Acute Ischemic Stroke Care: Updates for 2019

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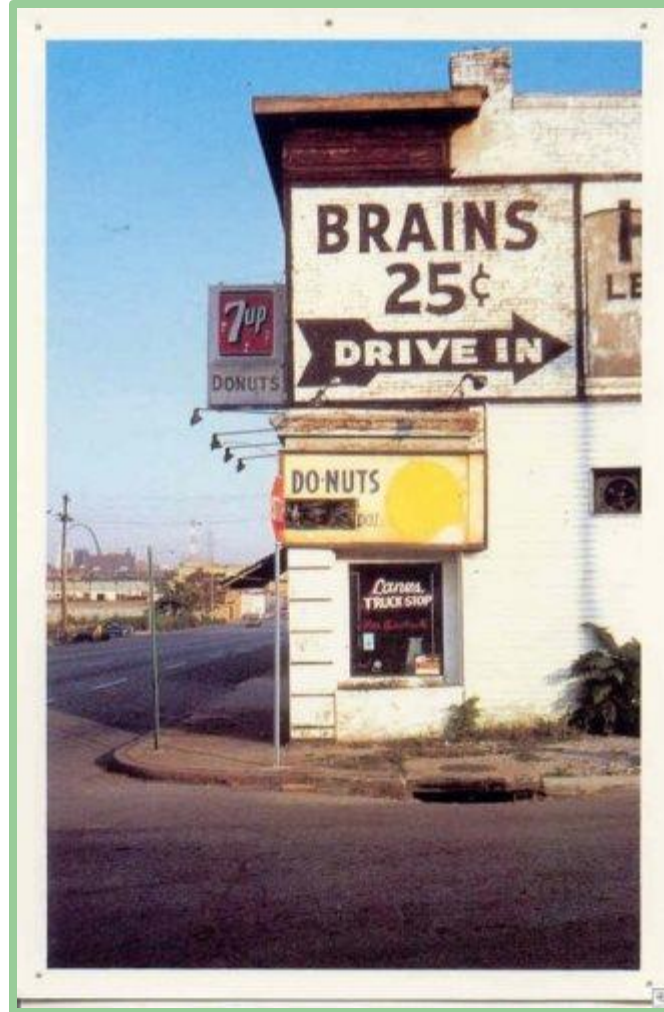
Neurocritical Care and Vascular Neurology

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
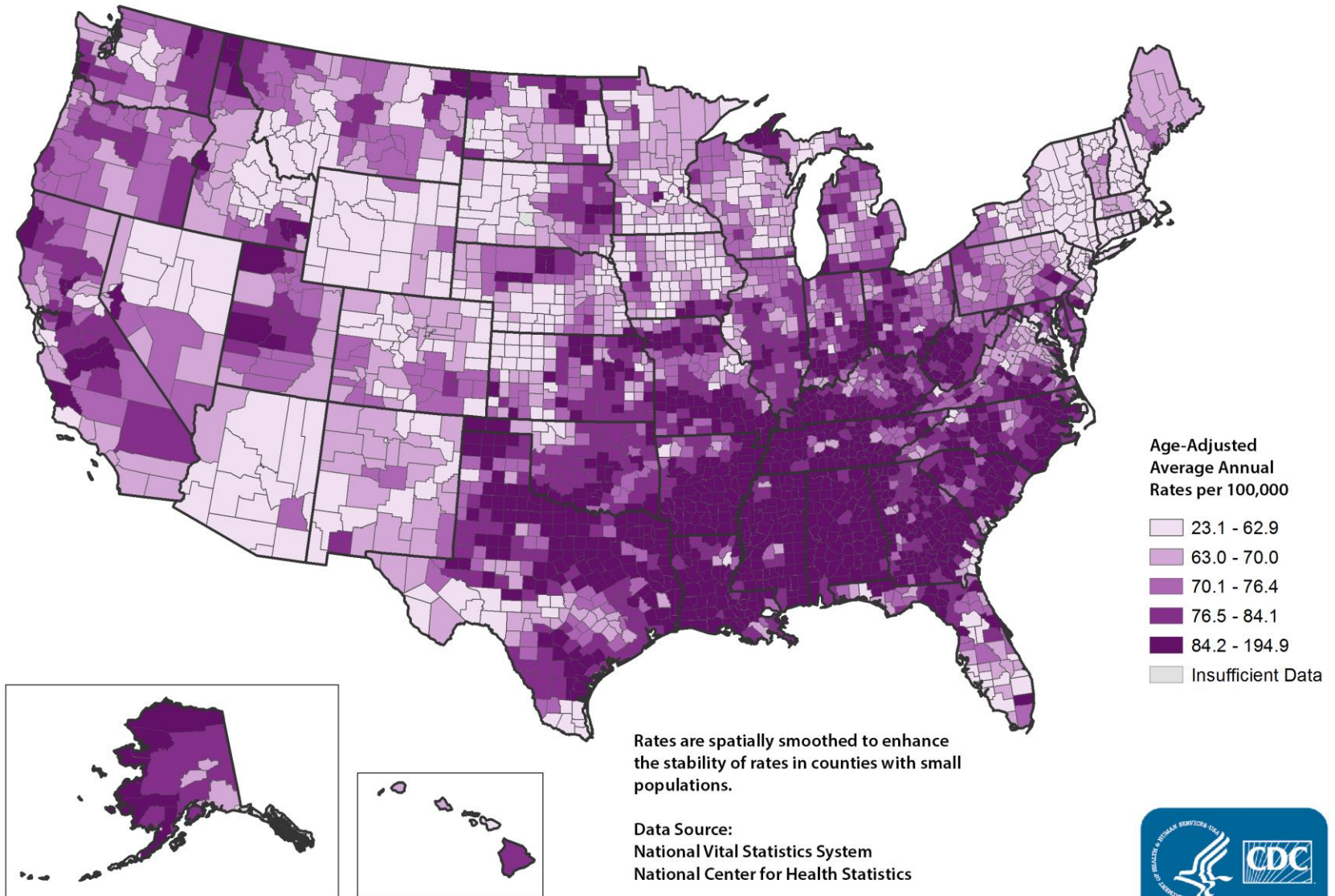
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Disclosures

- None

Stroke Epidemiology

- Roughly 800,000 strokes every year in the US
  - About one every 40 seconds
- ~$38.6 billion per year, direct and indirect costs
- Fifth most common cause of death in the US
  - Behind heart disease, cancer, trauma and lower respiratory disease
- Leading cause of long term disability in adults
  - Over 4 million stroke survivors in the US

Berry, Jarett D., et al. Heart Disease and Stroke Statistics--2013 Update:
A Report from the American Heart Association. Circulation. 127, 2013.

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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
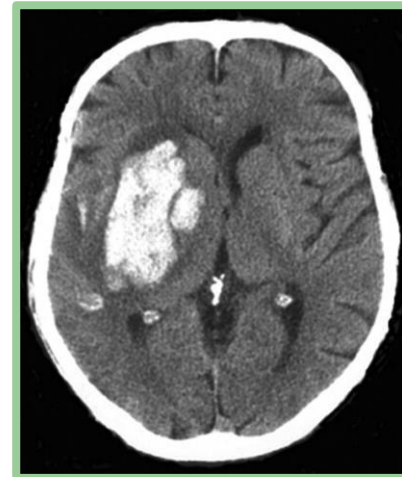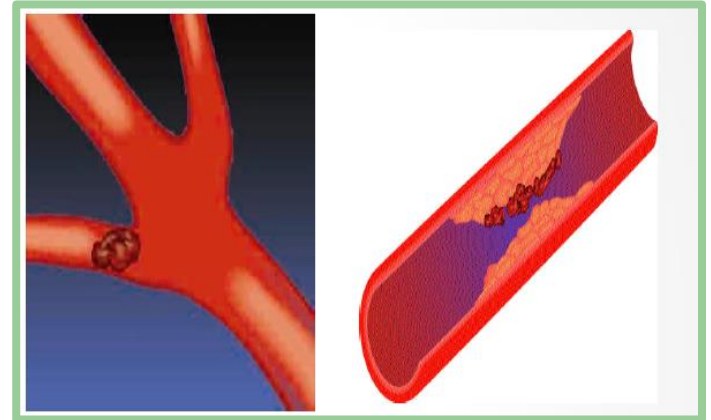National Center for Health Statistics

Types of Stroke

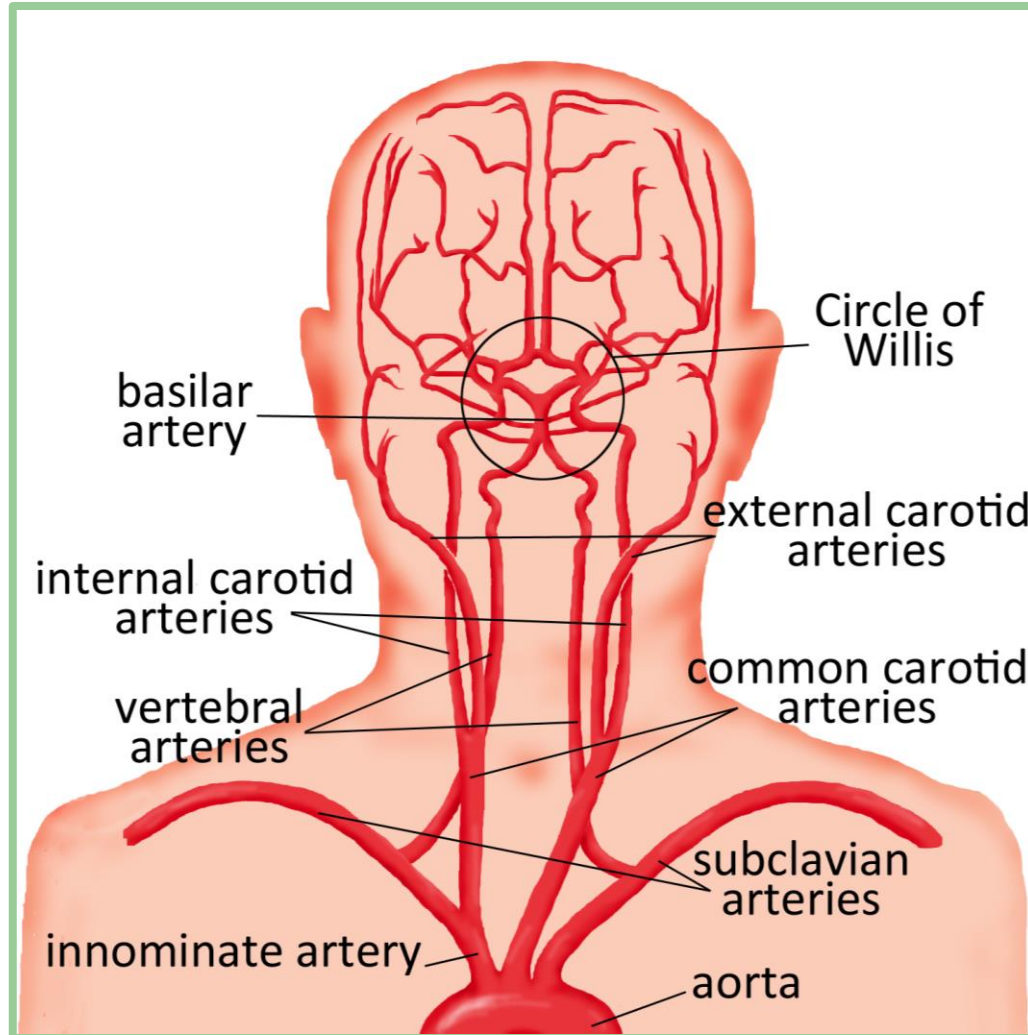Ischemic → lack of blood flow

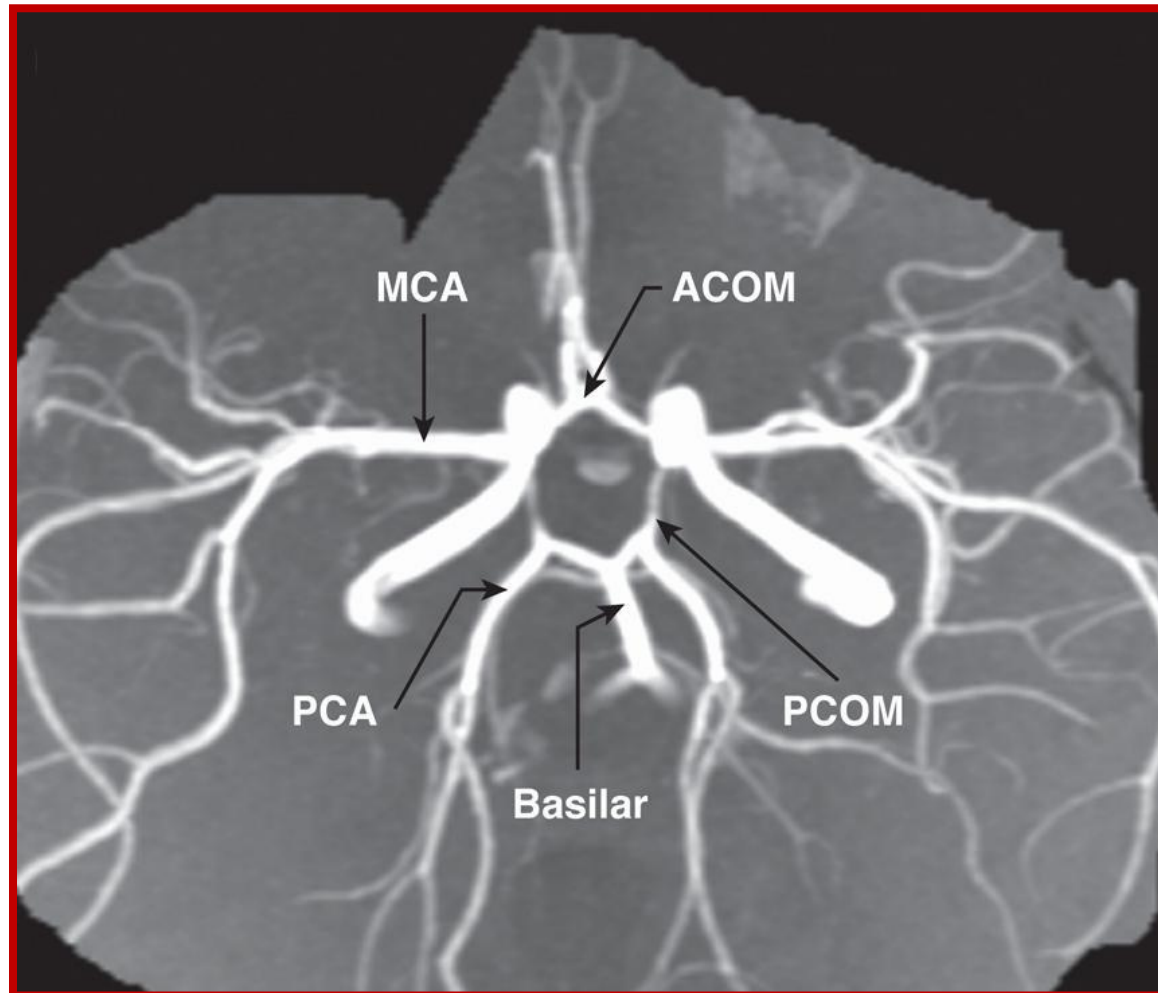- 87% of all strokes

Hemorrhagic → ruptured vessel
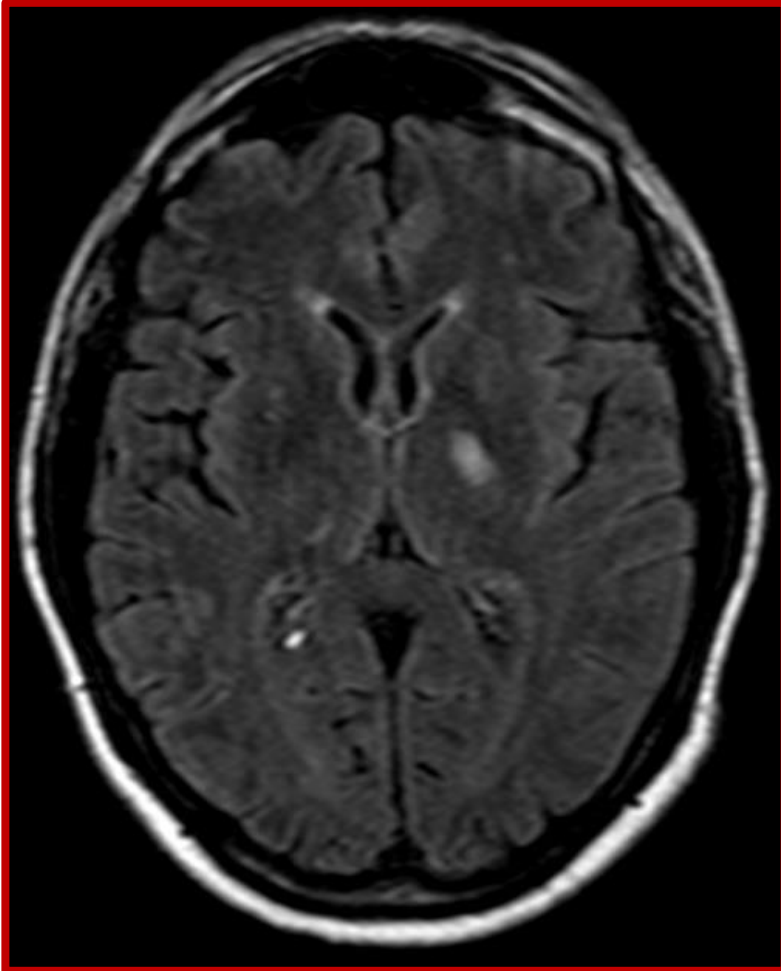
- 13% of all strokes

Neurovascular Anatomy

Neurovascular Anatomy

Cerebrovascular Syndromes
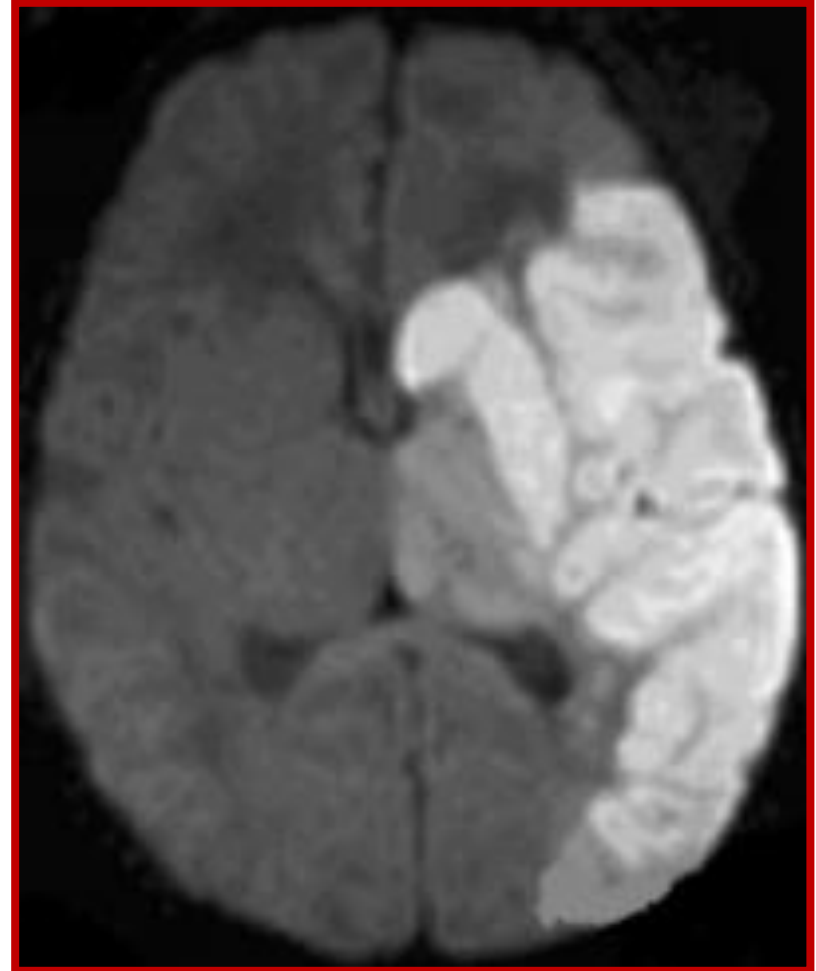

Small Vessel Stroke (Lacune)

Large Vessel Stroke: L MCA Occlusion

CBF thresholds for preservation of function and structure
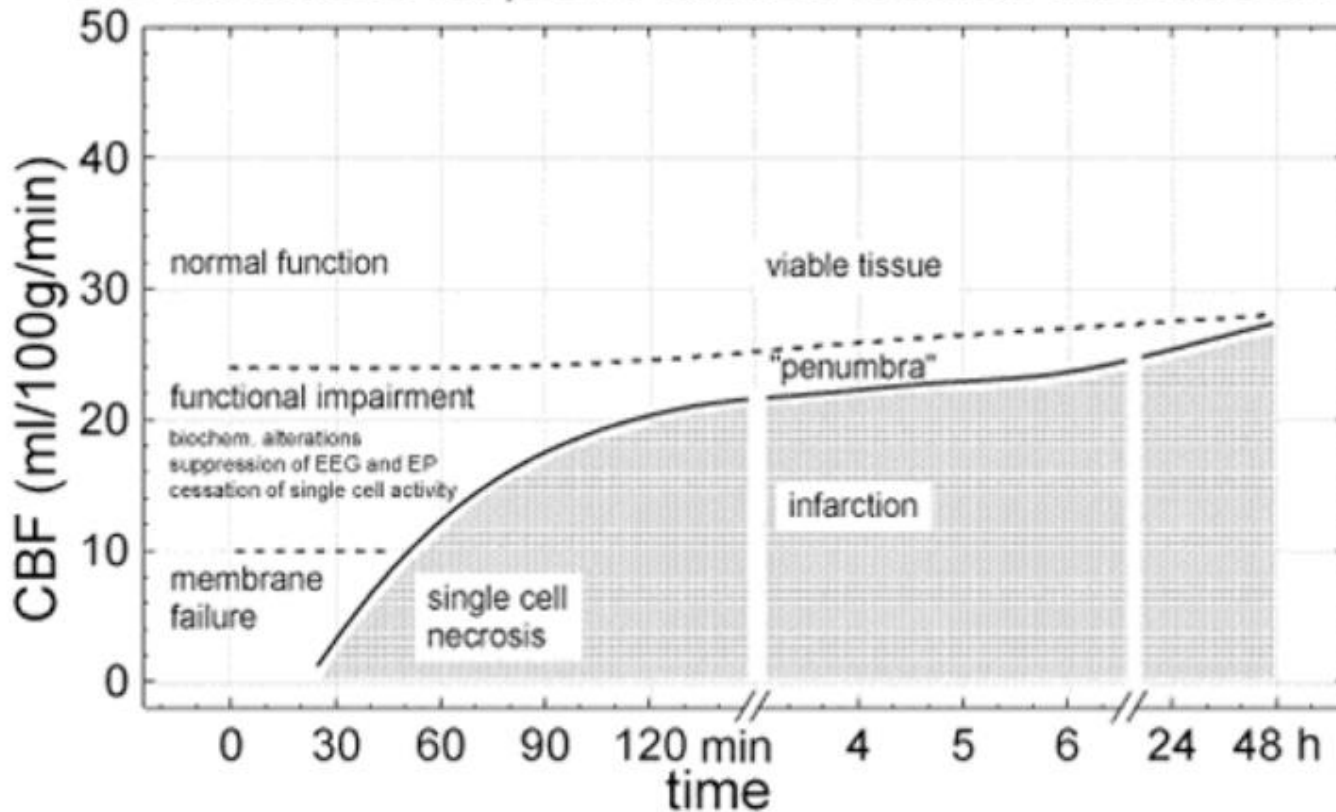
*The size of the infarct depends upon both the **degree** and the **duration** of ischemia.*
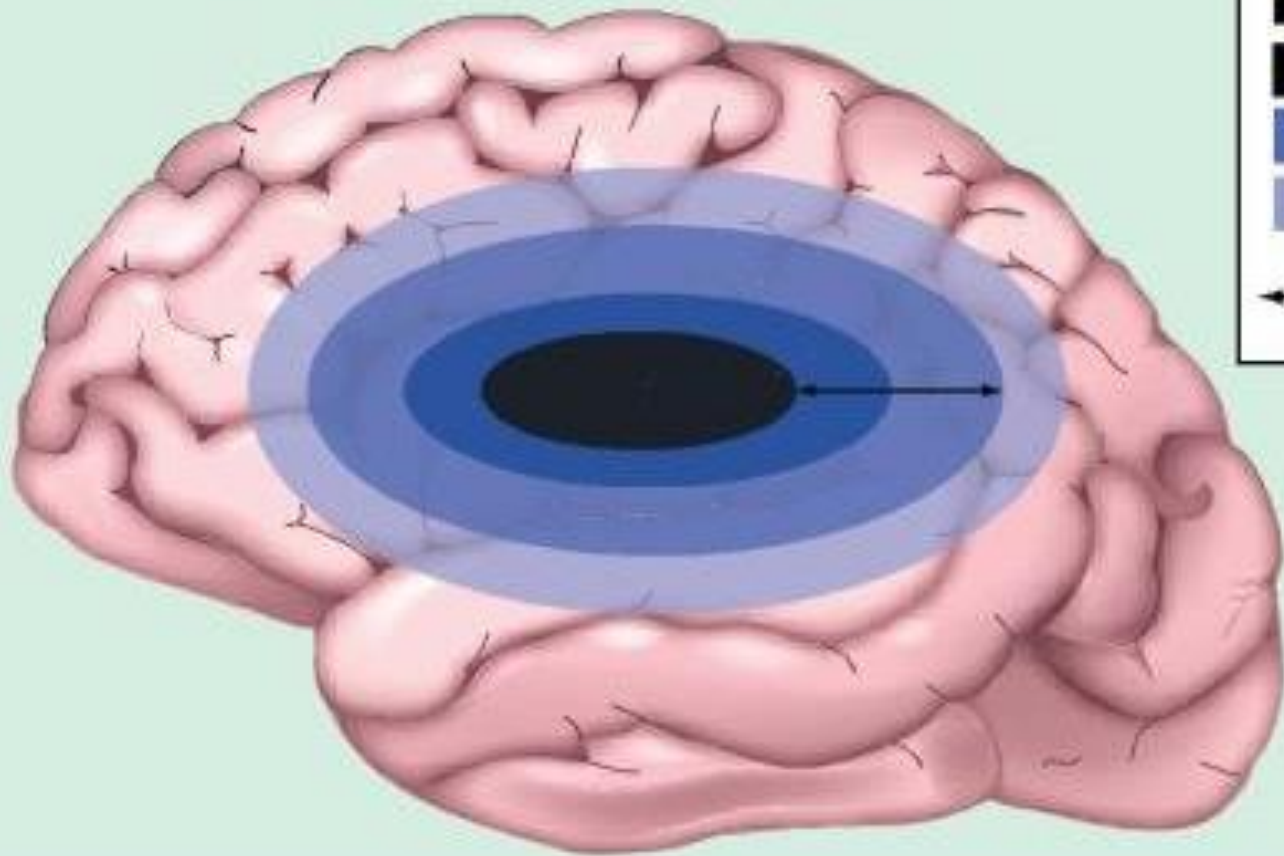
Core
Diffusion abnormality
Perfusion abnormality
Benign oligoemia
Potentially salvagable tissue

Source: Expert Rev Neurother © 2009 Expert Reviews Ltd

https://www.medscape.com/viewarticle/707722_4
Expert Rev Neurother. 2009;9(6):885-895.

Left and Right Hemisphere Stroke: Common Patterns

Dominant (Usually LEFT)	Non-Dominant (Usually RIGHT)
• Aphasia	• Neglect of left visual field
• Right hemiparesis	• Extinction of left-sided stimuli
• Right-sided sensory loss	• Left hemiparesis
• Right visual field defect	• Left-sided sensory loss
• Poor right conjugate gaze	• Left visual field defect
• Dysarthria	• Poor left conjugate gaze
• Difficulty reading, writing, or calculating	• Dysarthria
	• Spatial disorientation

Adams HP et al. Circulation. 1994; 90:1588-1601

Brainstem Strokes

- Unexplained coma/loss of consciousness (Basilar artery thrombosis/occlusion)

- Motor or sensory loss in all four limbs

- Crossed signs

- Limb or gait ataxia

- Dysarthria

- Dysconjugate gaze

- Nystagmus

- Bilateral visual field defects

Adams HP et al. Circulation. 1994; 90:1588-1601

Common Stroke Mimics

Stroke Mimics
Seizure and post-seizure paralysis (Todd's paralysis)
Hypoglycemia
Migraine
Hypertensive Encephalopathy
Brain Tumors
Alcohol Intoxication
Drug overdose/Toxicity
Metabolic Disorders
Neuropathies (Bell's Palsy)
Cerebral Infections

Summers, D., Leonard, A., Wentworth, D., Saver, J. L., Simpson, J., Spilker, J. A., et al. Comprehensive Overview of Nursing and Interdisciplinary Care of the Acute Ischemic Stroke Patient. American Heart Association,2911-2944, 2009

Treatment of (Hyper)Acute Stroke

WITH A STROKE, TIME LOST IS BRAIN LOST.
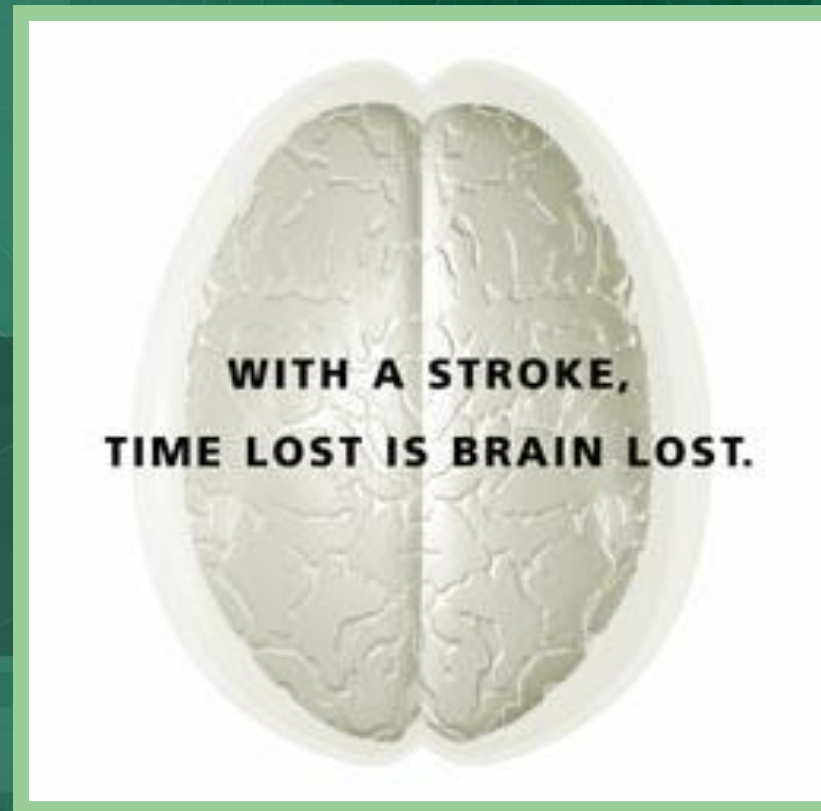
Stroke Care

- ***Stroke Chain of Survival*** links actions to be taken by patients, family members, and healthcare providers to maximize stroke recovery.

Emergency Dispatch

- Use of 911 system is recommended for symptoms of stroke

- Many callers do not use the word "stroke"

- Dispatchers should recognize the seriousness of stroke and be familiar with stroke symptoms

- Strokes should be dispatched as a high priority call, send closest unit- similar to acute MI or trauma

- An EMD call-receiving algorithm is recommended to ask appropriate questions to callers

https://www.acls.net/acls-suspected-stroke-algorithm.htm
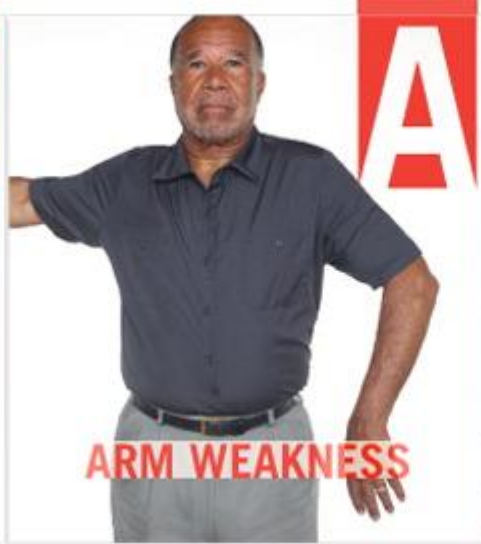
F FACE DROOPING
A ARM WEAKNESS
S SPEECH DIFFICULTY
T TIME TO CALL 911

Pre-hospital Stroke Assessment

- Stroke assessment tools help EMS identify a stroke quickly
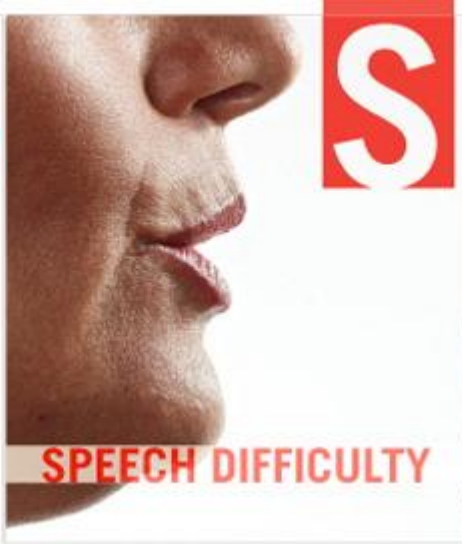
- Pre-hospital stroke assessment training raises accuracy of stroke identification

- Paramedics demonstrated a sensitivity of 61-66% without training and **86-97%** with training

EMS Stroke Identification*

% of Stroke Identification Sensitivity

■ No Training in Use of Stroke Assessment Tool

■ Training in Use of Stroke Assessment Tool

Stroke Assessment Tool Training

Maggiore, W. A. (2012). 'Time is Brain' in Prehospital Stroke Treatment . *Journal of Emergency Medical Services* , 1- 9.
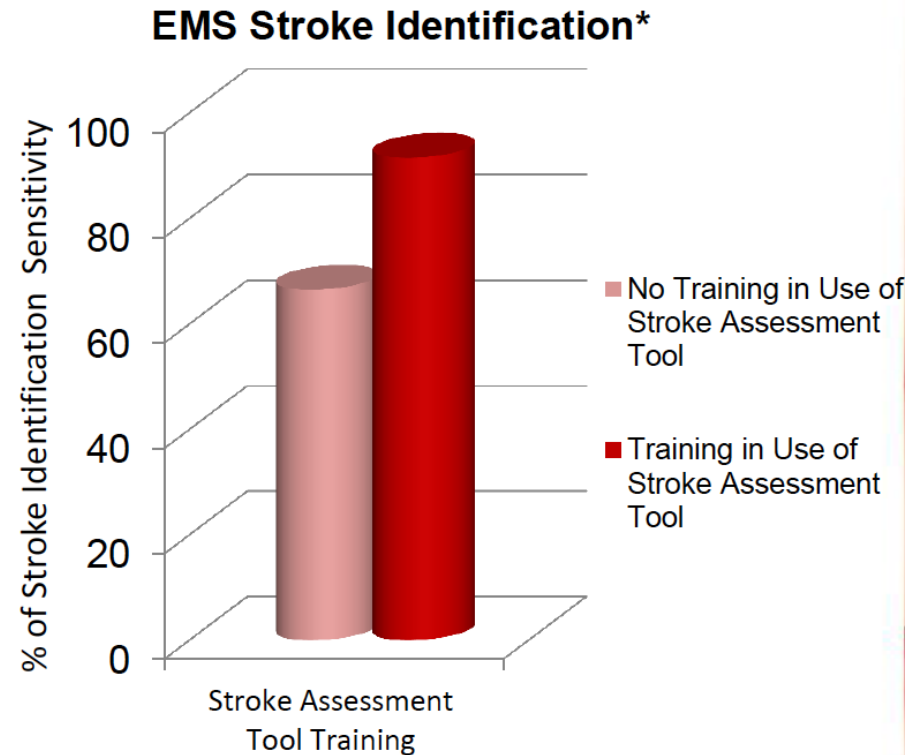
Pre-hospital Stroke Assessment

Cincinnati Prehospital Stroke Scale

Facial Droop

Normal: Left and Right side of face move equally
Abnormal: One side of face does not move at all

Arm Drift

Normal: Both left and right arm move together or not at all
Abnormal: One arm does not move equally with the other

Speech

Normal: Patient uses correct words with no slurring
Abnormal: Patient has slurred speech, uses inappropriate words or cannot speak

Kothari RU, Pancioli A, Liu T., Brott T., Broderick J. "Cincinnati Prehospital Stroke Scale: reproducibility and validity." *Ann Emerg Med.* 1999 Apr;33(4):373-8.
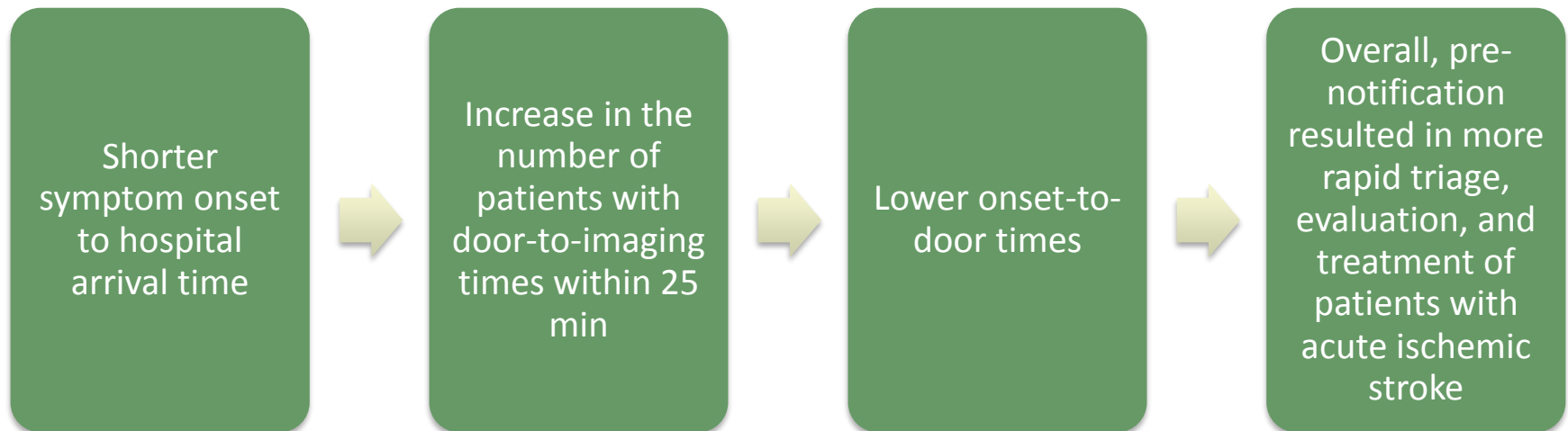
Prehospital Stroke Care

- Minimize scene time (≤ 15 minutes)

- Establish **Last Known Normal** time

- Bring a **knowledgeable friend or family member** with the stroke patient

Pre-notification

EMS professionals can notify hospital staff that a stroke patient is being sent to the hospital prior to them arriving at the hospital

The sooner the patient gets to medical treatment, the greater potential for a better outcome

| Shorter symptom onset to hospital arrival time | → | Increase in the number of patients with door-to-imaging times within 25 min | → | Lower onset-to-door times | → | Overall, pre-notification resulted in more rapid triage, evaluation, and treatment of patients with acute ischemic stroke |

Lin, C. B., Peterson, et al. (2012). Emergency Medical Service Hospital Pre-Notification is Associated with Improved Evaluation and Treatment of Acute Ischemic Stroke. *Journal of the American Heart Association* , 1-9.

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Ongoing Assessment en route

- <u>History from family member</u> (SAMPLE)

  S-Symptoms/ onset (When was the person last seen normal?)

  A-Allergies

  M-Medications-*anticoagulants* (<u>warfarin</u>), antithrombotics, insulin, antihypertensives, antiepileptics

  P-Past Medical History-Hypertension, Diabetes (hypoglycemic patients may have symptoms that mimic stroke), seizures, prior stroke, aneurysms

  L-Last oral intake

  E-Events Prior-stroke, MI, trauma, surgery, bleeding

Management en route

Not recommended

- Dextrose-containing fluids in nonhypoglycemic patients

- Blood pressure reduction (can cause hypotension, decrease cerebral perfusion and worsen stroke) unless >220/120

Emergency Medical Stroke Assessment (EMSA)

	Score if Abnormal
E: Eye Movement	
Horizontal Gaze Ask patient to keep their head still and follow your finger left to right with their eyes Abnormal: Patient is unable to follow as well in one direction compared to the other	1 Point
M: Motor – Face, Arm, or Leg Weakness	
Facial Weakness Ask patient to show their teeth or smile Abnormal: One side of the face does not move as well as the other	1 Point
Arm Weakness Ask patient to hold out both arms, palms up, for 10 seconds with eyes closed Abnormal: One arm does not move or drifts down compared to the other	1 Point
Leg Weakness Ask patient to lift up one leg and then the other for 5 seconds Abnormal: One leg does not move or drifts down compared to the other	1 Point
SA: Slurred Speech or Aphasia	
Naming Ask patient to name your watch and pen Abnormal: Patient slurs words, says the wrong words, or is unable to speak **Repetition** Ask patient to repeat "They heard him speak on the radio last night" after you Abnormal: Patient slurs words, says the wrong words, or is unable to speak	2 Points

Hospital Treatment

Acute Stroke: Initial Evaluation

- CT of the brain without contrast

- Electrocardiogram

- Chest x-ray

- Hematologic studies (complete blood count, platelet count, prothrombin time, partial thromboplastin time)

  - **Platelet Count and Coagulation profile are not necessary prior to tPA** if patient is not taking Oral anticoagulants and has no suspected bleeding disorder.

- Serum electrolytes

- Blood glucose

- Renal and hepatic chemical analyses

- National Institutes of Health Scale (NIHSS) score

Stroke specific interventions

Depend on Last known normal time

- IV Thrombolytic Agents

Depend on advanced imaging (CTA/CTP or MRA/MRP)

- Intra-arterial approaches (neurointerventional clot retrieval)

IV tPA (alteplase)

Last known normal time ≤ 4.5 hours

No hemorrhage on CT

Disabling neurological deficit

No contraindications to tPA

IV alteplase (tPA)
- FDA approved for ≤ 3 hours of onset of symptoms
- AHA/ASA approved for use between 3-4.5 h with additional exclusion criteria

Exclusion criteria

Significant head trauma or prior stroke in previous 3 months

Symptoms suggest subarachnoid hemorrhage

Arterial puncture at non-compressible site in previous 7 days

History of previous intracranial hemorrhage

Intracranial neoplasm, arteriovenous malformation, or aneurysm

Recent intracranial or intraspinal surgery

Elevated blood pressure (systolic >185 mm Hg or diastolic >110 mm Hg)

Active internal bleeding

Acute bleeding diathesis, including but not limited to

    Platelet count <100 000/mm3

    Heparin received within 48 hours, resulting in abnormally elevated aPTT

    greater than the upper limit of normal

    Current use of anticoagulant with INR >1.7 or PT >15 seconds

    Current use of direct thrombin inhibitors or direct factor Xa inhibitors with

    elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and

    ECT; TT; or appropriate factor Xa activity assays)

Blood glucose concentration <50 mg/dL (2.7 mmol/L)

CT demonstrates multilobar infarction (hypodensity >1/3 cerebral hemisphere)

Relative *exclusion* criteria

- Careful consideration and weighing of risk to benefit
- Patients may receive TPA despite 1 or more relative contraindications
- Consider risk to benefit of IV tPA administration carefully if any of these relative contraindications are present:

  - Only minor or rapidly improving stroke symptoms (clearing spontaneously)
  - Pregnancy
  - Seizure at onset with postictal residual neurological impairments
  - Major surgery or serious trauma within previous 14 days
  - Recent gastrointestinal or urinary tract hemorrhage (within previous 21 days)
  - Recent acute myocardial infarction (within previous 3 months)

Beyond rt-PA

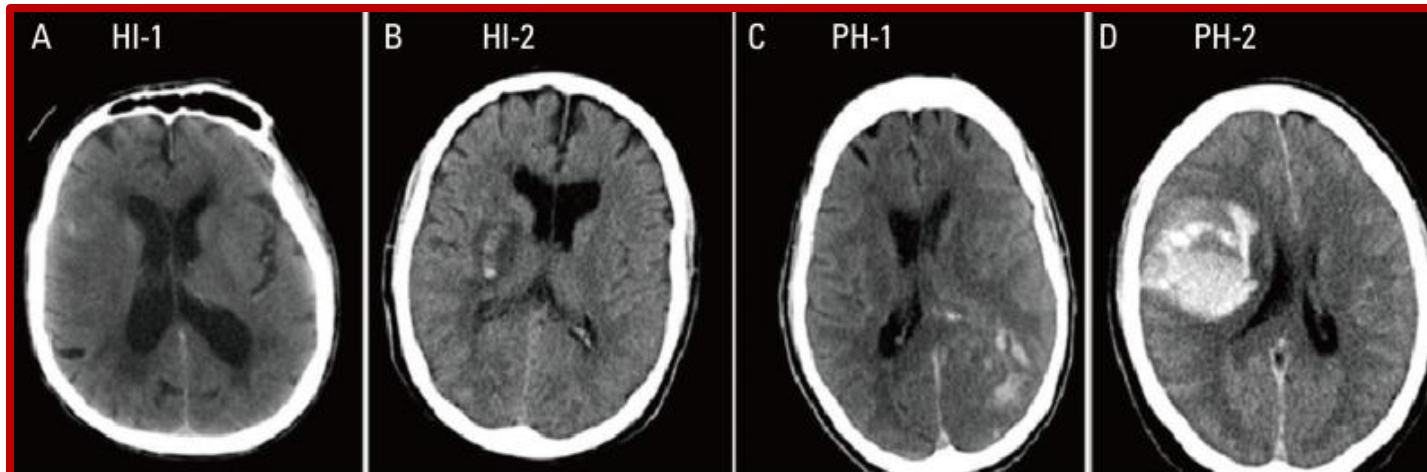TPA for Cerebral Ischemia within 3 Hours of Onset-Changes in Outcome Due to Treatment
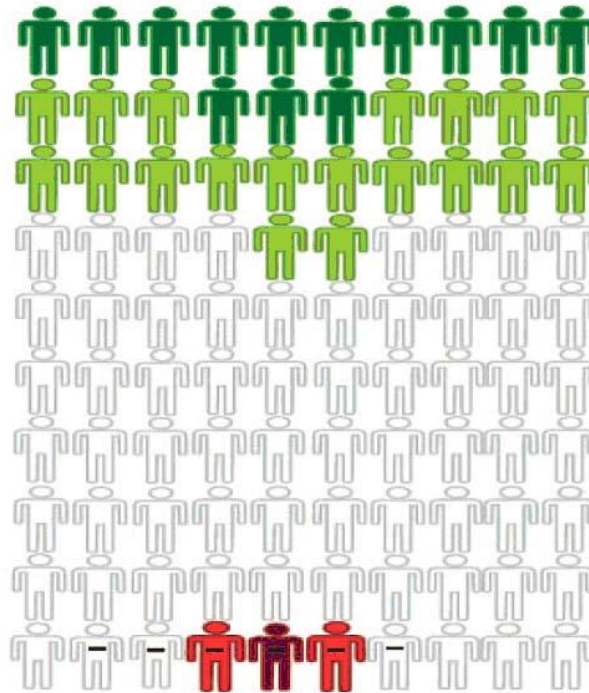
Changes in final outcome as a result of treatment:

- Normal or nearly normal
- Better
- No major change
- Worse
- Severely disabled or dead

Early course:
- No early worsening with brain bleeding
- Early worsening with brain bleeding

Stroke. 2010;41:00-00.

Hemorrhage After tPA

A	Hemorrhagic infarction - 1	Isolated petechial staining of infarcted tissue without mass effect
B	Hemorrhagic infarction - 2	Onfluent patechiae in infarcted tissue without mass effect
C	Parenchymal Hemorrhage - 1	Homogeneous high attenuation lesion with minimal mass effect occupying less than 30% of the infarcted area
D	Parenchymal Hemorrhage - 2	Lesion occupying more than 30% of the infarcted area with definite mass effect. Possible extension of hemorrhage into the ventricular space, As well as any hemorrhage outside the infracted area

Does tPA kill patients?

- Despite an increase in fatal intracerebral hemorrhages at 7 days (IST-3), all-cause mortality at 90 days and 6 months is not affected.

- A recent meta-analysis of RCTs of IV tPA versus placebo showed:

  - tPA does not impact all-cause mortality at any time point: 7 days, 30 days, 90 days, and 6 months

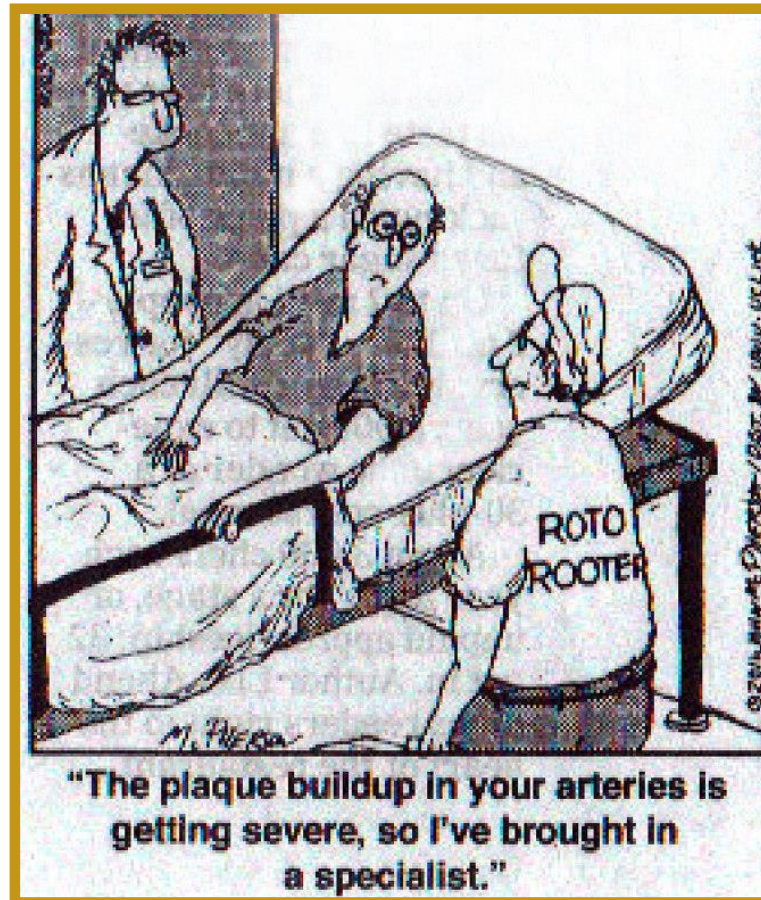Emberson et al. L**ancet**. 2014 Nov 29;384(9958):1929-35
IST-3 collaborative group. **Lancet**. 2012 Aug 25;380(9843):730.
Uhrig et al. International Stroke Conference -2015

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What about other thrombolytics?

- Tenecteplase: widely used for MI, not approved for stroke

  - Greater fibrin specificity, longer half life, less susceptible to Plasminogen Activator Inhibitor-1

- NOR-TEST: randomized open label phase 3 trial of tPA vs. TNK for AIS

  - Enrolled predominantly minor strokes (average NIHSS was 5)

  - Essentially no difference in outcome or rates of SAE

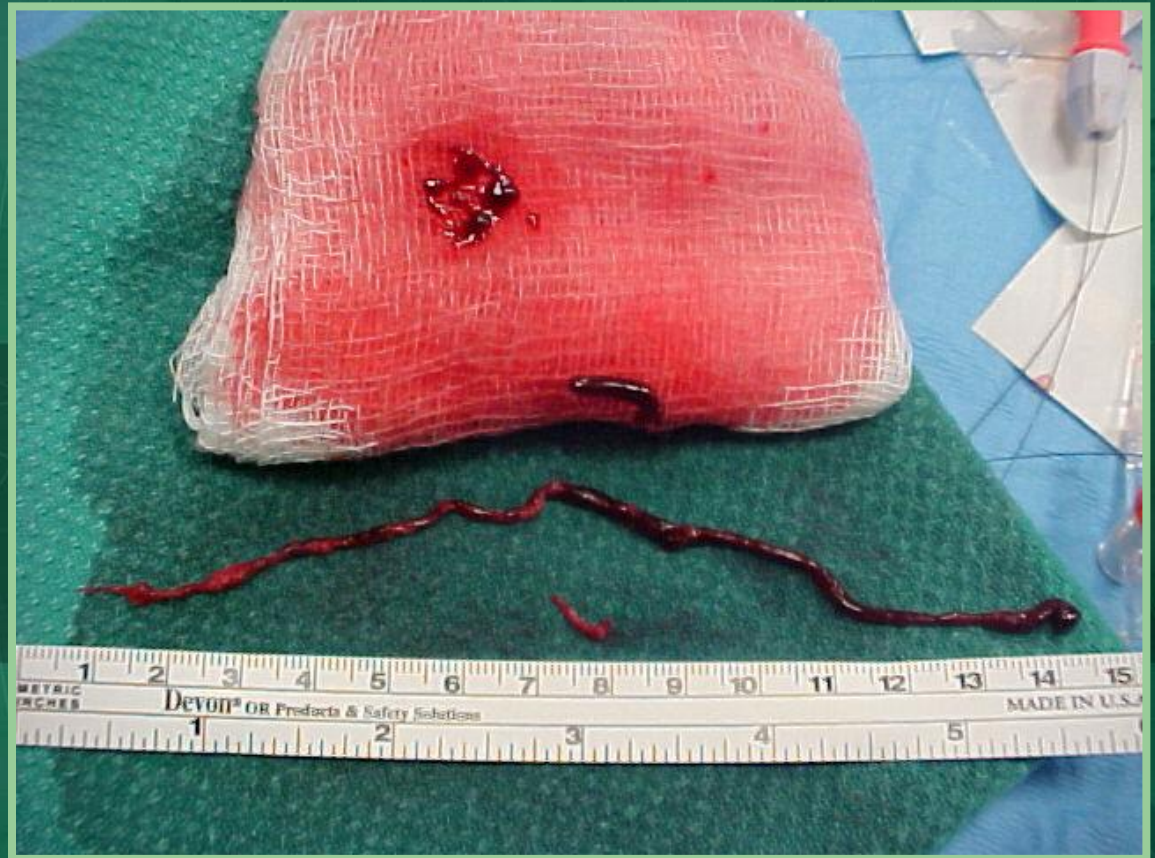- 2018 AHA Guidelines: TNK (0.4 mg/kg bolus) may be a reasonable alternative for patients with minor stroke

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What About Endovascular?

"The plaque buildup in your arteries is getting severe, so I've brought in a specialist."

# Intra-arterial Thrombolysis

Embolectomy: Stent-Retriever

Smith et al. *Stroke*, July 2005

Time-Based Reperfusion Trials

- 5 trials reported in 2014-2015→ total of 1287 patients

- Randomized patients with ICA or MCA occlusion to IAT vs usual care

  - tPA was administered if the patient was eligible (83%)

    - MR CLEAN: enrolled within 6 hours of onset

    - ESCAPE: up to 12 hours, used CT and CTA

    - SWIFT PRIME: within 4.5 hours (included only tPA recipients), varied imaging criteria

    - REVASCAT: enrolled within 8 hours of onset, used ASPECTS score

    - EXTEND IA: enrolled within 4.5 hours of onset, used perfusion imaging

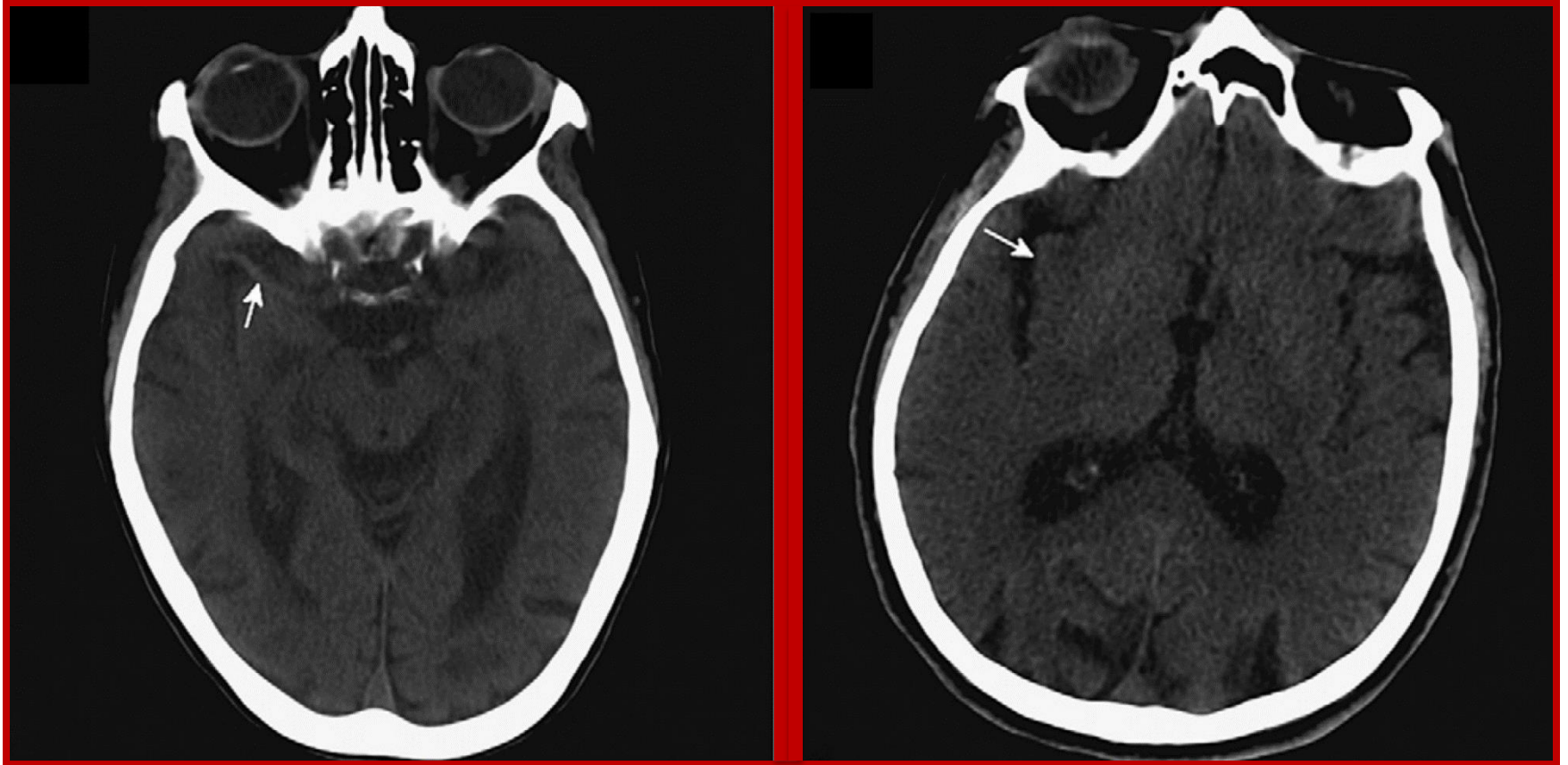# Pooled analysis
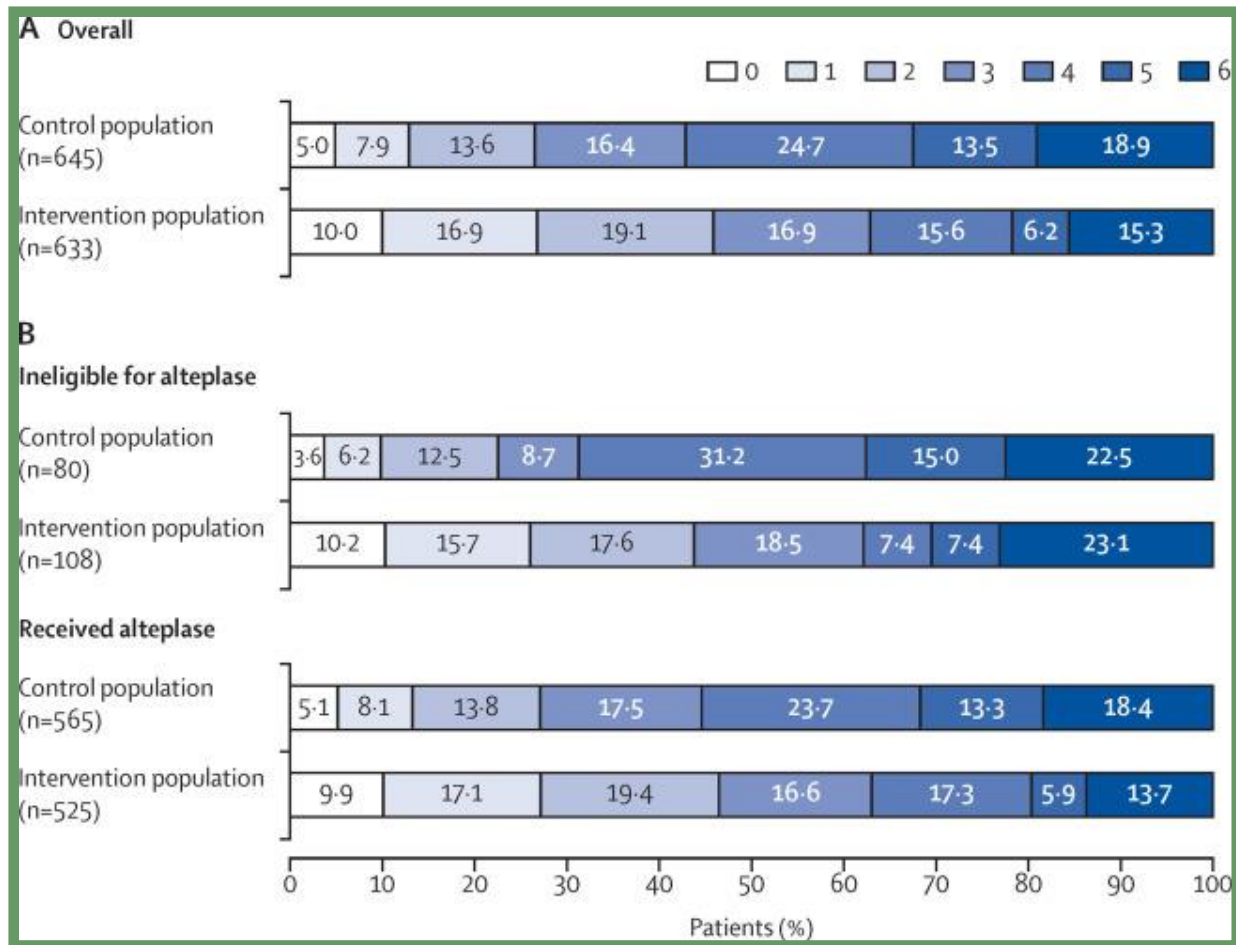
Lancet 2016; 387: 1723–31

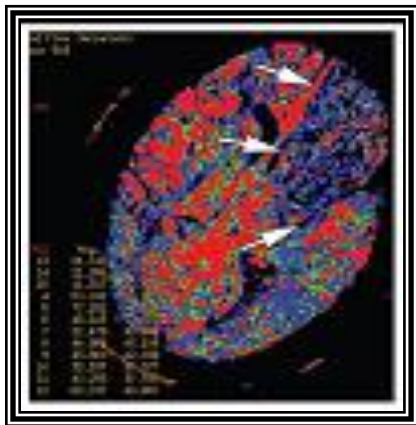# CT Angiography
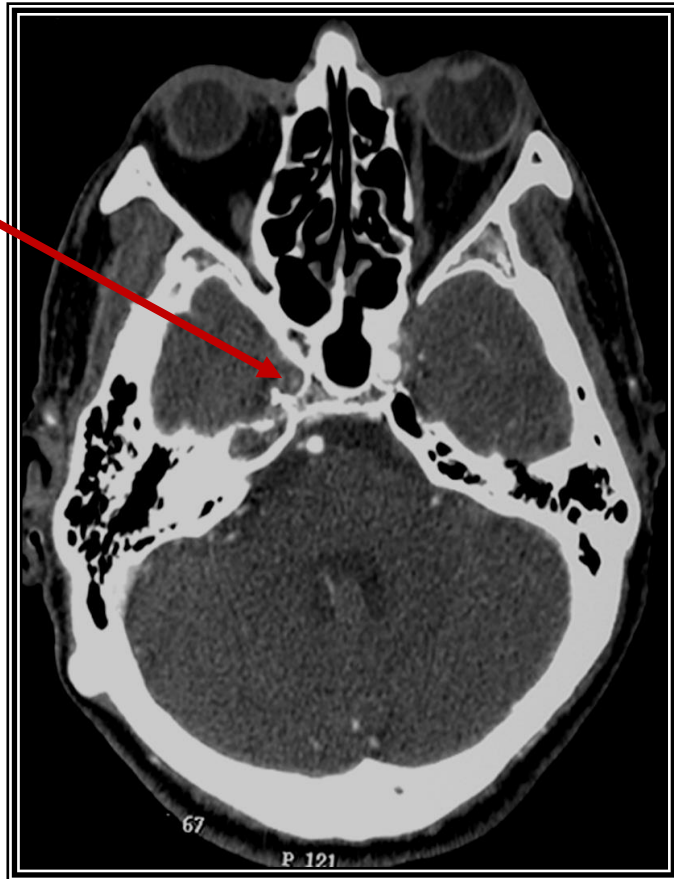
R ICA Occlusion

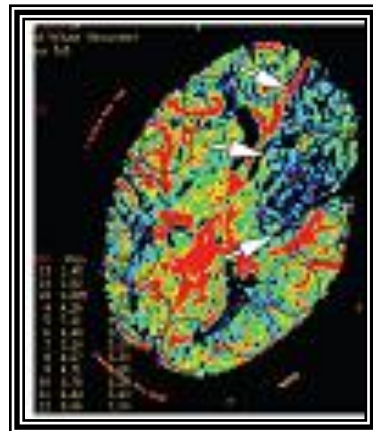**Poor R MCA flow**

Imaging-Based Reperfusion Trials
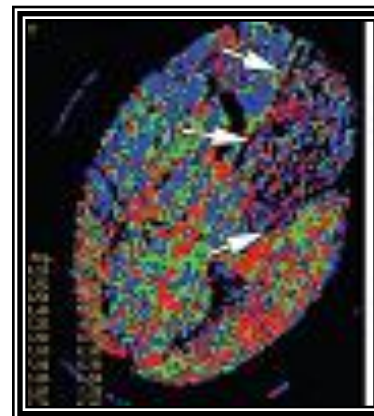
CT Perfusion

- Provides an indirect measure of the metabolic state of the tissue
  - Useful for identification of penumbra vs. core (ie, salvagable tissue)
- INFARCT will have ↑ MTT, ↓ CBF, & ↓ CBV
- TISSUE AT RISK will have ↑ MTT, ↓ CBF, & ↑ or normal CBV due to autoregulation

| CBF | CBV | MTT | Follow-Up CT |

Hoeffner *et. al.* Cerebral perfusion CT: technique and clinical application. Radiology 2004; 231:632–644.
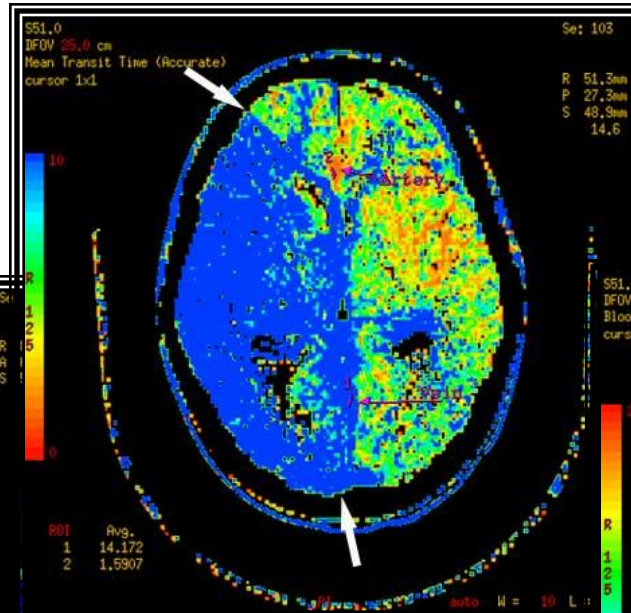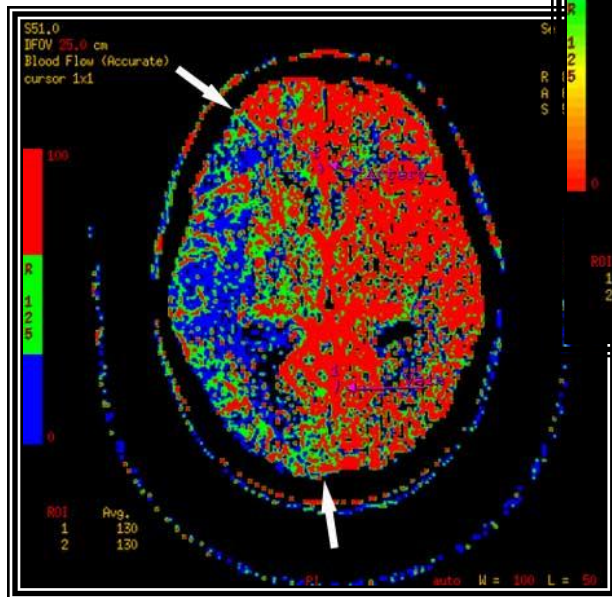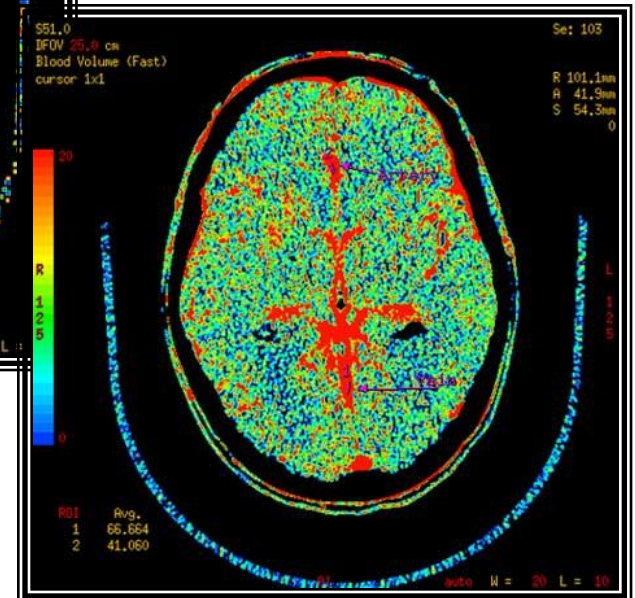
CT Perfusion

Blood Flow

(> 50 mL/100g/min)

Mean Transit Time

(< 6 sec)

Blood Volume

(>2.5 mL/100g)

ORIGINAL ARTICLE

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. [...]

DEFUSE:
RCT, 182 patients; terminated early for efficacy (goal 476)
--used MRI or CTP

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*

ABSTRACT

DAWN:
RCT, included 206 patients
--used MRI or CTP to select

Example of Perfusion Imaging Showing a Disproportionately Large Region of Hypoperfusion as Compared with the Size of Early Infarction.
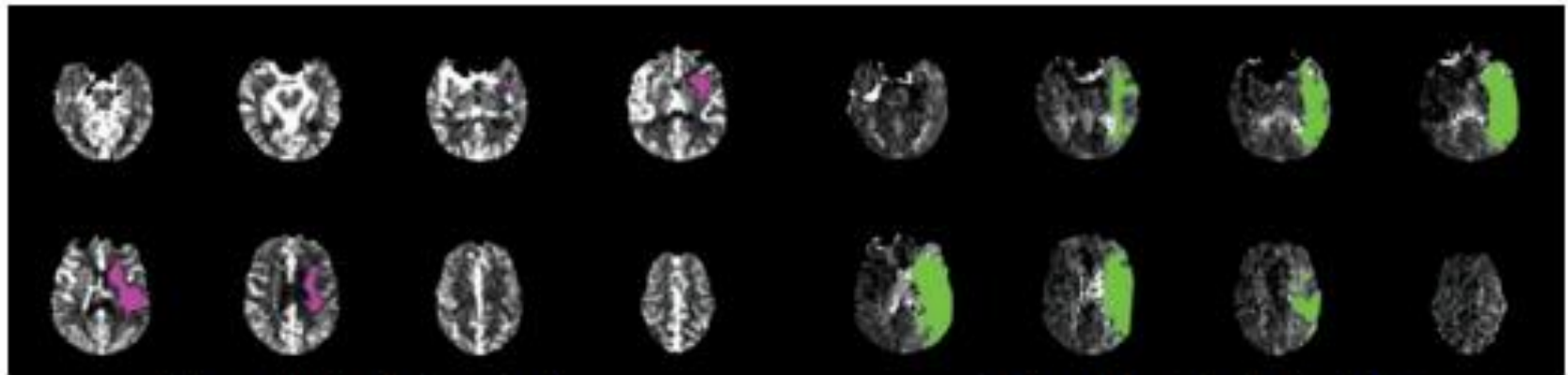
Volume of Ischemic Core, 23 ml   Volume of Perfusion Lesion, 128 ml

Mismatch volume, 105 ml
Mismatch ratio, 5.6

Eligible for randomization if:
- Core infarct < 70 mL
- Ratio of Penumbra: Core Infarct of >= 1.8
- Absolute penumbra volume > 15 mL

GW Albers et al. N Engl J Med 2018;378:708-718.

DEFUSE 3: Outcomes

Table 2. Clinical and Imaging Outcomes.

Outcome	Endovascular Therapy (N = 92)*	Medical Therapy (N = 90)	Odds Ratio or Risk Ratio (95% CI)†	P Value
Primary efficacy outcome: median score on modified Rankin scale at 90 days (IQR)‡	3 (1–4)	4 (3–6)	2.77 (1.63–4.70)§	<0.001
Secondary efficacy outcome: functional independence at 90 days — no. (%)¶	41 (45)	15 (17)	2.67 (1.60–4.48)	<0.001
Safety outcomes — no. (%)				
Death at 90 days	13 (14)	23 (26)	0.55 (0.30–1.02)	0.05
Symptomatic intracranial hemorrhage‖	6 (7)	4 (4)	1.47 (0.40–6.55)	0.75
Early neurologic deterioration	8 (9)	11 (12)	0.71 (0.30–1.69)	0.44
Parenchymal hematoma type 2	8 (9)	3 (3)	2.61 (0.73–14.69)	0.21
Imaging outcomes**				
Median infarct volume at 24 hr (IQR) — ml	35 (18–82)	41 (25–106)	—	0.19
Median infarct growth at 24 hr (IQR) — ml	23 (10–75)	33 (18–75)	—	0.08
Reperfusion >90% at 24 hr — no./total no. (%)	59/75 (79)	12/67 (18)	4.39 (2.60–7.43)	<0.001
Complete recanalization at 24 hr — no./total no. (%)	65/83 (78)	14/77 (18)	4.31 (2.65–7.01)	<0.001
TICI score of 2b or 3 — no./total no. (%)	69/91 (76)	—	—	

When is IAT Considered?

- Acute stroke due to occlusion of a large vessel

- Onset within 6 hours
- *OR,* favorable perfusion pattern
  - Small area of completed infarction

- *OR,* acute basilar artery occlusion, regardless of imaging

In Summary:

- Any patient with clinical suspicion for stroke:

  - If onset occurred within 4.5 hours, consider treatment with thrombolysis

- If there's clinical suspicion for large vessel occlusion:

  - Determine eligibility for thrombolysis

    AND

  - Consider transfer to a center with IAT capability

UAB MEDICINE

COMPREHENSIVE NEUROVASCULAR & STROKE CENTER