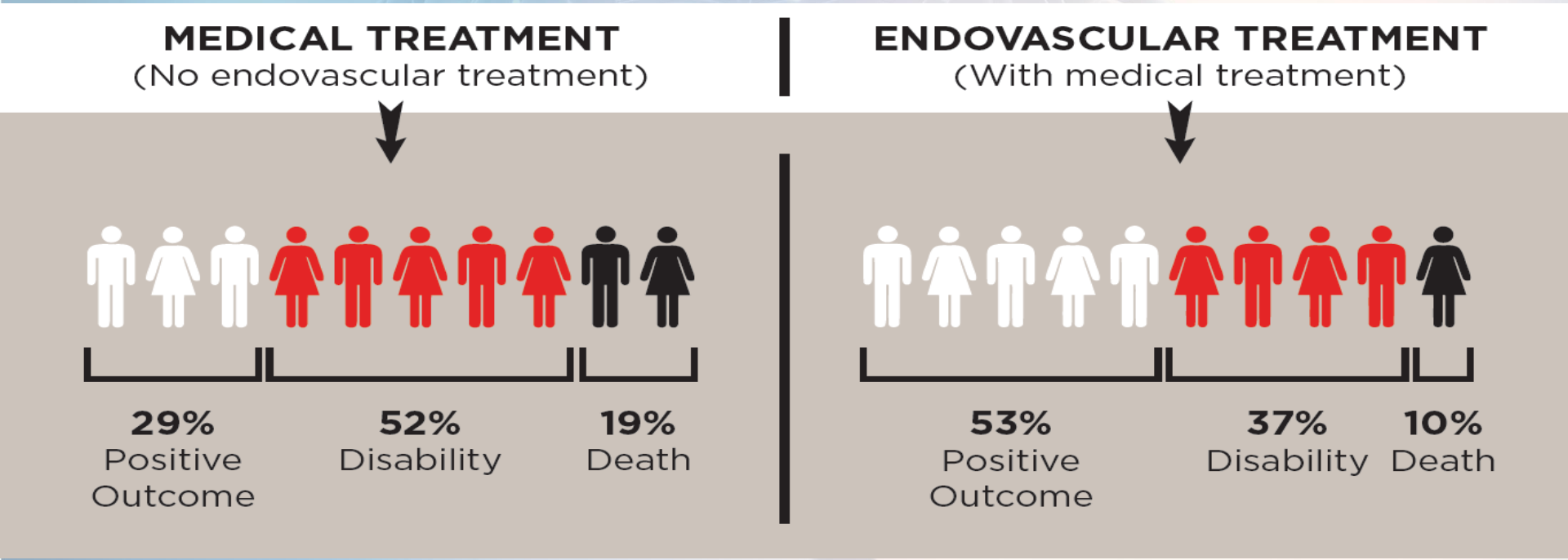
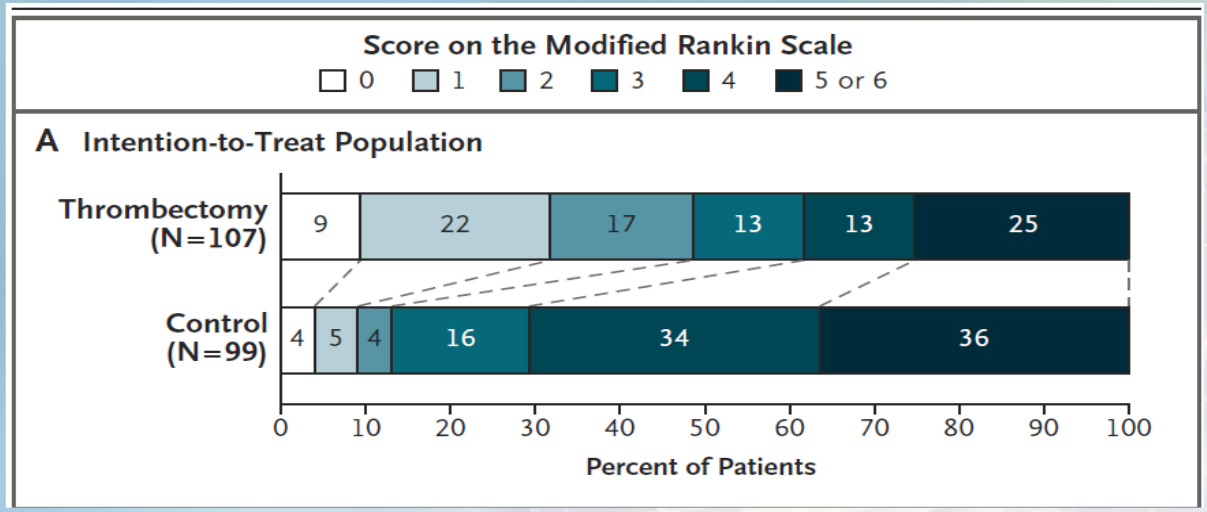
ESCAPE Outcomes



THINK ABOUT IT

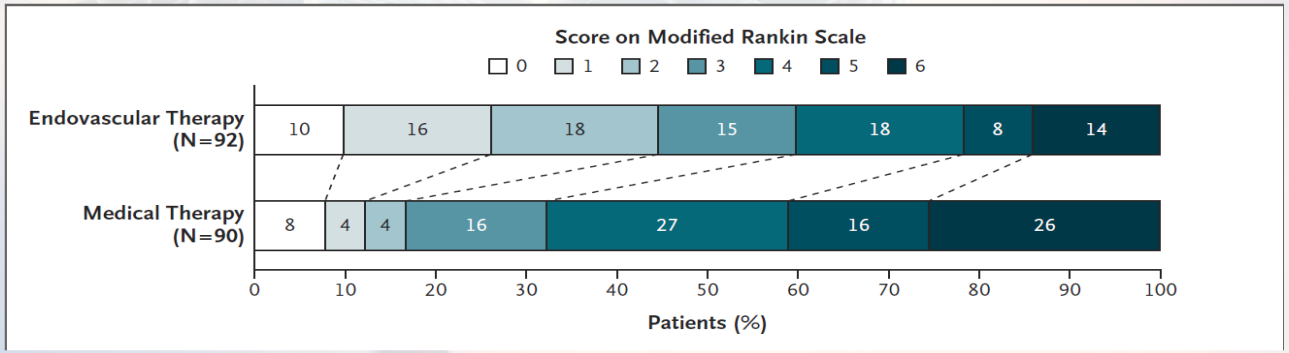
In order to have one additional stroke patient be independent at 90 days

Primary PCI vs. Thrombolysis for STEMI: Prevention of MI/Stroke/Death



DAWN

DEFUSE 3



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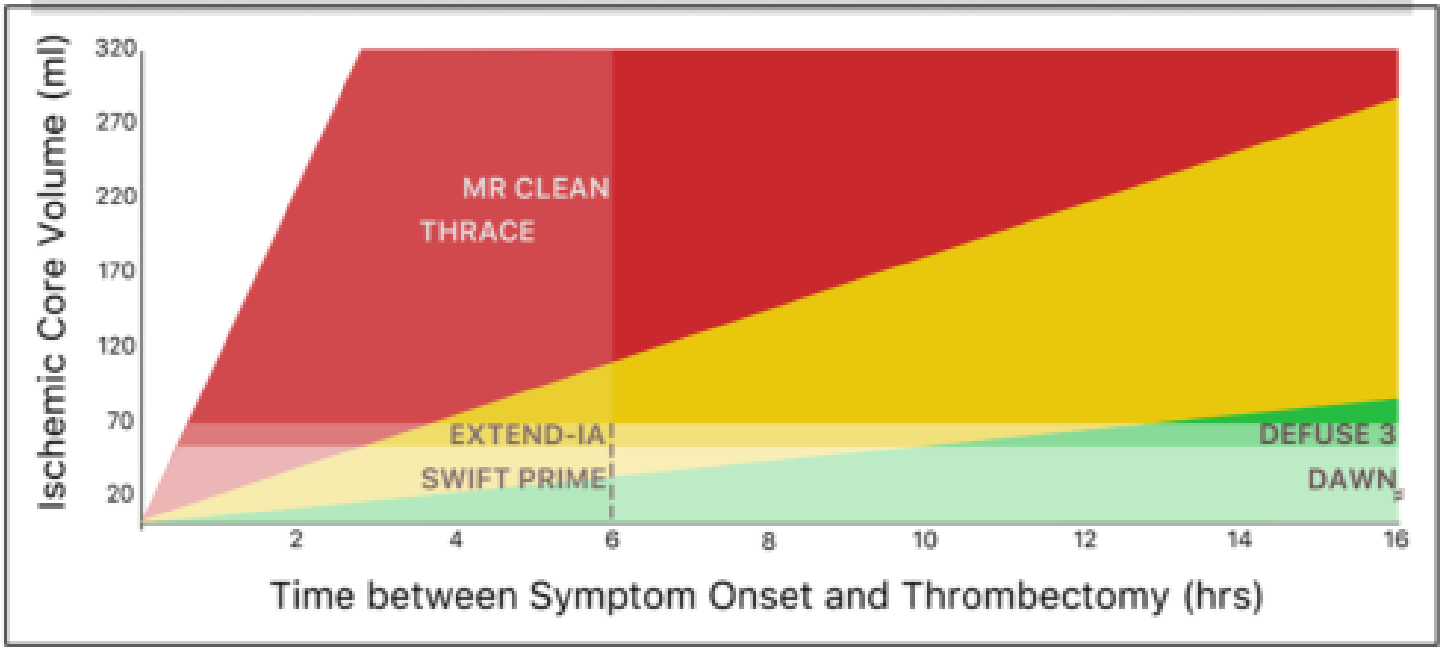
Conclusions from DAWN and DEFUSE 3

Selection should be based on imaging, not time



AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

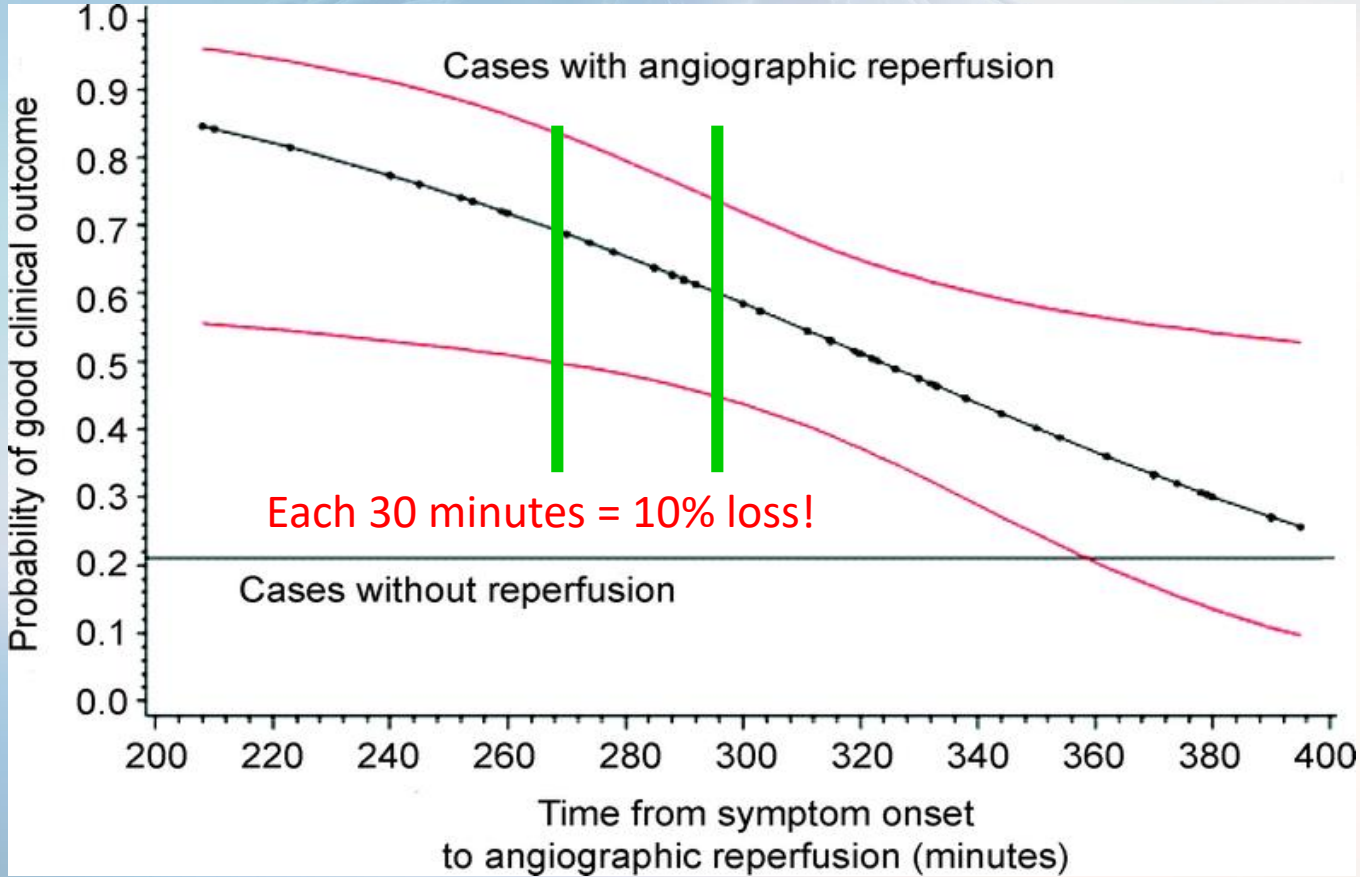
Endorsed by the Society for Academic Emergency Medicine

William J. Powers, MD, FAHA, Chair; Alejandro A. Rabinstein, MD, FAHA, Vice Chair; Teri Ackerson, BSN, RN; Opeolu M. Adeoye, MD, MS, FAHA; Nicholas C. Bambakidis, MD, FAHA; Kyra Becker, MD, FAHA; José Biller, MD, FAHA; Michael Brown, MD, MSc; Bart M. Demaerschalk, MD, MSc, FAHA; Brian Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; Thabele M. Leslie-Mazwi, MD; Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA; Phillip A. Scott, MD, MBA, FAHA; Kevin N. Sheth, MD, FAHA; Andrew M. Southerland, MD, MSc; Deborah V. Summers, MSN, RN, FAHA; David L. Tirschwell, MD, MSc, FAHA; on behalf of the American Heart Association Stroke Council

3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A	New recommendation.
8. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R	New recommendation.
The DAWN trial used clinical imaging mismatch (a combination of NIHSS score and imaging findings on CTP or DW-MRI) as eligibility criteria to select patients with large anterior circulation vessel occlusion for treatment with mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in function outcome at 90 days in the treatment group (mRS score 0–2, 49% versus 13%; adjusted difference, 33%; 95% CI, 21–44; posterior probability of superiority >0.999).[108] In DAWN, there were few strokes with witnessed onset (12%).The DEFUSE 3 trial used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last seen well for mechanical thrombectomy. This trial showed a benefit in functional outcome at 90 days in the treated group (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67; 95% CI, 1.60–4.48; $P<0.0001$).[109] Benefit was independently demonstrated for the subgroup of patients who met DAWN eligibility criteria and for the subgroup who did not. DAWN and DEFUSE 3 are the only RCTs showing benefit of mechanical thrombectomy >6 hours from onset. Therefore, only the eligibility criteria from these trials should be used for patient selection. Although future RCTs may demonstrate that additional eligibility criteria can be used to select patients who benefit from mechanical thrombectomy, at this time, the DAWN and DEFUSE-3 eligibility should be strictly adhered to in clinical practice.			See Table XXIII in online Data Supplement 1.

9. The technical goal of the thrombectomy procedure should be reperfusion to a modified Thrombolysis in Cerebral Infarction (mTICI) 2b/3 angiographic result to maximize the probability of a good functional clinical outcome.	**I**	**A**	Recommendation reworded for clarity from 2015 Endovascular. See Table LXXXIII in online Data Supplement 1 for original wording.
Mechanical thrombectomy aims to achieve reperfusion, not simply recanalization. A variety of reperfusion scores exist, but the mTICI score is the current assessment tool of choice, with proven value in predicting clinical outcomes.[176,177] All recent endovascular trials used the mTICI 2b/3 threshold for adequate reperfusion, with high rates achieved. In HERMES, 402 of 570 patients (71%) were successfully reperfused to mTICI 2b/3.[172] Earlier trials with less efficient devices showed lower recanalization rates, 1 factor in their inability to demonstrate benefit from the procedure (IMS III, 41%; MR RESCUE, 25%). The additional benefit of pursuing mTICI of 3 rather than 2b deserves further investigation.			
10. As with IV alteplase, reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcomes. To ensure benefit, reperfusion to TICI grade 2b/3 should be achieved as early as possible within the therapeutic window.	**I**	**B-R**	Recommendation revised from 2015 Endovascular.

Timing is Critical



Khatri et al; *Neurology* 2009

Time is Brain Analysis with EVT

JAMA | Original Investigation

Time to Treatment With Endovascular Thrombectomy and Outcomes From Ischemic Stroke: A Meta-analysis

Jeffrey L. Saver, MD; Mayank Goyal, MD; Aad van der Lugt, MD; Bijoy K. Menon, MD; Charles B. L. M. Majoie, MD; Diederik W. Dippel, MD; Bruce C. Campbell, MD, PhD; Raul G. Nogueira, MD; Andrew M. Demchuk, MD; Alejandro Tomasello, MD; Pere Cardona, MD; Thomas G. Devlin, MD; Donald F. Frei, MD; Richard du Mesnil de Rochemont, MD; Olvert A. Berkhemer, MD; Tudor G. Jovin, MD; Adnan H. Siddiqui, MD, PhD; Wim H. van Zwam, MD; Stephen M. Davis, MD; Carlos Castaño, MD; Biggya L. Sapkota, MD; Puck S. Fransen, MD; Carlos Molina, MD; Robert J. van Oostenbrugge, MD; Ángel Chamorro, MD; Hester Lingsma, PhD; Frank L. Silver, MD; Geoffrey A. Donnan, MD; Ashfaq Shuaib, MD; Scott Brown, PhD; Bruce Stouch, PhD; Peter J. Mitchell, MD; Antoni Davalos, MD; Yvo B. W. E. M. Roos, MD; Michael D. Hill, MD, MS; for the HERMES Collaborators

JAMA. 2016;316(12):1279-1288. doi:10.1001/jama.2016.13647

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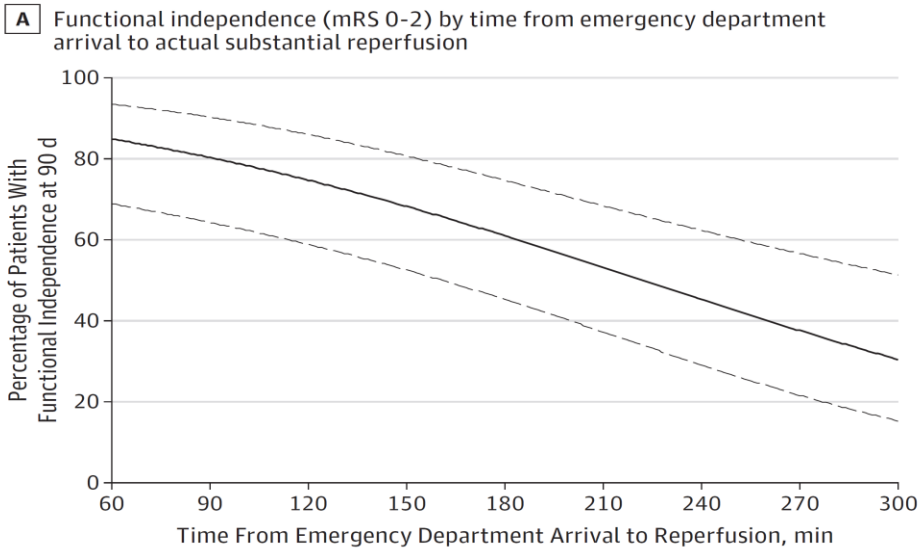
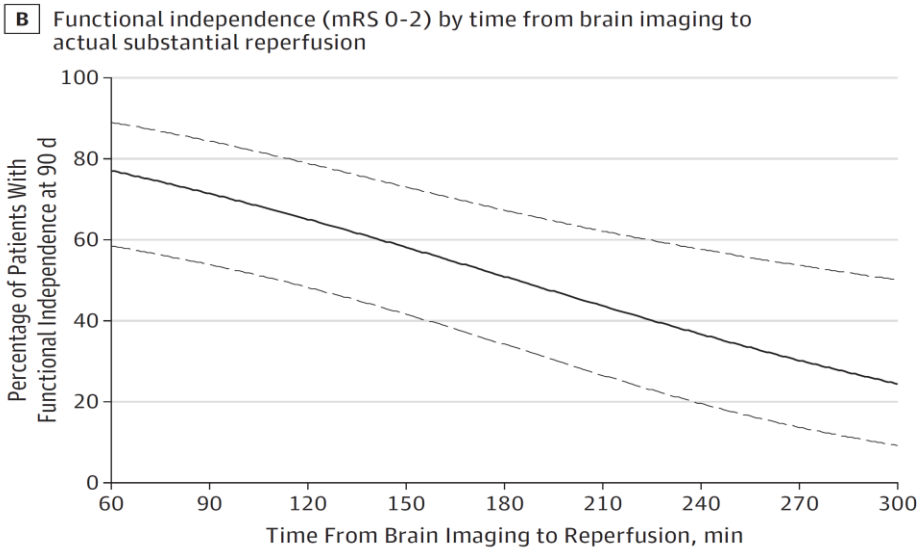
Process Efficiencies Matter after arrival at Endovascular Hospital

Figure 3. Relation Between In-Hospital Treatment Speeds and Functional Independence (mRS 0-2) at 3 Months Among Direct Arrival Patients in the Endovascular Thrombectomy Group Achieving Substantial Reperfusion (mTICI score, 2b or 3)





JAMA. 2016;316(12):1279-1288. doi:10.1001/jama.2016.13647

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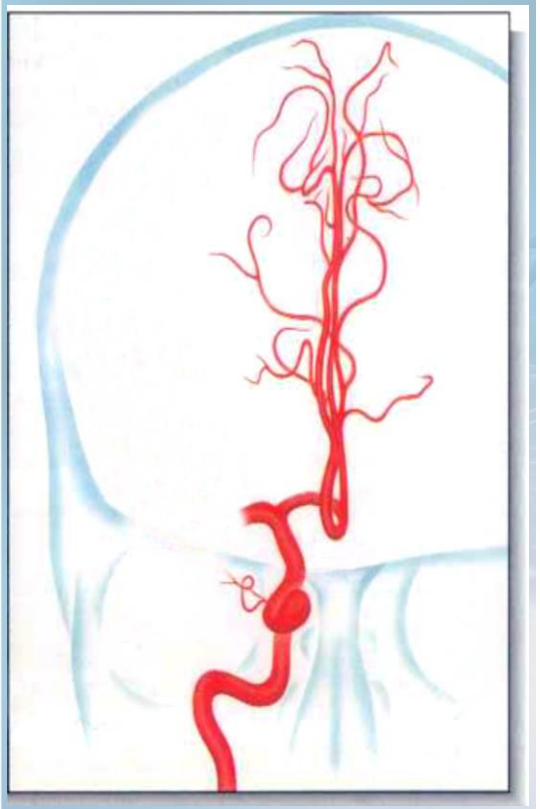

< 60 minutes

- Neurological evaluation
- Imaging evaluation
- Thrombectomy

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Boulder Community Hospital

CLARA BARTON Hospital

The Medical Center of Aurora

ROSE Medical Center

Presbyterian/St. Luke's Medical Center

Good Samaritan Medical Center

Banner Health North Colorado Medical Center

Cheyenne Regional Medical Center

Lutheran Medical Center

Banner Health McKee Medical Center

PIONEERS Medical Center

Sky Ridge Medical Center

North Suburban Medical Center

Longmont United Hospital

Rice County District Hospital

Valley View Hospital

Mt. San Rafael Hospital

GUNNISON VALLEY HEALTH

Vail Valley Medical Center

Banner Health Sterling Regional MedCenter

SOUTHEAST COLORADO HOSPITAL DISTRICT
The Hub Of Quality Care in Southeast Colorado

Prowers Medical Center

Hamilton County Hospital

Gove County Medical Center

anner Health East Morgan County Hospital

ASPEN VALLEY HOSPITAL

Holyoke Medical Center

Yuma District Hospital And Clinic

Banner Health Community Hospital

NEOSHO MEMORIAL REGIONAL MEDICAL CENTER

MONTROSE MEMORIAL HOSPITAL

ROOKS COUNTY RCH HEALTH CENTER

PAGOSA SPRINGS Medical Center
Better health and wellness where you live

WESLEY Medical Center

GALICHIA Heart Hospital

SWEDISH STROKE TEAM

Swedish Medical Center

STROKE CARE

Swedish Medical Center Neurovascular Team

- 14 + hospitalist neurologists
  - Evaluate patients from 60 telemedicine hospitals in the western USA
  - Neurologist meets ALL stroke patients upon arrival
  - In suspected LVO patients, the INR team meets the patient upon arrival in CT - 24/7/365
- 4 neuro-interventional surgeons
- 6 stroke nurse practitioners

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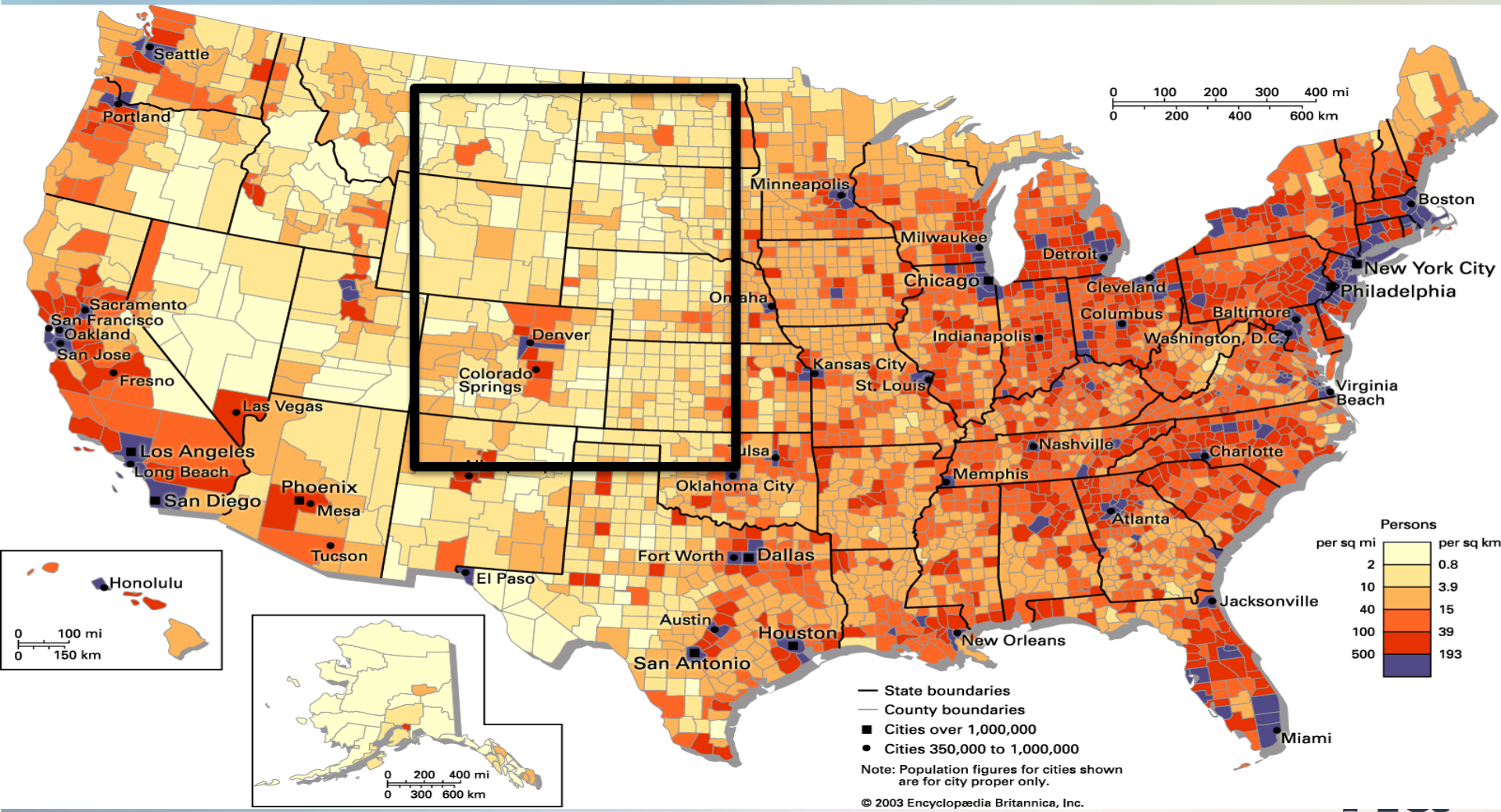
COMPREHENSIVE STROKE CENTERS

SOURCE: American Heart Association

Swedish Medical Center Spoke and Hub Treatment Area – 10 million population



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Air Ambulance 2010 Program of the Year!

HealthONE AIRLIFE DENVER

It's About The Experience!

Named #1 in the Country by the national Association of Air Medical Services (AAMS)

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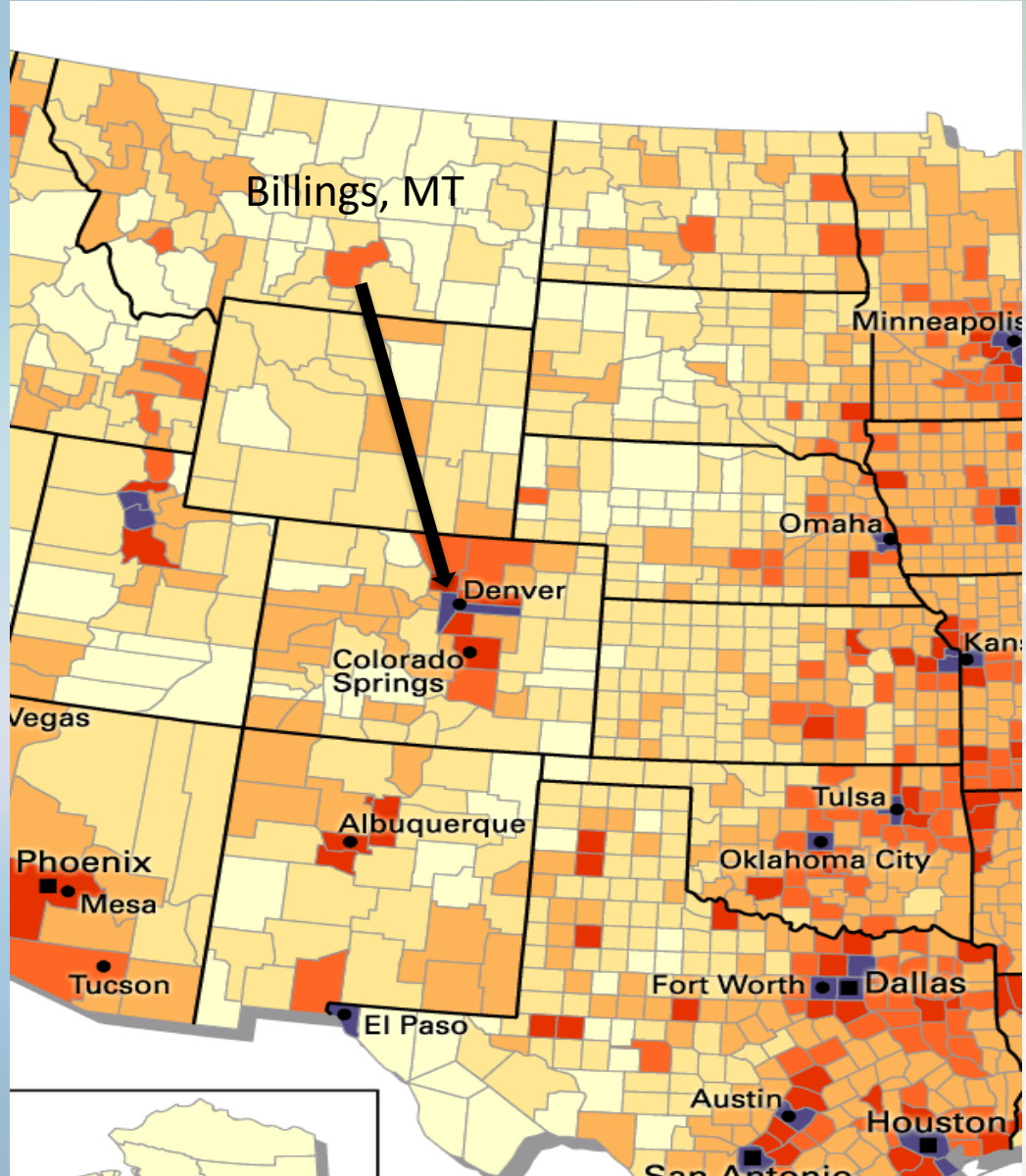
Sunday November 20, 2016

- 29 y.o. male transferred from Billings, Montana
- Marfans syndrome, intubated before transfer



2 hour fixed wing flight
600 miles

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Sunday November 20, 2016

- 29 y.o. male transferred from Billings, Montana
- Marfans syndrome, intubated before transfer
- Door - 3:50 pm
- CT - 4:00 pm

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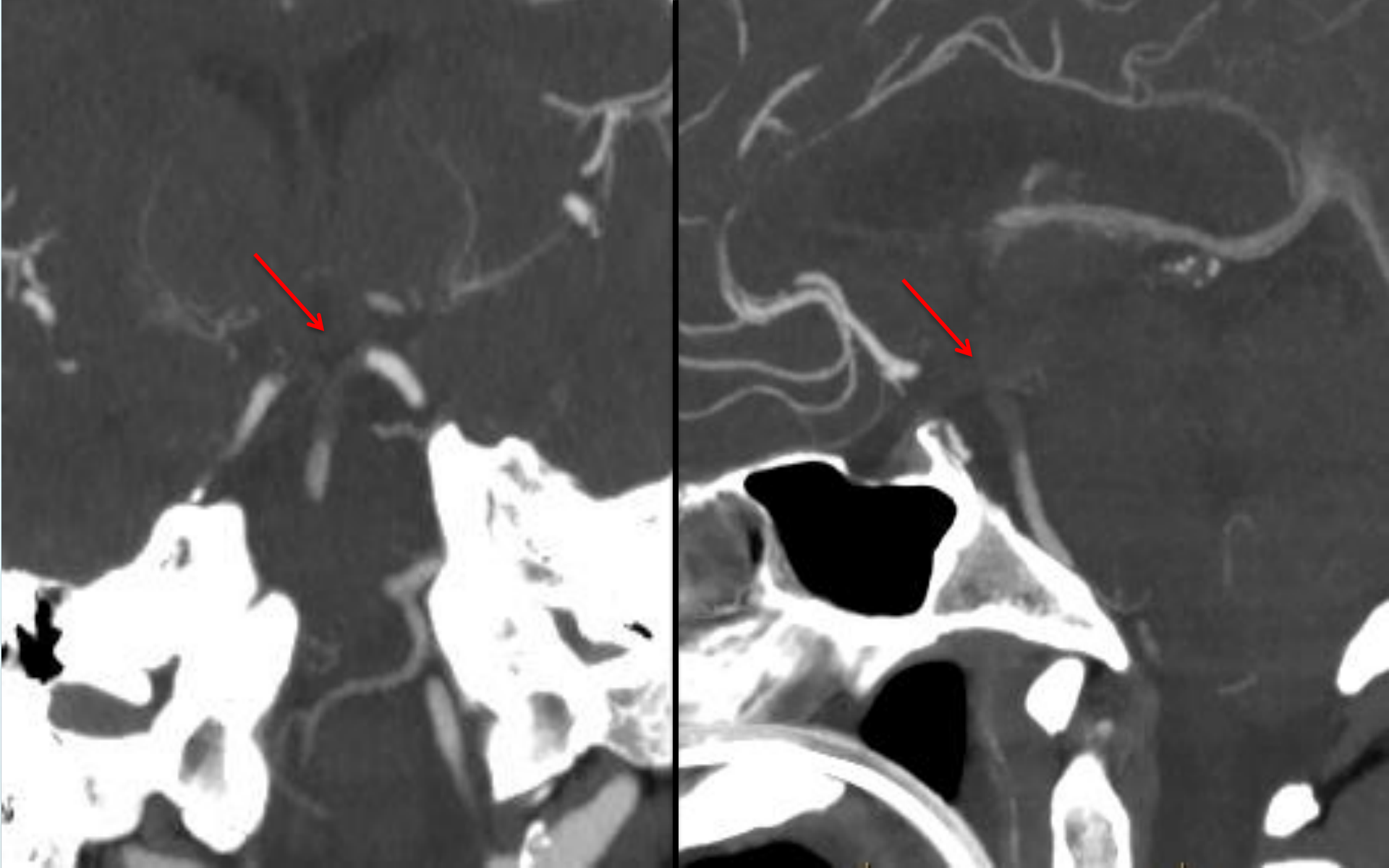

Sunday November 20, 2016

- 29 y.o. male transferred from Billings, Montana
- Marfans syndrome, intubated before transfer
- Door – 3:50 pm
- CT - 4:00 pm
- Access - 4:23 pm

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4:23 pm
Compressio

TICI 3 recanalization – 1 pass ACE 68

Sunday November 20, 2016

- 29 y.o. male transferred from Billings, Montana
- Marfans syndrome, intubated before transfer
- Door – 3:50 pm
- CT - 4:00 pm
- Access - 4:23 pm
- Recan. - 4:36 pm

Door – recanalization

46 minutes

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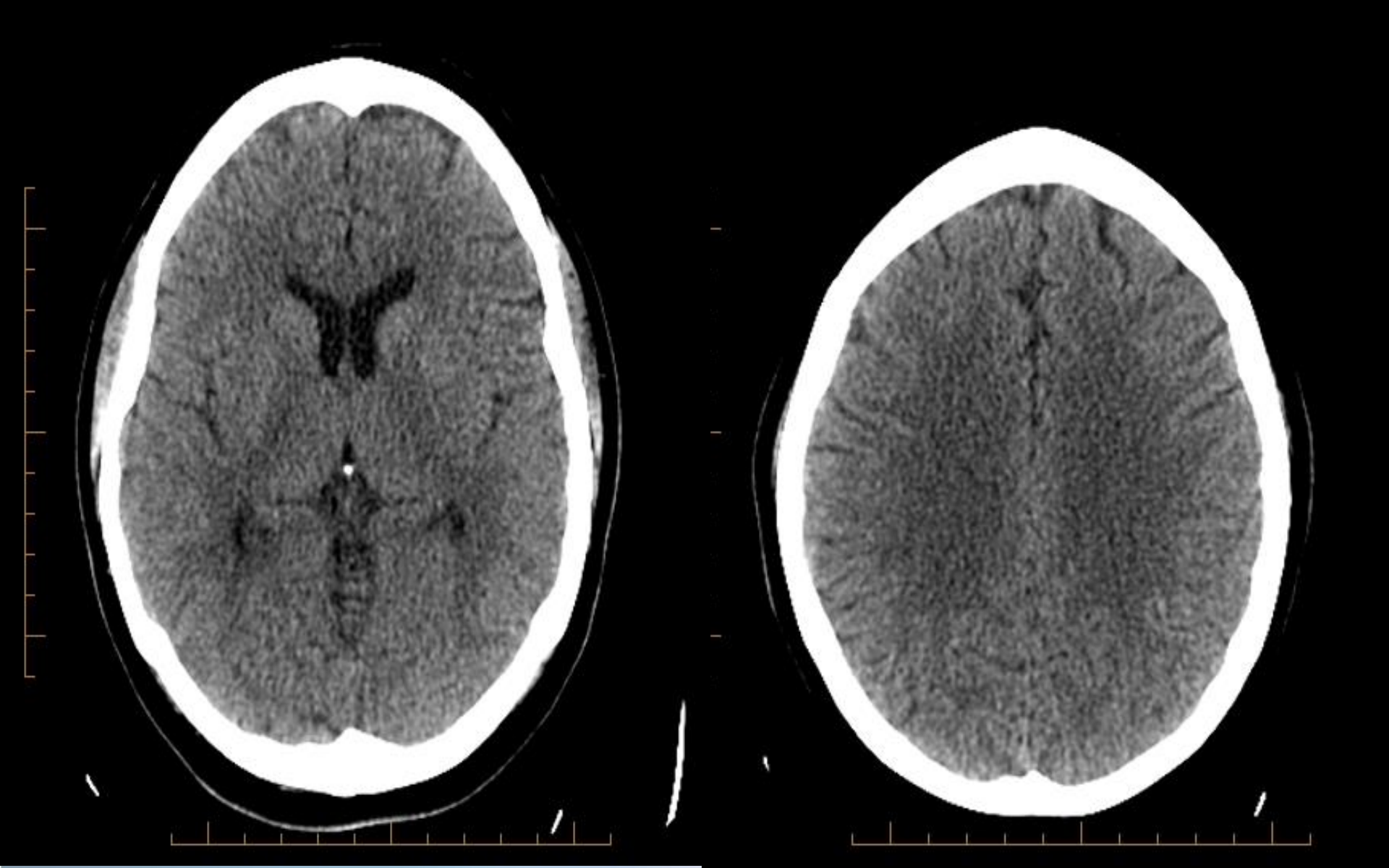
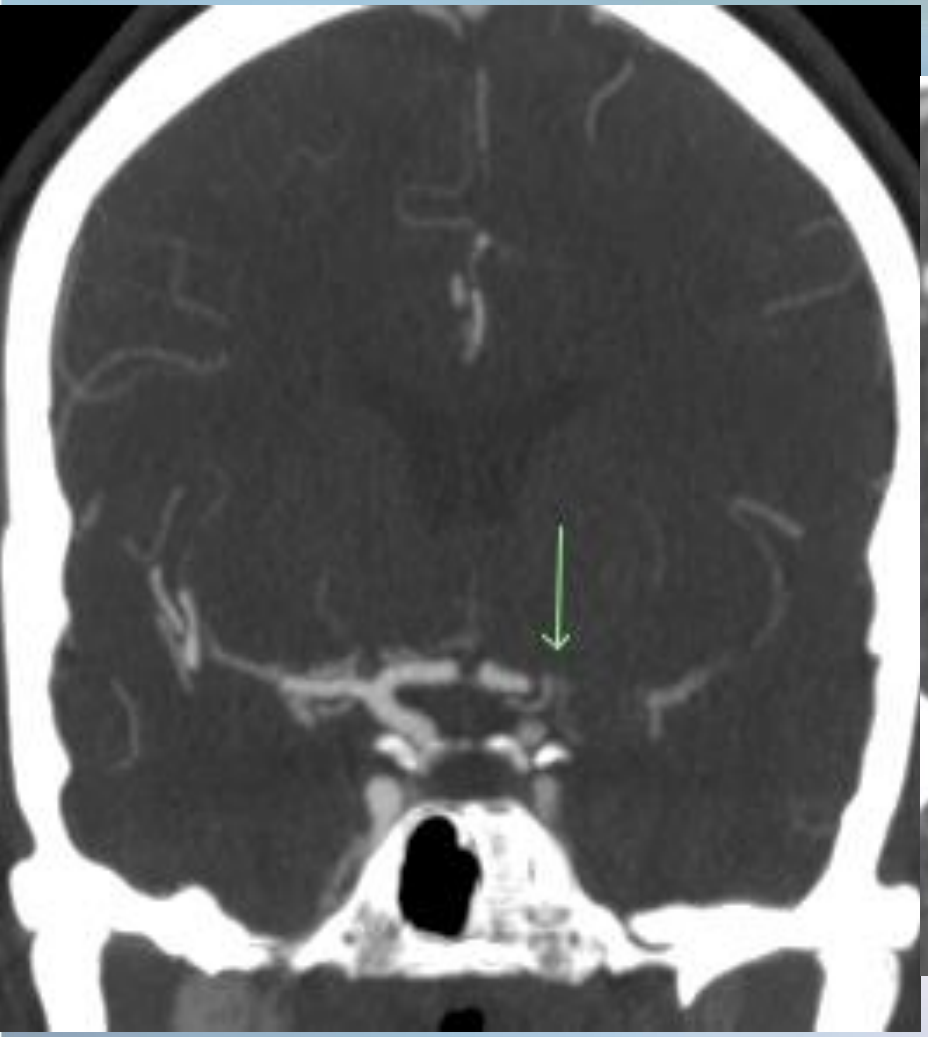
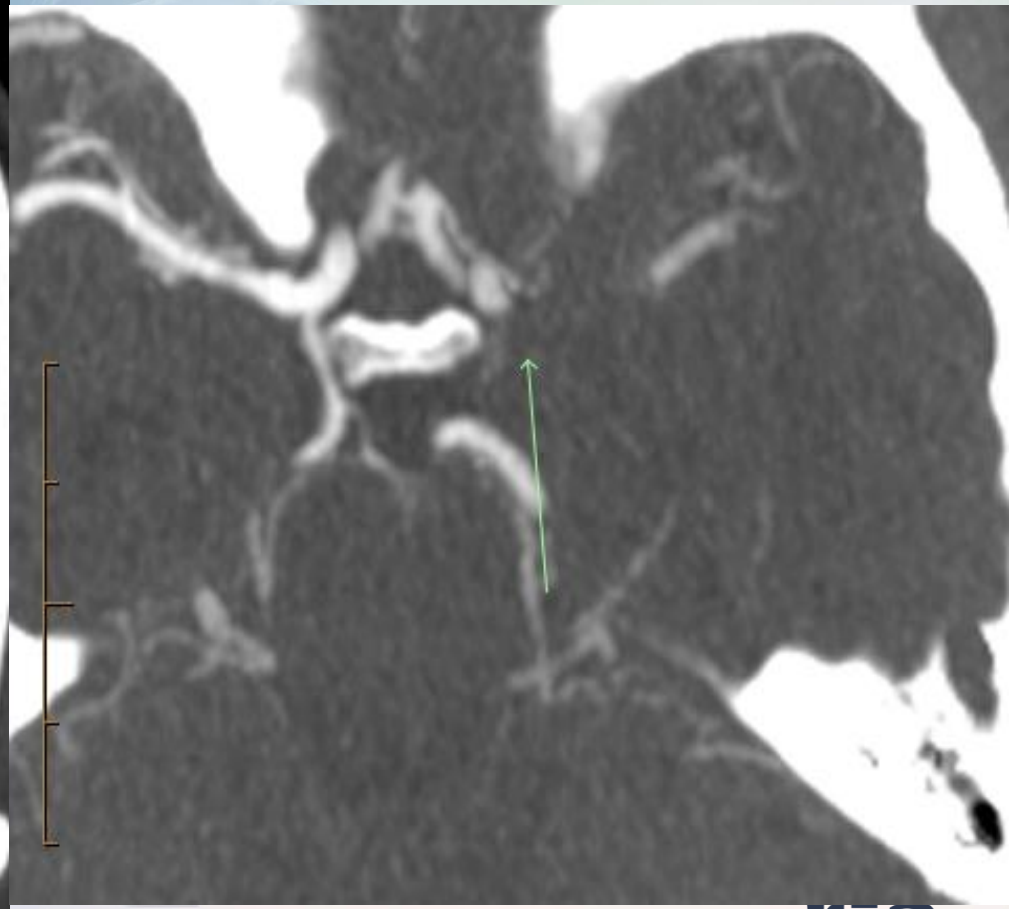
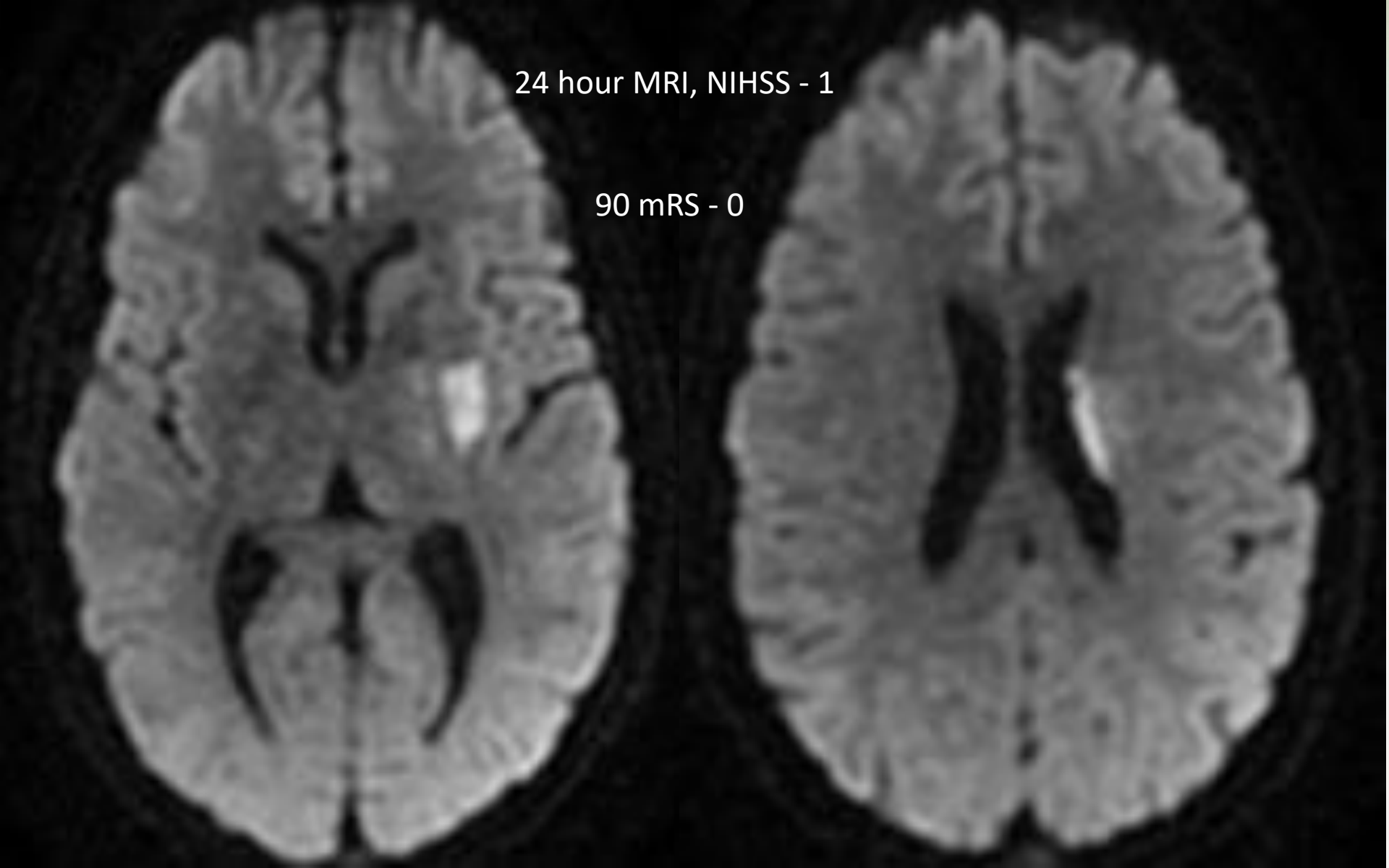
Friday night, 7:00 pm, at my home, with visiting physicians from Japan

- 31 y.o. female – aphasia, right hemiplegia
- Cardiomyopathy, ejection fraction 10%
- Not therapeutic on coumadin
- CT/CTA at a hospital 9 miles away at 6:42 pm
  - Reviewed prior to arrival



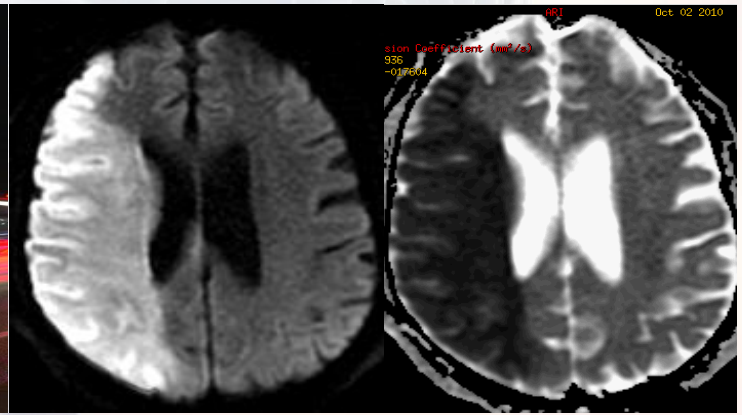





24 hour MRI, NIHSS - 1
90 mRS - 0

LVO Stroke - Time is Brain

- 1.8 million neurons lost each minute
- Probability of a good outcome reduced 10% every 30 minutes until treated[1]
- Every 30 minute delay to revascularization = 7% increased risk of moderate to severe disability and 11.8% increase in mortality[2]



1. Stroke 2006; 37: 263–266

2. Linfante et al. Predictors of mortality in acute ischemic stroke intervention: analyis of the North American Solitaire Acute Stroke Registry. Stroke 2015;46;2305-8.

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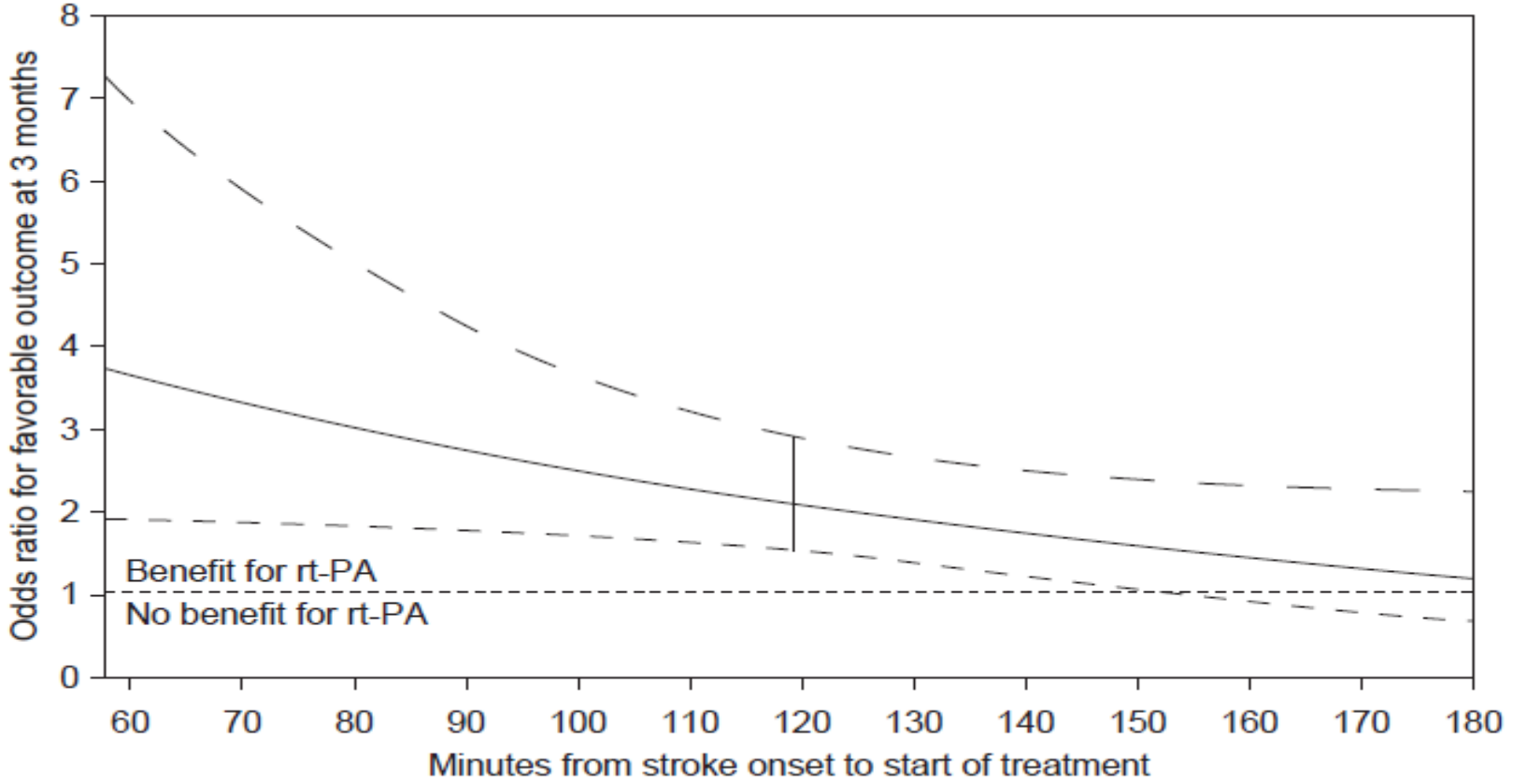
Passage of time from the start of the stroke occurs differently for every patient

- Data supports a time window, but is the window the same for all patients?
  - **Wake up Stroke:** “last time known well” excludes many from treatment
  - **Posterior Strokes:** tolerate ischemia longer than anterior stroke and may have viable penumbra beyond 6 or 8 hours
  - **Collateral Circulation:** affects a patient’s ability to tolerate an occluded vessel

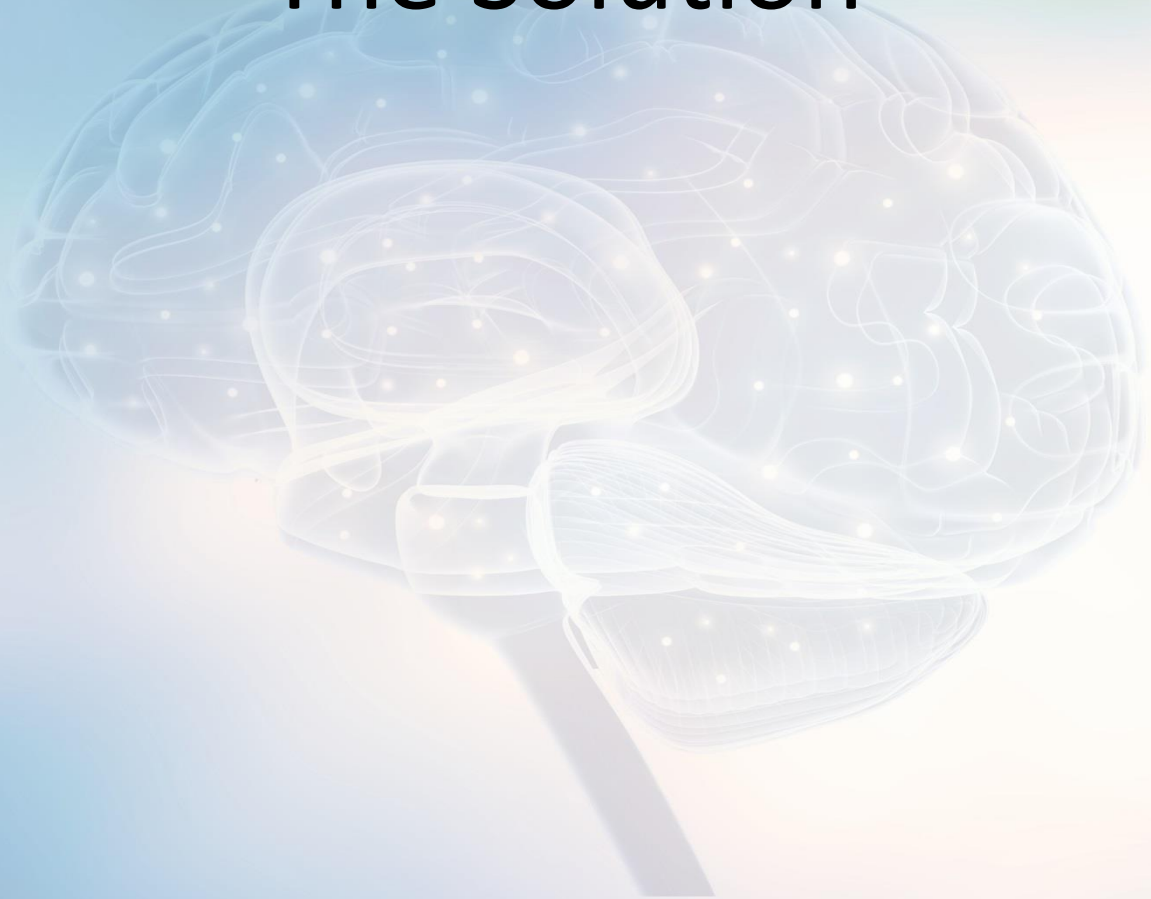
- An alternative to the traditional time window may be advanced imaging techniques in selected patients
  - CT Perfusion
  - MRI Diffusion/Perfusion

Early Treatment = Better **Outcome**



Marler J.R. et. al., Early Stroke Treatment Associated with Better Outcome, The NINDS rt-PA Stroke Study Neurology 55 December 2000.

The Solution



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LVO Stroke Treatment – A Team Sport

- Community Education
- EMS appropriate triage to IA capable facility
- Rapid ED evaluation and triage to endovascular
- Acute Neurology/Neurointerventional Surgery consultation
- t-PA and/or Embolectomy
- Neurocritical care
- Rehabilitation
- Risk factor modification

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Stroke Chain of Survival

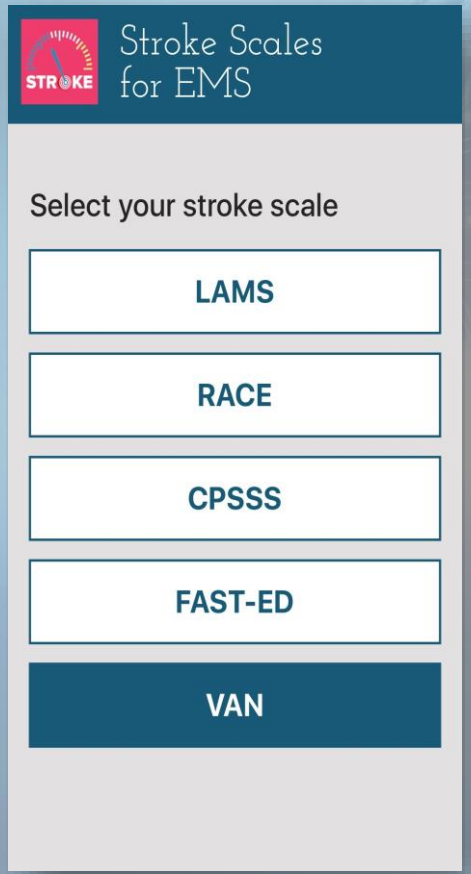
- Detection: Early stroke recognition
- Dispatch: Early EMS activation
- Delivery: Transport, triage & management
- Door: ED triage
- Data: ED evaluation & management
- Decision: Neurology input, therapy selection
- Drug: Thrombolytics & Endovascular therapies
- Disposition: Admission or transfer

Is it a stroke? Check these signs FAST!

Act FAST. Call 9-1-1 at any sign of stroke!

Massachusetts Department of Public Health

Stroke scales mobile app



- Tool for first responders to assess stroke severity in the field
- Based on results, app recommends the type of facility to which the stroke patient should be transported.

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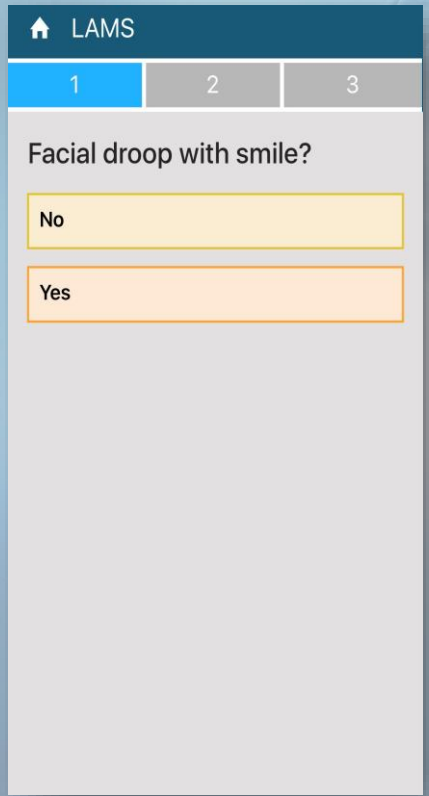
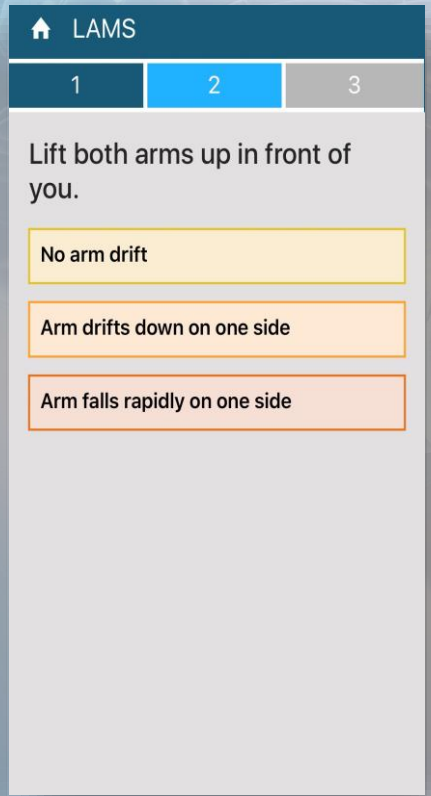
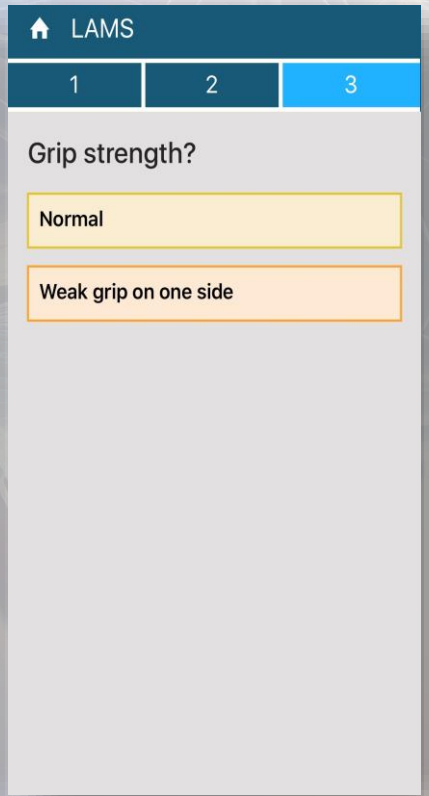
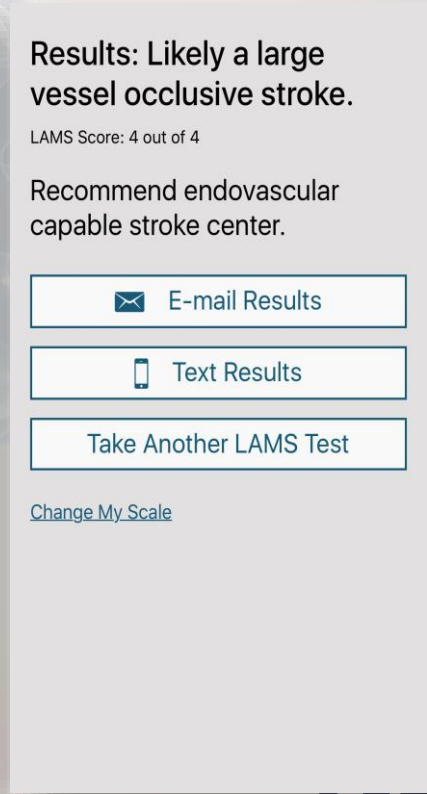
Stroke scales mobile app









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Thank You

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