Recent Stroke Guidelines: What Should I Be Doing Differently?

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Disclosures

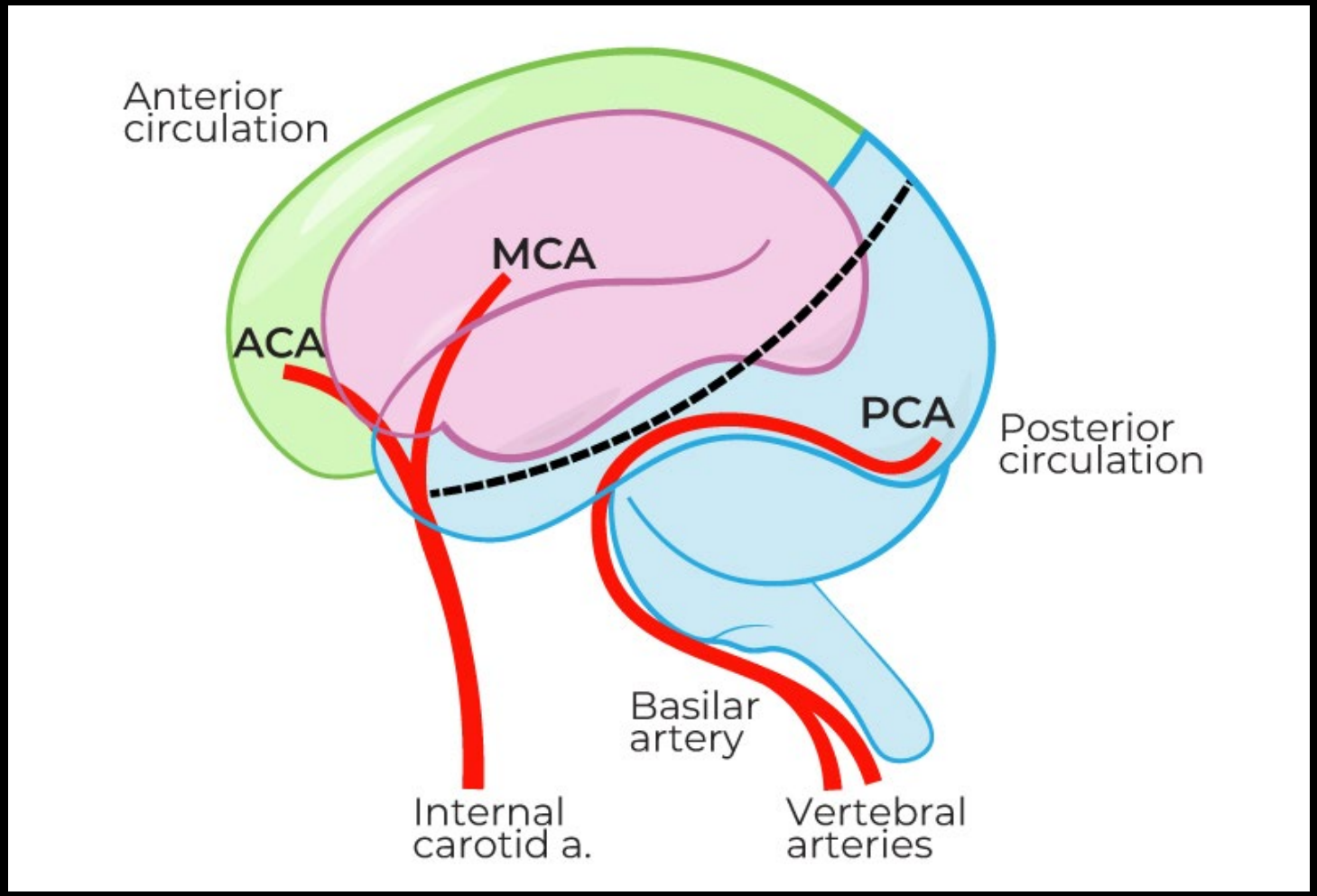
- US Department of Defense (HT9425-24-1-1072): to study outcomes in patients with TBI
- US Department of Defense: to study blood-based biomarkers in TBI
- Abbott Laboratories to advance development of Abbott’s TBI test for diagnosis and determination of severity of brain injury in adults and children

Plan

- Reviewing stroke definitions
- Recent stroke studies
- HREM takeaways

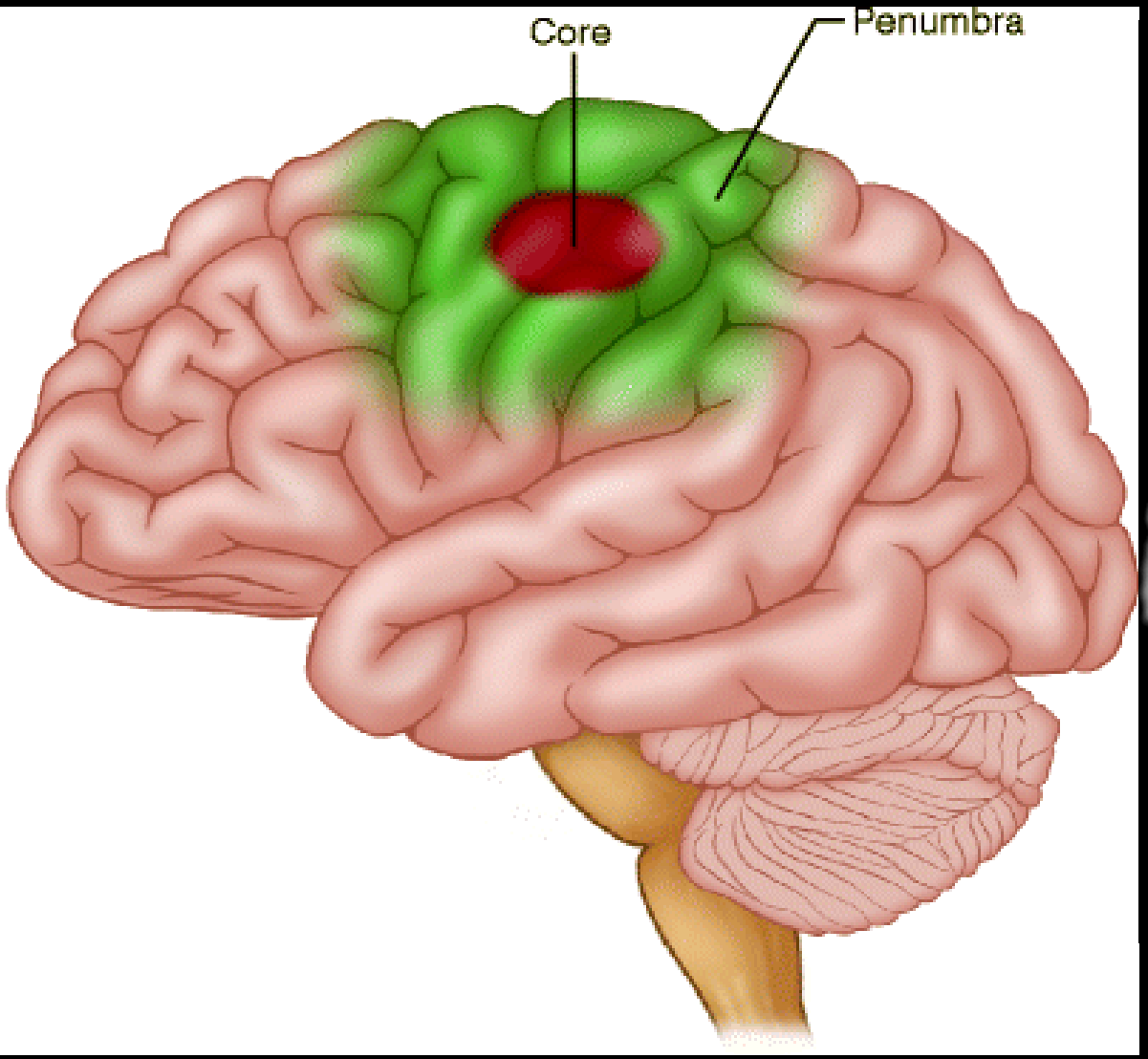
Definitions

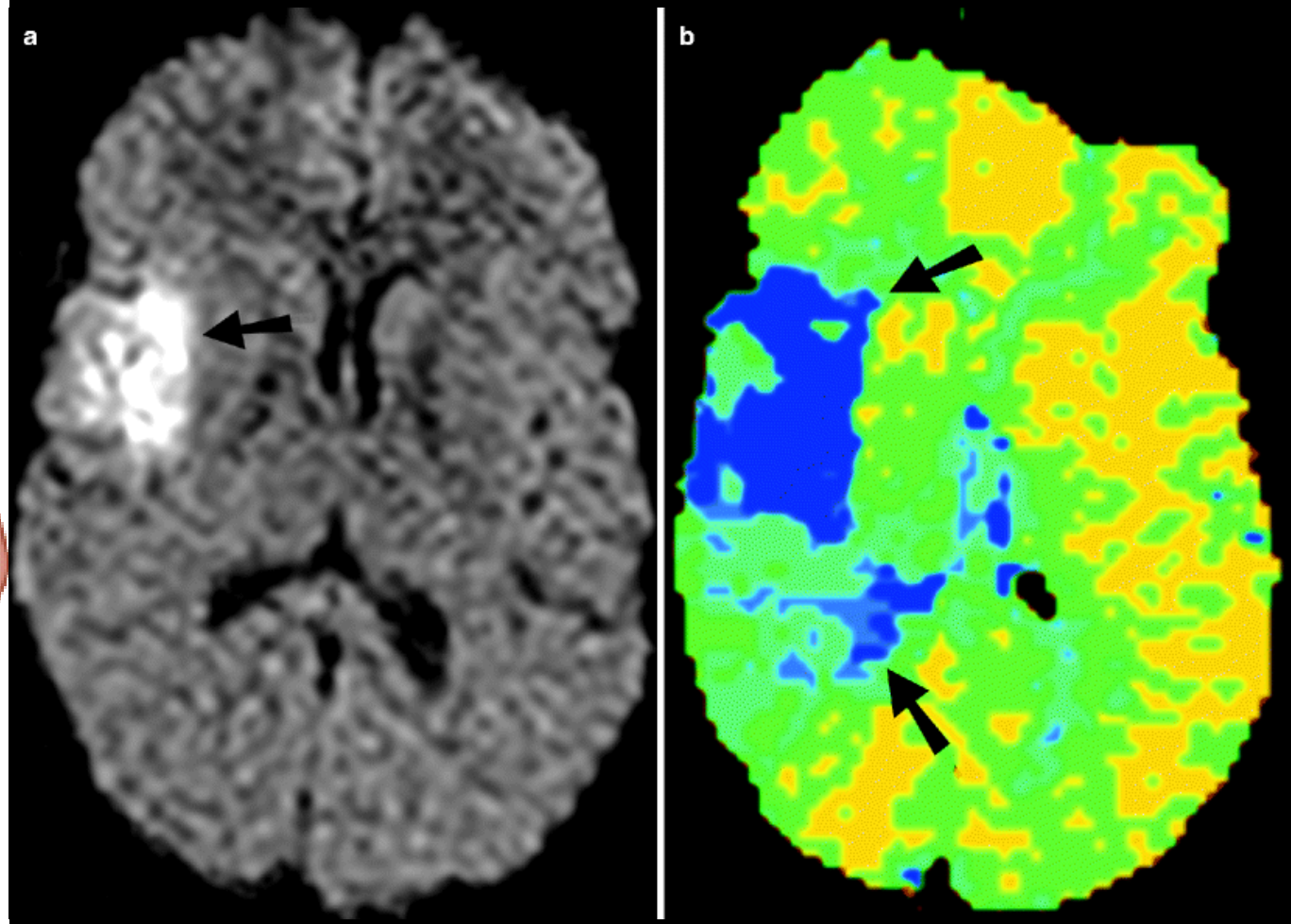
Anterior circulation



https://ditki.com/course/usmle-comlex-high-yield/neuroanatomy/cerebrovascular-supply/71/leptomeningeal-cerebral-arteries/notes

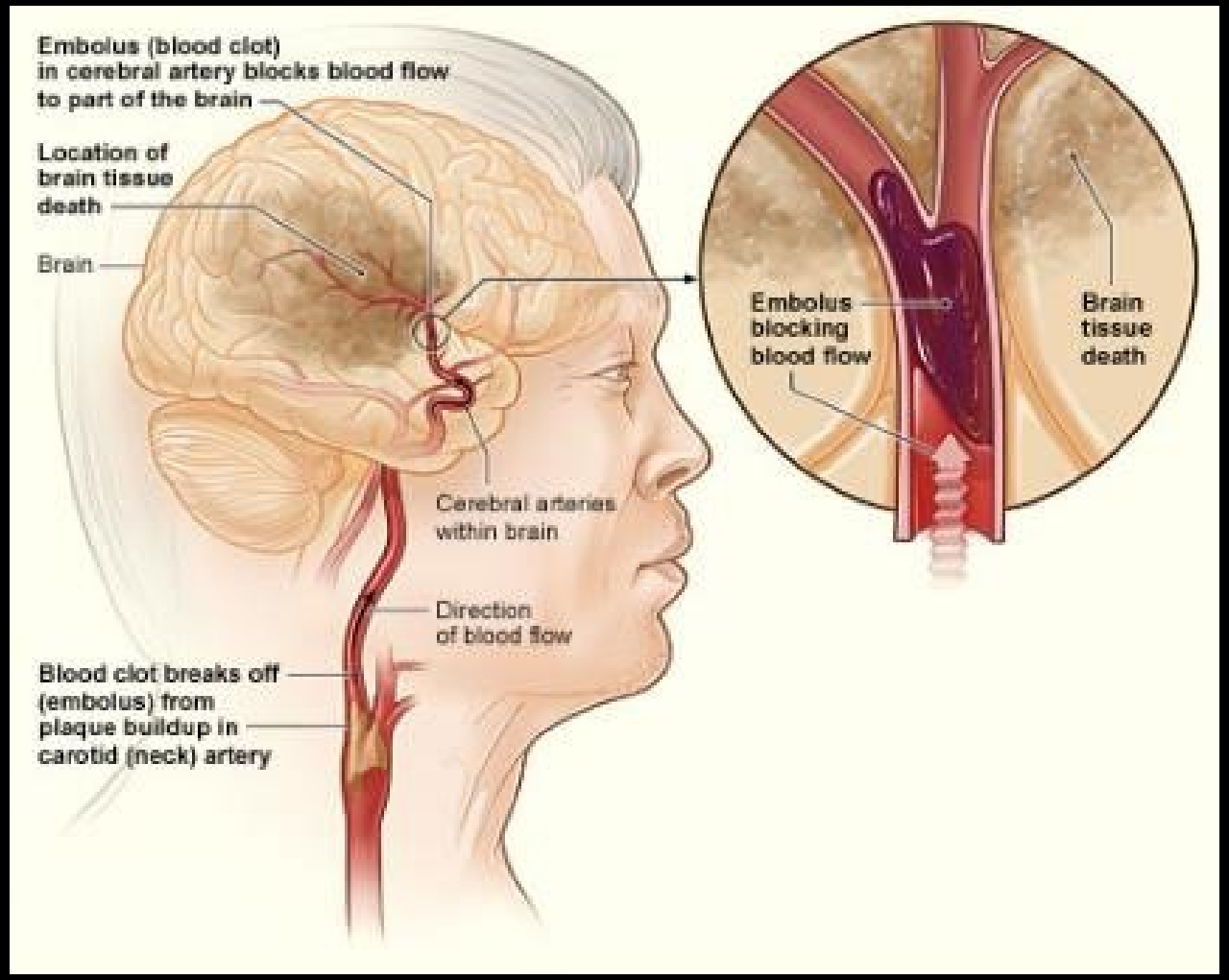
Core infarct





https://radiologykey.com/stroke-and-its-imaging-evaluation/

Stroke causes

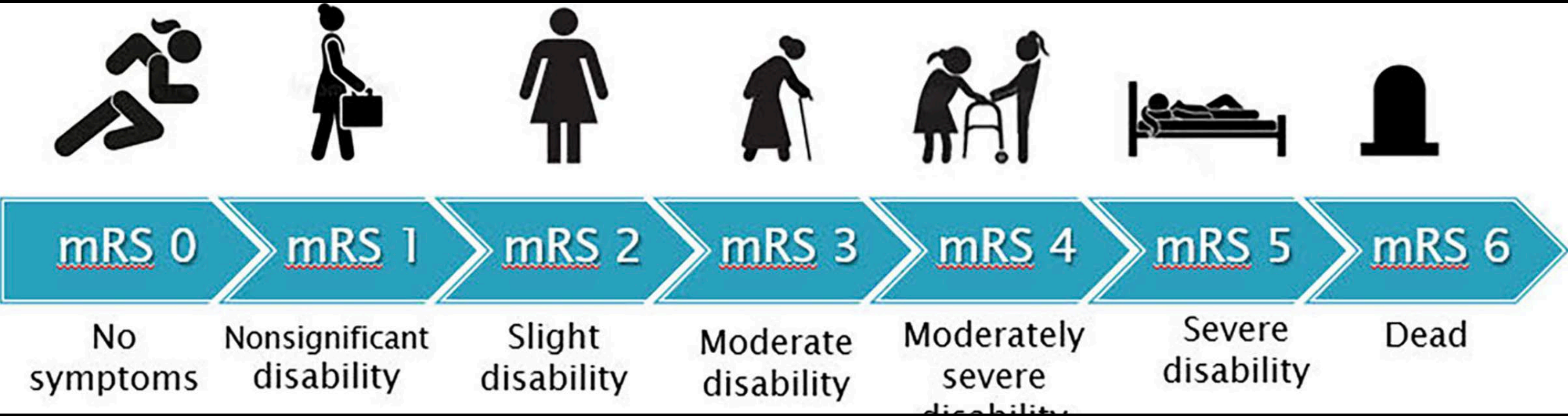


https://www.nhlbi.nih.gov/health/stroke/causes

EVT

- EVT = thrombectomy = embolectomy

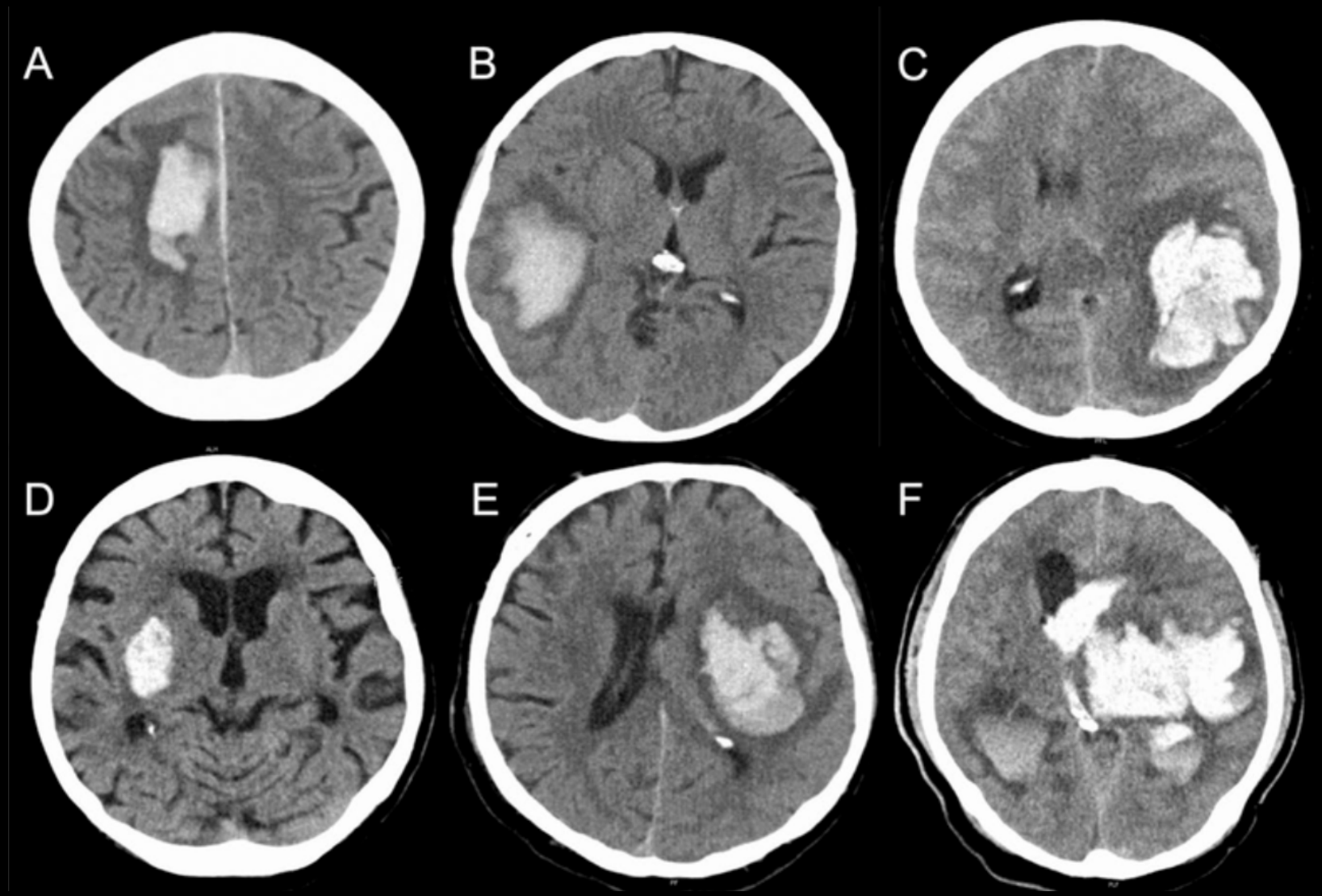
Modified Rankin Scale



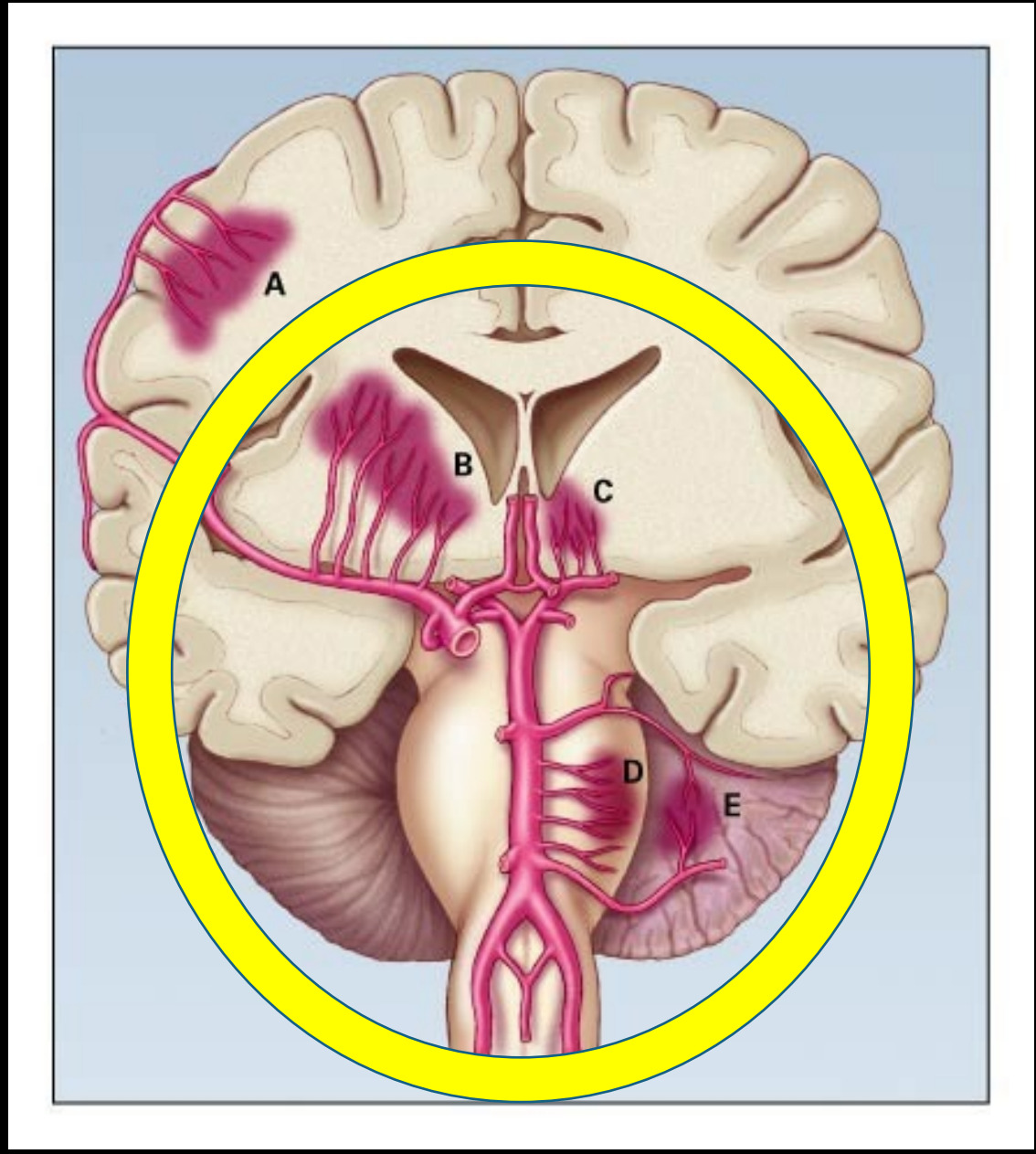
Jeffrey L. Saver, MD Napasri Chaisinanunkul, MD Bruce C.V. Campbell, MBBS, BMedSc, PhD, James C. Grotta, MD, Michael D. Hill, MD, MSc, Pooja Khatri, MD, MS, Jaren Landen, PhD, Maarten G. Lansberg, MD, Chitra Venkatasubramanian, MD, and Gregory W. Albers, MD
StrokeVolume 52, Number 9 https://doi.org/10.1161/STROKEAHA.121.034480

MeVO occlusion

- An acute stroke caused by a clot in medium sized cerebral arteries
  - M2/M3, A2/A3, P2/P3



Haupenthal, David & Schwab, Stefan & Kuramatsu, Joji. (2023). Hematoma expansion in intracerebral hemorrhage – the right target?. Neurological Research and Practice. 5. 10.1186/s42466-023-00256-6.



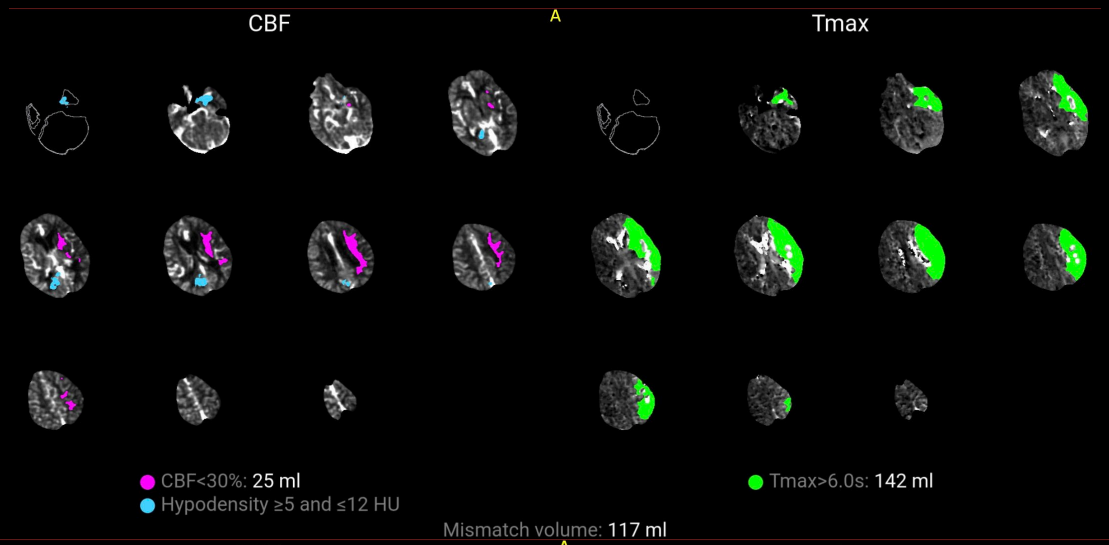
Qureshi AI, Tuhrim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. N Engl J Med. 2001;344(19):1450-1460. doi:10.1056/NEJM200105103441907.

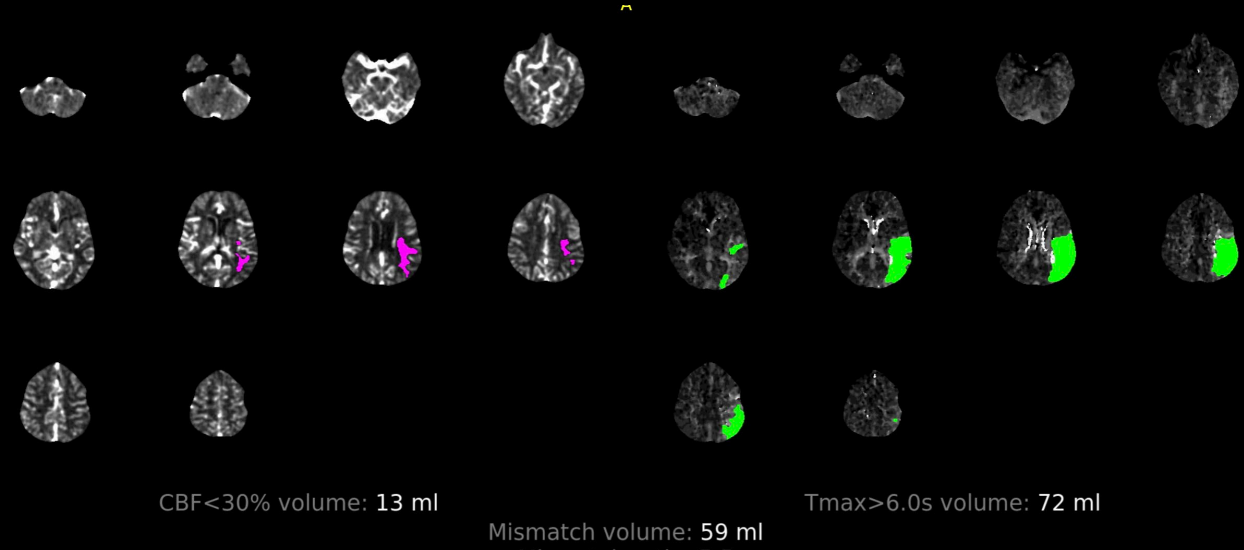
Recent Stroke Studies

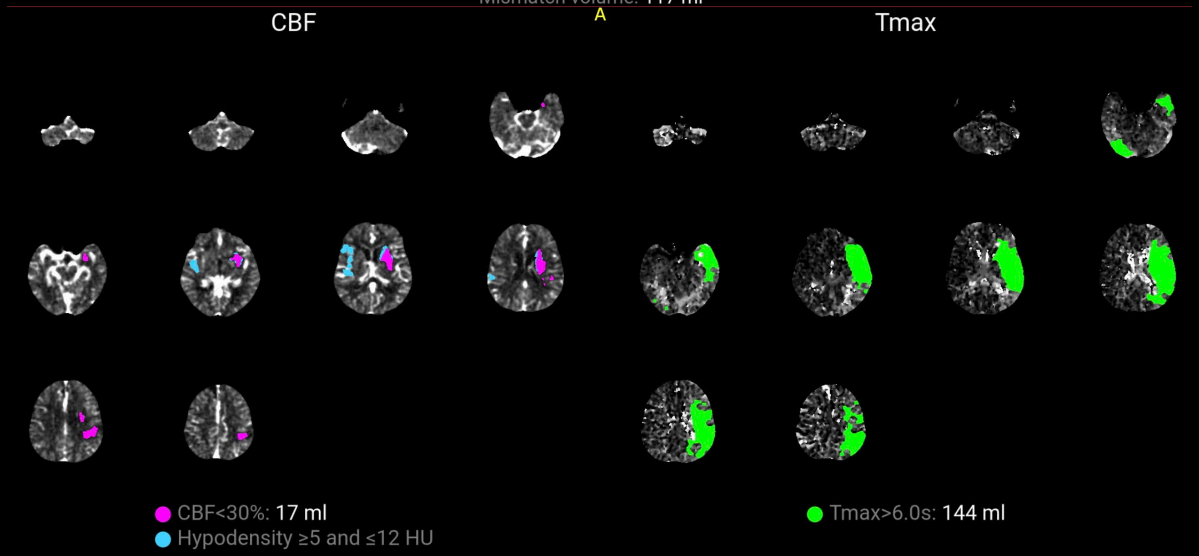
ATLAS

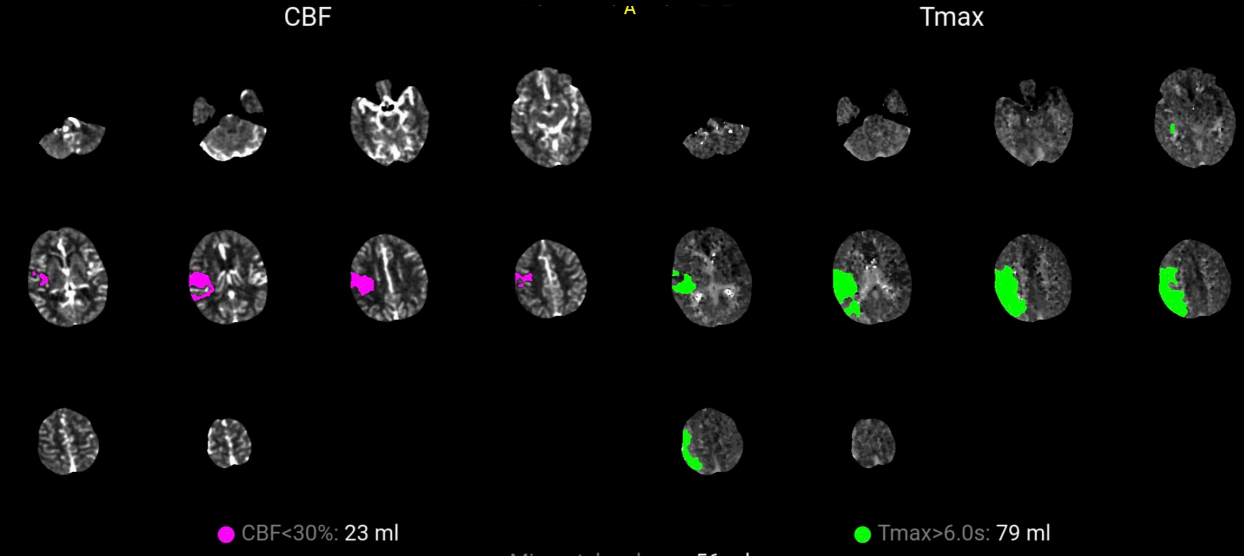
- Meta-analysis: is EVT beneficial for large ischemic cores

ATLAS


CBF
Tmax
CBF<30%: 25 ml
Hypodensity ≥5 and ≤12 HU
Tmax>6.0s: 142 ml
Mismatch volume: 117 ml


CBF<30% volume: 13 ml
Tmax>6.0s volume: 72 ml
Mismatch volume: 59 ml


CBF
Tmax
CBF<30%: 17 ml
Hypodensity ≥5 and ≤12 HU
Tmax>6.0s: 144 ml
Mismatch volume: 127 ml
Mismatch ratio: 8.5


CBF
Tmax
CBF<30%: 23 ml
Tmax>6.0s: 79 ml
Mismatch volume: 56 ml
Mismatch ratio: 3.4

ATLAS

- Over 1,800 patients
- Primary outcome: 90-day mRS
- Primary outcome: 20% with thrombectomy, 7% with medical therapy achieved mRS 0-2
- Mortality: 31% thrombectomy, 37% medical therapy

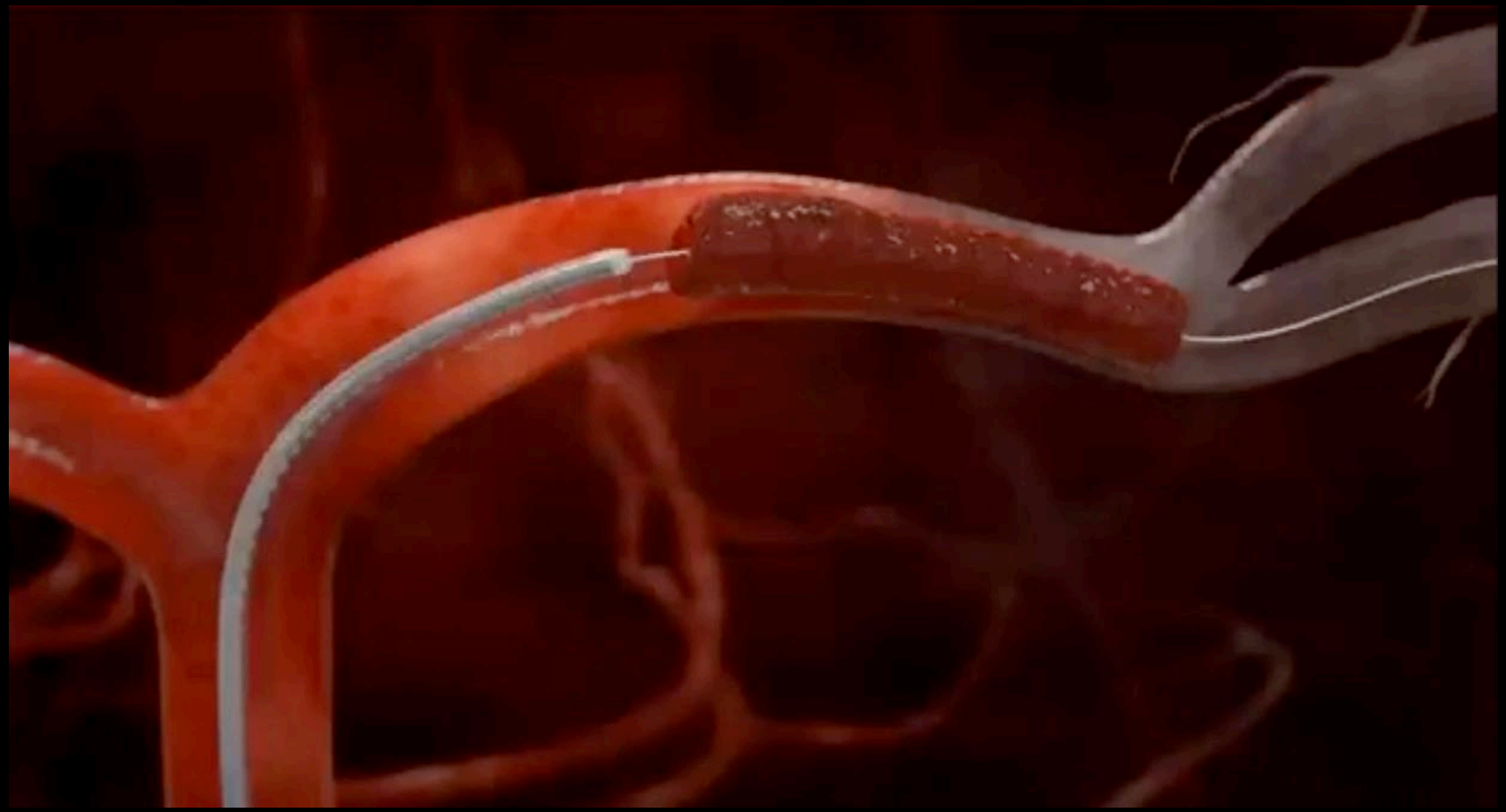
ATLAS

- Bottom line: up to 149mL (large core), EVT is beneficial

TRIMUS

- Large registry
- Question: looking at mild stroke (low NIHSS) but have LVO in proximal vessel, EVT vs. medical treatment

EVT



Courtesy of Stryker

TRIMUS

- Population: NIHSS 0-5, treated 3-4 hours after symptom onset
- Primary outcome: mRS 0-1 at 90 days
- Primary outcome: both groups had 54% rate of mRS 0-1
- Subgroup: potential benefit with EVT for anterior circulation

TRIMUS

- Bottom line: no clear-cut benefit to EVT for mild strokes, current guidelines = EVT for NIHSS 6 and above
- Potential benefit for anterior circulation strokes

ORIGINAL ARTICLE

Endovascular Treatment of Stroke Due to Medium-Vessel Occlusion

Authors: Mayank Goyal, M.D., Ph.D., Johanna M. Ospel, Ph.D., Aravind Ganesh, D.Phil., Dar Dowlatshahi, M.D., Ph.D., David Volders, M.D., Markus A. Möhlenbruch, M.D. , Mouhammad A. Jumaa, M.D., +76 , for the ESCAPE-MeVO Investigators* Author Info & Affiliations

Published February 5, 2025 | N Engl J Med 2025;392:1385-1395 | DOI: 10.1056/NEJMoa2411668

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ESCAPE MeVO

- Question: no current indication for EVT in MeVO occlusions
- Patients enrolled within 12 hours, median age 75
- Primary outcome: functional status at 90 days
- 60% received IV thrombolysis
- Primary outcome: no difference in functional status
- Mortality: 13% in EVT, 8% in medical therapy

ESCAPE MeVO

- Bottom line: no current indication for EVT in MeVO occlusions
- So… still get TNK → transfer for embolectomy more questionable

MeVO

HPI

Certified interpreter used in Cantonese (Chinese)

74yo M no PMHx, no meds, NKDA BIBEMS as Mission Protocol for sudden onset L sided weakness, slurred speech at 1110 this AM. He frequently visits a work site where all employees know him when he leaned up against a wall suddenly at 1110, had L facial droop, drooling, L arm and leg weakness, R gaze deviation and difficulty speaking. Baseline is A&Ox4, walks unassisted. There was no complaint of pain, no fall. Patient cannot answer any further questions due to difficulty speaking.

MeVO

Vitals

ED Triage Vitals [08/21/25 1151]

Temp	
Heart Rate	**90**
Resp	**18**
BP	**(!) 168/99**
SpO2	**99 %**
Temp src	
FiO2	
BP Palpated	

Physical Exam

Vitals and nursing note reviewed.

Constitutional:
- Appearance: He is not diaphoretic.

HENT:
- Head: Atraumatic.

Eyes:
- Comments: **R gaze deviation**

Cardiovascular:
- Rate and Rhythm: Normal rate.

Pulmonary:
- Effort: Pulmonary effort is normal.

Abdominal:
- General: There is no distension.
- Palpations: Abdomen is soft.
- Tenderness: There is no abdominal tenderness.

Musculoskeletal:
- General: No swelling or tenderness.
- Cervical back: Normal range of motion.

Skin:
- General: Skin is warm and dry.

Neurological:
- Mental Status: He is alert.
- Comments: **Slurred speech**

R gaze deviation

L facial droop with drooling

Flaccid L arm and L leg

Freely moving R arm and leg AG

MeVO

ED Course & Medical Decision Making

Medical Decision Making

74M no PMHx, no meds with sudden onset L sided weakness, R gaze deviation c/f R MCA stroke. No known meds. Delay to TNK due to unable to obtain hx from patient, unable to reach wife and son. Neuro at bedside within 2 minutes of arrival. Plan for TNK, CTA to rule out LVO, NIR if LVO, stroke labs, admit to neuro ICU.

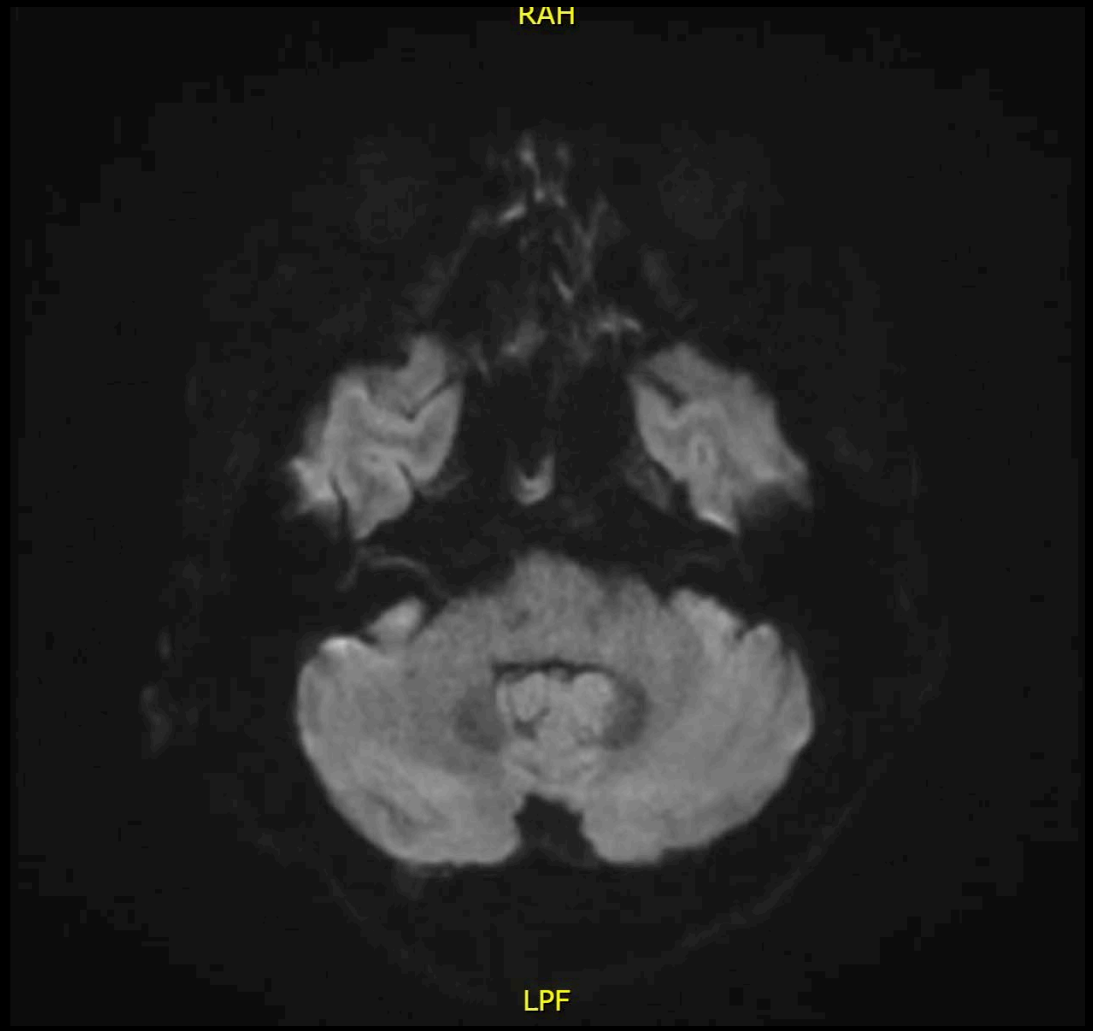
MeVO

MTT: Mean Transit Time
CBV: Cerebral Blood Volume

MeVO

- 1144: Hospital arrival
- 1147: CT Scan
- 1155: Mix TNK
- 1156: Preparing to give TNK
- 1200: Per son on phone, no blood thinners, no allergies
- 1201: 13mg TNK given
- 1300: Much improved exam. No more R gaze. Moving L side.

MeVO



DWI: Diffusion Weighted Imaging
ADC: Apparent Diffusion Coefficient
FLAIR: Fluid-Attenuated Inversion Recovery

Original Investigation

Intra-arterial Tenecteplase for Acute Stroke After Successful Endovascular Therapy

The ANGEL-TNK Randomized Clinical Trial

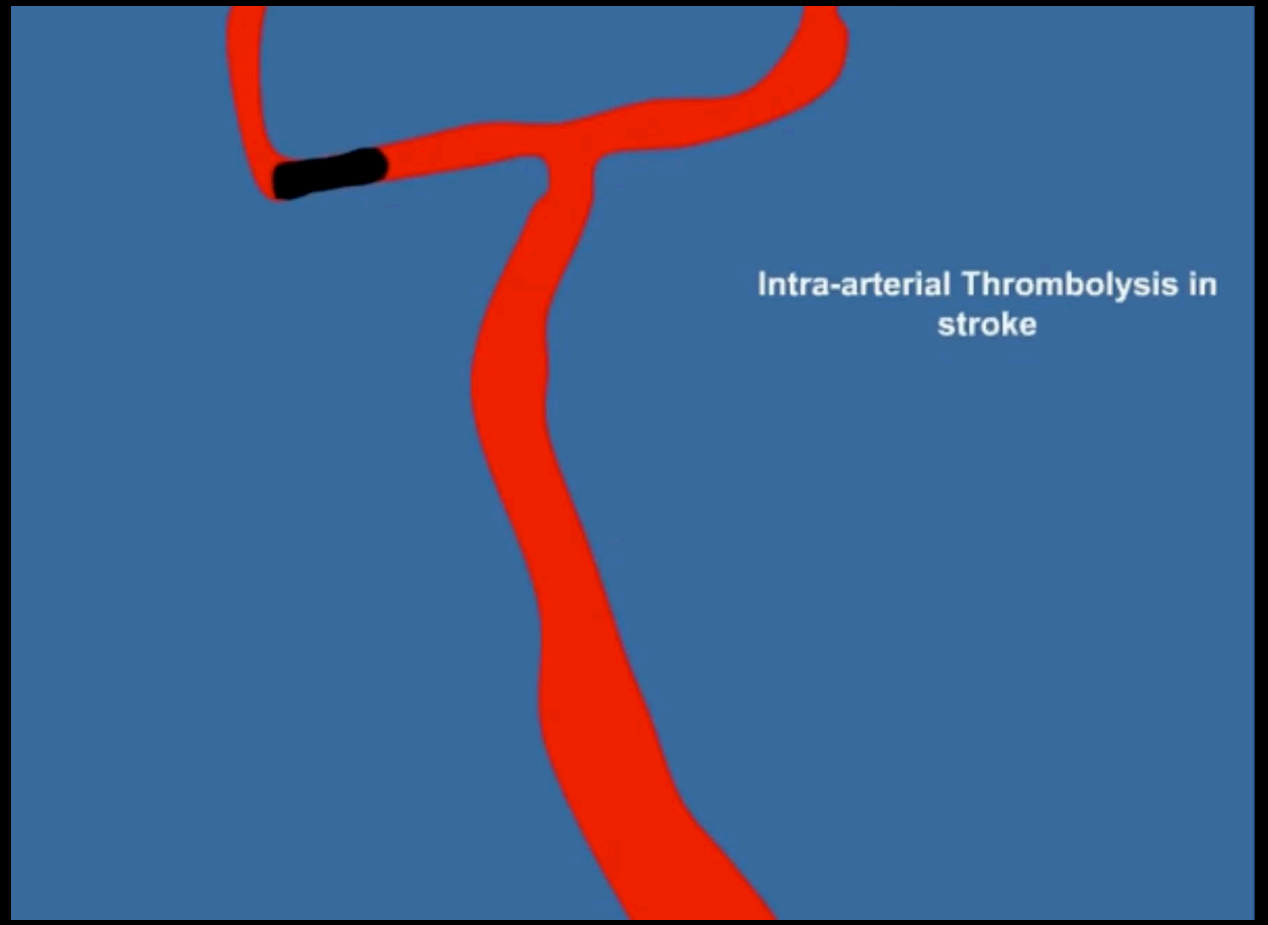
Zhongrong Miao, PhD[1,2]; Gang Luo, PhD[1]; Ligang Song, MD[1]; et al

» Author Affiliations | Article Information

ANGEL TNK

- Chasing thrombectomy with intra-arterial thrombolysis
- Rationale: following thrombectomy, sometimes clot fragments go into smaller vessels
- Treated up to 24 hours after TNK with low dose intra-arterial TNK

Intra-arterial Thrombolysis



ANGEL TNK

- Outcome: The primary outcome was mRS of 0-1at 90 days, 40.5% with TNK and 26% in control group
- Bleeding and mortality similar in both groups

ANGEL TNK

- Bottom line: Coming soon! Chasing thrombectomy with intra-arterial thrombolysis

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Early Minimally Invasive Removal of Intracerebral Hemorrhage

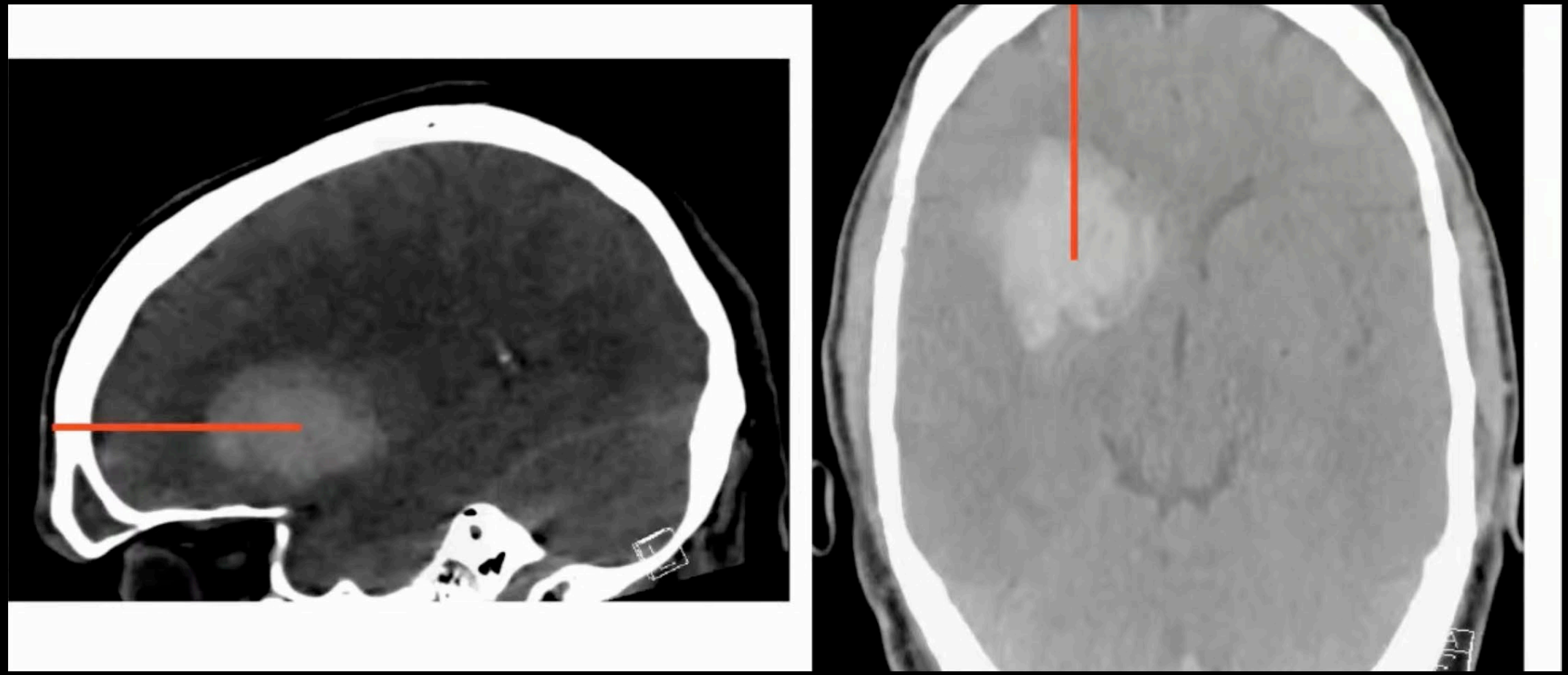
Authors: Gustavo Pradilla, M.D. , Jonathan J. Ratcliff, M.D., M.P.H., Alex J. Hall, D.H.Sc. , Benjamin R. Saville, Ph.D., Jason W. Allen, M.D., Ph.D., Giorgio Paulon, Ph.D., Anna McGlothlin, Ph.D. , +20 , for the ENRICH trial investigators* Author Info & Affiliations

Published April 10, 2024 | N Engl J Med 2024;390:1277-1289 | DOI: 10.1056/NEJMoa2308440 | VOL. 390 NO. 14

ENRICH

- Design: early (within 24 hours) minimally invasive surgical removal of hematoma vs. guideline-based medical management in ICH
- Intervention: Adults within 24 hours of lobar or anterior basal ganglia ICH with hematoma volume of 30-80mL

Minimally Invasive ICH Evacuation



Dr. Christopher Kellner/Mt. Sinai Hospital

ENRICH

- Primary efficacy end point: mean score for disability on mRS at 180 days
- Results: mean mRS score better with surgery than medical management alone but benefit is likely attributable to lobar hemorrhages
- Fewer patients died within 30 days in surgical group

ENRICH

- Bottom line: ICH, especially lobar hemorrhages do better with surgery than medical management

The Lancet
Volume 402, Issue 10395, 1–7 July 2023, Pages 27-40

Articles

The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial

Prof Lu Ma MD [a] *, Xin Hu MD [a] *, Lili Song PhD [c d] *, Xiaoying Chen PhD [d] *, Menglu Ouyang PhD [c d], Prof Laurent Billot MRes [d], Qiang Li MBiostat [d], Alejandra Malavera MD [d], Xi Li MM [a], Prof Paula Muñoz-Venturelli PhD [d e], Prof Asita de Silva DPhil [f], Prof Nguyen Huy Thang MD [g], Prof Kolawole W Wahab MD [h], Prof Jeyaraj D Pandian MD [i], Prof Mohammad Wasay MD [j], Prof Octavio M Pontes-Neto PhD [k], Prof Carlos Abanto MD [l], Prof Antonio Arauz PhD [m], Haiping Shi MM [n], Guanghai Tang MBBS [o]...Huy Thai

INTERACT-3

- Multicenter, prospective, randomized, open-treatment, blinded trial
- N=2,839
  - intensive-treatment (n=1,403)
  - guideline-recommended (standard-treatment) (n=1,436)
- Primary outcome: death or major disability
  - Major disability: mRS 3 to 5 at 90 days after randomization
- ≥2 systolic BP of ≥150 and ≤220 mmHg, recorded ≥2 minutes apart
- Treatment goal of systolic BP <140 mm Hg within 1 hour after randomization and of maintaining this level for the next 7 days
- **Death or major disability:** 52.0% vs. 55.6% (OR 0.87; 95% CI 0.75-1.01; P=0.06)

INTERACT-3

- Bottom line: In ICH, BP goal of SBP 130-140
- Clevidipine: extremely rapid onset (2–4 minutes) and offset (5–15 minutes) of action

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 18, 2024 VOL. 391 NO. 3

Tenecteplase for Ischemic Stroke at 4.5 to 24 Hours without Thrombectomy

Yunyun Xiong, M.D., Ph.D., Bruce C.V. Campbell, M.B., B.S., Ph.D., Lee H. Schwamm, M.D., Xia Meng, M.D., Ph.D., Aoming Jin, Ph.D., Mark W. Parsons, M.B., B.S., Ph.D., Marc Fisher, M.D., Yong Jiang, Ph.D., Fengyuan Che, M.D., Lihua Wang, M.D., Ph.D., Li Zhou, M.D., Hongguo Dai, M.D., Xintong Liu, M.D., Yuesong Pan, Ph.D., Chunmiao Duan, M.D., Yuming Xu, M.D., Ph.D., Anding Xu, M.D., Ph.D., Lixia Zong, M.D., Ph.D., Zefeng Tan, M.D., Ph.D., Wanxing Ye, Ph.D., Hao Wang, M.D., Ziran Wang, M.D., Manjun Hao, M.D., Zhixin Cao, M.D., Liyuan Wang, M.D., Shuangzhe Wu, M.D., Hao Li, Ph.D., Zixiao Li, M.D., Ph.D., Xingquan Zhao, M.D., Ph.D., and Yongjun Wang, M.D., for the TRACE-III Investigators*

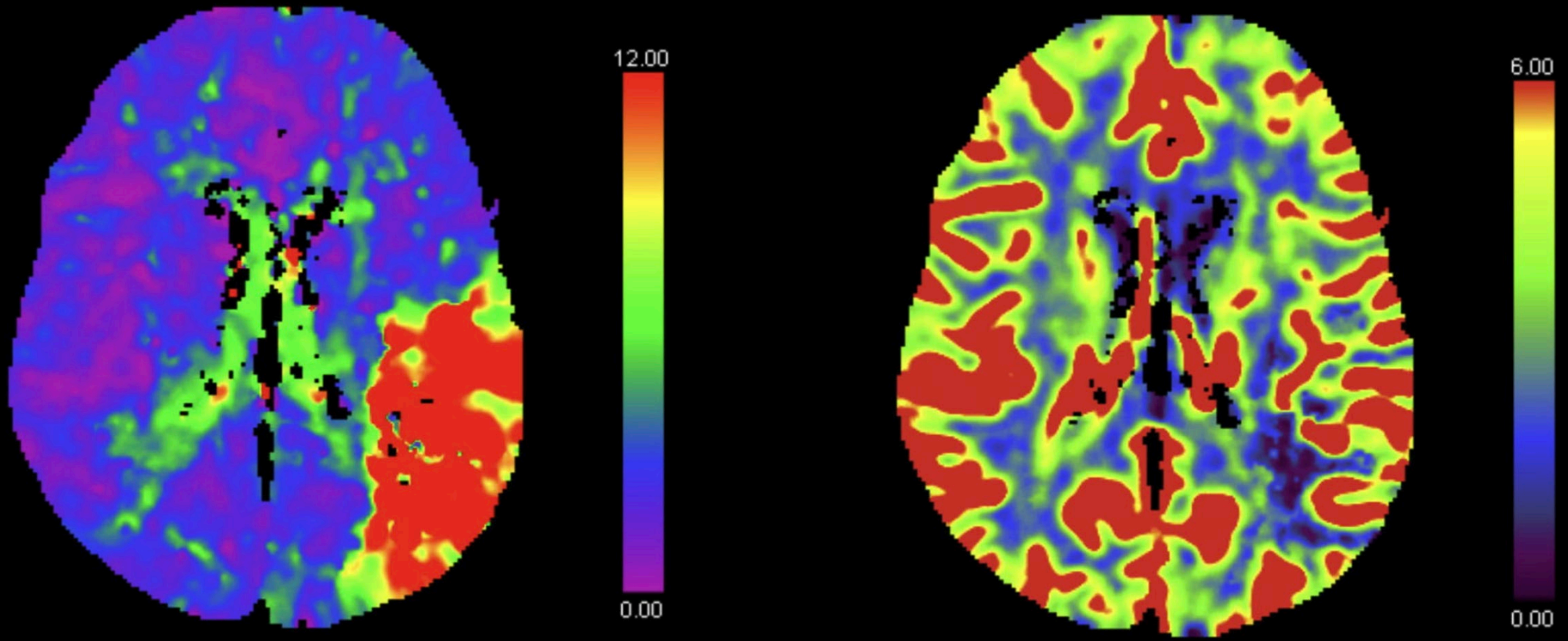
WAKE UP, EXTEND, & TRACE-III...

- Stroke symptom onset 2.5 to 24 hours prior
  - For those with 'wake up' stroke, this time was the last time seen normal.
- Pre-stroke modified Rankin score ≤1
- Baseline NIHSS between ranging from 6 to 25
- Salvageable brain tissue on perfusion imaging
- 38% had wake-up strokes
- Tenecteplase vs. usual care
- Outcome: absence of disability (mRS <= 1) at 90 days
  - 33% vs 24% (RR 1.37; 95% CI 1.04 to 1.81; P=0.03; NNT=11)

WAKE UP, EXTEND, & TRACE-III…

- Bottom line: Strokes out to 24 hours should be treated as acute ischemic strokes
- But… need CT perfusion or MRI
- So… if NIHSS 6-25 transfer out if < 24 hours

Core-to-Penumbra Ratio < 50%?



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intravenous Tenecteplase before Thrombectomy in Stroke

Authors: Zhongming Qiu, M.D. , Fengli Li, M.D., Hongfei Sang, M.D., Guangxiong Yuan, M.D., Dongjing Xie, M.D., Kai Zhou, M.D., Maohua Li, M.D., +59 , for the BRIDGE-TNK Trial Investigators* Author Info & Affiliations

Published May 21, 2025 | N Engl J Med 2025;393:139-150 | DOI: 10.1056/NEJMoa2503867 | VOL. 393 NO. 2

BRIDGE TNK

- Rationale: TNK in combination with thrombectomy vs. EVT alone
- 550 patients enrolled, median NIHSS 16
- Primary outcome: mRS 0-2 at 90 days
- Primary outcome: 53% in TNK with EVT group, 44% in EVT alone
- Caveat: Enrolled patients had to present to treating hospitals, short time delays = 16 minutes between TNK and EVT

BRIDGE TNK

- Bottom line: TNK in combination with thrombectomy works better than EVT alone
- So… if you transfer out for EVT, give the TNK and then transfer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Tirofiban Infusion after Intravenous Thrombolysis for Stroke

Authors: Chunrong Tao, M.D., Ph.D., Tianlong Liu, M.D., Tao Cui, M.D., Jie Liu, M.D., Zongliang Li, M.D., Youquan Ren, M.D., Xingli Zhao, M.D., +47 , for the ASSET-IT Investigators* Author Info & Affiliations

Published July 3, 2025 | N Engl J Med 2025;393:1191-1201 | DOI: 10.1056/NEJMoa2503678 | VOL. 393 NO. 12

ASSET-IT

- Rationale: if stroke is due to atherosclerosis, can re-occlude after TNK
- Study: IV tirofiban (anti-platelet) as adjunct to TNK within 4.5 hours
- 832 patients enrolled, median NIHSS 6
- Treatment: Tirofiban 24-hour infusion
- Primary outcome: mRS 0-1 at 90 days
- Primary outcome: 66% in IV tirofiban group vs. 55% in placebo
- Symptomatic ICH 1.7% in treatment arm (very low)

ASSET-IT

- Bottom line: Possibly coming soon! IV anti-platelet as adjunct to TNK within 4.5 hours

HREM Takeaways:

- EVT beneficial for large ischemic cores
- No clear-cut benefit to EVT for mild strokes → EVT for NIHSS 6 and above
- No current indication for EVT in MeVO occlusions
- The near future: Treating up to 24 hours after TNK with low dose intra-arterial TNK to treat broken clots
- The near future: aspiration of lobar hemorrhages >>> deep hemorrhages
- TNK in combination with thrombectomy is better than EVT alone

Thank you!

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