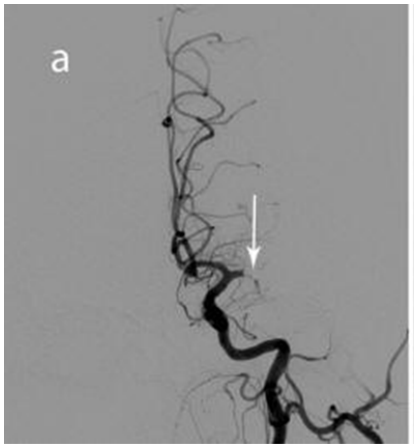
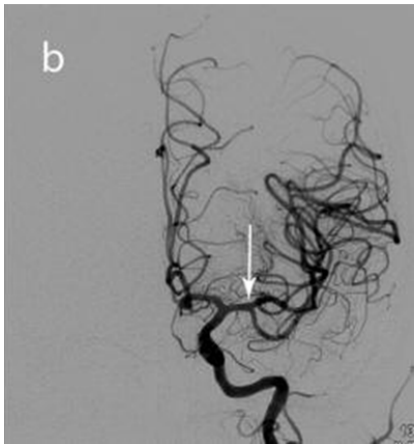
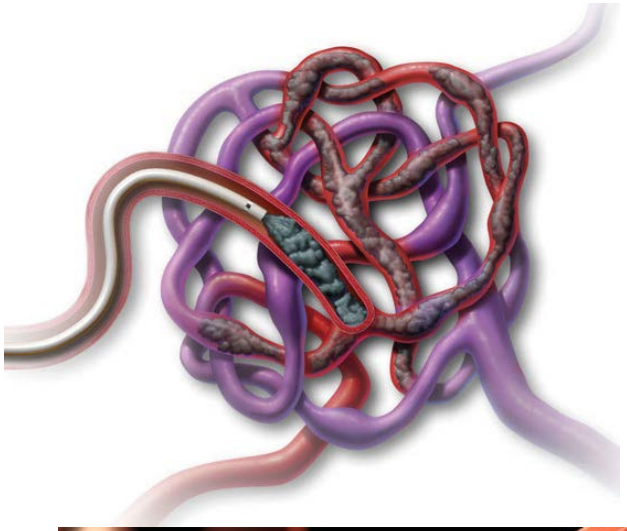
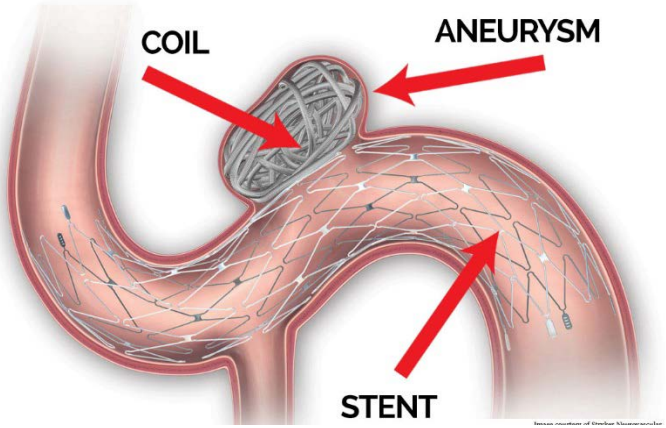








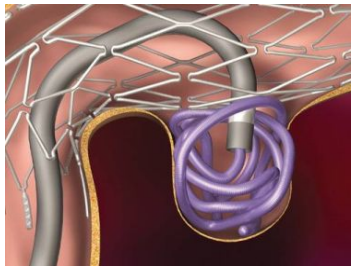
Neuro-Endovascular Management of LVO Stroke & Other Neurovascular Disorders

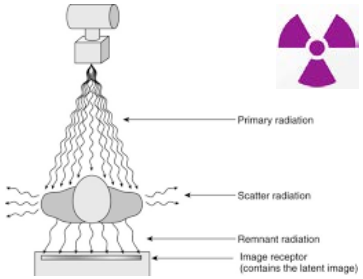
Avera eCARE Education – August 13, 2019

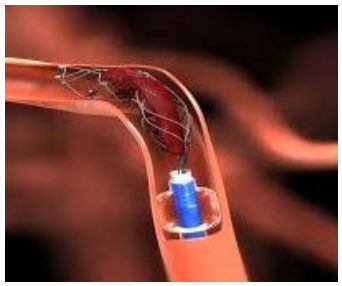
Alex J. Linn, M.D.
Neuro-Endovascular Surgery -&- Vascular Neurology
Ellen Gulbrandson, RN
Stroke Coordinator

Avera

Field Politics & The Naming Crisis







ESN - Endovascular Surgical Neuroradiology

NIS - Neuro-Interventional Surgery

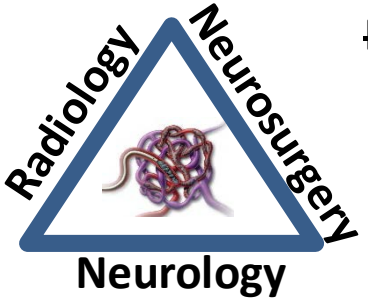
NES - Neuro-Endovascular Surgery

INR – Interventional Neuroradiology

ENS - Endovascular Neurosurgery

I~~N~~R – Interventional ~~Neuro~~Radiology

~~E~~NS - ~~Endovascular~~ Neurosurgery



CNSES – Central Nervous System Endovascular Surgery

INC – Interventional NeuroCardiology

IVN – Interventional Neurology

EVN - Endovascular Neurology

LECTURE OBJECTIVES

1) The LVO Stroke:

- *What is an LVO?*
- *Stroke & LVO data*

2) Rapid Evaluation & Neuroimaging Tools:

- *The Hyperacute Stroke Algorithm*
- *Confirming the LVO*

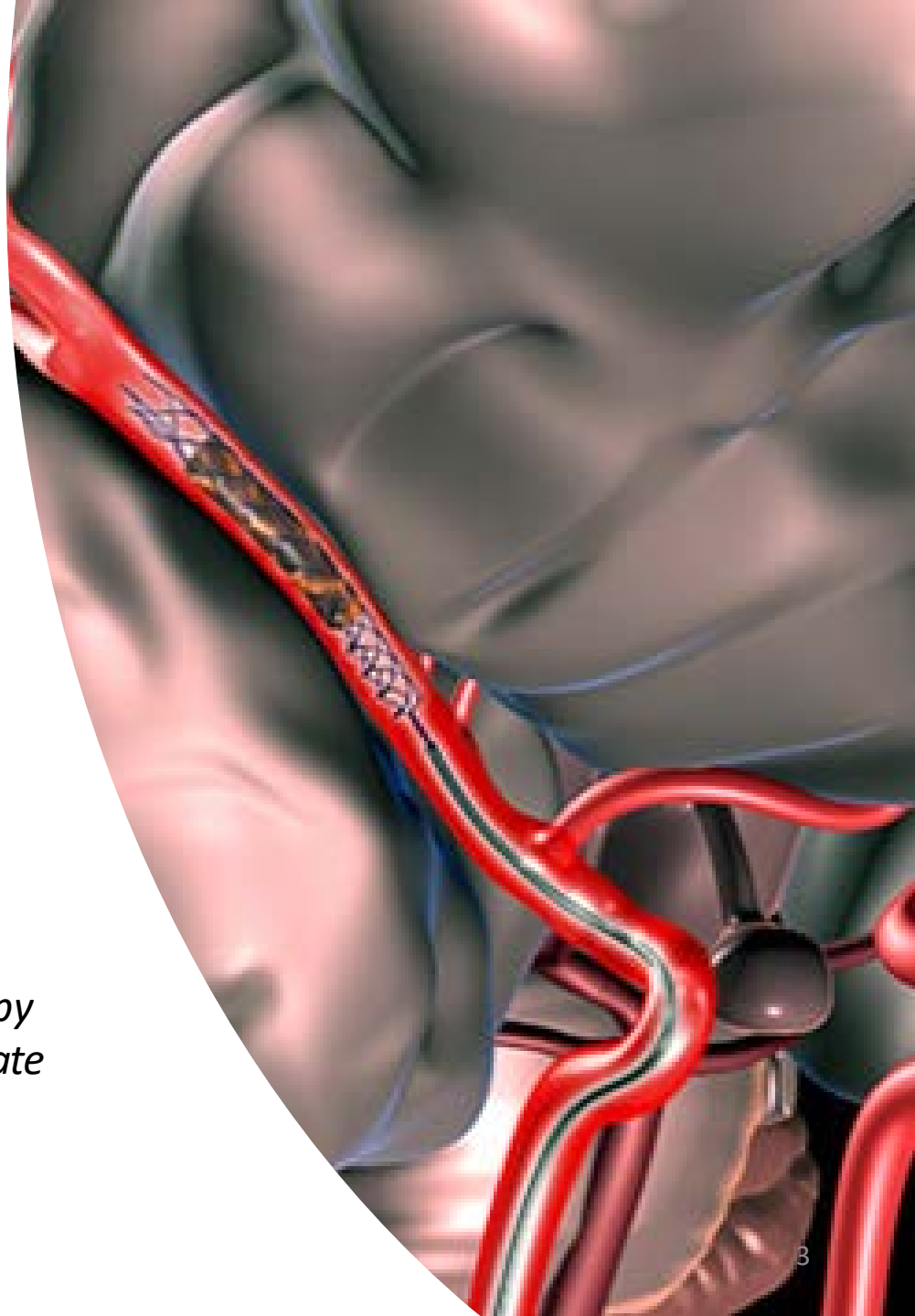
3) Managing the LVO:

- *The treatment*
- *The evidence*

4) Expanding the LVO Treatment Window:

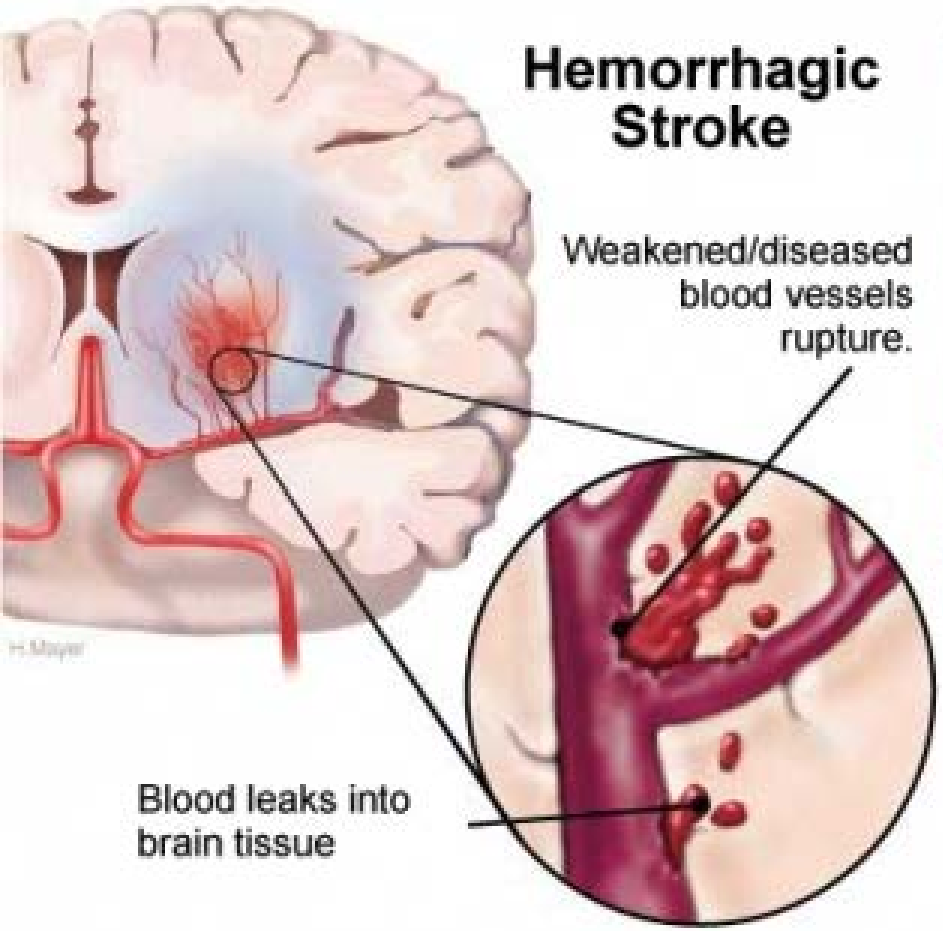
- *Extending the acute LVO stroke therapy window to 24 hours (for the appropriate patients)*

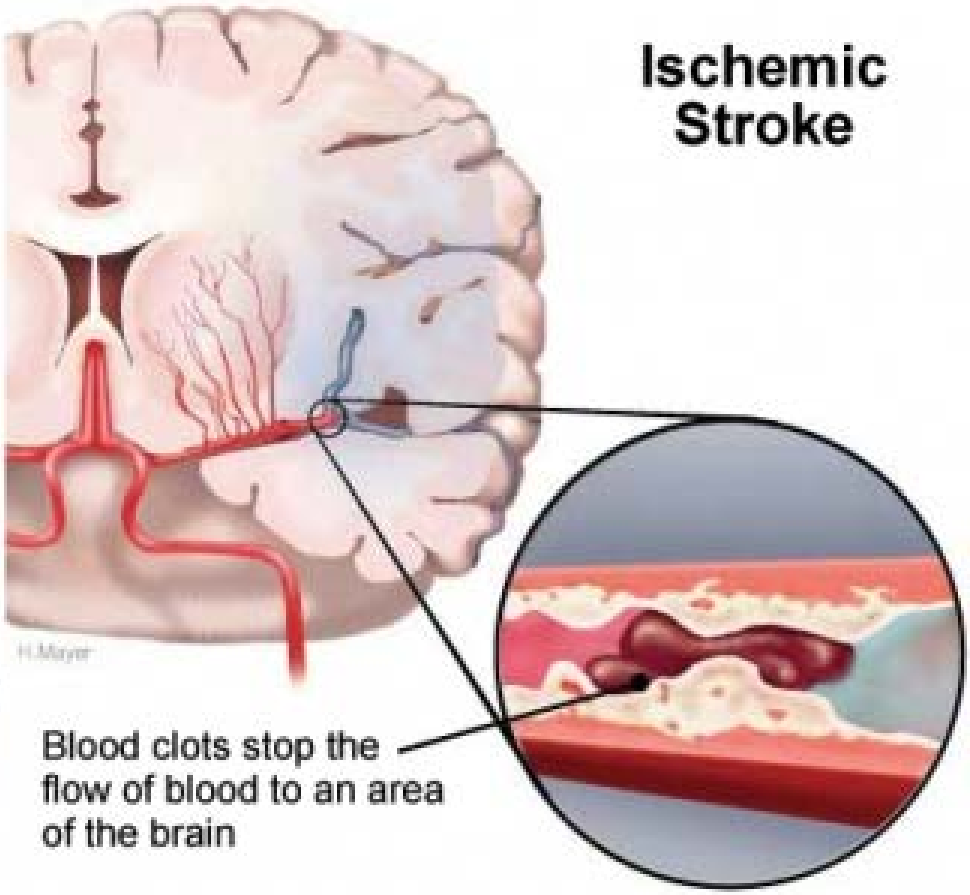
5) Other neuro-endovascular services



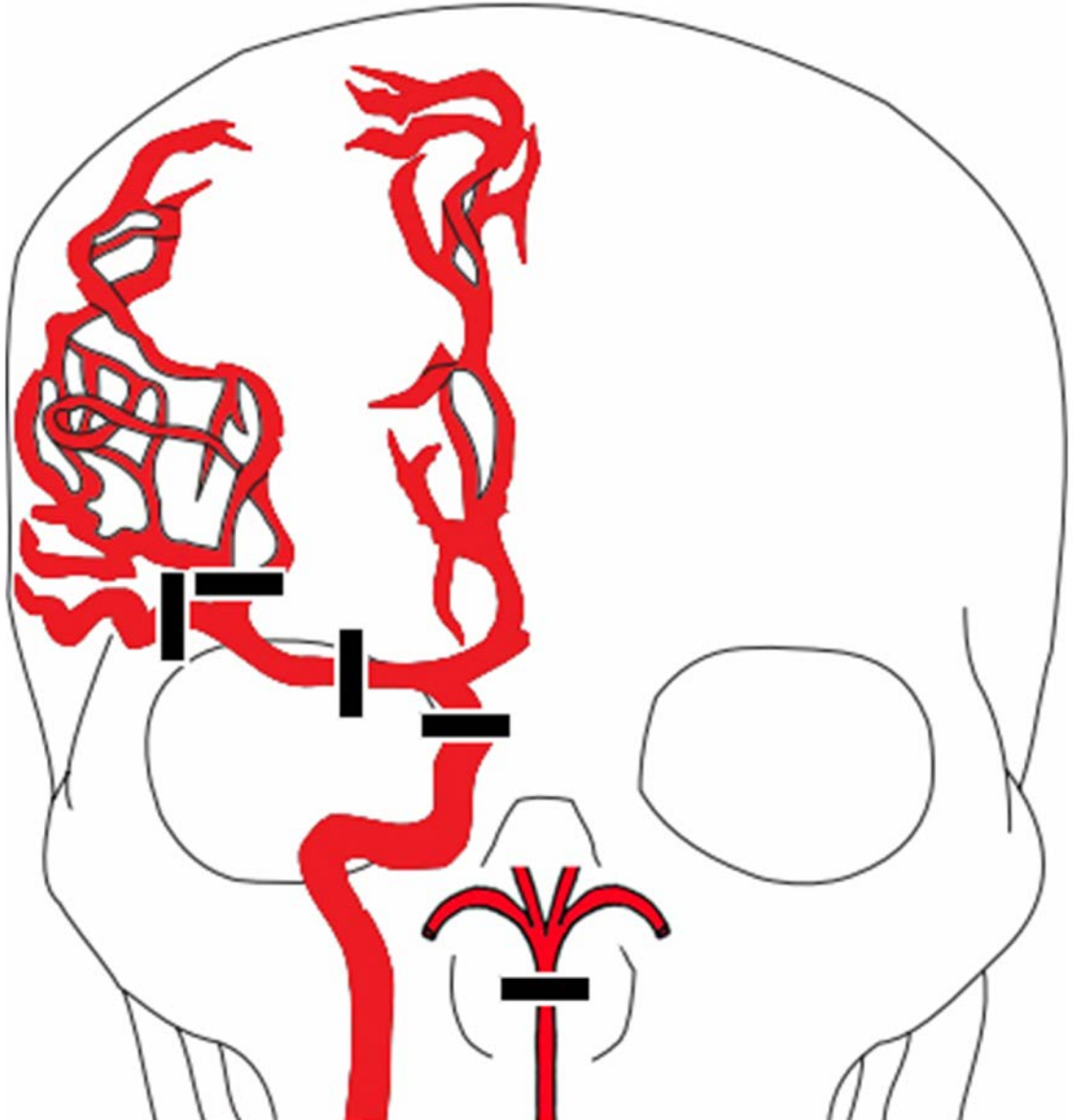
The LVO Stroke

STROKE
Hemorrhagic (~13%) -vs- Ischemic (~87%)





The Large Vessel Occlusion Stroke



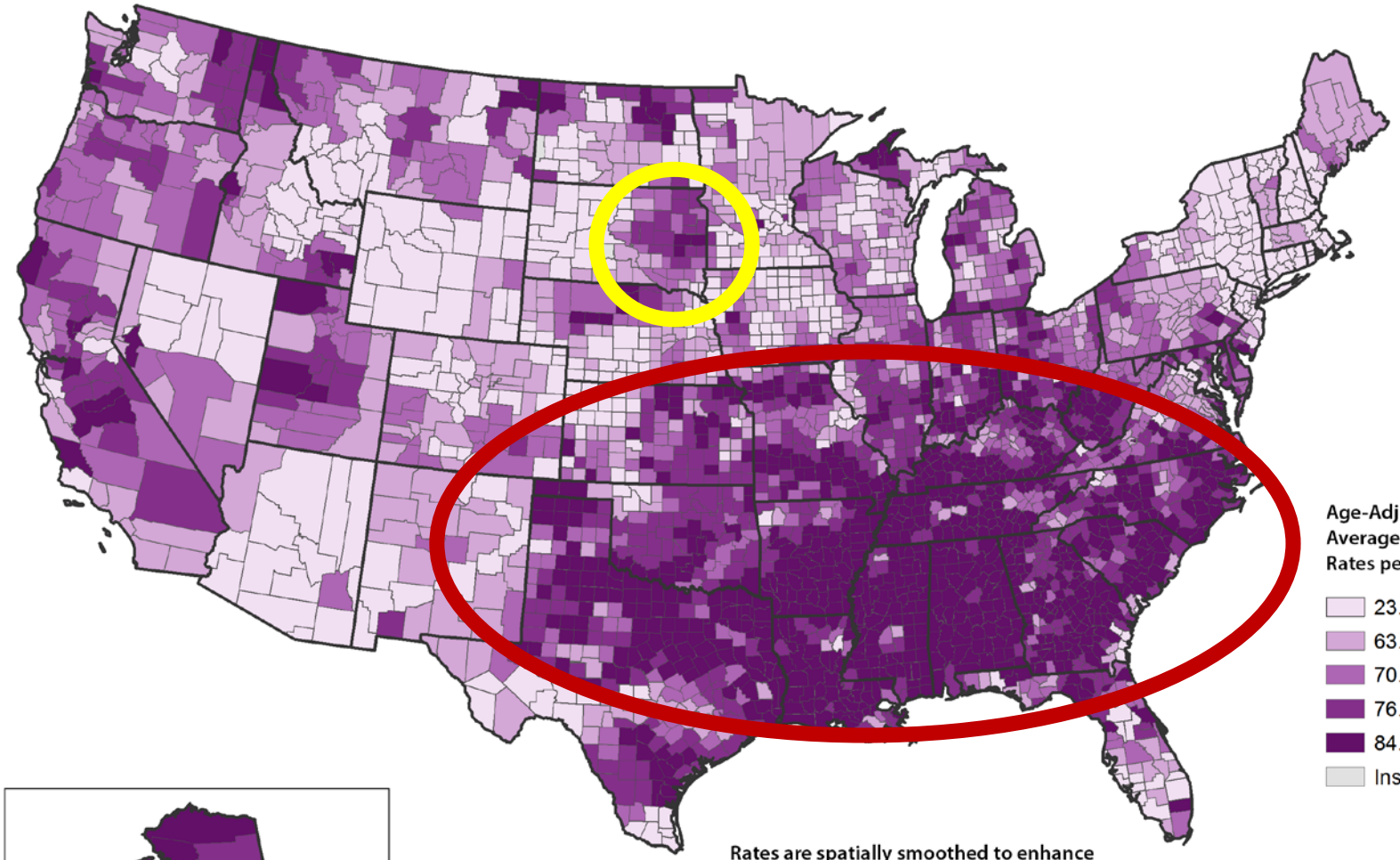
General Stroke Facts

- Currently the 5th leading cause of death in US
- Kills 140,000 Americans each year (*1 out of every 20 deaths*)
- 795,000 people per year in US have a stroke (*610,000 with first time stroke*)
- Cost to the US per year: $34,000,000,000.00
- A leading cause of long-term disability

LVO Stroke Facts

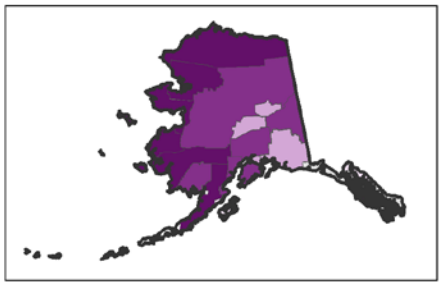
- LVO
  - Carotids, Verts$^{\pm}$, MCA M1 ± M2, Basilar
- MVO (distal LVO)
  - ACA A1/A2, MCA M2, PCA P1
- LVO = ~10% of all ischemic strokes
- If NIHSS > 10
  - 81% PPV for LVO (48% sensitive) [Maas '09]
- Many LVO patients present with NIHSS < 10
- IV tPA works on ~10% of LVO's

Stroke Death Rates, 2014 - 2016
Adults, Ages 35+, by County



Age-Adjusted
Average Annual
Rates per 100,000

- 23.1 - 62.9
- 63.0 - 70.0
- 70.1 - 76.4
- 76.5 - 84.1
- 84.2 - 194.9
- Insufficient Data



Rates are spatially smoothed to enhance the stability of rates in counties with small populations.

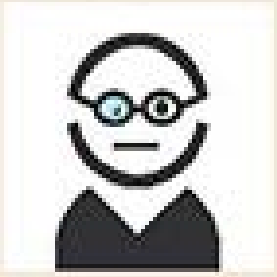
Data Source:
National Vital Statistics System
National Center for Health Statistics

COMMUNITY EDUCATION

SIGNS OF STROKE – BE FAST

B	E	F	A	S	T
Balance	Eyes	Face	Arms	Speech	Time

B is for Balance: Does the person have a sudden loss of balance?



E is for Eye: Has the person lost vision in one or both eyes?

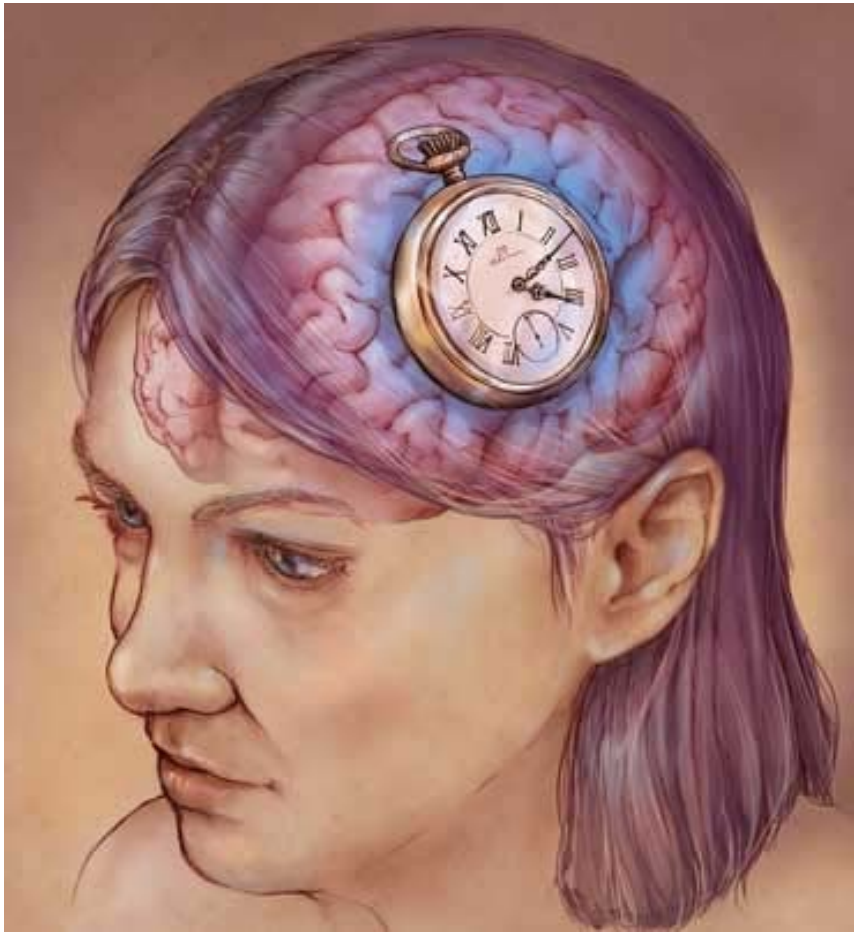
F is for Face: Does the person's face look uneven?

A is for Arm: Is one arm hanging down?

S is for Speech: Is the person's speech slurred? Does the person have trouble speaking or seem confused?

T is for Time: Call 911 now!

Timing is Everything…



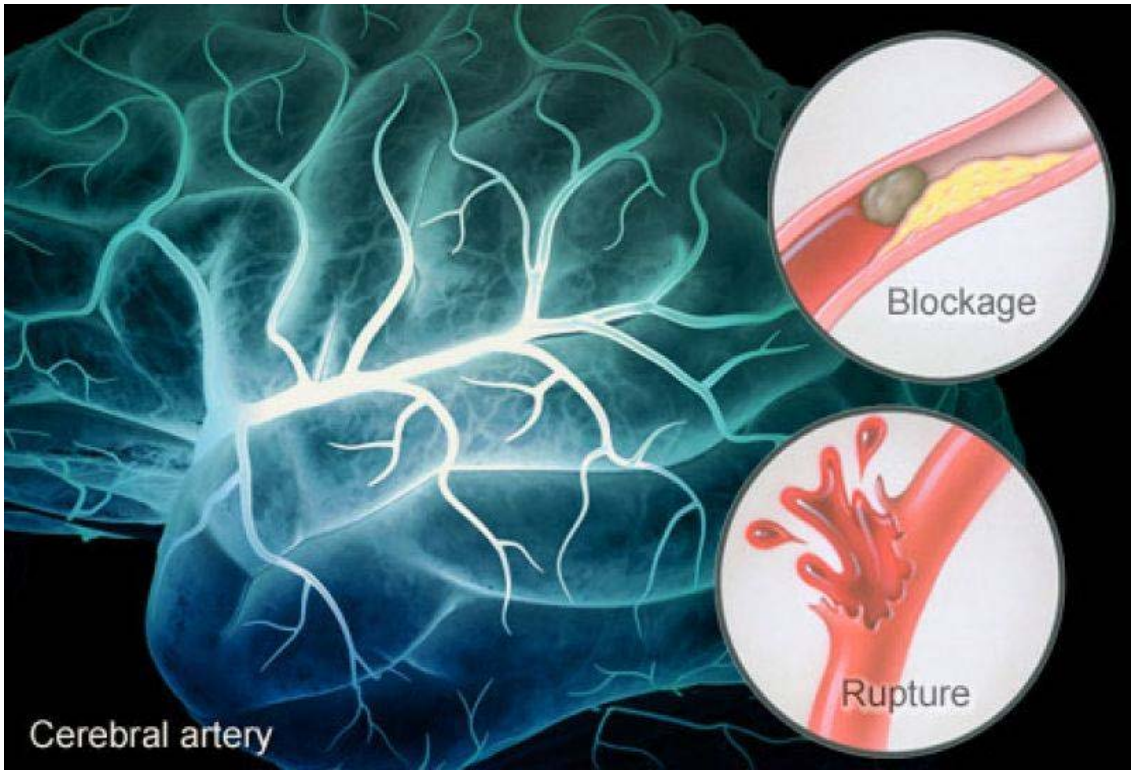
TIME = BRAIN

("1.8 million" neurons lost per minute)

VARIABLE TIME TO INFARCT

(Not all brains are created equally)

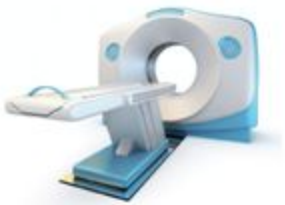
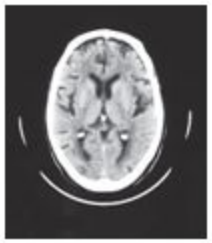
Rapid Evaluation & Neuroimaging Tools



NIH-recommended Emergency Department Response Times

DTN ≤60 min: the "golden hour" for evaluating and treating acute stroke




This paradigm is ~~becoming~~ outdated!
-Prefer direct to CT scanner upon pt arrival to ER
-Prefer tPA within 45 min

T=0	≤10 min	≤ 15 min	≤ 25 min	≤ 45 min	≤ 60 min
Suspected stroke patient arrives at stroke unit	Initial MD evaluation (including patient history, lab work initiation, & NIHSS)	Stroke team notified (including neurologic expertise)	CT scan initiated	CT & labs interpreted	rt-PA given if patient is eligible

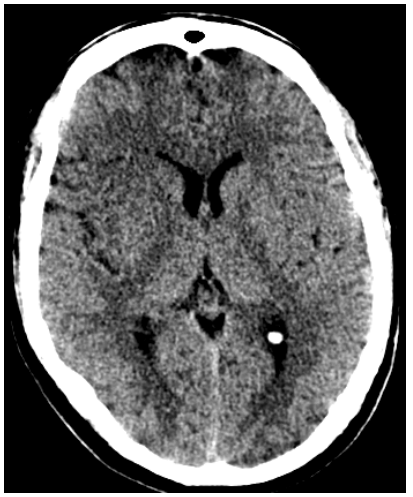
IDEALLY performed prehospital

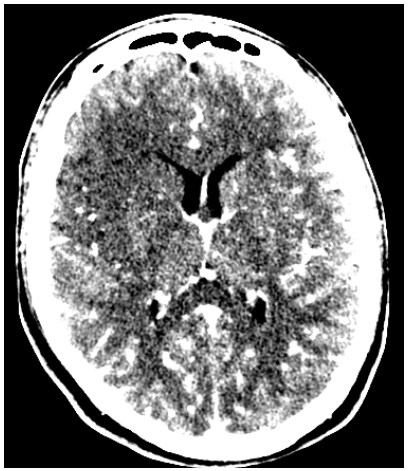
NINDS NIH website. Stroke proceedings. Latest update 2008.

Actilyse® alteplase
Act FAST

The Hyperacute Stroke Algorithm: Immediate Needs

- Possible Acute Stroke?
  - EMS alerts ER
  - Activate Stroke Team, eEmergency services
- Direct to CT scanner (if vitals stable)
  - **CT Brain wo contrast**
    - Window for ASPECTS (W: 40 | C: 40)
  - **CTA Head/Neck w/ contrast (or CTP)**
    - Look for large vessel occlusion (LVO)
- Time of Last Known Well (LKW)
- VAN Assessment
- NIH Stroke Scale
  - Exam of pertinent neurologic deficits
- Determine Treatment Options
  - IV tPA and/or endovascular therapy





The VAN Assessment

- Tool to identify symptoms congruent with a LVO stroke
- VAN Assessment:
  - Unilateral **weakness**?
    - No, stop, VAN (-)
    - Yes, continue with VAN
  - **V**isual field cut -OR- **A**phasia -OR- **N**eglect?
- 100% sensitive – 90% specific
- 73% PPV – 100% NPV

NIHSS ≥ 6:
100% sen – 74% spe
58% ppv – 100% npv

NATIONAL INSTITUTES OF HEALTH STROKE SCALE:

1a. Level of Consciousness:
[ ] 0: Alert and attentive.
[ ] 1: Not alert; but arousable by minor stimulation.
[ ] 2: Not alert; requires stimulation.
[ ] 3: Comatose (*no movement at all*).

1b. Level of Consciousness Questions:
[ ] 0: Both correct; *AGE & MONTH.*
[ ] 1: One correct.
[ ] 2: Neither correct (*comatose*).

1c. Level of Consciousness Commands:
[ ] 0: Both correct; *OPEN/CLOSE EYES & GRIP/RELEASE HAND(S).*
[ ] 1: One correct.
[ ] 2: Neither correct (*comatose*).

2. Best Gaze:
[ ] 0: Normal.
[ ] 1: Partial gaze palsy (*can overcome w/ Doll's*).
[ ] 2: Forced deviation (*total gaze paresis*).

3. Visual Fields: (*if extinction; score 1*)
[ ] 0: No visual loss.
[ ] 1: Partial hemianopsia (*ex: quadrantanopia*).
[ ] 2: Complete hemianopsia.
[ ] 3. Bilateral hemianopsia (*blind including cortical blindness)* (*comatose w/ no blink to threat*).

4. Facial Palsy:
[ ] 0: Normal.
[ ] 1: Minor, lower.
[ ] 2: Complete, lower (*UMN pattern*).
[ ] 3: Complete, total (*brainstem or PNS*).

5a. Motor Arm, Left:
[ ] 0: Does not drift (*10 seconds*).
[ ] 1: Drift, but does not hit bed.
[ ] 2: Some anti-gravity, but hits bed.
[ ] 3: No anti-gravity.
[ ] 4: No movement.

5b. Motor Arm, Right:
[ ] 0: Does not drift (*10 seconds*).
[ ] 1: Drift, but does not hit bed.
[ ] 2: Some anti-gravity, but hits bed.
[ ] 3: No anti-gravity.
[ ] 4: No movement.

6a. Motor Leg, Left:
[ ] 0: Does not drift (*5 seconds*).
[ ] 1: Drift, but does not hit bed.
[ ] 2: Some anti-gravity, but hits bed.
[ ] 3: No anti-gravity.
[ ] 4: No movement.

6b. Motor Leg, Right:
[ ] 0: Does not drift (*5 seconds*).
[ ] 1: Drift, but does not hit bed.
[ ] 2: Some anti-gravity, but hits bed.
[ ] 3: No anti-gravity.
[ ] 4: No movement.

7. Limb Ataxia (*out of proportion to weakness*):
[ ] 0: Absent (*comatose*).
[ ] 1: Present in one limb.
[ ] 2: Present in two limbs.
[ ] UN: Amputation or joint fusion; explanation: _____.

8. Sensory (*pin-prick*):
[ ] 0: Normal.
[ ] 1: Mild to moderate sensory loss.
[ ] 2: Severe or total sensory loss (*comatose*).

9. Best Language:
[ ] 0: No aphasia.
[ ] 1: Mild to moderate aphasia.
[ ] 2: Severe aphasia.
[ ] 3: Mute, global aphasia (*comatose*).

10. Dysarthria:
[ ] 0: Normal.
[ ] 1: Mild to moderate dysarthria.
[ ] 2: Severe dysarthria (*comatose*).
[ ] UN: Intubated or other barrier; explanation: _____.

11. Extinction and Inattention:
[ ] 0: No abnormality (*comatose*).
[ ] 1: Visual, tactile, auditory, spatial, or personal inattention / extinction (*only one modality*).
[ ] 2: Profound hemi-inattention or extinction to more than one modality.

Total NIH Stroke Scale: _____.

AVERA HSA (HYPERACUTE STROKE ALGORITHM) FLOW CHART – 7/15/2019

"PART 1 – tPA & THE TARGET LVO"

Pre-ER

- EMS Stroke Alert – Notify ER with ETA.
- Update 5 min prior to ER door arrival.

- ER Dispatch: Ask Pt age, sex, LKW, VAN ?'s.
- ER Dispatch: Advise EMS to keep HOB flat, attempt R-AC 18-20 g IV access, start/give NS 1L bolus wide open (if time).
- ER HUC activate HSA. Register Pt w/ Doe name, age, sex. Print wrist band & labels.

Pre-ER Arrival

Patient Arrives to ER (Goal ER Arrival to Eval Start = 0 min) – Initial HSA team gathers at ER door 5 min prior to Pt arrival

0-5 min

- Initial HSA team meets Pt & EMS at ER door entrance in hallway.
- EMS provides brief 15 sec story. • ER HUC → apply Pt ID band.
- ER Doc → quick ABC eval. • NCC-SC → quick VAN score.

- **HSA Team:**
  (in order of role)
  1) ER Doc (ER)
  2) NCC-SC (ER)
  3) ER RN+PM's (ER).
  4) CT Tech (CT).
  5) Lab-Phleb (CT).
  6) Rad Doc (CT).
  7) Neuro Doc (CT).
  8) Pharmacist (CT).
  9) NES Doc (VAN+).

ABC Unstable

- ER Doc stabilize, then resume HSA.

ABC Stable
VAN Negative

- Go directly to CT scanner.
- Do not notify NES Doc.
- NCC-SC begin NIHSS en route.

ABC Stable
VAN Positive

- Go directly to CT scanner.
- **Notify NES Doc of VAN (+).**
- NCC-SC begin NIHSS en route.

Patient Arrives to CT Scanner (Goal ER Arrival to CT Arrival < 5 min) – CT Tech puts scale cradle on table's lower end

5-30 min

VAN Negative

LKW < 4.5 hrs

- CT-B (*Skip CTA for now*).
- CT-B + **CT-Ang**-H/N.
  (if no IV access, proceed with algorithm below).
- ER RN + PM's obtain patient weight w/ crane.
- Lab-Phleb draws rainbow set of tubes.
- NCC-SC: Finish NIHSS, pre-mRS, & tPA checklist.
- Rad Doc interpret imaging.
- ER + Neuro Docs assess possible IV tPA (< 4.5 hrs).
- Pharmacist mix tPA & ER RN begin tPA.
- Proceed with **CT-Ang**-H/N (*if not already done*).

LKW > 4.5 hrs

- CT-B + **CT-Ang**-H/N.
  (if no IV access, proceed with algorithm below).
- ER RN + PM's obtain patient weight w/ crane.
- Lab-Phleb draws rainbow set of tubes.
- NCC-SC: Finish NIHSS, pre-mRS, & tPA checklist.
- Rad Doc interpret imaging.
- ER + Neuro Docs assess possible IV tPA (< 4.5 hrs).
- Pharmacist mix tPA & ER RN begin tPA.
- Proceed with **CT-Ang**-H/N (*if not already done*).

-GWTG DTN goal < 45 min.
-Avera DTN goal < 30 min.

- Return to ER to assigned bed.
  (If Rad Doc interprets LVO (+) → Notify NES Doc).
  -END HSA PROTOCOL-

VAN Positive

LKW < 6.0 hrs

- CT-B + **CT-Ang**-H/N.
  (if no IV access, get CT-B, get IV, then CTA / CTP).
- ER RN + PM's obtain patient weight w/ crane.
- Lab-Phleb draws rainbow set of tubes.
- NCC-SC: Finish NIHSS, pre-mRS, & tPA checklist.
- NES Doc review + Rad Doc interpret imaging.
- ER + Neuro Docs assess possible IV tPA (< 4.5 hrs).
- Pharmacist mix tPA & ER RN begin tPA.
- NES Doc makes decision for MER w/ NCC-SC.

LKW > 6.0 hrs

- CT-B + **CT-Perf**-H/N.
  (if no IV access, get CT-B, get IV, then CTA / CTP).
- ER RN + PM's obtain patient weight w/ crane.
- Lab-Phleb draws rainbow set of tubes.
- NCC-SC: Finish NIHSS, pre-mRS, & tPA checklist.
- NES Doc review + Rad Doc interpret imaging.
- ER + Neuro Docs assess possible IV tPA (< 4.5 hrs).
- Pharmacist mix tPA & ER RN begin tPA.
- NES Doc makes decision for MER w/ NCC-SC.

No plans for MER

Activate MER Pathway

- Go directly to lab w/ TLS team.
- ER HUC activate on-call lab staff.

Rare MER Pathway

"PART 2 – THE MER PATHWAY"

Patient Arrives to Cath Lab (Goal ER Arrival to Cath Lab Arrival < 30 min) – TLS team begins MER setup process

30-50 min

- NES Doc gains consent (if already in hospital) -OR- NES Doc en route.
- ER + Neuro Docs assist w/ brief consent (50% better outcome -VS- 3-5% no change / worse outcome).
- TLS team move Pt to angiosuite table, connect monitors, & prepare lab per NCC-SC's direction.
- Stroke specific quick pack opened & prepared on sterile back table.
- Sterile drape placed over patient with R-CFA site ready for access.

50-60 min

NES Doc

- NES Doc arrive.
- NES Doc quick Pt status update.
- NES Doc gain arterial access:
  -GWTG DTP goal < 90 min.
  -Avera DTP goal < 60 min.

On-Call Lab Staff

- On-call lab staff arrive 1 by 1.
- Relieve TLS team 1 by 1.
- Each give 30 sec Pt info handoff.
- TLS members return to prior duties.
- NCC-SC stays for procedure.

MER Procedure Underway

60-90 min

- NES Doc & lab staff continue to rapidly approach "Target LVO."
- First endovascular treatment device(s) deployed for first reperfusion achieved.
  -GWTG DTR (ER door-to-reperfusion) goal < 120 min.
  -Avera DTR (ER door-to-reperfusion) goal < 90 min.
- Continue MER, additional attempts (+/-), for goal **TICI-2b or better** (as appropriate).
- Complete neuro-angiography imaging. Finalize procedure.

MER Procedure Complete

Post-MER

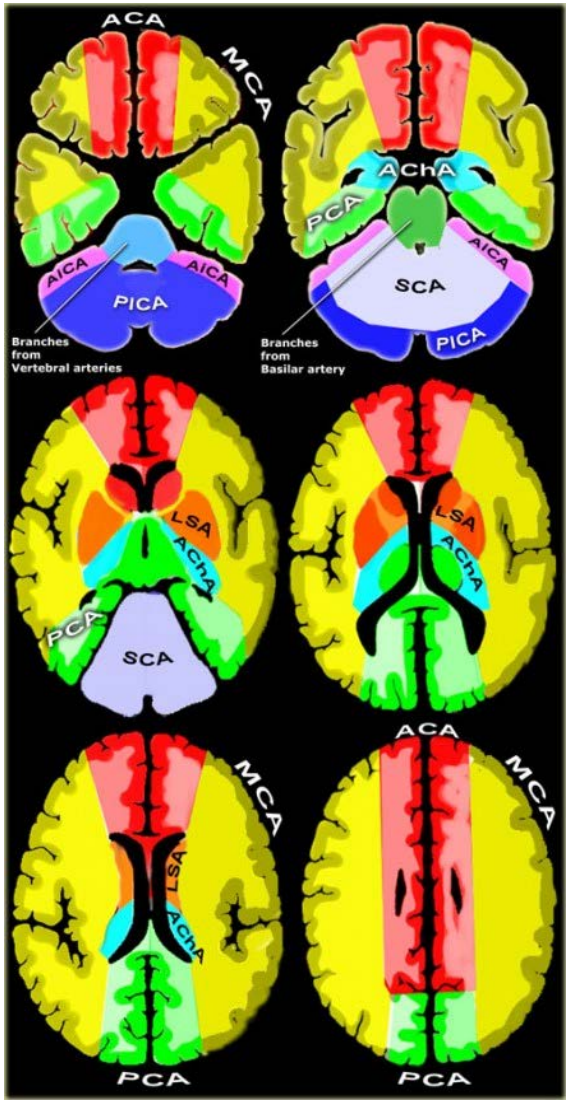
- Go directly to CT scanner w/ NCC-SC & lab team. Repeat CT Brain wo study.
- Transfer to Neuro Critical Care Unit for post-MER +/- post-tPA care.

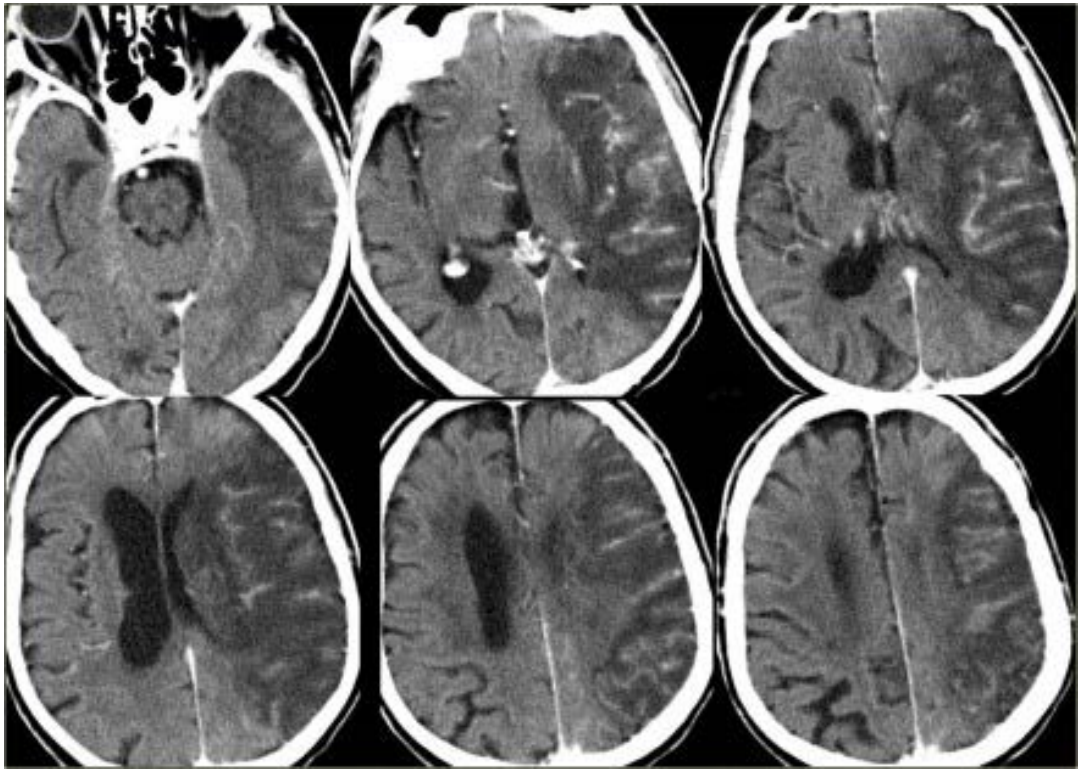
-END HSA PROTOCOL-

Avera eCARE Emergency

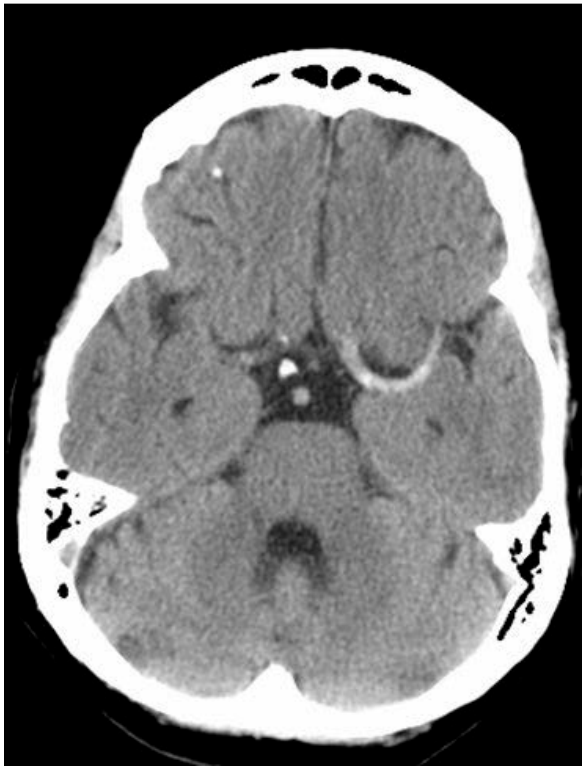
- Assistance with treatment decision making, triage, transport
- ED Physician
- ED RN
- Avera Neurology
- Avera Neuro-Endovascular Surgery

Large Artery Distributions
Vascular Territorial Strokes

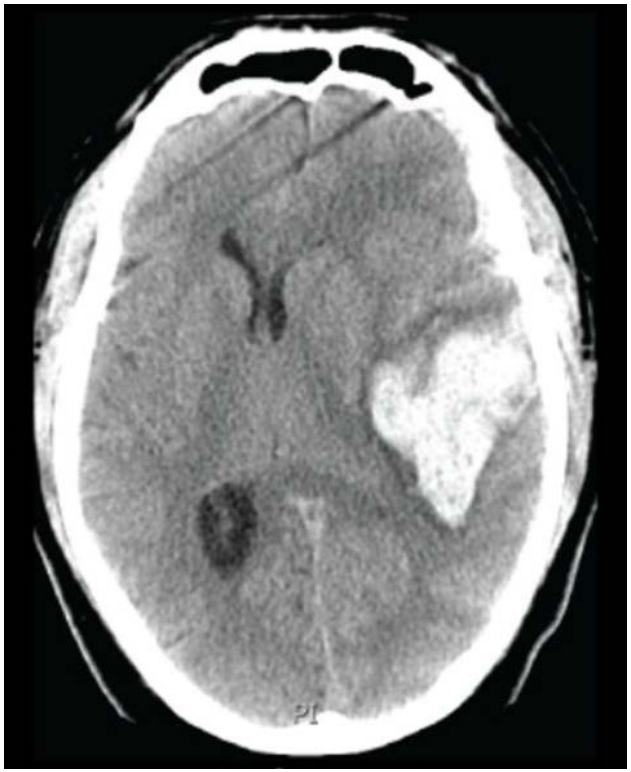




BRAIN ATTACK - INITIAL CT SCAN

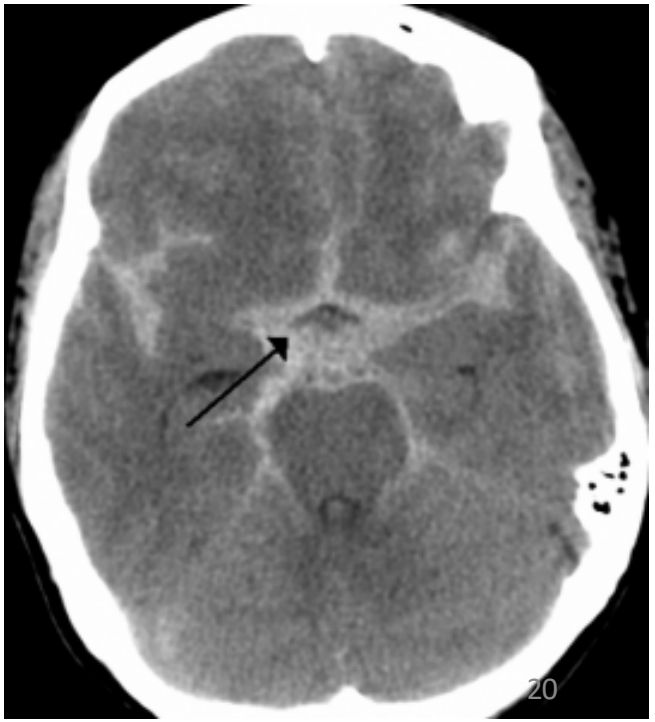


Ischemic

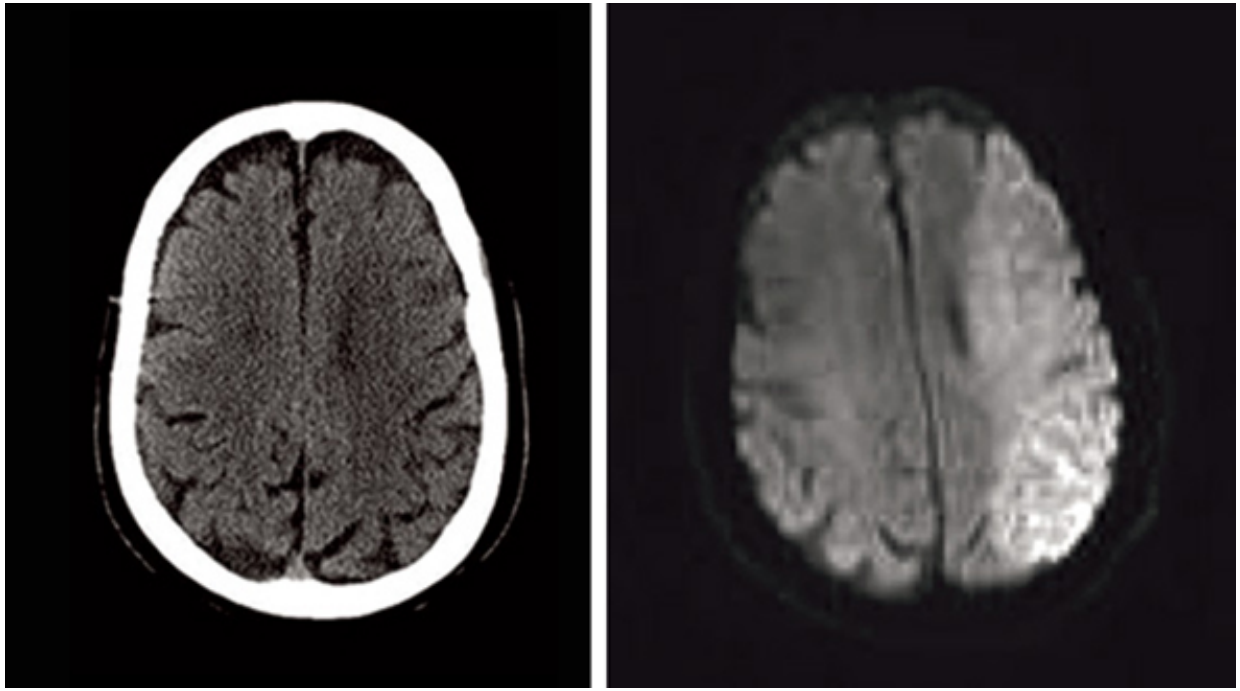


Hemorrhagic

Aneurysmal SAH



CT vs MRI in Acute Ischemic Stroke



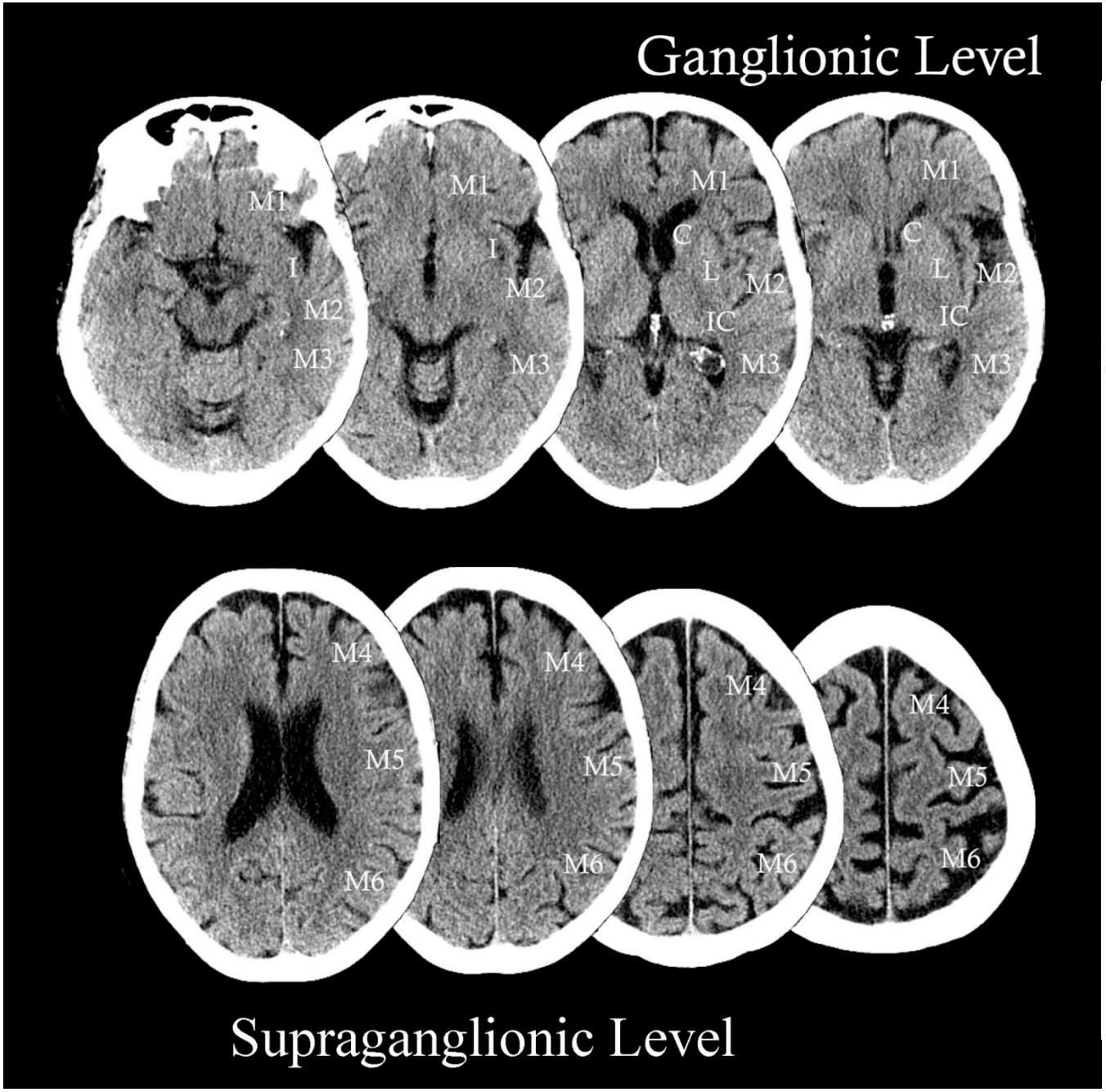
Bottom line:

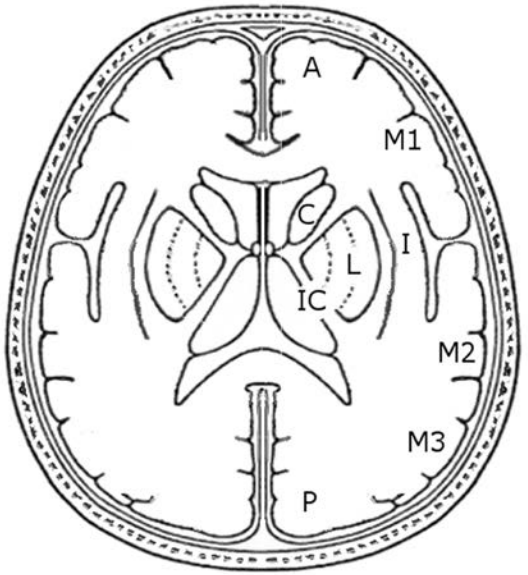
- MRI takes MUCH longer to scan…
- Requires screening for metal implants/foreign bodies…
- Use CT ASPECTS!

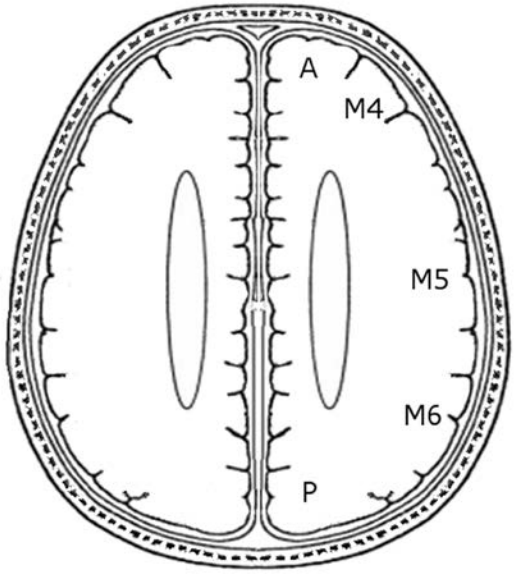
ASPECTS AJNR 2001

FACULTY OF MEDICINE | UNIVERSITY OF CALGARY

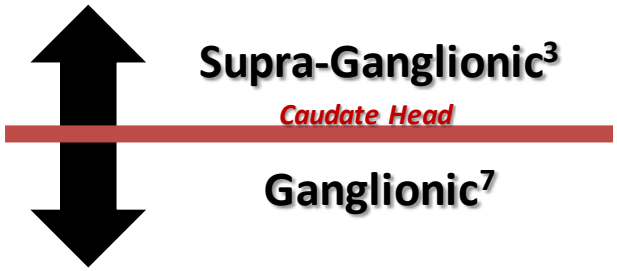
- ASPECTS = “Alberta Stroke Program Early CT Score”
- Validated clinical tool to predict early ischemic changes in acute ischemic stroke
- Requires “some level” of neuroimaging experience
- This is difficult! → Practice makes perfect…
  - *Only “Canadians” can see the subtle difference (?)*


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

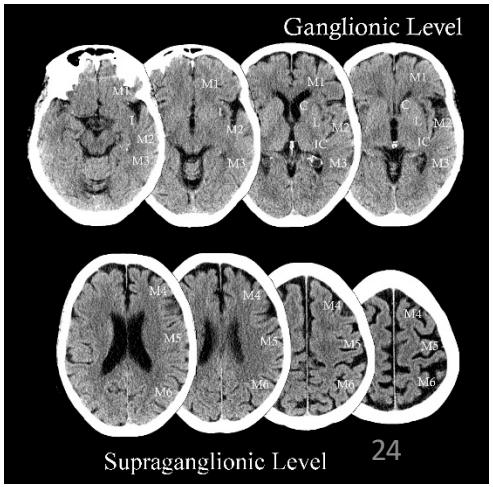

A
M1
C
L
I
IC
M2
M3
P


A
M4
M5
M6
P

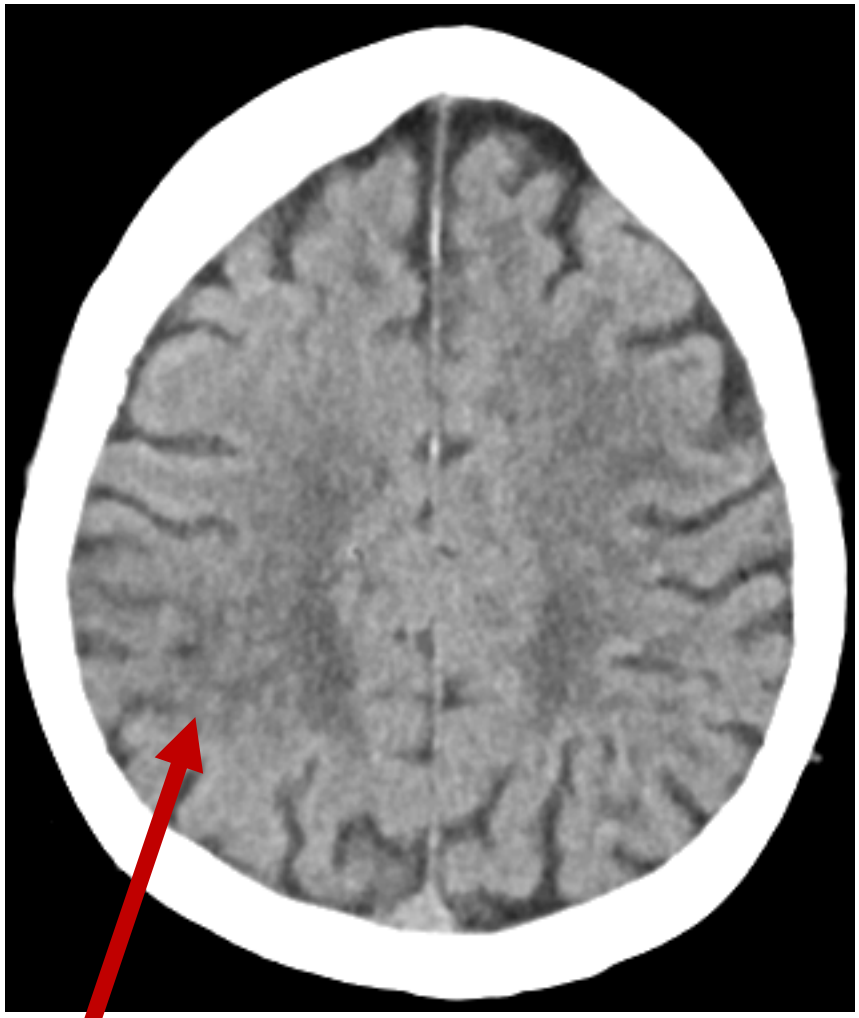
Grading ASPECTS



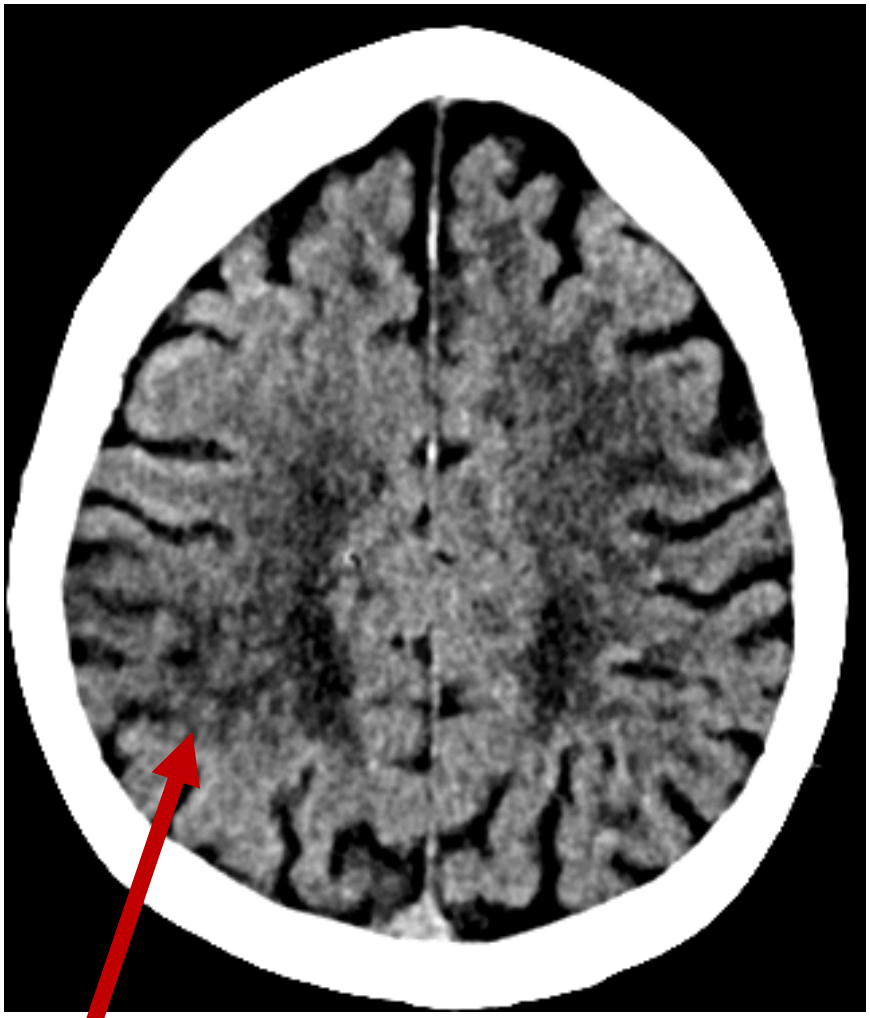
- 10-point quantitative score, left or right hemisphere, clinically determined
- Look at all cuts. Follow the 2-cut rule…
- 4 inner or basal ganglia regions:
  - Ganglionic (deep structures):
    - C, L, IC, Ins.
- 6 outer or cortex regions:
  - Ganglionic: (caudate head or below):
    - M1, M2, M3.
  - Supra-ganglionic: (above caudate head):
    - M4, M5, M6.



CT STANDARD -vs- CT ASPECTS

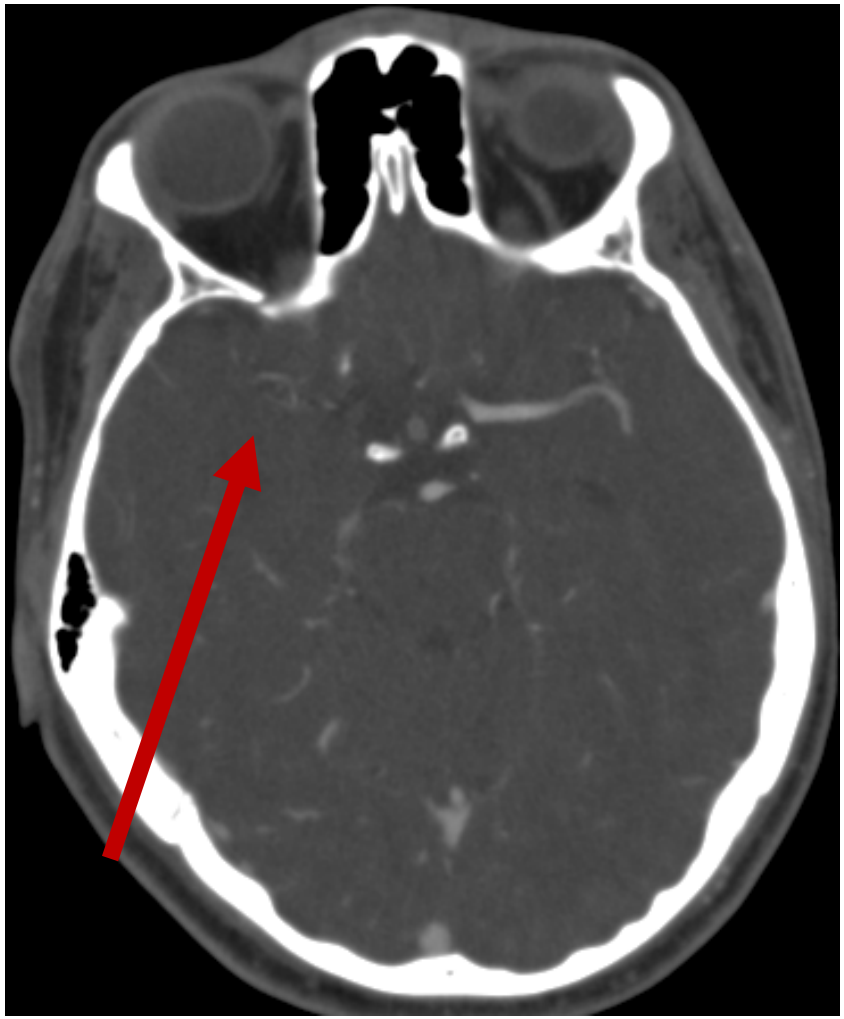


W: 90 | C: 30

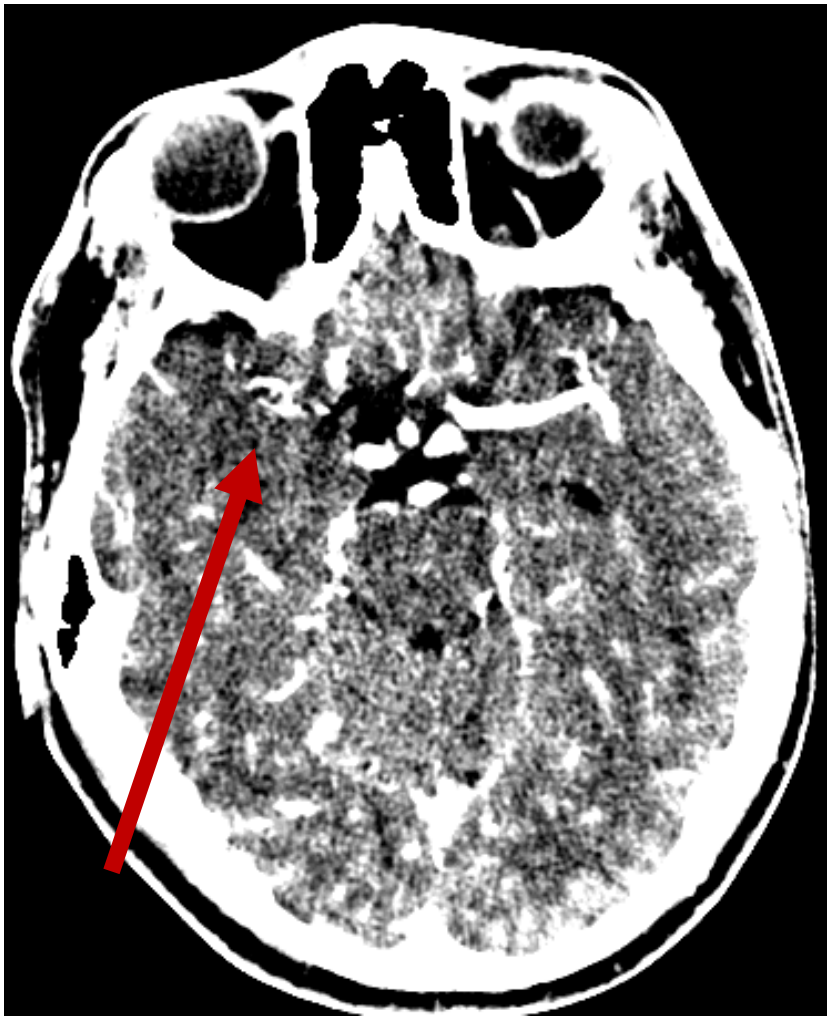


W: 40 | C: 40

CTA STANDARD -vs- CTA ASPECTS

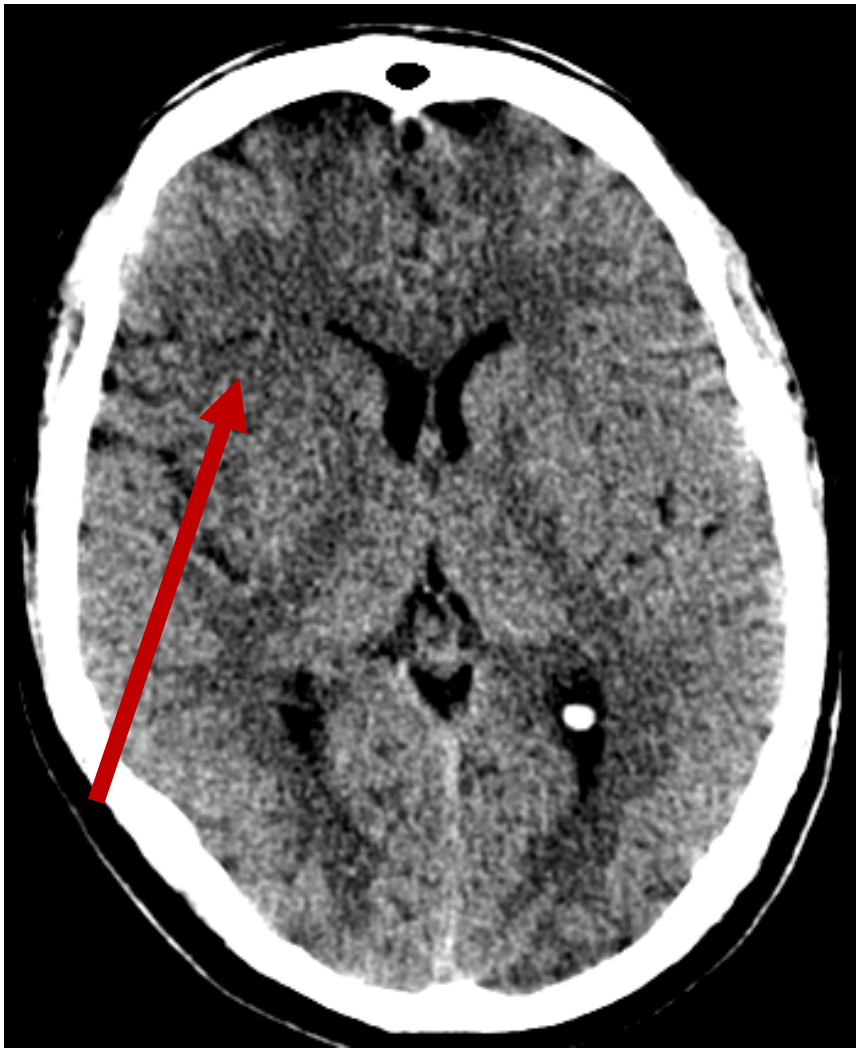


W: ~800 | C: ~200

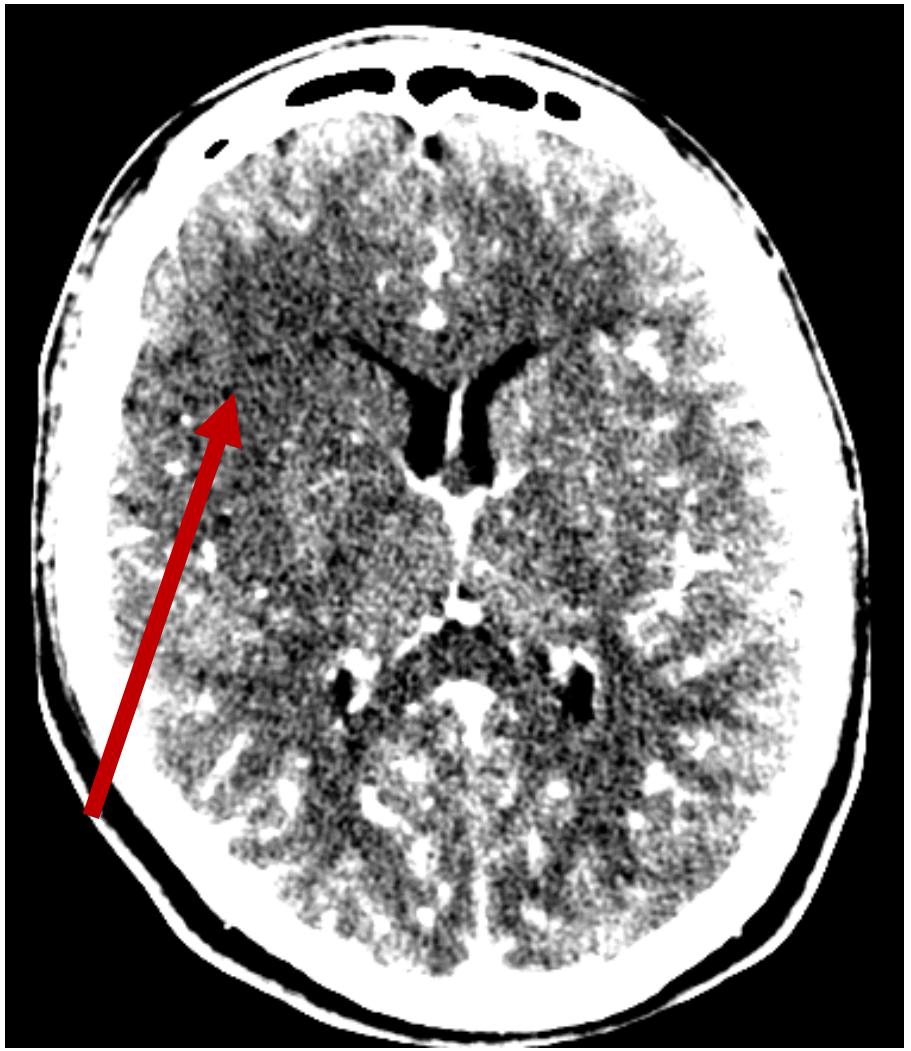


W: 40 | C: 40

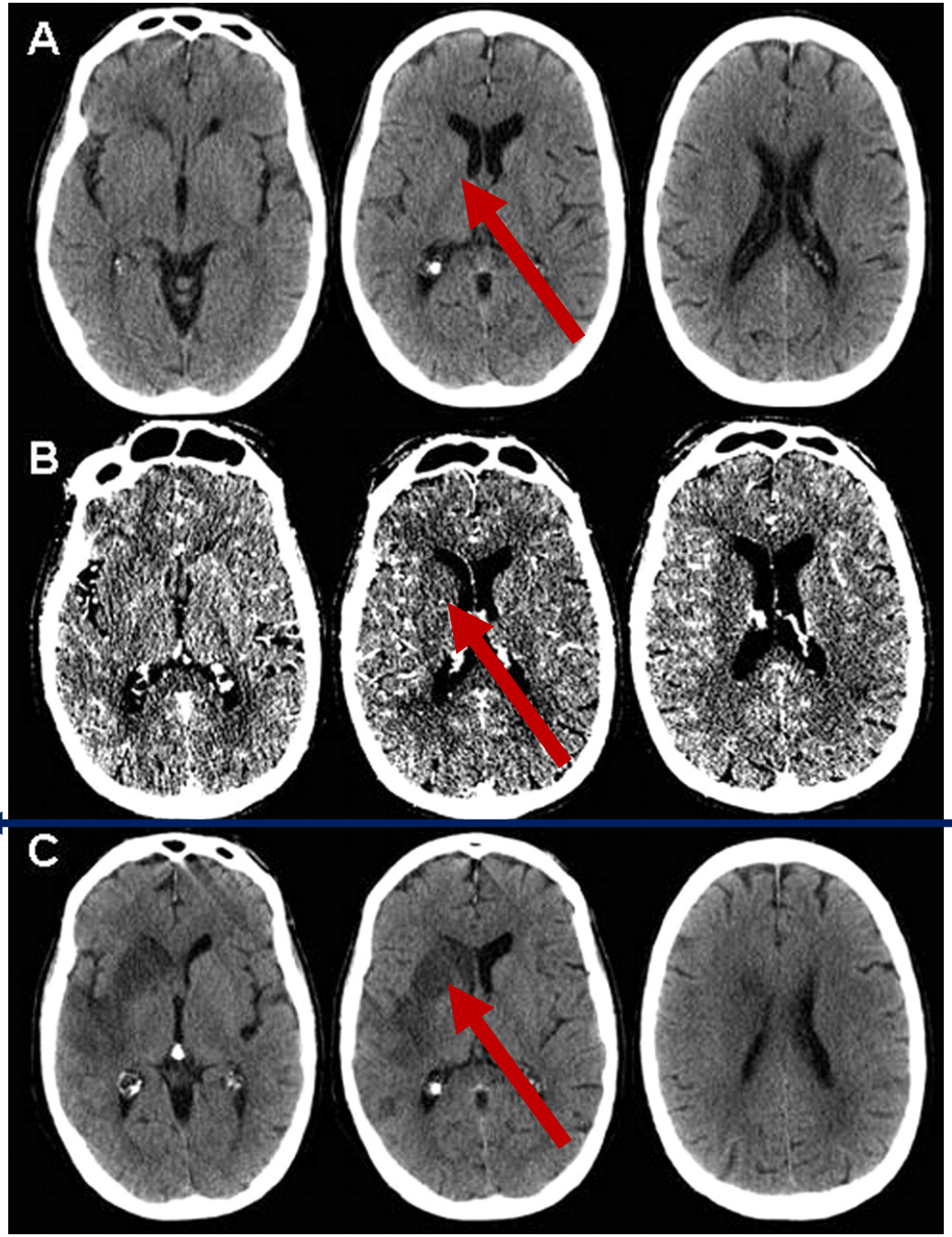
CT ASPECTS -vs- CTA ASPECTS



W: 40 | C: 40



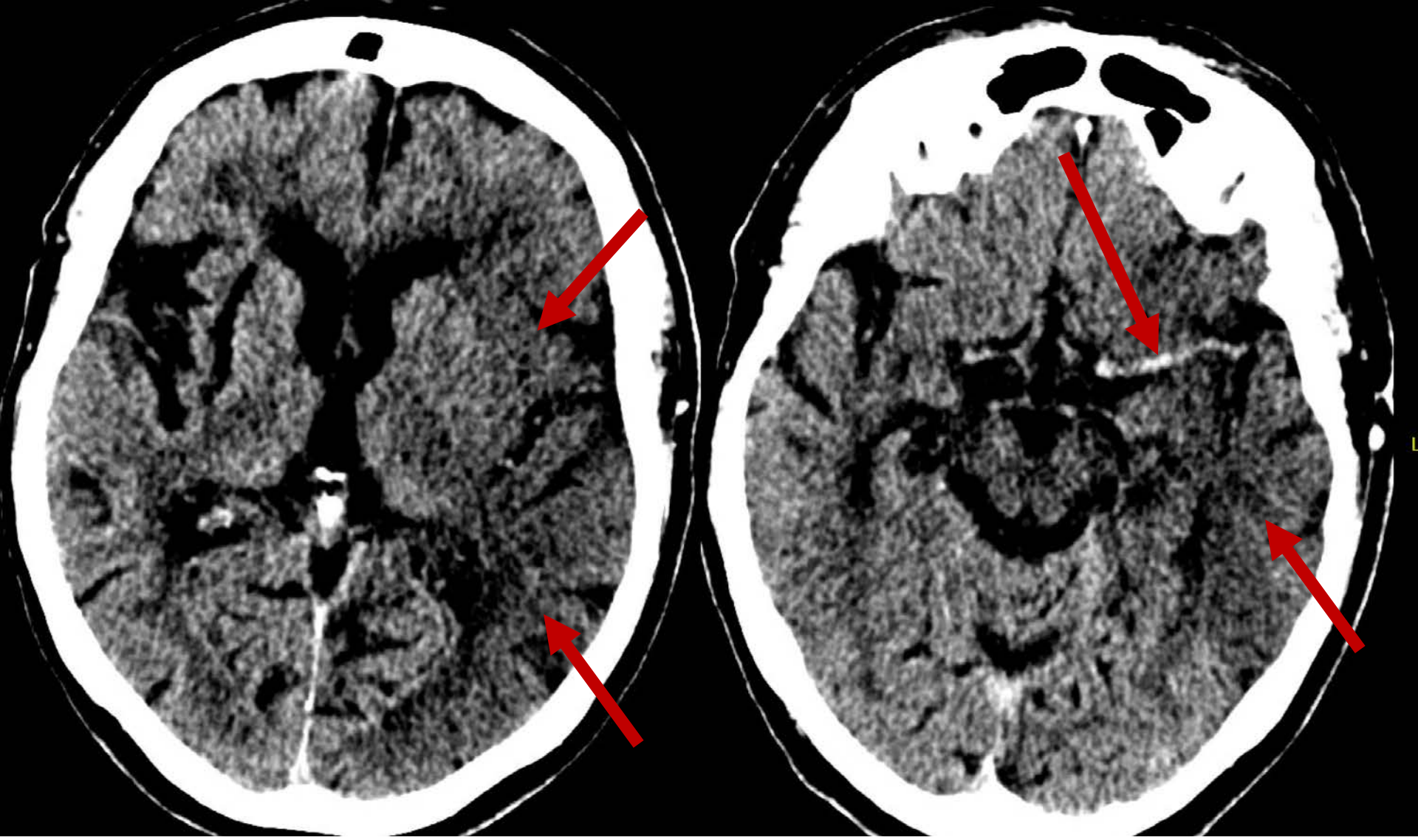
W: 40 | C: 40



A. CT

B. CTA-SI

C. Follow Up CT

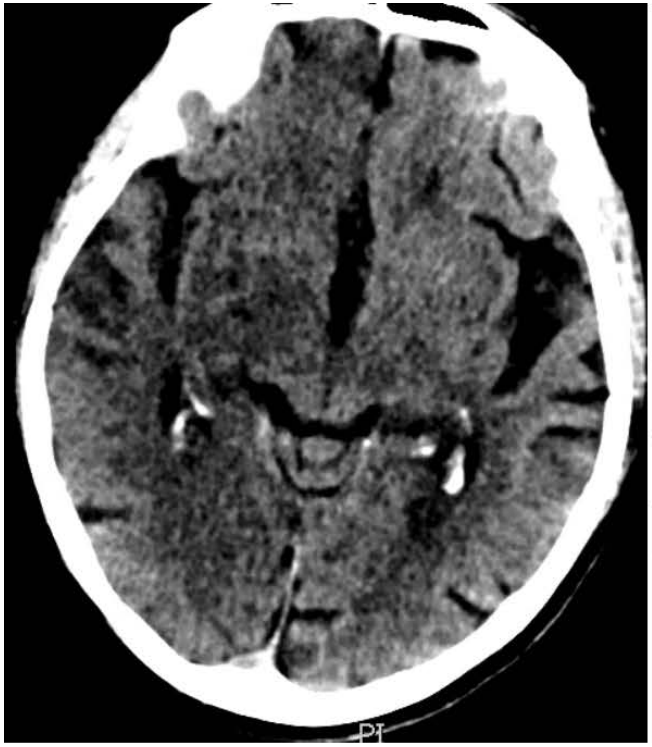


When is it Too Late? → ~ASPECTS ≤ 5

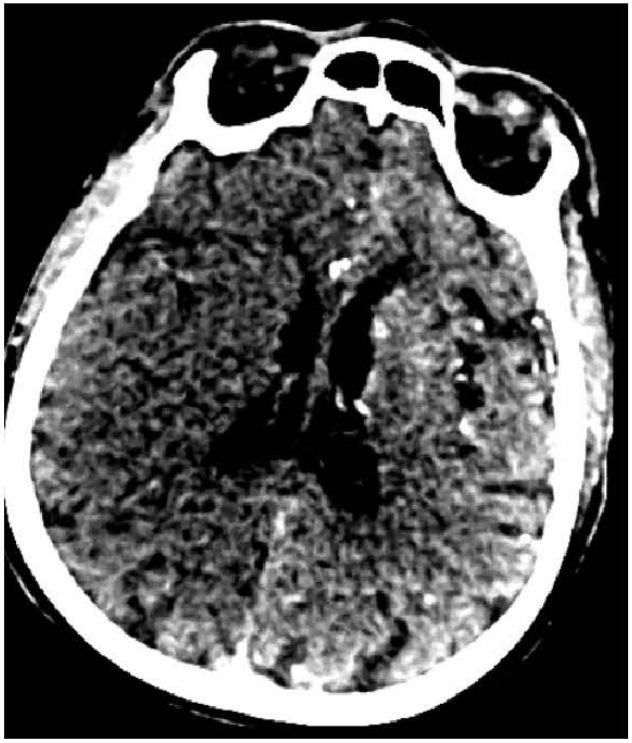
Caution: Interpreting radiologist read this as “no acute findings”

Far Too Late… The Wipe Out

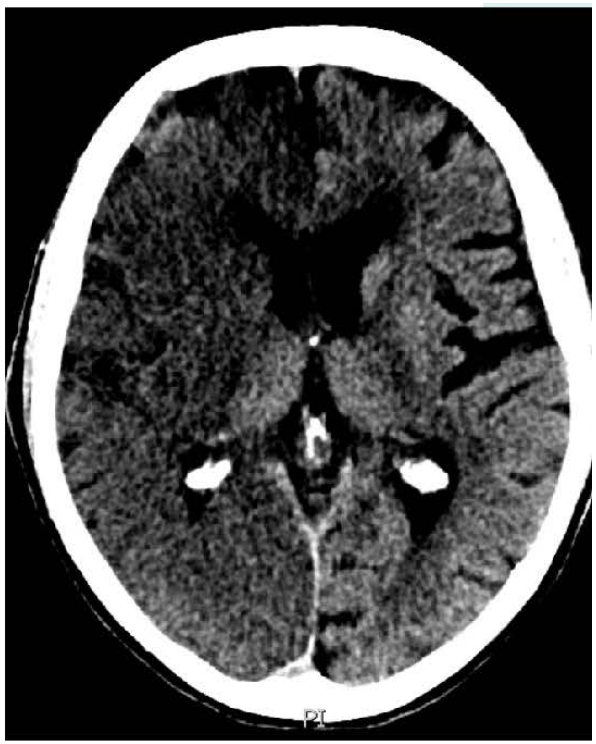
Sx onset +1 hr



Sx onset +2 hrs



Sx onset +7-8 hrs

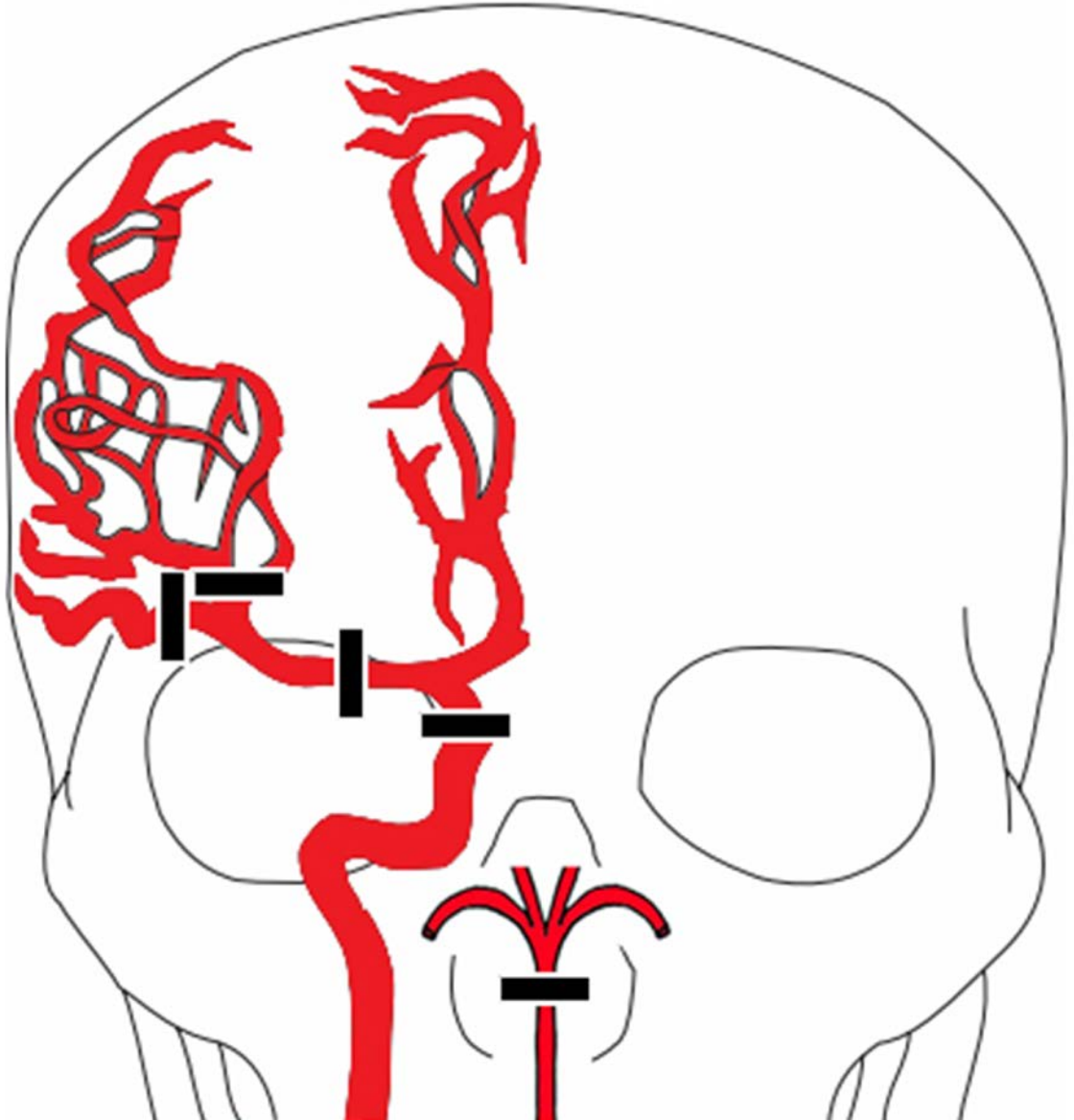


Sun 1/07/2018 - 95F, presented with AMS & left-sided weakness, became unresponsive, prompting intubation. First CT Brain wo on left, 1 hour after symptom onset, with ASPECTS of 9, diffuse subtle changes already. CTA ASPECTS in middle, 2 hours after symptom onset, score 0, suggesting diffuse core rapidly developing. Repeat CT Brain wo upon arrival to comprehensive stroke center, about 7-8 hours after symptom onset, massive R-MCA core, ASPECTS 0.

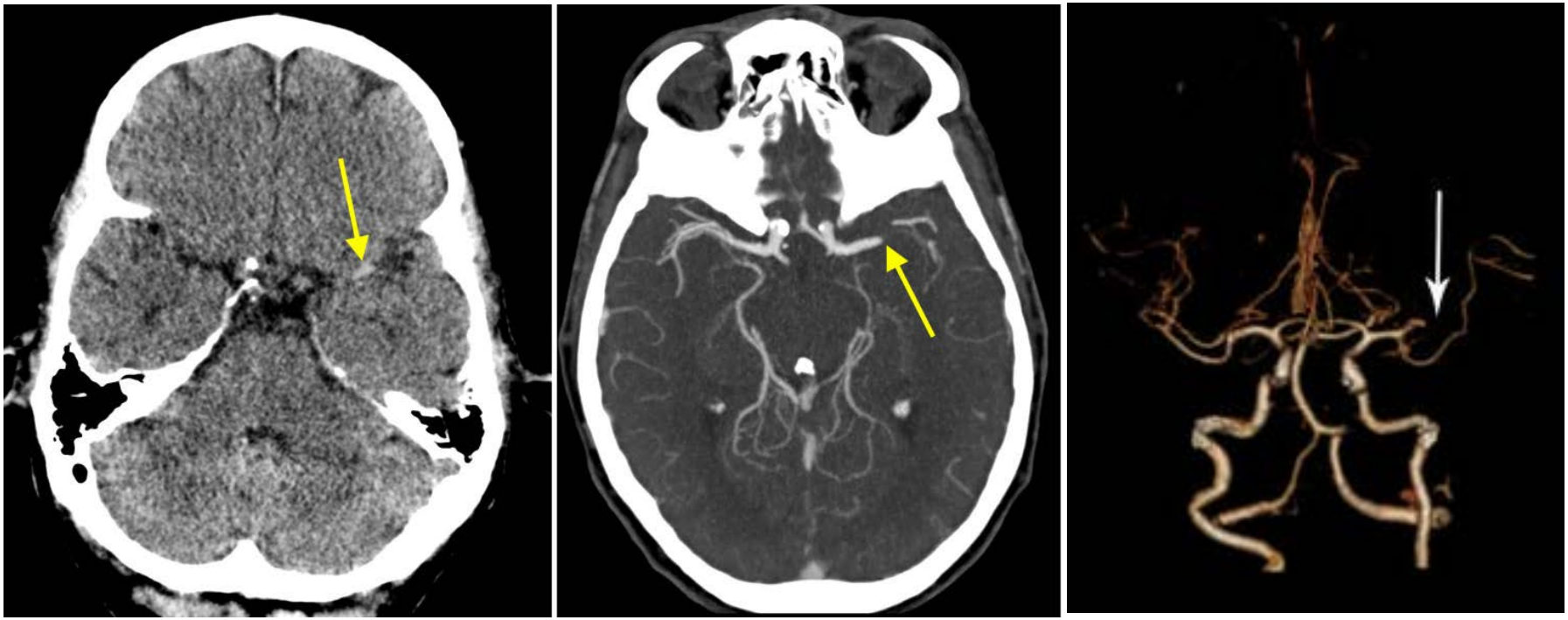
Searching for the Target LVO

8. For patients who otherwise meet criteria for EVT, a noninvasive intracranial vascular study is recommended during the initial imaging evaluation of the acute stroke patient, but should not delay IV alteplase if indicated. For patients who qualify for IV alteplase according to guidelines from professional medical societies, initiating IV alteplase before noninvasive vascular imaging is recommended for patients who have not had noninvasive vascular imaging as part of their initial imaging assessment for stroke. Noninvasive intracranial vascular imaging should then be obtained as quickly as possible.	**I**	**A**	Recommendation reworded for clarity from 2015 Endovascular. Class and LOE unchanged. See Table LXXXIII in online Data Supplement 1 for original wording.
9. For patients who otherwise meet criteria for EVT, it is reasonable to proceed with CTA if indicated in patients with suspected intracranial LVO before obtaining a serum creatinine concentration in patients without a history of renal impairment.	**IIa**	**B-NR**	New recommendation.
10. In patients who are potential candidates for mechanical thrombectomy, imaging of the extracranial carotid and vertebral arteries, in addition to the intracranial circulation, is reasonable to provide useful information on patient eligibility and endovascular procedural planning.	**IIa**	**C-EO**	New recommendation.

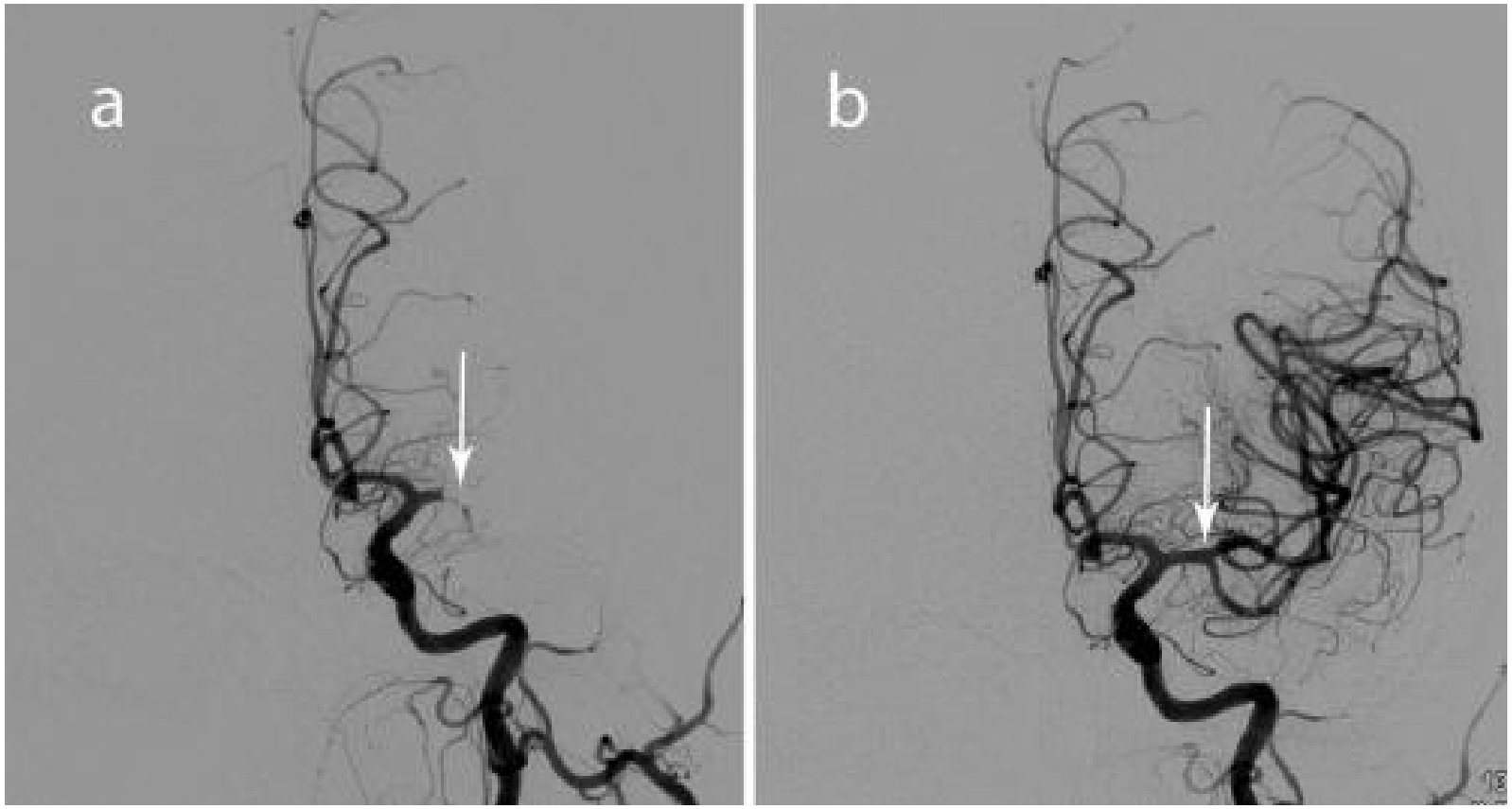
"Target LVO" – Large Vessel Occlusion



"**Target LVO**" – Large Vessel Occlusion

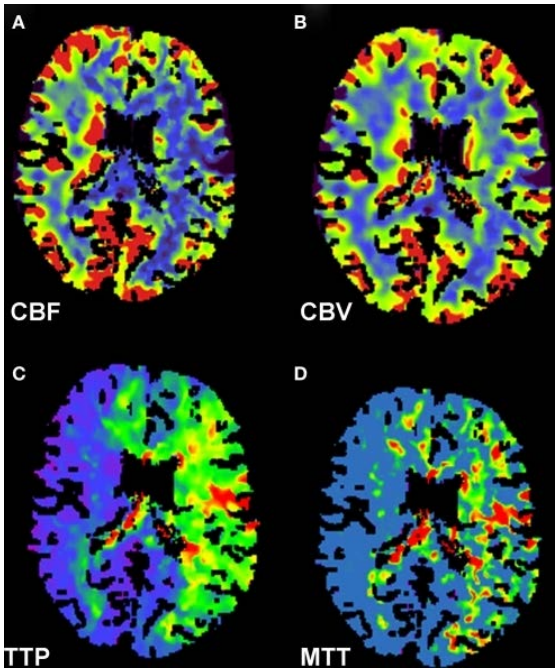


The "**Target LVO**" in the Cath Lab



CT Perfusion Imaging

- Generally NOT necessary within the standard 6-hour thrombectomy window
- Available at Avera McKennan for patients with LKW of 6-24 hours prior to presentation



11. Additional imaging beyond CT and CTA or MRI and magnetic resonance angiography (MRA) such as perfusion studies for selecting patients for mechanical thrombectomy in <6 hours is not recommended.	**III: No Benefit**	**B-R**	New recommendation.

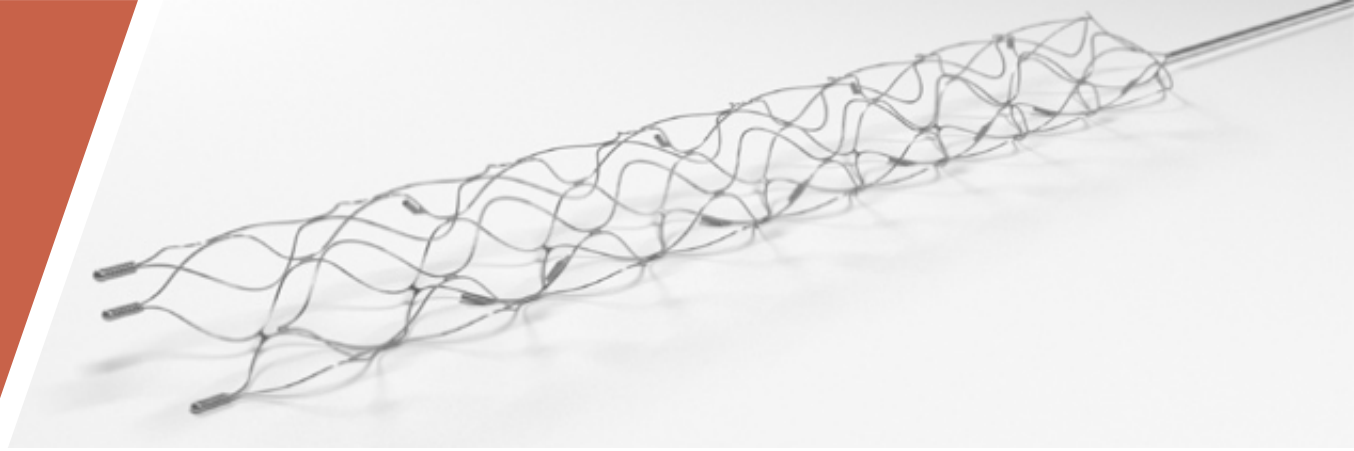
CTA vs. CT Perfusion

CTA Head / Carotid

- Identify blockage in cerebral vasculature
- IV contrast dye used
- LKW < 6 hours
  - Assume tissue surrounding occlusion is salvageable

CT Perfusion

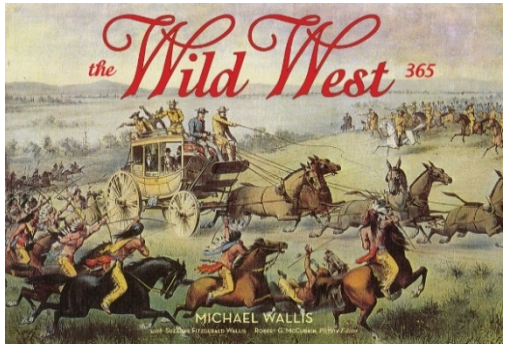
- Identify how well brain tissue around occlusion is being perfused
- Measures volume of salvageable tissue around an infarct
- LKW 6-24 hours
  - Risk v. benefit of endovascular intervention



Managing the LVO

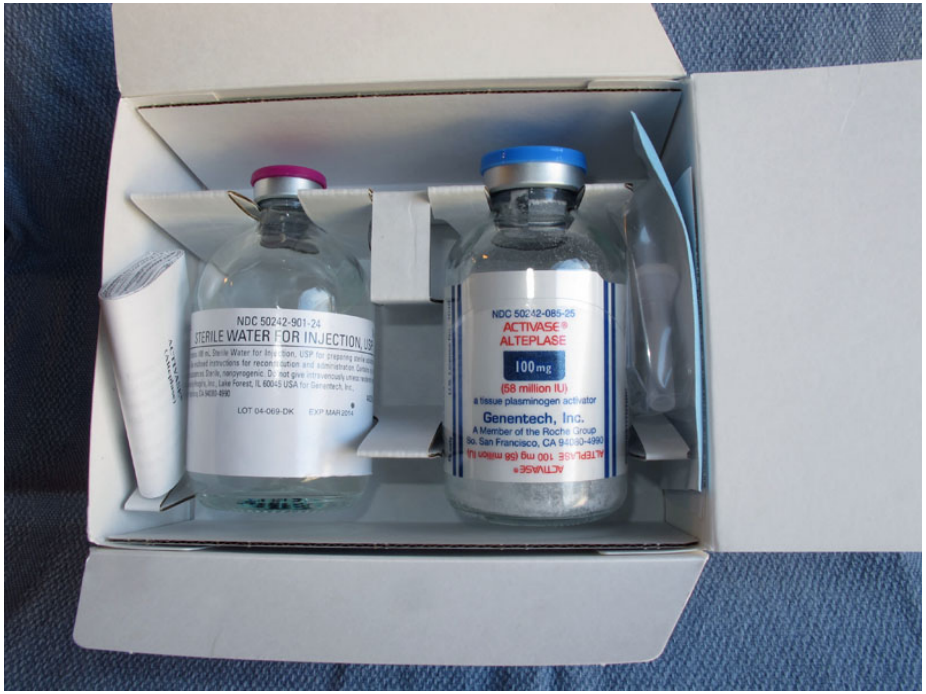
Acute Ischemic Stroke Treatment

- Revolution of acute stroke management over the last ~20-25 years
- Systemic IV tPA offered acute treatment option, at last:
  - NINDS, 1995; etc.



- Endovascular mechanical thrombectomy for LVO's (large vessel occlusions):
  - 5 major trials, 2015, & beyond
  - 2 extended window trials, 2017-2018
- **Rapid neuroimaging tools are critical**

tPA for the LVO Acute Ischemic Stroke

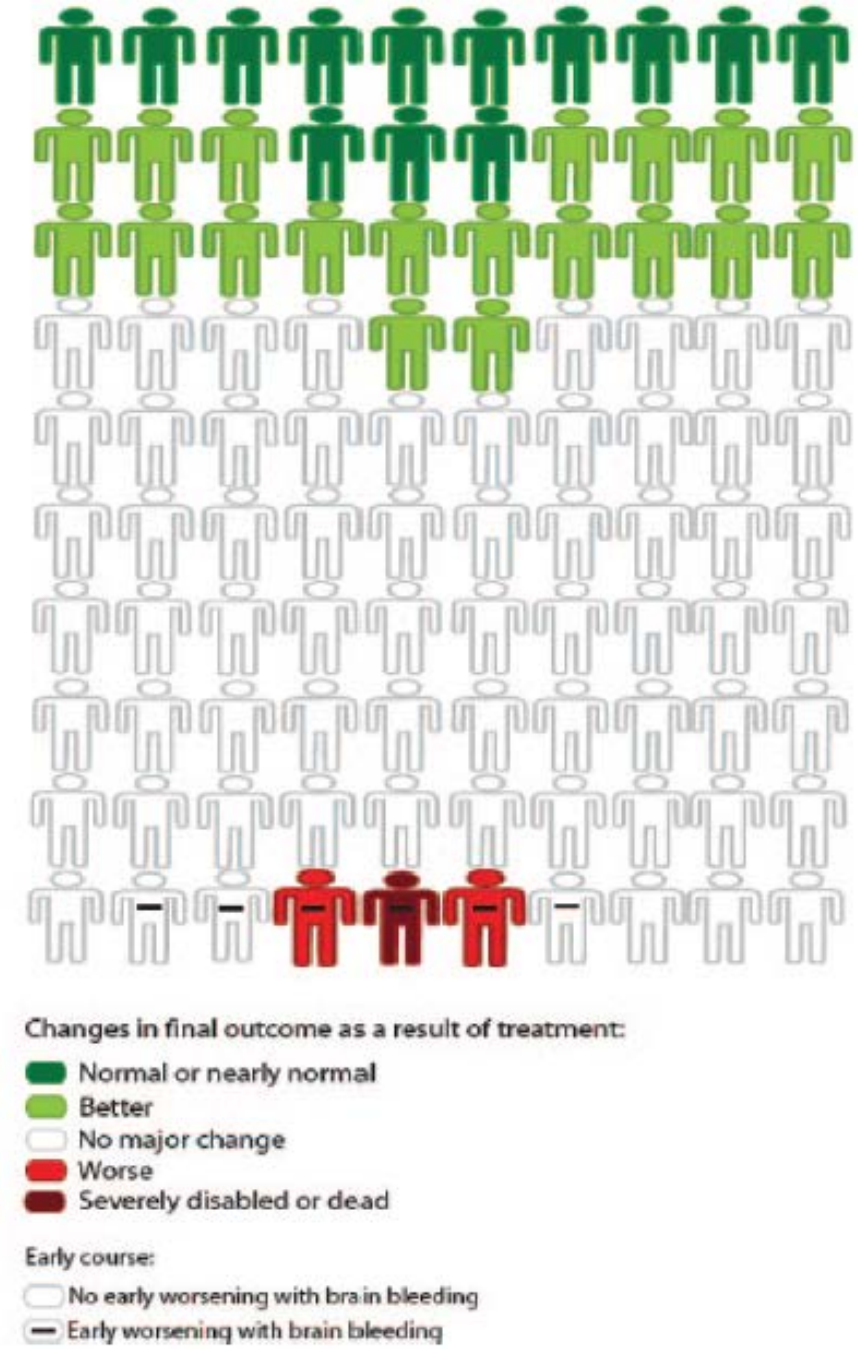


3.7. Mechanical Thrombectomy	COR	LOE	New, Revised, or Unchanged
1. Patients eligible for IV alteplase should receive IV alteplase even if EVTs are being considered.	I	A	Recommendation reworded for clarity from 2015 Endovascular. See Table LXXXIII in online Data Supplement 1 for original wording.
2. In patients under consideration for mechanical thrombectomy, observation after IV alteplase to assess for clinical response should not be performed.	III: Harm	B-R	Recommendation revised from 2015 Endovascular.

IV tPA Risks & Benefits

32 vs 3

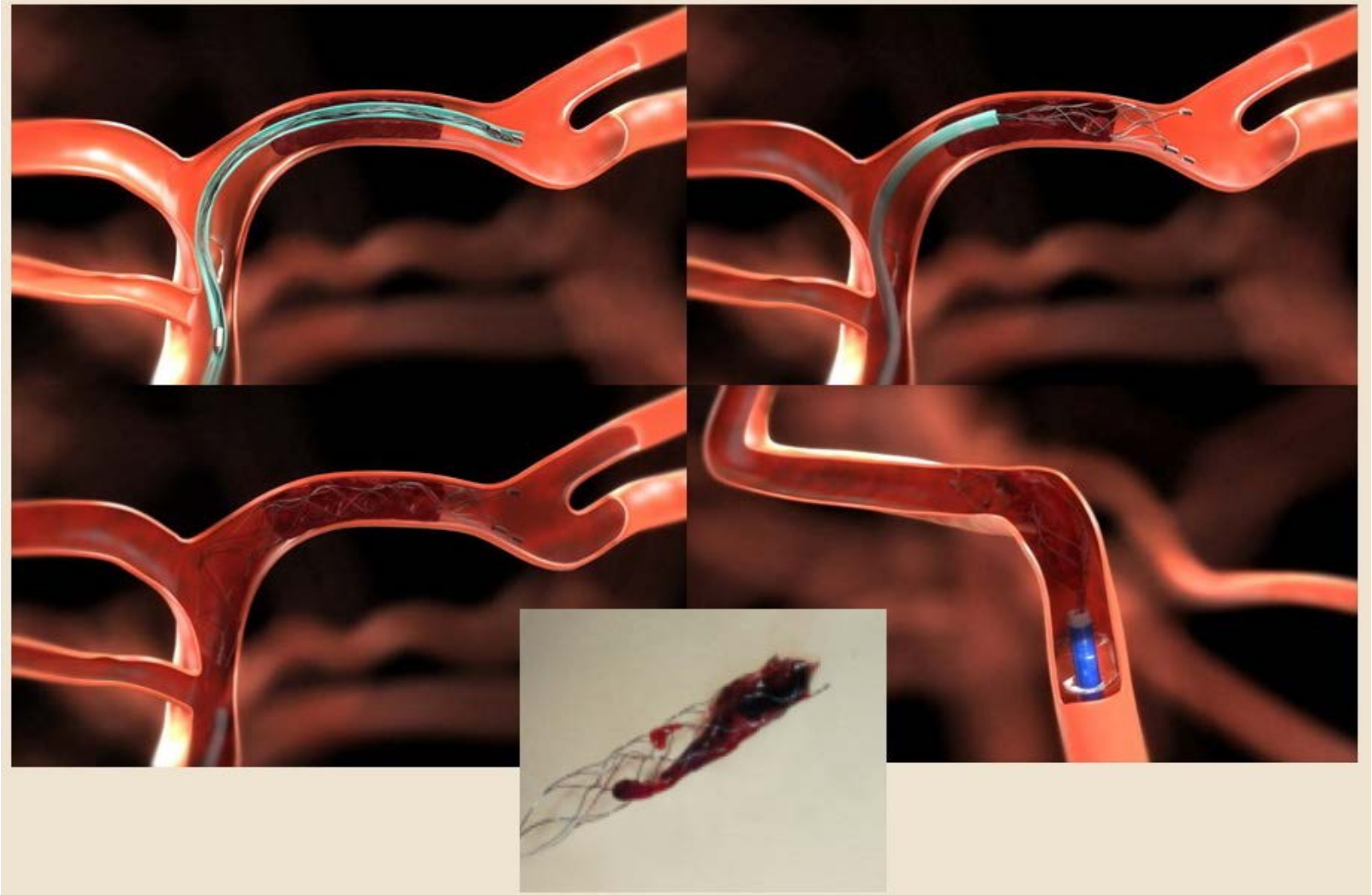
(per 100)

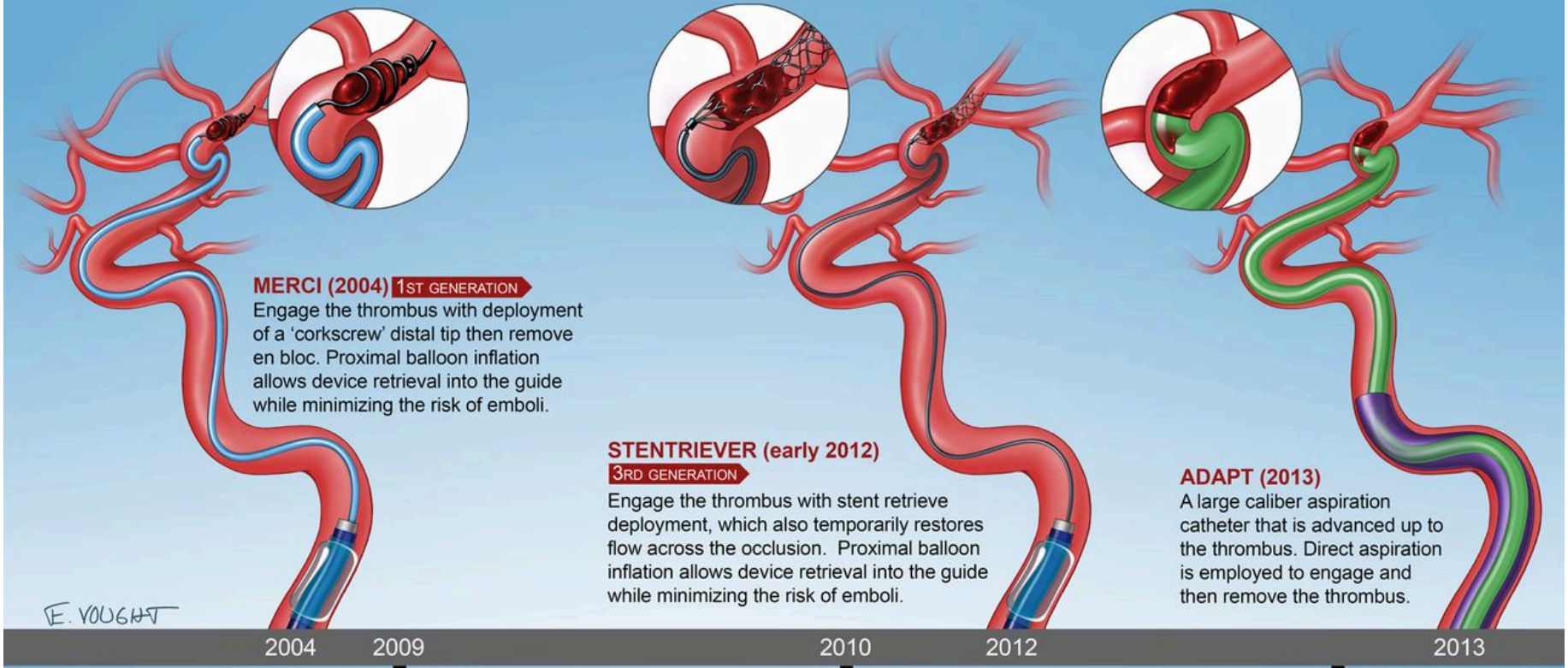


Stroke – ELVO Management

ELVO: Emergency Large Vessel Occlusion

Endovascular Mechanical Thrombectomy



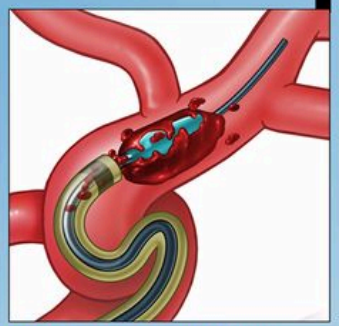


MERCI (2004) 1ST GENERATION
Engage the thrombus with deployment of a 'corkscrew' distal tip then remove en bloc. Proximal balloon inflation allows device retrieval into the guide while minimizing the risk of emboli.

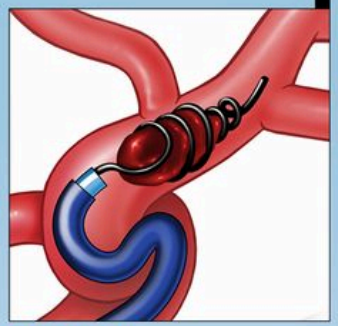
STENTRIEVER (early 2012)
3RD GENERATION
Engage the thrombus with stent retrieve deployment, which also temporarily restores flow across the occlusion. Proximal balloon inflation allows device retrieval into the guide while minimizing the risk of emboli.

ADAPT (2013)
A large caliber aspiration catheter that is advanced up to the thrombus. Direct aspiration is employed to engage and then remove the thrombus.

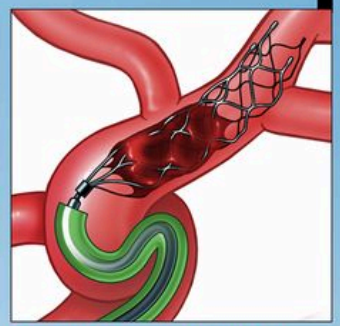
2004 2009 2010 2012 2013



PENUMBRA (2009) 2ND GENERATION
The penumbra aspiration system involves maceration of the thrombus with a separator under direct aspiration to prevent showering of fragments. Once the catheter system is delivered to the target vessel, ongoing clot maceration is performed without the need to re-access.



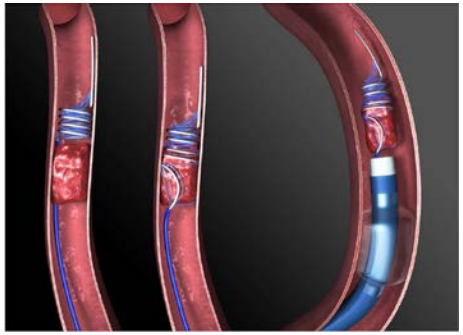
DAC (2010)
The DAC is positioned immediately adjacent to the thrombus and aspiration is applied to minimize emboli and optimize the vectors during pulling of the device.

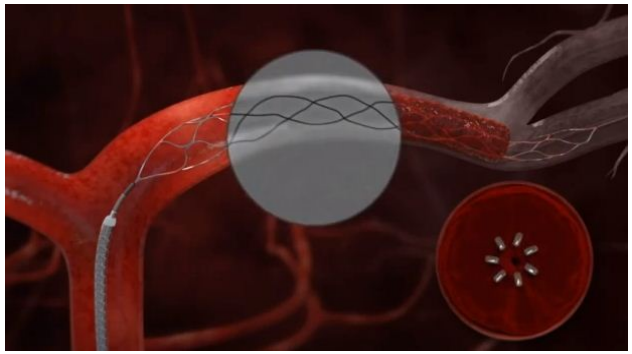


SOLUMBRA (late 2012)
To minimize the distance the stent retriever must travel while engaging the thrombus and mitigate the possibility of losing purchase of the clot, the stent retriever is then pulled directly into a large bore intermediate catheter while maintaining aspiration.

Thrombectomy Devices

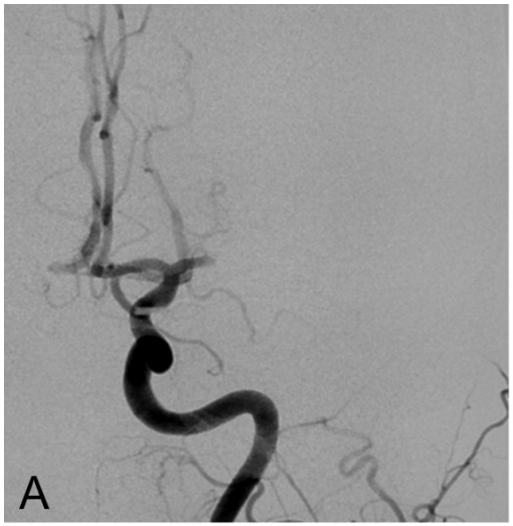
MERCI **SOLITAIRE** **TREVO**

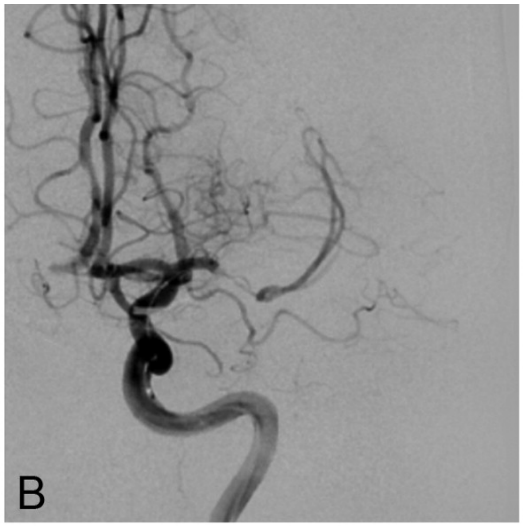


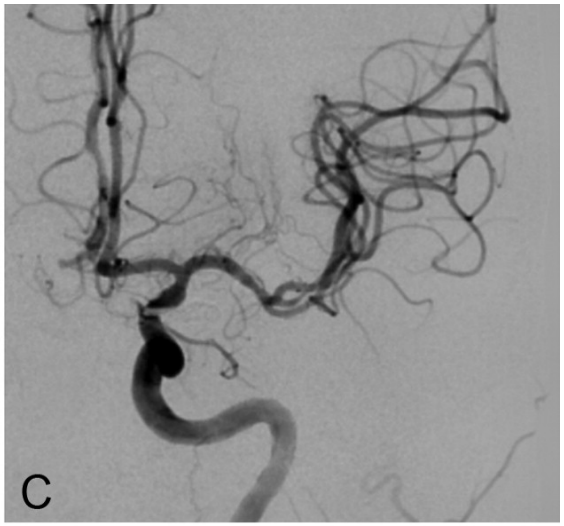


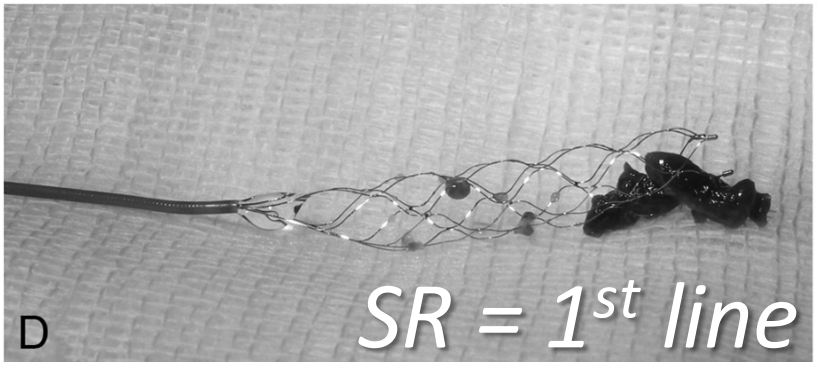
11. Use of stent retrievers is indicated in preference to the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) device.	I	A	Recommendation unchanged from 2015 Endovascular.

The Solitaire Stent-Retriever









3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
12. The use of mechanical thrombectomy devices other than stent retrievers as first-line devices for mechanical thrombectomy may be reasonable in some circumstances, but stent retrievers remain the first choice.	**IIb**	**B-R**	Recommendation revised from 2015 Endovascular.

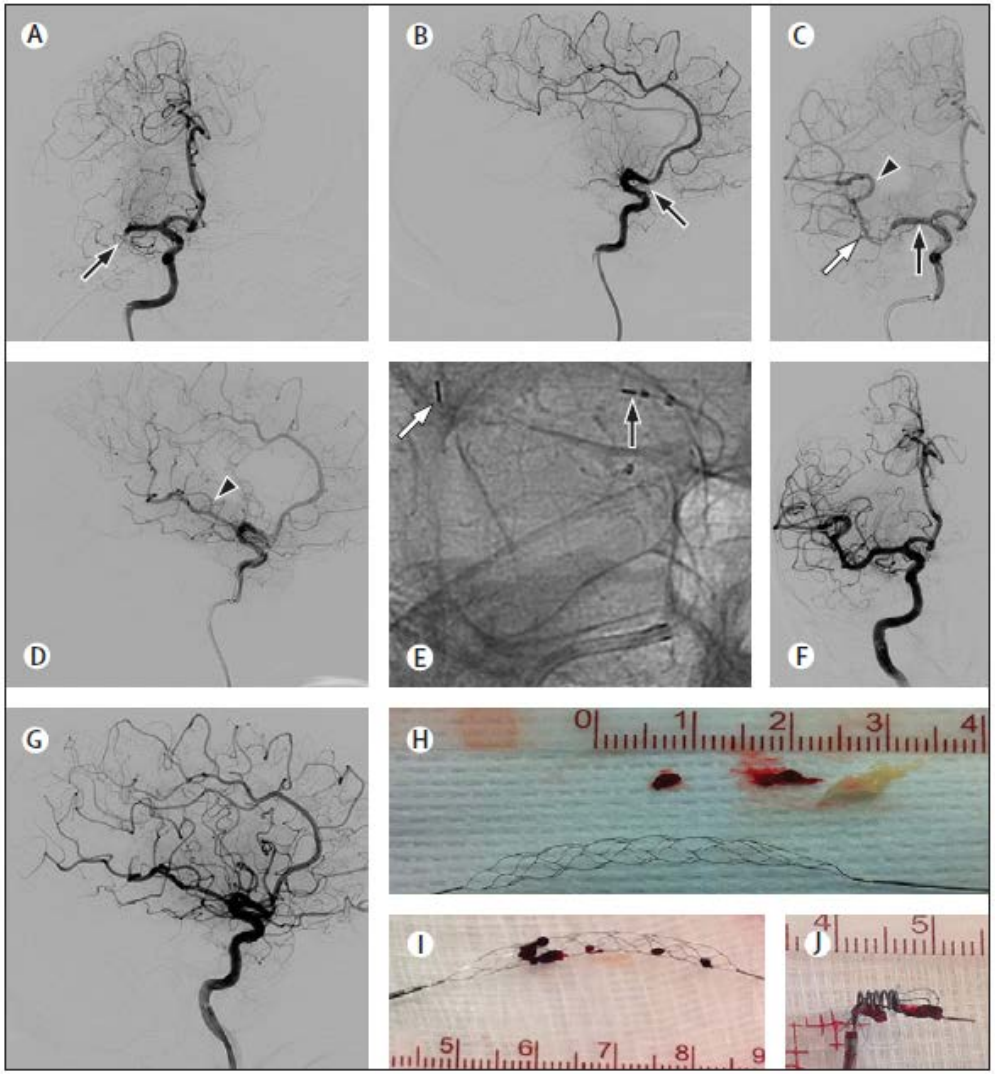


***Figure 1*: Example angiography and devices**

(A–H) Angiography images of a 67-year-old woman presenting with left hemiplegia and dysarthria (NIHSS 12). Intravenous recombinant tissue plasminogen activator was given 115 min after symptom onset without improvement. (A–B) Angiography before treatment showing complete occlusion of the M1 segment of the right MCA (arrows). (C–E) Angiography after deployment of the Trevo Retriever across the occluded segment showing a perfusion channel with contrast opacification of the distal MCA territory (arrowheads). Black arrows in panels C–E show the proximal Trevo markers and white arrows show the distal Trevo markers. (E) Magnified native image of panel C. (F–G) Angiography after treatment showing near complete reperfusion of the right MCA territory (TICI 2b). At 90 days, the patient's NIHSS was 0 and modified Rankin scale score was 1. (H) Trevo device and retrieved complex thromboembolic material. (I–J) Thrombus incorporation by the Trevo (I) and Merci (J) retrievers. NIHSS=National Institutes of Health Stroke Scale. MCA=middle cerebral artery. TICI=thrombolysis in cerebral infarction grading scale score.

WHY WE DO WHAT WE DO

Endovascular Therapy Clinical Evidence

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European Heart Journal
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FASTTRACK CLINICAL RESEARCH
Vascular medicine

Endovascular therapy for acute ischaemic stroke: a systematic review and meta-analysis of randomized trials

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Endovascular Therapy Clinical Evidence

Early Failures → Later Success Stories

Table I Characteristics of included trials

Variable	IMS III 2013	MR RESCUE 2013		SYNTHESIS Expansion 2013	MR CLEAN 2015	ESCAPE 2015	EXTEND-IA 2015	SWIFT PRIME 2015	REVASCAT 2015
		Penumbral	Non-penumbral						
	EVT/control	EVT/control	EVT/control	EVT/control	EVT/control	EVT/control	EVT/control	EVT/control	EVT/control
Total	434/222	34/34	30/20	181/181	233/267	165/ 150	35/35	98/98	103/103
Follow-up (days)	90	90	90	90	90	90	90	90	90
Location	58 centres in USA, Canada, Australia, and Europe	22 sites, North America		24 sites, Italy	16 sites, The Netherlands	22 centres worldwide in USA, Canada, UK, and South Korea	14 centres in Australia and New Zealand	39 sites, USA and Europe	4 centres in Spain
Trial design	PROBE design	PROBE design		PROBE design	PROBE design	PROBE design	PROBE design	PROBE design	PROBE design
IV tPA in EVT group	Yes	Yes		No	Yes	Yes	Yes	Yes	Yes
Maximum delay for initiation of EVT (h)	5	8		6	6	12	6	6	8
Premature termination and reason	Yes, because of futility	No		No	No	Yes, because of external evidence/ efficacy	Yes, because of external evidence/efficacy	Yes, because of external evidence/ efficacy	Yes, because of external evidence/ efficacy
Vessel imaging required CTA/MRA/ DSA	Not required in initial protocol, later amendment	Yes		No	Yes	Yes	Yes	Yes	Yes
Other imaging modality for trial inclusion	NCCT	NCCT		NCCT	NCCT	NCCT, collateral assessment on multiphase CTA	NCCT, CT perfusion imaging	NCCT, CT perfusion imaging (81%), MRI (in few patients)	NCCT, MRI
Control group therapy	IV tPA	IV tPA		IV tPA	IV alteplase or urokinase	IV alteplase	IV alteplase	IV tPA	IV alteplase (when eligible)
Primary efficacy outcome	mRS of 2 or less at 90 days	mRS at 90 days		mRS at 90 days	mRS at 90 days	mRS at 90 days	Median reperfusion at 24 h and early neurological improvement	mRS at 90 days	Severity of global disability at 90 days on mRS

Endovascular Therapy Clinical Evidence

Meta-Analysis of 5 Newer Trials (2015 onward)

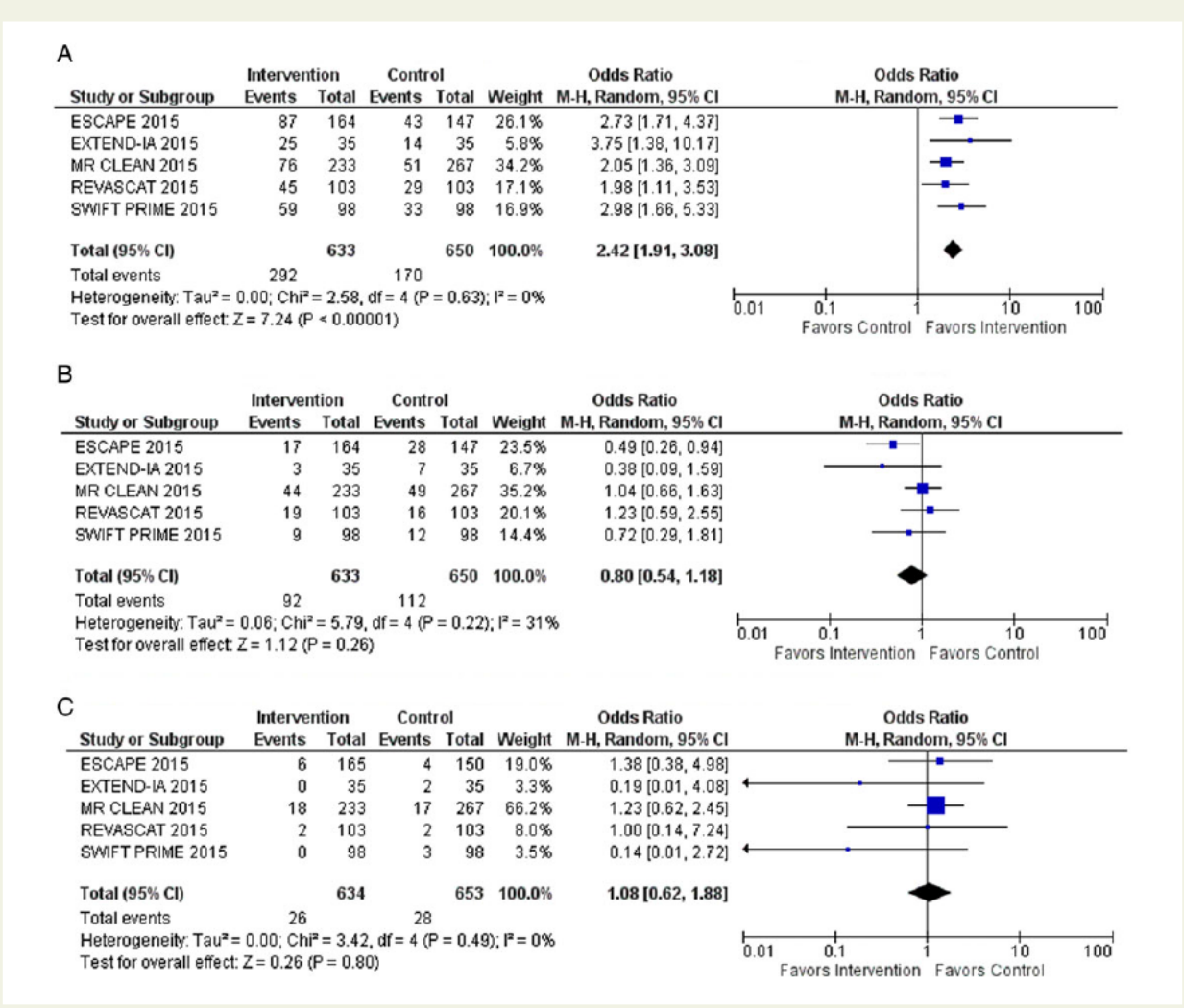


Figure 2 Analysis limited to newer (2014–15) trials: (*A*) functional independence (90-day mRS of 0–2) with EVT; (*B*) mortality with EVT; and (*C*) sICH with EVT.

A) **All 5 trials favored intervention for functional outcome**.

B) **Decrease in mortality** in the intervention arm (*in all but 1 trial*).

C) **No significant difference in sICH** (*note that SWIFT PRIME and EXTEND-IA had no symptomatic ICH*).

Endovascular Trial Overview

Study	Onset to tPA control, median time (min)	Onset to tPA endo, median time (min)	Onset to groin, median time (min)	Study CT to groin, median time (min)	Onset to reperfusion, median time (min)	mTICI 2b-3 (%)	TICI 2b-3 (%)	90 day mRS 0-2 control, (%)	90 day mRS 0-2 endo, (%)
MR CLEAN	87	87	260			58.7		19.1	32.6
REVASCAT	105	117	269		355	65.7		28.2	43.7
ESCAPE	125	110		51	241		72.4	29.3	53
SWIFT PRIME	117	110.5	224	57		83		35	60
EXTEND IA	145	127	210	93	248	86		40	71

Collective Expectations:

CT head to groin puncture < 60 minutes

CT head to reperfusion < 90 minutes

TICI or mTICI of 2b-3 in 70% or more of patients

Overall reperfusion under 4 hours from stroke onset

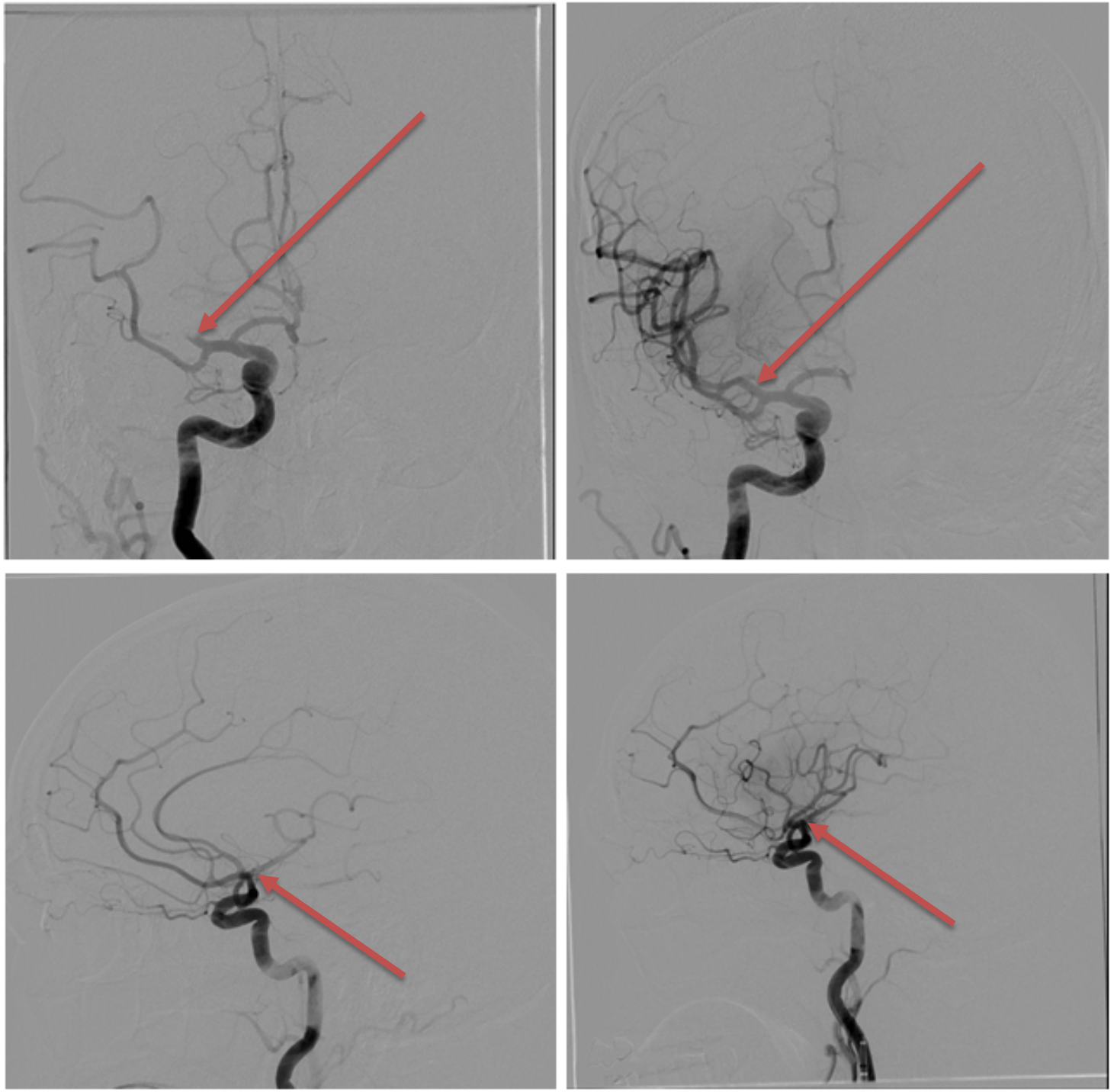
Endovascular Therapy
Clinical Evidence - Conclusions

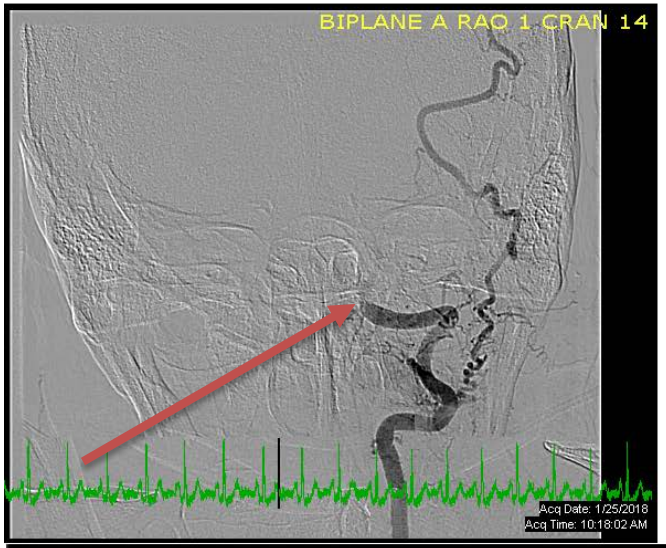
- EVT (endovascular therapy) significantly improved functional outcomes in a "selected group of individuals" with confirmed "target" large vessel ischemic strokes (within 6 hours from LKW)

3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
3 Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.	I	A	Recommendation revised from 2015 Endovascular.

From “Slam Dunk” to “Ambiguous”

4. 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**	Recommendation reworded for clarity from 2015 Endovascular. Class unchanged. LOE revised. See Table LXXXIII in online Data Supplement 1 for original wording.
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-EO**	Recommendation reworded for clarity from 2015 Endovascular. Class unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table LXXXIII in online Data Supplement 1 for original wording.
6. 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). Additional randomized trial data are needed.	**IIb**	**B-R**	Recommendation unchanged from 2015 Endovascular.

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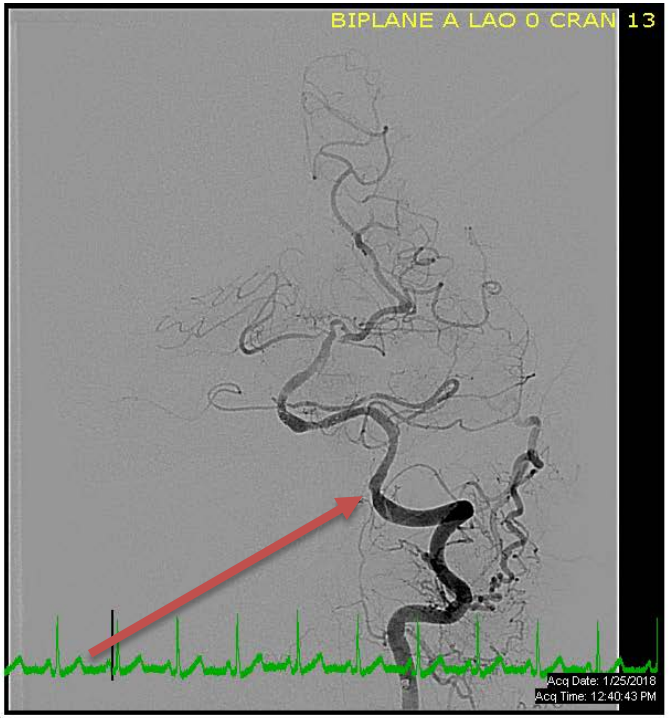
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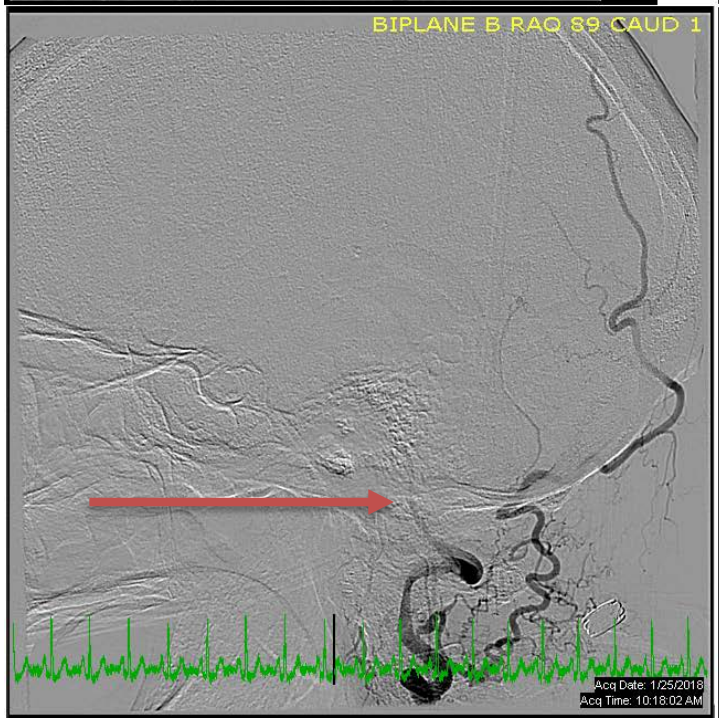
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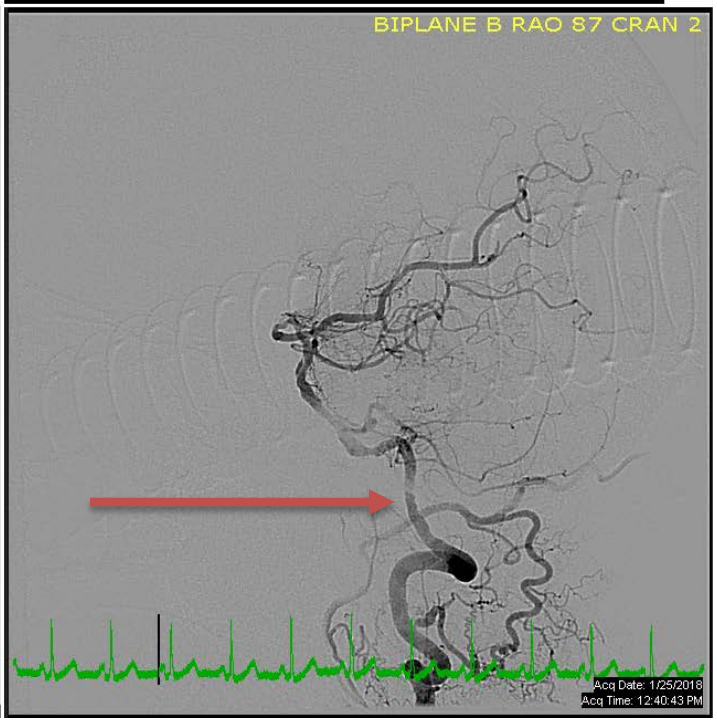
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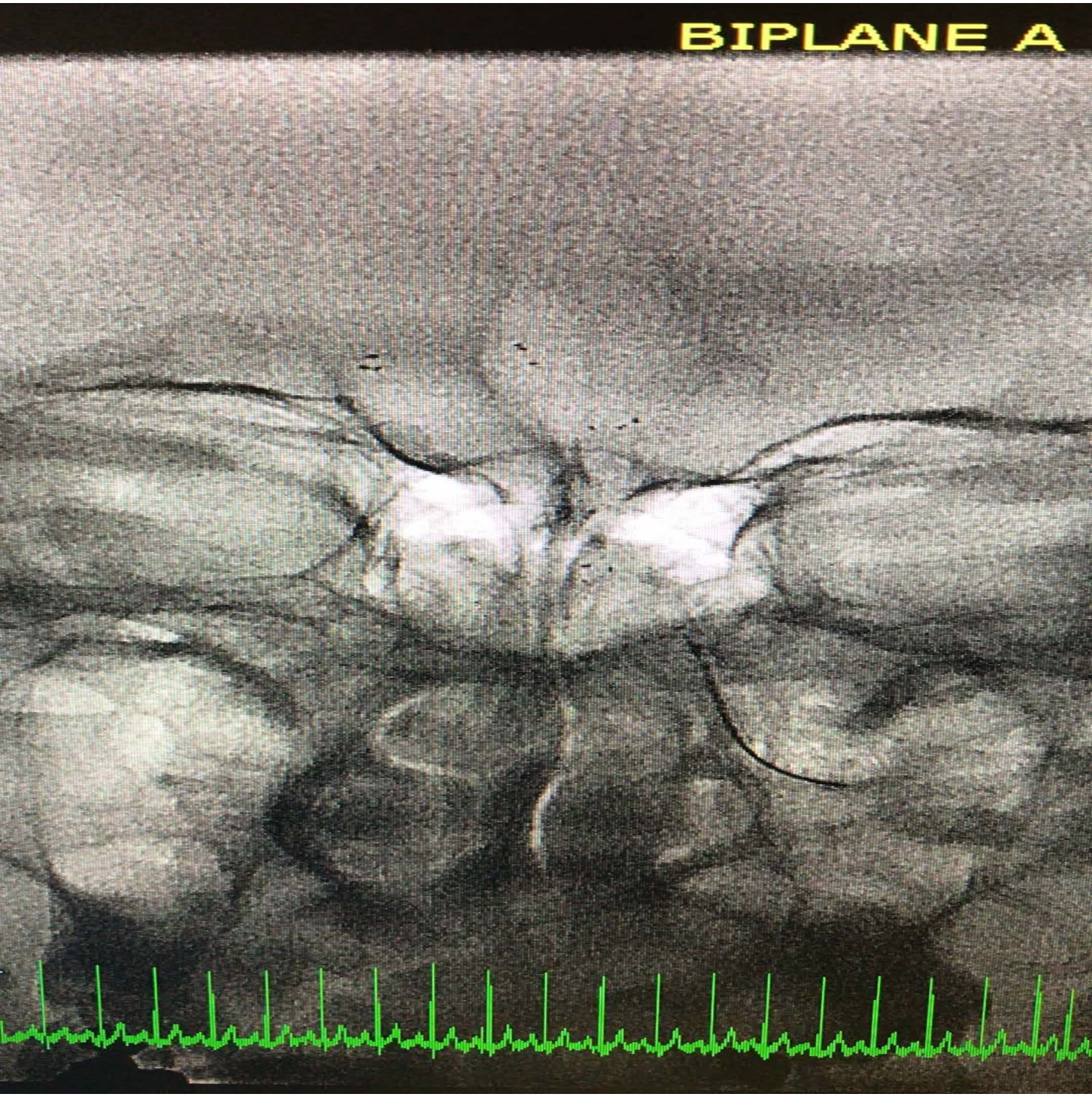

BIPLANE A

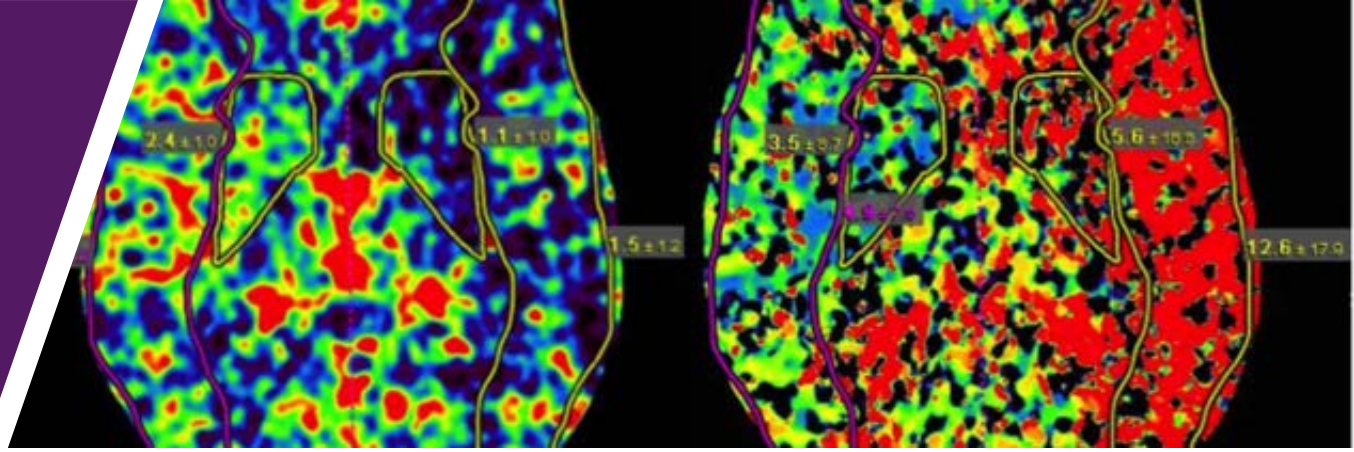
(m²)TICI Scoring

- Grade 0: No perfusion.
- Grade 1: Minimal perfusion.
- Grade 2: Partial perfusion.
  - *2a: partial filling of vascular territory.*
  - *2b: > 50% filling of vascular territory.*
  - *2c: > 90% filling of vascular territory.*
- Grade 3: Normal/complete perfusion.

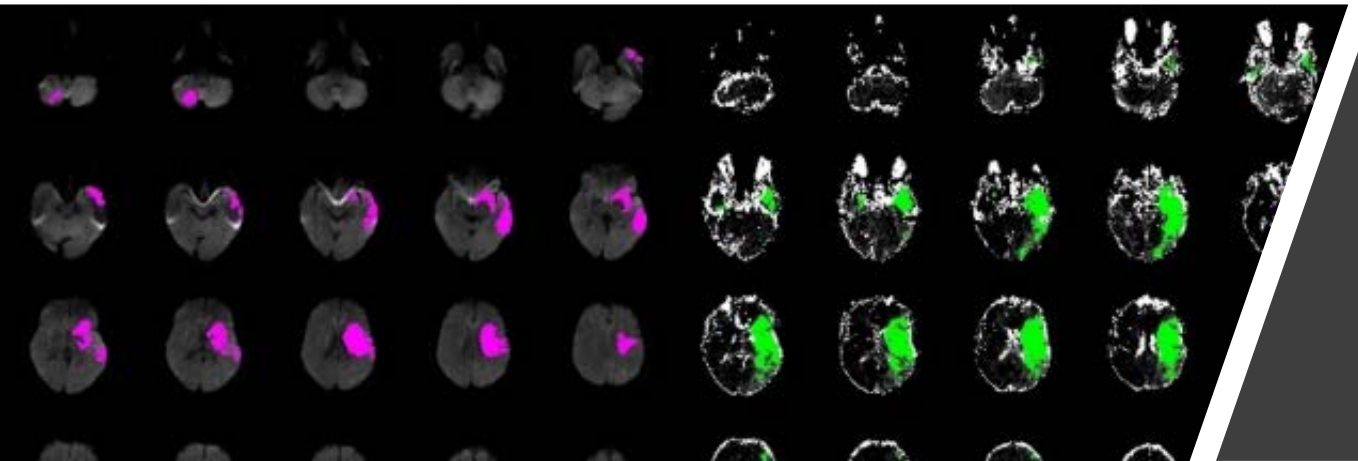
The general goal is 2B or better…
or as Shakespeare would say:

"2B, or not 2B?
That is the question!"

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.

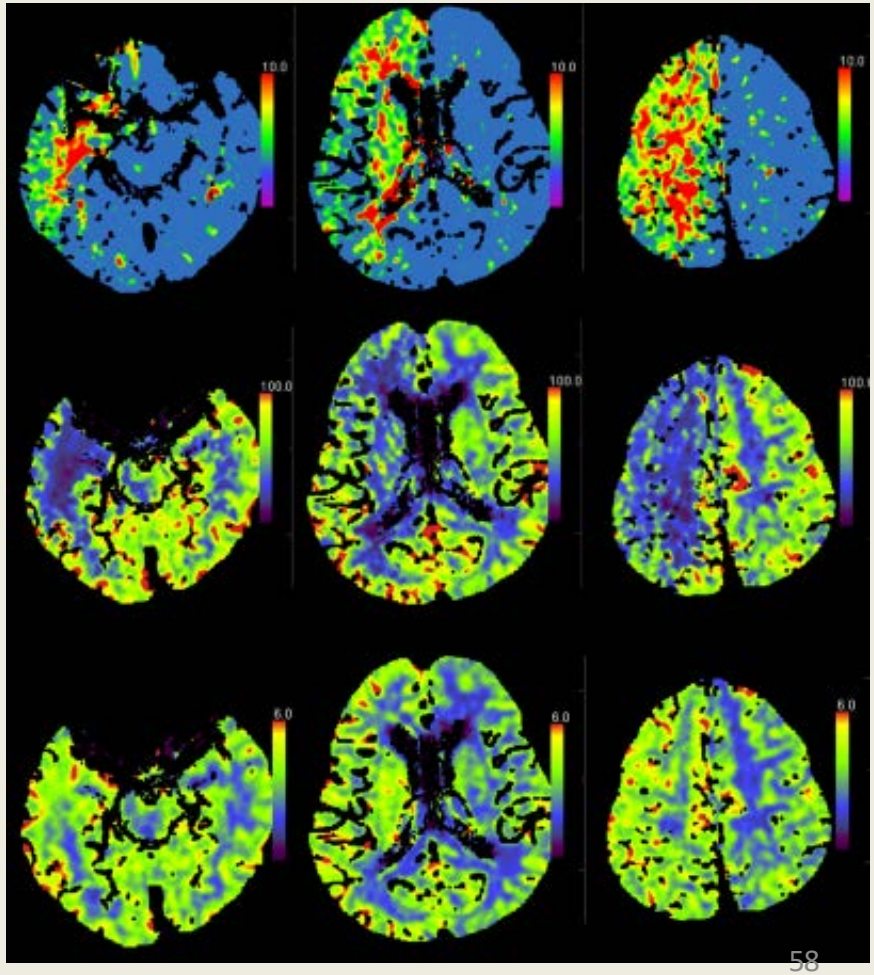


Expanding the LVO Treatment Window



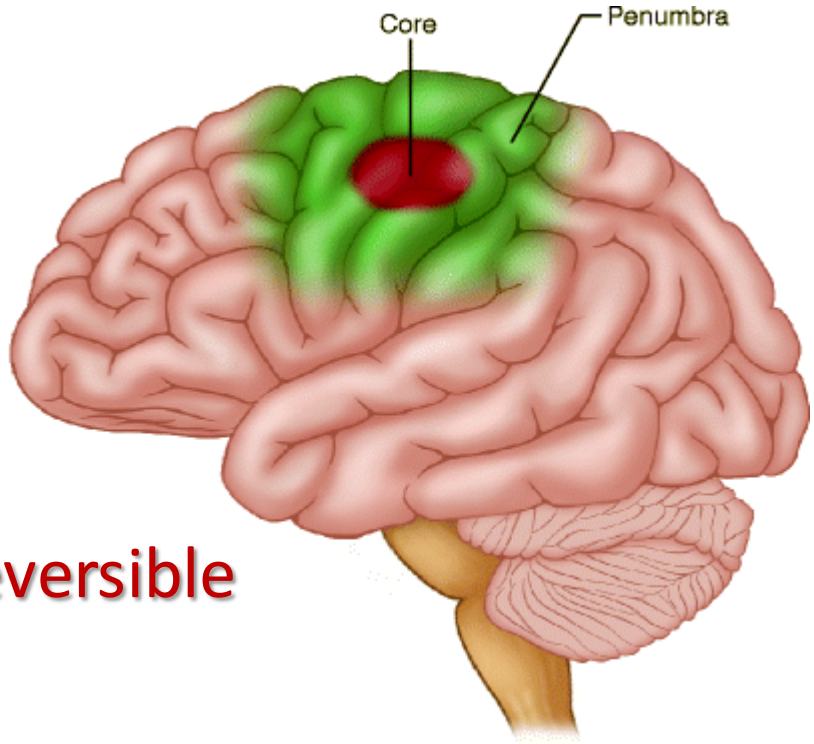
Perfusion Imaging

- Modalities:
  - CTP
  - MRP



The Big "Perfusion" Question

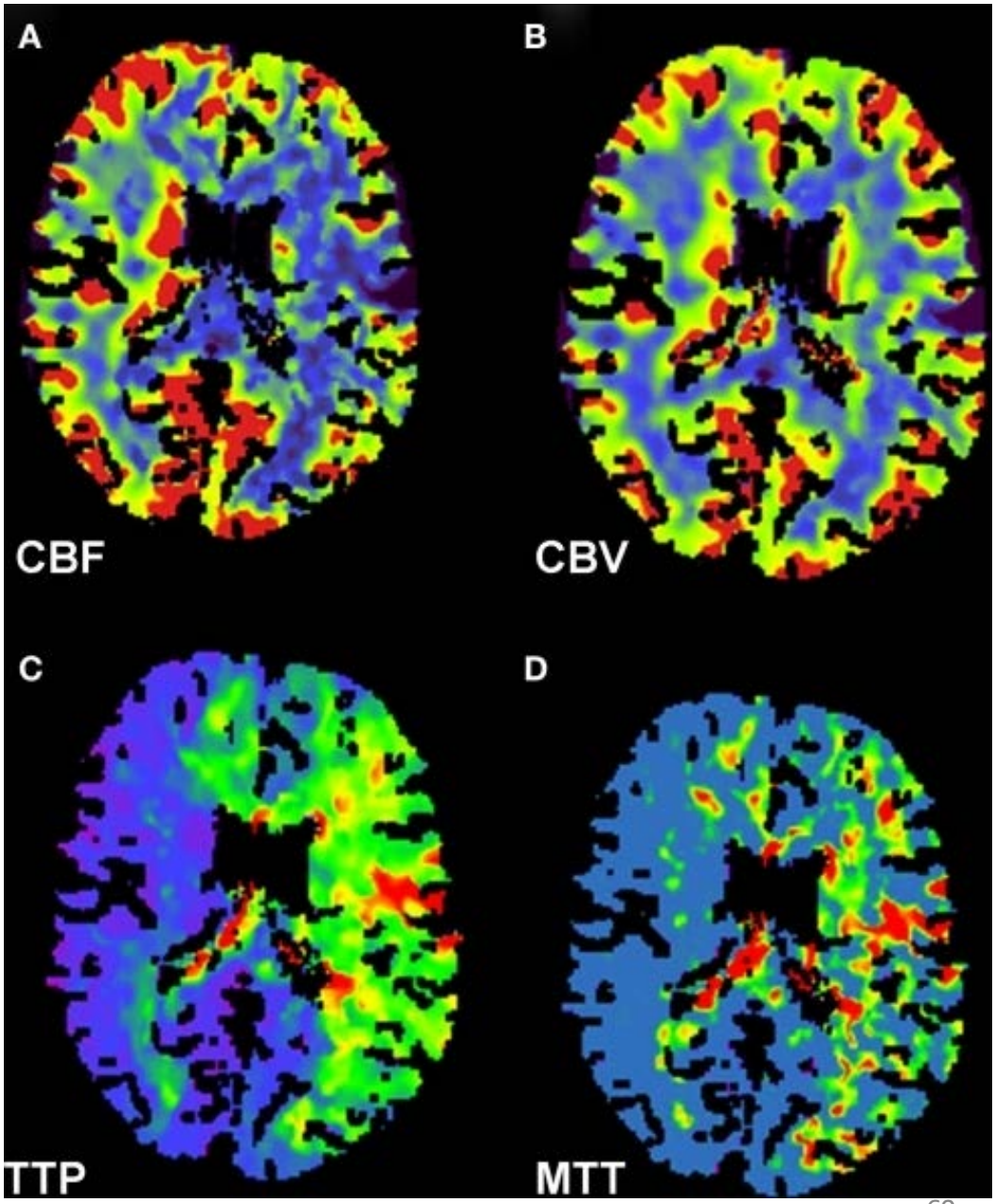
Core vs Penumbra



- Stroke Core:
  - Dead brain tissue → not reversible
- Stroke Penumbra:
  - At risk brain tissue → reversible

- Stroke Core

- Stroke Penumbra



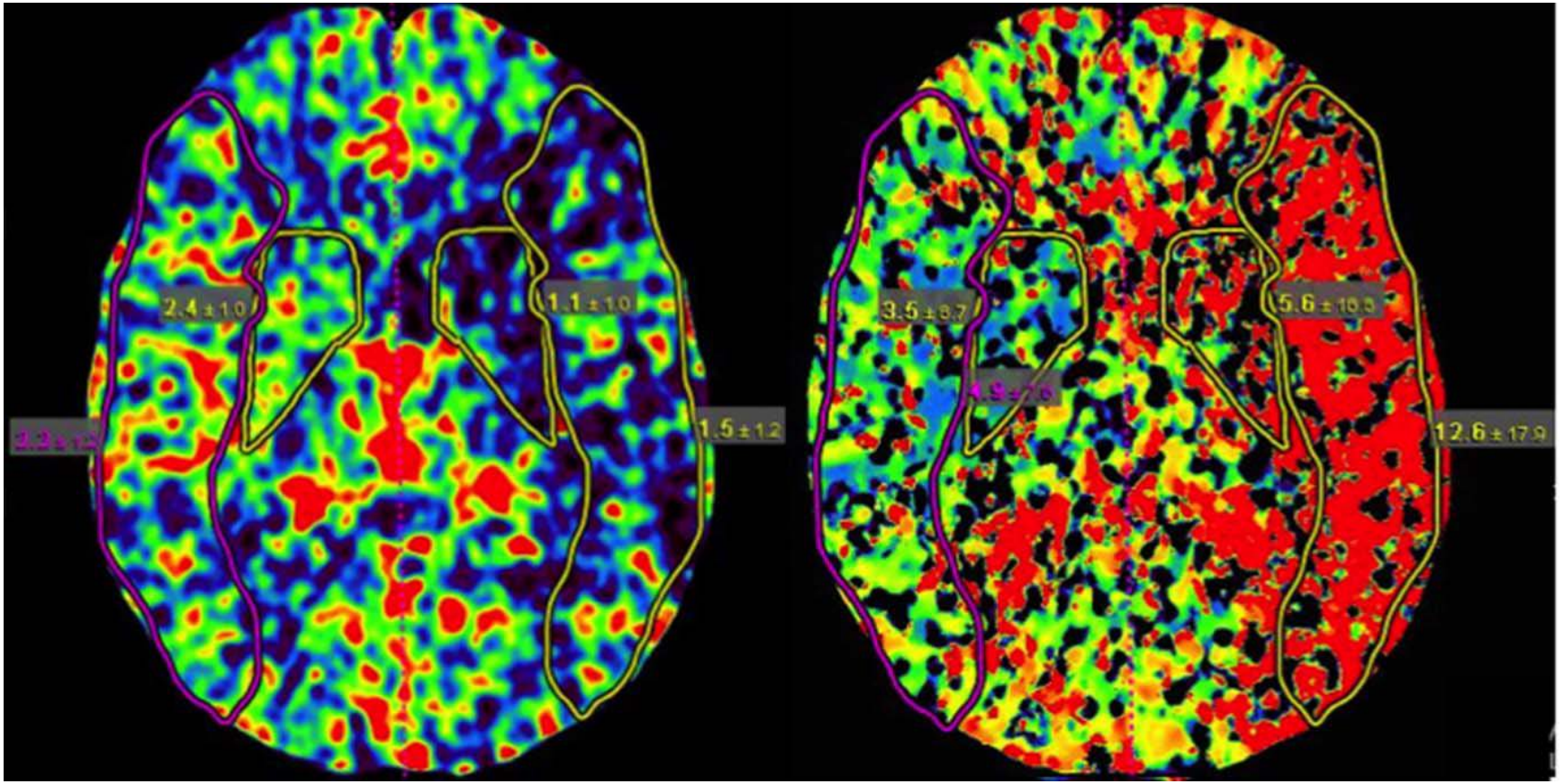


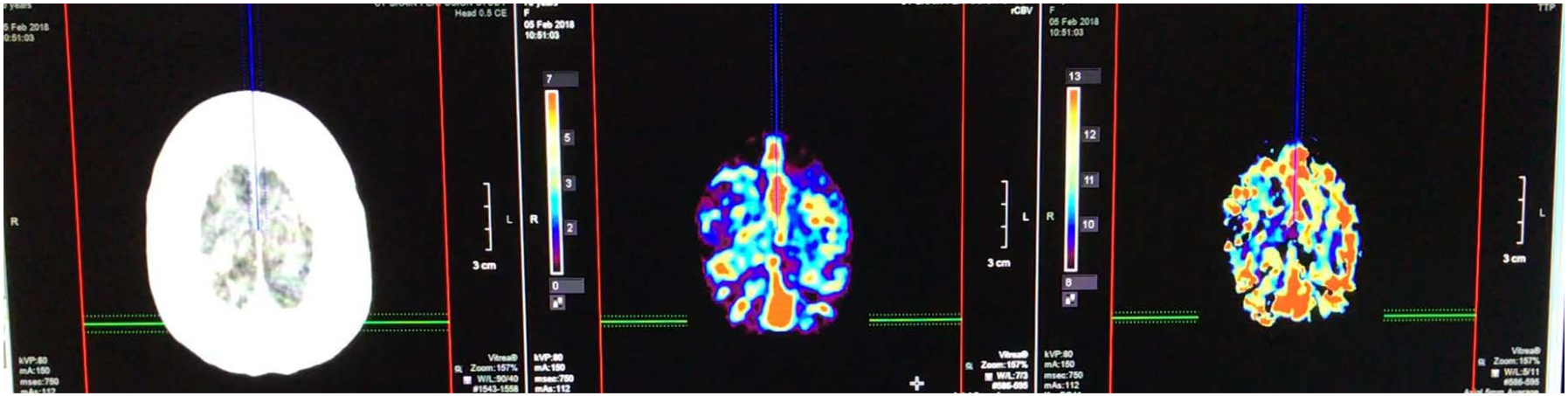
Figure 1. Perfusion maps in a case of **left MCA M1** segment occlusion. Numbers indicate absolute values of **CBV (left)** and **MTT/TTP (right)** maps of the affected territory (left hemisphere) and the contralateral control side (right hemisphere). Values are calculated separately for the territory of the basal ganglia and the supraganglionic (cortical) regions.

CT Perfusion - Axial Maps

Source 0.5 mm

CBV

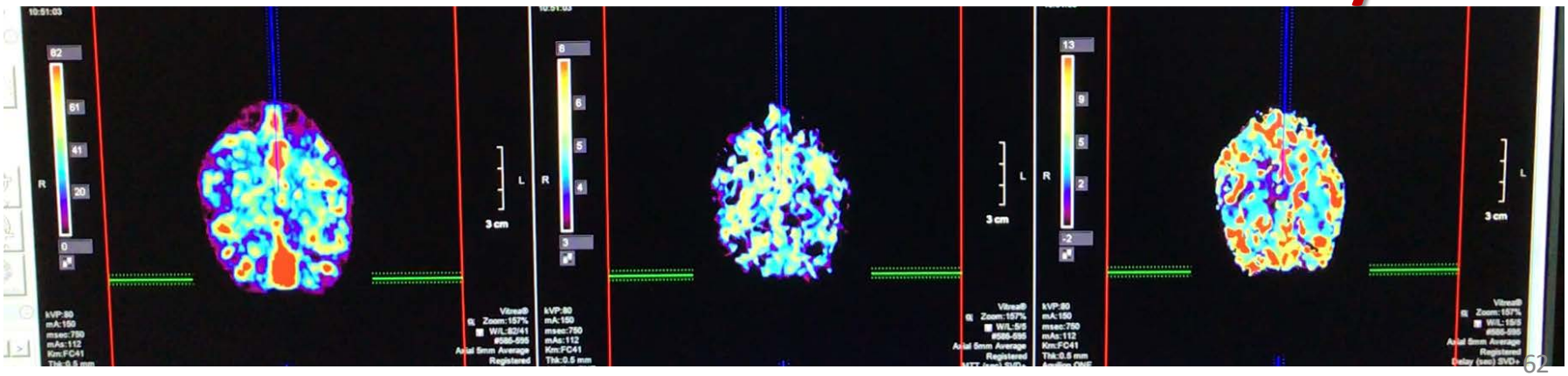
TTP



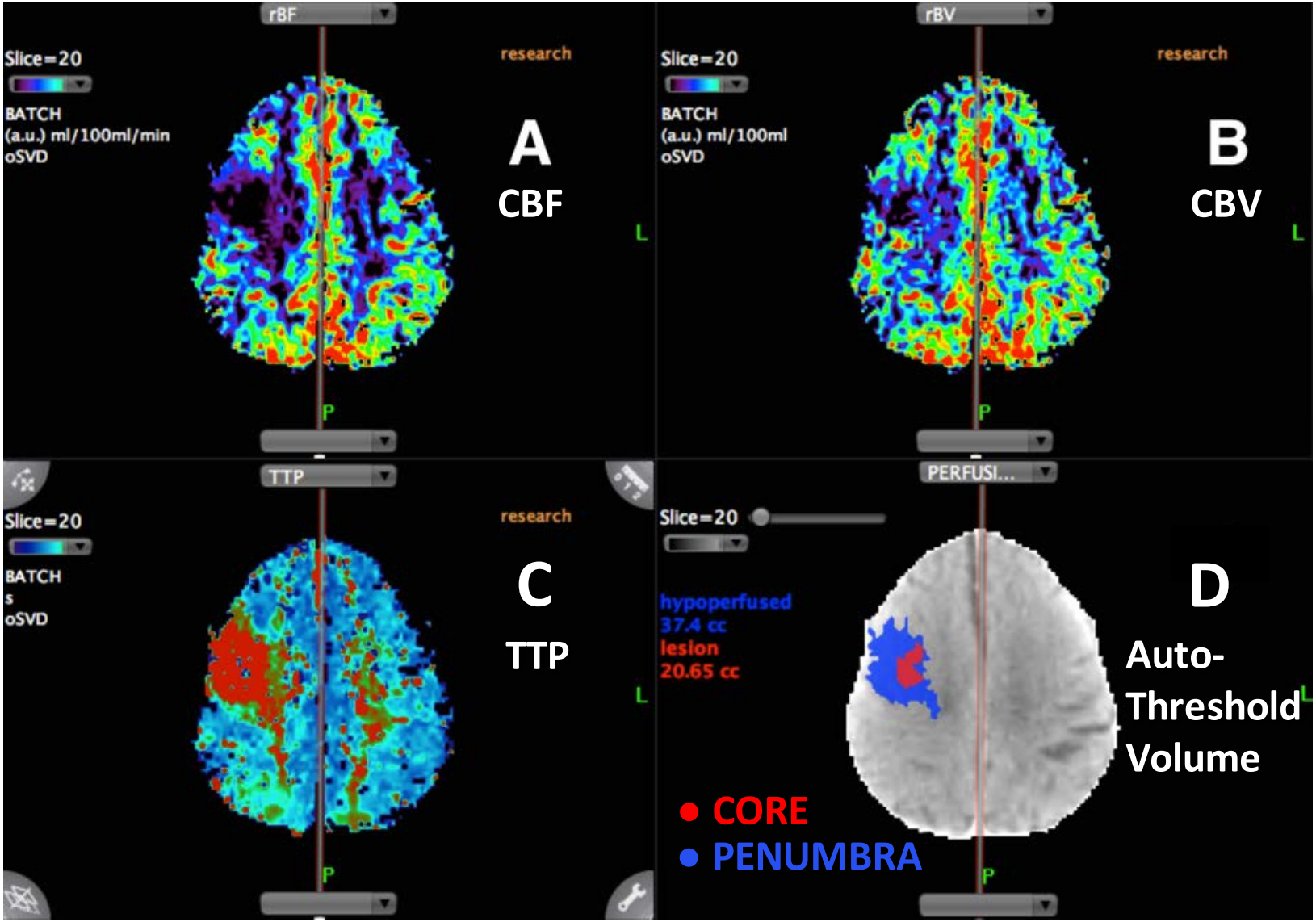
CBF

MTT

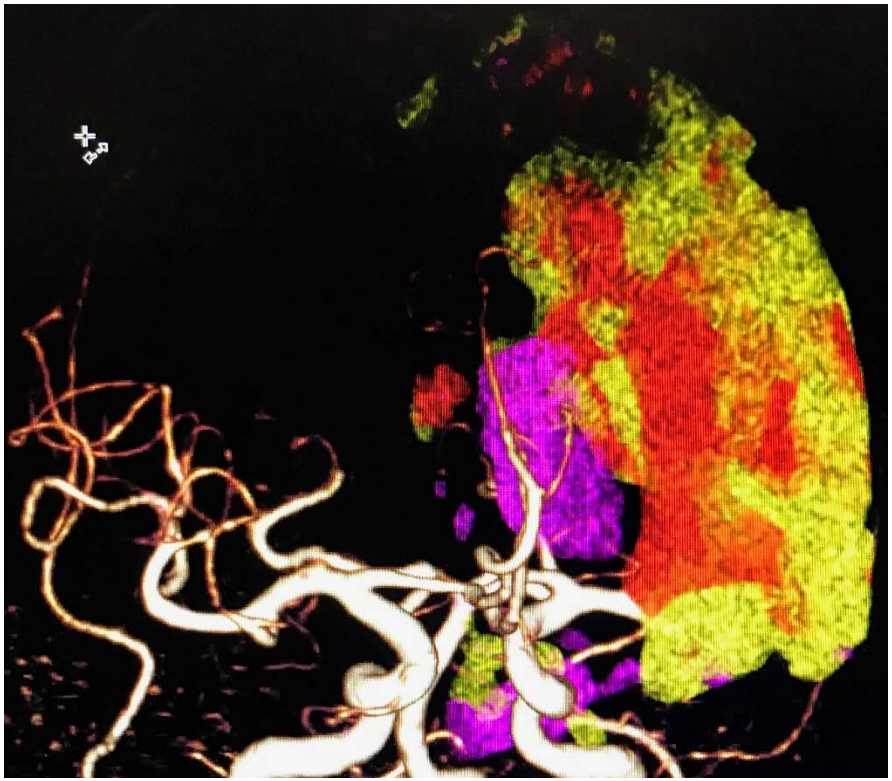
Delay

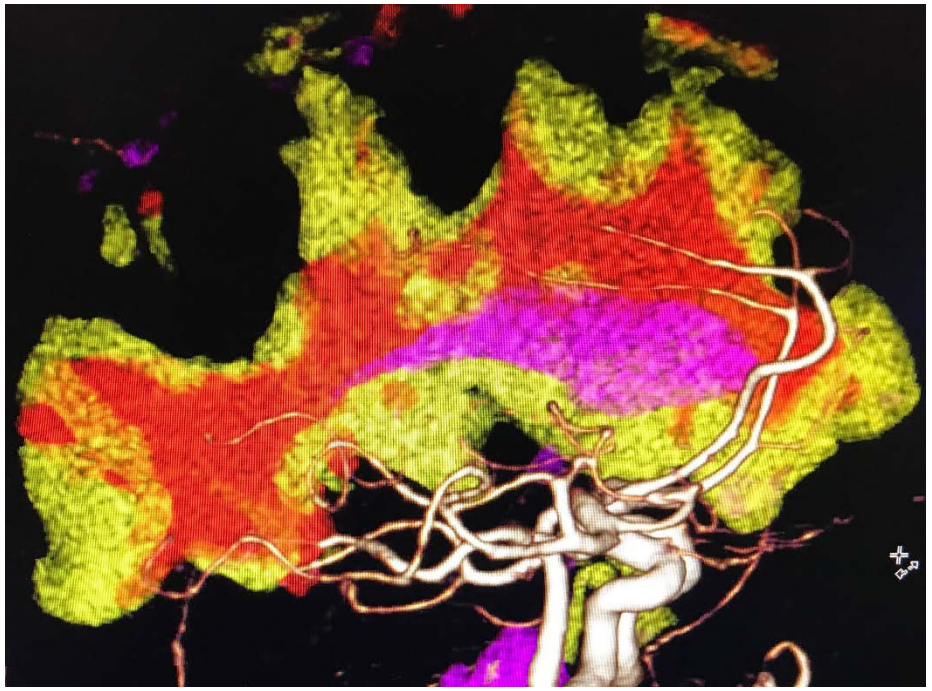


Automation → Olea Sphere Analysis

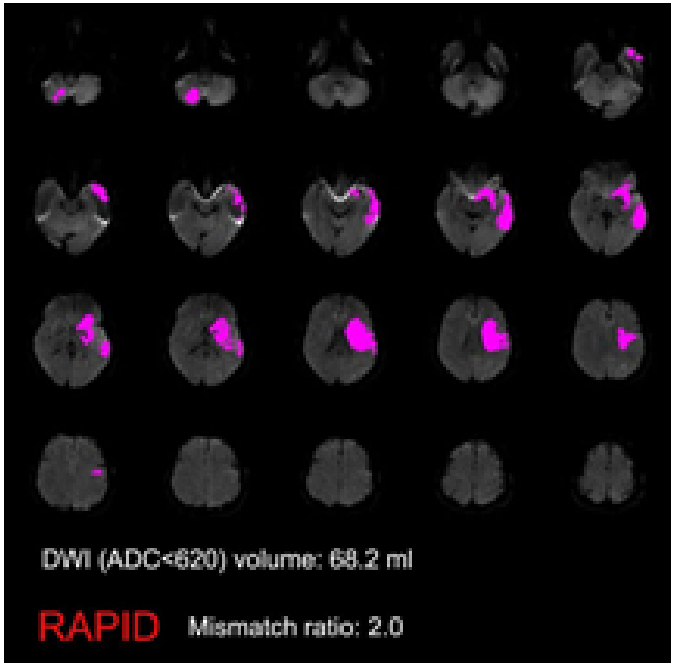


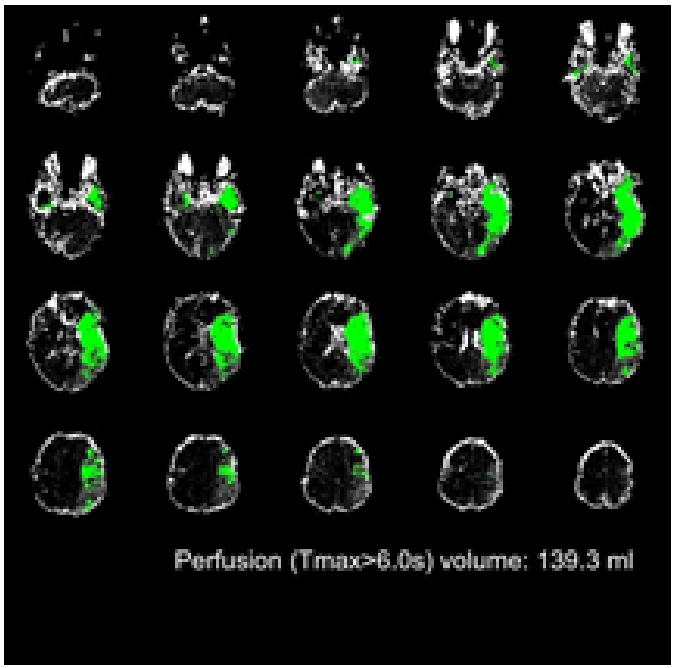
Automation → Vital Vitrea Analysis





New Data
DAWN (‘17)
DEFUSE-3 (’18)

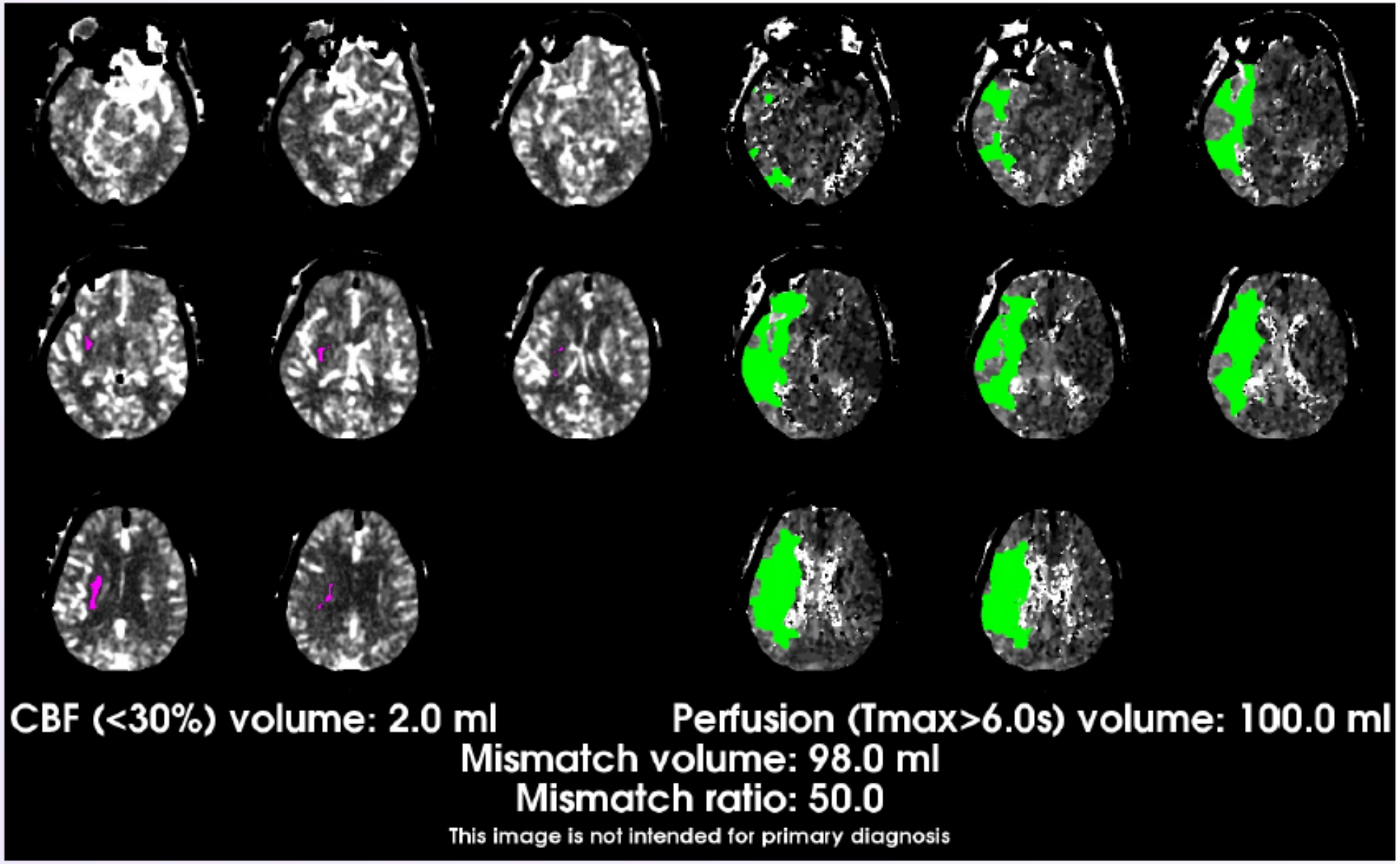




Extended Window for Thrombectomy?

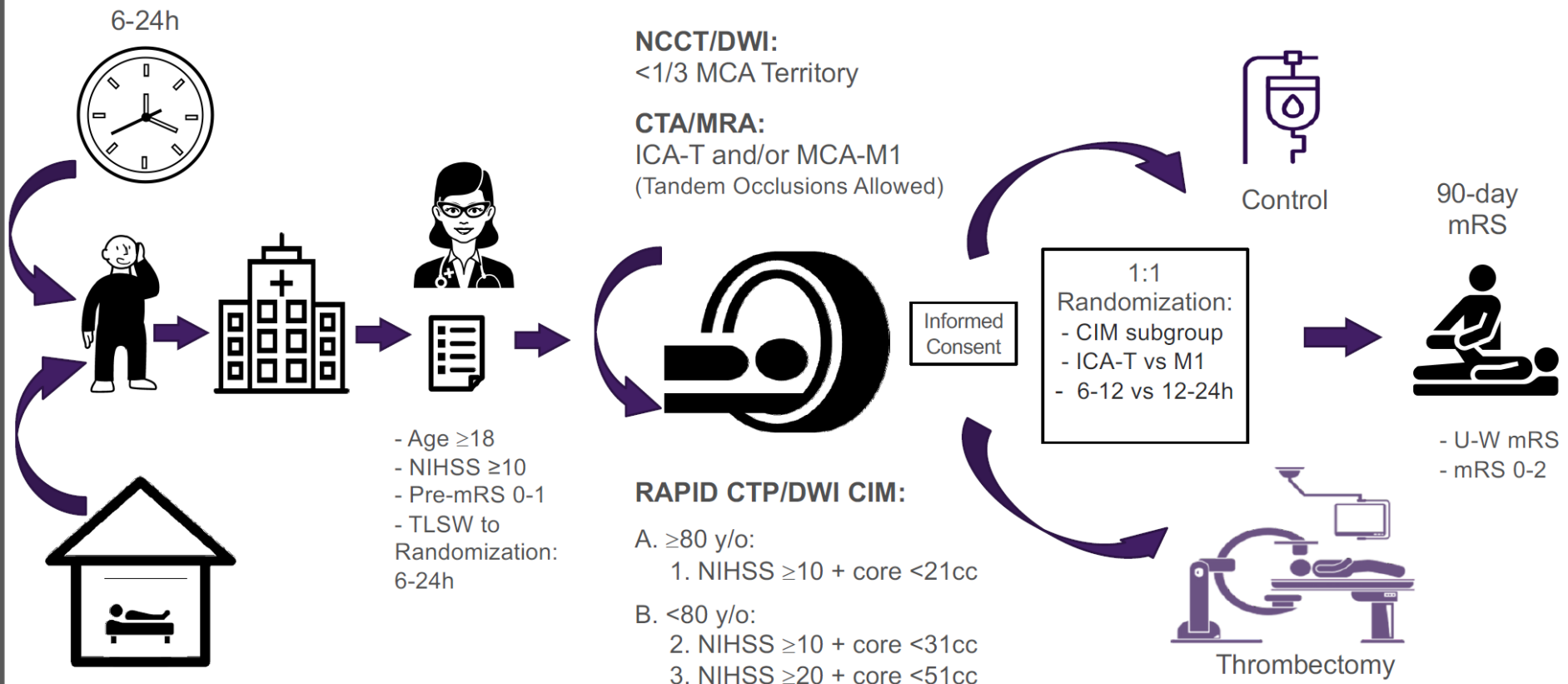
DAWN Trial -&- DEFUSE-3 Trial

CT or MR Perfusion → RAPID


CBF (<30%) volume: 2.0 ml
Perfusion (Tmax>6.0s) volume: 100.0 ml
Mismatch volume: 98.0 ml
Mismatch ratio: 50.0
This image is not intended for primary diagnosis

DAWN™
TRIAL

Study Methods: Workflow



Inclusion Criteria Comparison

FACTORS	DAWN '17	DEFUSE-3 '18
Age:	18+	18-90
NIHSS:	10+ or 20+	6+
Pre-stroke mRS:	0-1	0-2
LKW to Puncture:	6-24 hrs	6-16 hrs
CT or MR core:	MCA < 1/3	ASPECTS 6+
Target LVO:	ICA-T and/or MCA M1	ICA and/or MCA M1

Inclusion Criteria Comparison

RAPID Perfusion	DAWN '17	DEFUSE-3 '18
Penumbra/Core Ratio:		1.8 or more
Penumbra/Core Diff:		15 mL or more
Core:	50 mL or less Age < 80 & NIHSS 20+	70 mL or less
	30 mL or less Age < 80 & NIHSS 10+	*NOTE: Only 61.5% of DEFUSE-3 patients met the more strict DAWN inclusion criteria.*
	20 mL or less Age 80+ & NIHSS 10+	
Endovascular Device:	Trevo only!	Any FDA-approved thrombectomy device
Endovascular Roadblock:	Angioplasty of cervical ICA (no stenting)	Angioplasty or stenting of cervical ICA

Patient Characteristics

FACTORS	DAWN '17		DEFUSE-3 '18	
	EVT:	Control:	EVT:	Control:
Age:	69	71	70	71
Male Sex (%):	39%	52%	50%	49%
NIHSS:	17	17	16	16
Stroke Witnessed (%):	10%	14%	34%	39%
A-Fib (%):	40%	24%		
Rx with IV tPA (%):	5%	13%	11%	9%

Patient Characteristics

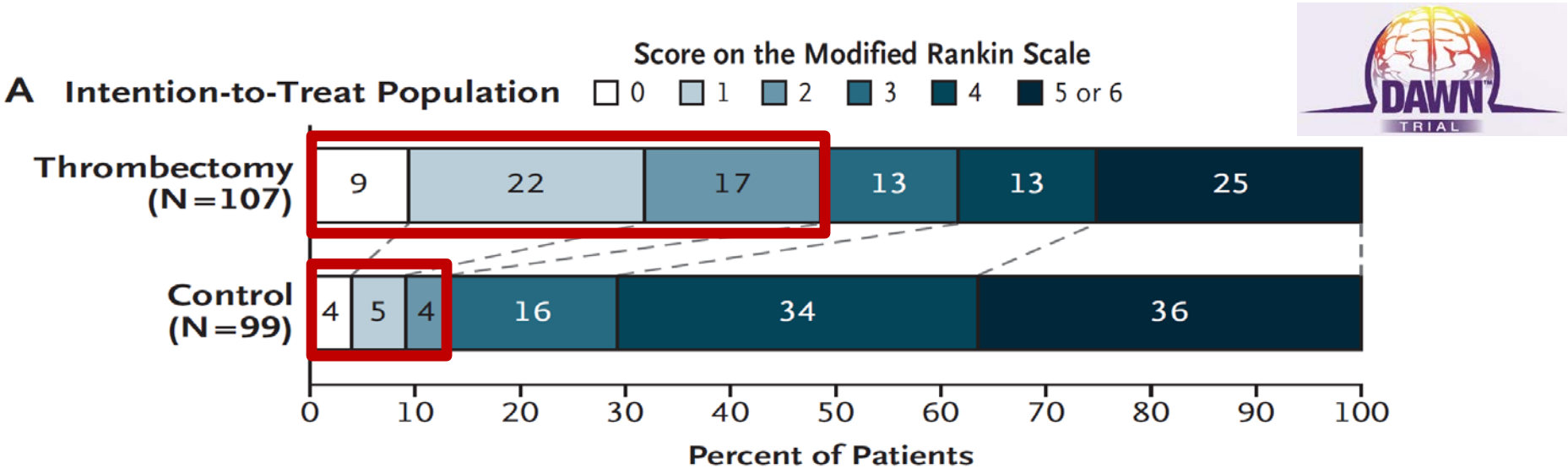
FACTORS	DAWN '17		DEFUSE-3 '18	
	EVT:	Control:	EVT:	Control:
Stroke Core (mL):	7.6 mL	8.9 mL	9.4 mL	10.1 mL
Stroke Penumbra (mL):			114.7 mL	116.1 mL
ICA Occlusion (%)*:	21%	19%	35%	40%
MCA M1 Occlusion (%):	78%	78%	65%	60%
CT ASPECTS:			8	8

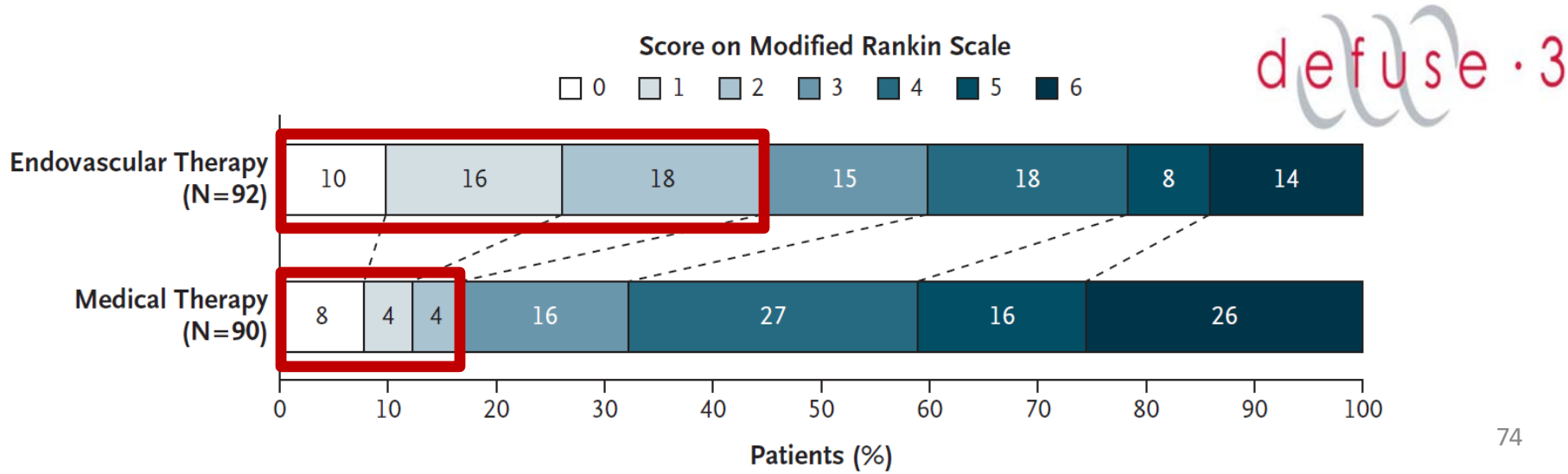
**DAWN = ICA-T only.*
**DEFUSE-3 = any ICA occlusion.*

mRS - Modified Rankin Scale

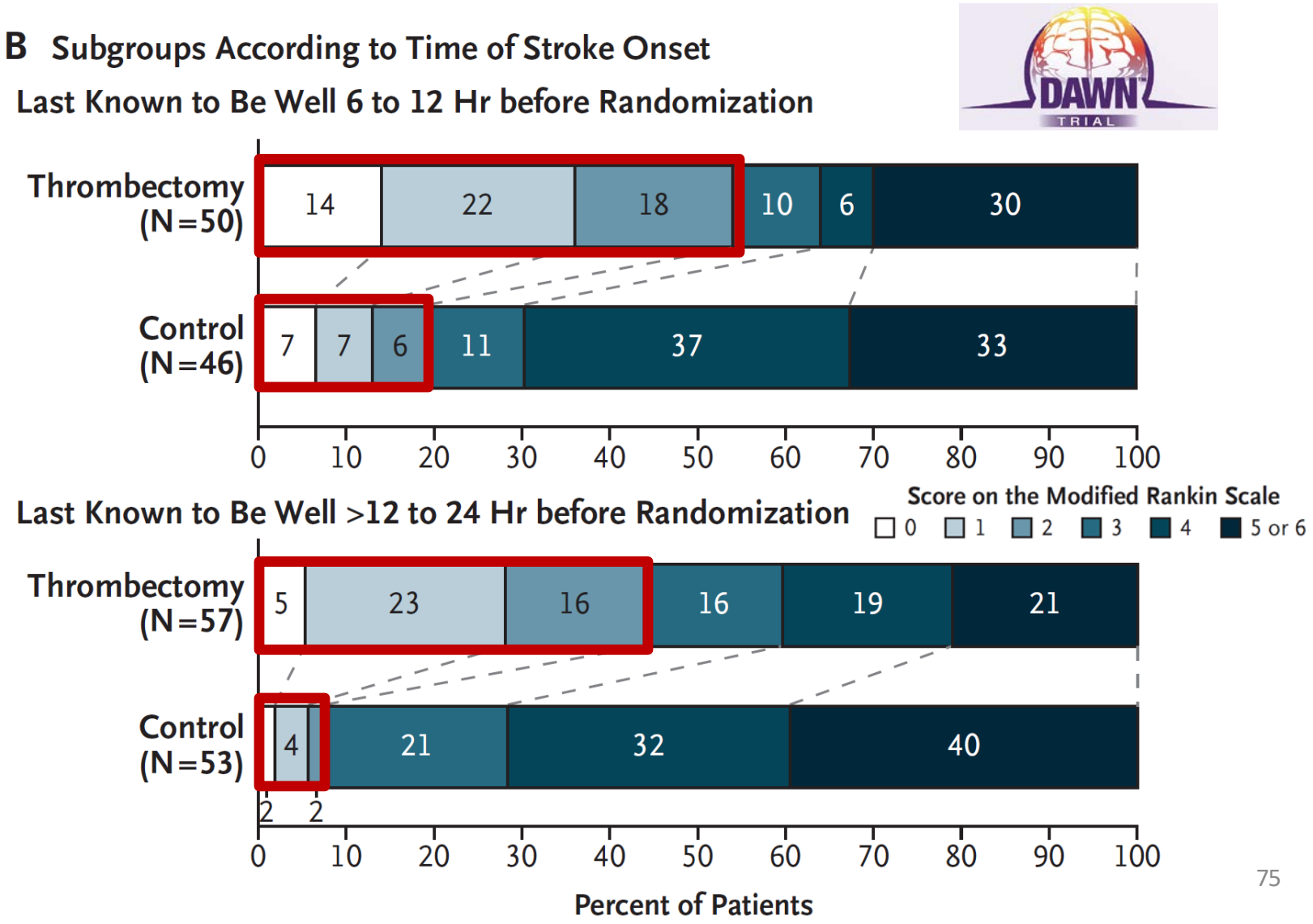
- 0 - No symptoms.
- 1 - No significant disability. Able to carry out all usual activities, despite some symptoms.
- 2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
- 3 - Moderate disability. Requires some help, but able to walk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

90-Day mRS – Primary Result



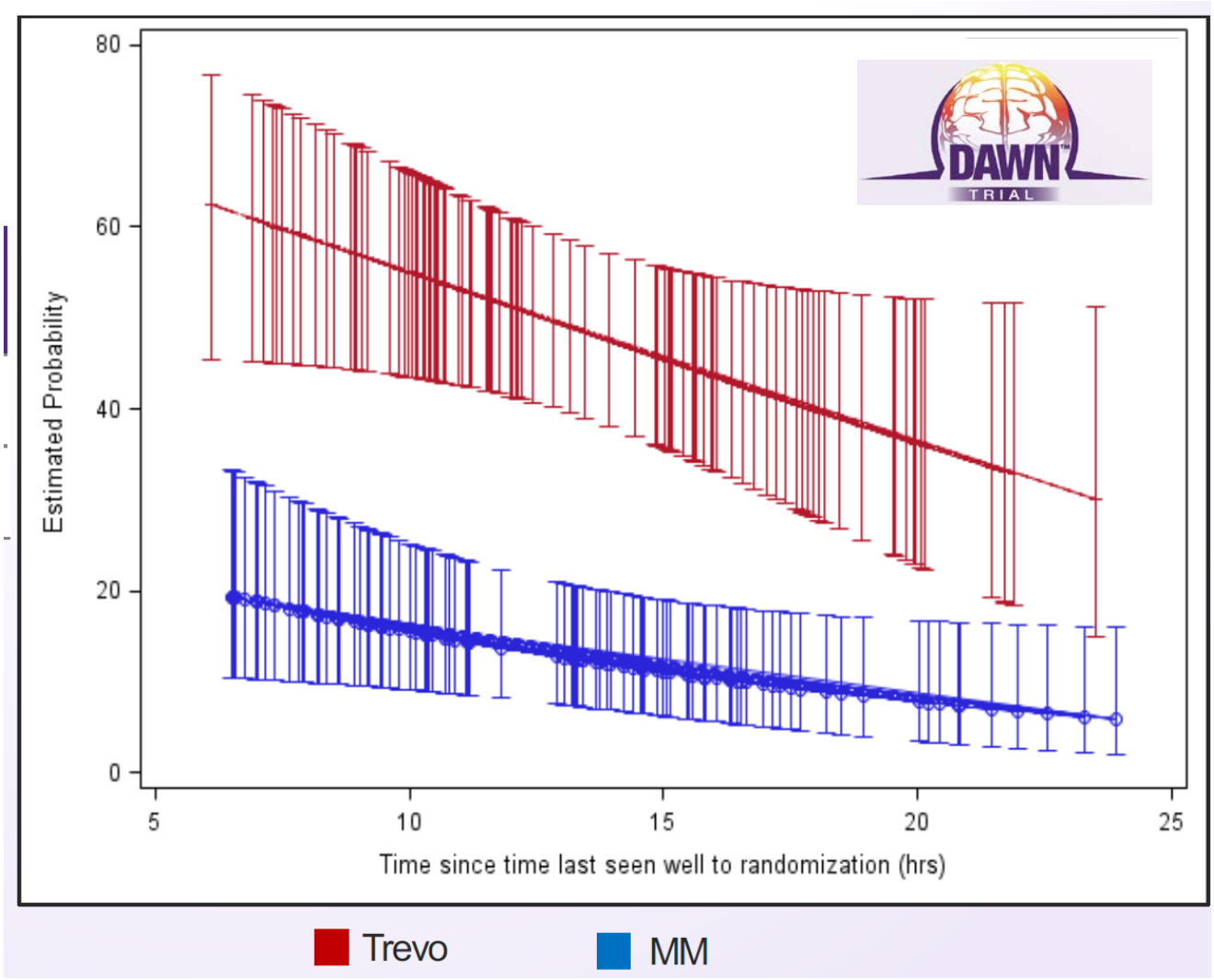


DAWN's "12th Hour" Sub-Analysis



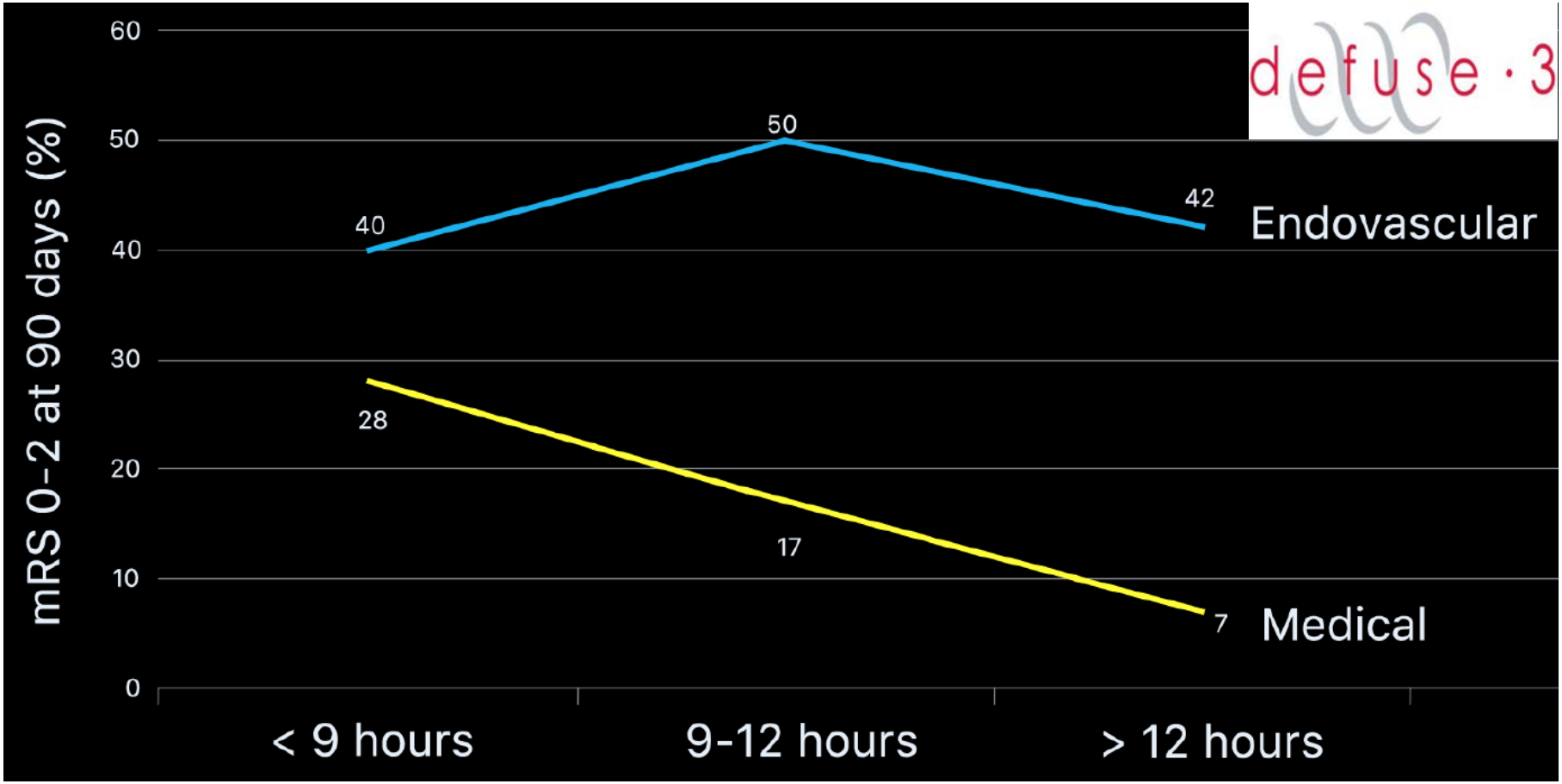
DAWN – LKW to Randomization

Probability of 90-Day mRS of 0-2



DEFUSE-3 – LKW to Randomization

Percentage of 90-Day mRS of 0-2



The Bad Outcomes

FACTORS	DAWN '17		DEFUSE-3 '18	
	EVT:	Control:	EVT:	Control:
sICH (%):	6%	3%	7%	4%
Neuro Deterioration:	14%	26%	9%	12%
Death by Stroke @ 90d:	16%	18%		
Any Death @ 90d:	19%	18%	14%	26%
Procedure Complication:	7%	0%	(>3%)	(0%)

Conclusions

- Thrombectomy with Trevo in DAWN-eligible patients is associated with improvement in clinical outcomes across the entire range of utility weighted mRS and with higher rates of functional independence (mRS 0-2) compared to standard medical therapy (48.6% vs 13.1%, probability of superiority >0.999, NNT = 2.8)
- For every 100 patients treated with endovascular therapy, 49 will have a less disabled outcome as a result of treatment, including 36 who will be functionally independent
- The treatment effect size in DAWN is the highest out of any stroke trials to date and suggests that the presence of Clinical-Core Mismatch is a critical predictor of treatment effect independent of time to presentation
- Treatment effect persisted throughout 24 hours from TLKW; however, earlier treated patients do better
- Thrombectomy with the Trevo device in patients presenting beyond 6 hours of TLSW had comparable safety profile to thrombectomy performed within 6 hours

DAWN™ TRIAL

defuse·3

Conclusions

- DEFUSE 3 extends late window therapy to larger population identified by CT perfusion or diffusion/perfusion mismatch
- Considerable clinical benefit across the disability spectrum
- Immediate impact on treatment guidelines
- Substantial effect on stroke imaging, triage and treatment
- New perspective on “time is brain”

Extended Window LVO Guidelines

2.2. Brain Imaging (Continued)	COR	LOE	New, Revised, or Unchanged
12. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation, obtaining CTP, DW-MRI, or MRI perfusion is recommended to aid in patient selection for mechanical thrombectomy, but only when imaging and other eligibility criteria from RCTs showing benefit are being strictly applied in selecting patients for mechanical thrombectomy.	I	A	New recommendation.
The DAWN trial (Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo) used clinical imaging mismatch (a combination of NIHSS and imaging findings on CTP or DW-MRI) as an eligibility criterion to select patients with large anterior circulation vessel occlusion for mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in functional 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] The DEFUSE 3 trial (Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution) 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.

Extended Window LVO Guidelines

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.

Tying it All Together

WATCHING THE CLOCK

By AMERICAN HEART ASSOCIATION NEWS

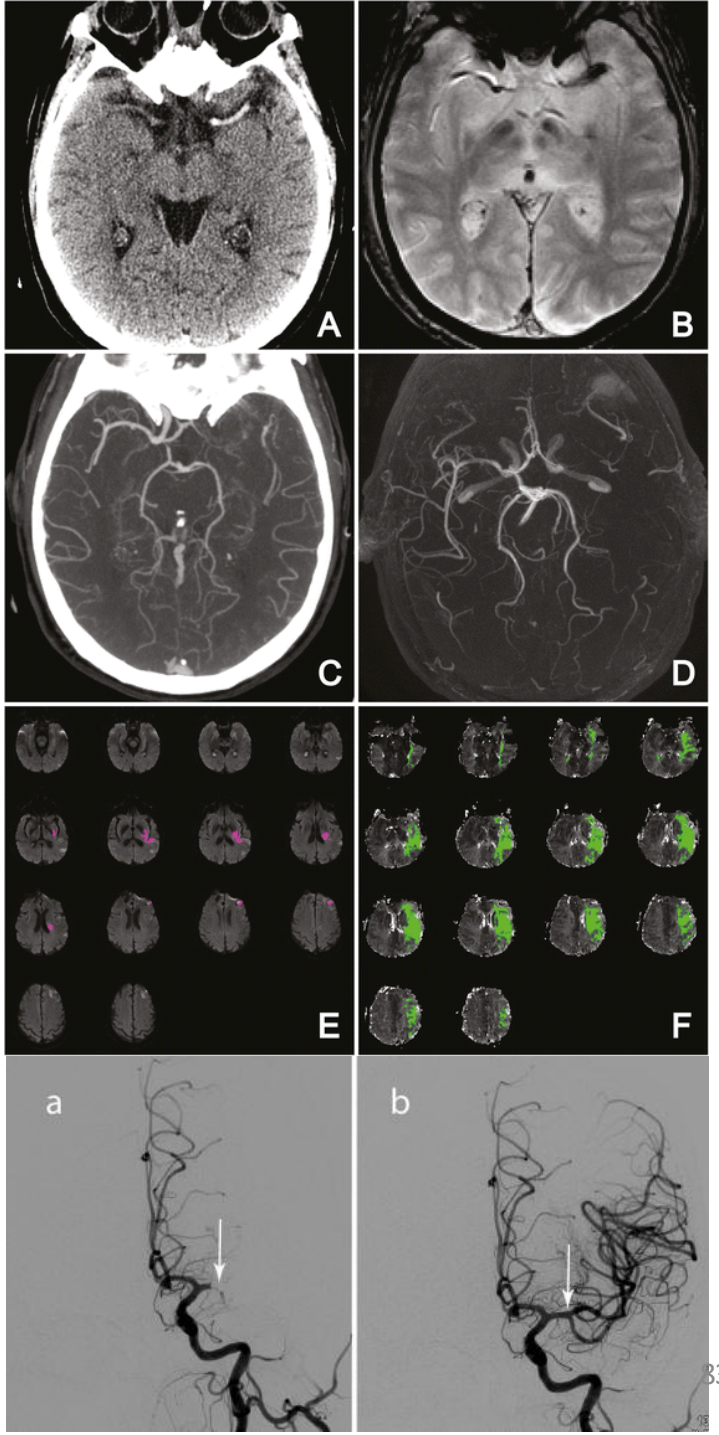
Under new treatment guidelines, people having mild strokes can now be considered for a medication given within several hours to help dissolve a clot. Clot-snaring devices can also now be used up to 24 hours after the start of a stroke in some patients with clots blocking a large vessel in the brain.

0 MINUTES
Onset of stroke symptoms

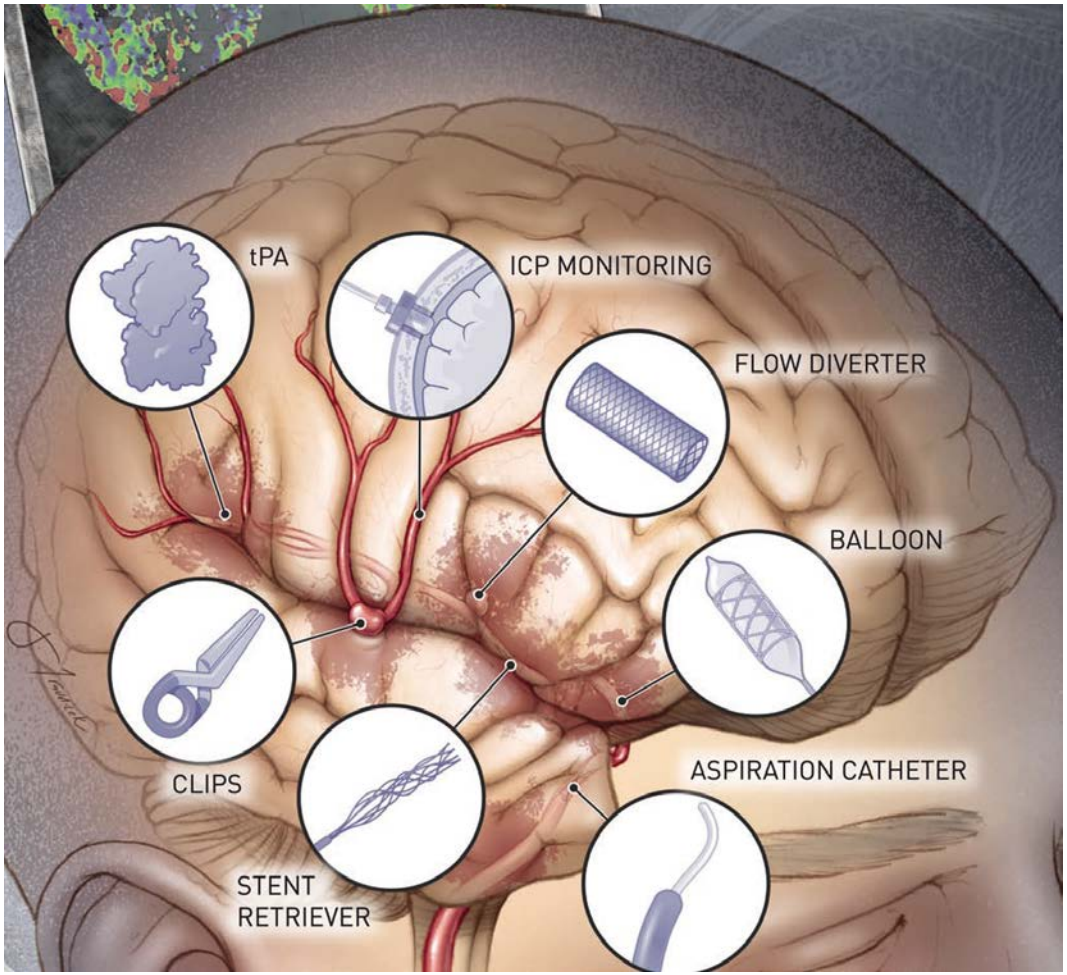
WITHIN 3-4½ HOURS
Clot-dissolving drug alteplase for mild and severe strokes

WITHIN 6-24 HOURS
Mechanical thrombectomy with stent retrievers for large-vessel clots

Source: American Heart Association/American Stroke Association
Published: Jan. 24, 2018

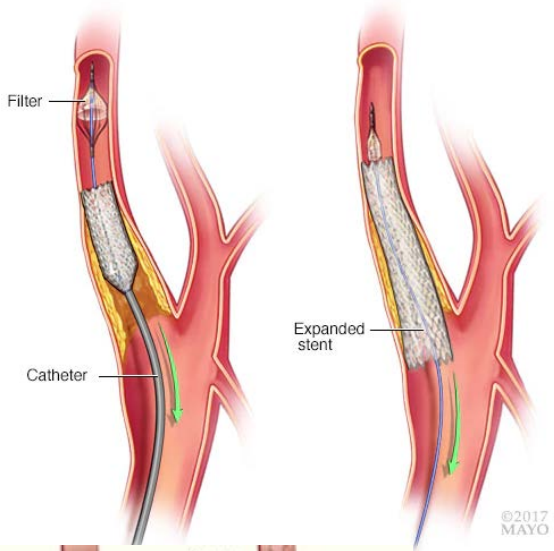


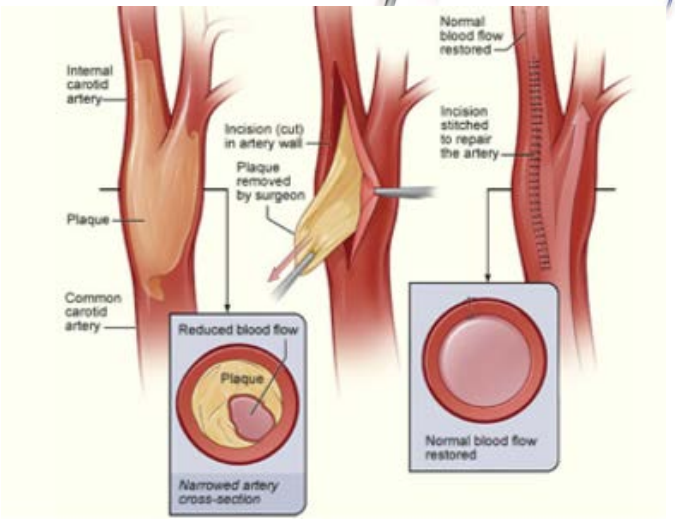
Management of Other Neurovascular Disorders



Carotid Revascularization

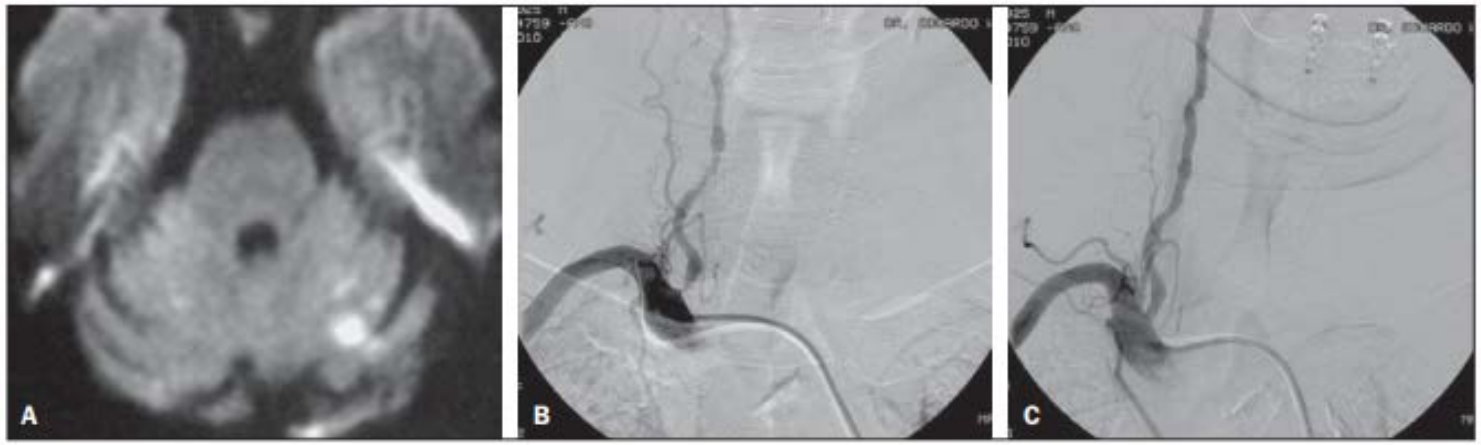
- Carotid atherosclerosis contributes to LVO stroke risk
- Carotid artery stenting (CAS), Carotid Endarterectomy (CEA)
  - Goal to reduce future risk of stroke





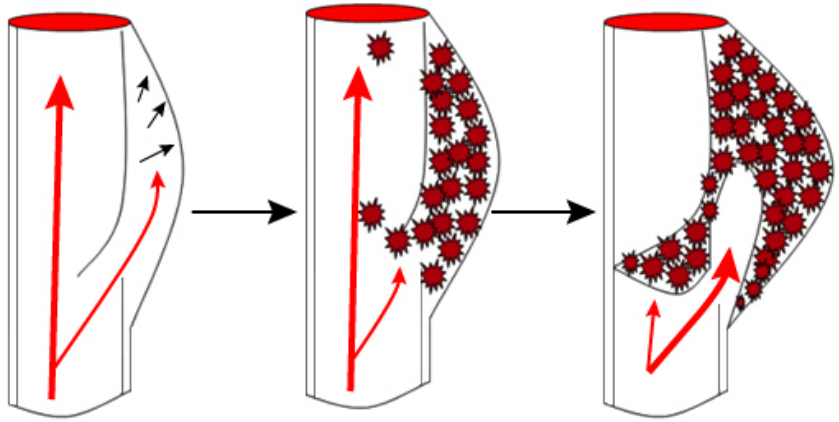
Vertebral Artery Stenosis

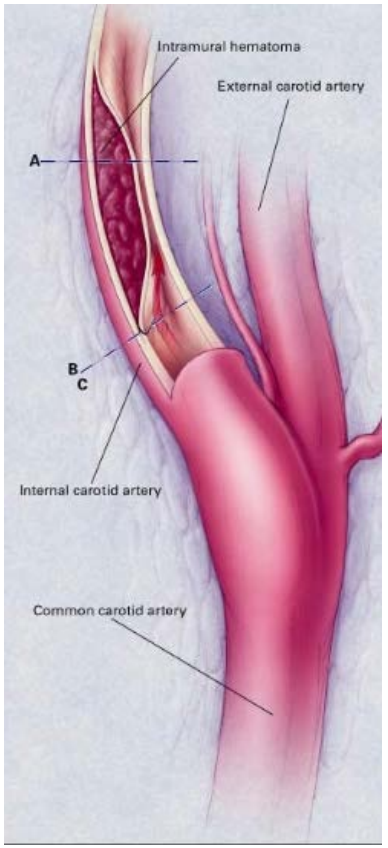
- VA stenosis contributes to heightened risk of posterior circulation stroke
- Angioplasty & stenting can be performed in select cases to increase perfusion



Carotid Artery Dissection

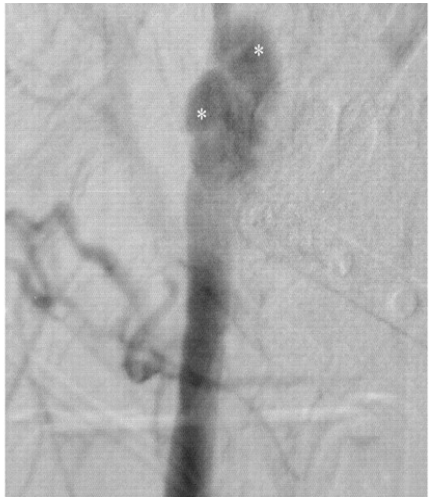
- Tear in inner lining of carotid artery leads to risk of:
  - Embolic stroke
  - Dissecting aneurysm
  - Hemorrhagic stroke

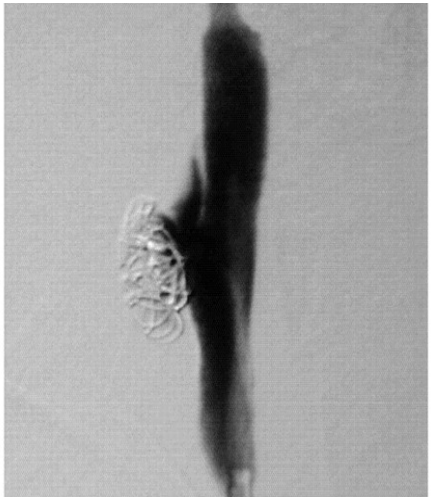


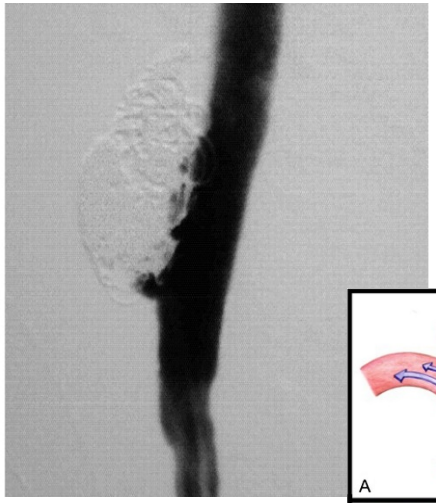


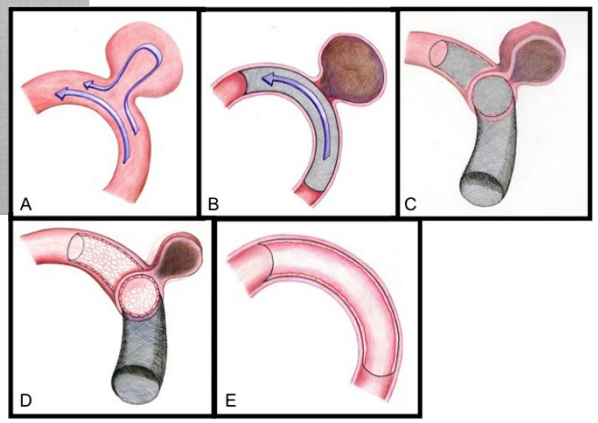
Carotid Artery Dissection Endovascular Treatment

- If patient develops pseudoaneurysm, this can be clipped, coiled, or treated with endovascular flow diversion.



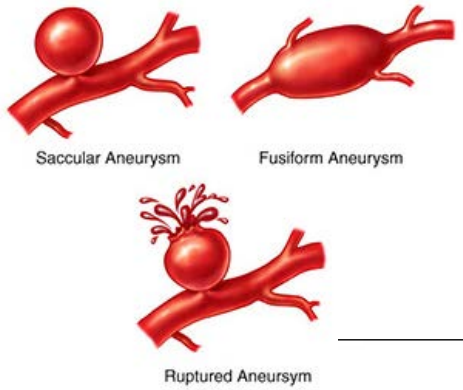


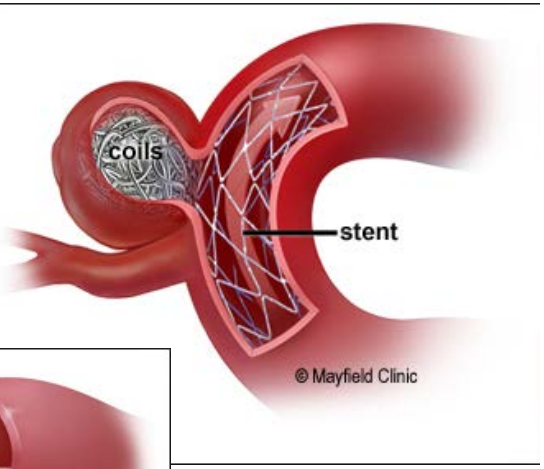


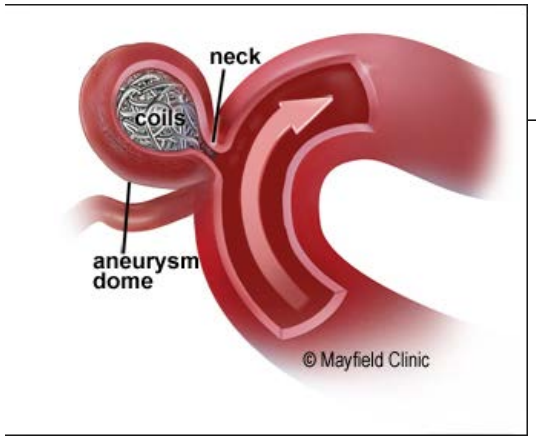


Intracranial Aneurysm Treatment

- Elective
  - Risk of rupture vs. risk of treatment
- aSAH
  - Ruptured aneurysm to be treated within 24 hours of bleeding event



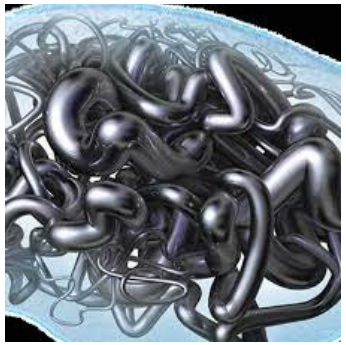




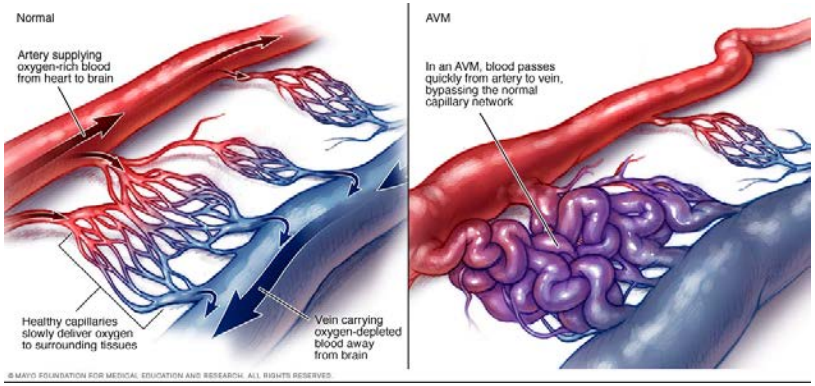
Intractable Epistaxis

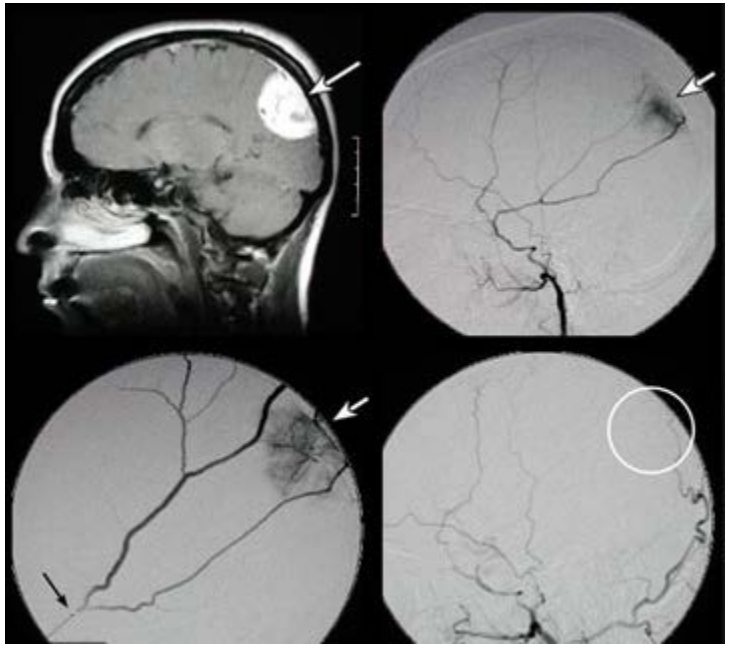
- Refractory epistaxis that cannot be managed by pressure, ice, cautery, ENT surgery.
- Usually originates from distal branches of the internal maxillary artery (IMAX)
- Internal maxillary artery embolization
  - Particle injection into the IMAX to reduce blood flow, control bleeding.

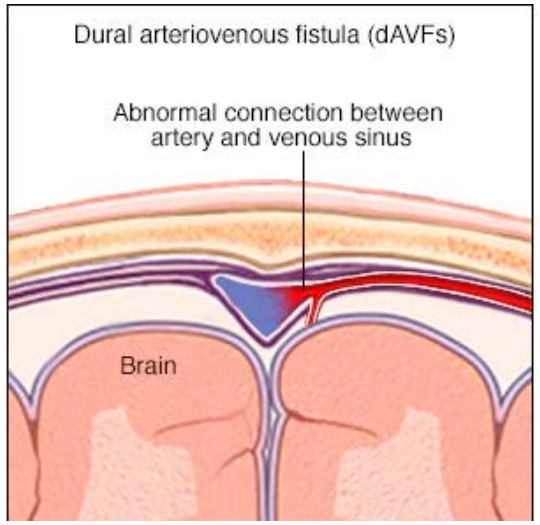
Reducing Bleed Risk: Embolization



- Arteriovenous malformation
- Dural AV fistula
- Tumor, meningioma



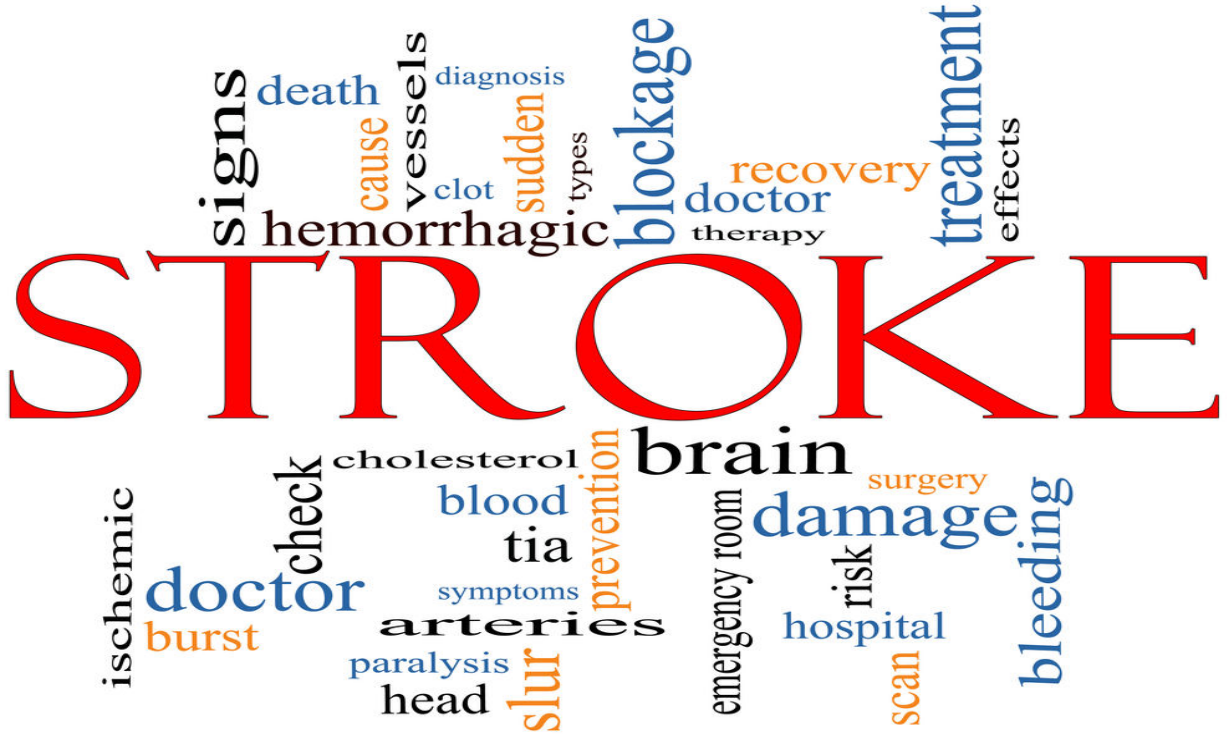




Wada Test

- Pre-epilepsy surgery evaluation to determine eloquence of targeted tissue for planned surgical excision.

THE END!



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- *The NEJM*
- *The 2018 ISC*
- *ASPECTS*
- *Meta-analysis of major 2015 EVT trials*
- *The DAWN Trial*
- *The DEFUSE-3 Trial*
- *The VAN Study*