Evolution of Endovascular Stroke Care

AHA Bi-State Stroke Symposium
Nov 2020

Koji Ebersole M.D.
Director of Endovascular Neurosurgery
Associate Professor Departments of Neurosurgery and Radiology
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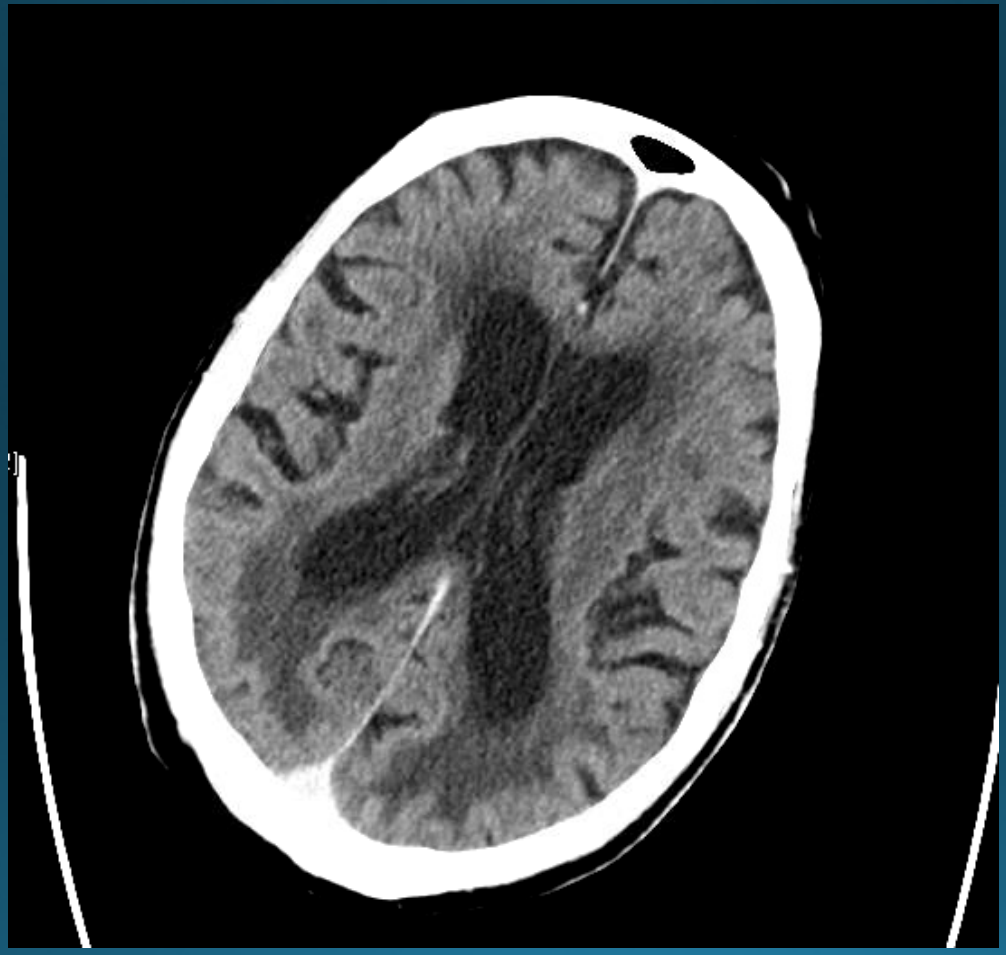
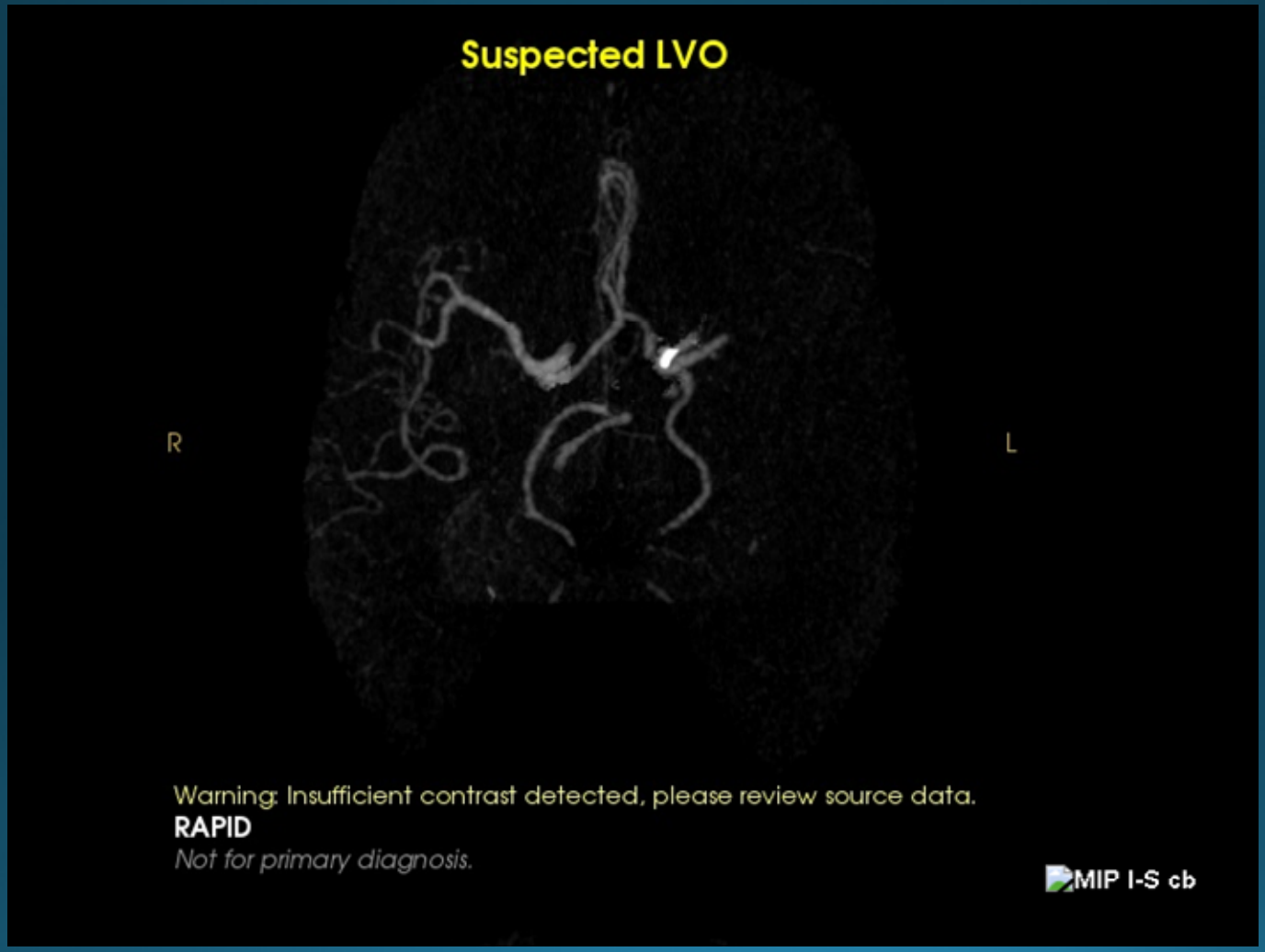
- Medical Consult/Physician Proctor Stryker Neurovascular

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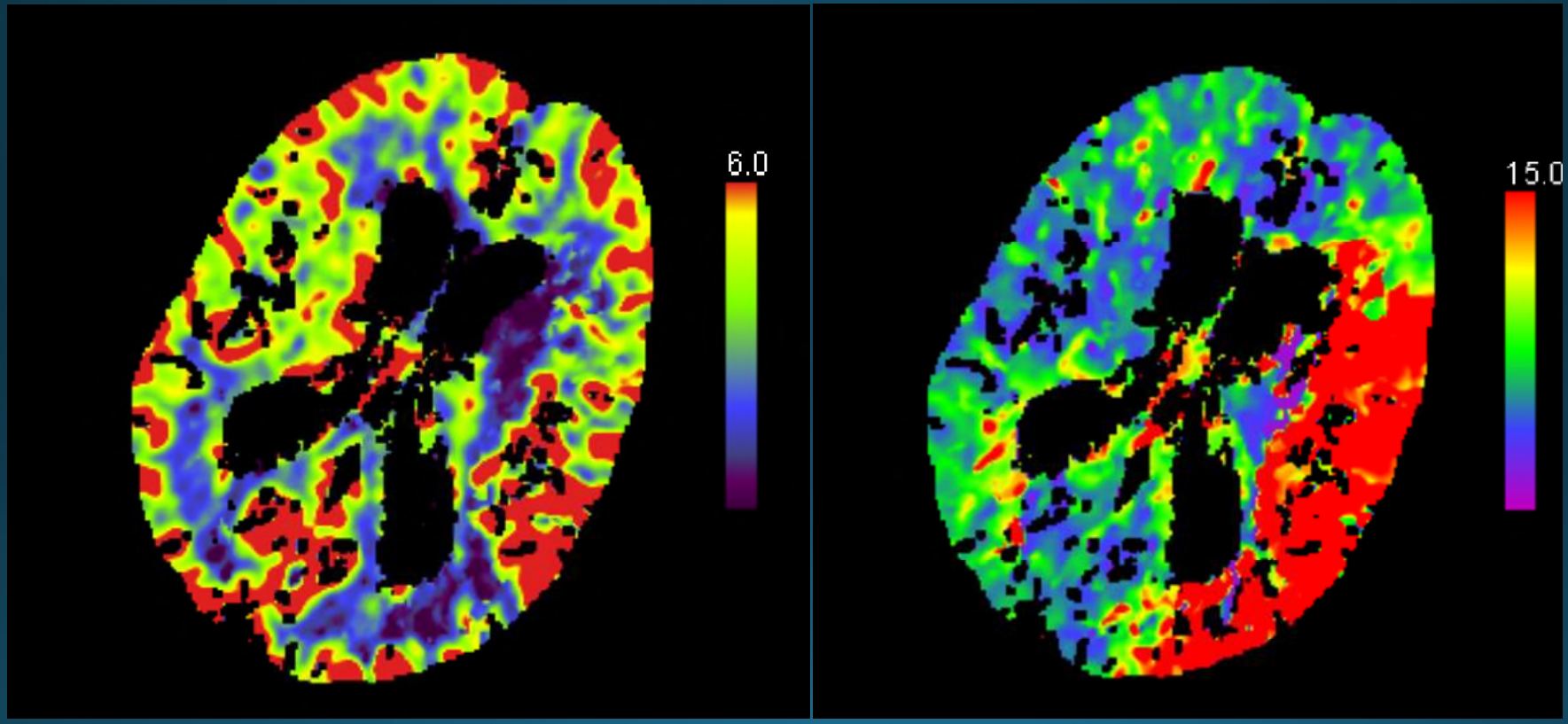
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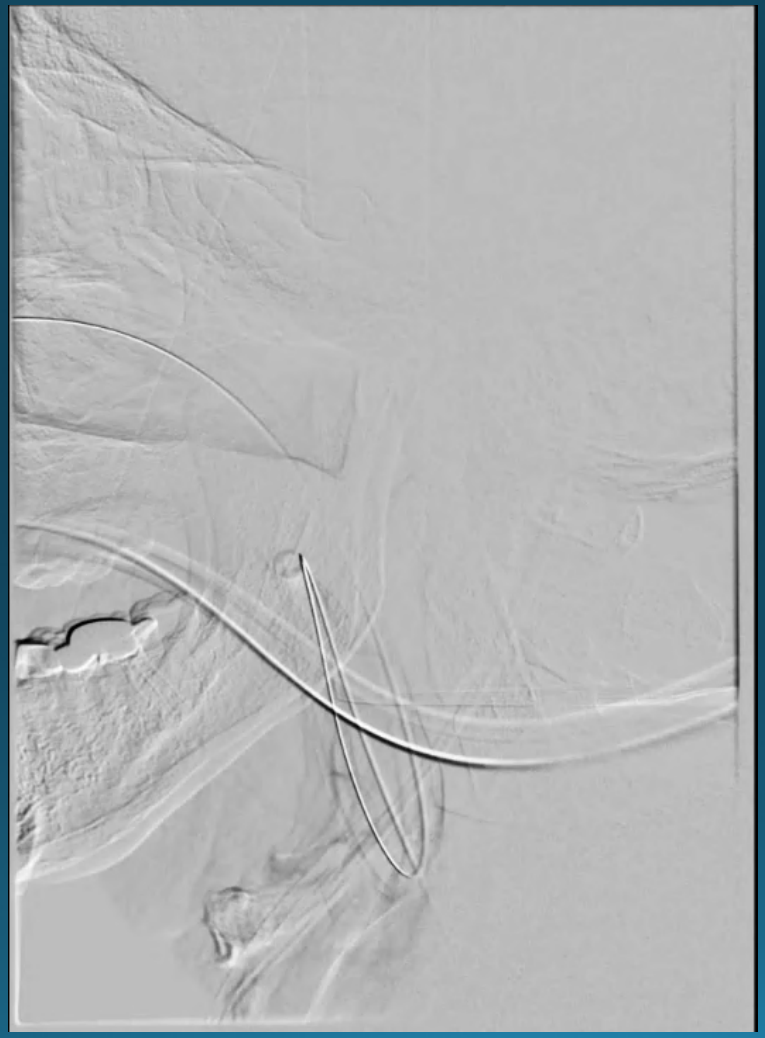

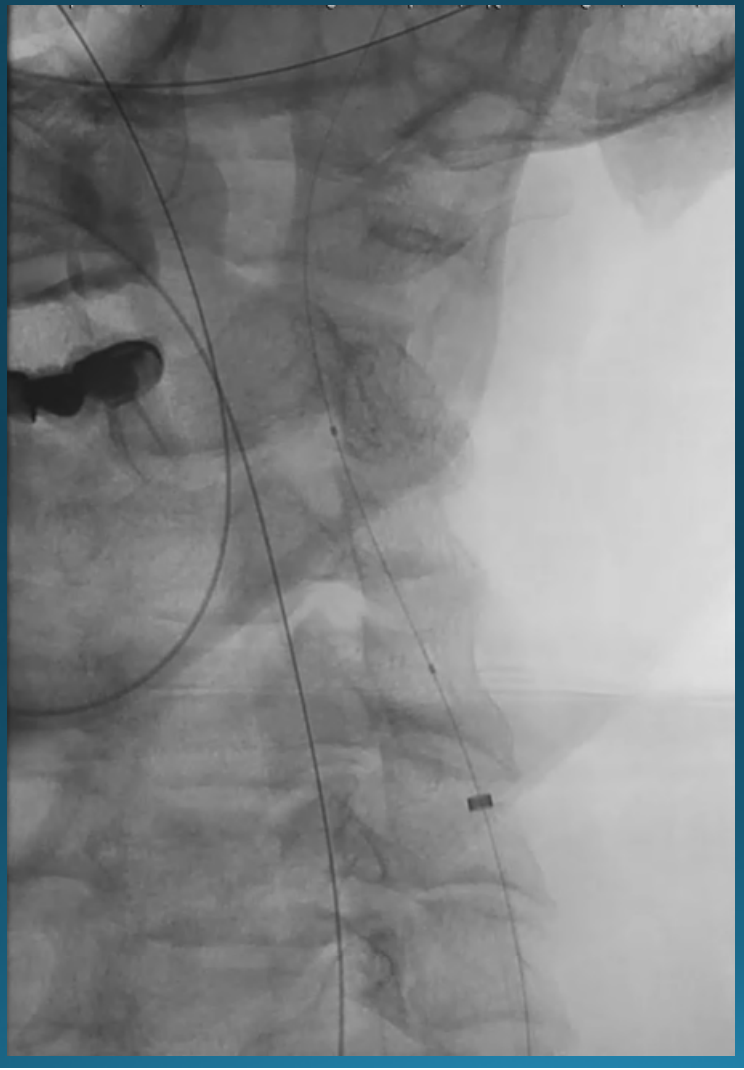

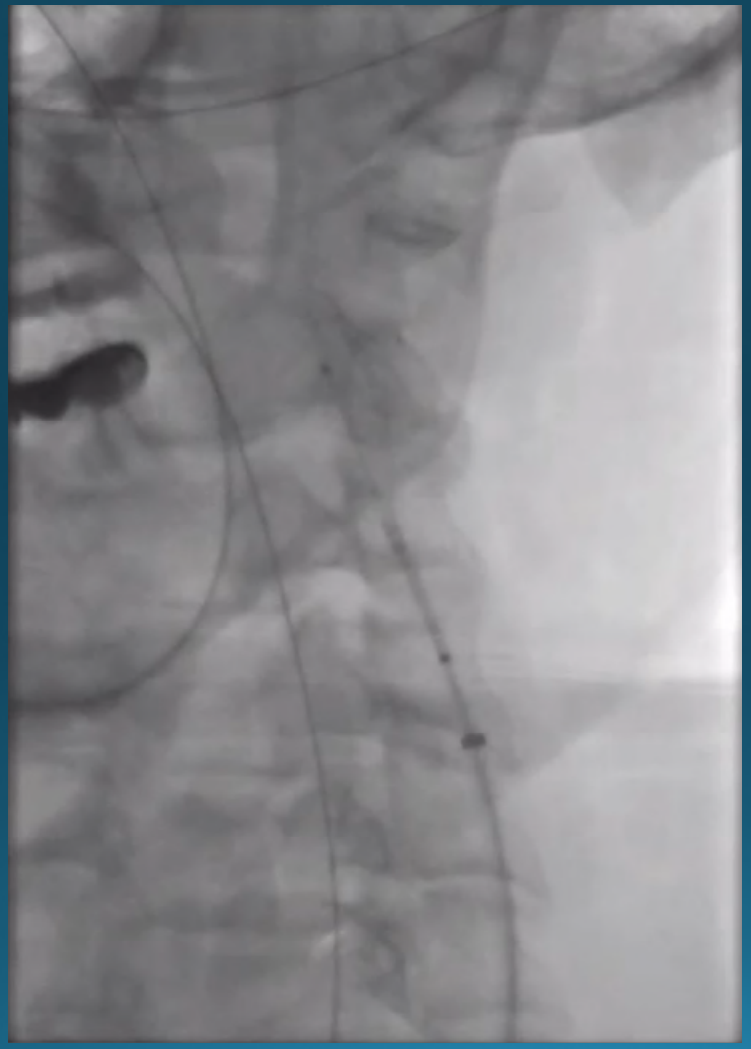

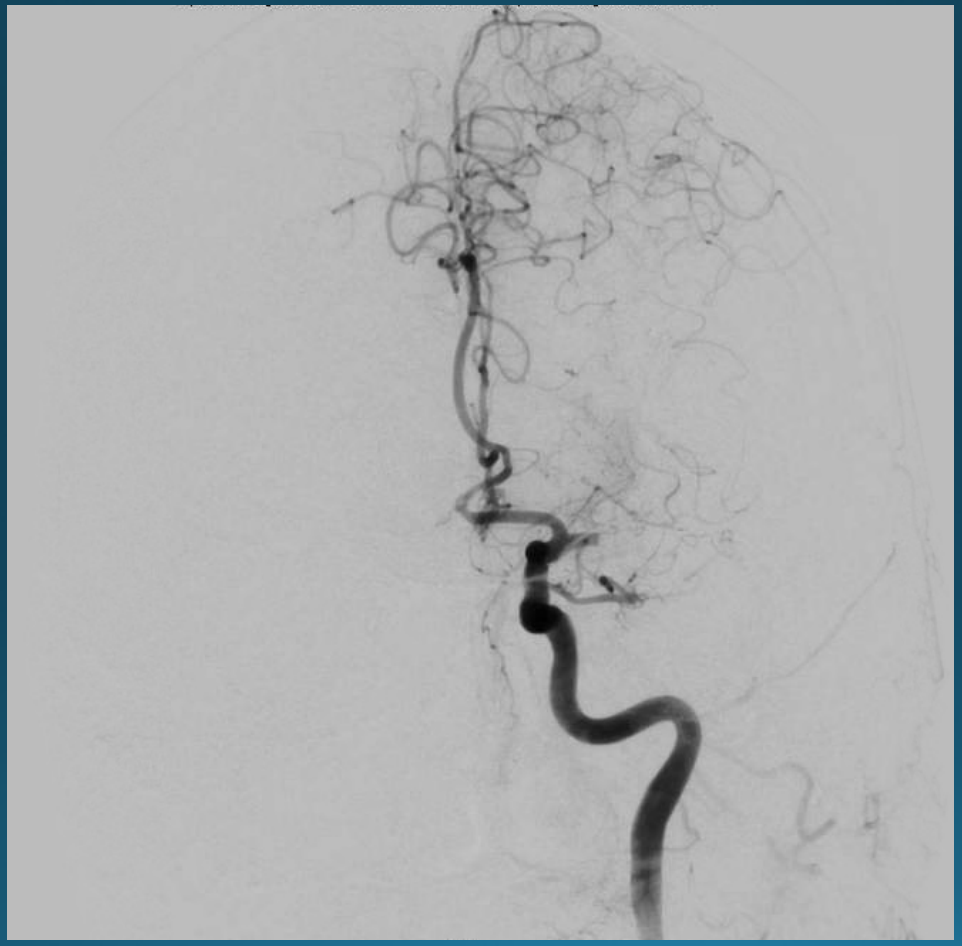

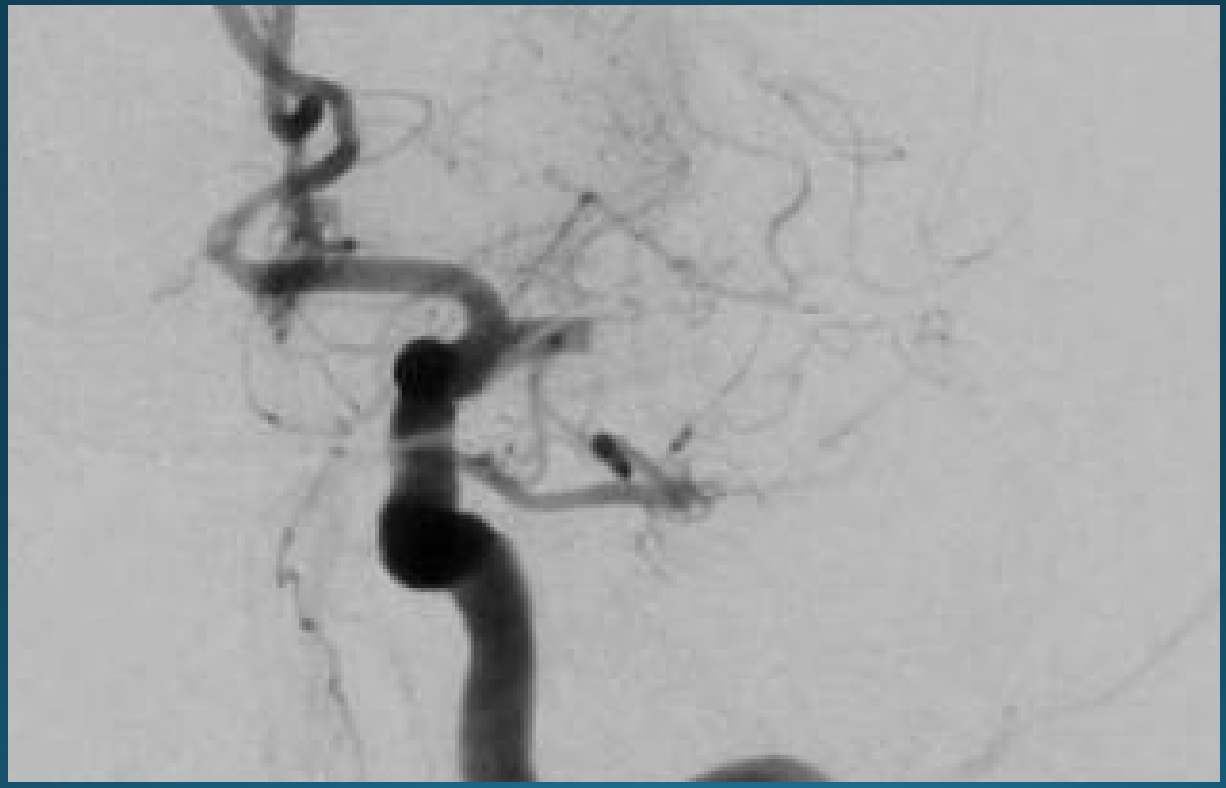

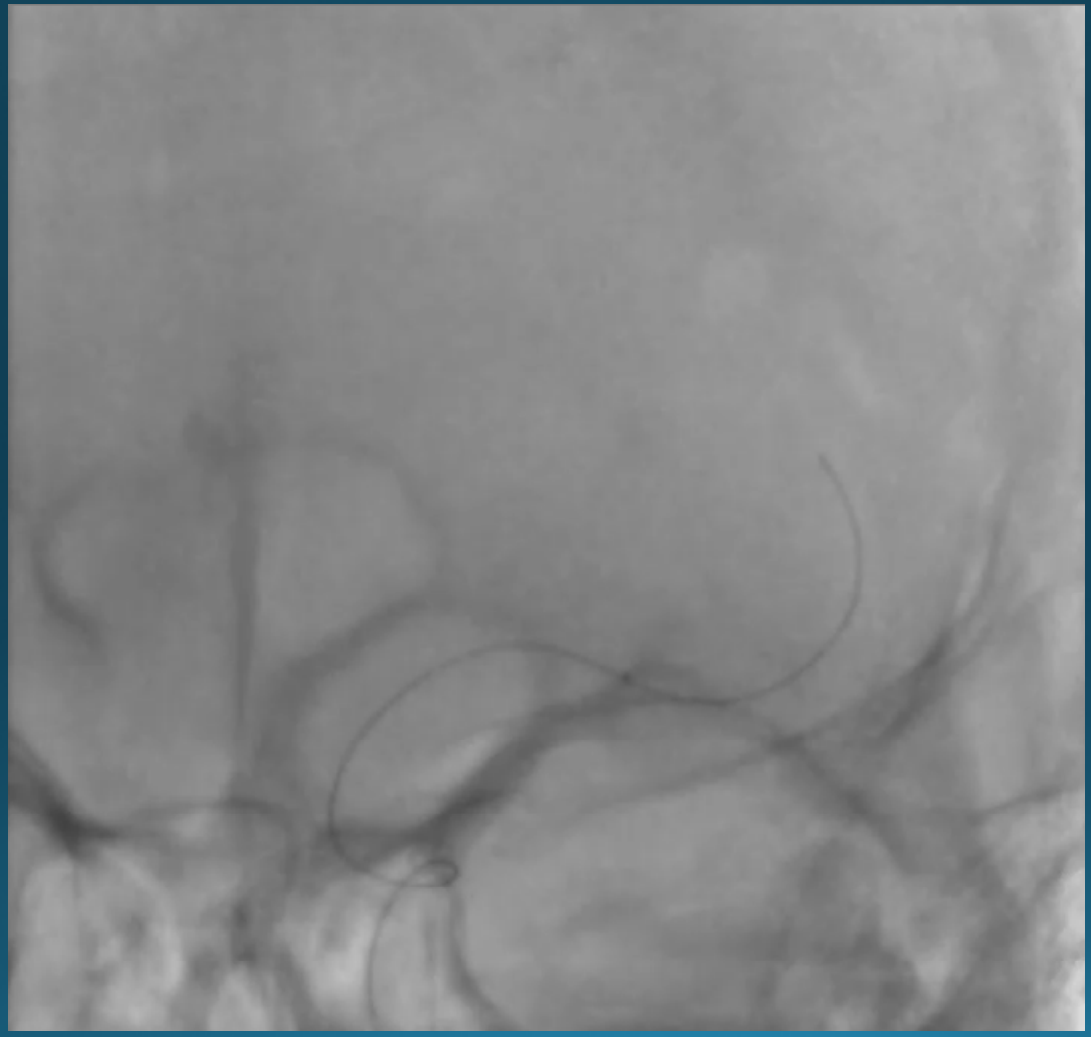

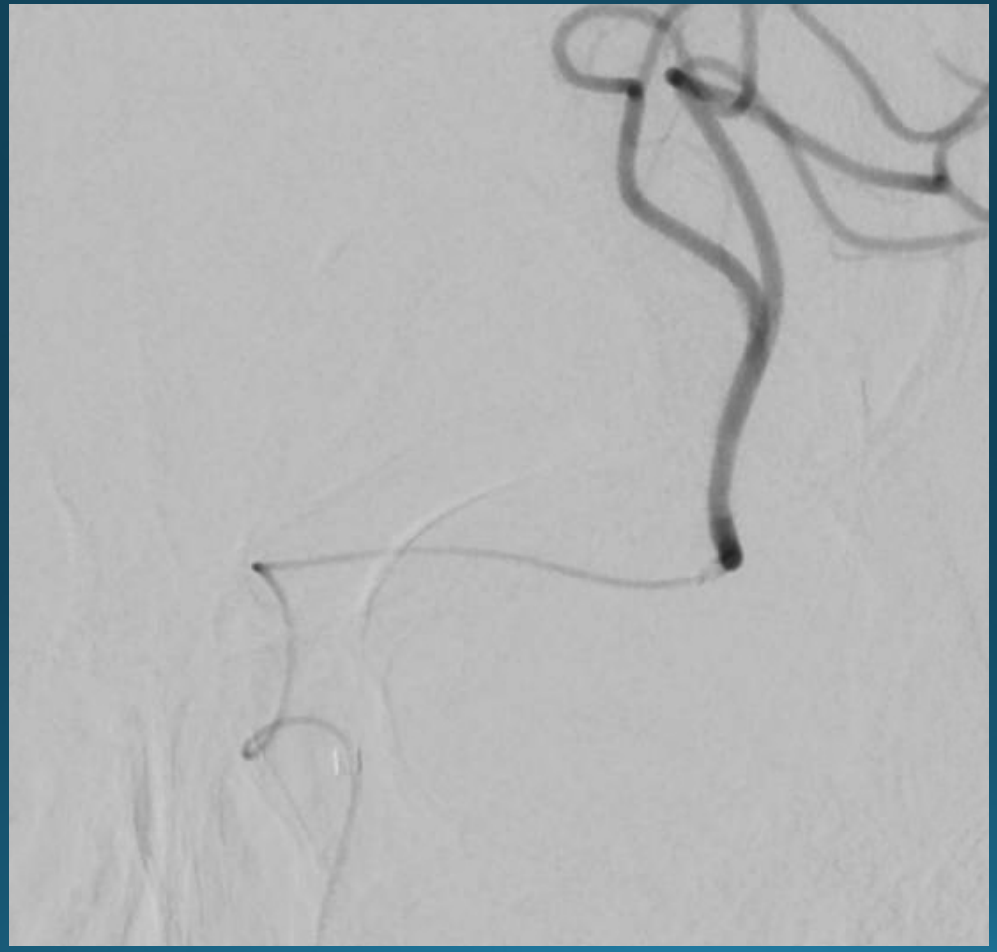

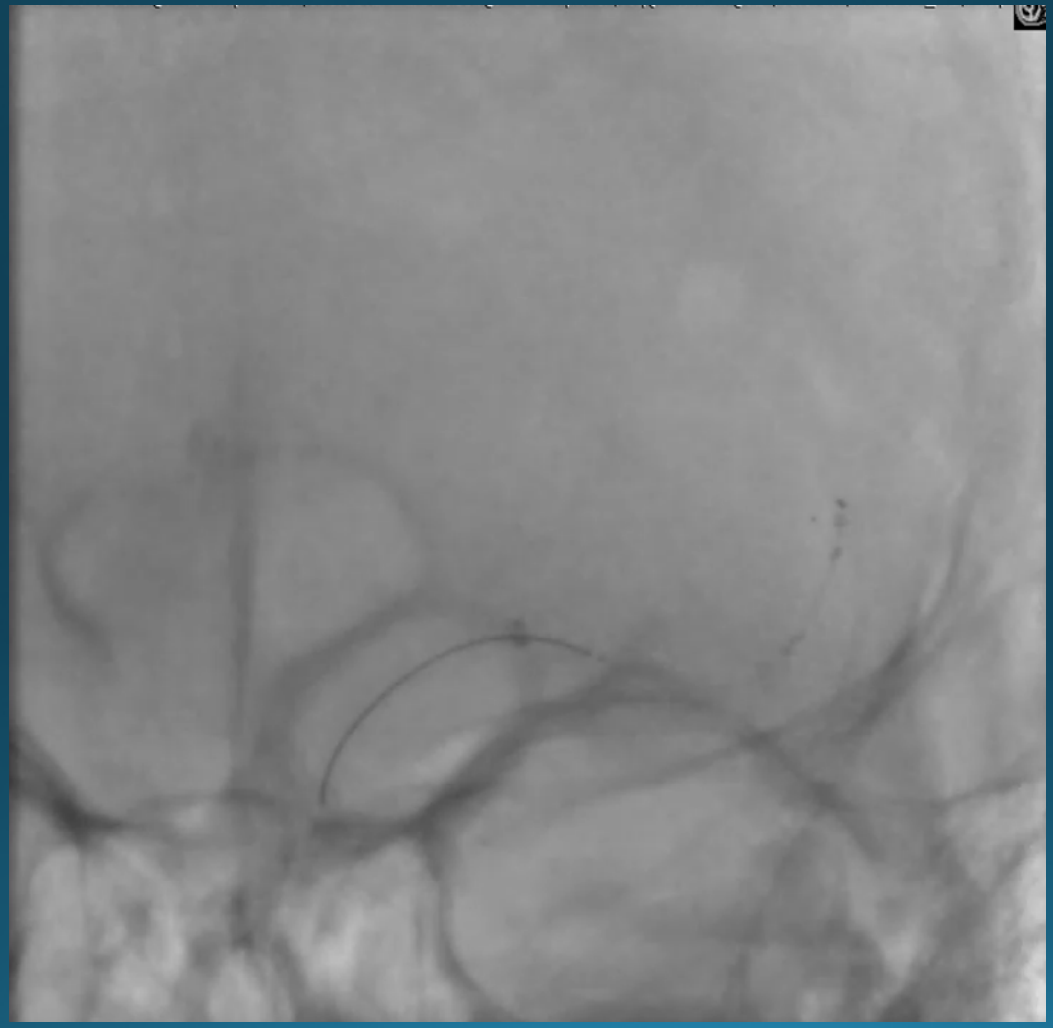

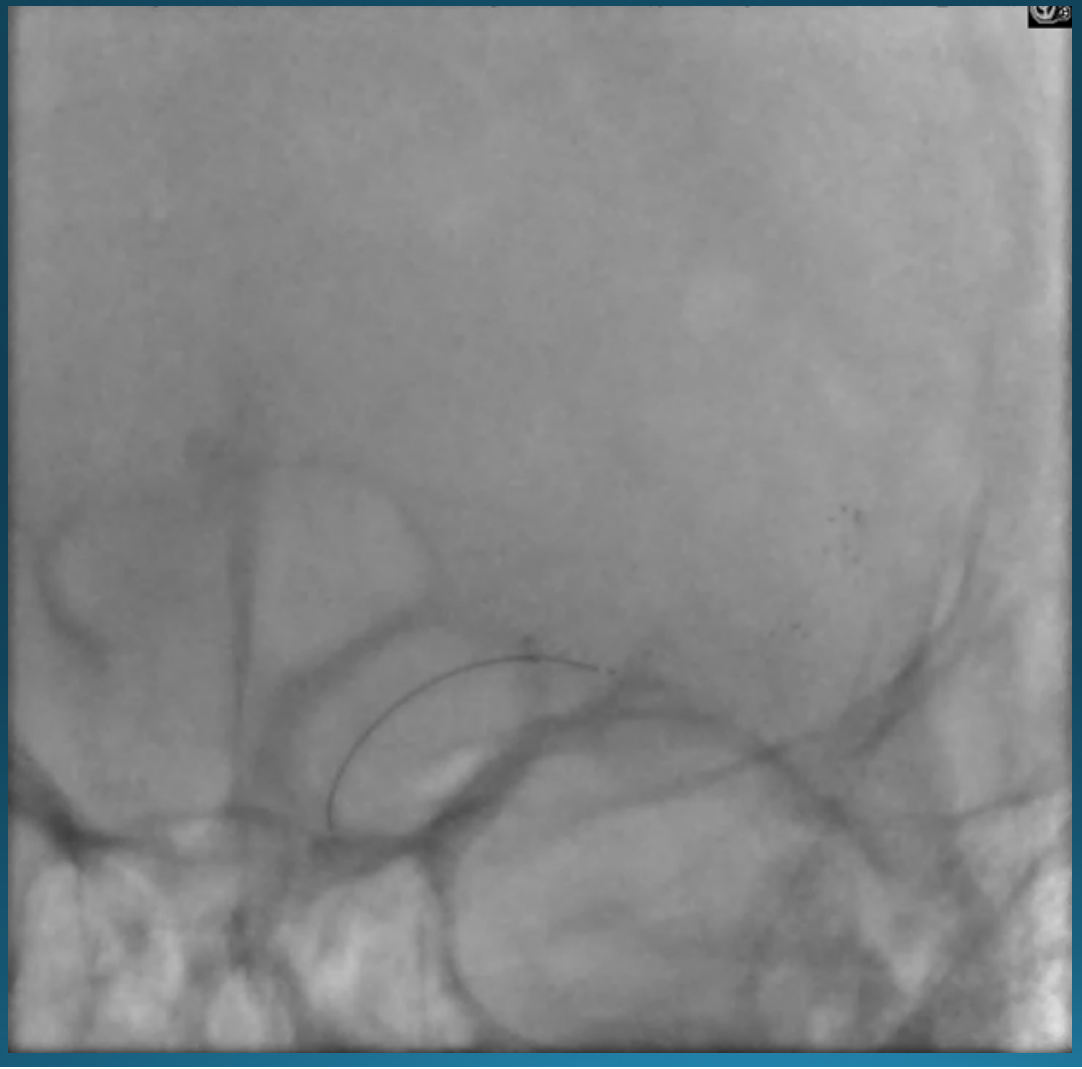

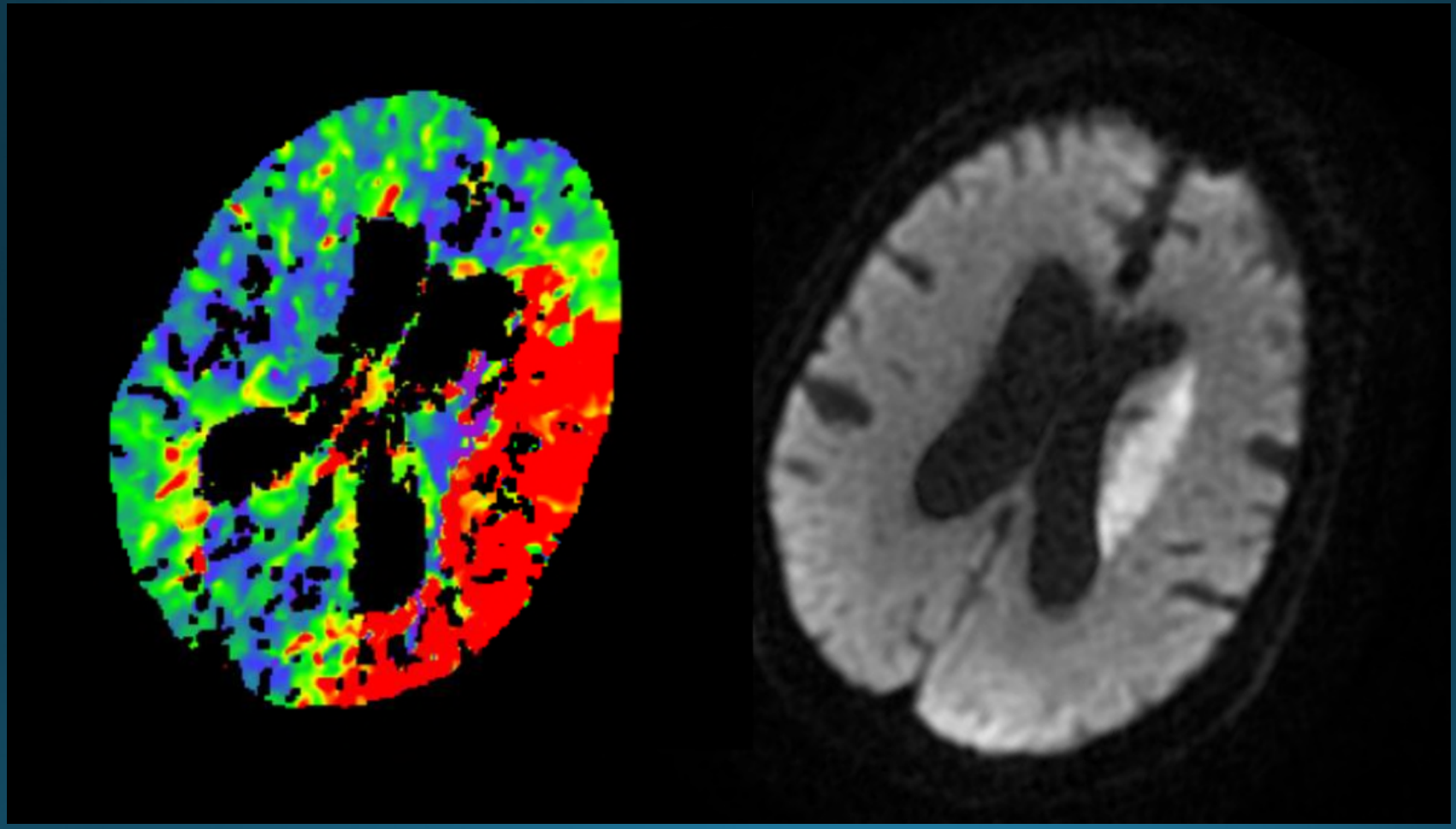

How did we get here?

1995: NINDS

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*

Abstract *Background.* Thrombolytic therapy for acute ischemic stroke has been approached cautiously because there were high rates of intracerebral hemorrhage in early clinical trials. We performed a randomized, double-blind trial of intravenous recombinant tissue plasminogen activator (t-PA) for ischemic stroke after recent pilot studies suggested that t-PA was beneficial when treatment was begun within three hours of the onset of stroke.

Methods. The trial had two parts. Part 1 (in which 291 patients were enrolled) tested whether t-PA had clinical activity, as indicated by an improvement of 4 points over base-line values in the score of the National Institutes of Health stroke scale (NIHSS) or the resolution of the neurologic deficit within 24 hours of the onset of stroke. Part 2 (in which 333 patients were enrolled) used a global test statistic to assess clinical outcome at three months, according to scores on the Barthel index, modified Rankin scale, Glasgow outcome scale, and NIHSS.

Results. In part 1, there was no significant difference between the group given t-PA and that given placebo in the percentages of patients with neurologic improvement at 24 hours, although a benefit was observed for the t-PA group at three months for all four outcome measures. In part 2, the long-term clinical benefit of t-PA predicted by the results of part 1 was confirmed (global odds ratio for a favorable outcome, 1.7; 95 percent confidence interval, 1.2 to 2.6). As compared with patients given placebo, patients treated with t-PA were at least 30 percent more likely to have minimal or no disability at three months on the assessment scales. Symptomatic intracerebral hemorrhage within 36 hours after the onset of stroke occurred in 6.4 percent of patients given t-PA but only 0.6 percent of patients given placebo ($P<0.001$). Mortality at three months was 17 percent in the t-PA group and 21 percent in the placebo group ($P=0.30$).

Conclusions. Despite an increased incidence of symptomatic intracerebral hemorrhage, treatment with intravenous t-PA within three hours of the onset of ischemic stroke improved clinical outcome at three months. (N Engl J Med 1995;333:1581-7.)

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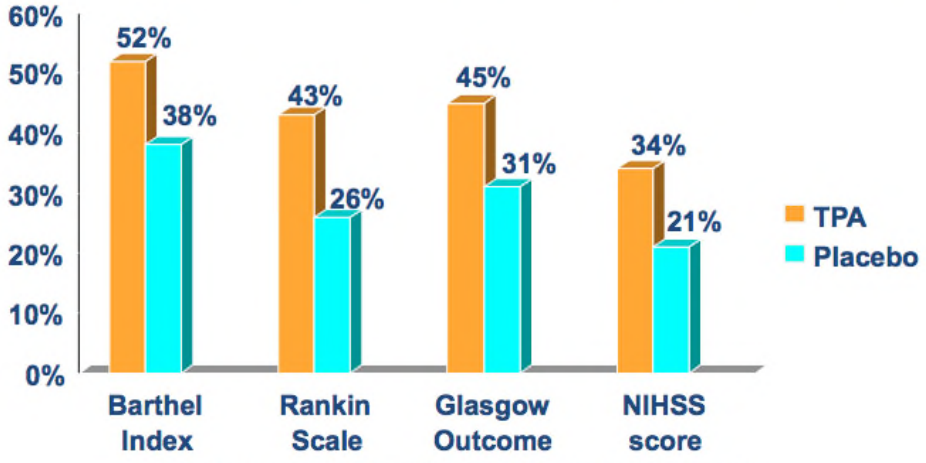
TARGET: STROKE
TIME LOST IS BRAIN LOST.

NINDS TPA Stroke Trial

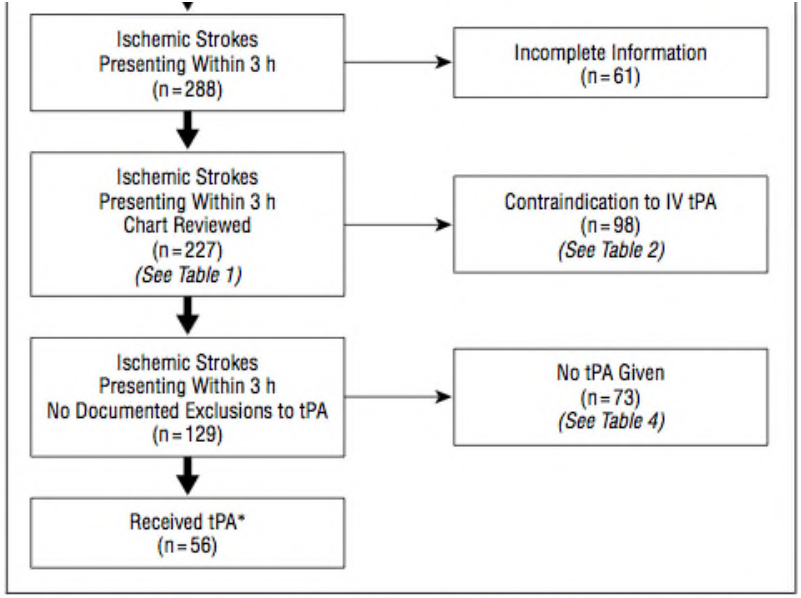
Excellent outcome at 3 months on all scales



Global outcome statistic: OR=1.7, 50% v. 38%= 12% benefit

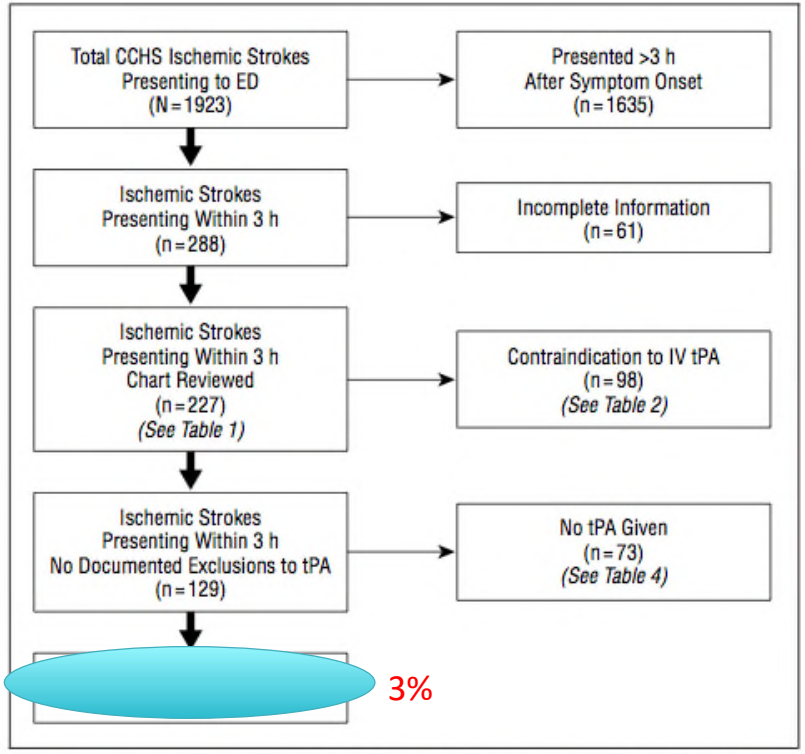
N Engl J Med 1995;333:1581-7

But many patients are not eligible at all…



Stroke admissions to the Cleveland Clinic Health System (CCHS) from June 15, 1999, to June 15, 2000. ED indicates emergency department; IV, intravenous; tPA, tissue plasminogen activator; and asterisk, the 56 patients included 9 patients treated with intra-arterial tPA.

Arch Neurol. 2004;61:346-350



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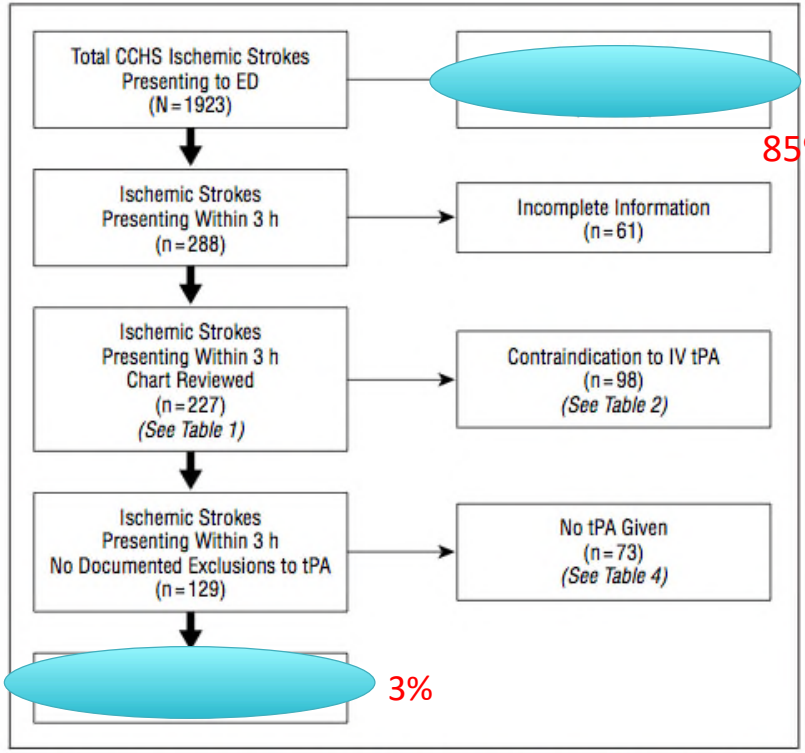

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Arch Neurol. 2004;61:346-350

2008: ECASS III

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 25, 2008 VOL. 359 NO. 13

Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke

Werner Hacke, M.D., Markku Kaste, M.D., Erich Bluhmki, Ph.D., Miroslav Brozman, M.D., Antoni Dávalos, M.D., Donata Guidetti, M.D., Vincent Larrue, M.D., Kennedy R. Lees, M.D., Zakaria Medeghri, M.D., Thomas Machnig, M.D., Dietmar Schneider, M.D., Rüdiger von Kummer, M.D., Nils Wahlgren, M.D., and Danilo Toni, M.D., for the ECASS Investigators*

ABSTRACT

BACKGROUND

Intravenous thrombolysis with alteplase is the only approved treatment for acute ischemic stroke, but its efficacy and safety when administered more than 3 hours after the onset of symptoms have not been established. We tested the efficacy and safety of alteplase administered between 3 and 4.5 hours after the onset of a stroke.

METHODS

After exclusion of patients with a brain hemorrhage or major infarction, as detected on a computed tomographic scan, we randomly assigned patients with acute ischemic stroke in a 1:1 double-blind fashion to receive treatment with intravenous alteplase (0.9 mg per kilogram of body weight) or placebo. The primary end point was disability at 90 days, dichotomized as a favorable outcome (a score of 0 or 1 on the modified Rankin scale, which has a range of 0 to 6, with 0 indicating no symptoms at all and 6 indicating death) or an unfavorable outcome (a score of 2 to 6 on the modified Rankin scale). The secondary end point was a global outcome analysis of four neurologic and disability scores combined. Safety end points included death, symptomatic intracranial hemorrhage, and other serious adverse events.

From the Department of Neurology, Universität Heidelberg, Heidelberg, Germany (W.H.); the Department of Neurology, Helsinki University Central Hospital, Helsinki (M.K.); the Department of Statistics, Boehringer Ingelheim, Biberach, Germany (E.B.); the Neurology Clinic, University Hospital Nitra, Nitra, Slovakia (M.B.); the Department of Neurosciences, Hospital Universitari Germans Trias i Pujol, Barcelona (A.D.); the Department of Neurology, Hospital of Piacenza, Piacenza, Italy (D.G.); the Department of Neurology, University of Toulouse, Toulouse, France (V.L.); the Faculty of Medicine, University of Glasgow, Glasgow, United Kingdom (K.R.L.); Boehringer Ingelheim, Reims, France (Z.M.); Boehringer Ingelheim, Ingelheim, Germany (T.M.); the Department of Neurology, Universität

IV tPA 3 – 4.5 meta-analysis

CME Availab

Efficacy and Safety of Tissue Plasminogen Activator 3 to 4.5 Hours After Acute Ischemic Stroke

A Metaanalysis

Maarten G. Lansberg, MD, PhD; Erich Bluhmki, PhD; Vincent N. Thijs, MD, PhD

Background and Purpose—The Third European Cooperative Acute Stroke Study (ECASS-3) demonstrated a benefit of treatment with intravenous tissue plasminogen activator (tPA) for acute stroke in the 3- to 4.5-hour time-window. Prior studies, however, have failed to demonstrate a significant benefit of tPA for patients treated beyond 3 hours. The purpose of this study was to produce reliable and precise estimates of the treatment effect of tPA by pooling data from all relevant studies.

Methods—A metaanalysis was undertaken to determine the efficacy of tPA in the 3- to 4.5-hour time-window. The effect of tPA on favorable outcome and mortality was assessed.

Results—The metaanalysis included data from patients treated in the 3- to 4.5-hour time-window in ECASS-1 (n=234), ECASS-2 (n=265), ECASS-3 (n=821) and The Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke (ATLANTIS) (n=302). tPA treatment was associated with an increased chance of favorable outcome (odds ratio 1.31; 95% CI: 1.10 to 1.56; P=0.002) and no significant difference in mortality (odds ratio 1.04; 95% CI: 0.75 to 1.43; P=0.83) compared to placebo treated patients.

Conclusions—Treatment with tPA in the 3- to 4.5-hour time-window is beneficial. It results in an increased rate of favorable outcome without adversely affecting mortality. **(*Stroke*. 2009;40:2438-2441.)**

Key Words: acute stroke ■ thrombolysis ■ metaanalysis

In 1996, based on the results of the 2-part National Institutes of Neurological Disorders and Stroke (NINDS) acute stroke trial, the FDA approved intravenous tissue plasminogen activator (tPA) for treatment of acute ischemic stroke up to 3 hours after symptom onset.[1] The recently published European Cooperative Acute Stroke Study (ECASS)-3 study results are the first data from a randomized placebo-controlled trial that demonstrate efficacy of intravenous tPA beyond the established 3-hour time-window.[2] In ECASS-3, 821 stroke patients were randomized between treatment with placebo and tPA in the 3- to 4.5-hour time-window after acute ischemic stroke. Compared to placebo-treated patients, tPA-treated patients experienced a 7.2% ciated with only a 2% increased rate of excellent outcome (not significant), a 5.4% higher rate of symptomatic intracerebral hemorrhage (P<0.001), and a 4% increased rate of death (P=0.09). The inferiority of the ATLANTIS results compared to ECASS-3 may be due to the longer treatment time-window in ATLANTIS part B (3- to 5-hour window with a median time-to-treatment of 4 hours 36 minutes in ATLANTIS part B versus a 3- to 4.5-hour time window with a median time to treatment of 3 hours 59 minutes in ECASS-3). The marginal significance with which superiority of tPA over placebo was demonstrated in ECASS-3 and the lack of a confirmatory randomized controlled trial of tPA in the 3- to 4.5-hour time-window

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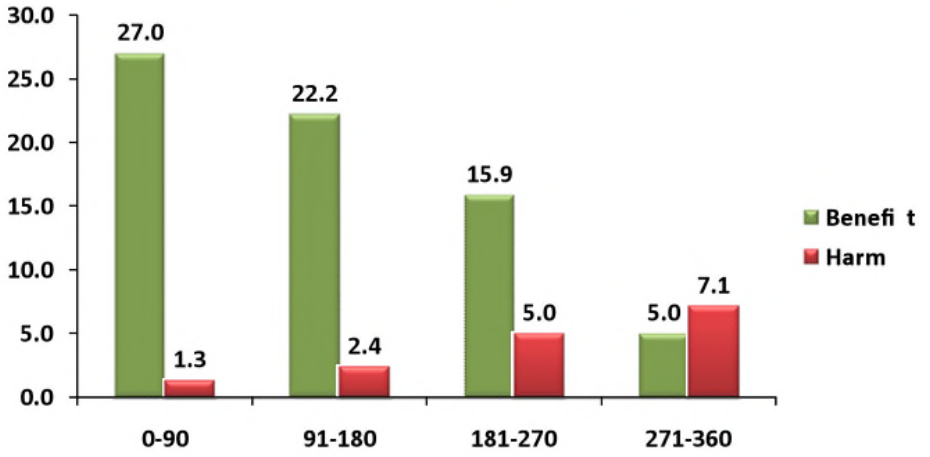
TARGET: STROKE
TIME LOST IS BRAIN LOST.

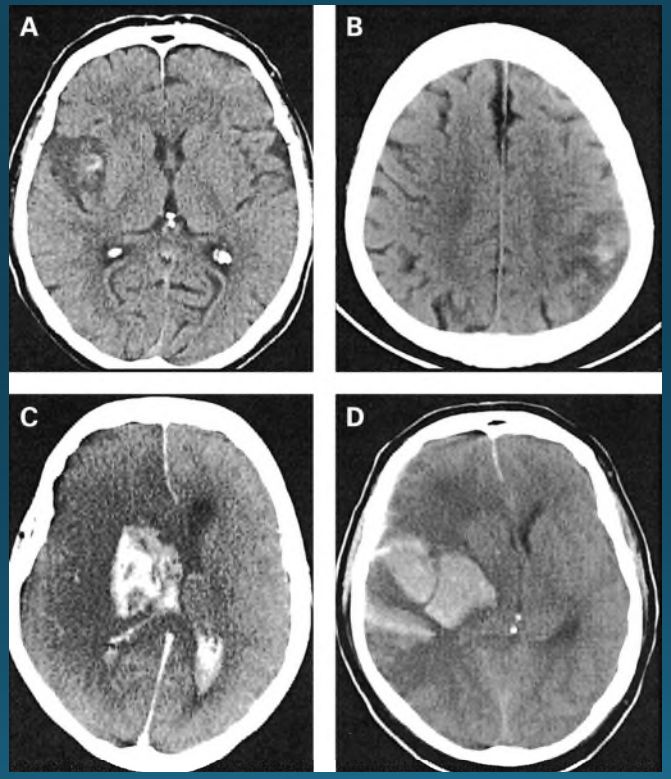
Number of Patients Who Benefit and Are Harmed per 100 Patients tPA Treated in Each Time Window



--Lansberg et al, Stroke 2009

3.0 - 4.5 hrs

European Cooperative Acute Stroke Study (ECASS) classification of intracerebral haemorrhage (ICH) following thrombolysis (from Berger and colleagues38).



Derex L , Nighoghossian N J Neurol Neurosurg Psychiatry 2008;79:1093-1099

Cerebrovascular Diseases

Cerebrovasc Dis 2007;24:1–10
DOI: 10.1159/000103110

Received: September 29, 2006
Accepted: December 21, 2006
Published online: May 22, 2007

Symptomatic Intracerebral Hemorrhage following Thrombolytic Therapy for Acute Ischemic Stroke: A Review of the Risk Factors

Maarten G. Lansberg Gregory W. Albers Christine A.C. Wijman

Stanford University, Stanford Stroke Center, Palo Alto, Calif., USA

- Risk of SICH with IV tPA is ~6%
- Fatality rate is between 50 and 80%
- Severe morbidity or mortality exceeds 90%

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

3.5. IV Alteplase	COR	LOE
1. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who may be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 6 to determine patient eligibility.	I	A
2. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is also recommended for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well. Physicians should review the criteria outlined in Table 6 determine patient eligibility.	I	B-R

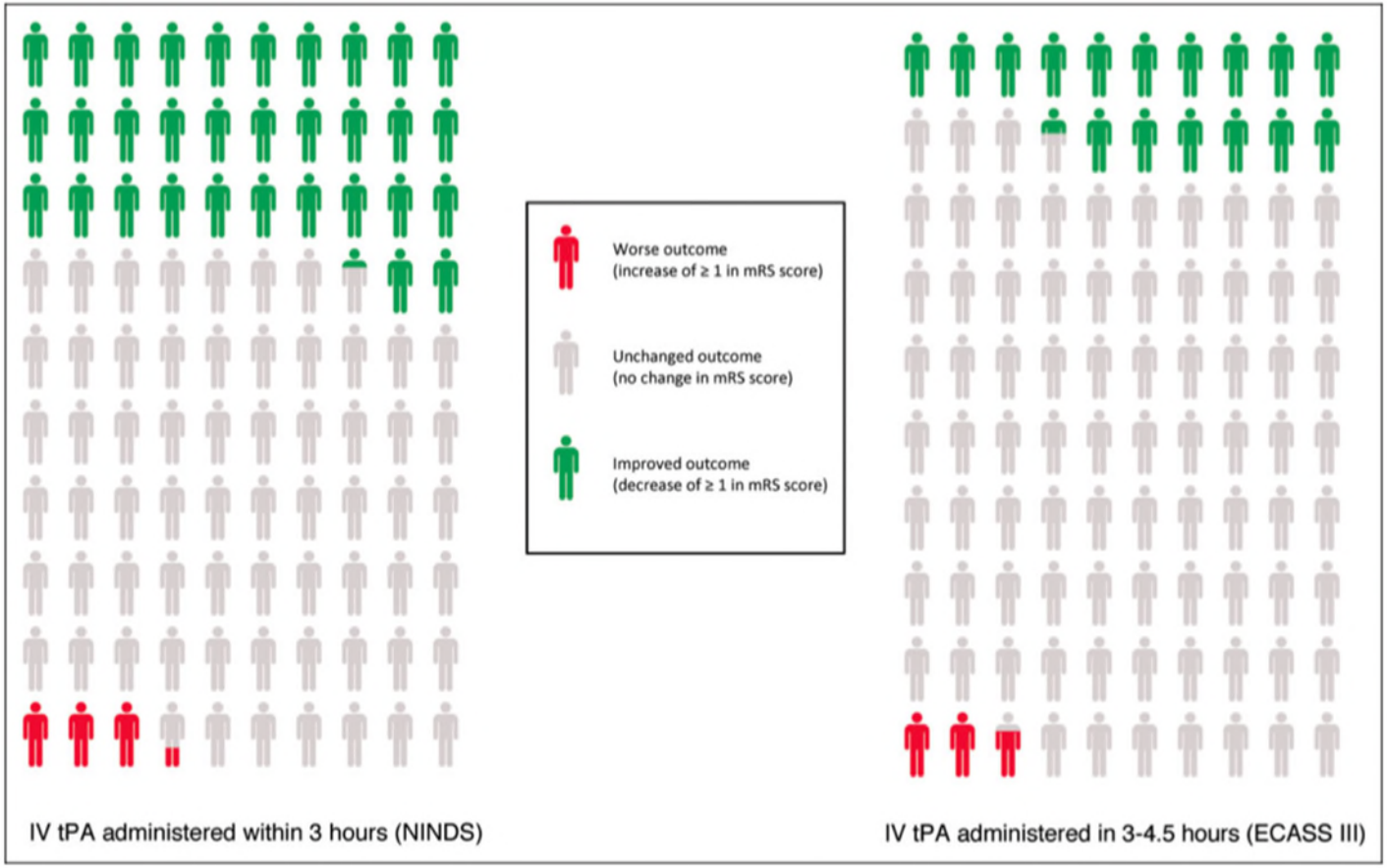
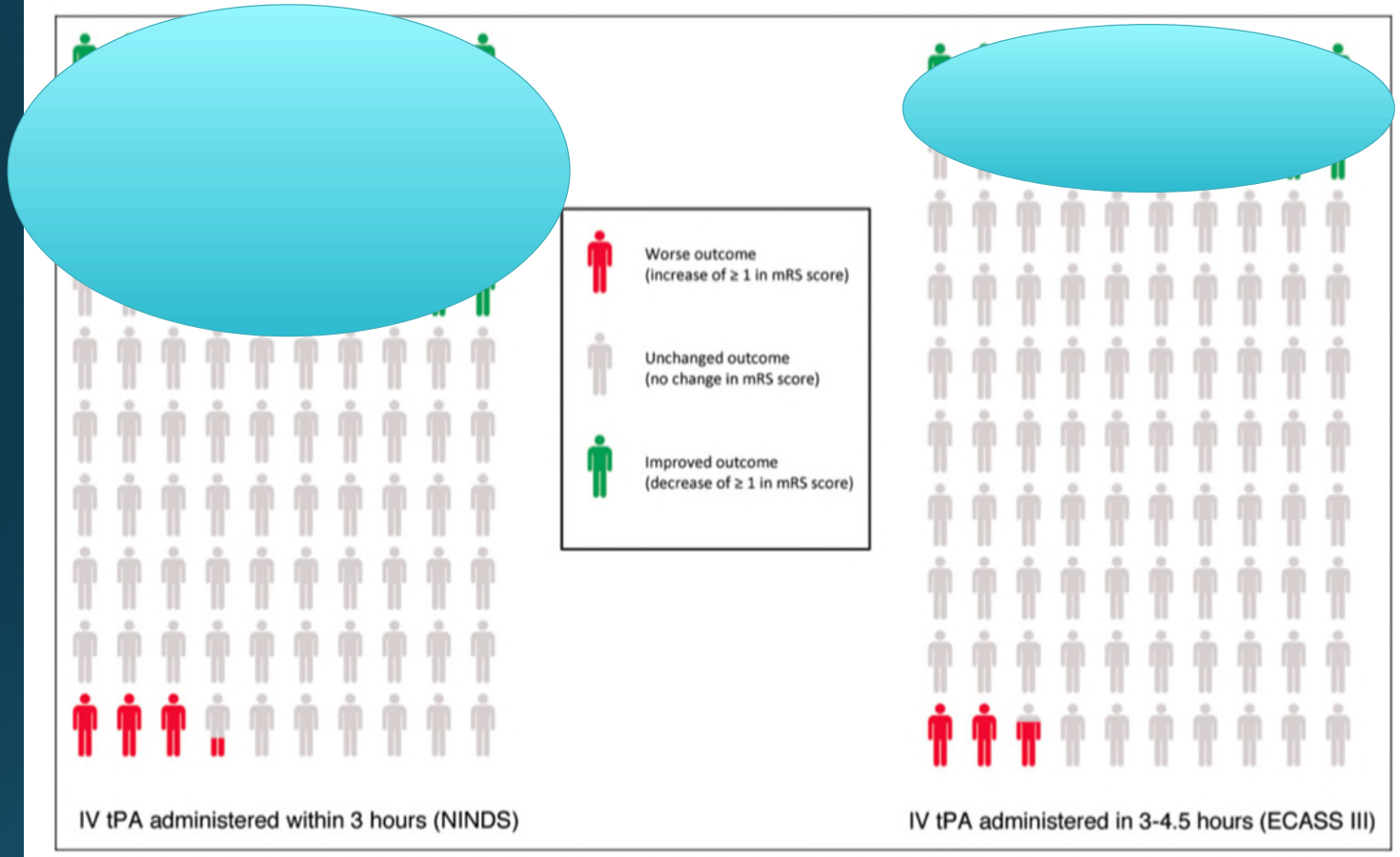


Figure 3. Number needed to treat to benefit and harm per 100 patients treated with intravenous recombinant tissue-type plasminogen activator (IV tPA) for acute ischemic stroke in the <3-hour versus 3- to 4.5-hour time windows.[24] mRS indicates modified Rankin scale; NINDS, National Institute of Neurologic Disorders and Stroke; ECASS-III, European Cooperative Acute Stroke Study-III.

Neurohospitalist. 2015 Jul; 5(3): 101–109.



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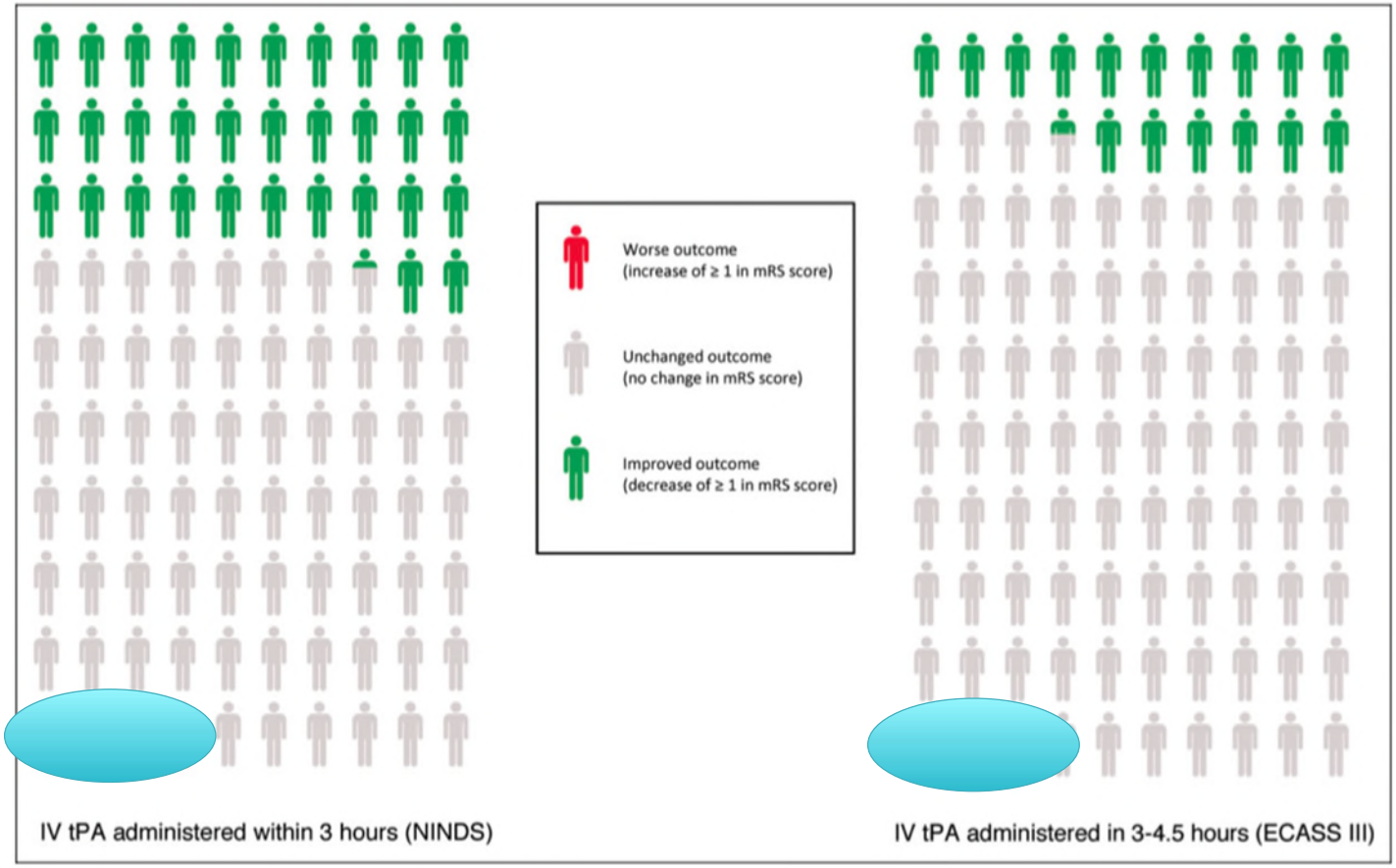

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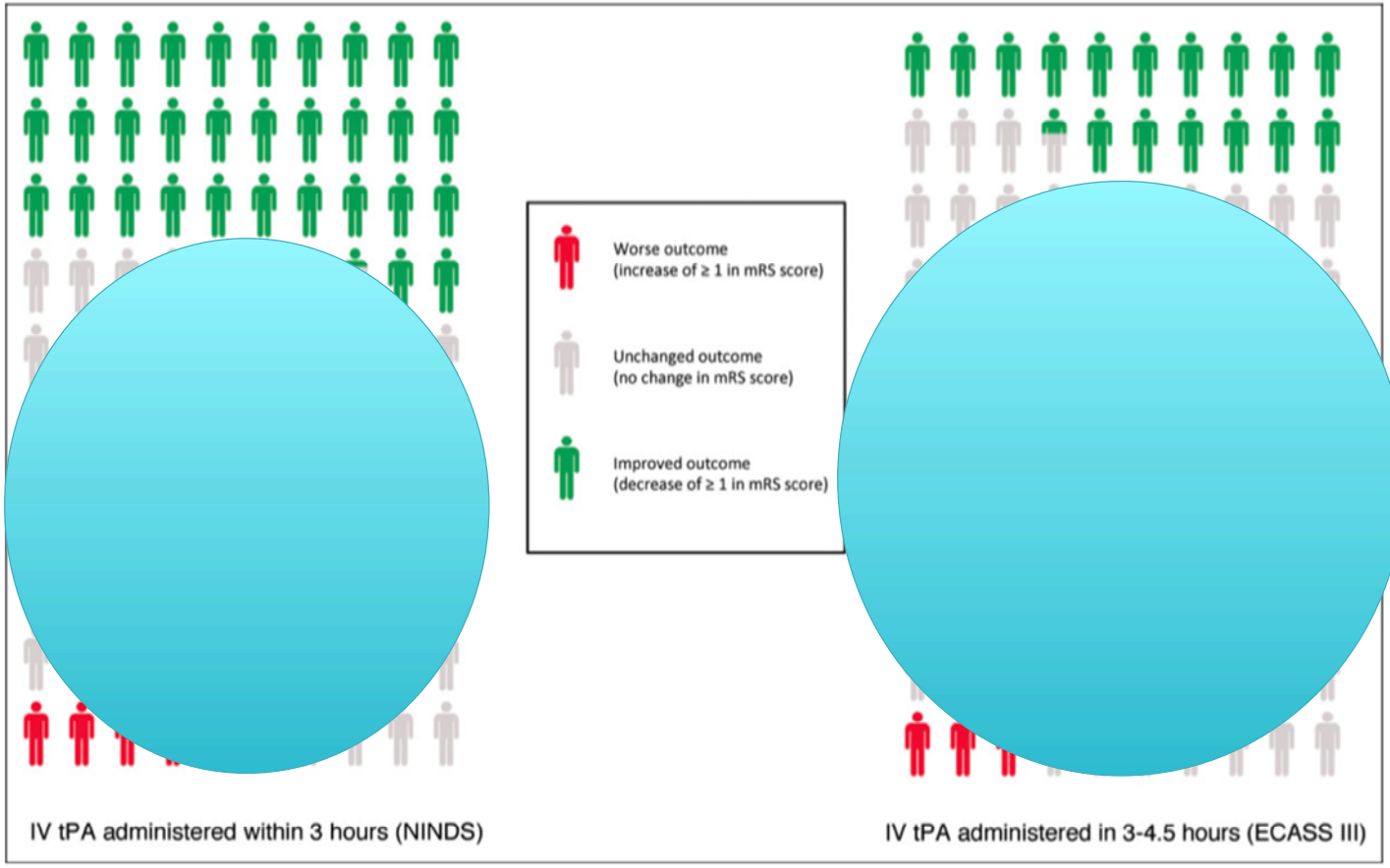

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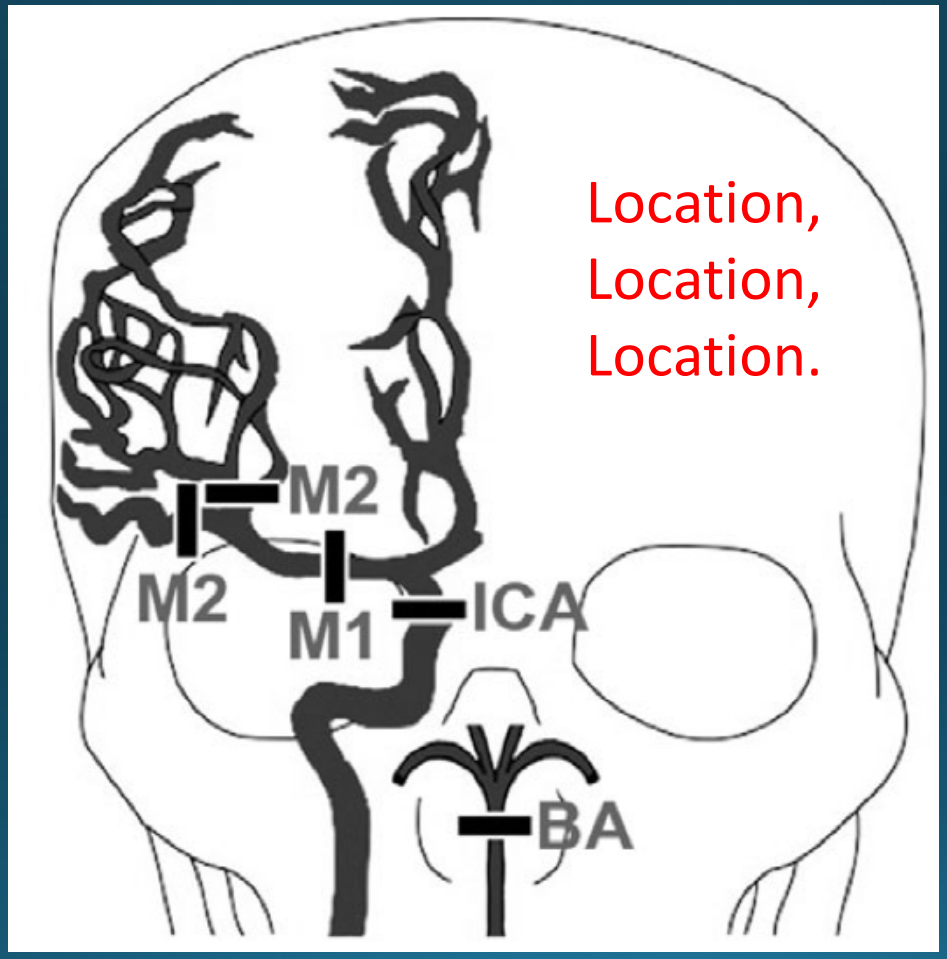
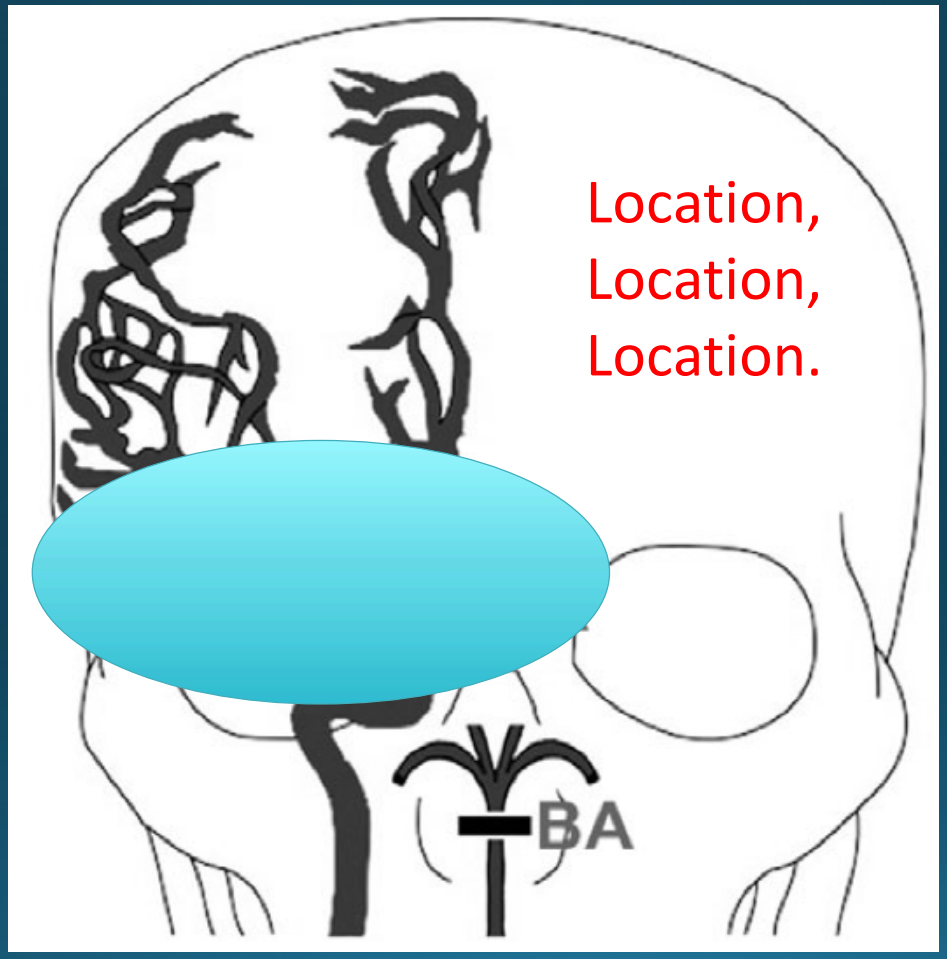


BASIS: Boston Acute Stroke Imaging Score - 2008



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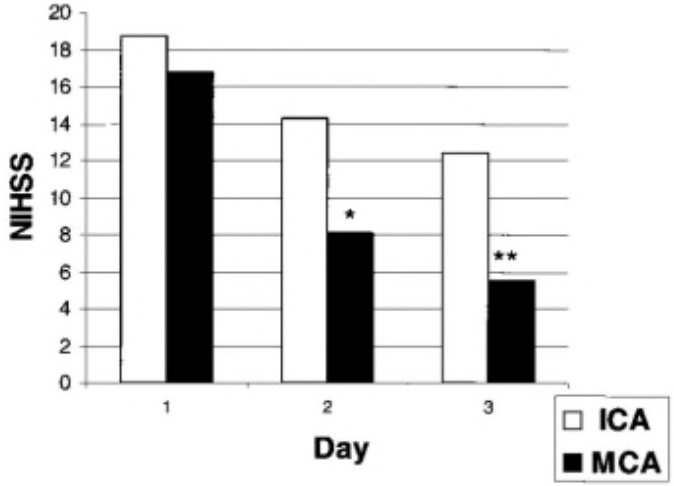
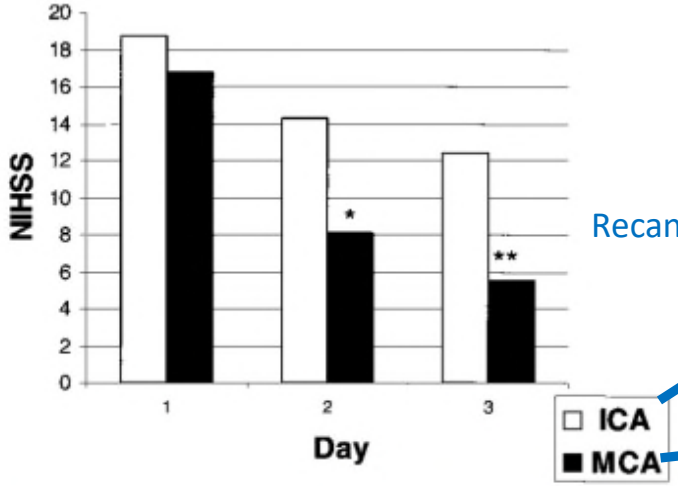


Figure 1. Comparison of NIHSS scores at days 1 (pre-tPA), 2, and 3 after tPA in patients with ICA-plus-MCA occlusion (□) vs patients with isolated MCA occlusion (■). *P=0.04; **P=0.03 (Wilcoxon rank sum).

Stroke. 2002;33:2066-2071



Recanalization at 3 days after tPA

31%

p<0.001

88%

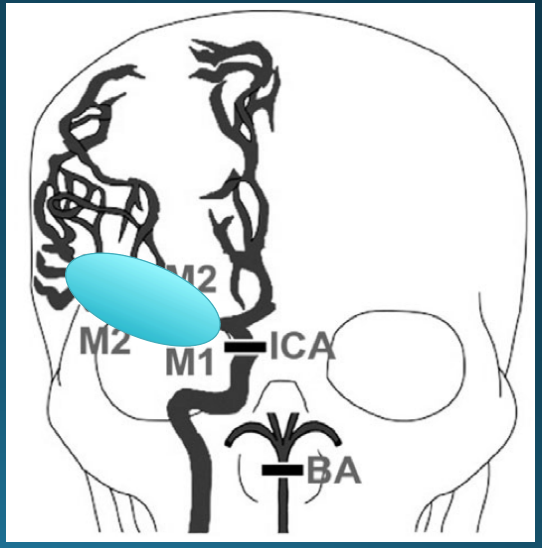
Figure 1. Comparison of NIHSS scores at days 1 (pre-tPA), 2, and 3 after tPA in patients with ICA-plus-MCA occlusion (□) vs patients with isolated MCA occlusion (■). **P*=0.04; ***P*=0.03 (Wilcoxon rank sum).

Stroke. 2002;33:2066-2071

Site of Arterial Occlusion Identified by Transcranial Doppler Predicts the Response to Intravenous Thrombolysis for Stroke

Likelihood of complete recanalization after IV tPA

- MCA M2
  - OR = 2 (95% CI: 1.1 to 3.1, *P*=0.005)
  - 44.2% (n=50 of 113)
- MCA M1
  - OR = 0.7 (95% CI: 0.4 to 1.1, *P*=0.13)
  - 30% (n=49 of 163)



(*Stroke*. 2007;38:948-954.)

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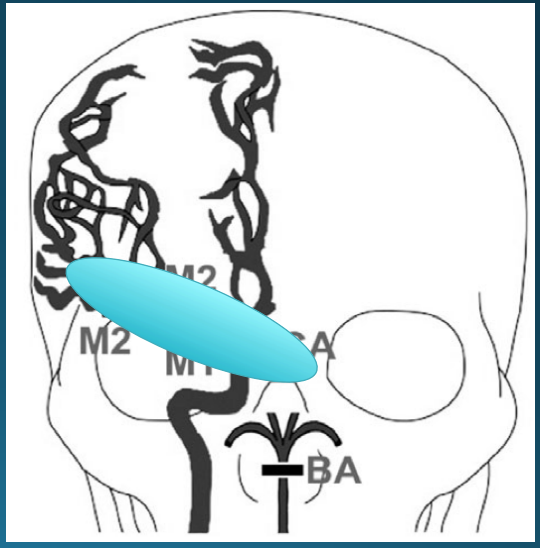
- MCA M1
  - OR = 0.7 (95% CI: 0.4 to 1.1, *P*=0.13)
  - 30% (n=49 of 163)
- Terminal ICA
  - OR = 0.1 (95% CI: 0.015 to 0.8, *P*=0.015)
  - 5.9% 1 of 17



(*Stroke*. 2007;38:948-954.)

Site of Arterial Occlusion Identified by Transcranial Doppler Predicts the Response to Intravenous Thrombolysis for Stroke

- Following IV tPA:
  - Patients with distal MCA occlusion are twice as likely to have a better outcome than those with proximal MCA occlusions.

(*Stroke*. 2007;38:948-954.)

Site of Arterial Occlusion Identified by Transcranial Doppler Predicts the Response to Intravenous Thrombolysis for Stroke

- Following IV tPA:
  - Patients with distal MCA occlusion are twice as likely to have a better outcome than those with proximal MCA occlusions.
  - Terminal ICA occlusions were the least likely to have clinical recovery

(*Stroke*. 2007;38:948-954.)

Size matters…

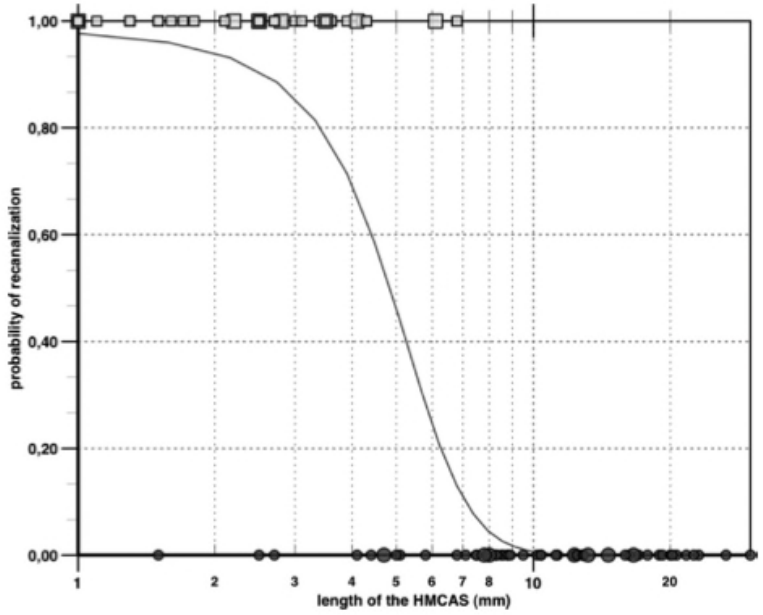


Figure 1. Logistic regression curve representing an estimate of the probability for successful recanalization of occluded vessels by intravenous thrombolysis (IVT) depending on thrombus length.

(*Stroke*. 2011;42:1775-1777.)

The Importance of Size

Successful Recanalization by Intravenous Thrombolysis in Acute Anterior Stroke Depends on Thrombus Length

Christian H. Riedel, MD; Philip Zimmermann, MD; Ulf Jensen-Kondering, MD; Robert Stingele, MD; Günther Deuschl, MD; Olav Jansen, MD

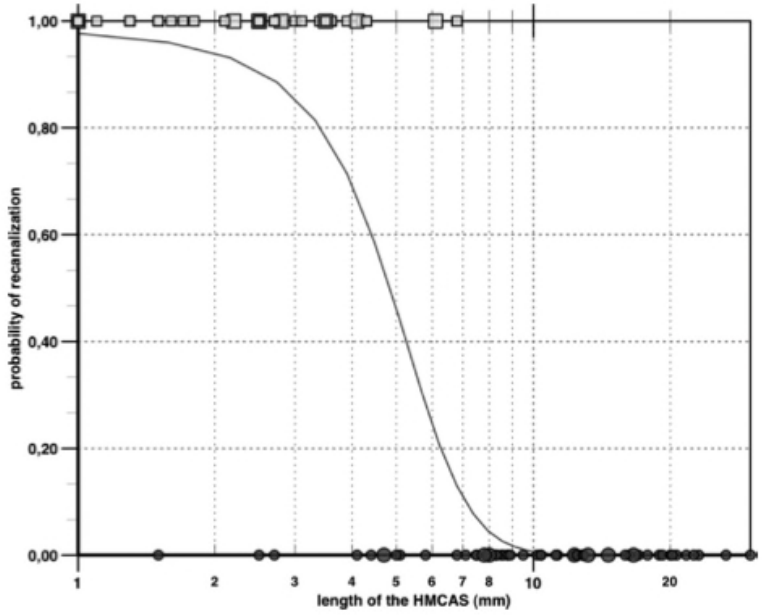


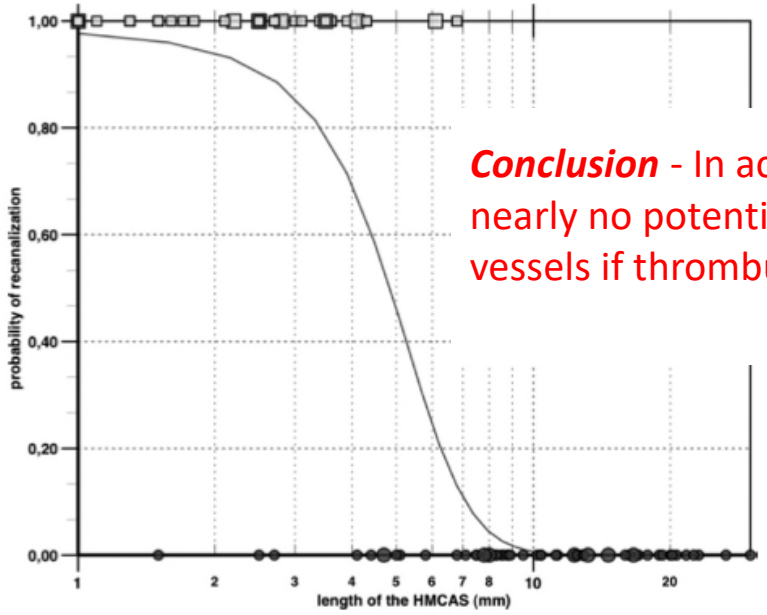
Figure 1. Logistic regression curve representing an estimate of the probability for successful recanalization of occluded vessels by intravenous thrombolysis (IVT) depending on thrombus length.

(*Stroke*. 2011;42:1775-1777.)

The Importance of Size

Successful Recanalization by Intravenous Thrombolysis in Acute Anterior Stroke Depends on Thrombus Length

Christian H. Riedel, MD; Philip Zimmermann, MD; Ulf Jensen-Kondering, MD; Robert Stingele, MD; Günther Deuschl, MD; Olav Jansen, MD



Conclusion - In acute MCA stroke, IV tPA has nearly no potential to recanalize occluded vessels if thrombus length exceeds 8mm

(*Stroke*. 2011;42:1775-1777.)

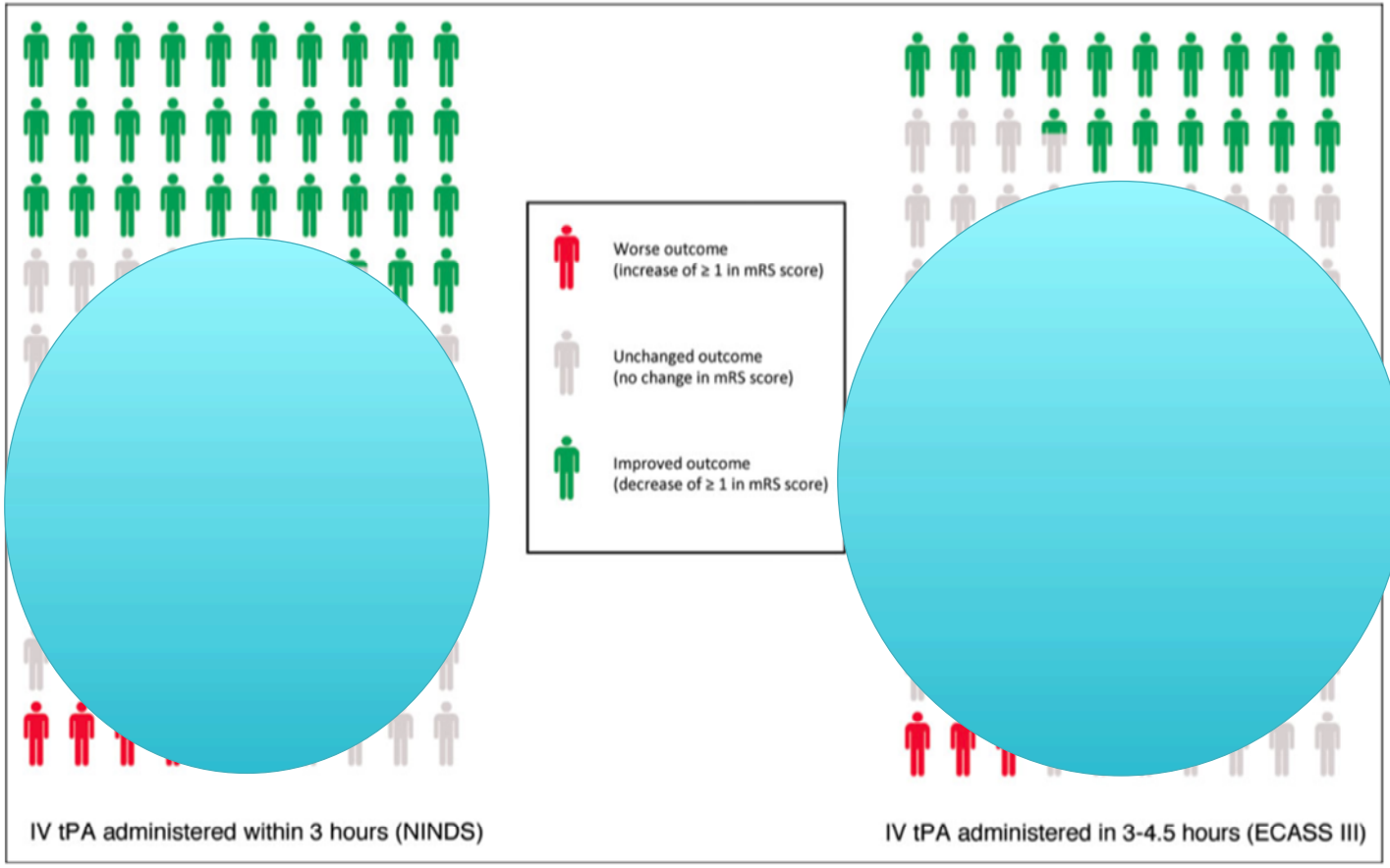
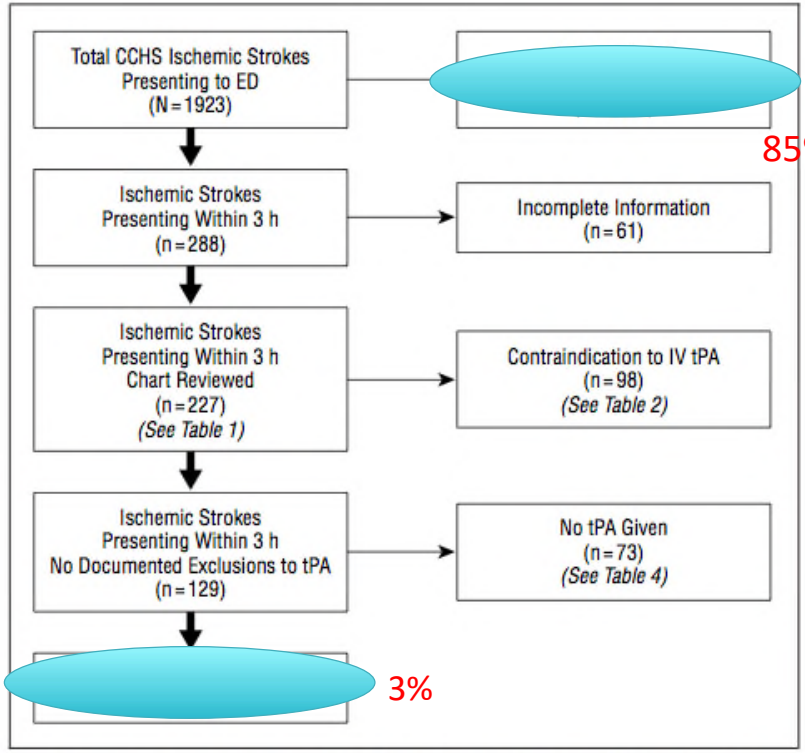


Figure 3. Number needed to treat to benefit and harm per 100 patients treated with intravenous recombinant tissue-type plasminogen activator (IV tPA) for acute ischemic stroke in the <3-hour versus 3- to 4.5-hour time windows.[24] mRS indicates modified Rankin scale; NINDS, National Institute of Neurologic Disorders and Stroke; ECASS-III, European Cooperative Acute Stroke Study-III.

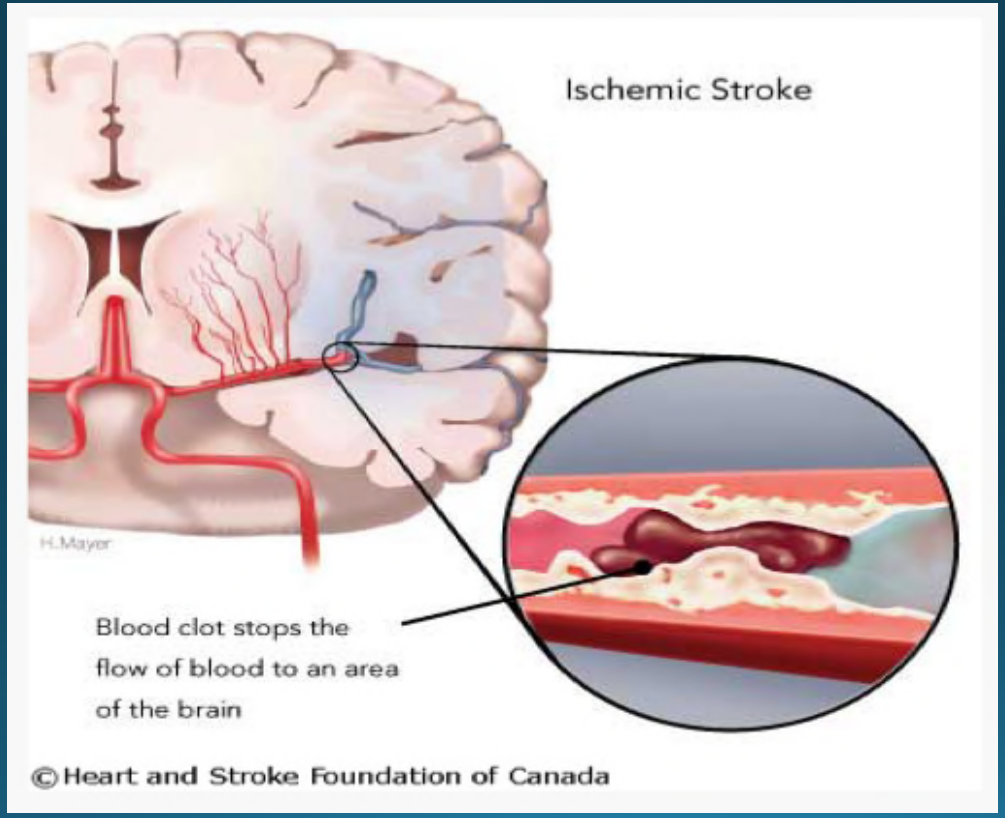
Neurohospitalist. 2015 Jul; 5(3): 101–109.



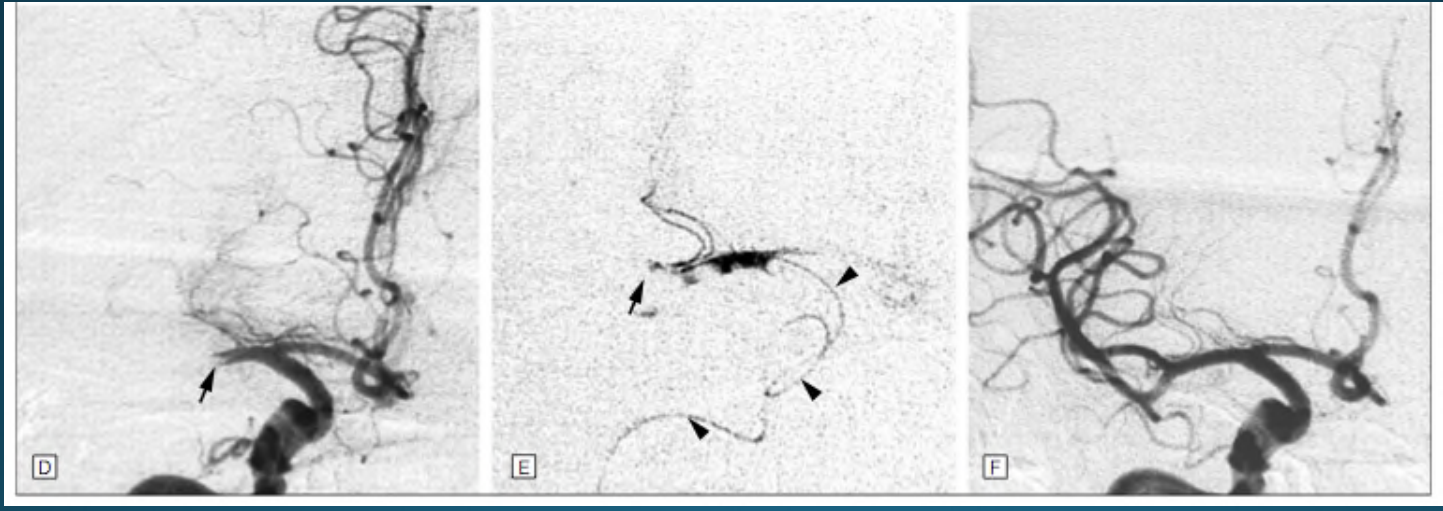
Stroke admissions to the Cleveland Clinic Health System (CCHS) from June 15, 1999, to June 15, 2000. ED indicates emergency department; IV, intravenous; tPA, tissue plasminogen activator; and asterisk, the 56 patients included 9 patients treated with intra-arterial tPA.

Arch Neurol. 2004;61:346-350

Wouldn’t it be better if we could target our therapies?



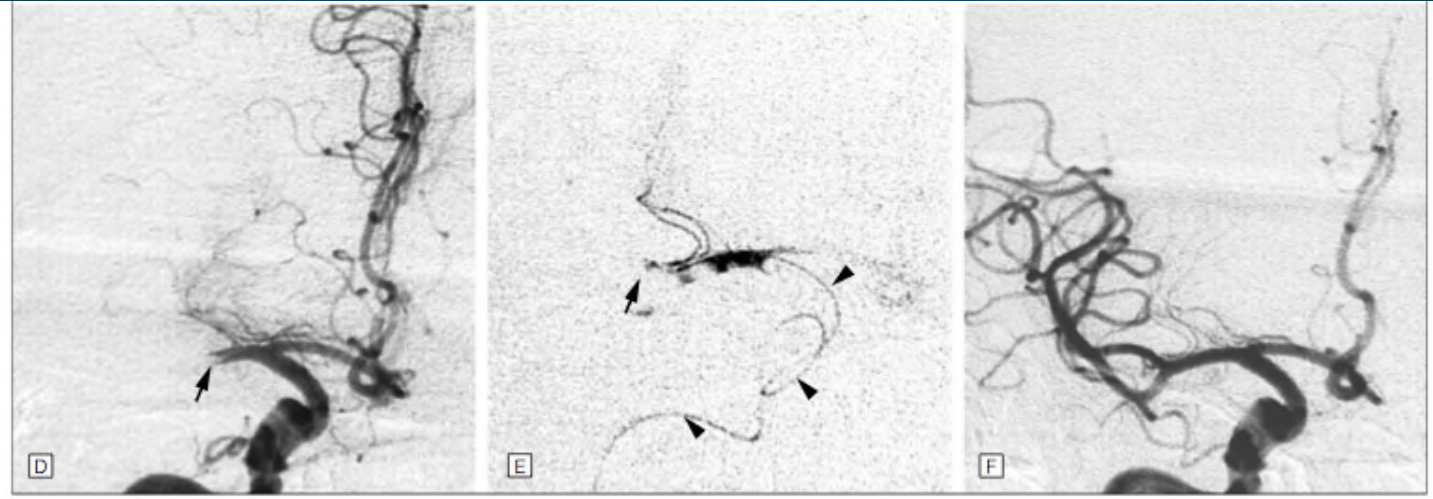
Not really a new idea….



Vol. 167, No. 14 1705

THROMBOLYSIS WITH FIBRINOLYSIN IN CEREBRAL ARTERIAL OCCLUSION

Bernard J. Sussman, M.D.
and
Thomas S. P. Fitch, M.D., Plainfield, N. J.

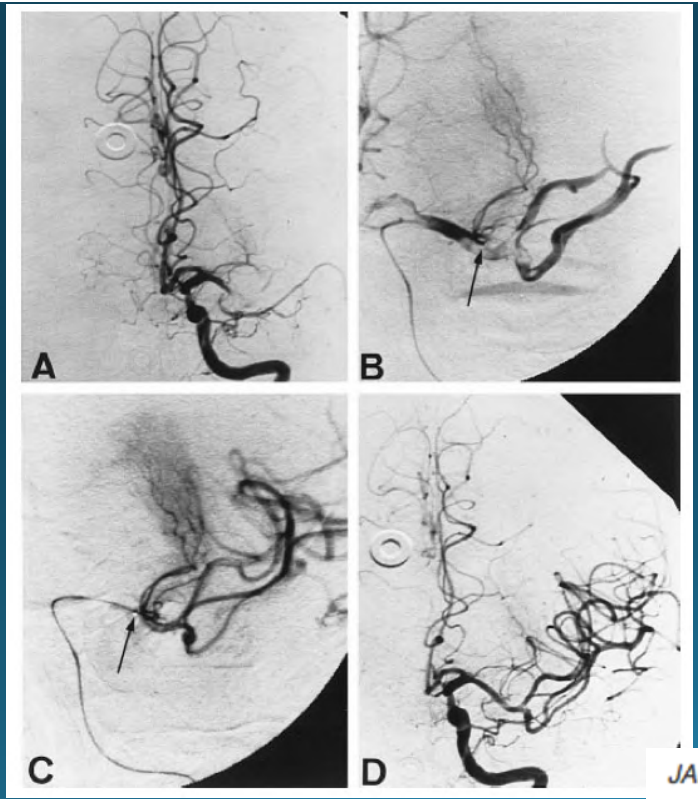


67(14):1705-1709.

Intra-arterial Prourokinase for Acute Ischemic Stroke

The PROACT II Study: A Randomized Controlled Trial FREE

Anthony Furlan, MD; Randall Higashida, MD; Lawrence Wechsler, MD; Michael Gent, DSc; Howard Rowley, MD; Carlos Kase, MD; Michael Pessin, MD; Arvind Ahuja, MD; Fred Callahan, MD; Wayne M. Clark, MD; Frank Silver, MD; Frank Rivera, MD;



JAMA. 1999;282(21):2003-2011.

Intra-arterial Prourokinase for Acute Ischemic Stroke

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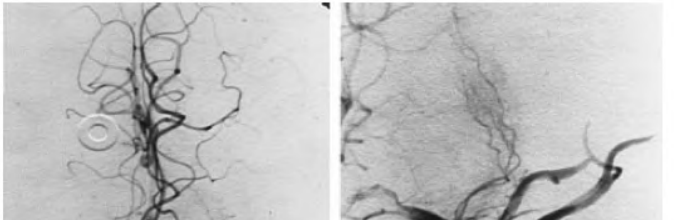
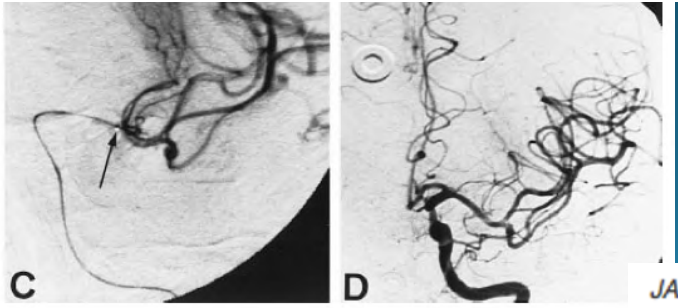


Conclusion – Despite increased SICH (~10%), IA r-proUK within 6 hrs of MCA stroke significantly improved clinical outcome at 90 days



JAMA. 1999;282(21):2003-2011.

AHA/ASA Guideline

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

1. Initial treatment with intra-arterial thrombolysis is beneficial for carefully selected patients with major ischemic strokes of <6 hours' duration caused by occlusions of the MCA.	I	B-R

AHA/ASA Guideline

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

1. Initial treatment with intra-arterial thrombolysis is beneficial for carefully selected patients with major ischemic strokes of <6 hours' duration caused by occlusions of the MCA.	I	B-R
2. Regarding the previous recommendation about intra-arterial thrombolysis, these data are derived from clinical trials that no longer reflect current practice, including the use of fibrinolytic drugs that are not available. A clinically beneficial dose of intra-arterial alteplase is not established, and alteplase does not have US Food and Drug Administration approval for intra-arterial use. As a consequence, mechanical thrombectomy with stent retrievers is recommended over intra-arterial thrombolysis as first-line therapy.	I	C-EO

Powers et al 2018 Guidelines for Management of Acute Ischemic Stroke

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

2. Intra-arterial fibrinolysis initiated within 6 hours of stroke onset in carefully selected patients who have contraindications to the use of IV alteplase might be considered, but the consequences are unknown.	IIb	C-EO

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

2. Intra-arterial fibrinolysis initiated within 6 hours of stroke onset in carefully selected patients who have contraindications to the use of IV alteplase might be considered, but the consequences are unknown.	**IIb**	**C-EO**
14. Use of salvage technical adjuncts including intra-arterial thrombolysis may be reasonable to achieve mTICI 2b/3 angiographic results. In THRACE, an intra-arterial lytic [alteplase] was used to a maximum dose of 0.3 mg/kg and allowed to establish goal reperfusion, only after mechanical thrombectomy was attempted.	**IIb**	**C-LD**

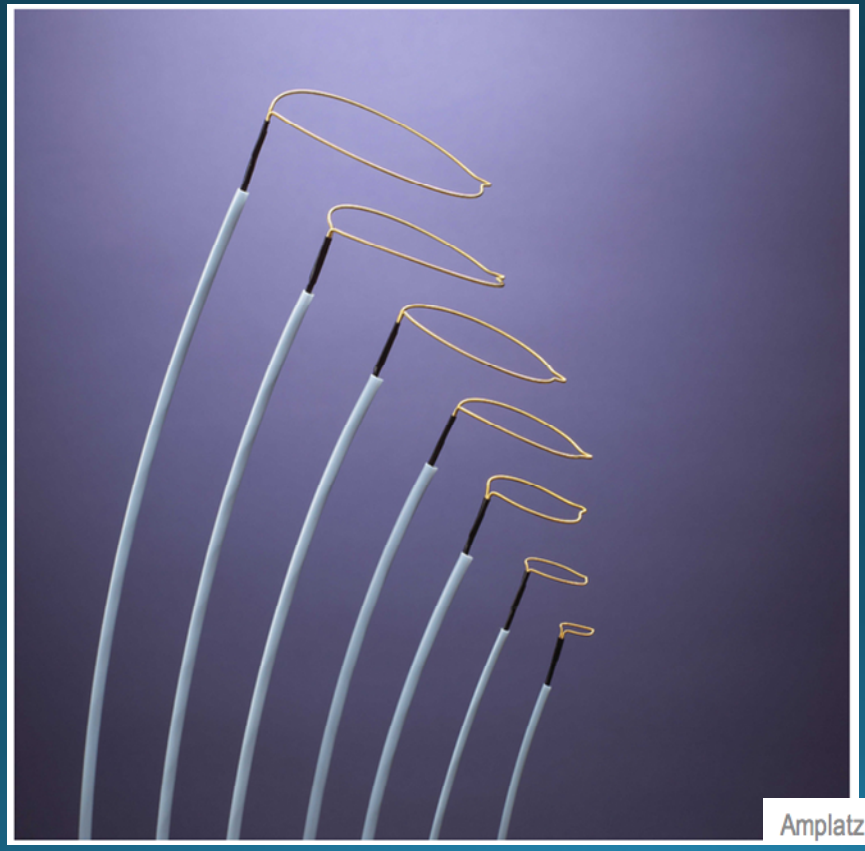
AHA/ASA Guideline

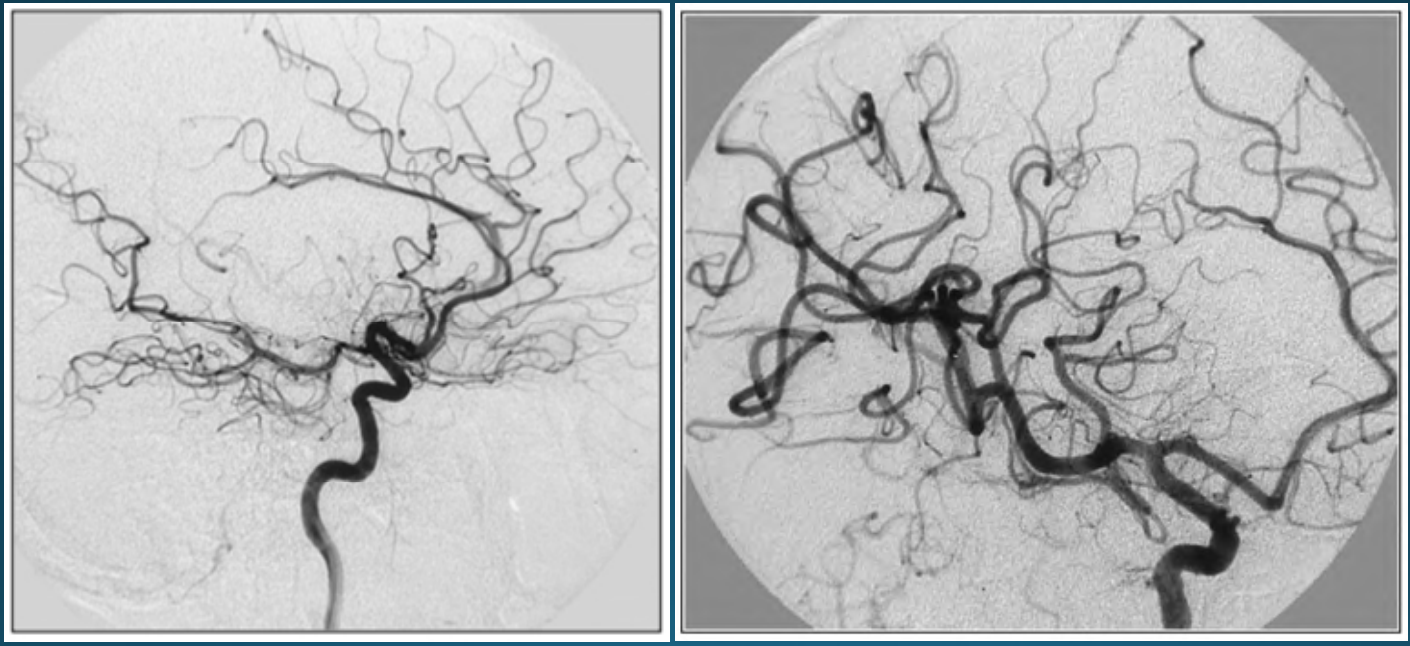
Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

1. Mechanical thrombectomy with stent retrievers is recommended over intra-arterial fibrinolysis as first-line therapy.	I	C-EO

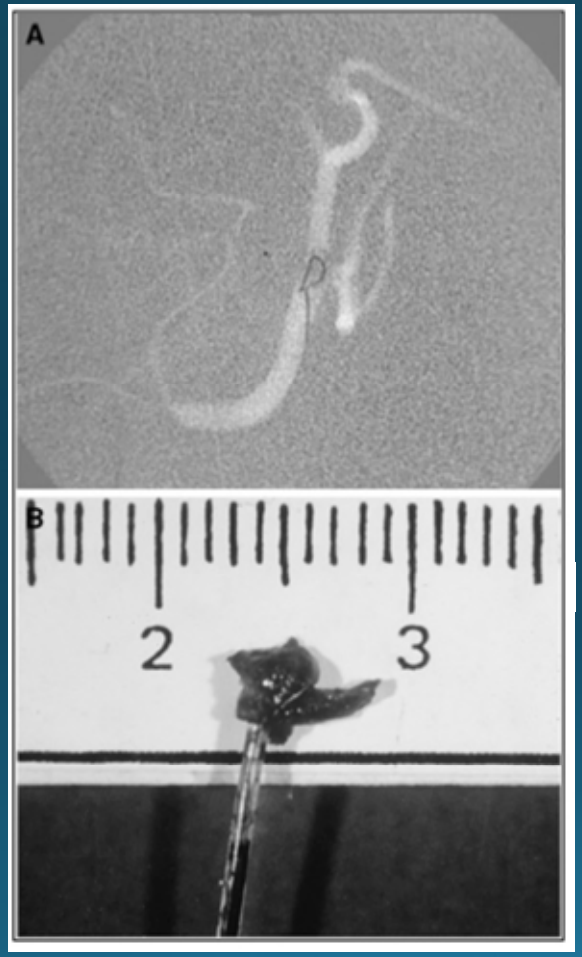
Thrombolysis without tPA…

Mechanical Thrombectomy

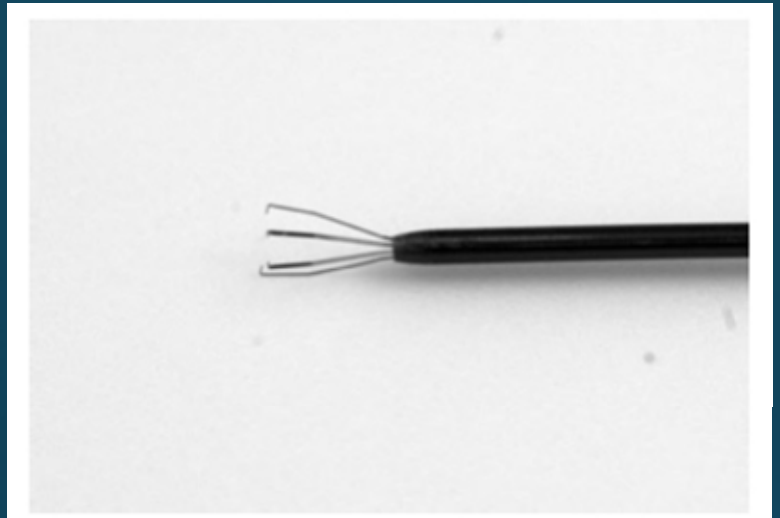




Neurosurgery. 46(6):1529-1531, June 2000.



Neurosurgery. 46(6):1529-1531, June 2000.




A
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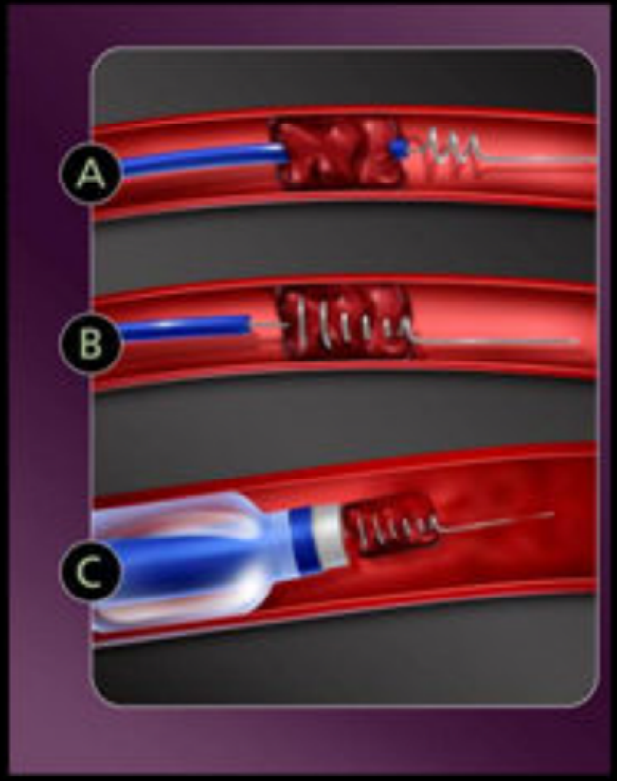
Kerber | AJNR 28 | May 2007 | www.ajnr.org

APM0119/A/2351, 2006-02


A
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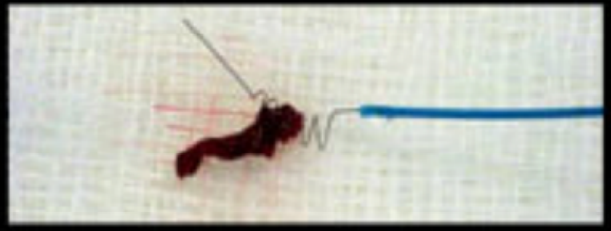

Merci Retriever Devices

X5, X6
Five helical loops, conical, X6 more resistant to stretching

L5, L6
Helical loops, cylindrical, arcading filaments

K-mini
Helical loops with counter-twist, cylindrical, smaller diameter

Safety and Efficacy of Mechanical Embolectomy in Acute Ischemic Stroke

Results of the MERCI Trial

Wade S. Smith, MD, PhD; Gene Sung, MD; Sidney Starkman, MD; Jeffrey L. Saver, MD; Chelsea S. Kidwell, MD; Y. Pierre Gobin, MD; Helmi L. Lutsep, MD; Gary M. Nesbit, MD; Thomas Grobelny, MD; Marilyn M. Rymer, MD; Isaac E. Silverman, MD; Randall T. Higashida, MD; Ronald F. Budzik, MD; Michael P. Marks, MD; for the MERCI Trial Investigators

- Revascularization 48% (vs 18% spontaneous historical control)
- SICH 7.8% (similar to NINDs, less than PROACT 10%)
- Good outcome 46% if revascularized vs 10% non-revascularized.

Stroke. 2005;36:1432-1440

Safety and Efficacy of Mechanical Embolectomy in Acute Ischemic Stroke

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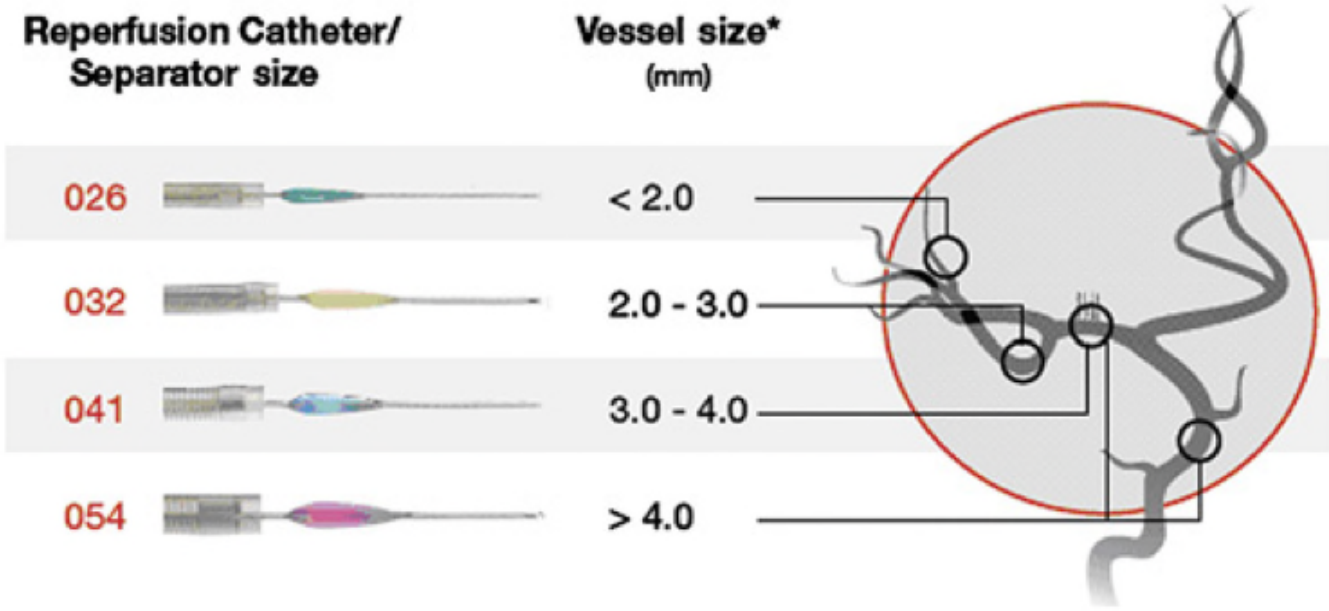
FDA cleared in **2004** for **restoring blood flow** in patients with acute stroke **up to 8 hrs** who:

- are ineligible for IV tPA
- IV tPA treatment has failed

Stroke. 2005;36:1432-1440

www.penumbrainc.com

Reperfusion Catheter/ Separator size	Vessel size* (mm)
026	< 2.0
032	2.0 - 3.0
041	3.0 - 4.0
054	> 4.0



The Penumbra Pivotal Stroke Trial

Safety and Effectiveness of a New Generation of Mechanical Devices for Clot Removal in Intracranial Large Vessel Occlusive Disease

The Penumbra Pivotal Stroke Trial Investigators

- 81.6 % vessel revascularization
- SICH 11.2%
- Good outcome 25% revascularized (vs 10%)

Stroke. 2009;40:2761-2768

The Penumbra Pivotal Stroke Trial

Safety and Effectiveness of a New Generation of Mechanical Devices for Clot Removal in Intracranial Large Vessel Occlusive Disease

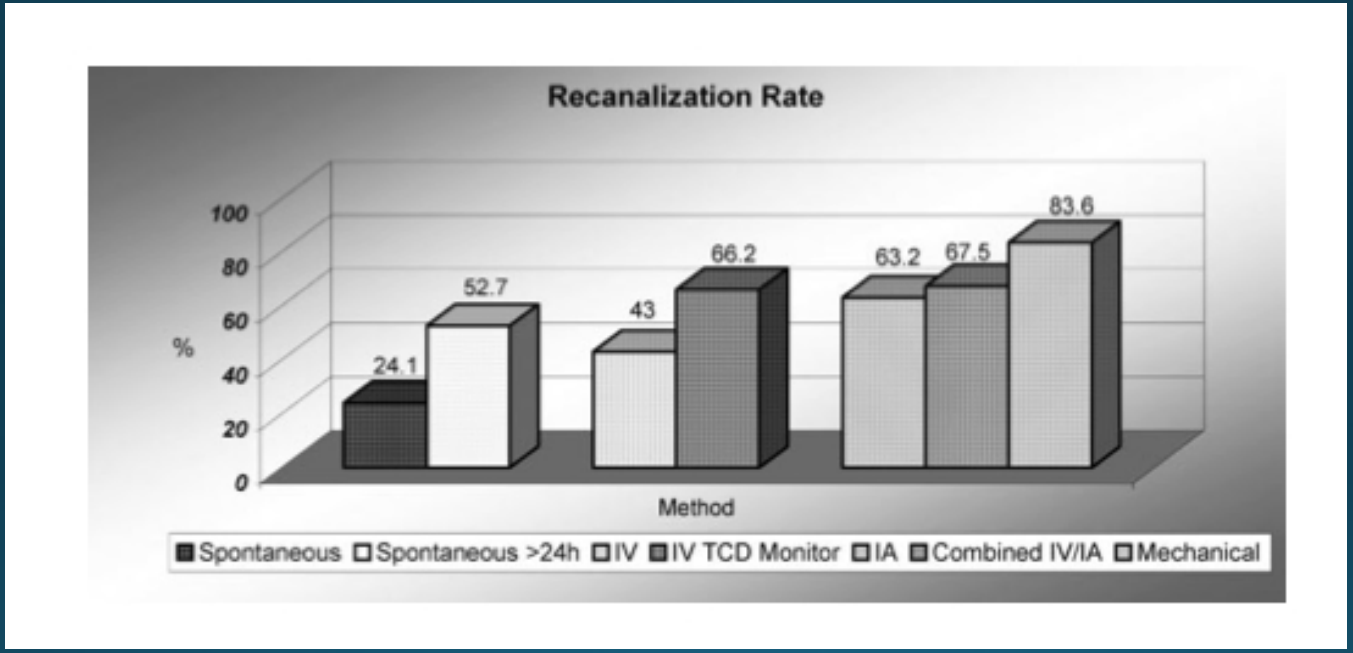
The Penumbra Pivotal Stroke Trial Investigators

FDA cleared in **2008** for restoring blood flow in patients with acute stroke up to 8 hrs who:

- are ineligible for IV tPA
- IV tPA treatment has failed

Stroke. 2009;40:2761-2768

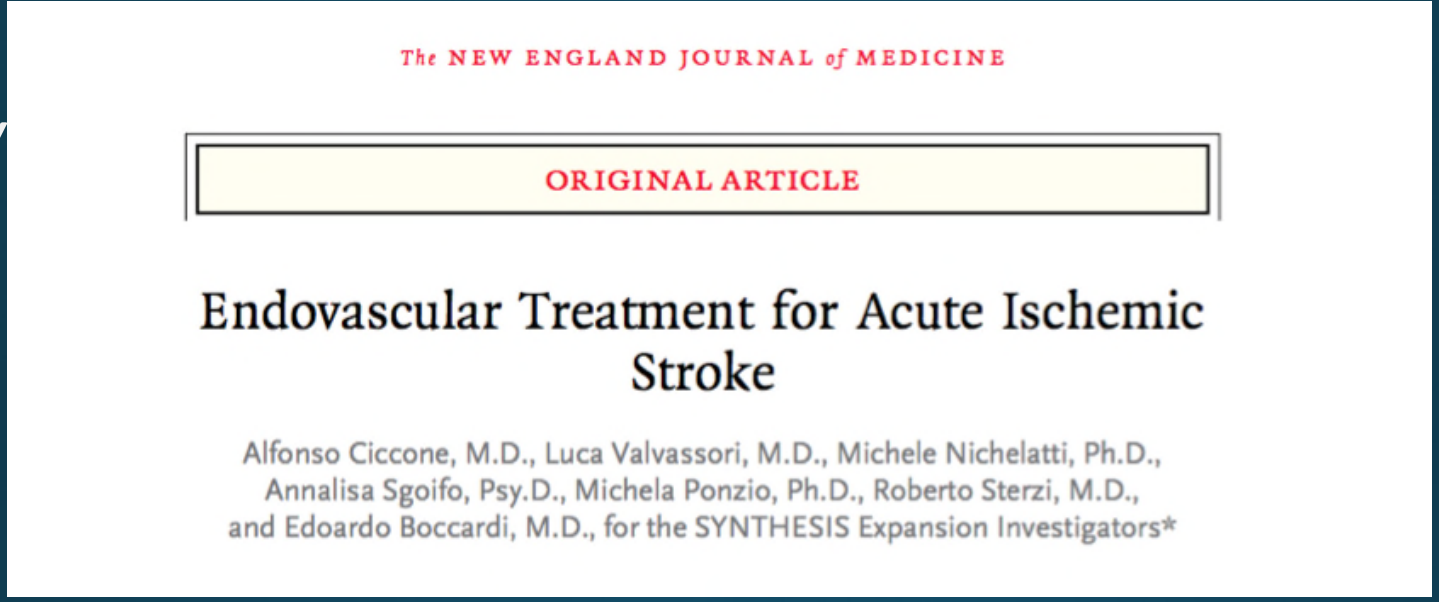
Collective Progress…



The Impact of Recanalization on Ischemic Stroke Outcome : A Meta-Analysis
Joung-Ho Rha and Jeffrey L. Saver
Stroke. 2007;38:967-973

Putting it all together…

SY



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Treatment for Acute Ischemic Stroke

Alfonso Ciccone, M.D., Luca Valvassori, M.D., Michele Nichelatti, Ph.D., Annalisa Sgoifo, Psy.D., Michela Ponzio, Ph.D., Roberto Sterzi, M.D., and Edoardo Boccardi, M.D., for the SYNTHESIS Expansion Investigators*

SYNTHESIS : IV tPA vs Endovascular therapy

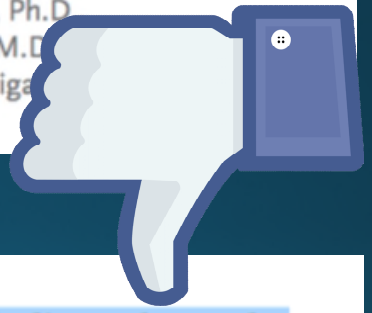
SY

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

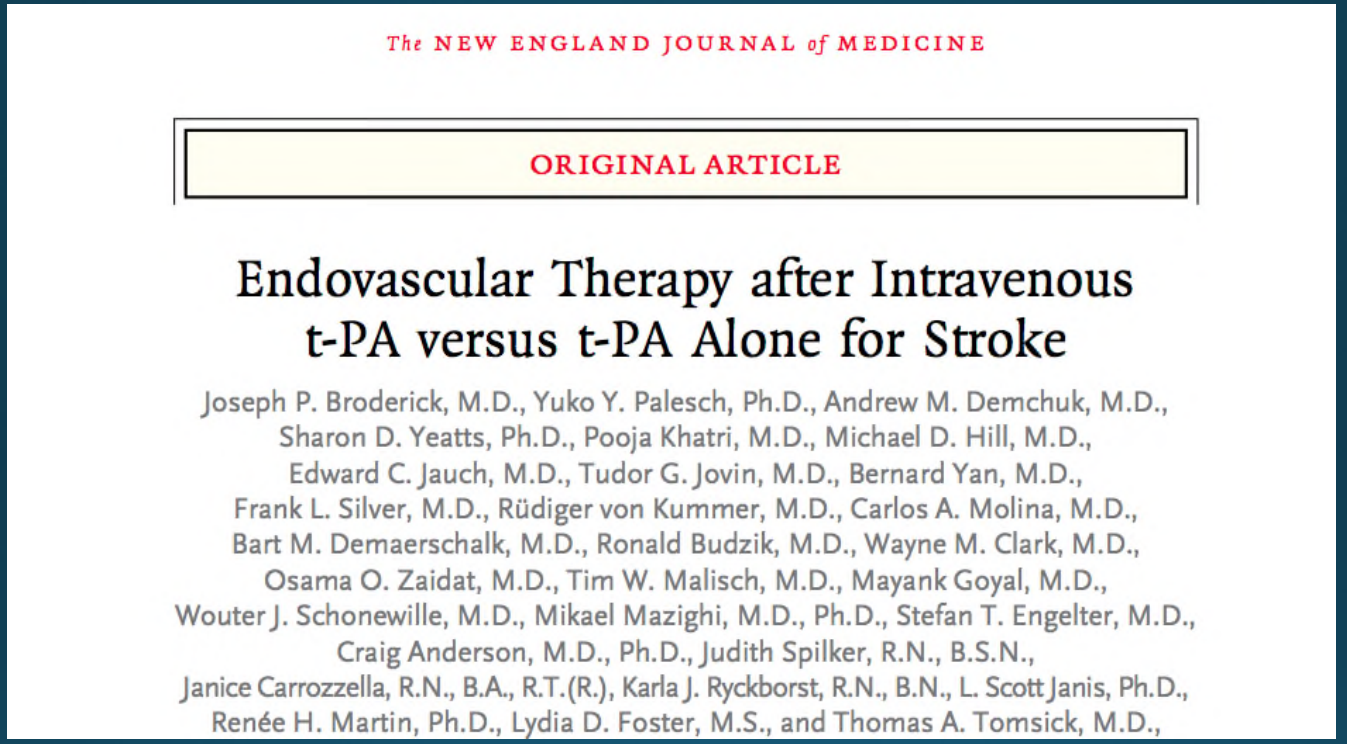
Endovascular Treatment for Acute Ischemic Stroke

Alfonso Ciccone, M.D., Luca Valvassori, M.D., Michele Nichelatti, Ph.D.,
Annalisa Sgoifo, Psy.D., Michela Ponzio, Ph.D., Roberto Sterzi, M.D.,
and Edoardo Boccardi, M.D., for the SYNTHESIS Expansion Investiga



CONCLUSIONS

The results of this trial in patients with acute ischemic stroke indicate that endovascular therapy is not superior to standard treatment with intravenous t-PA.



IMS III : IV tPA vs IV tPA plus clot retrieval

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke

CONCLUSIONS

The trial showed similar safety outcomes and no significant difference in functional independence with endovascular therapy after intravenous t-PA, as compared with intravenous t-PA alone. (Funded by the National Institutes of Health and others; ClinicalTrials.gov number, NCT00359424.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke

Chelsea S. Kidwell, M.D., Reza Jahan, M.D., Jeffrey Gornbein, Dr.P.H., Jeffry R. Alger, Ph.D., Val Nenov, Ph.D., Zahra Ajani, M.D., Lei Feng, M.D., Ph.D., Brett C. Meyer, M.D., Scott Olson, M.D., Lee H. Schwamm, M.D., Albert J. Yoo, M.D., Randolph S. Marshall, M.D., Philip M. Meyers, M.D., Dileep R. Yavagal, M.D., Max Wintermark, M.D., Judy Guzy, R.N., Sidney Starkman, M.D., and Jeffrey L. Saver, M.D., for the MR RESCUE Investigators*

MR Rescue : Standard care vs
Standard care + Clot retrieval + Penumbra imaging

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Imaging Selection and Endovascular Treatment for Ischemic St

CONCLUSIONS

A favorable penumbral pattern on neuroimaging did not identify patients who would differentially benefit from endovascular therapy for acute ischemic stroke, nor was embolectomy shown to be superior to standard care. (Funded by the National Institute of Neurological Disorders and Stroke; MR RESCUE ClinicalTrials.gov number, NCT00389467.)

What Happened?

- Most patients treated outside of trials
- Patient recruitment very slow
- Patient selection overly broad
- Assumption that newer approaches would render current standard of care unnecessary
- Confirmation of large vessel occlusion (LVO) not required
- Highly variable endovascular approaches, not utilizing state of the art technology

Moving Forward…

- Improve patient selection through imaging

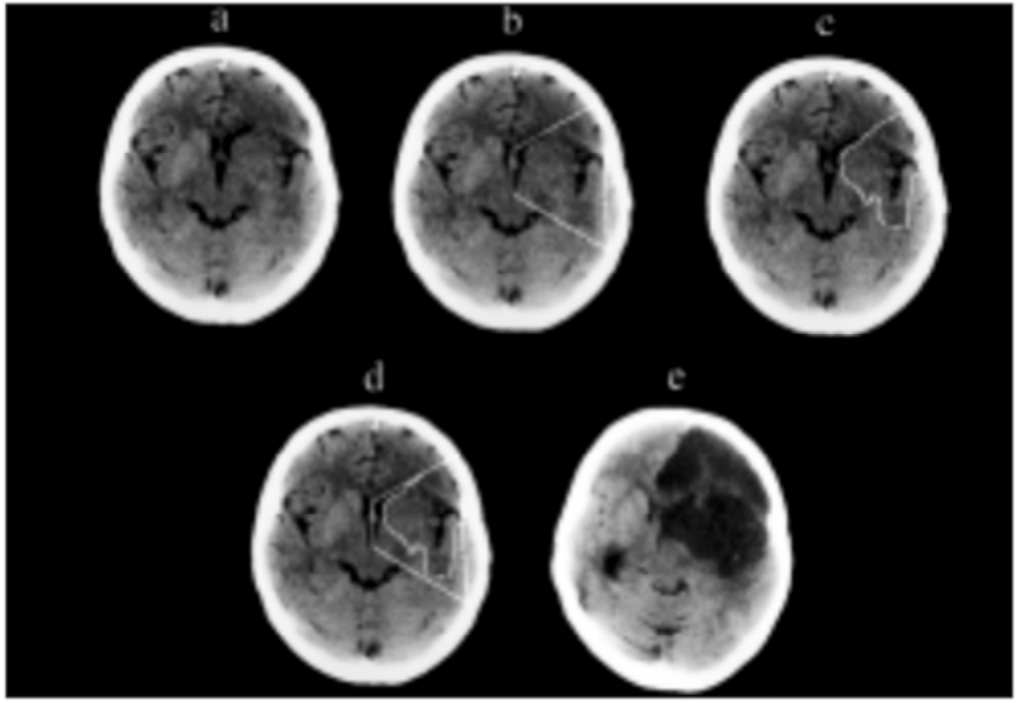
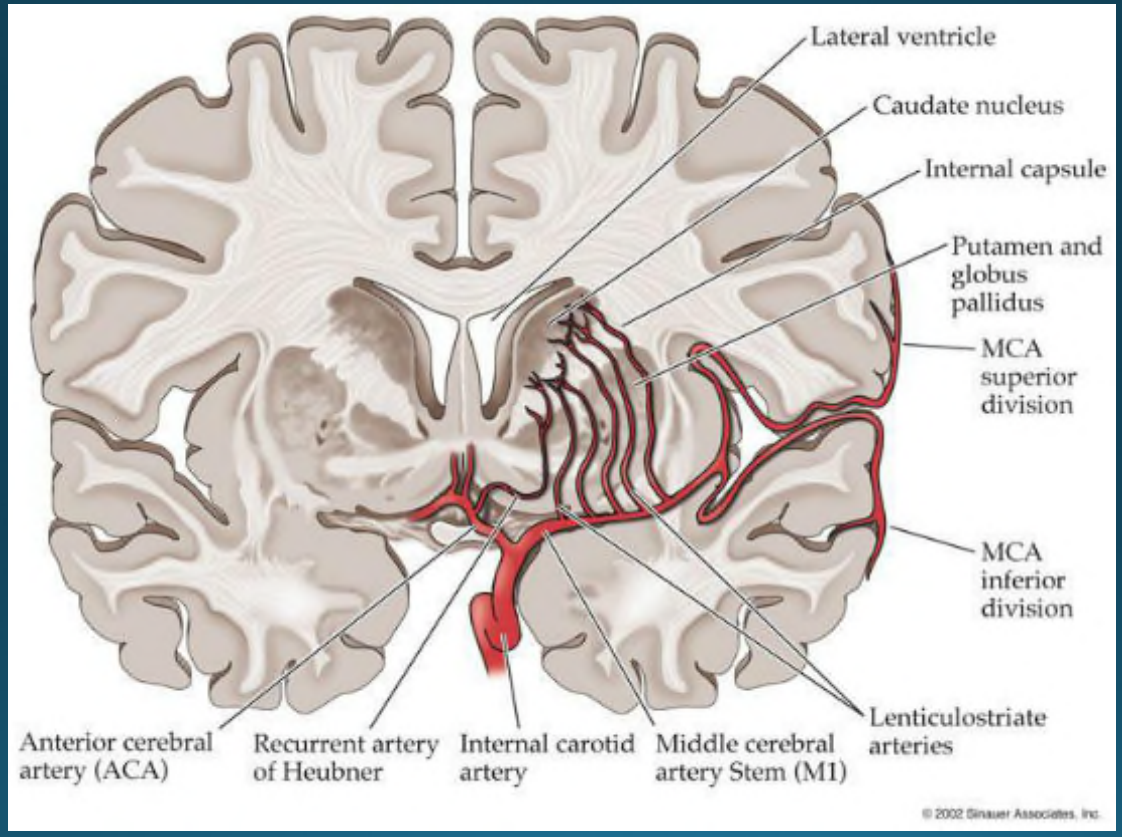
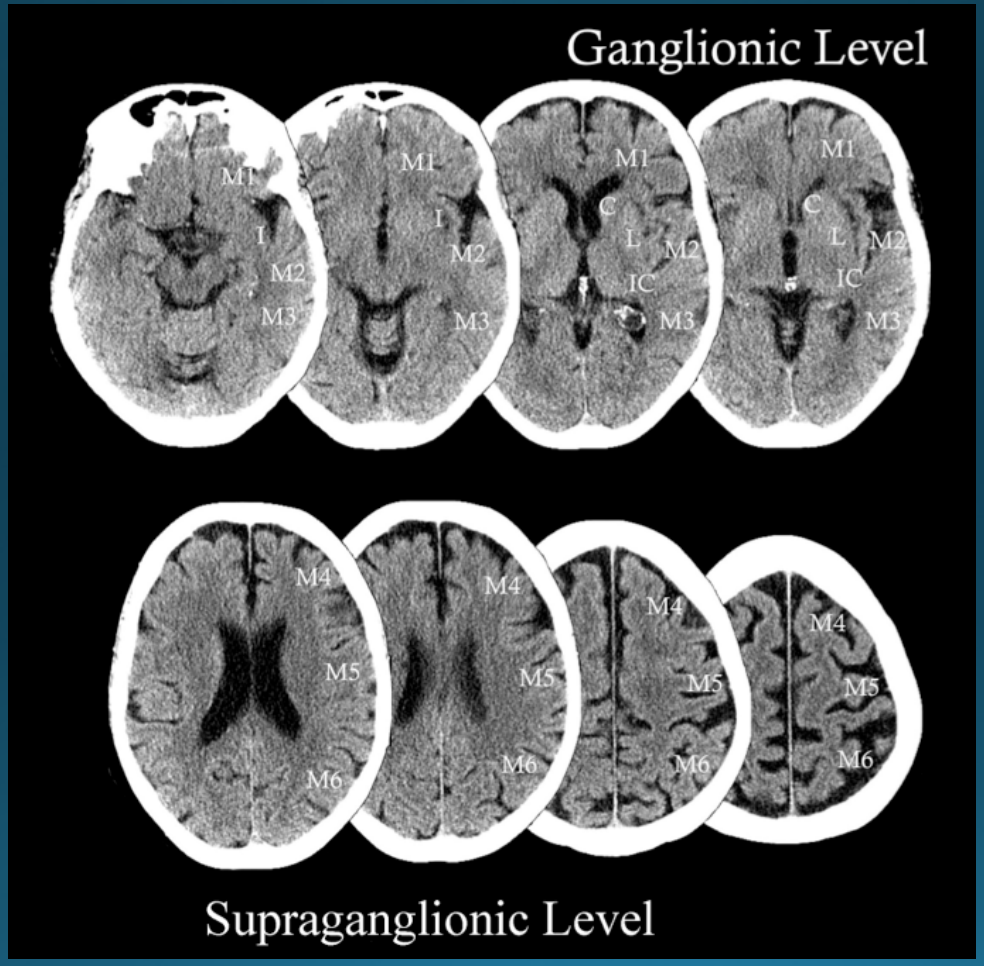


Figure 1: *"ICE" method of estimation of greater than one-third middle cerebral artery territory infarction on initial CT scan: a. Baseline scan; b. Idealized MCA territory (trapezoid) onto baseline scan; c. Closure around area of abnormality; d. Estimate of ratio; e. 24-hour scan.*

Can. J. Neurol. Sci. 2006; 33: 200-204


Lateral ventricle
Caudate nucleus
Internal capsule
Putamen and globus pallidus
MCA superior division
MCA inferior division
Lenticulostriate arteries
Anterior cerebral artery (ACA)
Recurrent artery of Heubner
Internal carotid artery
Middle cerebral artery Stem (M1)
© 2002 Sinauer Associates, Inc.


Ganglionic Level
M1
I
M2
M3
M1
I
M2
M3
M1
C
L
M2
IC
M3
M1
C
L
M2
IC
M3
M4
M5
M6
M4
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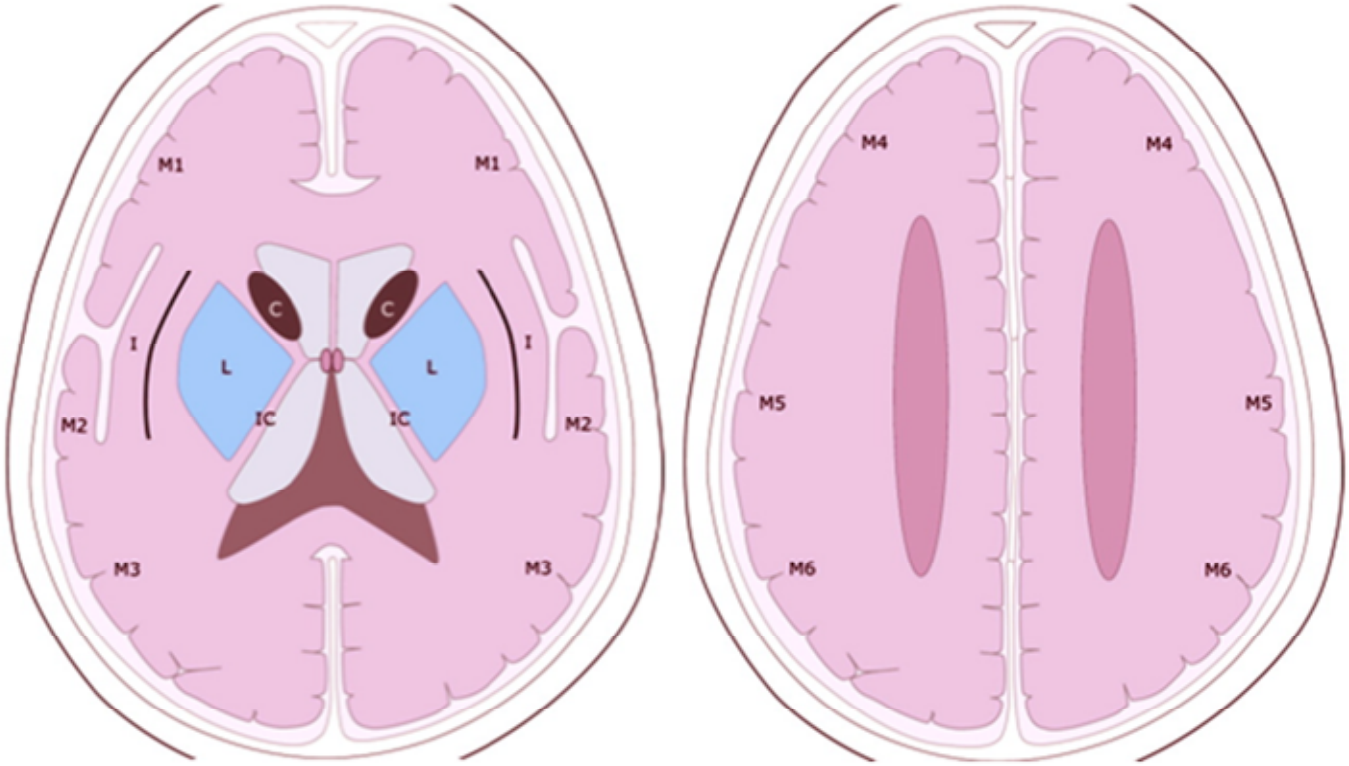
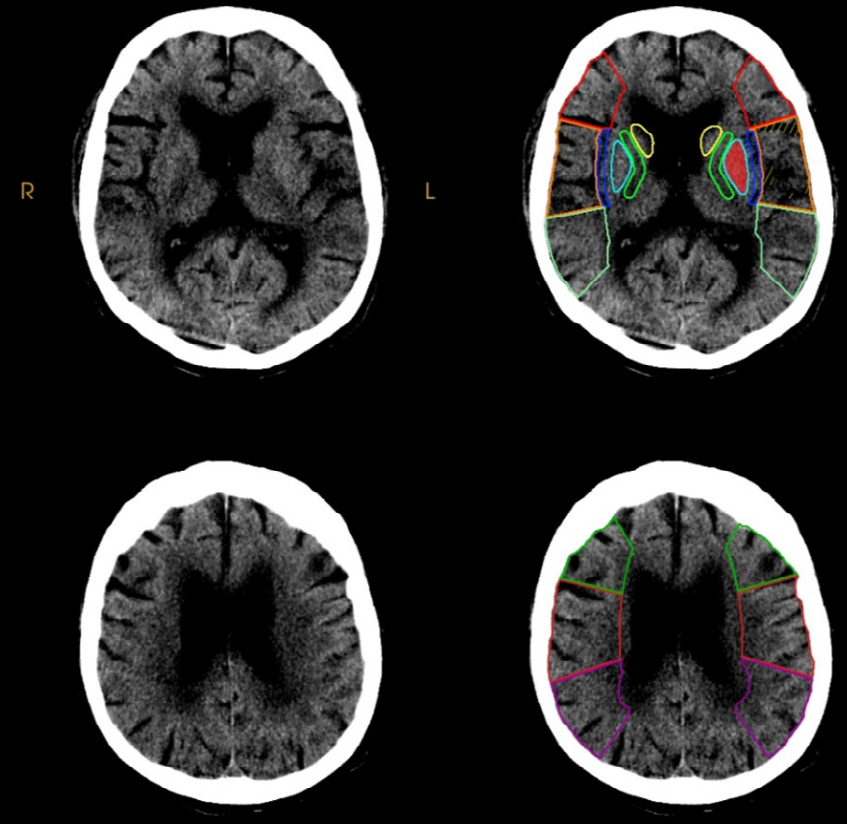
M6
M4
M5
M6
M4
M5
M6
Supraganglionic Level



Srinivasan A et al. Radiographics 2006;26:S75-S95



Hounsfield Units Mean

RIGHT		LEFT	
C	25.2	C	27.0
IC	29.6	IC	29.2
L	34.4	L	32.9
I	30.6	I	29.8
M1	32.4	M1	32.0
M2	31.5	M2	30.0
M3	32.5	M3	32.3
M4	32.1	M4	31.7
M5	30.8	M5	31.1
M6	30.1	M6	31.0

SCORE

9

Auto-generated ASPECTS

unreviewed

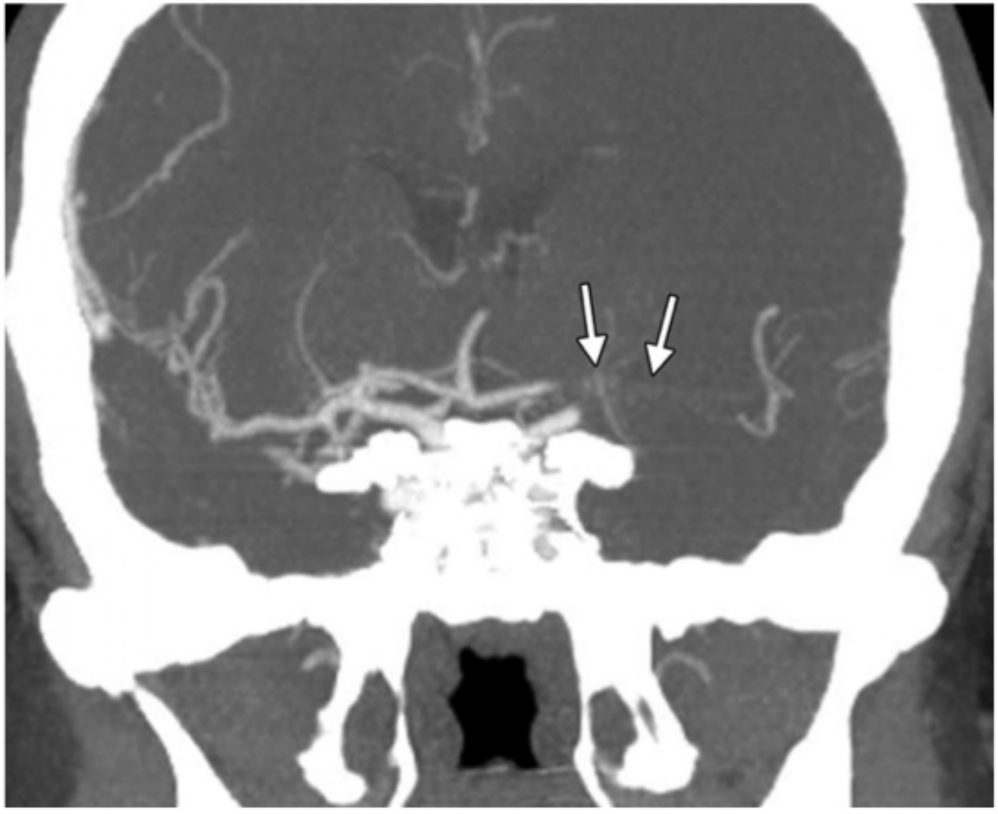
LVO not confirmed

RAPID

Use of Rapid ASPECTS in a setting other than early brain ischemia (within 6 hours) caused by occlusion of the ICA or MCA has not been tested.

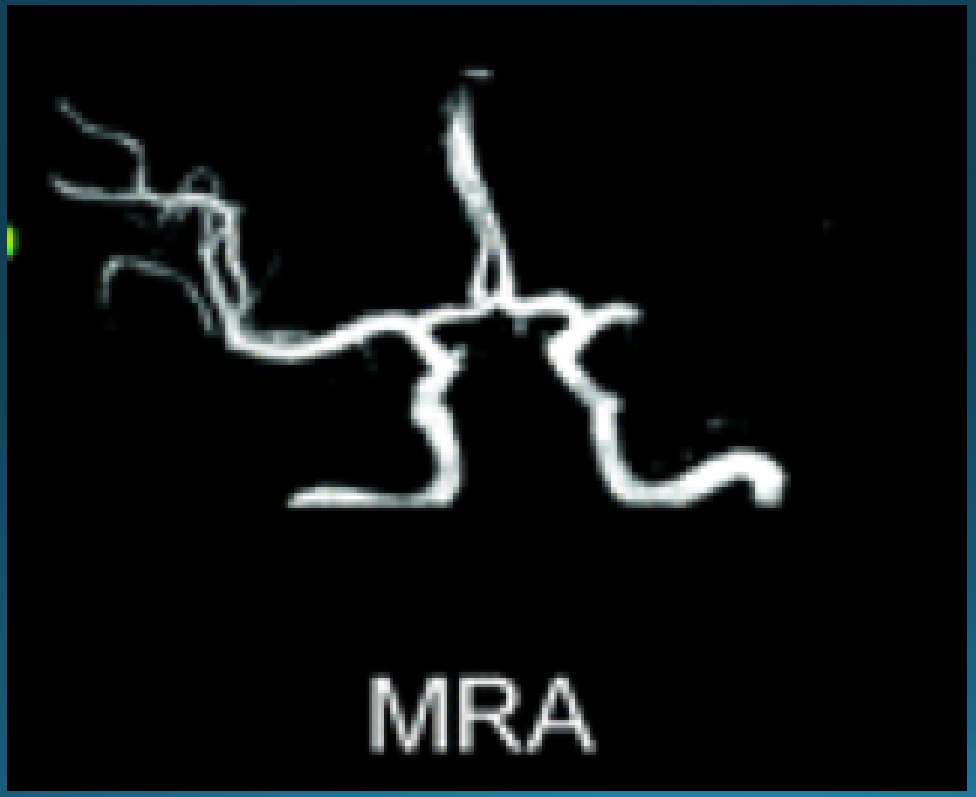
Not for primary diagnosis. For research purposes only.

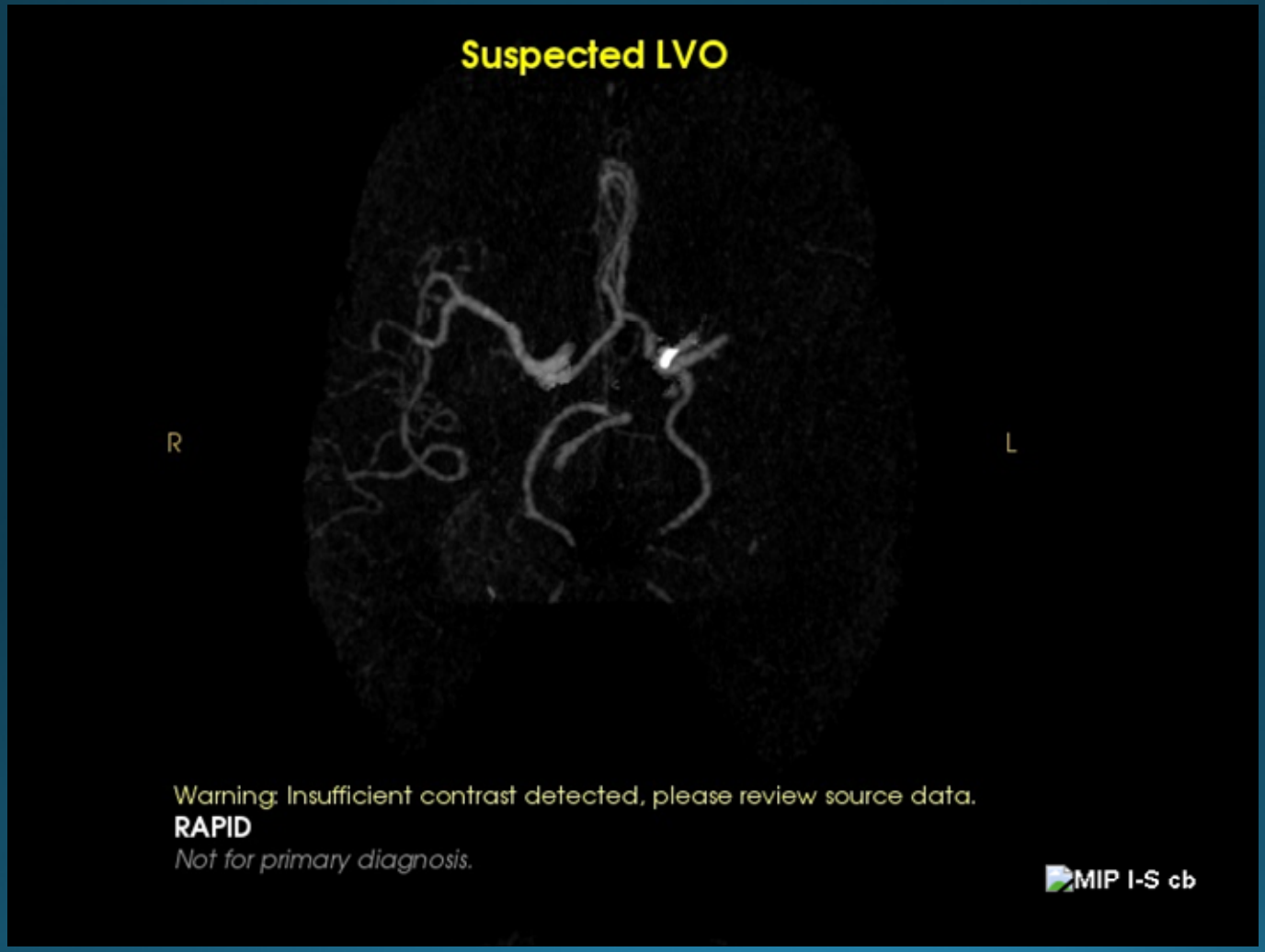
Confirm LVO



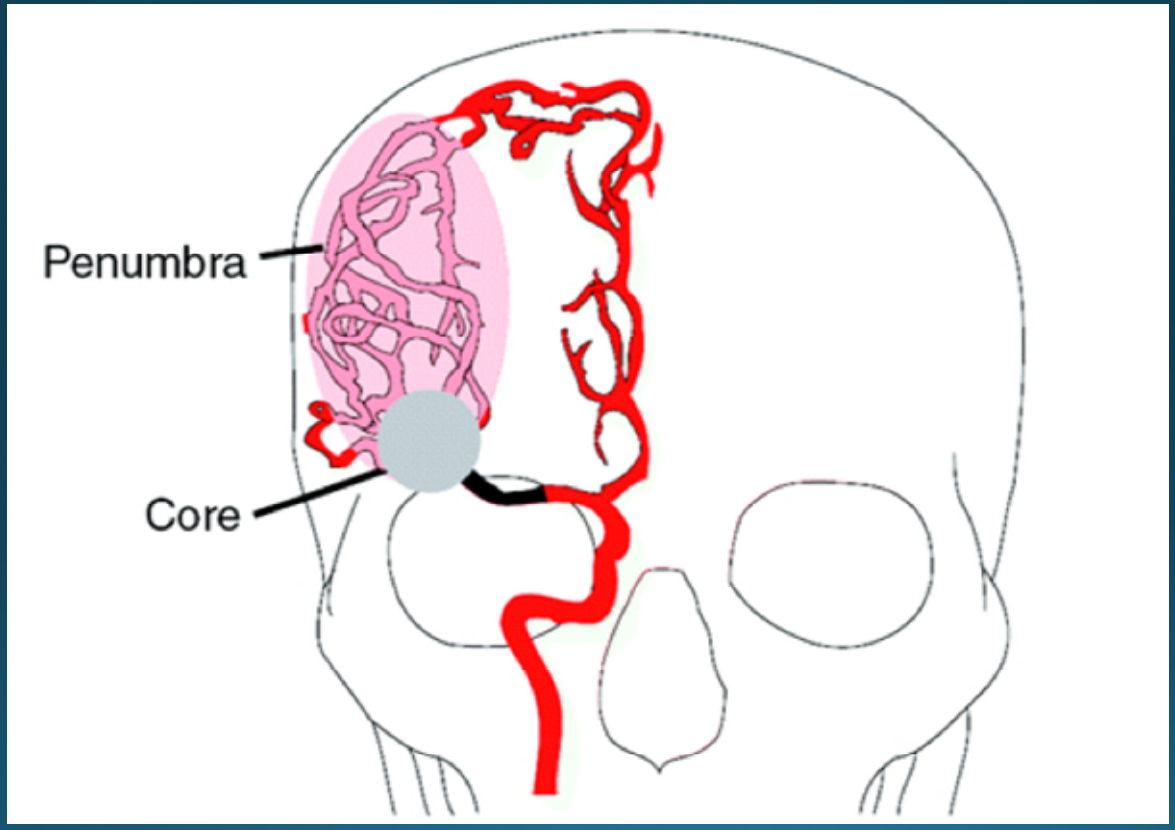
Srinivasan A et al. Radiographics 2006;26:S75-S95

Confirm LVO



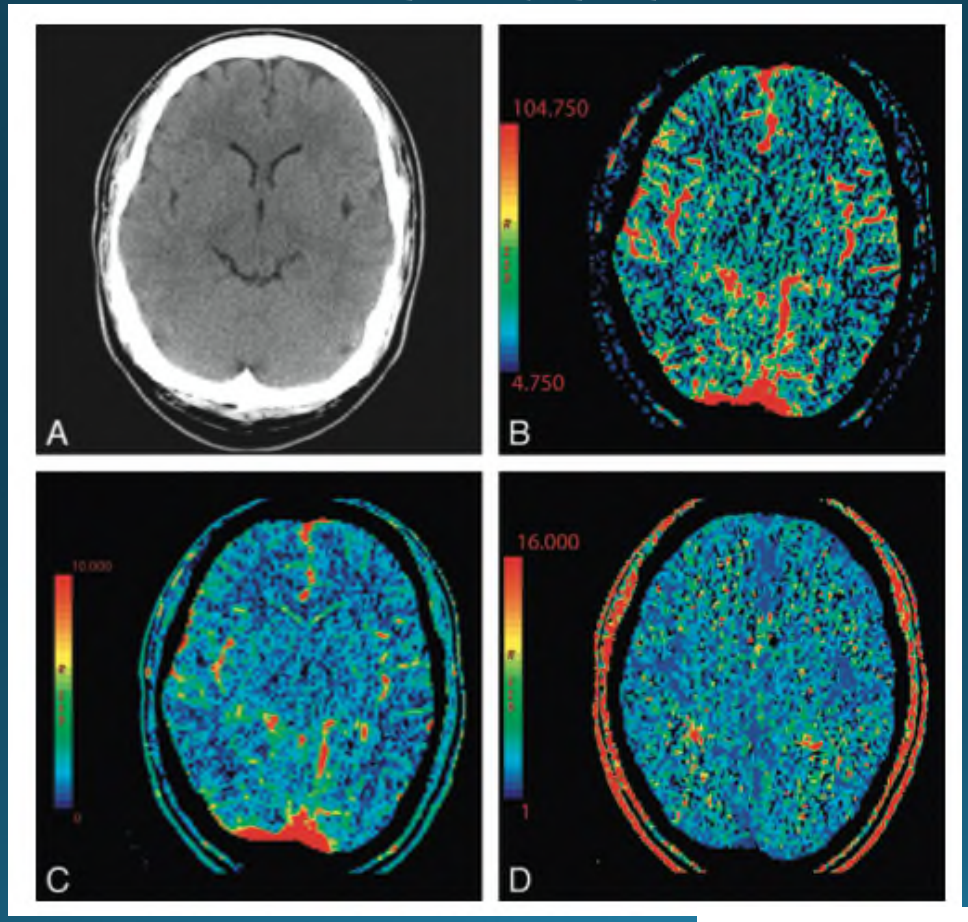

Suspected LVO
R
L
Warning: Insufficient contrast detected, please review source data.
RAPID
Not for primary diagnosis.
MIP I-S cb

“Physiologic” Imaging:

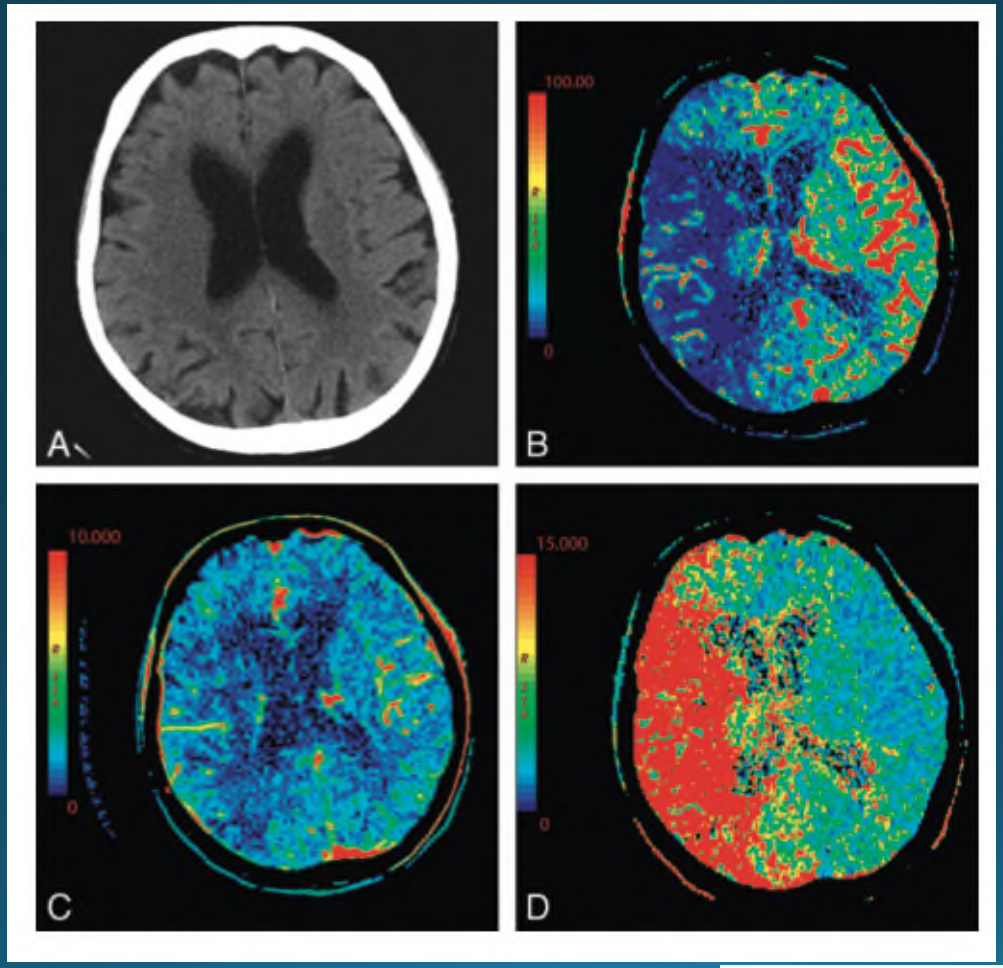


AJNR Am J Neuroradiol 27:728–35 | Apr 2006 | www.ajnr.org

CT-Perfusion



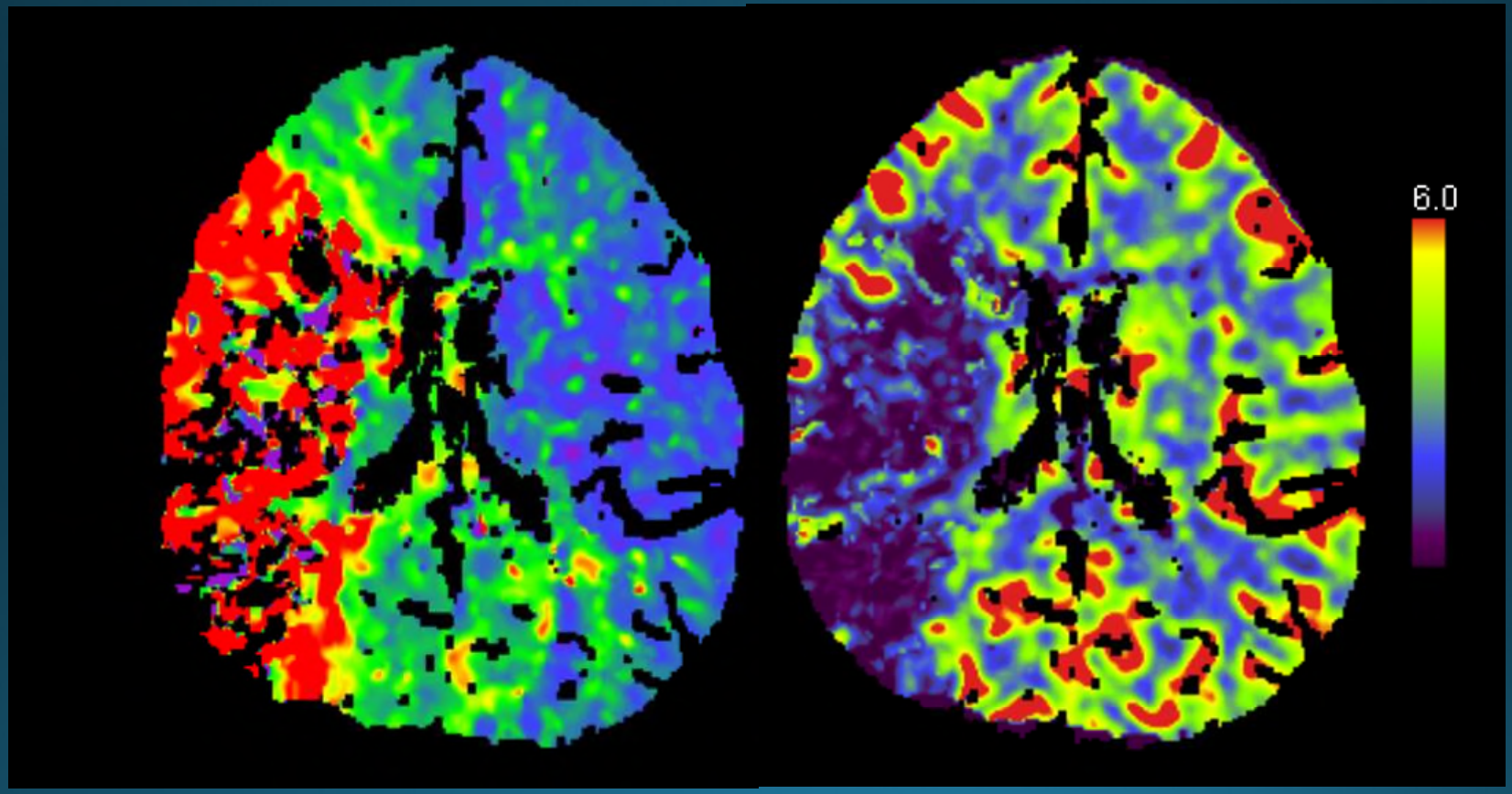
Lui | AJNR 31 | Oct 2010 | www.ajnr.org

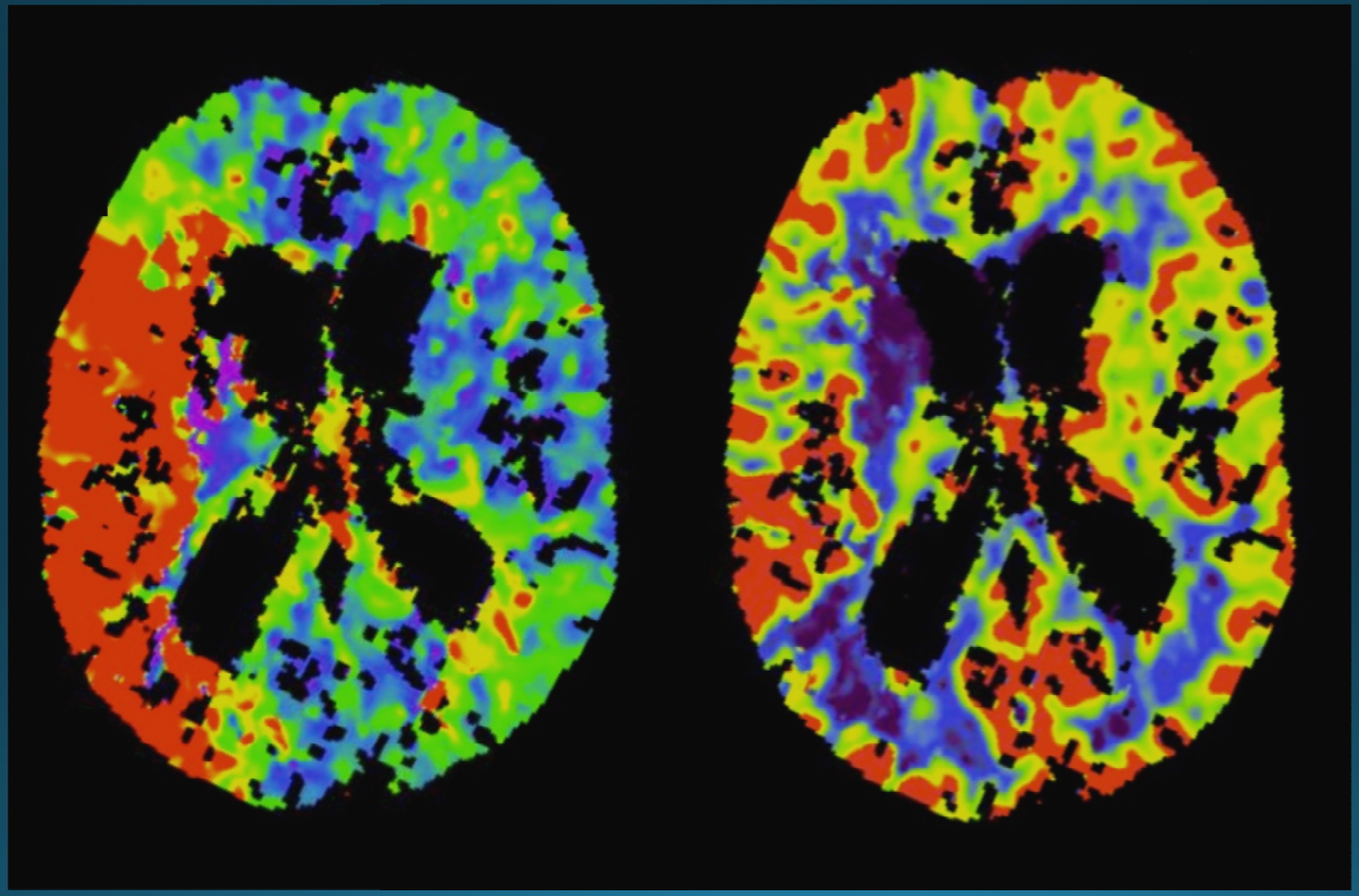


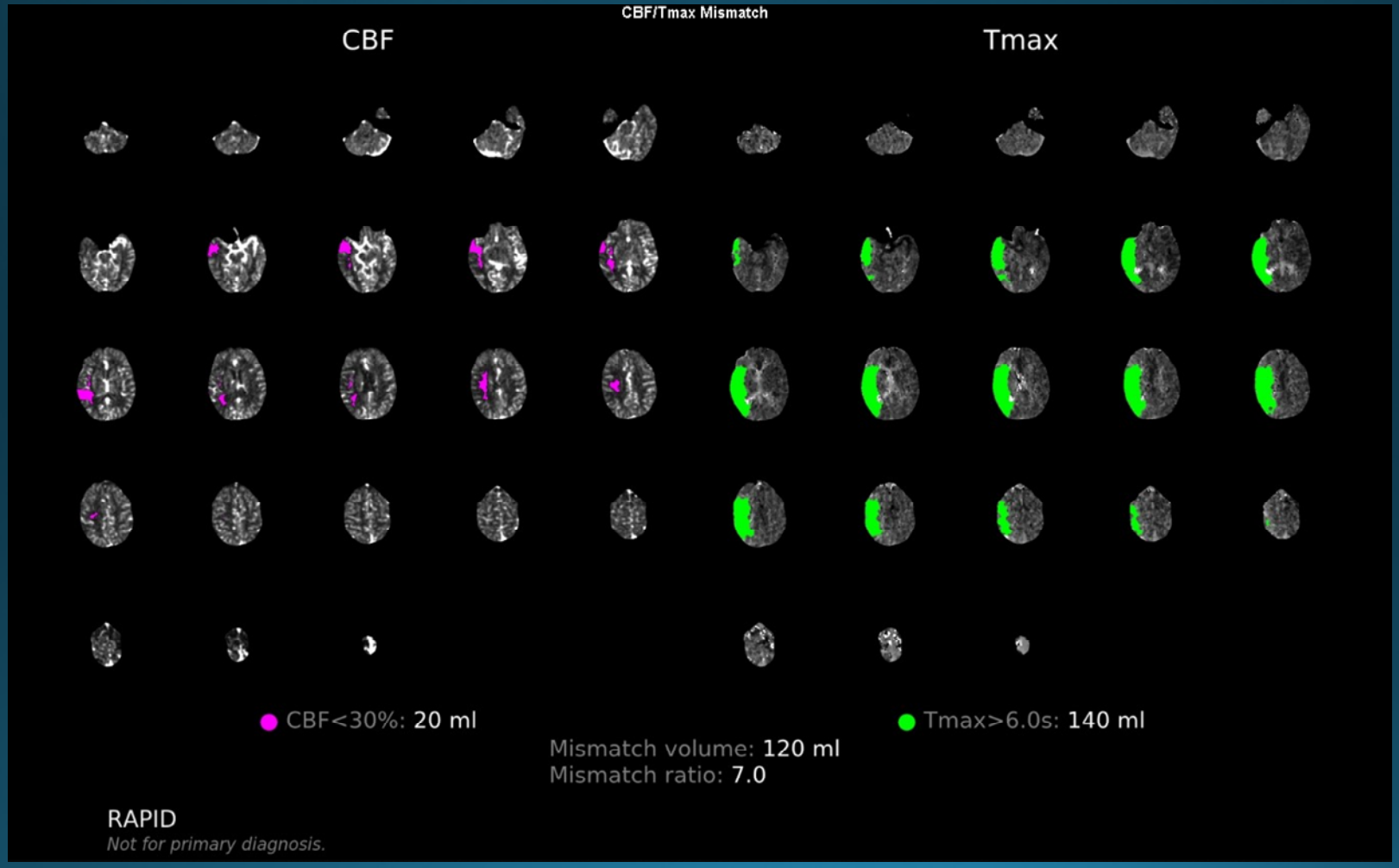
CBV

CBF

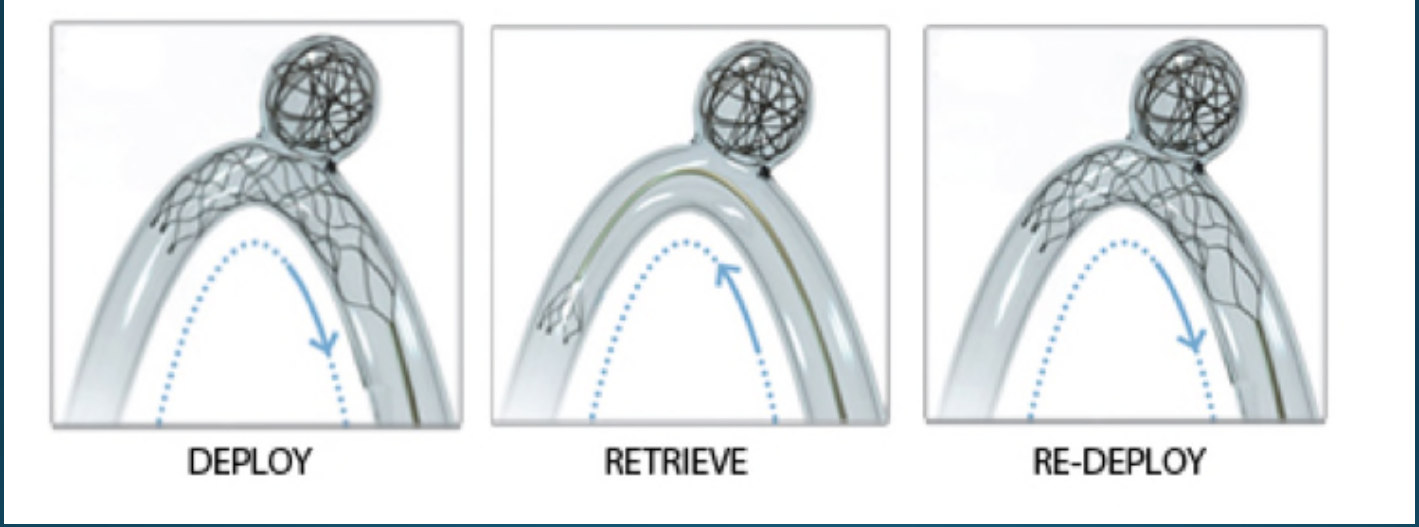
MTT


6.0



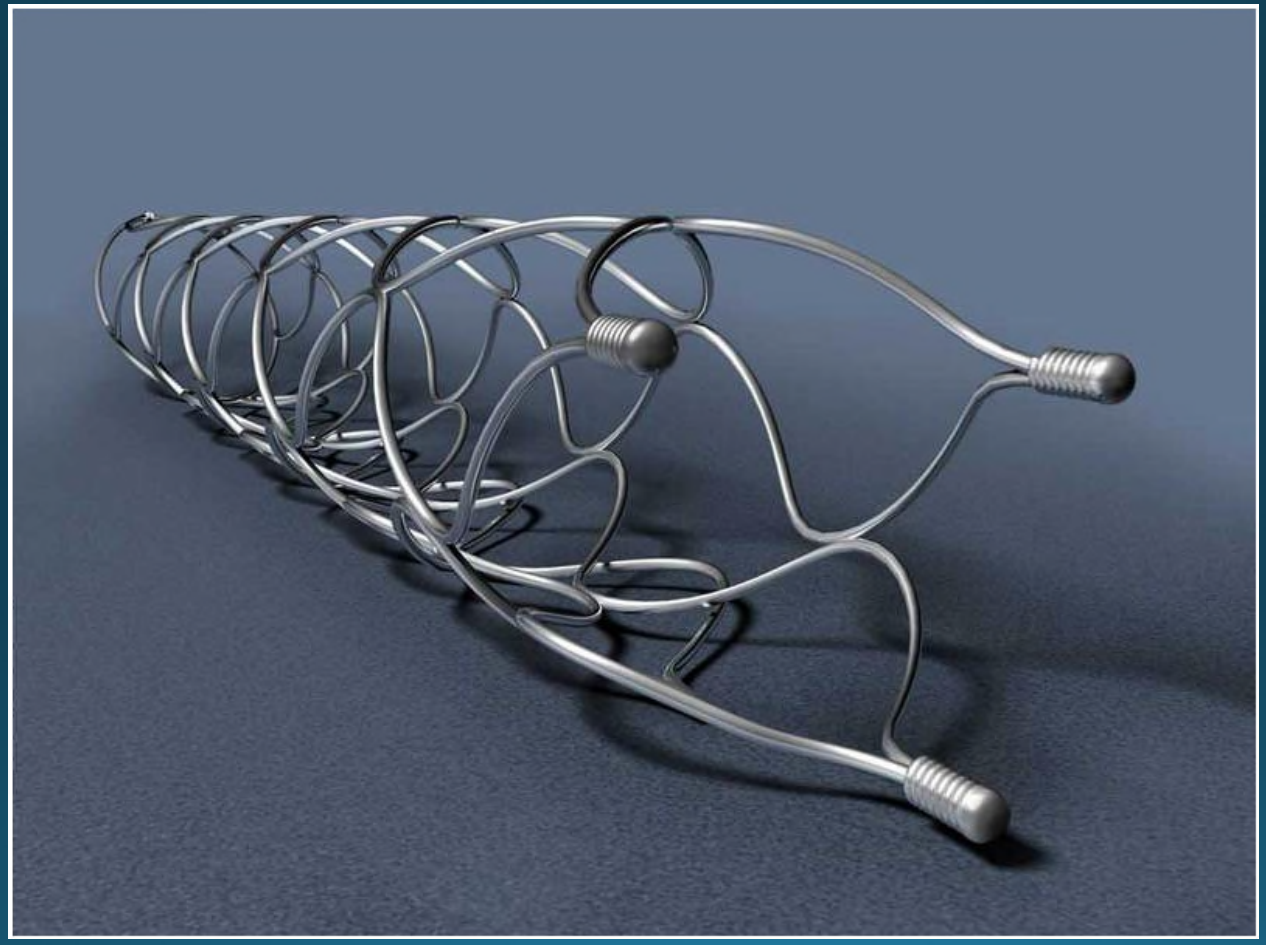

CBF/Tmax Mismatch
CBF
Tmax
CBF<30%: 20 ml
Tmax>6.0s: 140 ml
Mismatch volume: 120 ml
Mismatch ratio: 7.0
RAPID
Not for primary diagnosis.

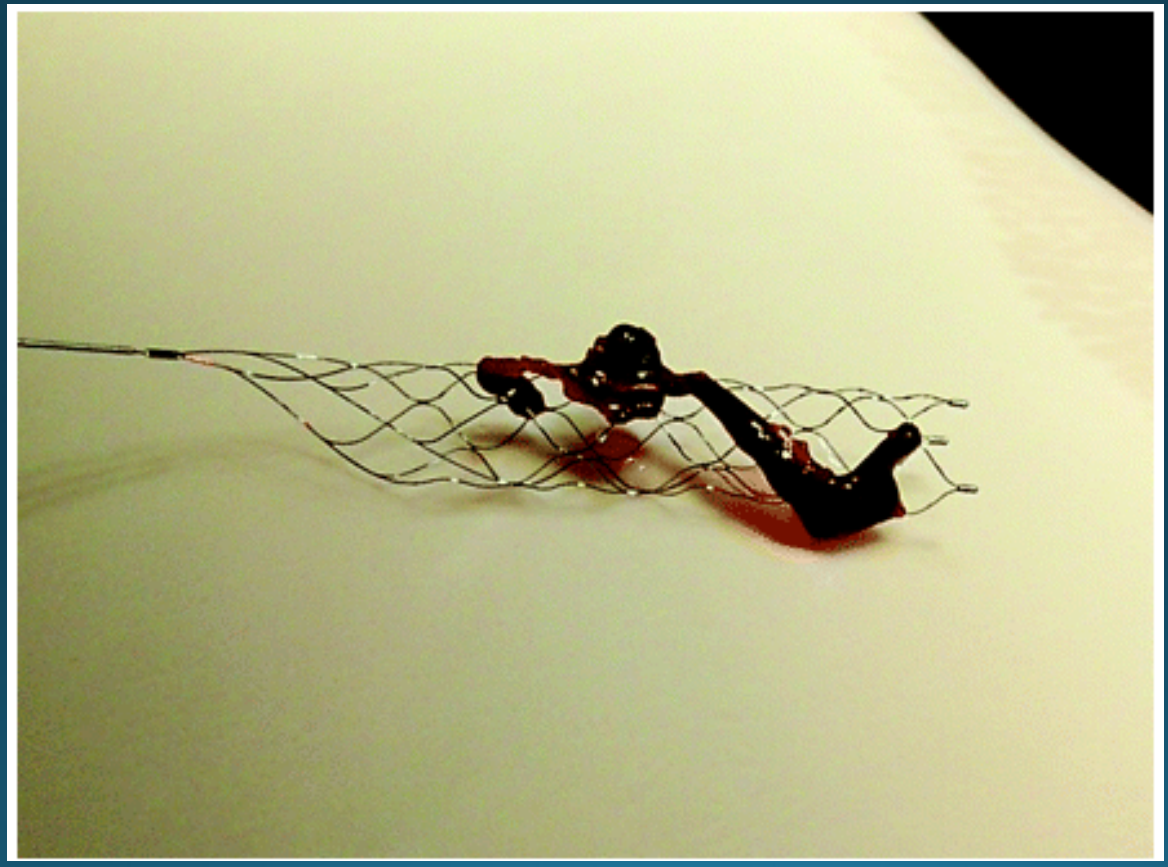
Better Instruments…



COVIDIEN

Solitaire™ FR Revascularization Device Product Animation





Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial

Jeffrey L Saver, Reza Jahan, Elad I Levy, Tudor G Jovin, Blaise Baxter, Raul G Nogueira, Wayne Clark, Ronald Budzik. Osama O Zaidat. for the SWIFT Trialists

Lancet 2012; 380: 1241–49

RCT: Standard Care + Solitaire

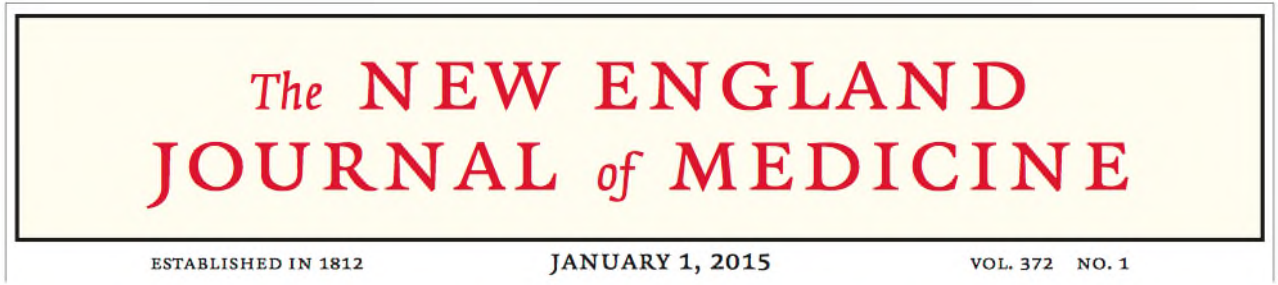
vs

Standard Care + Merci (up to 8hrs)

- Successful recanalization without SICH – 61% vs. 24%
- Rate SICH 2% vs. 11%
- Favorable 90-day neurologic outcome 58% vs. 33%
- 90-day mortality 17% vs. 38%
- Time to recanalization 36 min vs 52 min

- Study stopped prematurely due to overwhelming benefit for Solitaire. FDA approval.

Putting it all together…again…



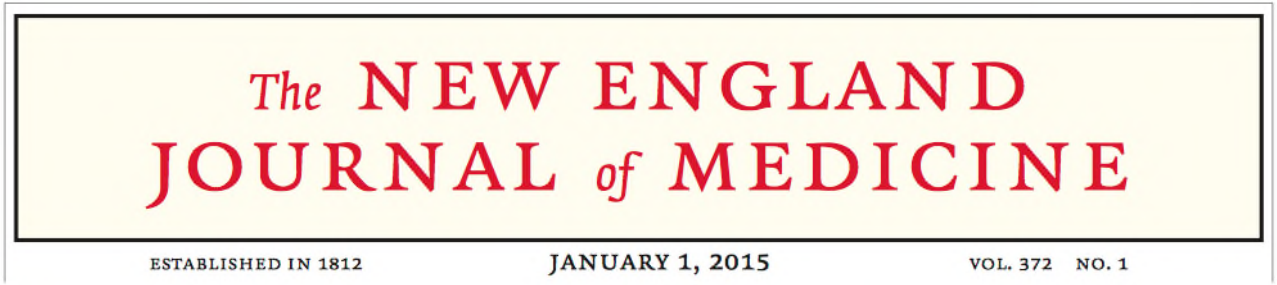
The NEW ENGLAND JOURNAL of MEDICINE

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

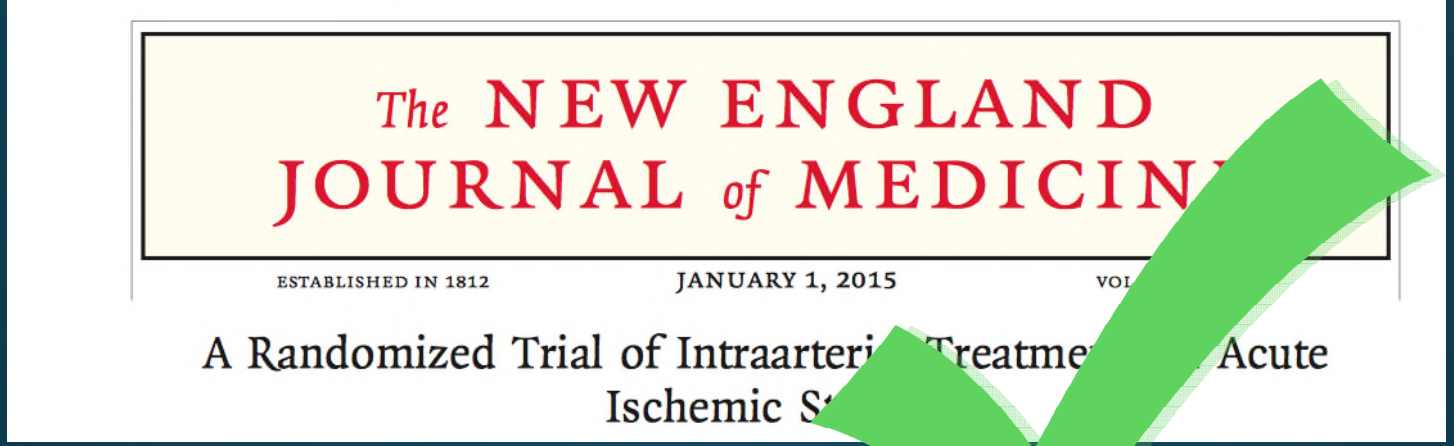
A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

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*

MR CLEAN TRIAL



- Multicenter RCT in Netherlands, all pts included
- Standard of care vs Standard of care plus Endovascular therapy
- Large vessel occlusion confirmed by advanced imaging
- Endovascular therapy within 6 hrs
- Majority stent-retriever (81%)



Functional Independence (mRS 0 to 2) 32.6% vs 19.1%

Absolute difference of 13.5 percentage points (95% CI, 5.9 to 21.2)

No significant difference in SICH

No significant difference in mortality

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*

ESCAPE TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

- RCT Worldwide
- Standard Care vs Standard Care + Endovascular
- LVO confirmed by CTA
- ASPECTS scoring
- Collateral assessment by multiphase CTA
- Up to 12 hrs
- Stent Retriever 86.1%

- Trial stopped early because of efficacy
- Functional independence (mRS 0-2 at 90 days)
  53% vs 29.3%, p<.001
- Absolute benefit of 23.7 percentage points
- Reduced mortality (10.4% vs 19%, p=0.04)
- SICH not significantly different

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*

EXTEND-IA TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

- RCT Austrailia and New Zealand
- IV tPA vs IV tPA plus Endovascular
- LVO confirmed by CTA
- CT Perfusion for core and penumbra
- Up to 4.5hrs
- Stent Retriever 100%

The NEW ENGLAND JOURNAL of MEDICINE

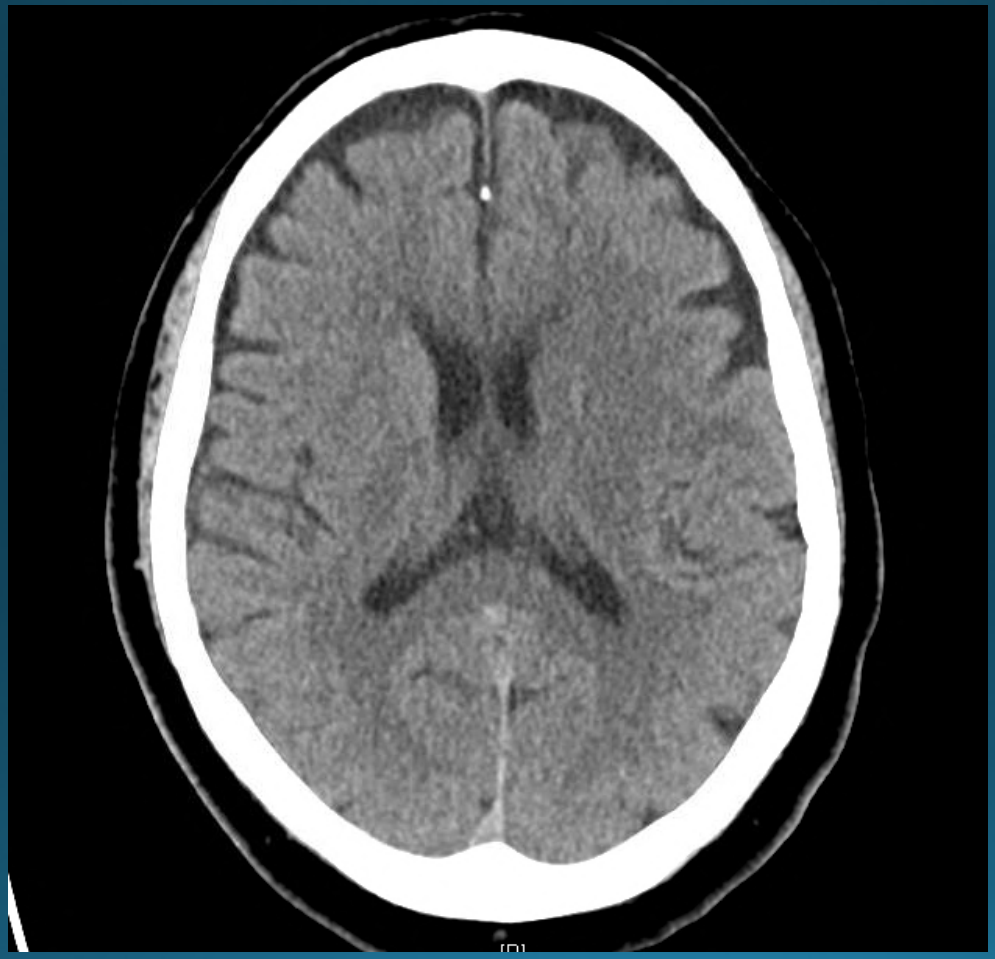
ORIGINAL ARTICLE

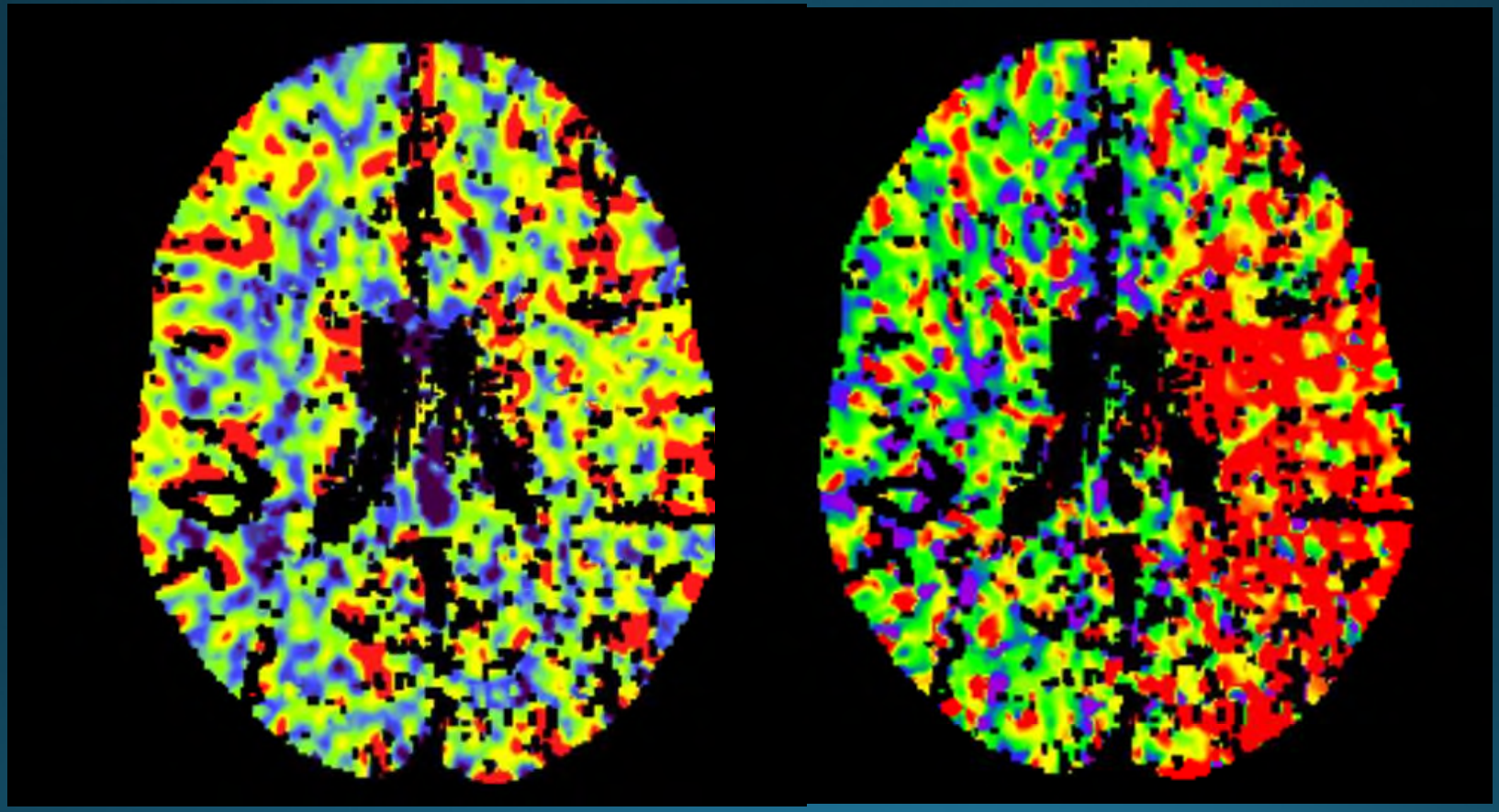
Endovascular Therapy for Ischemic [illegible]ke with Perfusion-Imaging Selec[illegible]

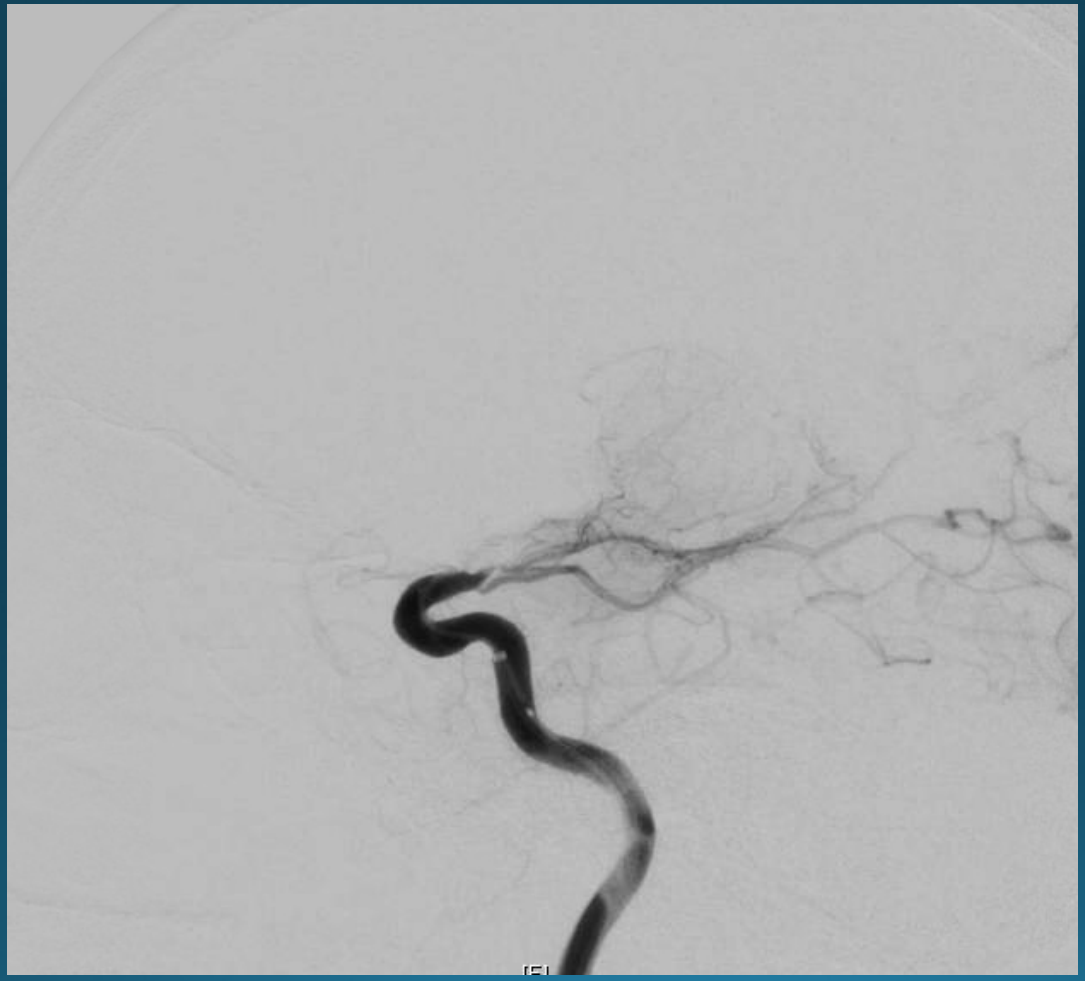
- Trial stopped early because of efficacy
- Functional outcome (mRS 0-2 at 90 days)
  80% vs 37%, p=0.002
- Reperfusion at 24 hrs
  100% vs 37%, p<0.001
- No significant difference in mortality
- No significant difference in SICH

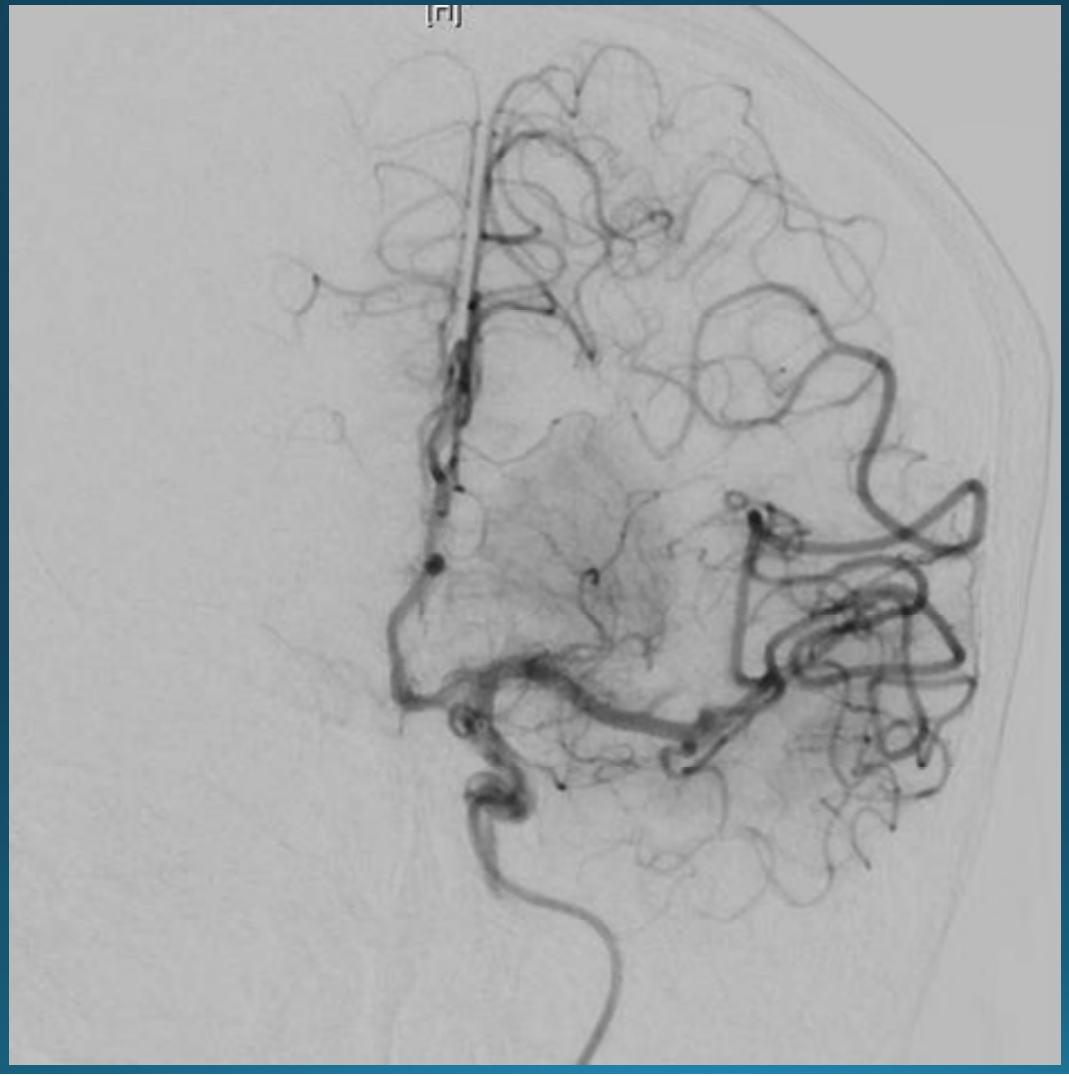
6 RCTs Confirm the Results

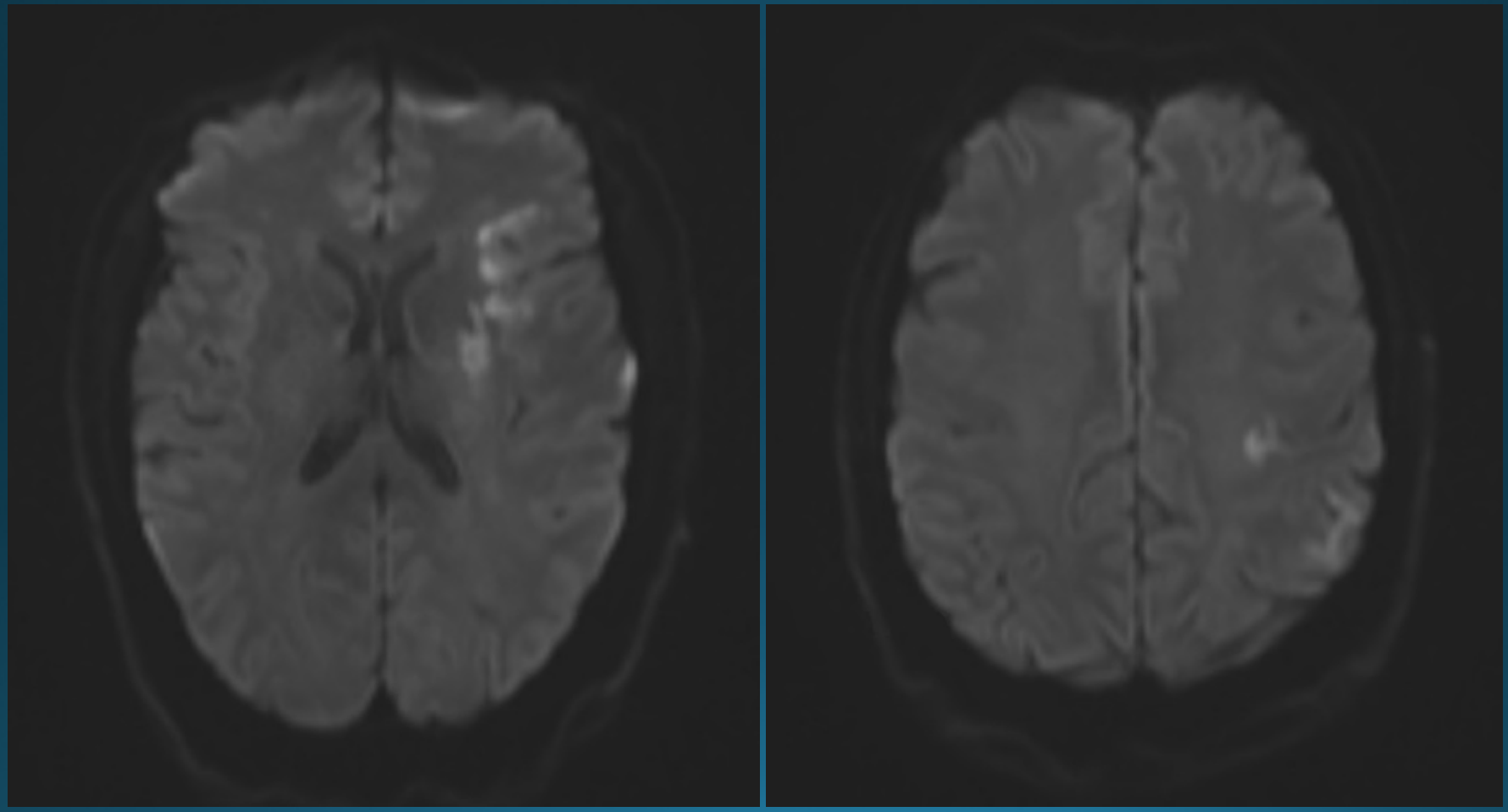
- MR CLEAN
- SWIFT PRIME
- EXTEND-IA
- ESCAPE
- REVASCAT
- THRACE











The Technical Goal:

AHA/ASA Guideline

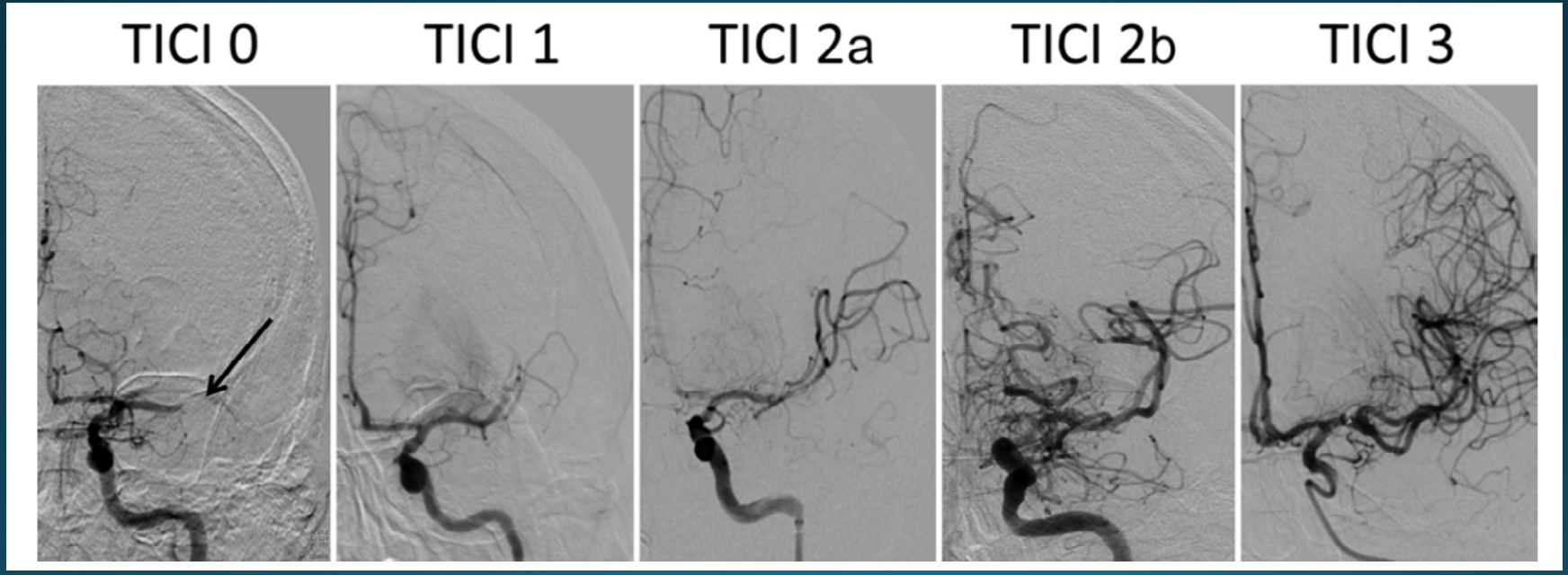
Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

2. The technical goal of the thrombectomy procedure should be reperfusion to a modified Thrombolysis in Cerebral Infarction (mTICI) grade 2b/3 angiographic result to maximize the probability of a good functional clinical outcome.	I	A

Powers et al 2019 Guidelines for Management of AIS

mTICI 2b: Antegrade reperfusion of greater than 50% affected target artery territory

mTICI 3: Complete revascularization



Neurosurg Focus 36 (1):E5, 2014

Neurology
THE MOST WIDELY READ AND HIGHLY CITED PEER-REVIEWED NEUROLOGY JOURNAL
The Official Journal of the American Academy of Neurology

Neurology. 2012 Sep 25; 79(13 Suppl 1): S110–S116.
doi: 10.1212/WNL.0b013e3182695916
PMCID: PMC4109231
PMID: 23008384

Revascularization grading in endovascular acute ischemic stroke therapy

- Evaluated 10 different grading scales of cerebral reperfusion

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THE MOST WIDELY READ AND HIGHLY CITED PEER-REVIEWED NEUROLOGY JOURNAL
The Official Journal of the American Academy of Neurology

Neurology. 2012 Sep 25; 79(13 Suppl 1): S110–S116.
doi: 10.1212/WNL.0b013e3182695916
PMCID: PMC4109231
PMID: 23008384

Revascularization grading in endovascular acute ischemic stroke therapy

Table 1 Criteria for an optimal revascularization scale

- Takes into account both recanalization and reperfusion
- Takes into account cerebral collateral circulations
- Reproducibility: intra- and inter-rater reliability
- Ease of use and application in daily practice, not trials-only scale
- Comparable results across clinical trials
- Prognostic significance and correlation with clinical outcome

Neurology®
THE MOST WIDELY READ AND HIGHLY CITED PEER-REVIEWED NEUROLOGY JOURNAL
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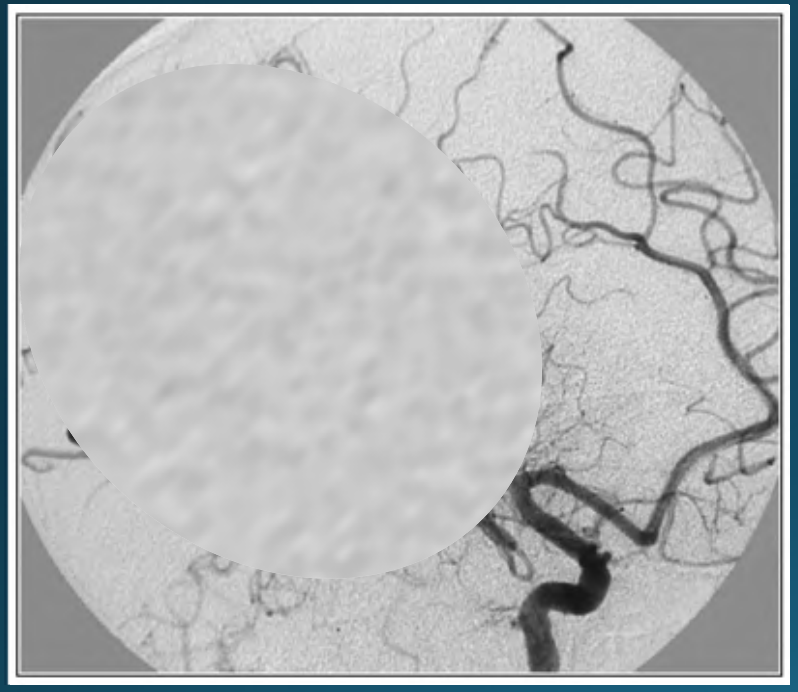
Neurology. 2012 Sep 25; 79(13 Suppl 1): S110–S116.
doi: 10.1212/WNL.0b013e3182695916

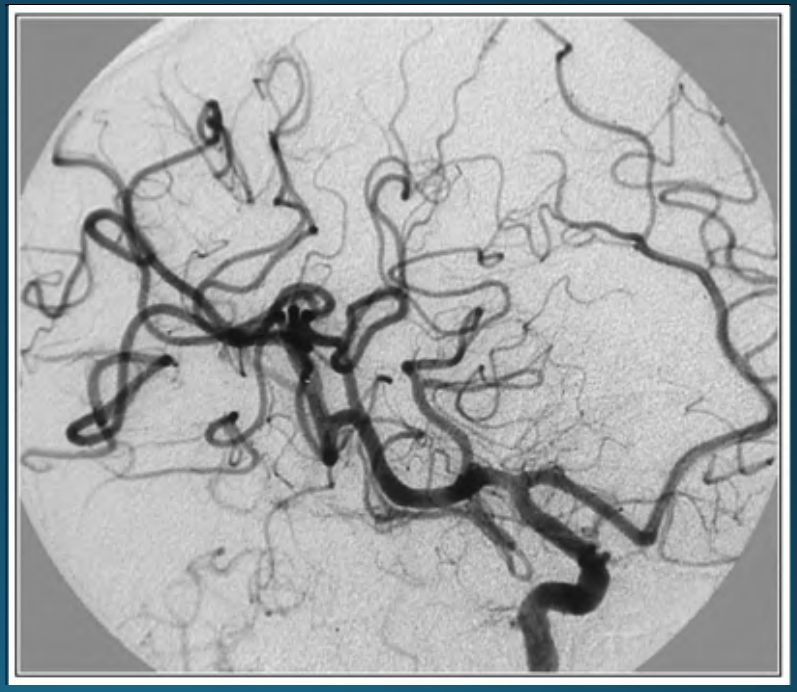
PMCID: PMC4109231
PMID: 23008384

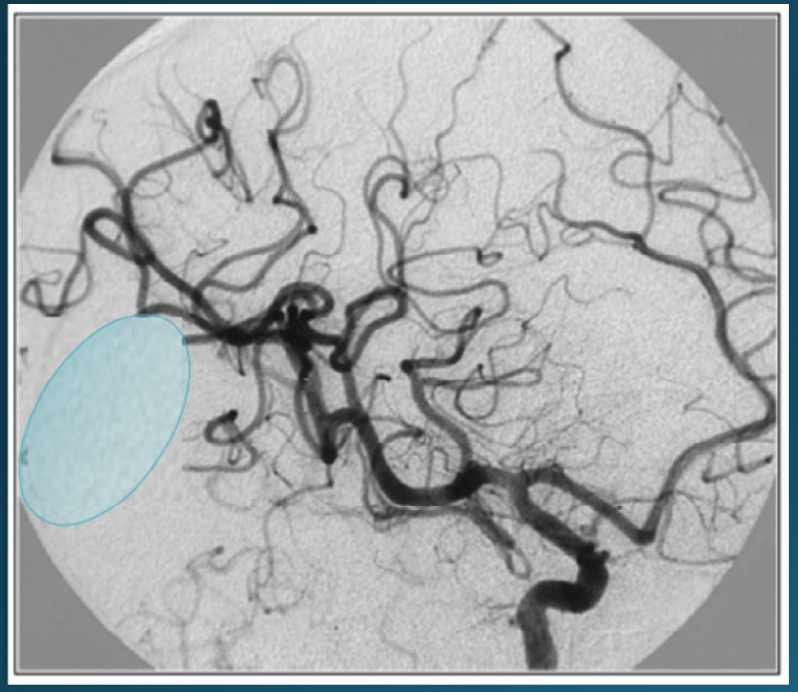
Revascularization grading in endovascular acute ischemic stroke therapy

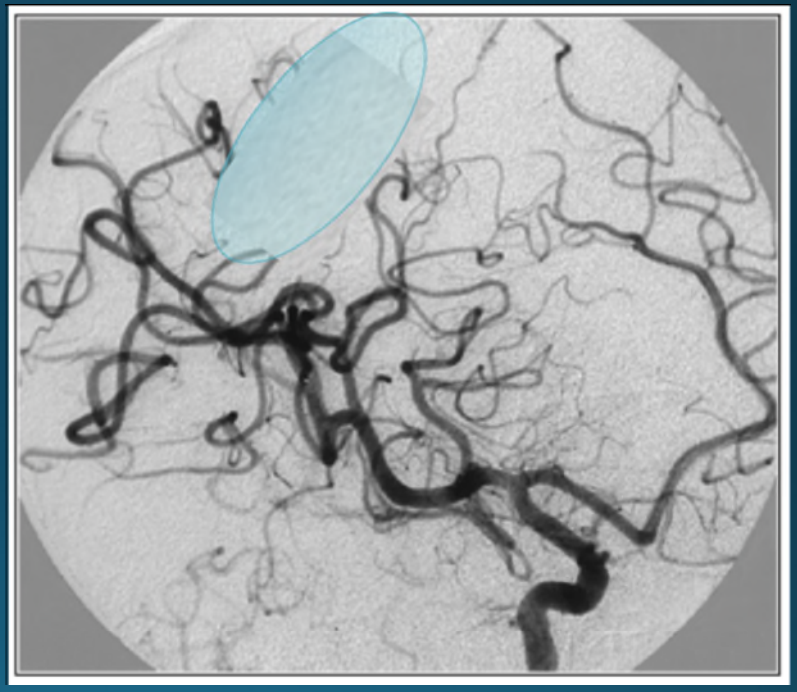
mTICI

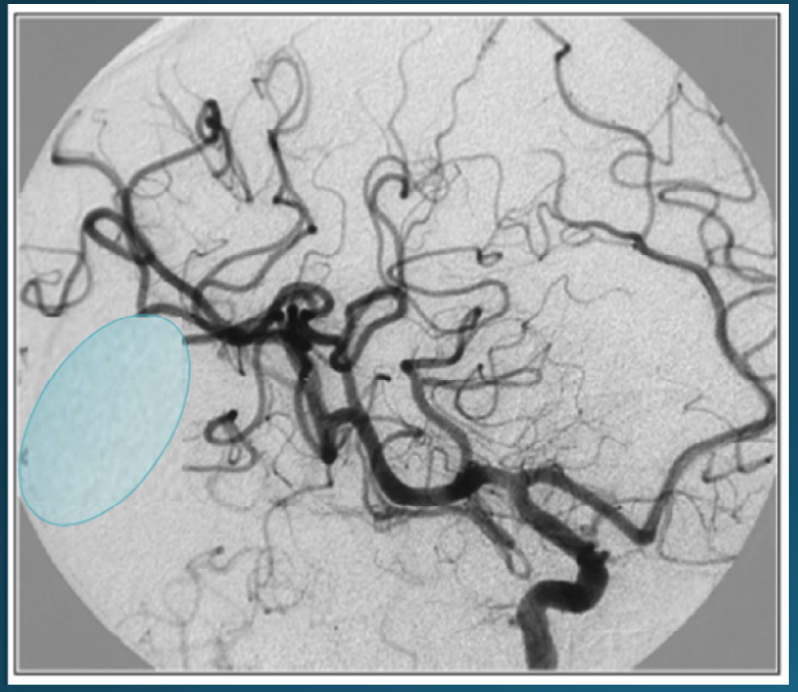
- ✓ Takes into account both recanalization and reperfusion
- ✓ Reproducibility: intra- and inter-rater reliability
- ✓ Ease of use and application in daily practice, not trials-only scale
- ✓ Comparable results across clinical trials

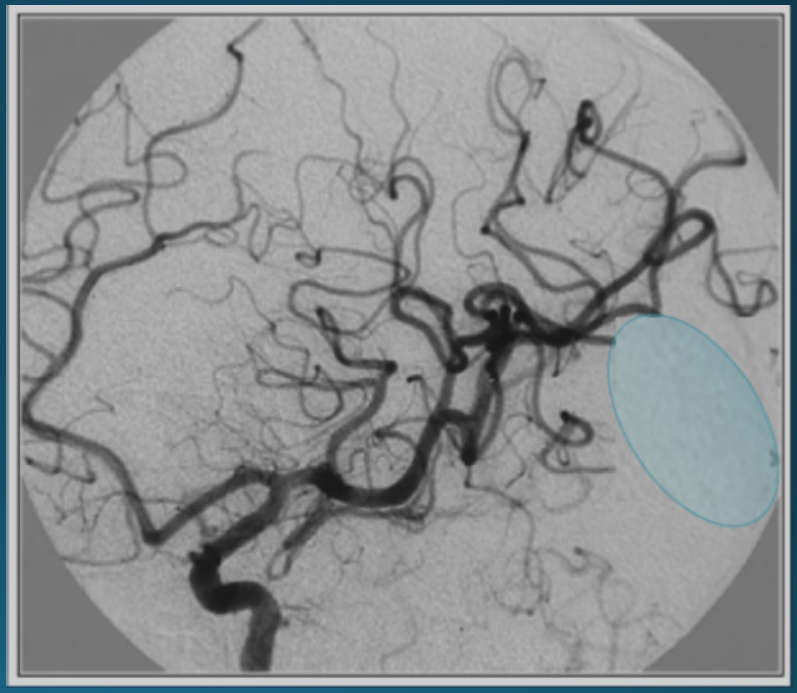


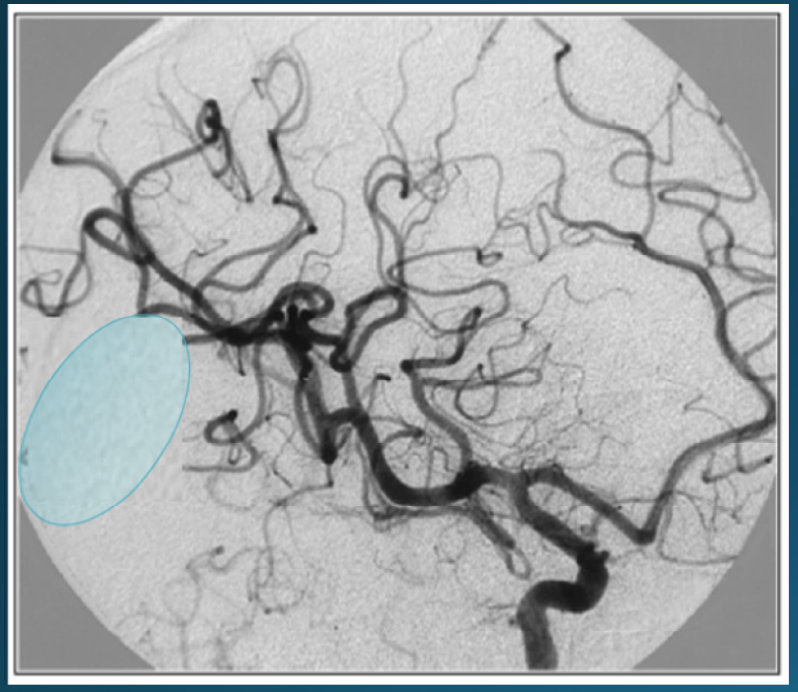


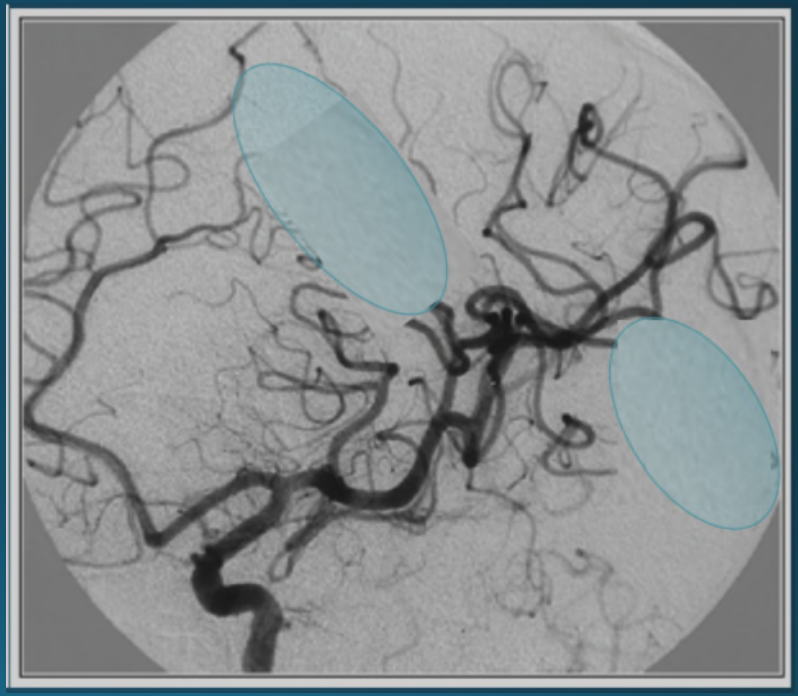












Systematic review and meta-analysis on outcome differences among patients with TICI2b versus TICI3 reperfusions: success revisited

- Fourteen studies
- 2379 successfully reperfused patients
- 1131 TICI3
- 1248 TICI2b

- TICI3 reperfusions were associated with
- higher rates functional independence (1.74, 95% cI 1.44 to 2.10)
- higher rates excellent functional outcomes (2.01, 95% cI 1.60 to 2.53)
- lower rates of mortality (sOR 0.59, 95% cI 0.37 to 0.92)
- lower rates of SICH (sOR 0.42, 95% cI 0.25 to 0.71)

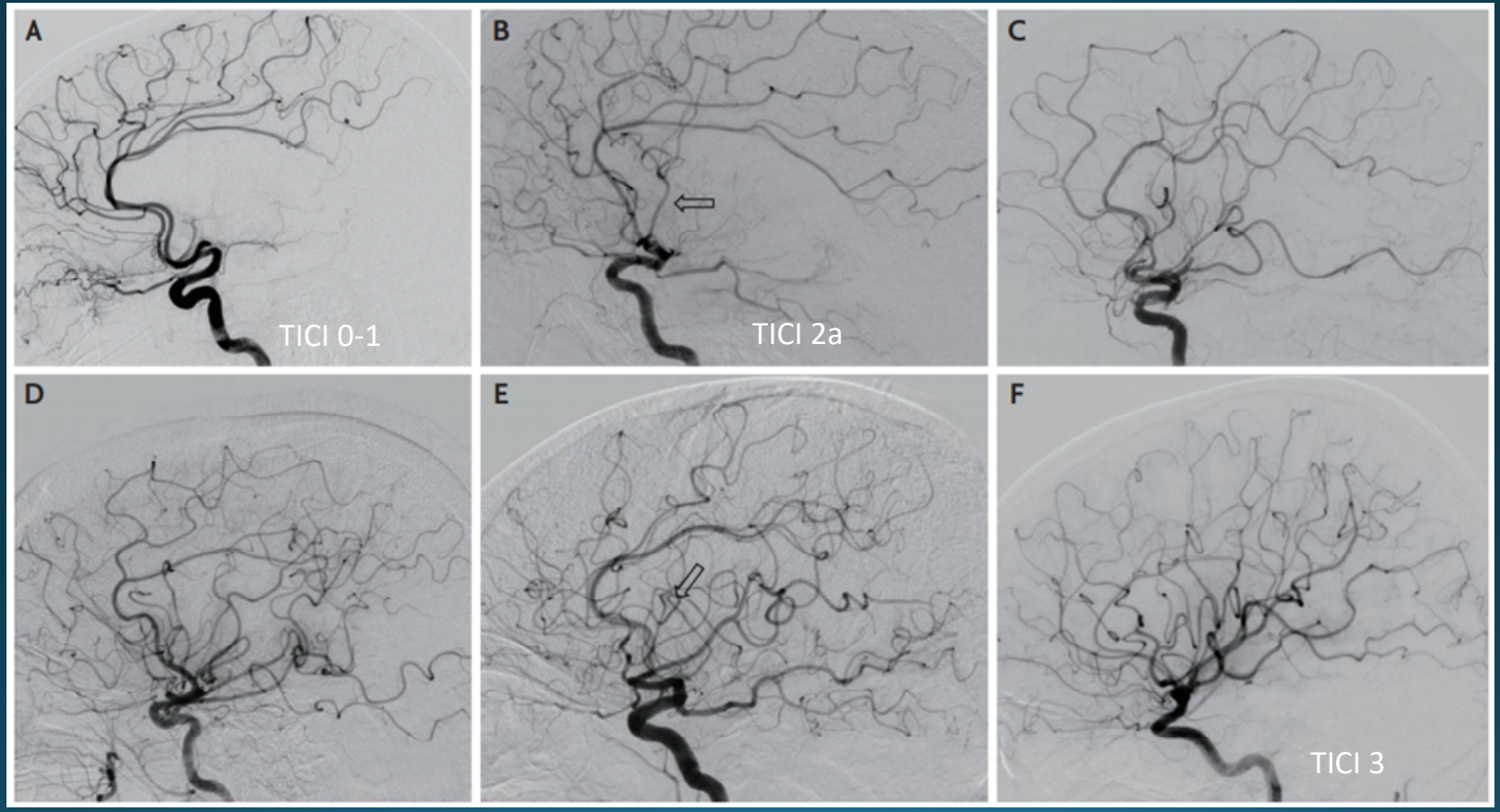
Kaesmacher J, *et al*. *J Neurol Neurosurg Psychiatry* 2018;**89**:910–917.

Systematic review and meta-analysis on outcome differences among patients with TICI2b versus TICI3 reperfusions: success revisited

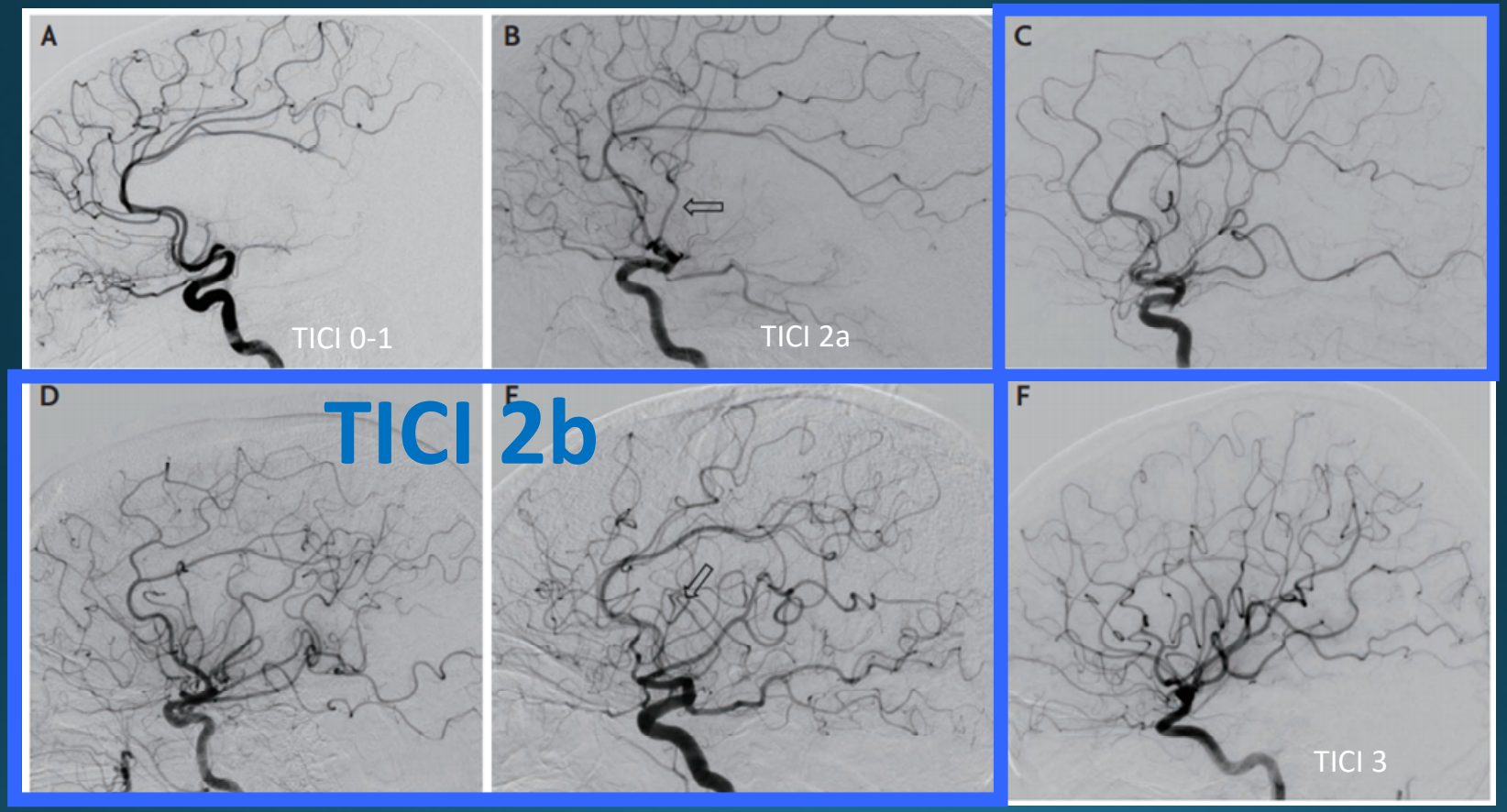
Conclusion:

- TICI3 reperfusion is associated with superior outcome and better safety profiles than TICI2b.
- This effect is independent of time and collaterals.

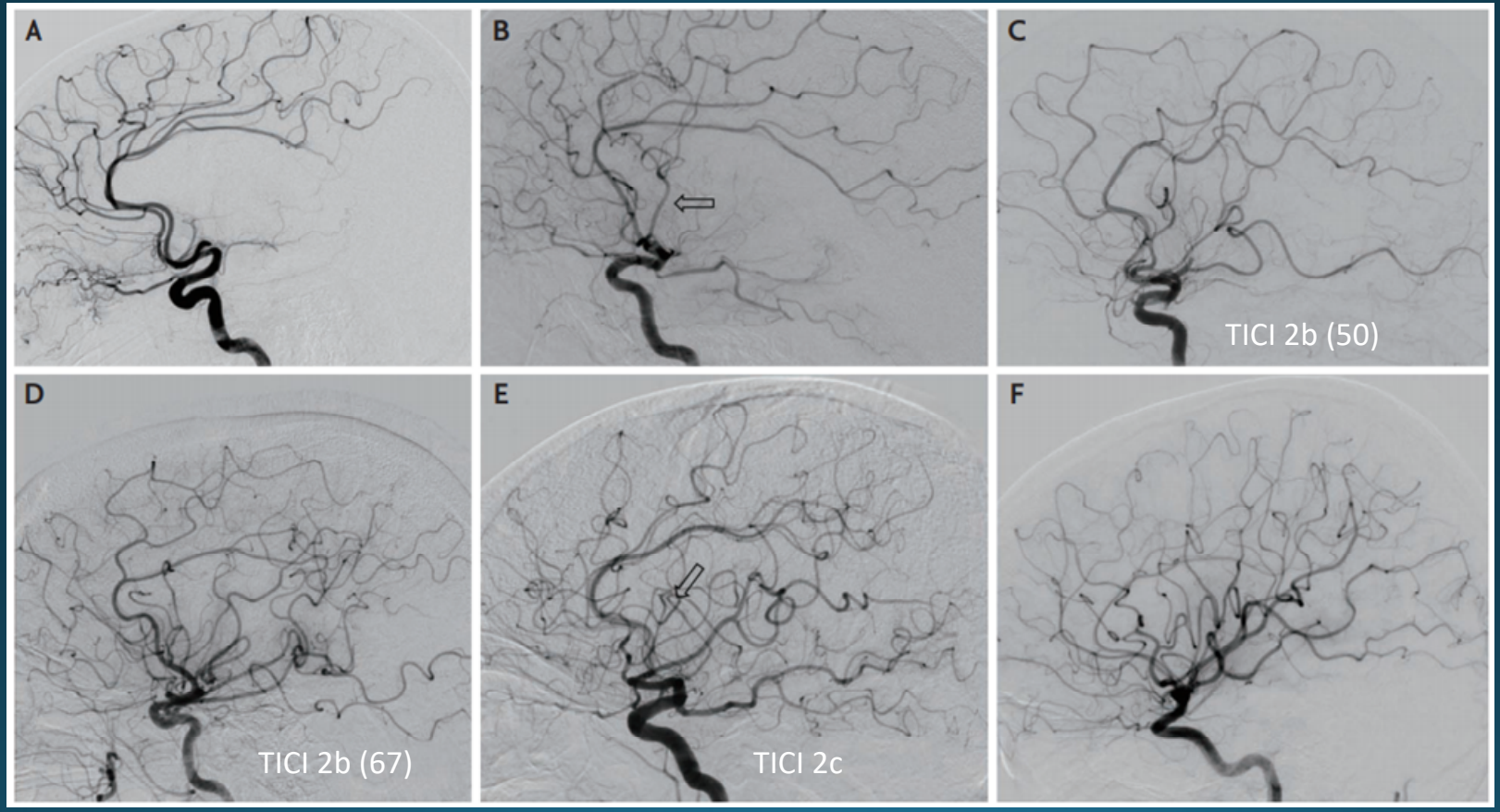
Kaesmacher J, *et al*. *J Neurol Neurosurg Psychiatry* 2018;**89**:910–917.



J Neurosonol Neuroimag 2018;10(2):95-99



J Neurosonol Neuroimag 2018;10(2):95-99



J Neurosonol Neuroimag 2018;10(2):95-99

6 RCTs Confirm the Results

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

Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials (HERMES) collaboration

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

Lancet 2016; 387: 1723–31

- Meta-analysis using patient level data, n=1287
  - 634 endovascular
  - 653 standard medical management

Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials (HERMES) collaboration

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

Lancet 2016; 387: 1723–31

- Overall odds ratio of improvement in mRS vs control at 90 days
  2.49 $p<0.0001$

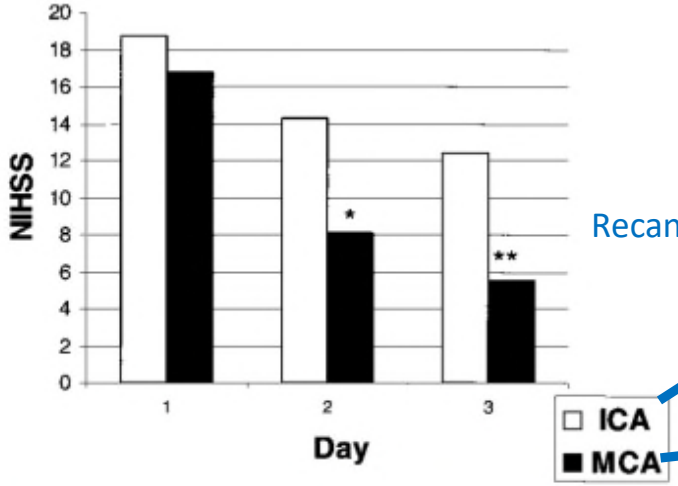
- Odds ratio of improved mRS at 90 days was time dependent
  - 3 hrs 2.79 Absolute risk reduction 39.2%
  - 6 hrs 1.98 Absolute risk reduction 30.2%
  - 8 hrs 1.57 Absolute risk reduction 15.7%

Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials (HERMES) collaboration

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

Lancet 2016; 387: 1723–31

- Independence (mRS 0-2) at 90 days 46.0% vs 26.5% p<0.0001
- 71.0% mTICI 2b/3
- Mortality 15.3% vs 18.9% p = 0.15
- SICH 4.4% vs 4.3% p=0.82
- NNT 2.6 [vs 10 at 0-3hr or 19 3-4.5hr IV tPA alone]



Recanalization at 3 days after tPA

31%

p<0.001

88%

Figure 1. Comparison of NIHSS scores at days 1 (pre-tPA), 2, and 3 after tPA in patients with ICA-plus-MCA occlusion (□) vs patients with isolated MCA occlusion (■). **P*=0.04; ***P*=0.03 (Wilcoxon rank sum).

Stroke. 2002;33:2066-2071

Size matters…

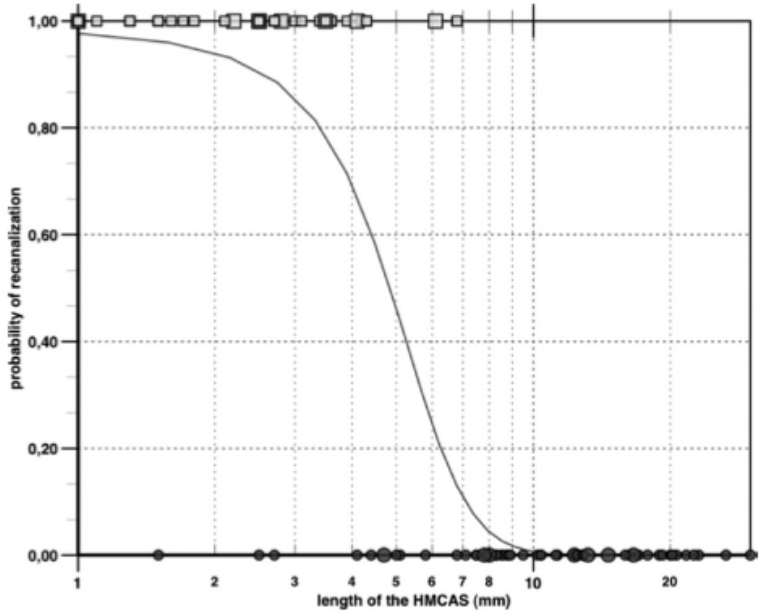


Figure 1. Logistic regression curve representing an estimate of the probability for successful recanalization of occluded vessels by intravenous thrombolysis (IVT) depending on thrombus length.

(*Stroke*. 2011;42:1775-1777.)

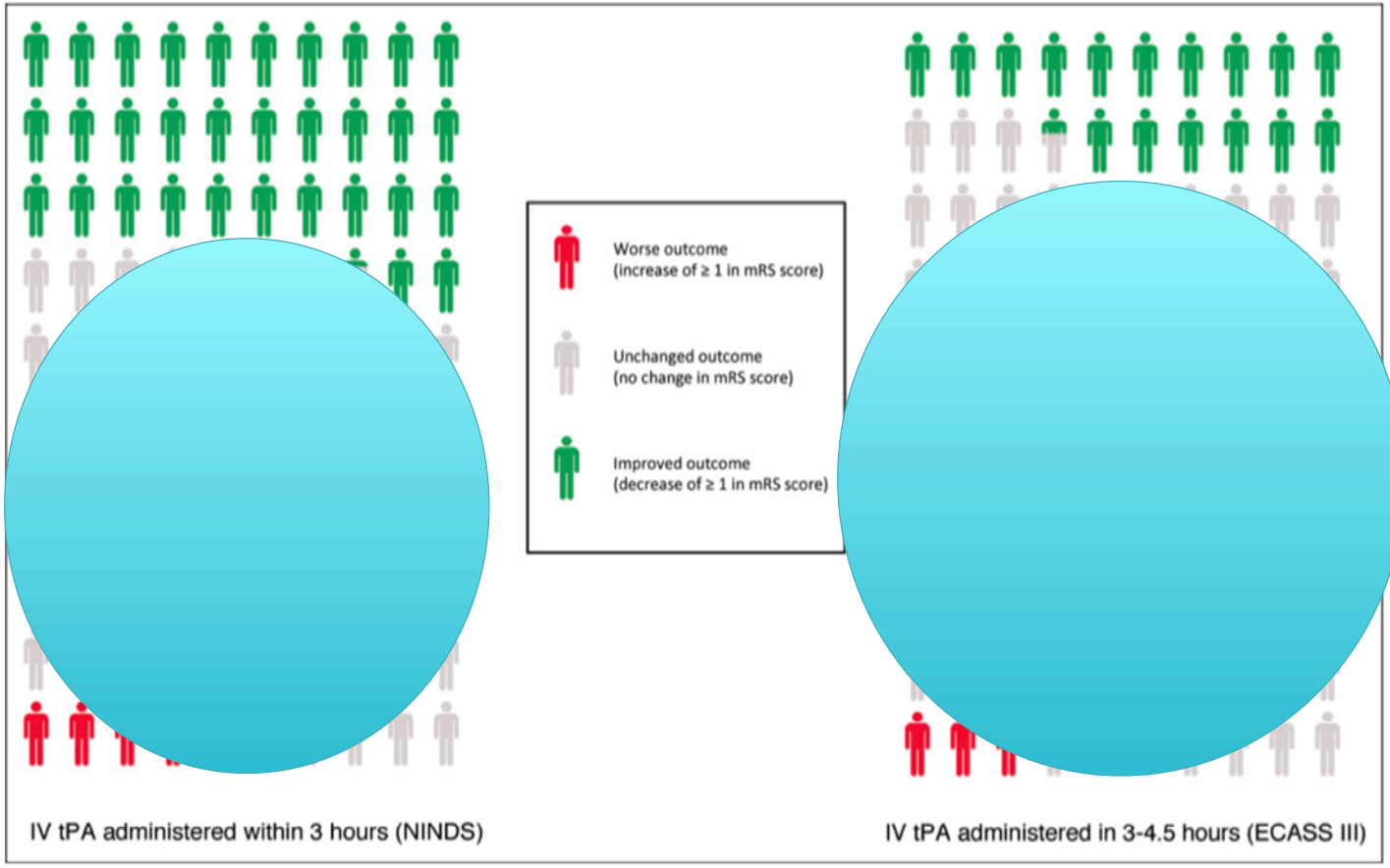
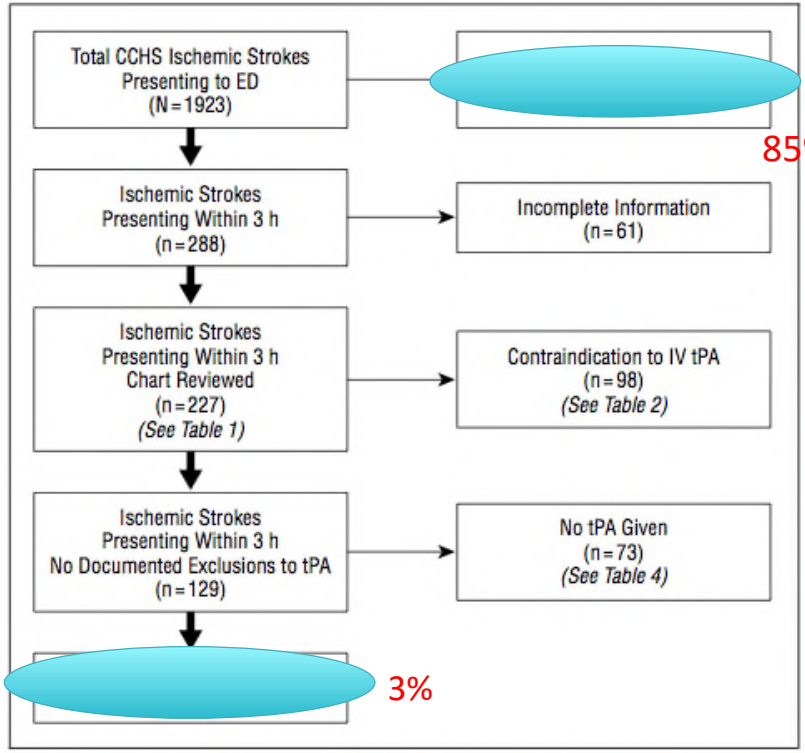


Figure 3. Number needed to treat to benefit and harm per 100 patients treated with intravenous recombinant tissue-type plasminogen activator (IV tPA) for acute ischemic stroke in the <3-hour versus 3- to 4.5-hour time windows.[24] mRS indicates modified Rankin scale; NINDS, National Institute of Neurologic Disorders and Stroke; ECASS-III, European Cooperative Acute Stroke Study-III.

Neurohospitalist. 2015 Jul; 5(3): 101–109.



Stroke admissions to the Cleveland Clinic Health System (CCHS) from June 15, 1999, to June 15, 2000. ED indicates emergency department; IV, intravenous; tPA, tissue plasminogen activator; and asterisk, the 56 patients included 9 patients treated with intra-arterial tPA.

Arch Neurol. 2004;61:346-350

A New Standard of Care:

A New Standard of Care:

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

Class IA Mechanical Thrombectomy Candidates:

(1) prestroke mRS score of 0 to 1
(2) NIHSS score of ≥6
(3) ASPECTS of ≥6
(4) causative occlusion of the internal carotid artery or MCA segment 1 (M1)
(5) treatment can be initiated (groin puncture) within 6 hours of symptom onset
(6) age ≥18 years

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Modified Rankin Scale (mRS)

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

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Powers et al 2019 Guidelines for Management of AIS

CT/CT Angiography and MRI Findings Predict Recurrent Stroke After Transient Ischemic Attack and Minor Stroke

Results of the Prospective CATCH Study

- CTA abnormalities (hazard ratio, 4.0; 95% CI, 2.0–8.5)

- DWI positivity (hazard ratio, 2.2; 95% CI, 1.05–4.7)
- Symptoms ongoing at first assessment (hazard ratio, 2.2; 95% CI, 1.02–4.9)

DOI: 10.1161/STROKEAHA.111.637421

Thrombectomy versus medical management for large vessel occlusion strokes with minimal symptoms: an analysis from STOPStroke and GESTOR cohorts

- 26 matched pairs endovascular vs medical

- Endovascular therapy was statistically associated with:
  - lower NIHSS at discharge (p=0.04),
  - favorable NIHSS shift (p=0.03),
  - increased independence at discharge (p=0.03)
  - increased independence at 3–6-months (p=0.04).

Haussen DC, *et al*. *J NeuroInterv Surg* 2018;**10**:325–329.

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Powers et al 2019 Guidelines for Management of AIS

How large is too large?

Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial

*Serge Bracard, Xavier Ducrocq, Jean Louis Mas, Marc Soudant, Catherine Oppenheim, Thierry Moulin, Francis Guillemin, on behalf of the THRACE investigators**

- 30% (17 of 57) patients who had poor baseline ASPECTS (0–4) had good clinical outcomes at 3 months.
- Although this proportion is lower than that of patients with better baseline ASPECTS (≥5), it is nonetheless not negligible

Lancet Neurol 2016; 15: 1138–47

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4. Although its benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6, and causative occlusion of the internal carotid artery (ICA) or proximal MCA (M1).	IIb	B-R

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Treatment and outcomes of acute basilar artery occlusion in the Basilar Artery International Cooperation Study (BASICS): a prospective registry study

- 592 patients who were analysed,
  - 183 were treated with antiplatelet or anticoagulation regimen
  - 121 with IV thrombolysis
  - 288 with endovascular intervention, chemical, mechanical, stenting etc

- Overall, 402 (68%) had a poor outcome (mRS 4, 5 or 6)


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RM Neuro
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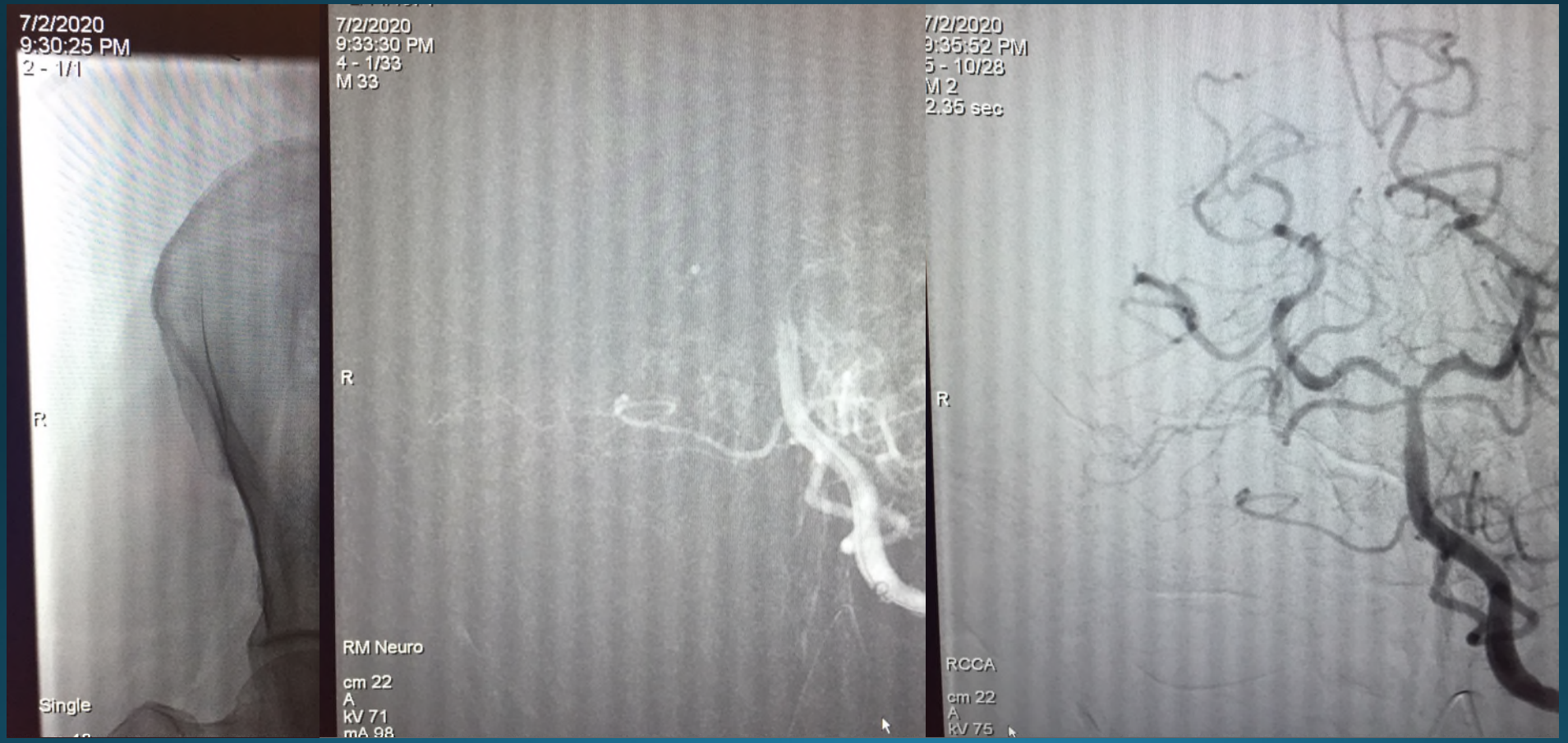
mA 98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3. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the MCA segment 2 (M2) or MCA segment 3 (M3) portion of the MCAs.	IIb	B-R
5. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries.	IIb	C-LD

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2 RCT extend the results up to 24hrs

- DEFUSE 3
- DAWN

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kasner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Mlynash, J.J. Heit, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators*

- Acute stroke last known well 6 to 16 hours
- Proximal MCA or ICA
- Perfusion imaging with mismatch
- Thrombectomy plus standard medical therapy vs standard medical therapy alone.

N ENGL J MED 378;8 NEJM.ORG FEBRUARY 22, 2018

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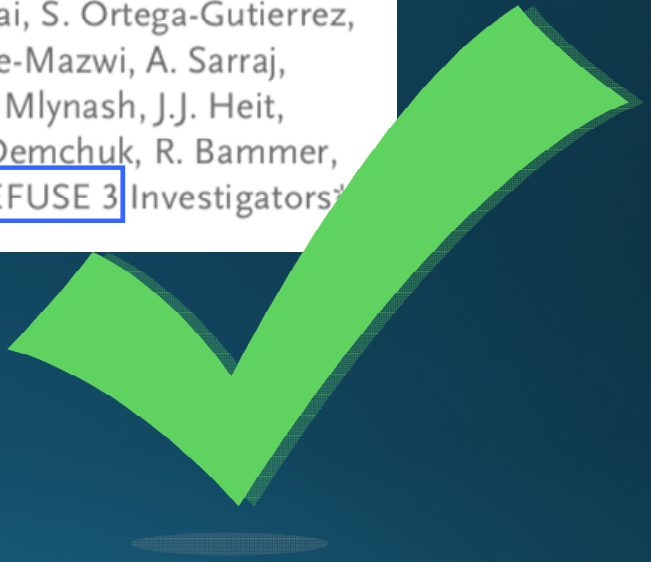

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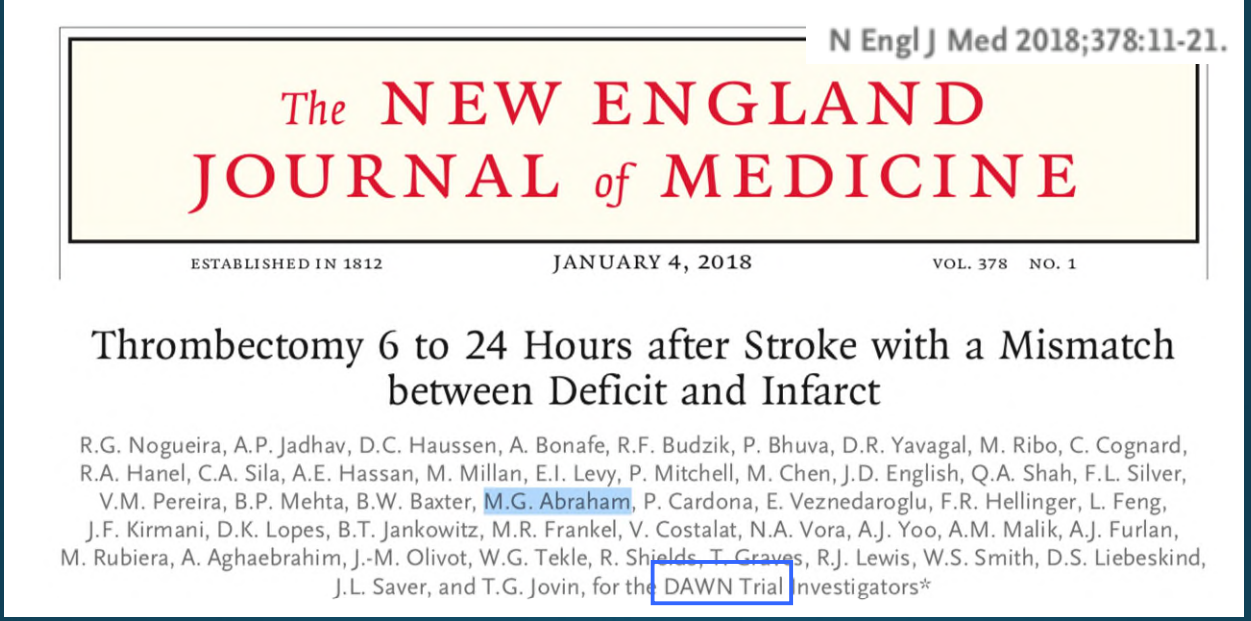

N Engl J Med 2018;378:11-21.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 4, 2018 VOL. 378 NO. 1

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators*

- Acute stroke last known well 6 to 24 hours
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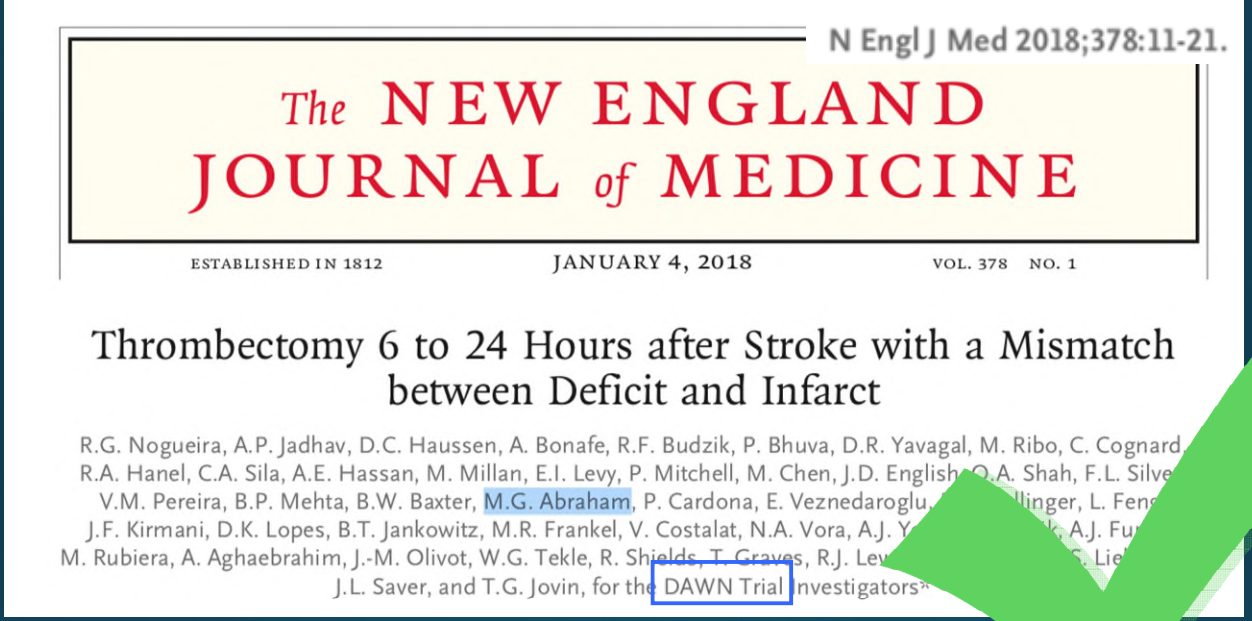
- Infarct volume imaged by CTP or MRI
- Mismatch between clinical severity and infarct volume
- Thrombectomy plus standard medical therapy vs standard medical therapy alone .



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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
8. In selected patients with AIS within 16 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

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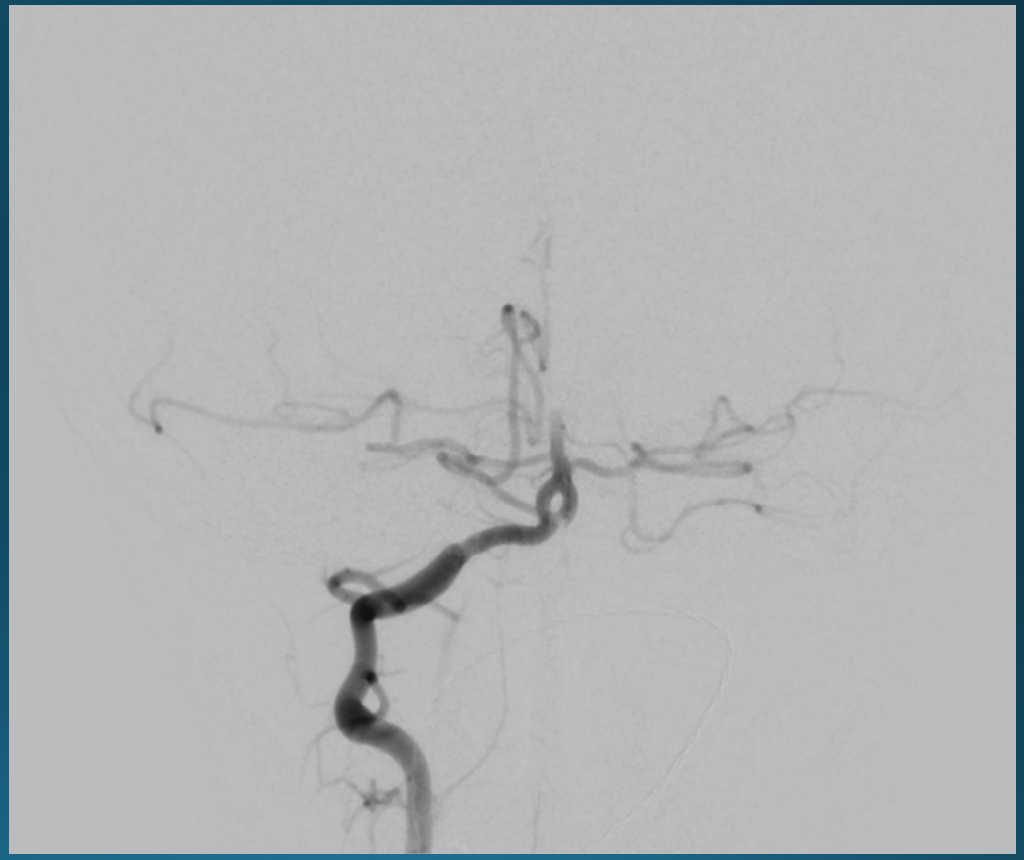

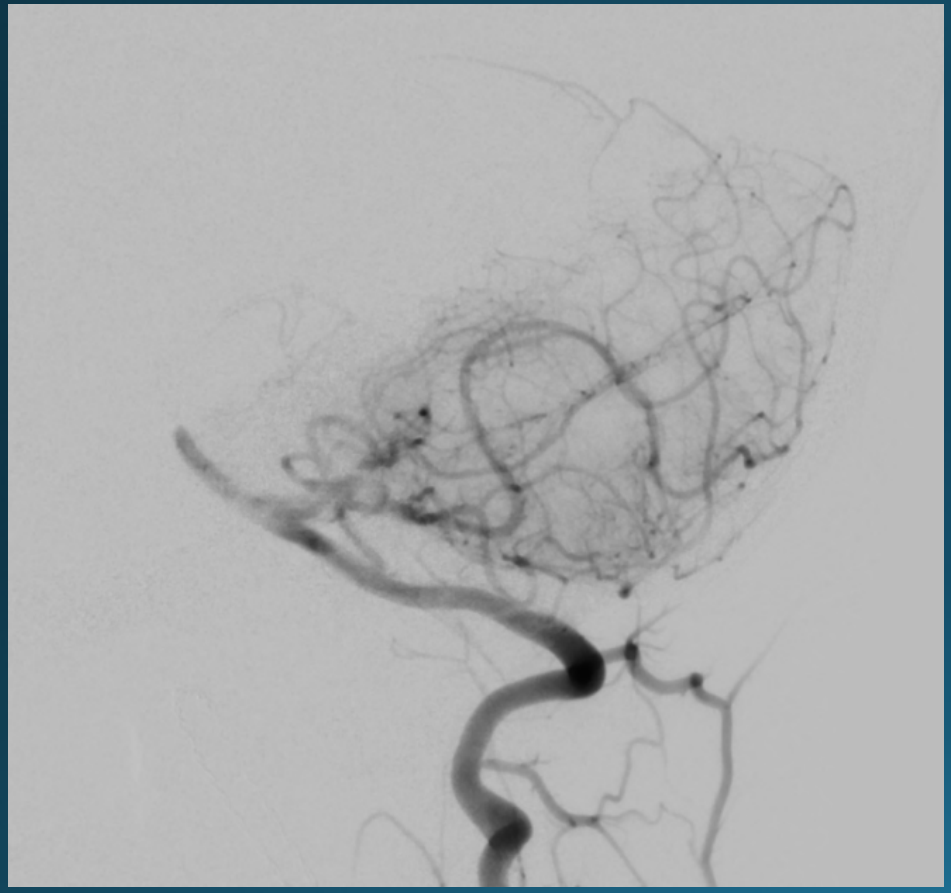

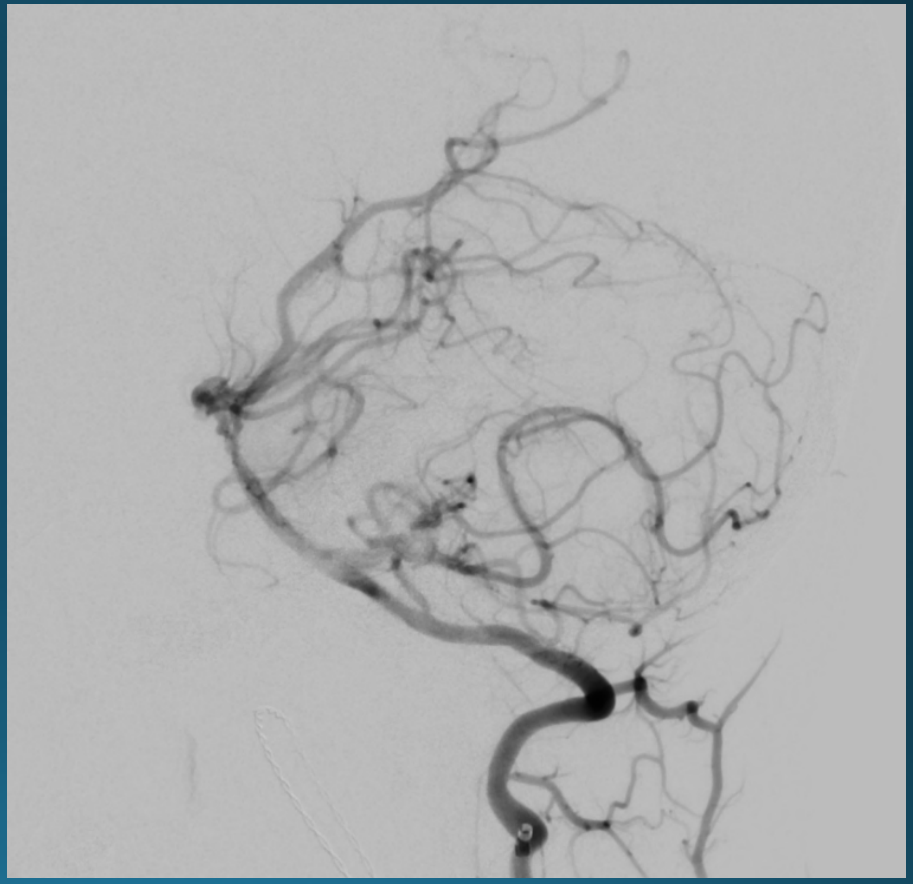

Thank You