# *Opening the Window for Stroke Intervention – How Far Can We Go?*

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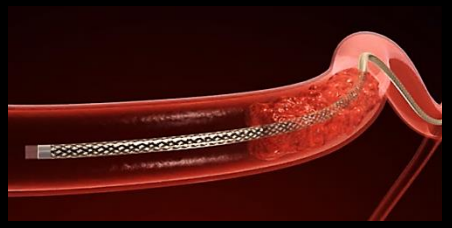

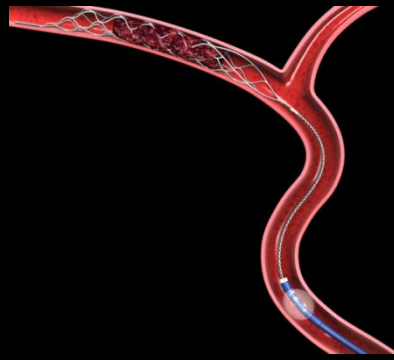

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# Disclosures:

## Stryker Neurovascular (unpaid)

- Trevo-2 Trial PI
- DAWN Trial PI

## Medtronic

- SWIFT and SWIFT-PRIME Trial Steering Committee (unpaid)
- STAR Trial Core Lab

## Penumbra (unpaid)

- 3-D Separator Trial Executive Committee

## Interventional Neurology Journal (unpaid)

- Editor-In-Chief

# Endovascular Therapy Recommendations: Protocol and Patient Selection

## Endovascular Protocol and Patient Selection

"Patients eligible for intravenous rtPA should receive intravenous rtPA even if intra-arterial treatments are being considered."

| Class I | Level of Evidence A | Unchanged Guideline |
|---|---|---|

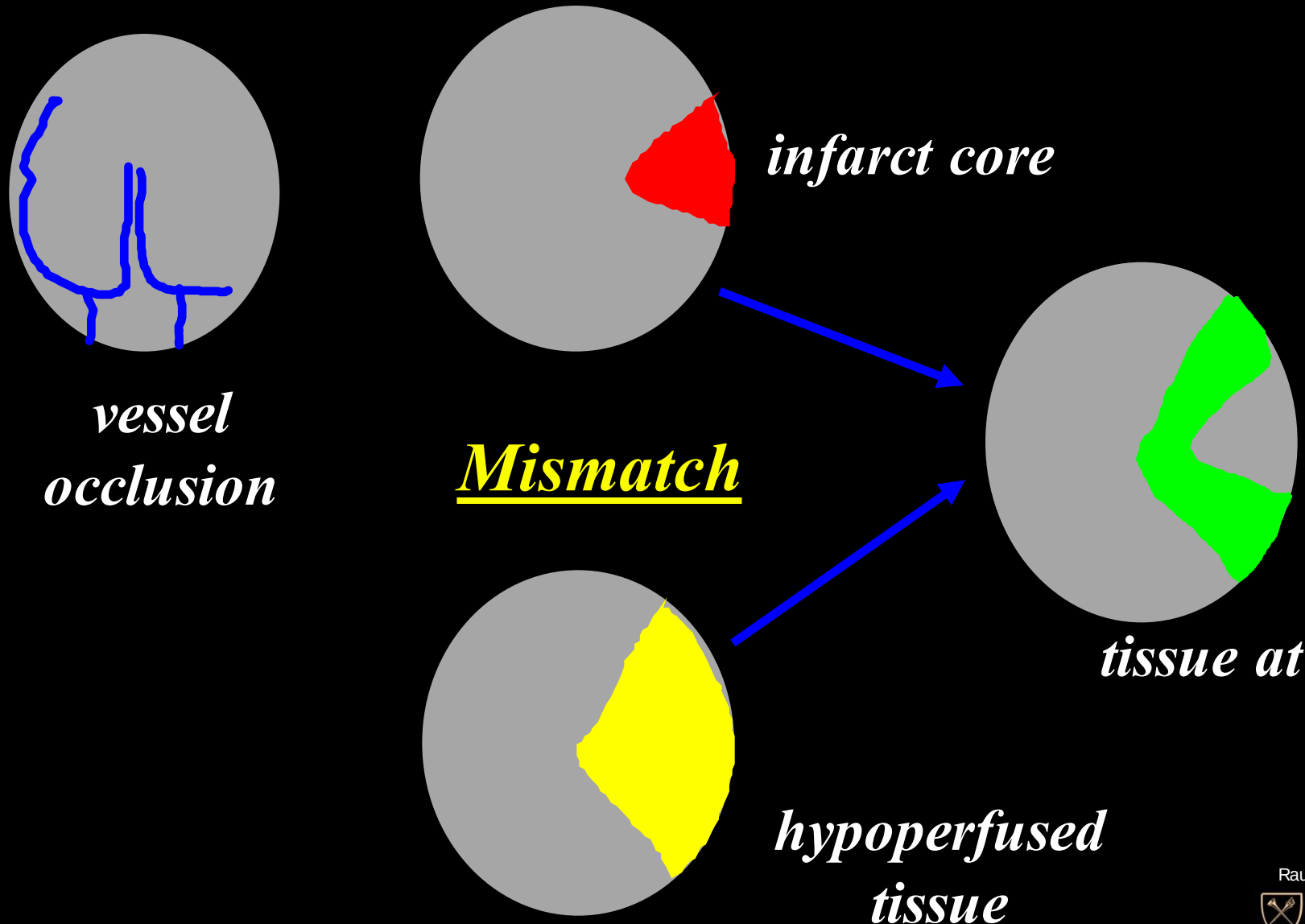
Patients should receive endovascular therapy with a stent retriever if they meet all the following criteria

a) prestroke mRS score 0 to 1,
b) acute ischemic stroke receiving intravenous r-tPA within 4.5 hours of onset according to guidelines from professional medical societies,
c) causative occlusion of the internal carotid artery or proximal MCA (M1),
d) age ≥18 years,
e) NIHSS score of ≥ 6,
f) ASPECTS of ≥ 6, and

| Class I | Level of Evidence A | New Recommendation |
|---|---|---|

William J. Powers, Colin P. Derdeyn, José Biller, Christopher S. Coffey, Brian L. Hoh, Edward C. Jauch, Karen C. Johnston, S. Claiborne Johnston, Alexander A. Khalessi, Chelsea S. Kidwell, James F. Meschia, Bruce Ovbiagele, and Dileep R. Yavagal. "2015 AHA/ASA Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association." American Heart Association Stroke Council. Stroke Published online June 29th 2015.

# Mismatch vs. Penumbra: Basic Concepts

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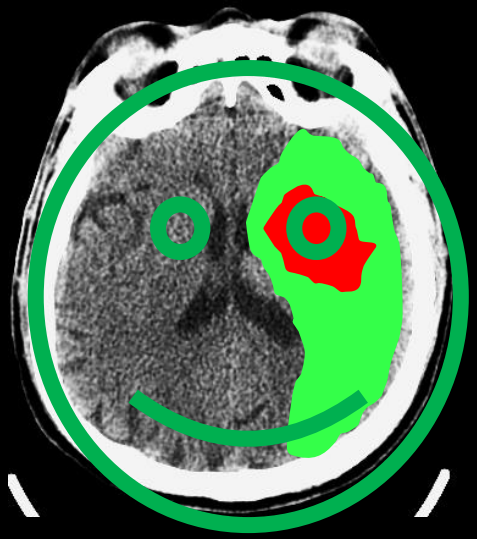
# The Fundament of Reperfusion: Penumbra – Core Mismatch

Enough Ischemic but Viable Brain that Can Be Rescued

ICA/MCA-M1 Occlusions:



NIHSS 25

ASPECTS 8

+Mismatch:

Penumbra>>Infarct

NIHSS 25

ASPECTS 3

-Mismatch:

Large Infarct

No Penumbra

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# The Fundament of Reperfusion: Penumbra – Core Mismatch

Enough Ischemic but Viable Brain that Can Be Rescued

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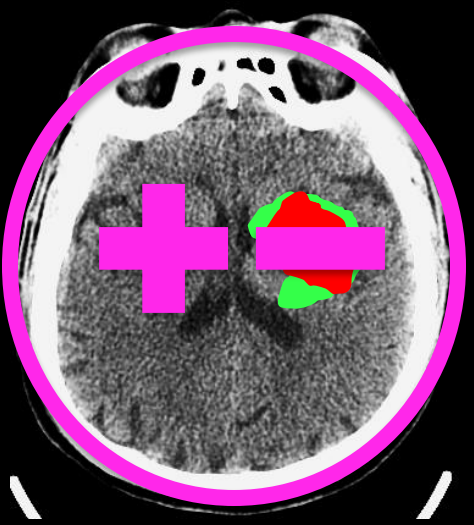

NIHSS 6

ASPECTS 8

Small Mismatch/Small Infarct: Penumbra>Infarct

NIHSS 18

ASPECTS 4

Large Mismatch/ Large Infarct: Penumbra>Infarct

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# How Far Can We Go?

- Controversies in LVOS Thrombectomy:
  - Is there an Upper Age Limit? No!
  - Best Management of the following is unknown at this time:
    - Low Baseline NIHSS (<6)
    - Distal Occlusions (?M2, M3, ACA, PCA)
    - Low Baseline ASPECTS (<6), Large Cores (>50-70cc)
    - Late Presenting (>6 hours)/ Wake-Up Strokes

# RCTs Advances in Patient Selection: Age

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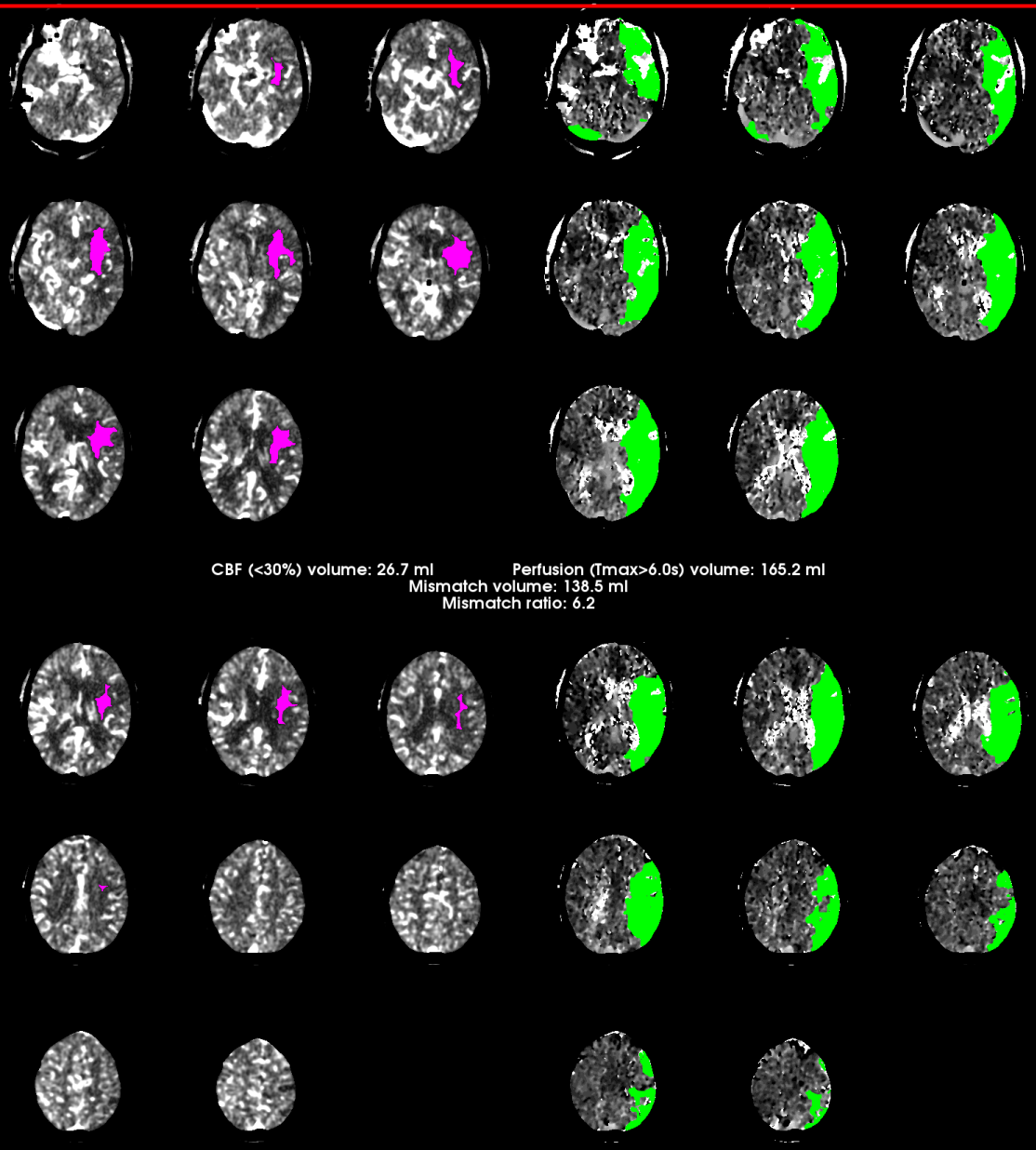
# IAT in the Elderly Revisited:

- 83 yo male PMHx of lower GI bleeding, AFib not on anticoagulants, and 4V CABG
- 1:45am: global aphasia and right hemiplegia
- 3:42am: IV tPA at OSH
- 5:20am: Grady CT
  - NIHSS = 26
  - Full LMCA syndrome
- CT perfusion demonstrated a deep territory infarct with a large mismatch

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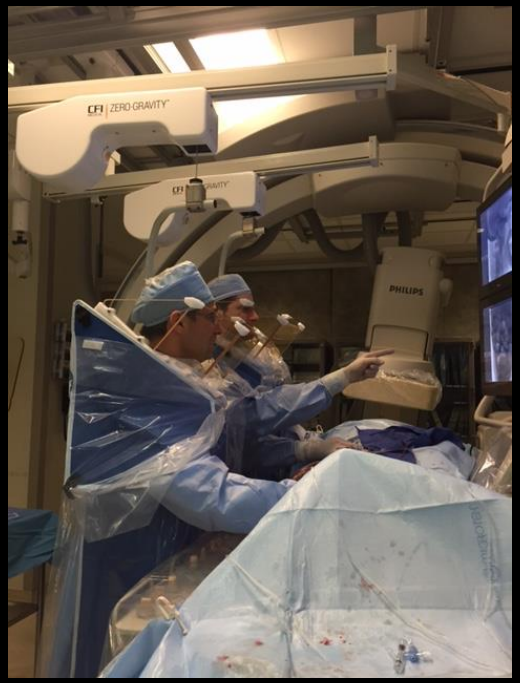
# Angio suite

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# Technique:

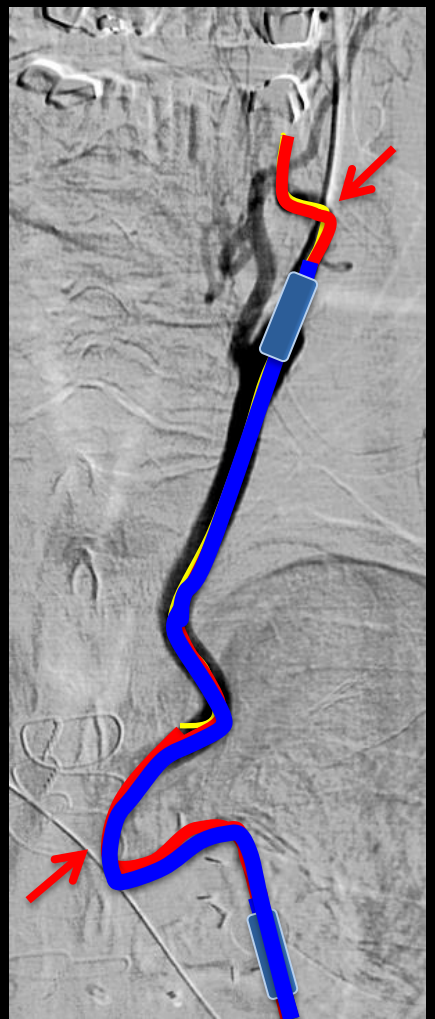
Principles: Simple and Fast!

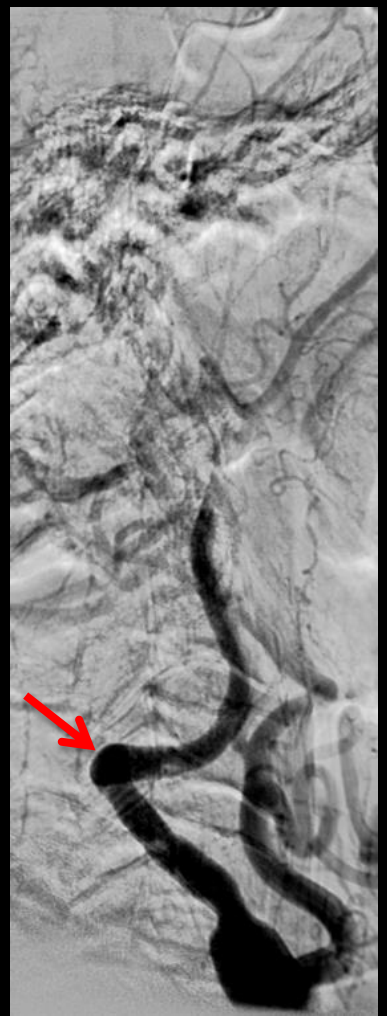
Coaxial Technique with 8-9F BGC and VTK (distal wire and VTK in ECA if extreme)
No Exchange

8-9F BGC

8-9F Sheath

5F 125cm
Vitek Cath

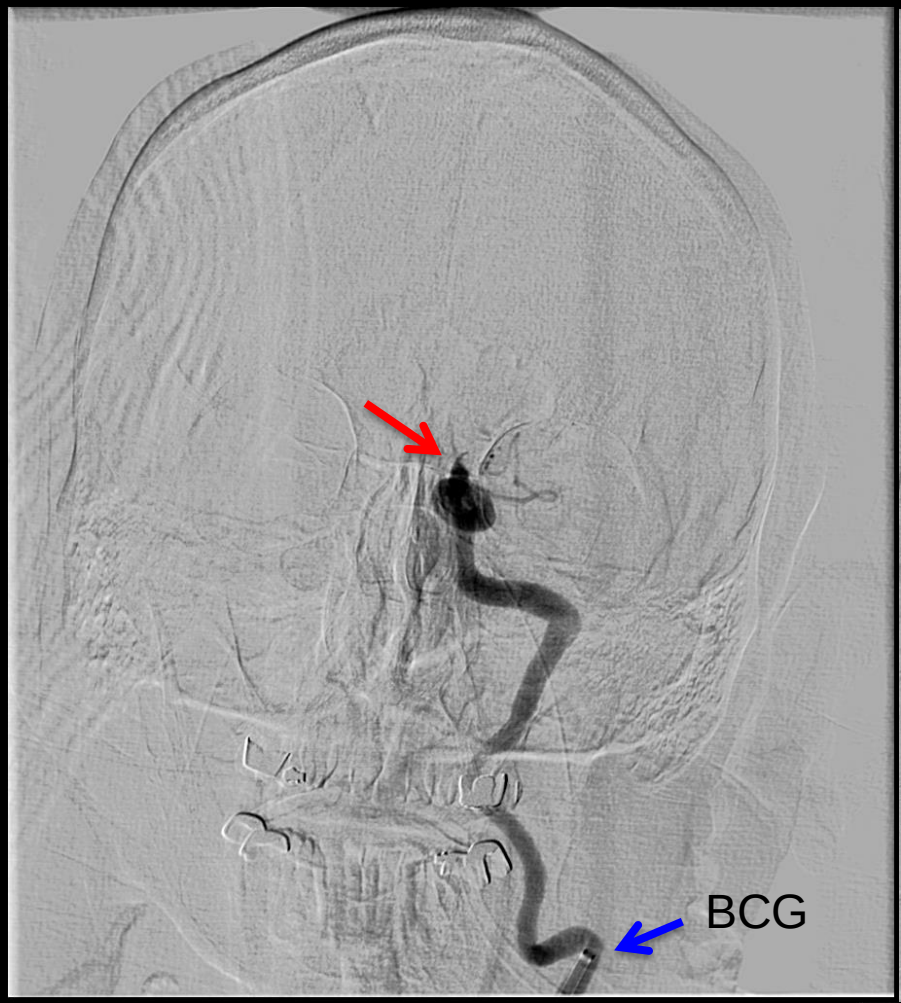


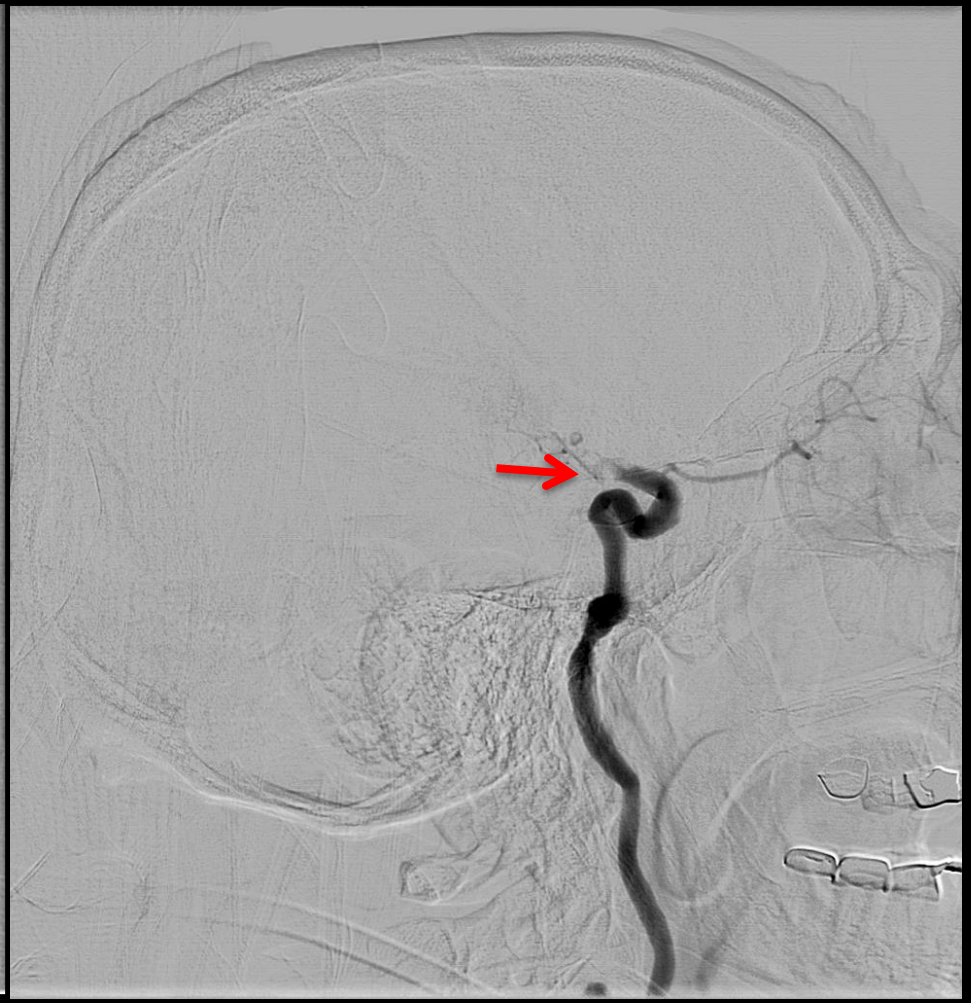


# Technique: Elderly/ Tortuosity

Principles: Simple and Fast!

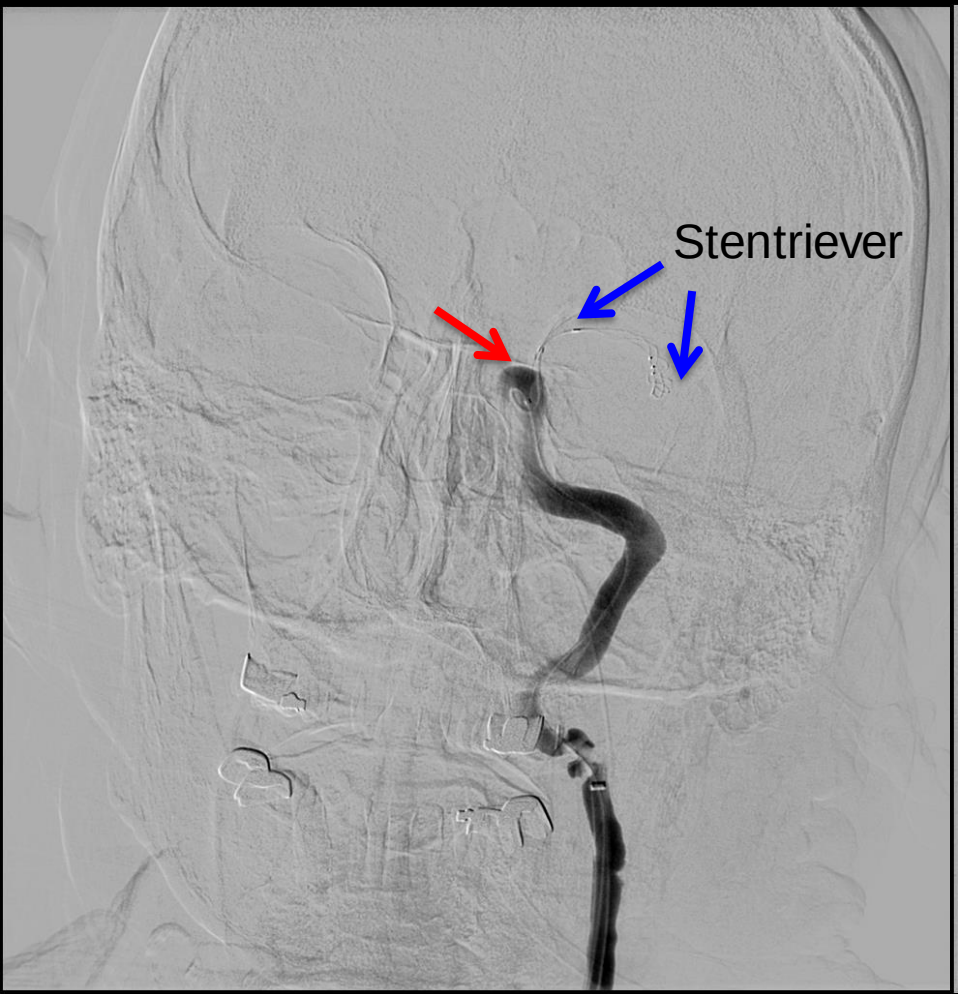
No Distal Access Catheter (will use only rarely if extreme)
Preferred Microcatheter for tortuous anatomy: Orion (compatible with all Stentrievers)

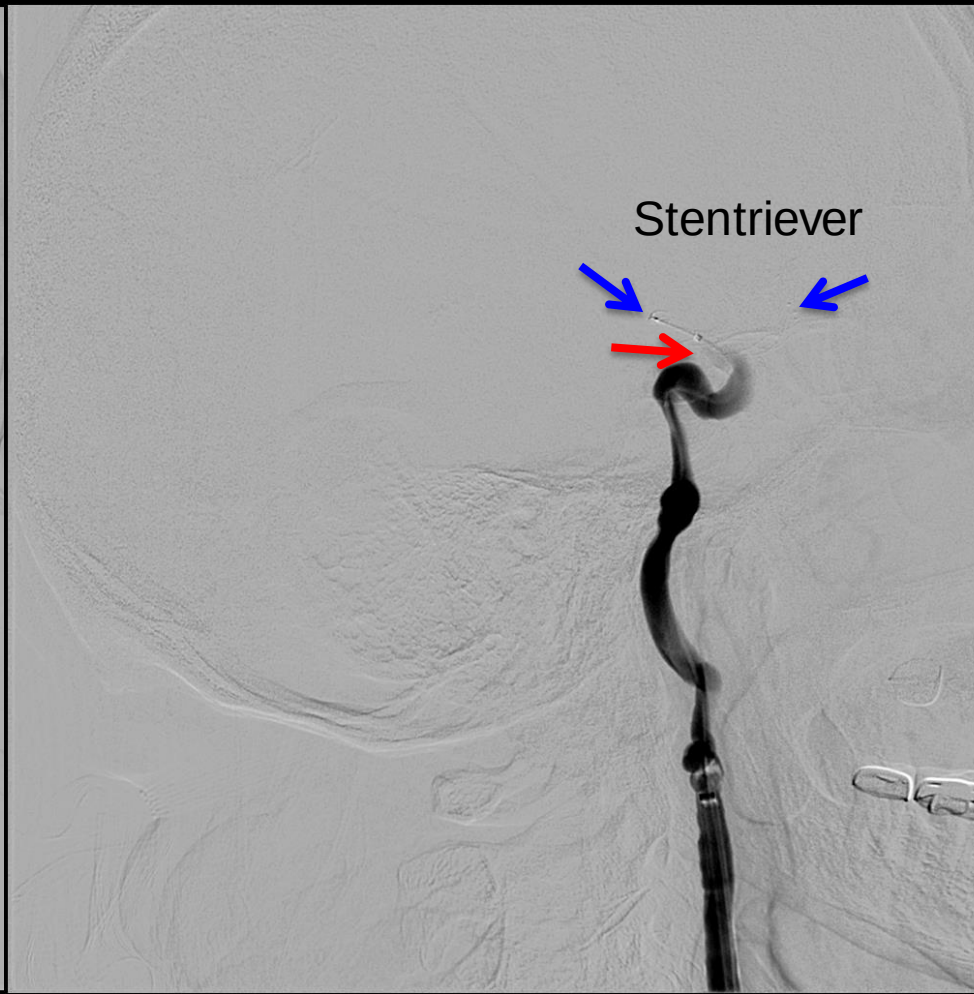


# Technique: Long Clots

Thrombus longer than device but device bridges distal end of thrombus and normal vessel – Optimal Radial Force of the Device and Cervical Aspiration with retrieve  the entire clot as a unit
5 minutes with device deployed



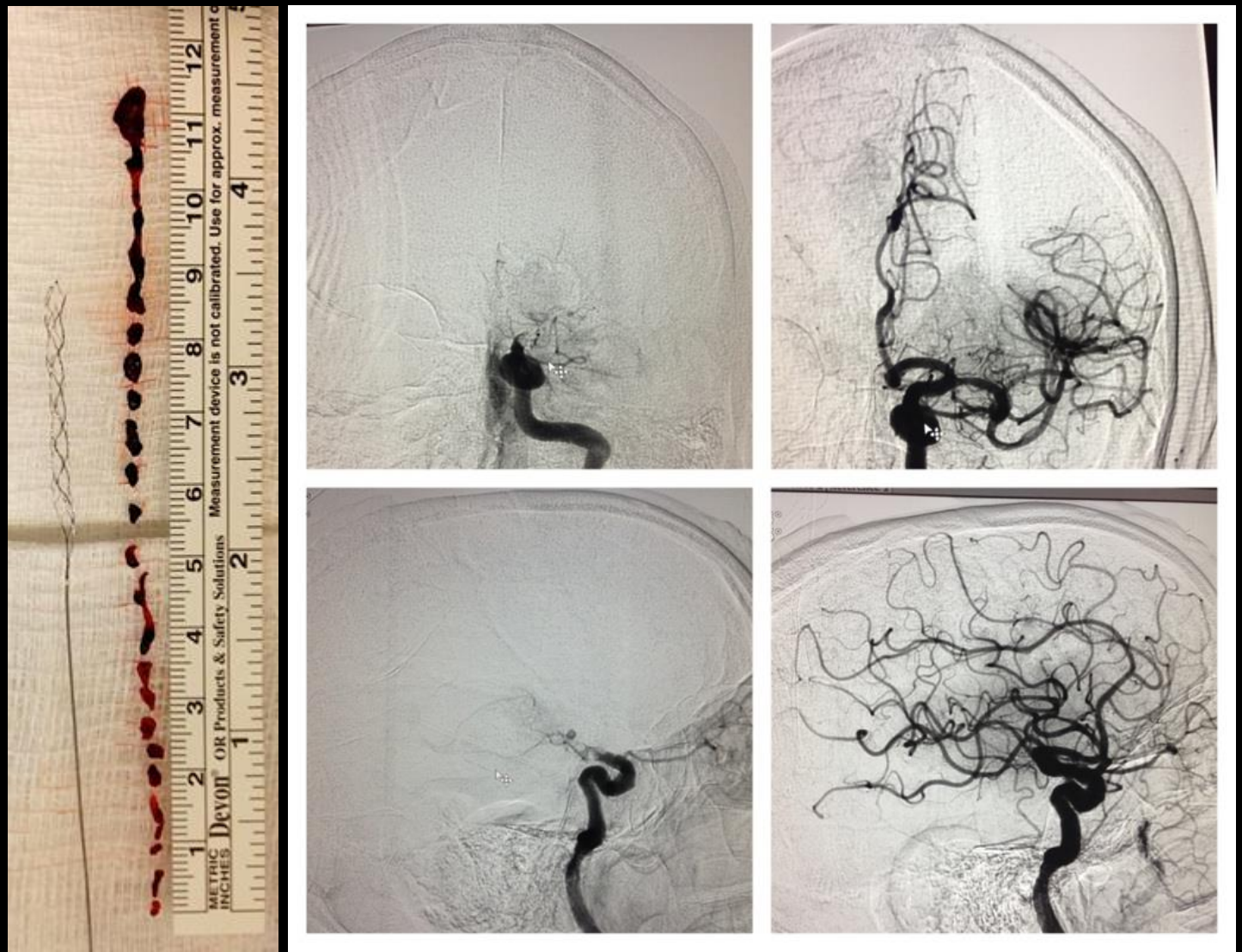
# Technique: Slow Pull with BCG Aspiration

One Pass Stent-Retriever = TICI 3

Groin to TICI 3 = 18min

# Clinical Outcome:

NIHSS down from 26 to 2 for mild paraphasic errors and mild facial droop

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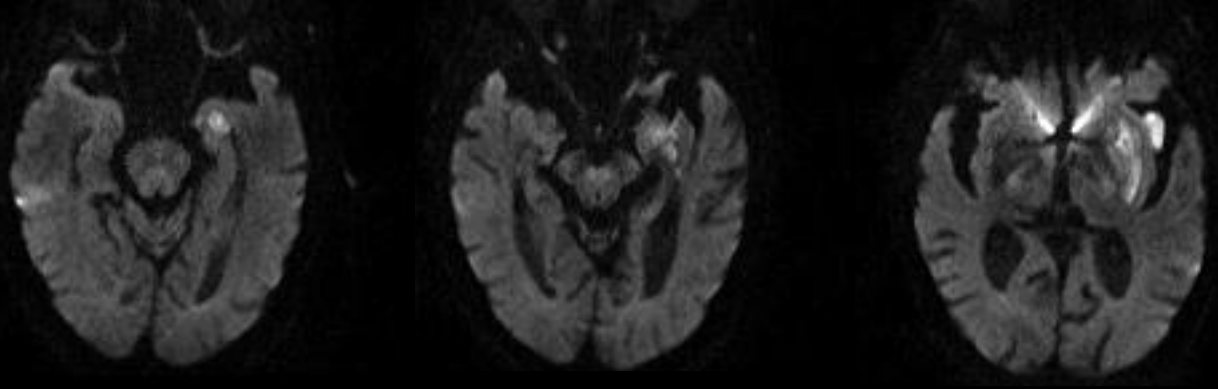
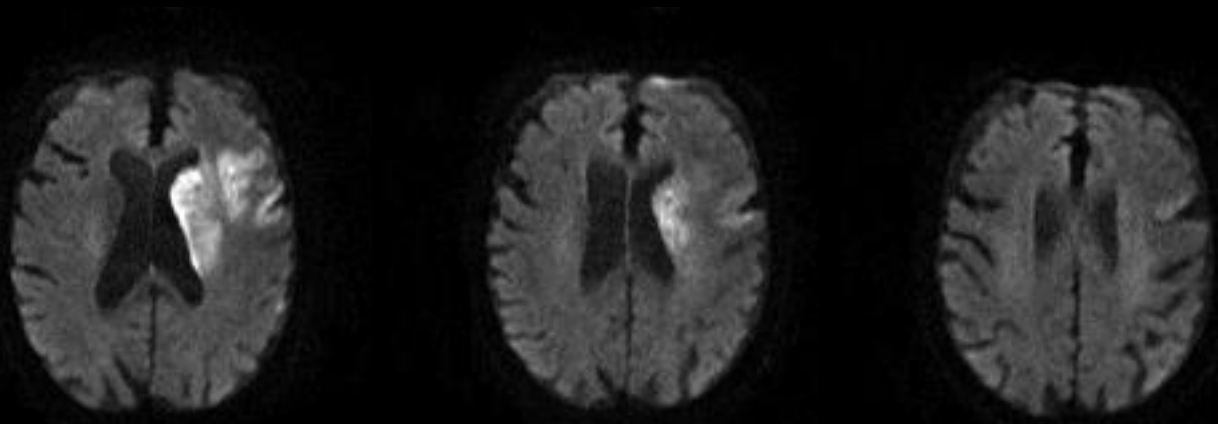


POST TREATMENT
NIHSS = 2

90-DAY mRS = 1



24-h Follow-up DWI (Post-Rx Core)

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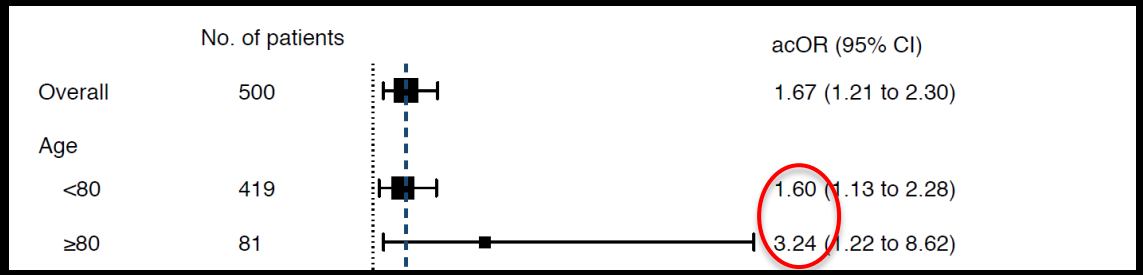
# IAT in the Elderly Revisited:

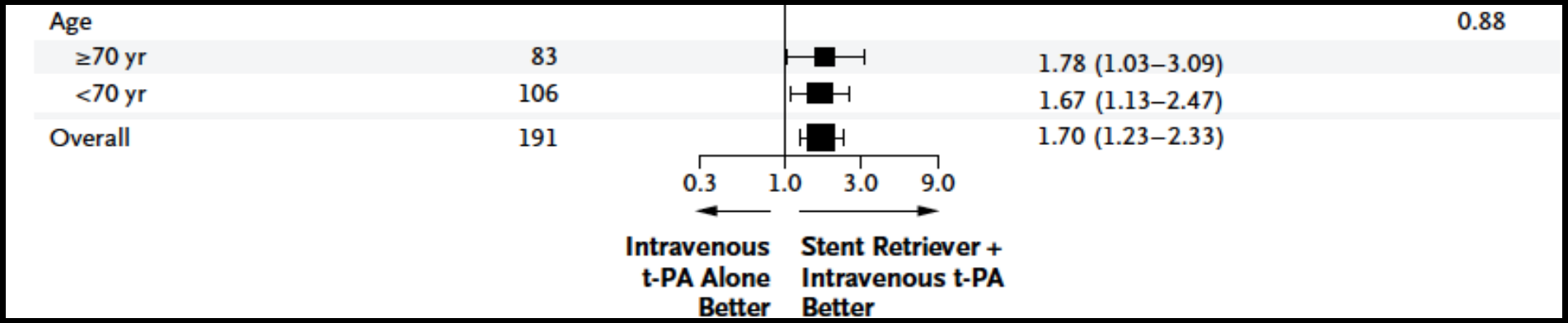
## RCT Subgroup Analyses: AGE

### ESCAPE

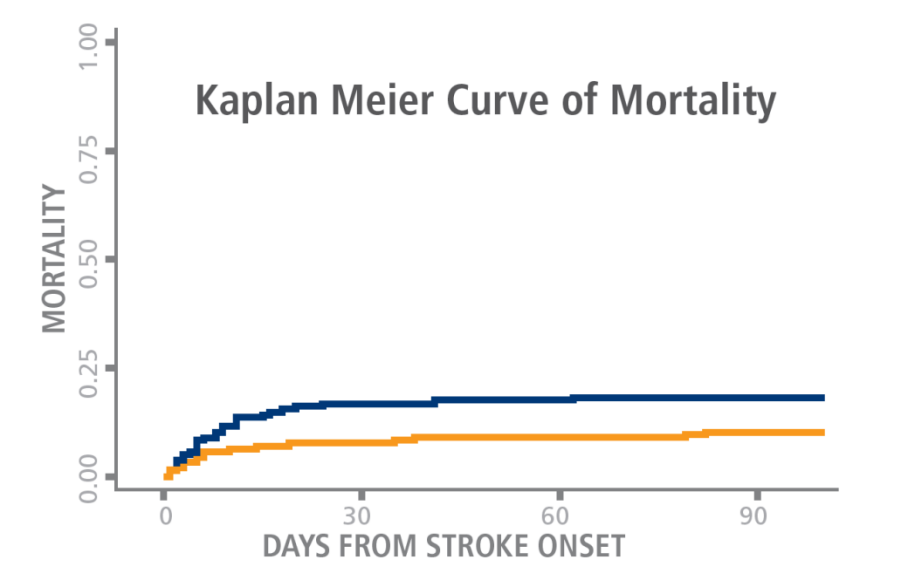

### MR CLEAN




### SWIFT PRIME

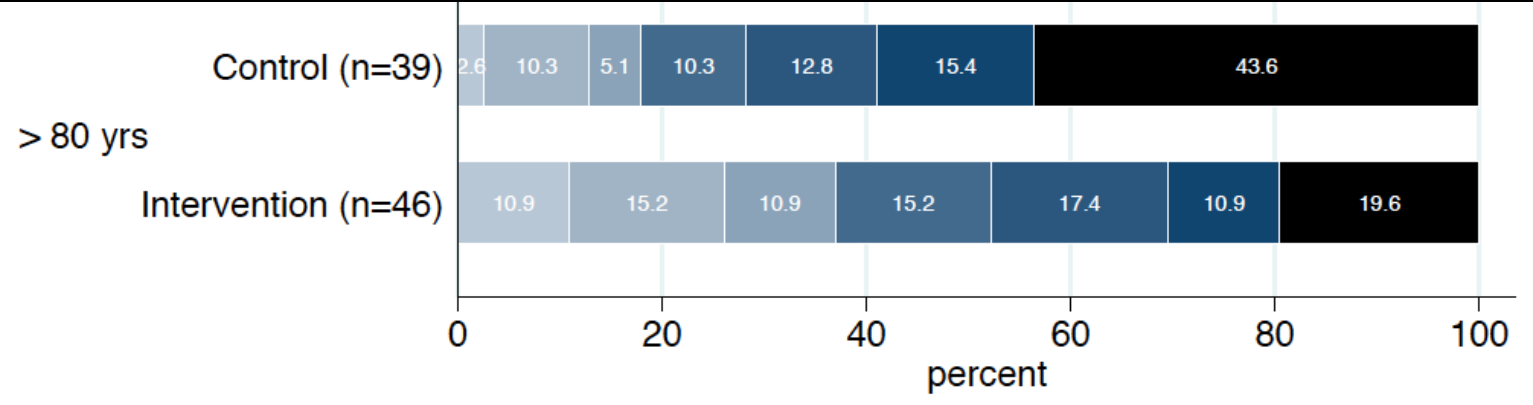


# ESCAPE: Reduction in Mortality




≤ 80 yrs: 7% vs. 10%

> 80 yrs: 20% vs. 44%

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# IAT in the Elderly Revisited:

- Single Center 102 Consecutive IAT for pts ≥80 yrs - Sept.2010-Sept.2014
  - Age: 84.8 yrs (80-100)
  - bNIHSS: 19.2 (4-33)
  - ASPECTS ≥7: 58%

**TABLE 2: Clinical and Radiographic outcome**

| | Overall (n=97) | Stentretriever (n=54) | ASPECTS ≥7 (n=56) | CT Perfusion (n=31) | IV t-Pa (n=50) |
|---|---|---|---|---|---|
| **Clinical outcome** | | | | | |
| 90-Day Good outcome (mRS 0-2) | 26/97(27%) | 18/54(33%) | 16/56(29%) | 11/31(35%) | 14/50(28%) |
| Symptomatic Hemorrhage | 8/97(8%) | 5/54(9%) | 3/56(5%) | 1/31(3%) | 4/50(8%) |
| 90-Day Mortality | 42/97(43%) | 20/54(37%) | 22/56(39%) | 13/31(42%) | 20/50(40%) |

  - Control pts ≥80 yrs: IST-3 trial: 6-month death/dependency = 75% if bNIHSS 6-14 and >95% if bNIHSS ≥15.

  - IV tPA pts ≥80 yrs:
    - SITS-ISTR/VISTA (n=2235; bNIHSS, 14): >2/3 dead/dependent at 3-months.
    - IST-3: 72.7% dead/dependent at 6-months.

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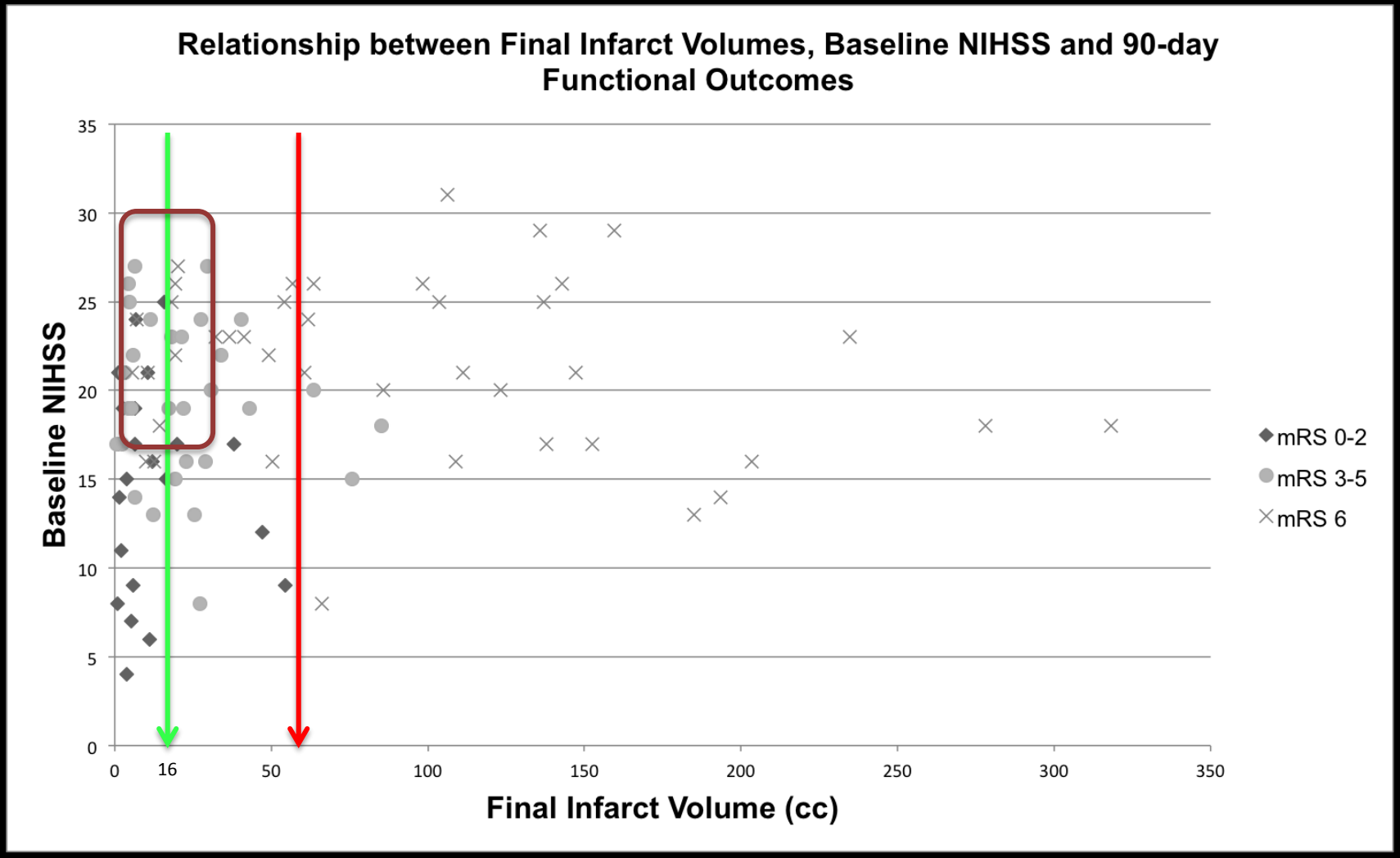
# IAT in the Elderly Revisited:

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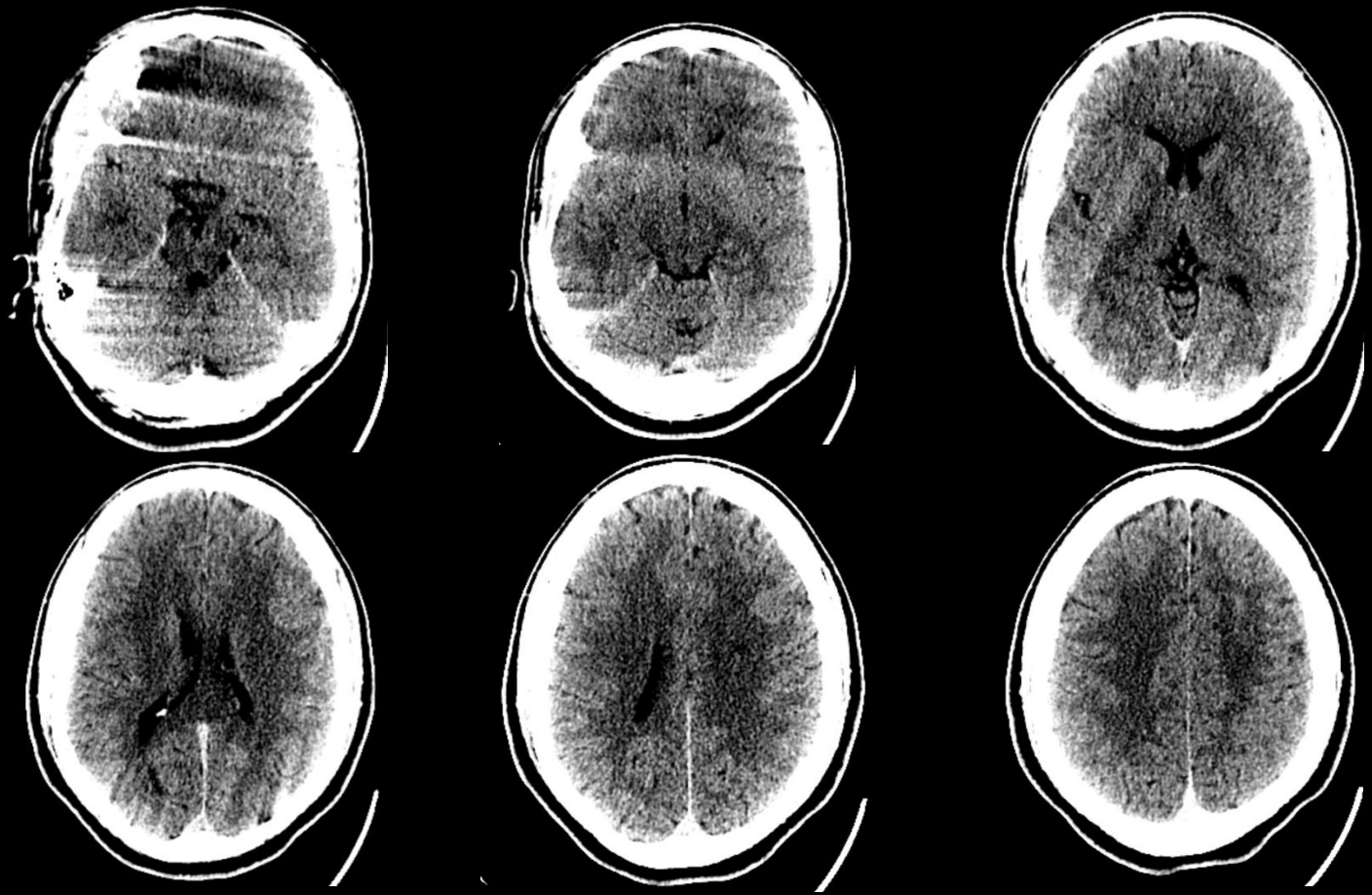
# Baseline Clinical Severity: Low NIHSS = Too Good to Treat?

# Too Good To Treat????

- 44 y/o man p/w LMCA sd. Fluctuating mild symptoms x 24-48 hours. NIHSS= 4
- Outside Window for IV tPA
- NCCT: ASPECTS = 8-9
- CTA: Left Intracranial ICA Occlusion



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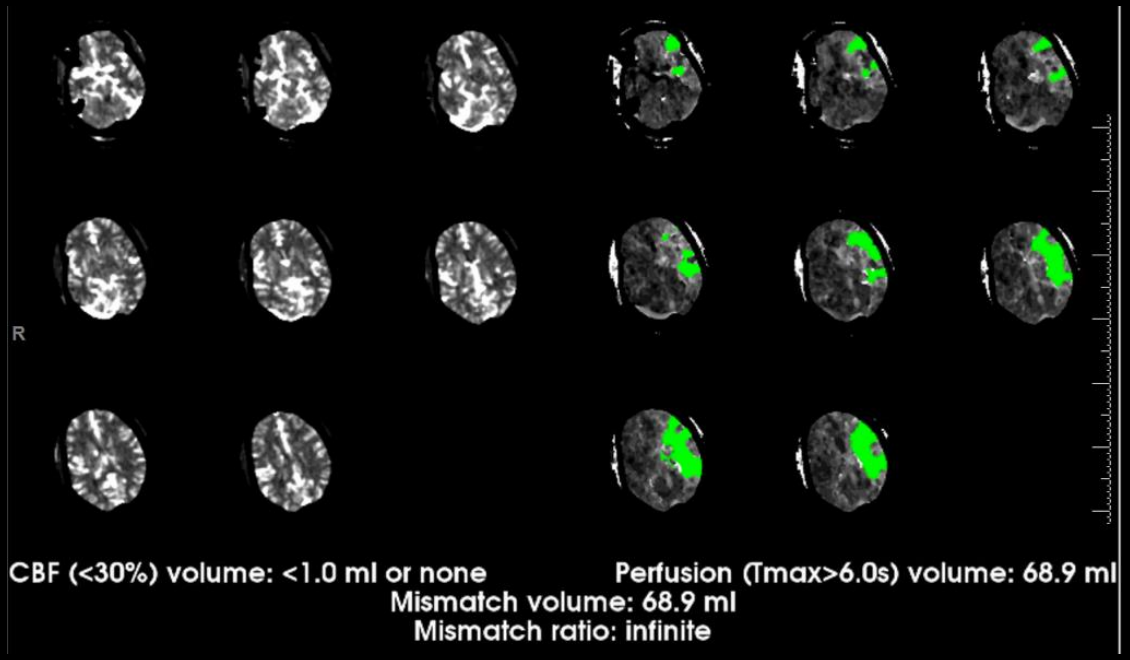


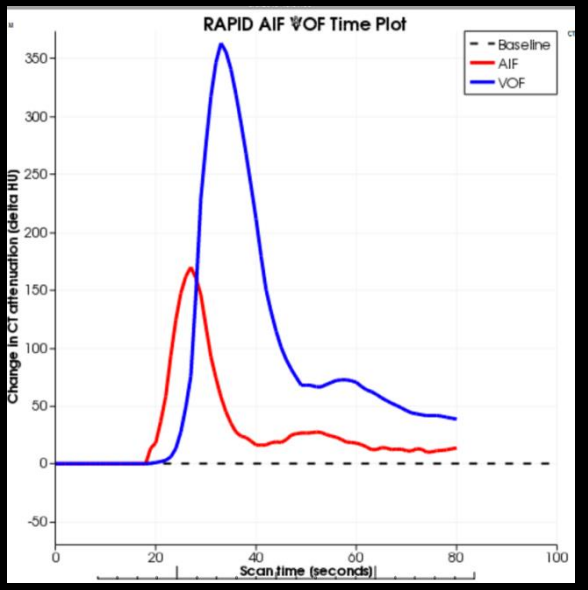


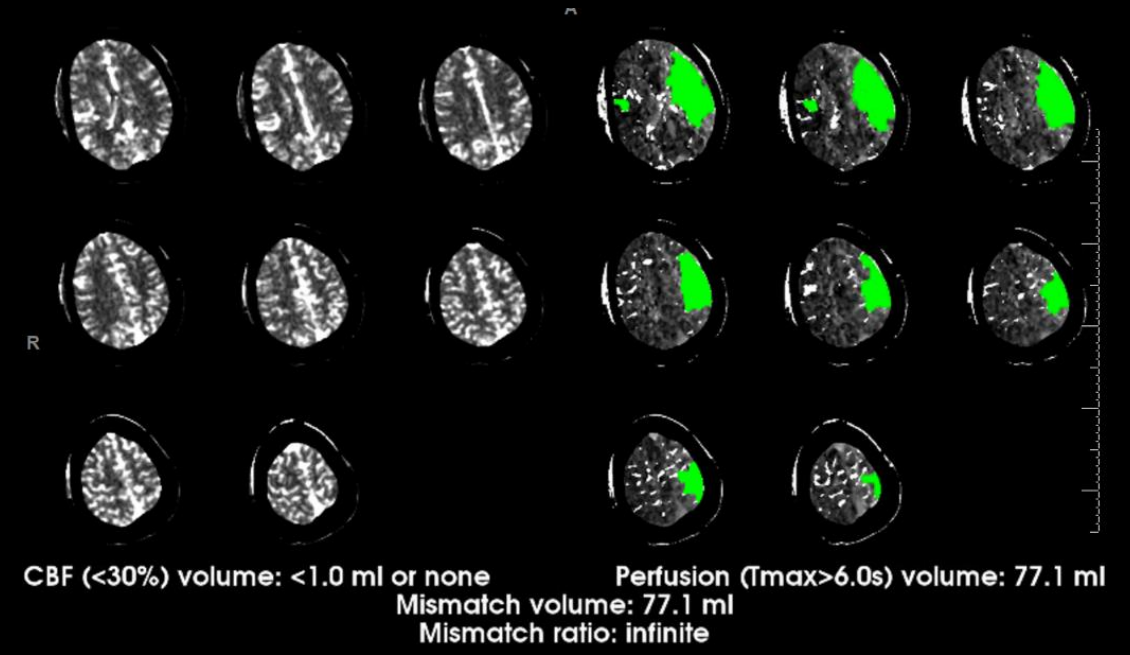


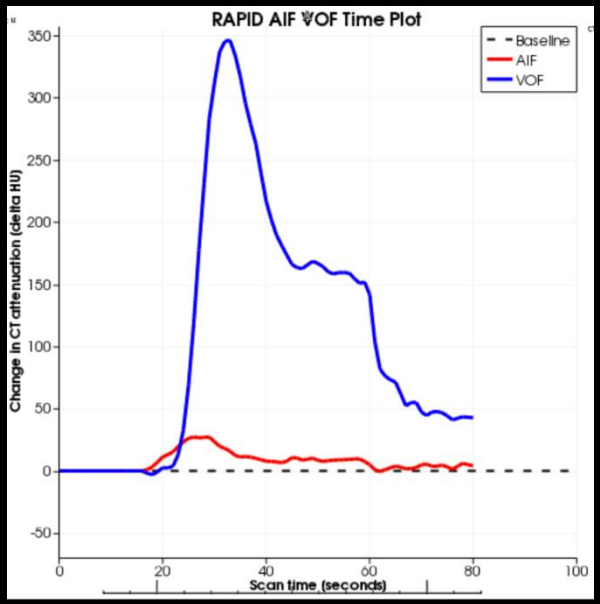


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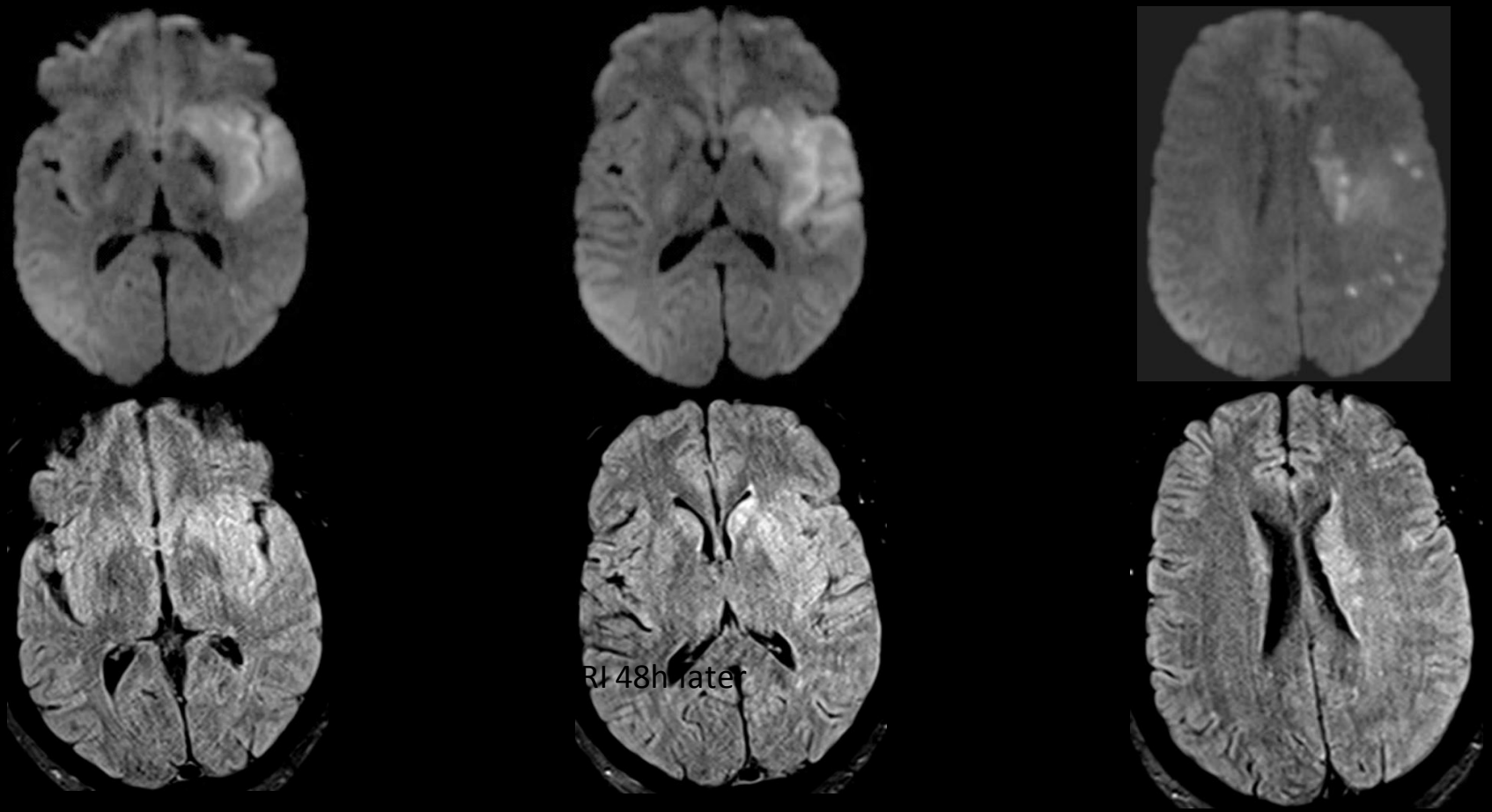
# Too Good To Treat????

- 48 hours later: clinically worse - R Hemiplegia
- NIHSS: 12
- Follow-up DWI and FLAIR



# Too Good To Treat????

## No IV tPA

# Outcomes in Mild or Rapidly Improving Stroke Not Treated With Intravenous Recombinant Tissue-Type Plasminogen Activator

## Findings From Get With The Guidelines–Stroke

Eric E. Smith, MD, MPH; Gregg C. Fonarow, MD; Mathew J. Reeves, PhD; Margueritte Cox, MS; DaiWai M. Olson, PhD, RN; Adrian F. Hernandez, MD; Lee H. Schwamm, MD

***Background and Purpose***—Mild or rapidly improving stroke is a frequently cited reason for not giving intravenous recombinant tissue-type plasminogen activator (rtPA), but some of these patients may have poor outcomes. We used data from a large nationwide study (Get With The Guidelines–Stroke) to determine risk factors for poor outcomes after mild or improving stroke at hospital discharge.

***Methods***—Between 2003 and 2009, there were 29 200 ischemic stroke patients (from 1092 hospitals) arriving within 2

mild/improving stroke. Among the 29 200 mild/improving cases, 28.3% were not discharged to home, and 28.5% were unable to ambulate without assistance at hospital discharge. The likelihood of home discharge was strongly

~~mild/improving stroke. Among the 29 200 mild/improving cases, 28.3% were not discharged to home, and 28.5%~~ were unable to ambulate without assistance at hospital discharge. The likelihood of home discharge was strongly related to initial National Institutes of Health Stroke Scale score ($P<0.001$). In multivariable-adjusted analysis, patients not discharged to home were more likely to be older, female, and black; have a higher National Institutes of Health Stroke Scale score and vascular risk factors; and were less likely to be taking lipid-lowering medication before admission.

***Conclusions***—In this large, nationwide study, a sizeable minority of patients who did not receive intravenous rtPA solely because of mild/improving stroke had poor short-term outcomes, raising the possibility that stroke-related disability is relatively common, even in "mild" stroke. A controlled trial of reperfusion therapy in this population may be warranted. (***Stroke***. **2011;42:3110-3115.**)

# Too Good To Treat????

## No IV tPA

### Ninety-Day Outcome Rates of a Prospective Cohort of Consecutive Patients With Mild Ischemic Stroke

Pooja Khatri, MD, MSc; Mark R. Conaway, PhD; Karen C. Johnston, MD, MSc; for the Acute Stroke Accurate Prediction Study (ASAP) Investigators

***Background and Purpose***—Prior studies have shown that patients with mild ischemic stroke have substantial disability rates at hospital discharge. We sought to determine disability rates at 90 days among patients not treated with thrombolytic therapy and explore the role of early neurological worsening.

***Methods***—We reviewed a prospective cohort of 136 consecutive patients with mild deficits (National Institutes of Health Stroke Scale score ≤5) presenting within 24 hours of onset and no baseline disability. Baseline MRIs were performed

***Results***—Among 136 patients, 40 (29%; 95% CI, 22%–38%) had poor outcomes (modified Rankin Scale score 2–6) at 90 days. Early worsening (4-point National Institutes of Health Stroke Scale increase; 25% versus 1%, $P<0.001$) and acute infarct growth (>10% on MRI–diffusion-weighted imaging; 79% versus 33%, $P=0.02$) from baseline to 5 days were more common among those with poor outcome.

***Conclusions***—Patients with mild ischemic stroke have substantial rates (29%) of disability at 90 days. (***Stroke*. 2012;43: 560-562.**)

# Too Good To Treat????

## + IV tPA

Original Investigation

### Outcomes in Mild Acute Ischemic Stroke Treated With Intravenous Thrombolysis

### A Retrospective Analysis of the Get With the Guidelines–Stroke Registry

Jose G. Romano, MD; Eric E. Smith, MD, MPH; Li Liang, PhD; Hannah Gardener, ScD; Sara Camp, RN, MSN; Laura Shuey, RN, MSN; Alison Cook, BS; Iszet Campo-Bustillo, MD, MPH; Pooja Khatri, MD; Deepak L. Bhatt, MD, MPH; Gregg C. Fonarow, MD; Ralph L. Sacco, MD, MS; Lee H. Schwamm, MD

**IMPORTANCE:** Mild strokes have been poorly represented in thrombolytic trials and only a few series have reported outcomes after treatment with intravenous (IV) recombinant tissue plasminogen activator (rtPA) after mild stroke.

**OBJECTIVE:** To report treatment complications and short-term outcomes in patients with mild stroke who have received treatment with IV rtPA.

**DESIGN, SETTING, AND PARTICIPANTS:** Retrospective analysis of patients treated in the emergency department of hospitals that use the Get With the Guidelines-Stroke registry, a prospectively collected quality improvement registry used by hospitals across the United States. Patients were those admitted between May 1, 2010, and October 1, 2012, with acute ischemic stroke within 4.5 hours from symptom onset and a baseline National Institutes of Health Stroke Scale score of 5 or less. Univariable and multivariable analyses were performed to identify factors independently associated with discharge outcomes and treatment complications.

**INTERVENTION:** Intravenous rtPA.

**MAIN OUTCOMES AND MEASURES:** Treatment complications included symptomatic intracranial hemorrhage, life-threatening or serious systemic hemorrhage, other serious complications, and undetermined complications. The short-term outcomes analyzed were in-hospital mortality, discharge to home, independent ambulation at discharge, and length of stay.

**RESULTS:** Among 33,995 patients who arrived within 4.5 hours of symptom onset and were treated with IV rtPA, 7621 (22.4%) had a National Institutes of Health Stroke Scale score of 5 or less and 5910 had complete data for analysis. Treatment complications were infrequent: symptomatic intracranial hemorrhage, 1.8%; life-threatening or serious systemic hemorrhage, 0.2%; other serious complications, 1.8%; and complications of undetermined cause, 2.4%. Mortality was low (1.3%), but at discharge 30.3% could not ambulate independently, 29.4% could not go directly home, and 73.0% had a length of stay of 3 days or longer. Worse short-term outcomes were seen in older patients, African American patients, diabetic patients, and those who arrived by ambulance, after hours, or with a higher National Institutes of Health Stroke Scale score.

**CONCLUSIONS AND RELEVANCE:** Many patients with ischemic stroke treated with IV rtPA have a mild stroke. Symptomatic intracranial hemorrhage is infrequent, but approximately 30% of these patients are unable to return directly home or ambulate independently at discharge. Additional studies are needed to identify strategies to improve the outcomes in patients with mild stroke who receive thrombolysis.

# Too Good To Treat????

## +/- IV tPA

### Effect of Intravenous Recombinant Tissue-Type Plasminogen Activator in Patients With Mild Stroke in the Third International Stroke Trial-3

#### Post Hoc Analysis

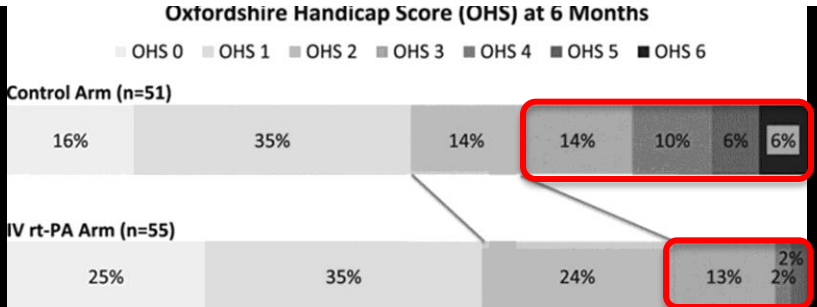
Pooja Khatri, MD, MSc; Darren Tayama, MD; Geoff Cohen, MSc; Richard I. Lindley, MD; Joanna M. Wardlaw, MD; Sharon D. Yeatts, PhD; Joseph P. Broderick, MD; Peter Sandercock, MD; on behalf of the PRISMS and IST-3 Collaborative Groups

***Background and Purpose***—Randomized trial evidence on the risk/benefit ratio of thrombolysis for mild stroke is limited. We sought to determine the efficacy of intravenous recombinant tissue-type plasminogen activator (IV r-tPA) in a subset of patients with mild deficit in the third International Stroke Trial (IST-3).

***Methods***—IST-3 compared IV r-tPA with control within 6 hours of onset in patients for whom IV r-tPA was considered promising but unproven. Analysis was restricted to subjects randomized within 3 hours of onset with a baseline National Institutes of Health Stroke Scale ≤5, pretreatment blood pressure <185/110, and no other r-tPA exclusion criteria. We compared r-tPA and control arms for primary (Oxfordshire Handicap Score [OHS] 0–2) and secondary (ordinal OHS and OHS 0–1) outcomes at 6 months.

***Results***—Among 3035 IST-3 subjects, 612 (20.2%) had an National Institutes of Health Stroke Scale ≤5; of these 106 (17.6%) met the restricted criteria. Allocation to r-tPA was associated with an increase in OHS 0 to 2 (84% r-tPA versus 65% control; adjusted odds ratio, 3.31; 95% confidence interval, 1.24–8.79) and a favorable shift in OHS distribution (adjusted odds ratio, 2.38; 95% confidence interval, 1.17–4.85). There was no significant effect of r-tPA on OHS 0 to 1 (60% versus 51%; adjusted odds ratio, 1.92; 95% confidence interval, 0.83–4.43).

***Conclusions***—This post hoc analysis in a highly selected sample of IST-3 supports the rationale of A Study of the Efficacy and Safety of Activase (Alteplase) in Patients With Mild Stroke (PRISMS) trial—a randomized, phase IIIb study to evaluate IV r-tPA in mild ischemic stroke. **(*Stroke*. 2015;46:2325-2327. DOI: 10.1161/STROKEAHA.115.009951.)**




36% Poor Outcomes

17% Poor Outcomes

# Too Good To Treat????

- Summary of the Data:
  - 20-30% of Low Baseline NIHSS AIS may not do well even after IV tPA.
  - Frequency of deterioration and bad outcomes likely significantly higher in the presence of LVOS
- Best Management:
  - No RCT data – two ongoing IV tPA RCTs (PRISMS)
  - If standard risk = offer treatment after careful discussion with patient/ family. Specially if:
    - Fluctuating NIHSS
    - Auto-hypertensive
    - + Clinical Stress Test (Sit up, Stand up)
    - CT Perfusion suggestive of potential collateral failure

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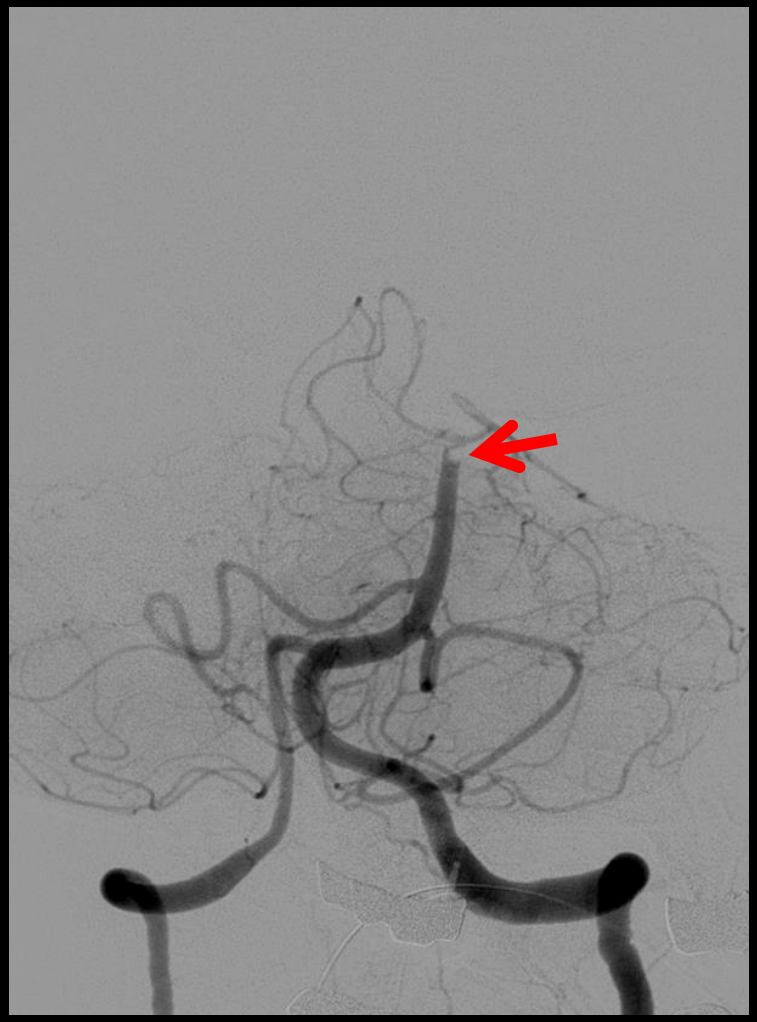
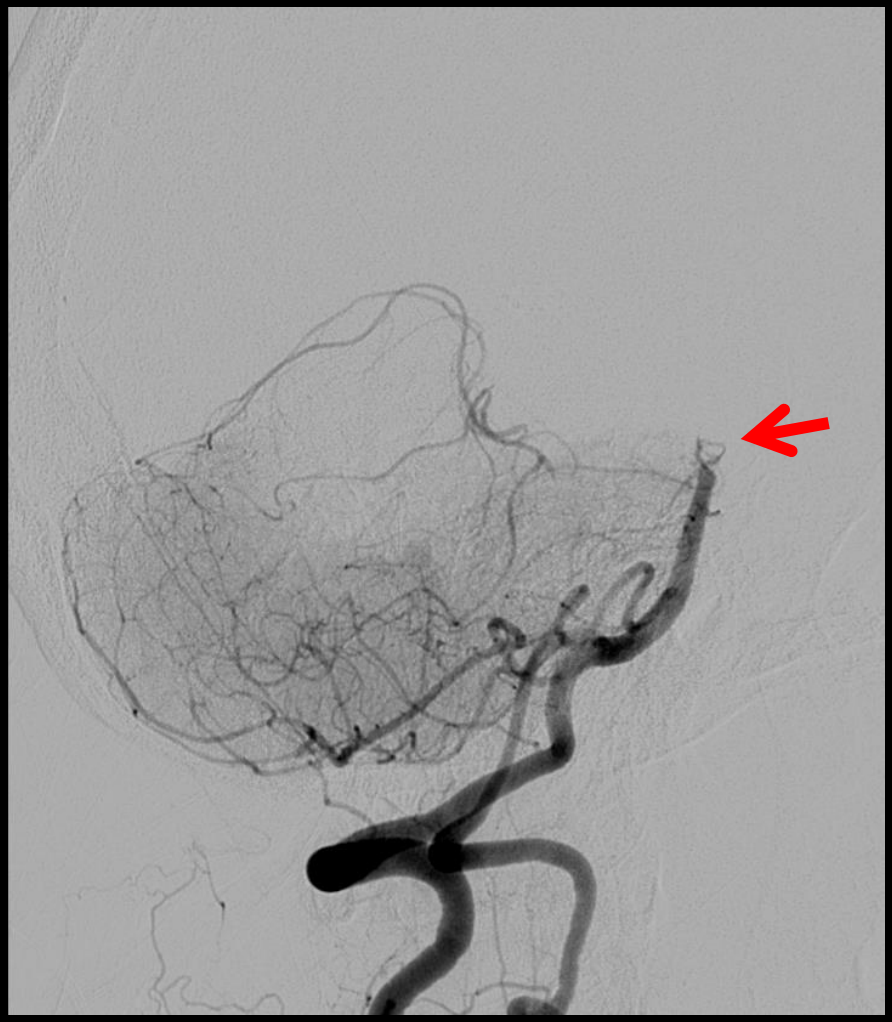
# Low NIHSS with Fluctuation:

76 y/o F presenting with diplopia, vertigo, and left hemiparesis
Symptoms improved to NIHSS 4





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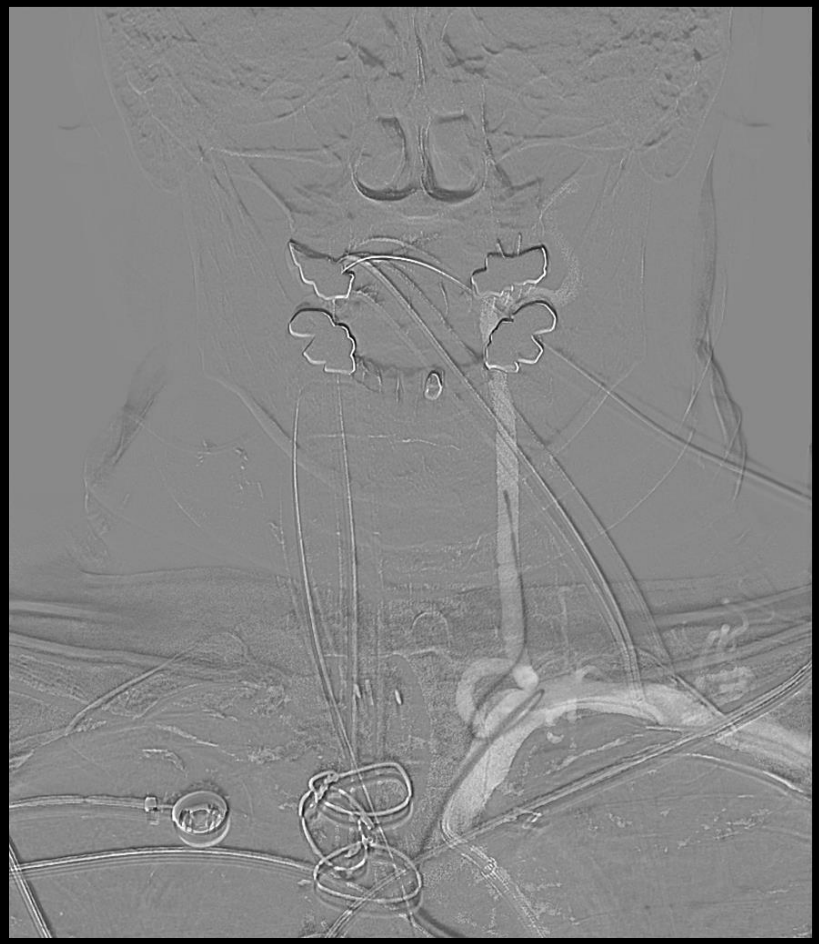
# Low NIHSS with Fluctuation:

## Marked Tortuousity of LVA



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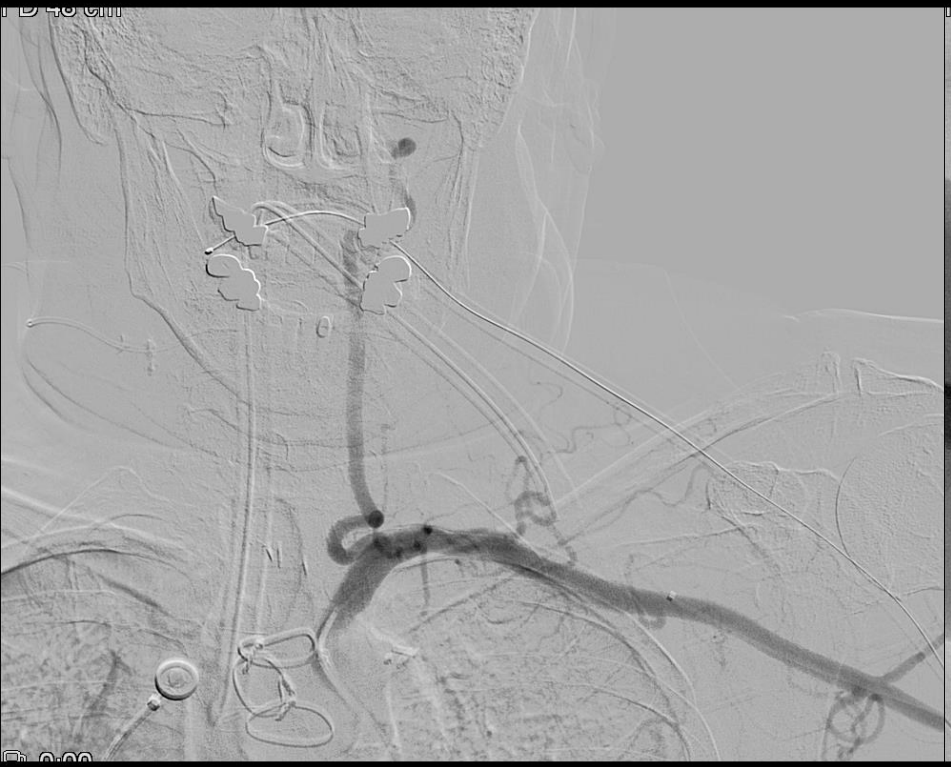
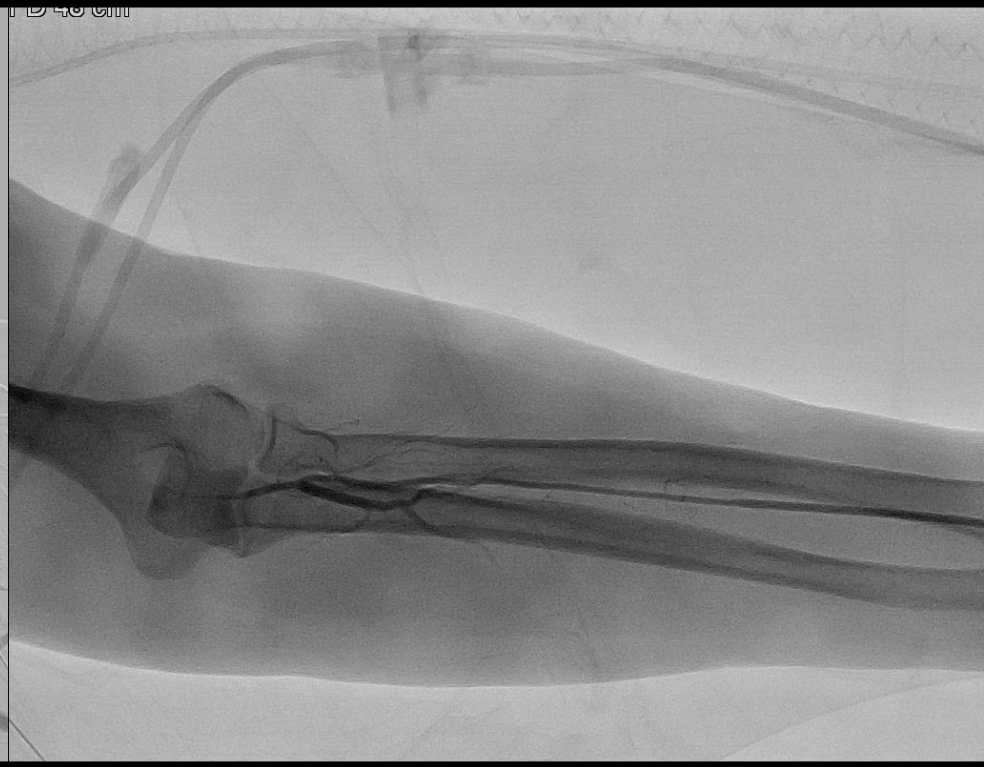
# Low NIHSS with Fluctuation:

## Transradial Approach





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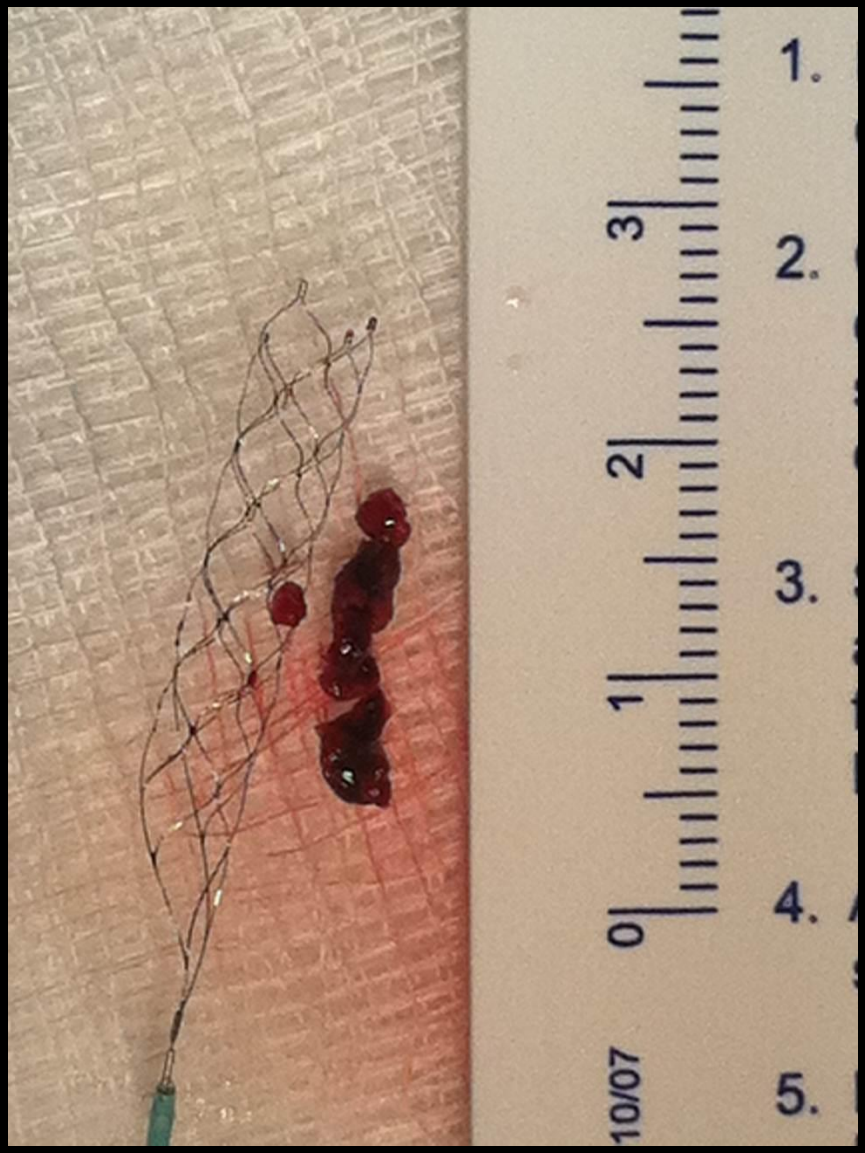
# Low NIHSS with Fluctuation:

**Full Reperfusion - TICI 3**

# Low NIHSS with Fluctuation:

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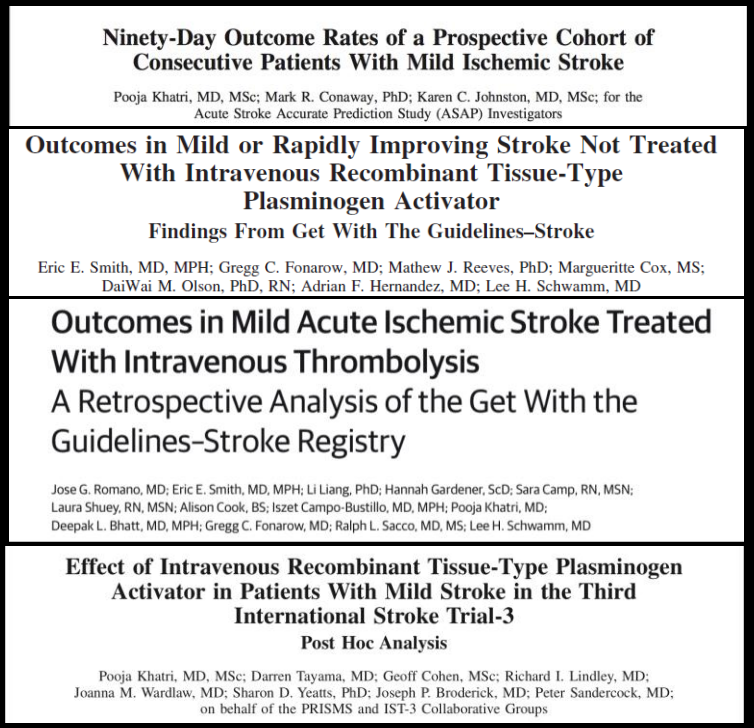
# Distal Occlusions?

# Occlusion Site, NIHSS, and Disability



**Ninety-Day Outcome Rates of a Prospective Cohort of Consecutive Patients With Mild Ischemic Stroke**

Pooja Khatri, MD, MSc; Mark R. Conaway, PhD; Karen C. Johnston, MD, MSc; for the Acute Stroke Accurate Prediction Study (ASAP) Investigators

**Outcomes in Mild or Rapidly Improving Stroke Not Treated With Intravenous Recombinant Tissue-Type Plasminogen Activator**

**Findings From Get With The Guidelines–Stroke**

Eric E. Smith, MD, MPH; Gregg C. Fonarow, MD; Mathew J. Reeves, PhD; Marguerite Cox, MS; DaiWai M. Olson, PhD, RN; Adrian F. Hernandez, MD; Lee H. Schwamm, MD

**Outcomes in Mild Acute Ischemic Stroke Treated With Intravenous Thrombolysis**

A Retrospective Analysis of the Get With the Guidelines–Stroke Registry

Jose G. Romano, MD; Eric E. Smith, MD, MPH; Li Liang, PhD; Hannah Gardener, ScD; Sara Camp, RN, MSN; Laura Shuey, RN, MSN; Alison Cook, BS; Iszet Campo-Bustillo, MD, MPH; Pooja Khatri, MD; Deepak L. Bhatt, MD, MPH; Gregg C. Fonarow, MD; Ralph L. Sacco, MD, MS; Lee H. Schwamm, MD

**Effect of Intravenous Recombinant Tissue-Type Plasminogen Activator in Patients With Mild Stroke in the Third International Stroke Trial-3**

**Post Hoc Analysis**

Pooja Khatri, MD, MSc; Darren Tayama, MD; Geoff Cohen, MSc; Richard I. Lindley, MD; Joanna M. Wardlaw, MD; Sharon D. Yeatts, PhD; Joseph P. Broderick, MD; Peter Sandercock, MD; on behalf of the PRISMS and IST-3 Collaborative Groups

## Low Baseline NIHSS:

20-30% of AIS with NIHSS ≦5 do not do well even after IV tPA

- Proximal Occlusions with Good Collaterals but Subsequent Failure
- Distal Occlusions in Eloquent Territories

## Mismatch between NIHSS and 90-day mRS/ Disability:

- ACA stroke with dense lower extremity plegia: NIHSS=4; 90-day mRS=4
- Left M3 stroke with receptive aphasia: NIHSS=5; 90-day mRS>2

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# Should We Treat MCA-M3, ACA, PCA Occlusions?

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# Can We Treat M3, ACA, PCA Occlusions?

## Yes, we have fine tuned tools for distal occlusions







CASE SERIES

### The Trevo XP 3×20 mm retriever ('Baby Trevo') for the treatment of distal intracranial occlusions

Diogo C Haussen, Andrey Lima, Raul G Nogueira

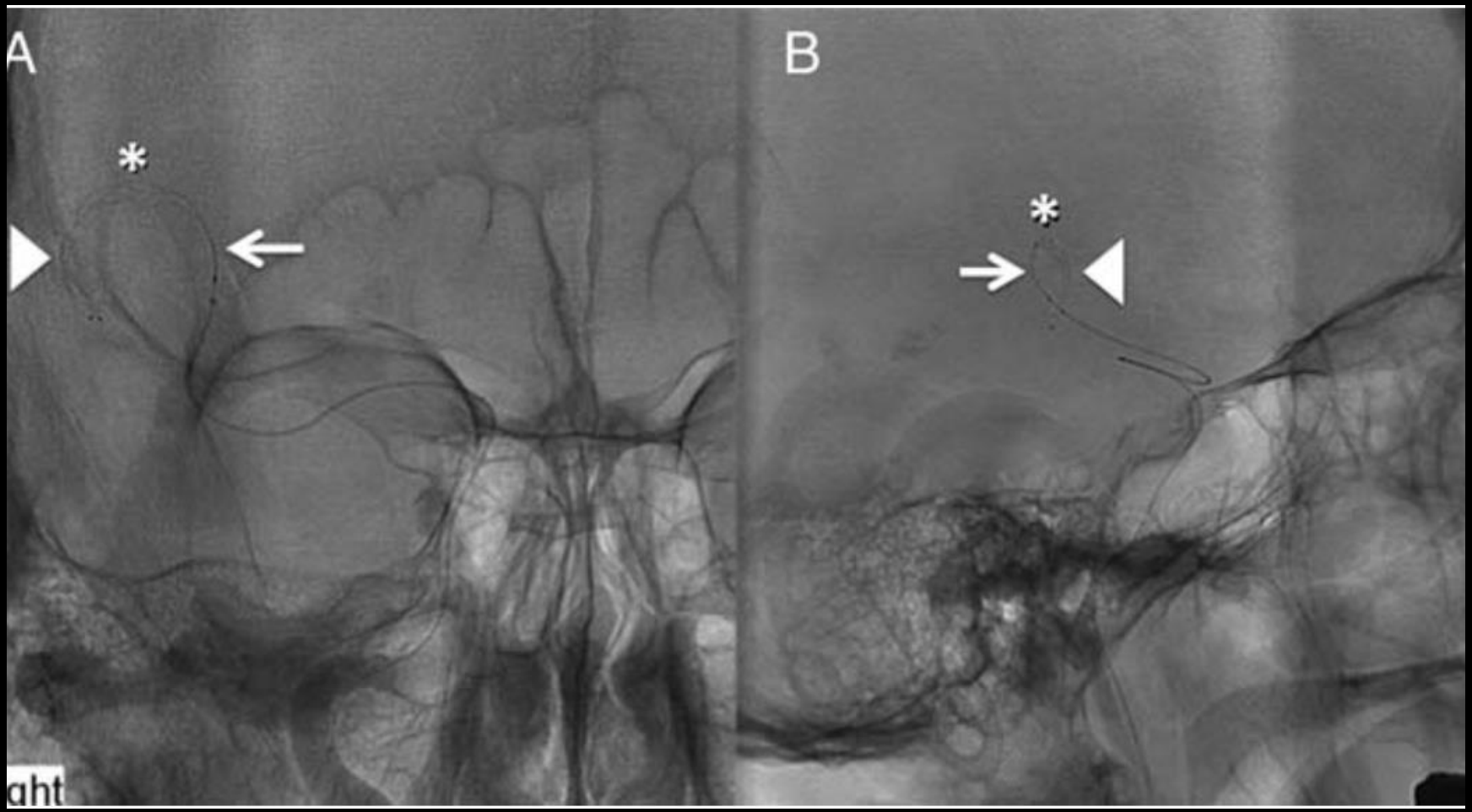
*J NeuroIntervent Surg* 2015;**0**:1–5. doi:10.1136/neurintsurg-2014-011613

**Table 1** Demographics and treatment variables

| Case No | Age (years) | NIHSS | Baseline occlusion | Treatment | Residual occlusion | Treatment | Overall reperfusion | Baby Trevo reperfusion |
|---|---|---|---|---|---|---|---|---|
| 1 | 64 | 12 | MCA M1 | Trevo 4×20 | MCA M3 (sup div) | Baby Trevo | TICI 2b | TICI 2a/AOL3 |
| 2 | 39 | 18 | MCA M1 | Trevo 4×20 | MCA M3 (sup div)* | Baby Trevo | TICI 2b | TICI 2b/AOL3 |
| 3 | 17 | 15 | MCA M3 (sup div)† | Baby Trevo (larger M3) | MCA M3 (smaller M3) | IA tPA | TICI 2b | TICI 2b/AOL3 |
| 4 | 57 | 25 | ICA terminus | Solitaire 6×30 | MCA M3 (sup and inf div) | Baby Trevo | TICI 2b | TICI 2b/AOL3‡ |
| 5 | 26 | 26 | BA proximal | Trevo 4×20 | PCA P3 | 3 Max/Baby Trevo | TICI 2b | TICI 2b/AOL3 |
| 6 | 70 | 14 | BA proximal | Trevo 4×20 | PCA P2–3 | Baby Trevo | TICI 2b | TICI 2a/AOL3 |
| 7 | 76 | 21 | ACA A4 | Baby Trevo (ACA) | – | – | TICI 3 | TICI 3/AOL3 |
| | | | MCA M1 | Solitaire (MCA) | MCA M3 (inf div) | 3 Max | | |
| 8 | 63 | 25 | ACA A3 | Baby Trevo (ACA) | ACA Callosomarginal | IA tPA/Baby Trevo | TICI 2b | TICI 3/AOL3 |
| | | | MCA M3s§ | | | | | |

# Stentriever in the MCA-M3

## Distal Curvy Anatomy but no “S”Curves

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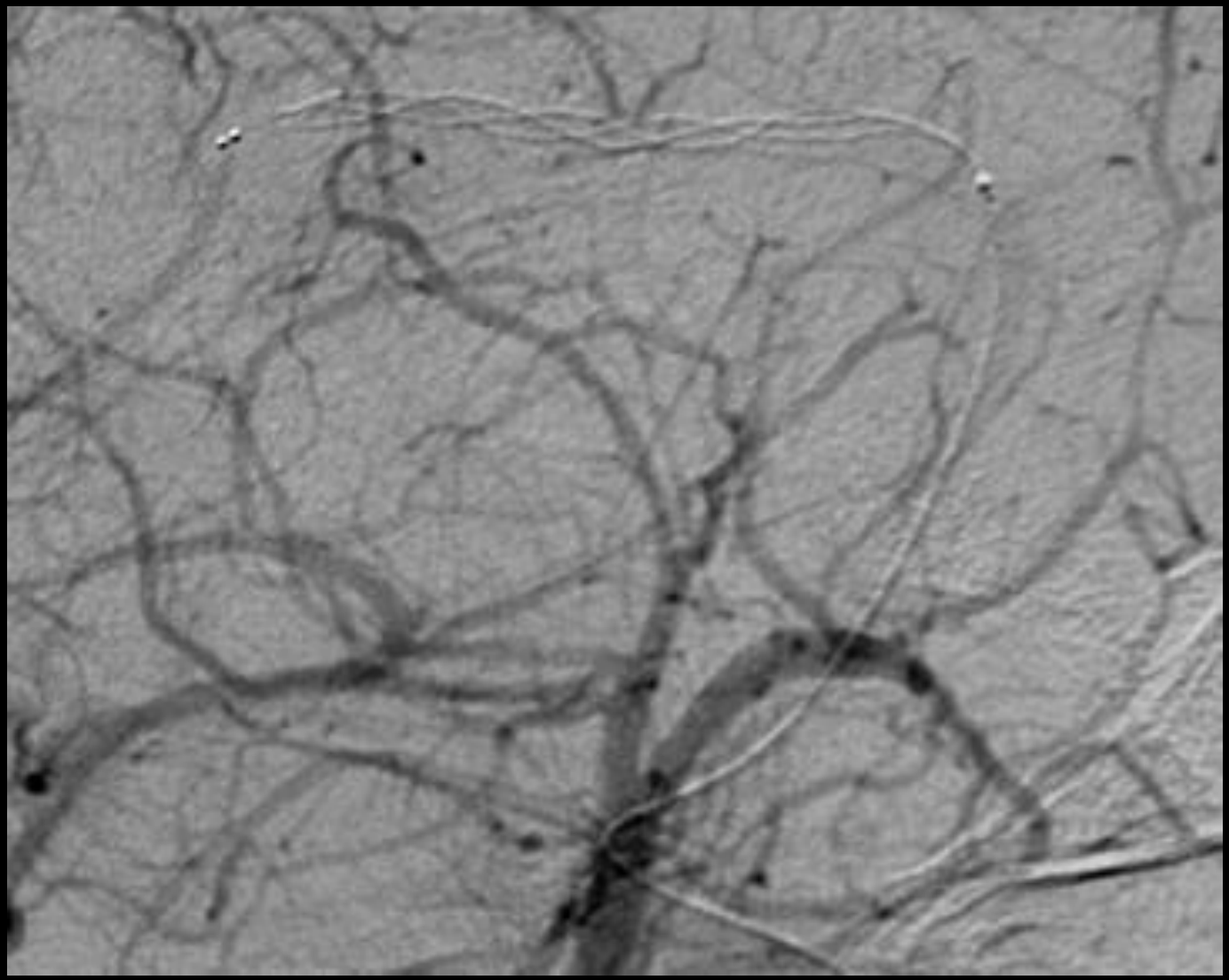
# Stentriever in the ACA-A2/3



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# Treatment of Distal Occlusions: Risks

Just because we can do it…
it doesn't mean we should always do it…

## Care with distal superior division branches!

82yo, baseline mRS=0, unknown onset (no IV tPA), NIHSS 12.

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# Should We Treat M3, ACA, PCA Occlusions?

## To Do or Not To Do: Basic Concepts

A. Tissue Viability

B. Eloquence of the Territory Supplied

C. Individualized Disability

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# Distal Occlusions and Tissue Viability

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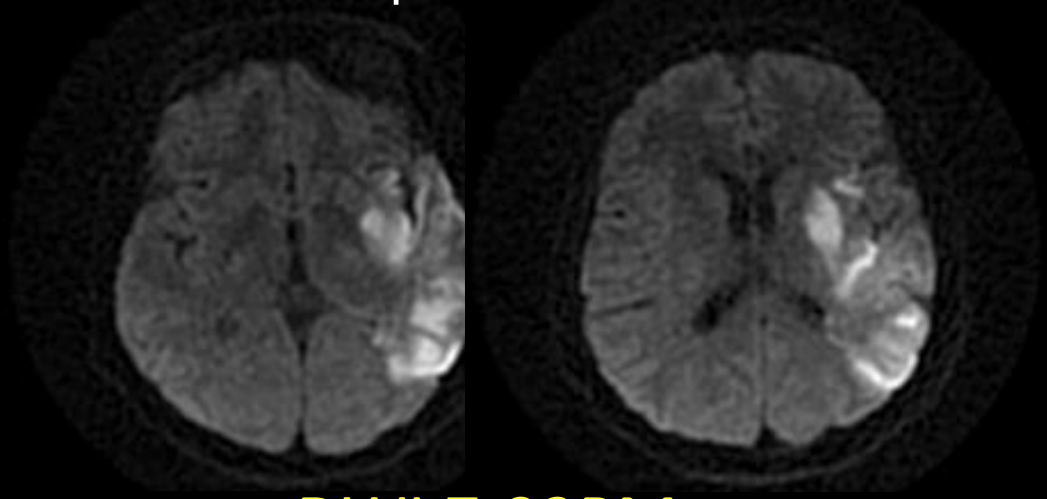
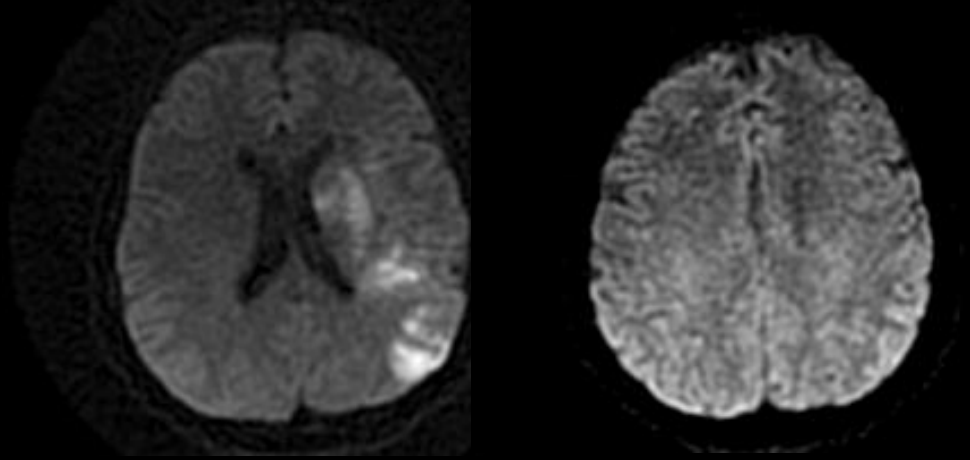
# Long/ Tandem Clots: M1-M3

39 yo 2 months pregnant, with acute onset of R HP, L gaze, and aphasia upon awakening at 4pm. Last known well unknown. On arrival at MSNC patient has NIHSS of 17



DWI 7:02PM



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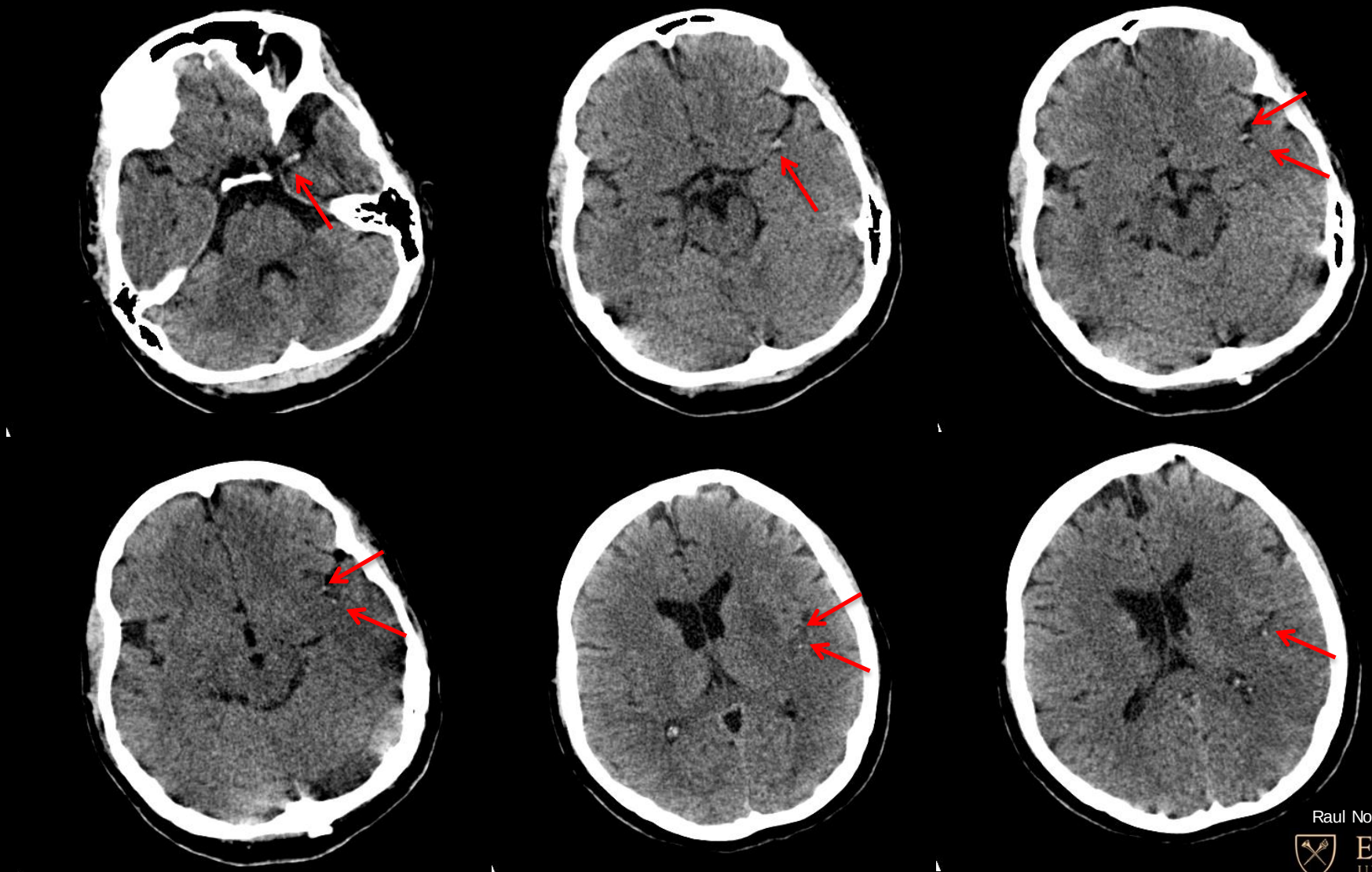
# Long/ Tandem Clots: M1-M3

## Non-Contrast CT: M1-M2-M3 Clots



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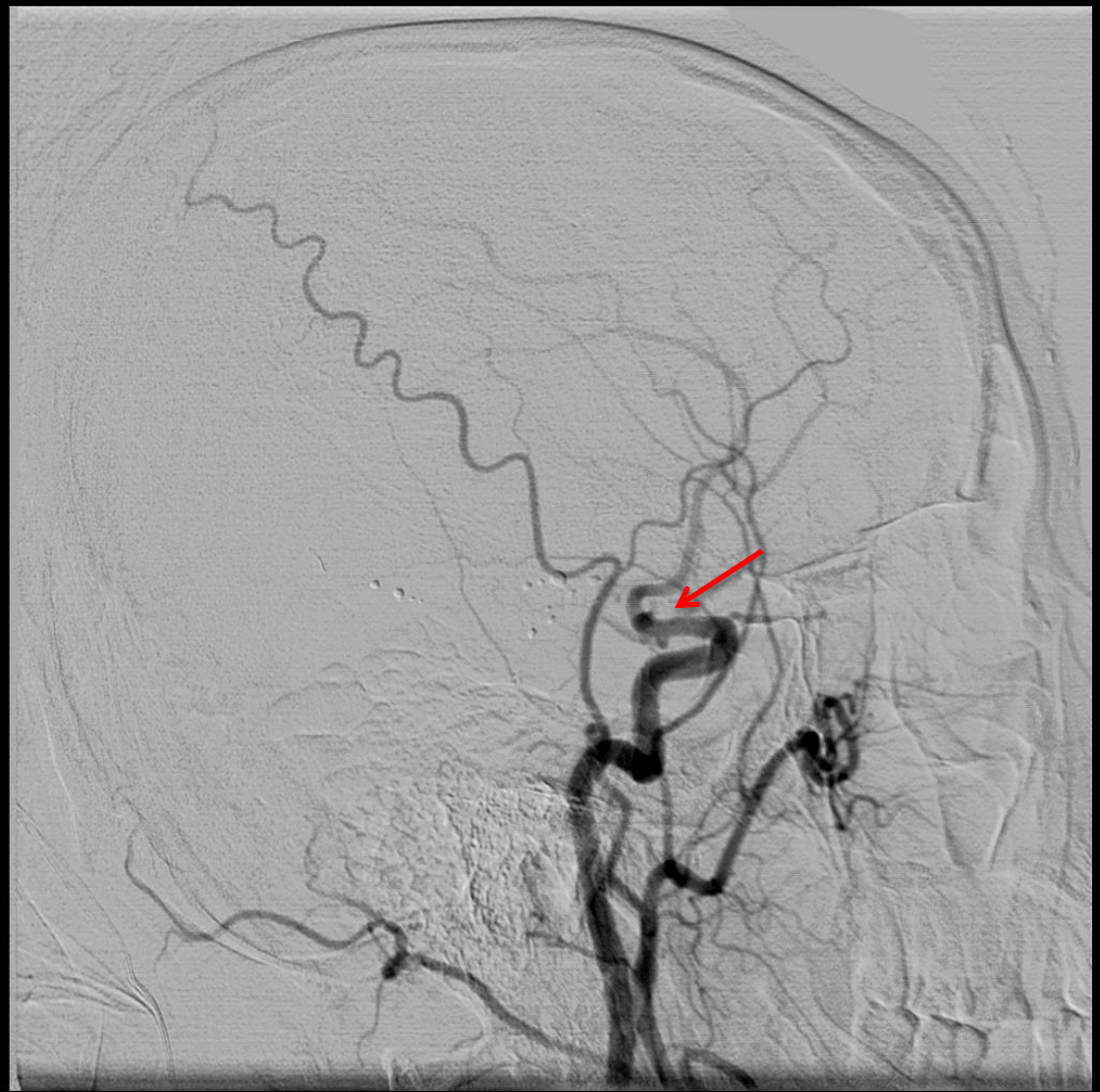
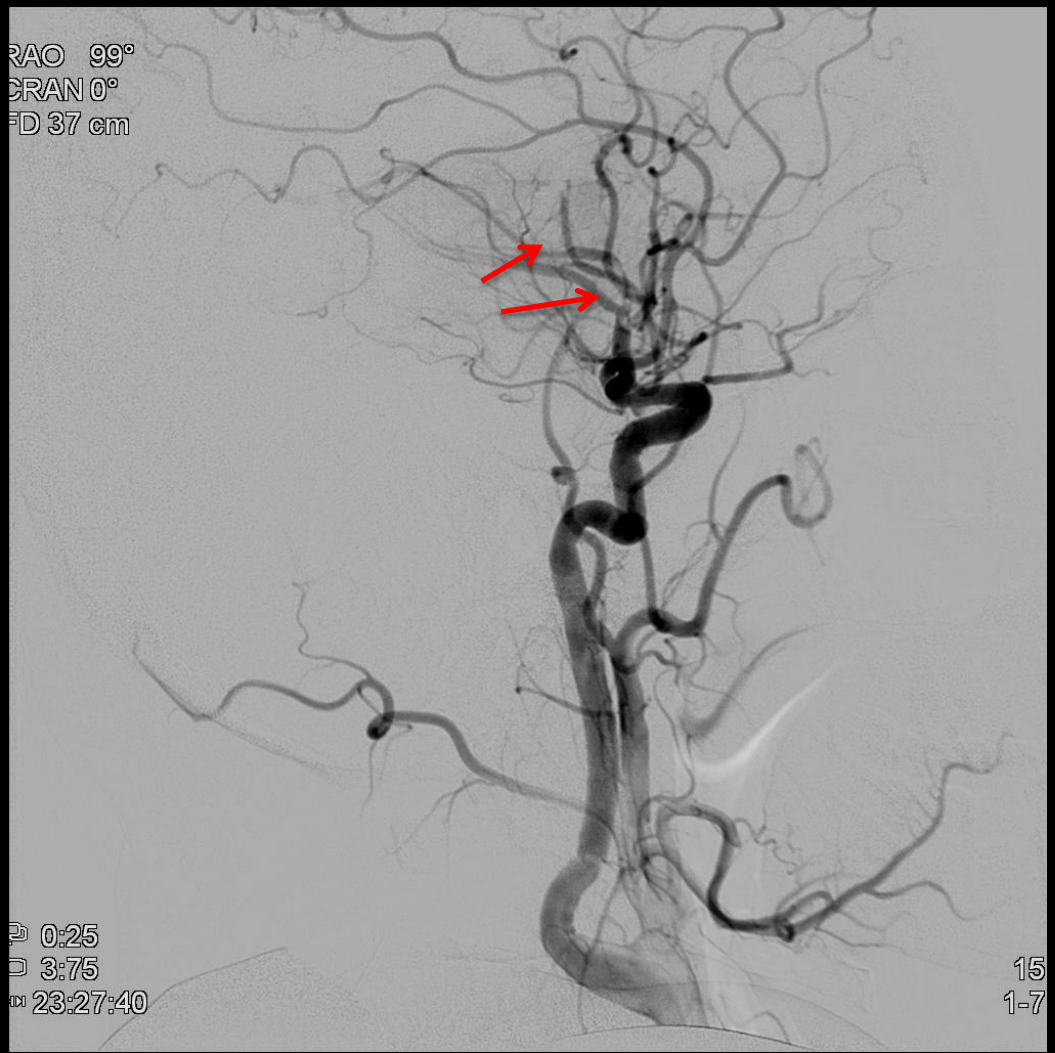
# Arterial Access 22:35 - Left M1 Occlusion

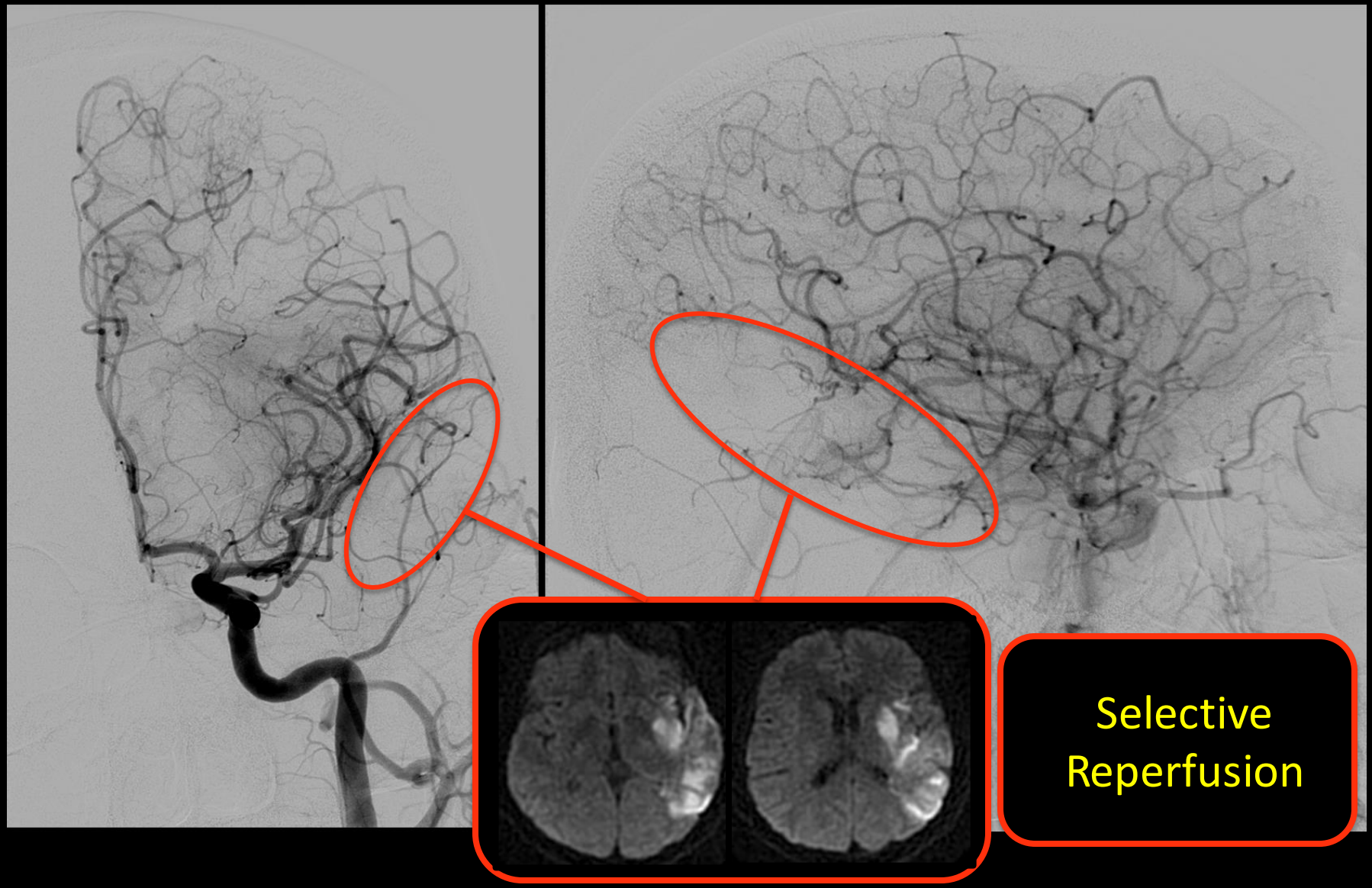


# Post Stentriever 4x20: Residual Distal M2-M3 Occlusion



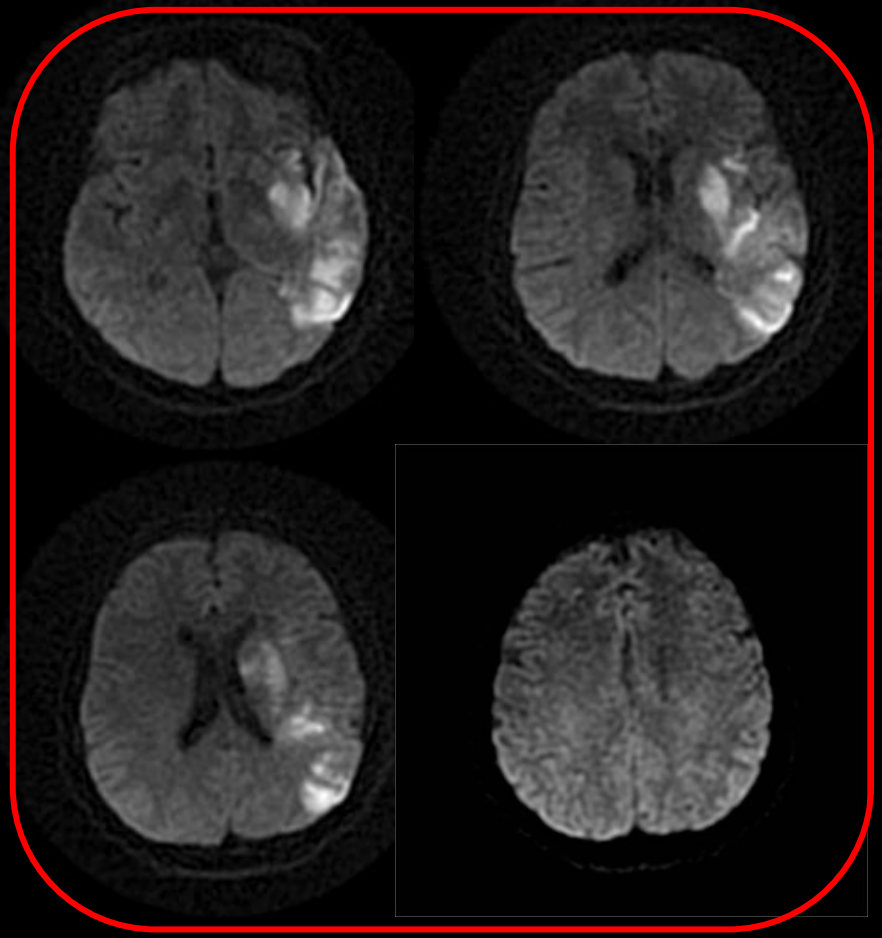
# Stentriever 3x20 in M2-M3

# TICI 2B but Full Reperfusion of the Target Territory

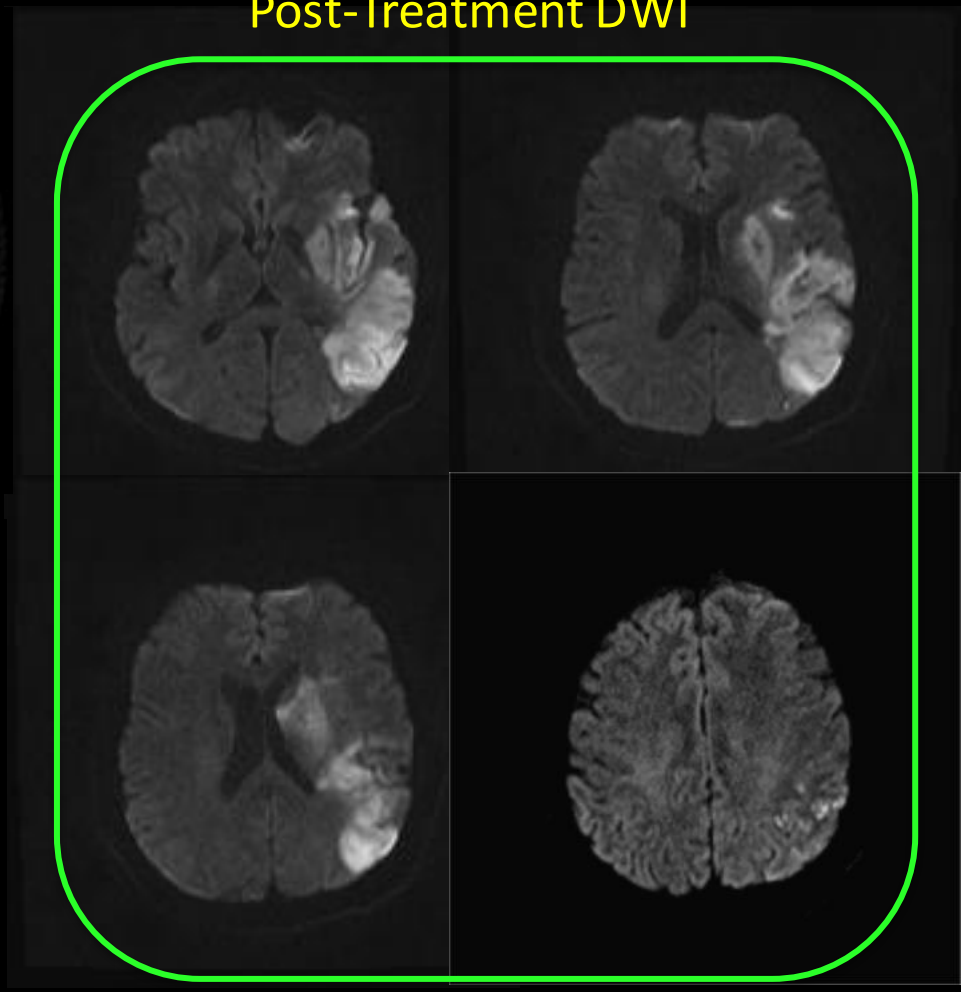


# Penumbral Area Completed Spared

Pre-Treatment DWI



Post-Treatment DWI



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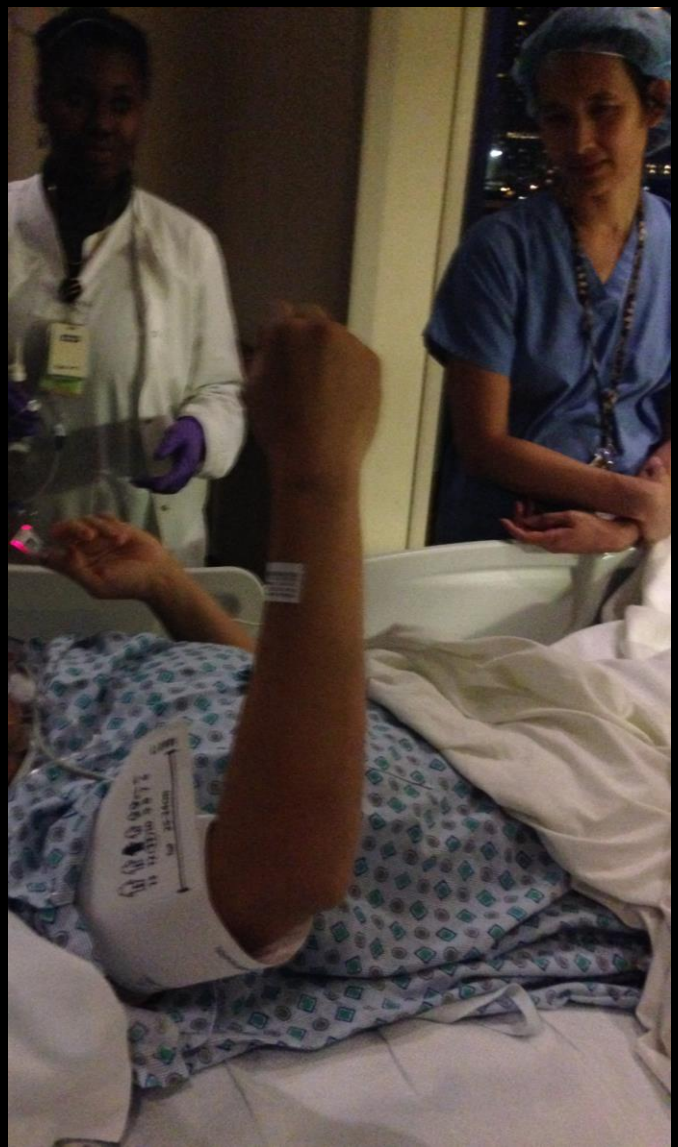
# She will be able to hold her baby!



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# Distal Occlusions and Eloquence of the Territory Supplied

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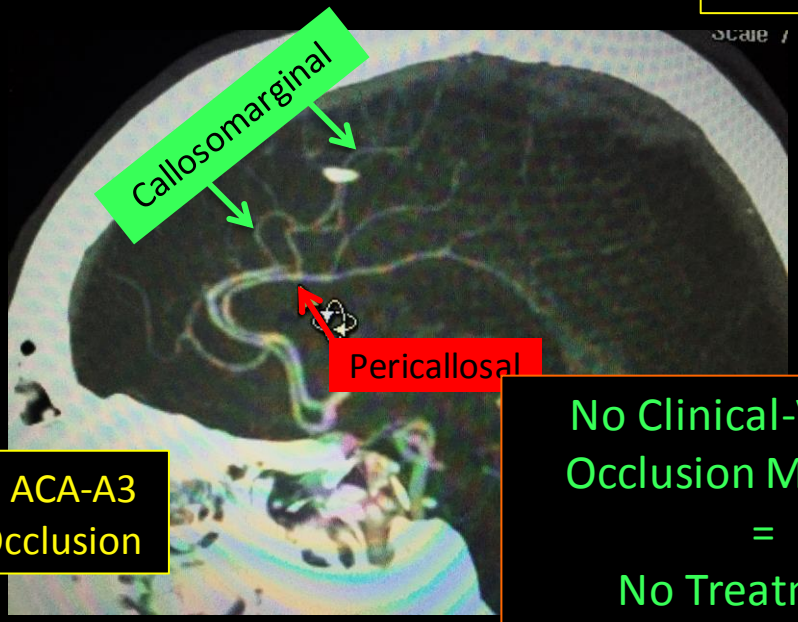
# ACA Occlusion #1

81 yo man h/o CHF and Afib on Warfarin (INR 1.3) - L LE plegia and mild L Face/UE paresis upon awakening. NIHSS: 6 (4+1+1). Family also described urinary incontinence and "odd behavior"/confusion

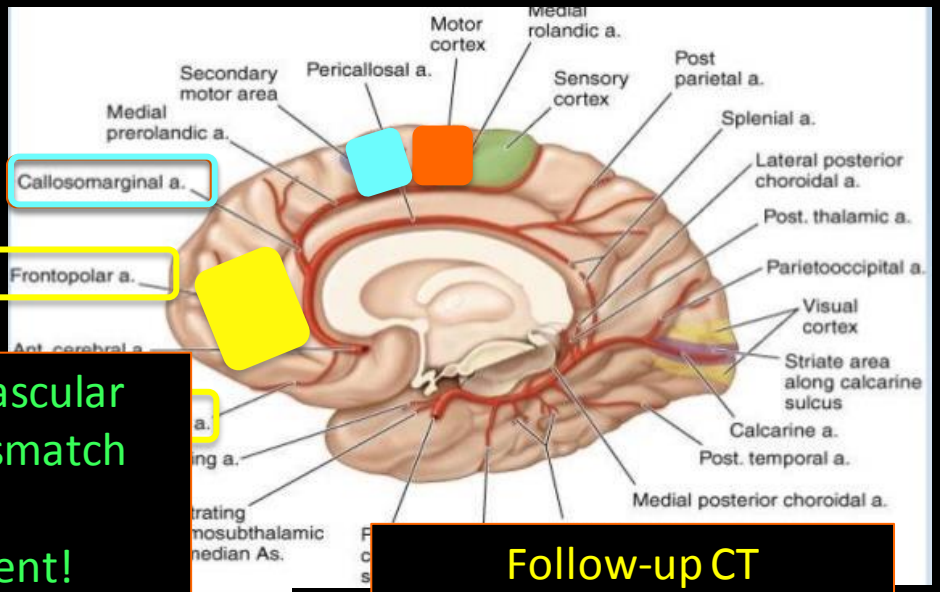
SMA

Motor Cortex

Prefrontal Cortex

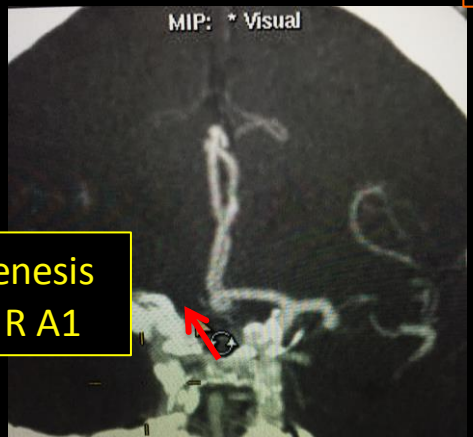



R ACA-A3 Occlusion

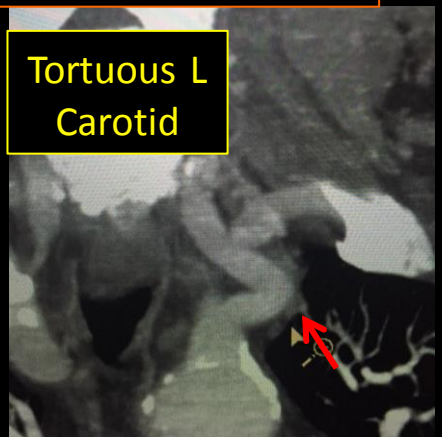



No Clinical-Vascular Occlusion Mismatch = No Treatment!

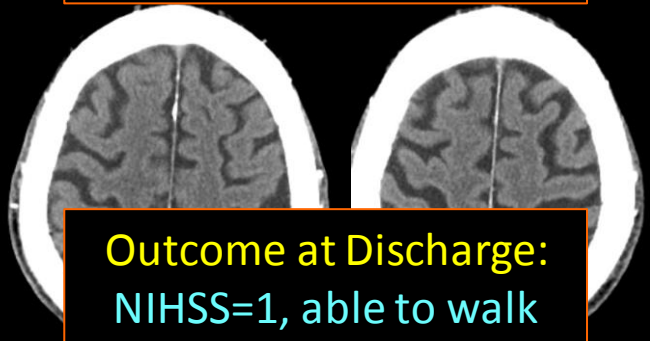
Follow-up CT




Agenesis of R A1



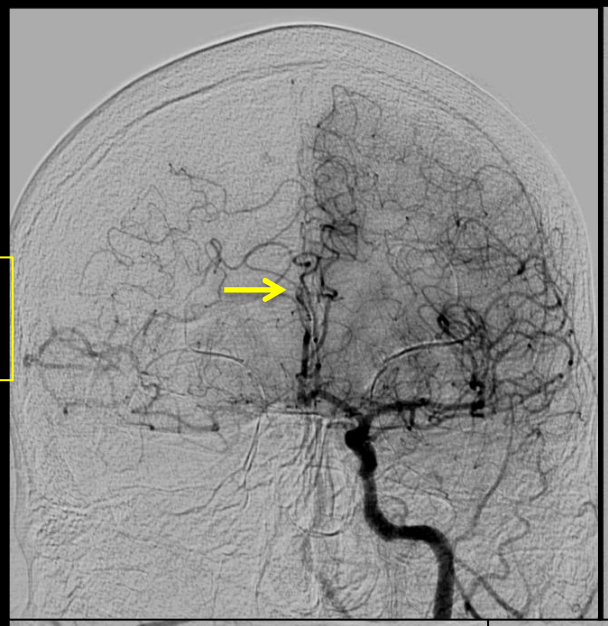
Tortuous L Carotid

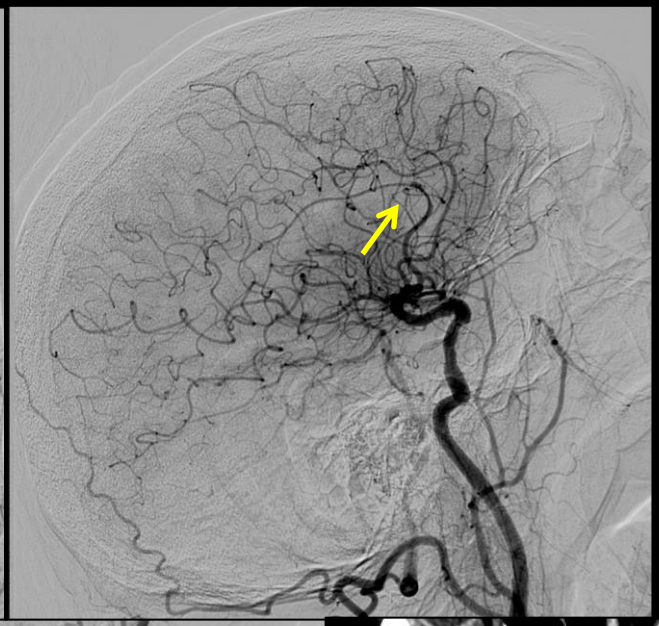


Outcome at Discharge: NIHSS=1, able to walk without assistance

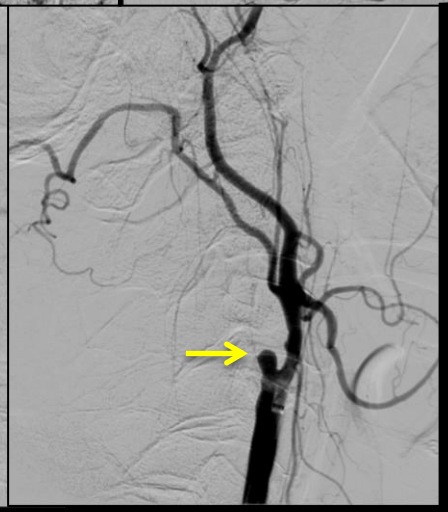
# ACA Occlusion #2

69 yo man h/o TIA awoke with LLE weakness. He progressed to full left hemiplegia over an hour while at OSH. Also L hemineglect, LHH, and R gaze preference (NIHSS=14)

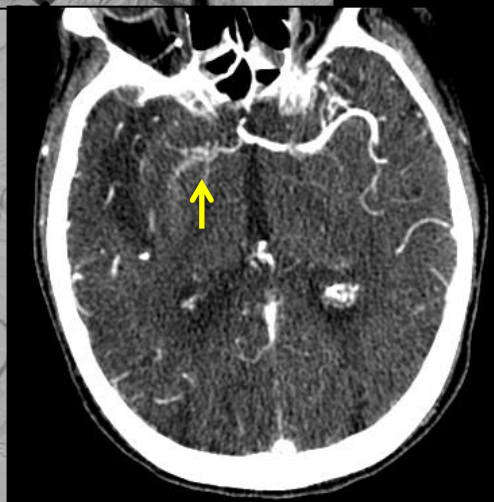




Distal R ACA-A2 Occlusion



Chronic ICA Occlusion



Tiny A1 and MCA

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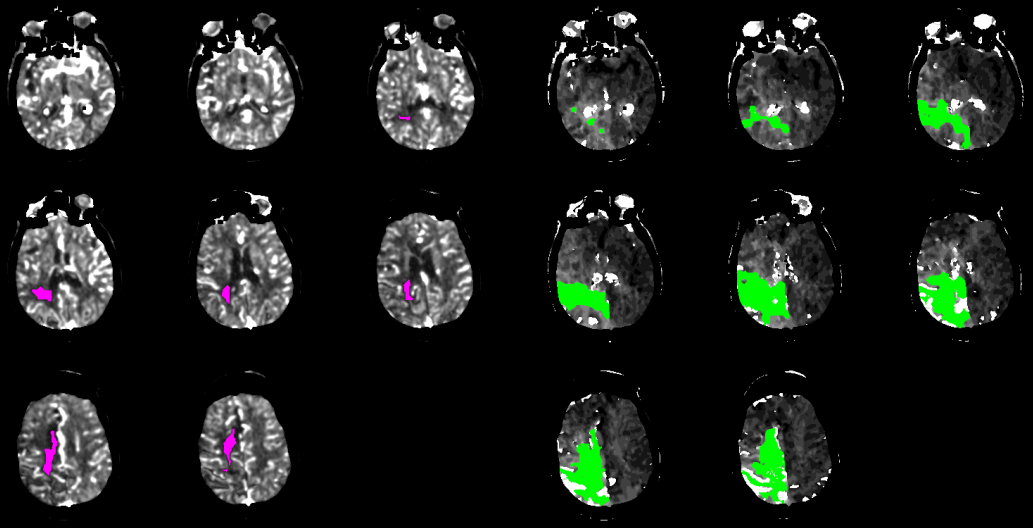
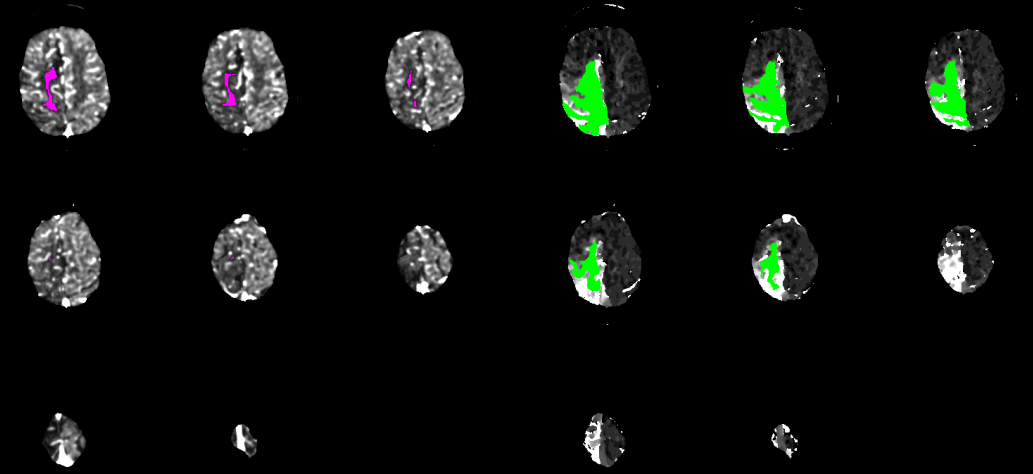
# ACA Occlusion #2

08/16/15



CBF (<30%) volume: 6.6 ml Perfusion (Tmax>6.0s) volume: 64.6 ml
Mismatch volume: 58.0 ml
Mismatch ratio: 9.8

~100 cc
MISMATCH!



CBF (<30%) volume: 3.5 ml Perfusion (Tmax>6.0s) volume: 39.3 ml
Mismatch volume: 35.8 ml
Mismatch ratio: 11.2

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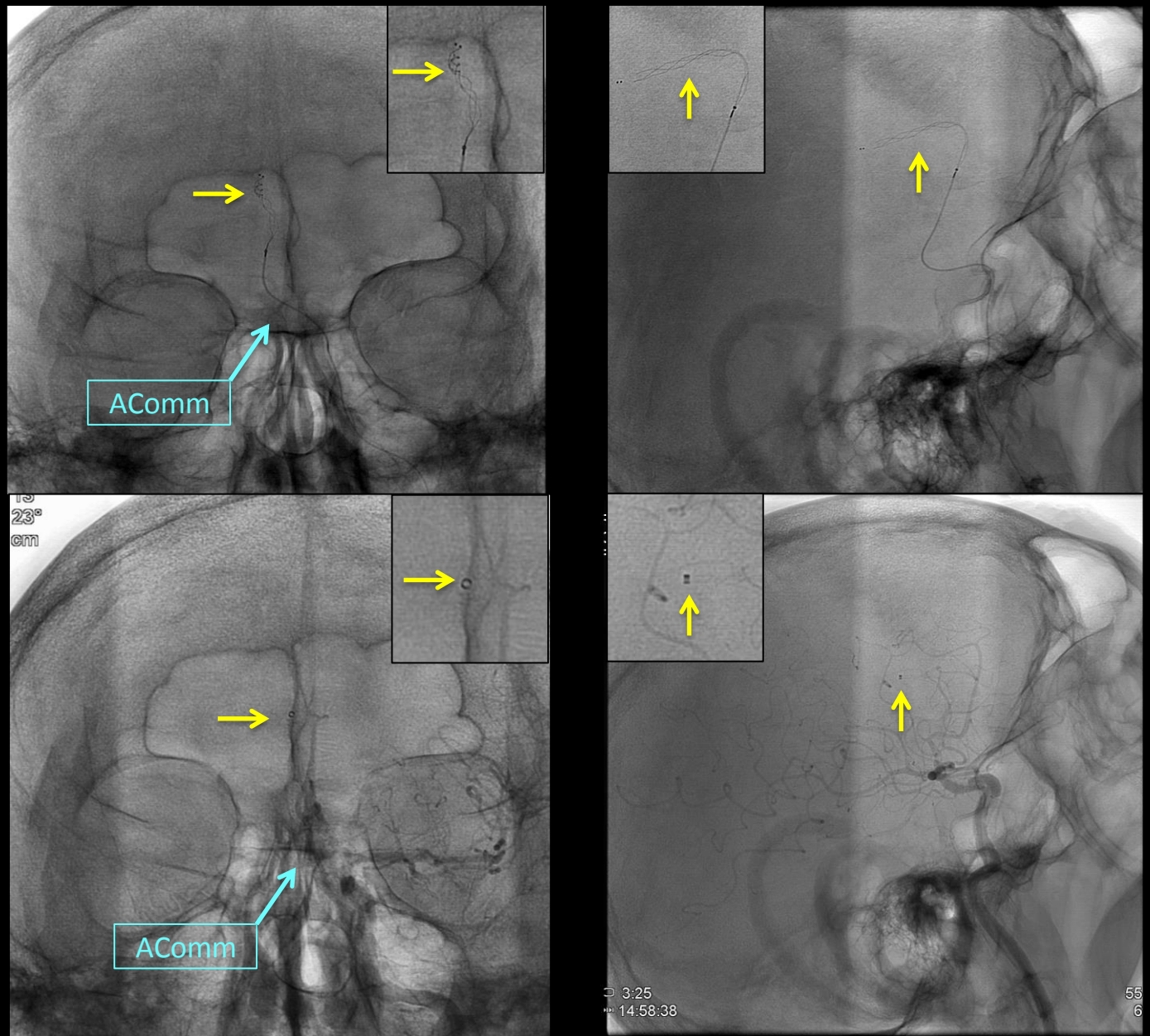
# ACA Occlusion #2

Trevo XP
3x20mm

Penumbra
3-Max

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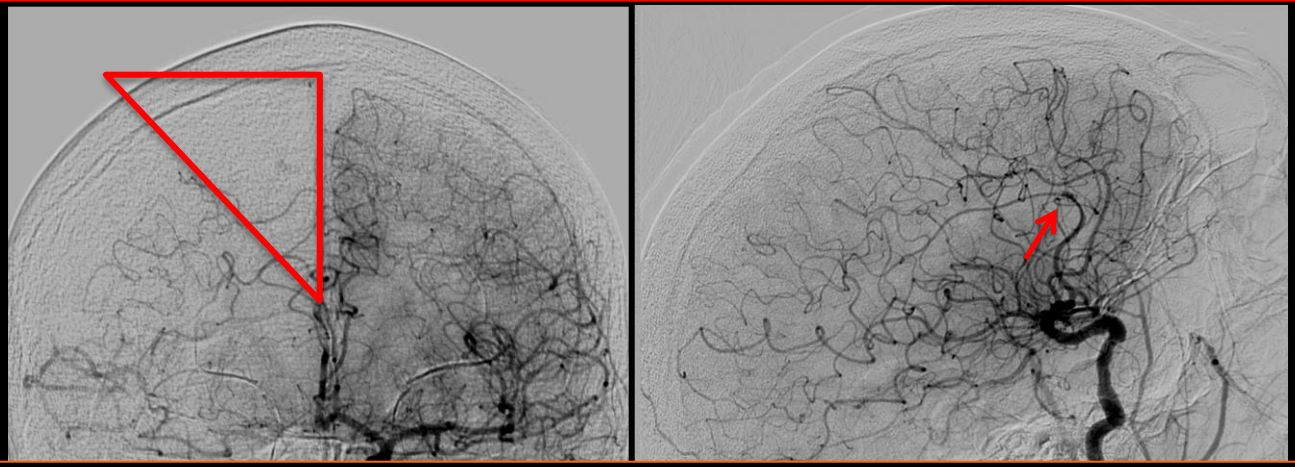
# ACA Occlusion #2

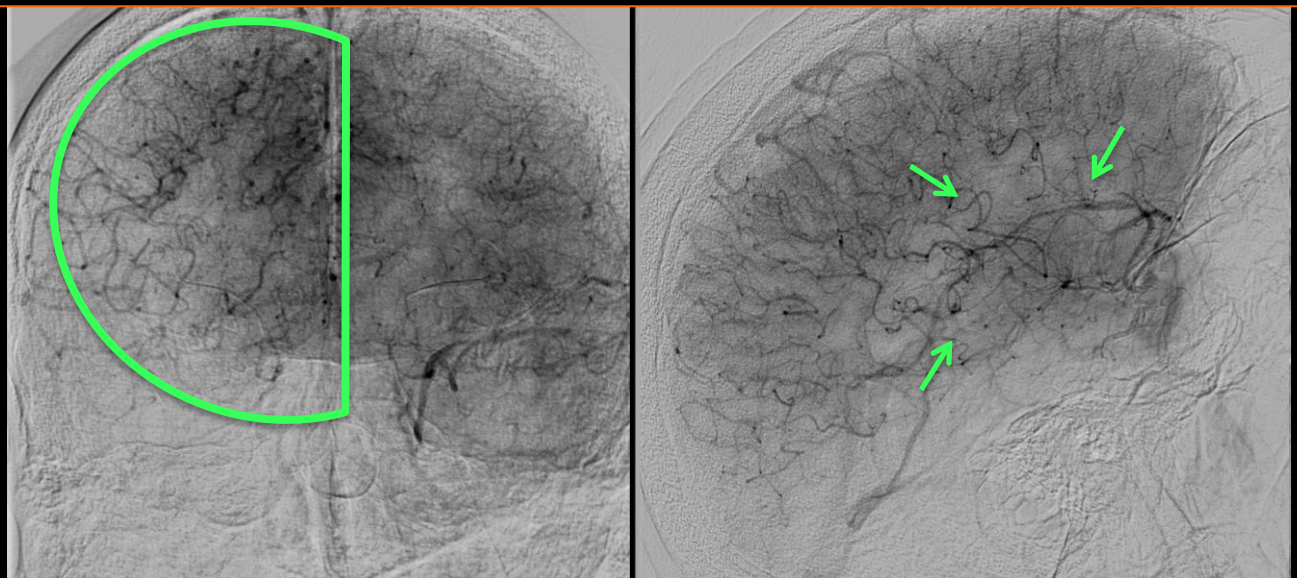
Pre-IAT



Chronic R Cervical + Cavernous ICA + Acute R ACA Occlusion
= AComm Crossing

TICI 3 Reperfusion

Post-IAT



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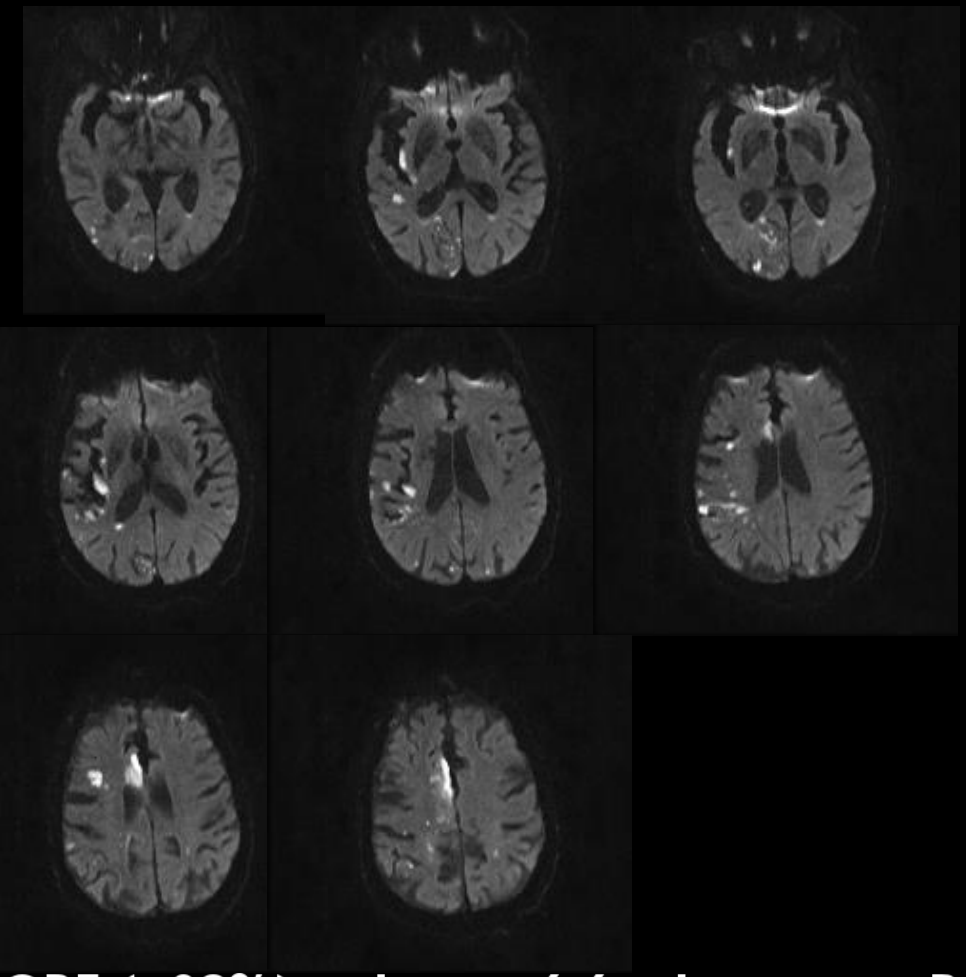
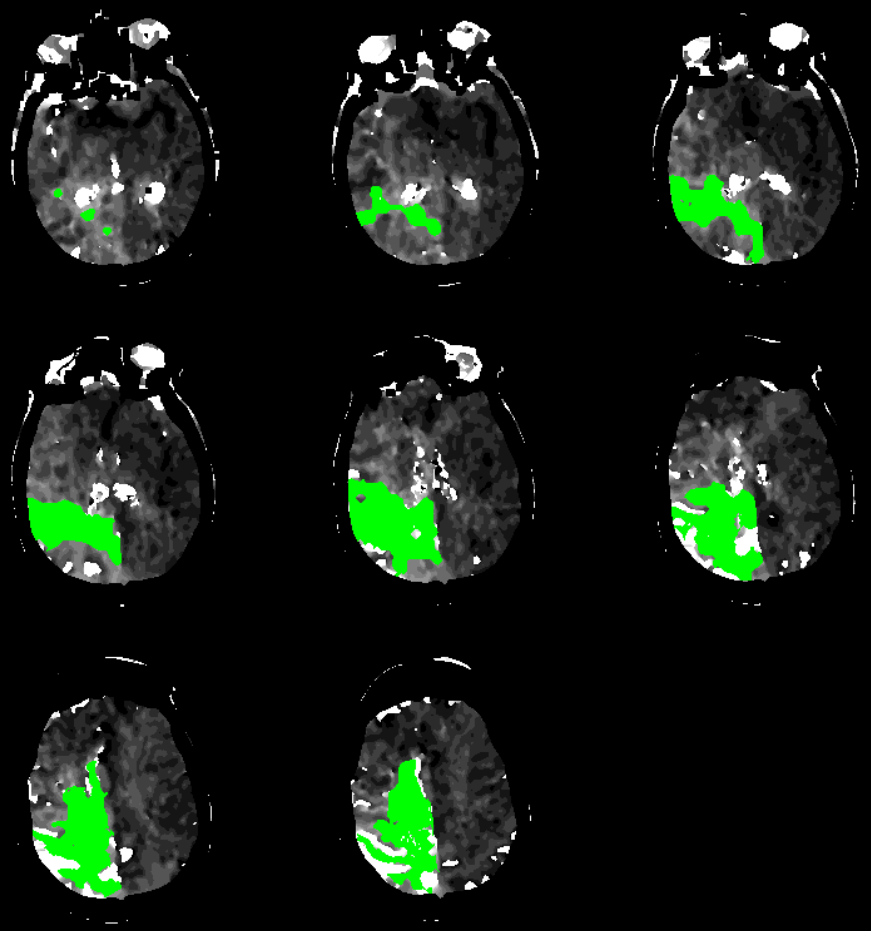
# ACA Occlusion #2





CBF (<30%) volume: 6.6 ml

Perfusion (Tmax>6.0s) volume: 64.6 ml

Mismatch volume: 58.0 ml

Mismatch ratio: 9.8

Follow-up MRI 08/19/15

Baseline CTP TMax 08/16/15

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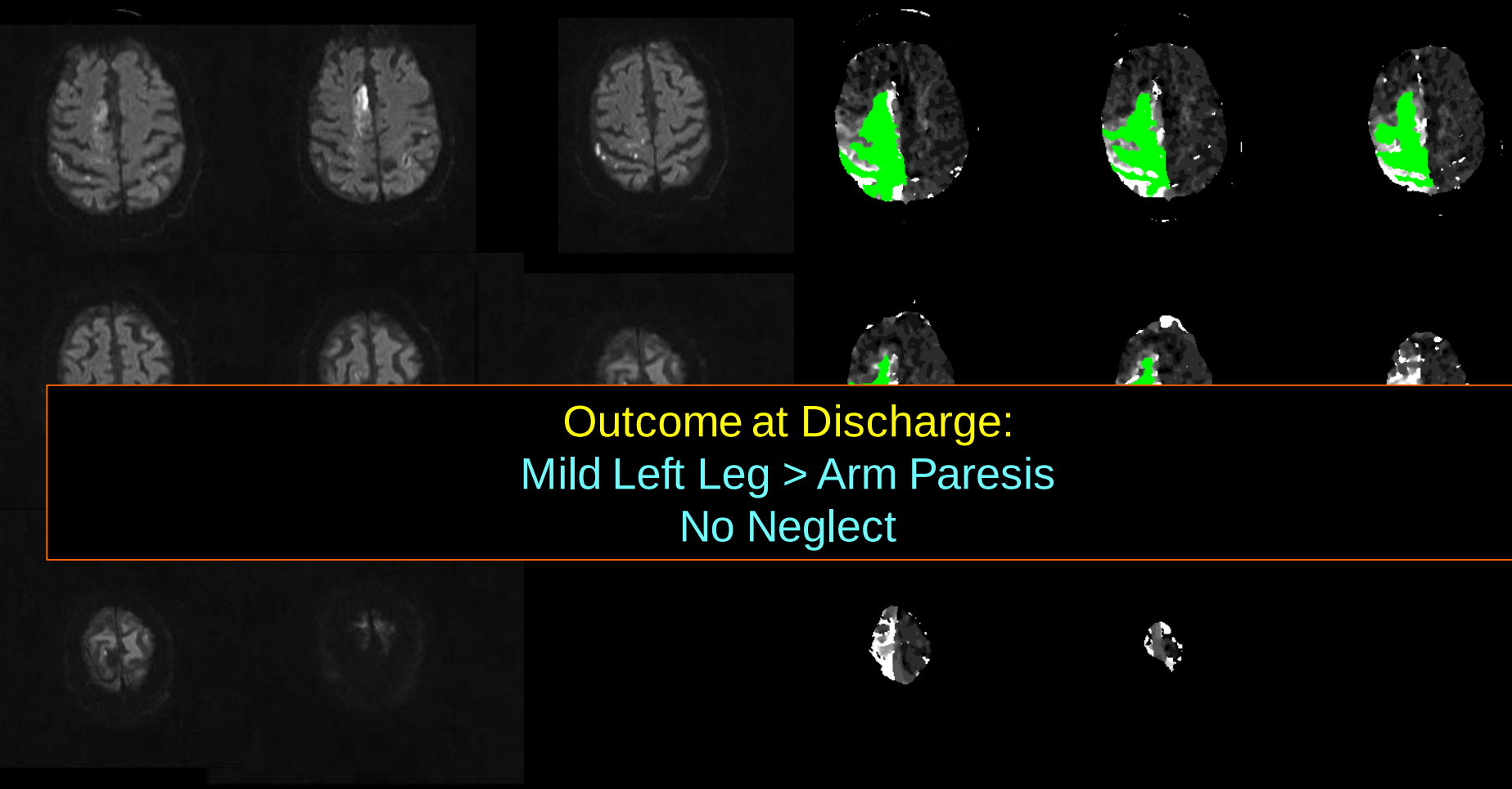
# ACA Occlusion #2



Outcome at Discharge:
Mild Left Leg > Arm Paresis
No Neglect

CBF (<30%) volume: 3.5 ml
Perfusion (Tmax>6.0s) volume: 39.3 ml
Mismatch volume: 35.8 ml
Mismatch ratio: 11.2

Follow-up MRI 08/19/15

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# Distal Occlusions and Individualized Disability

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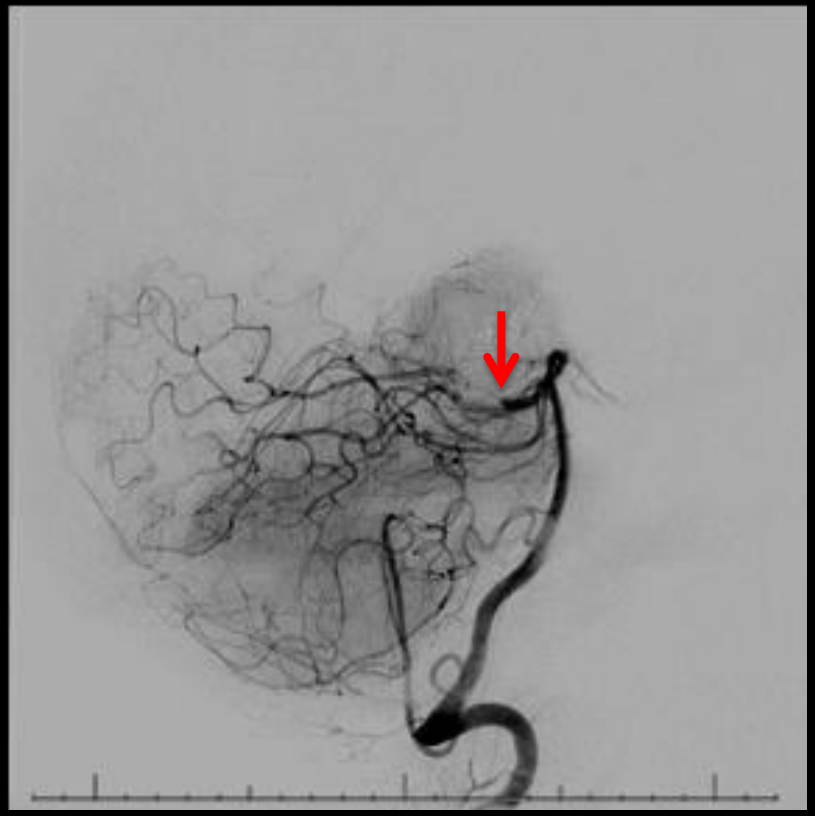
# D. Individualized Disability

## Left PCA-P2 Occlusion. Complete RHH. Normal CT – Should We Treat?

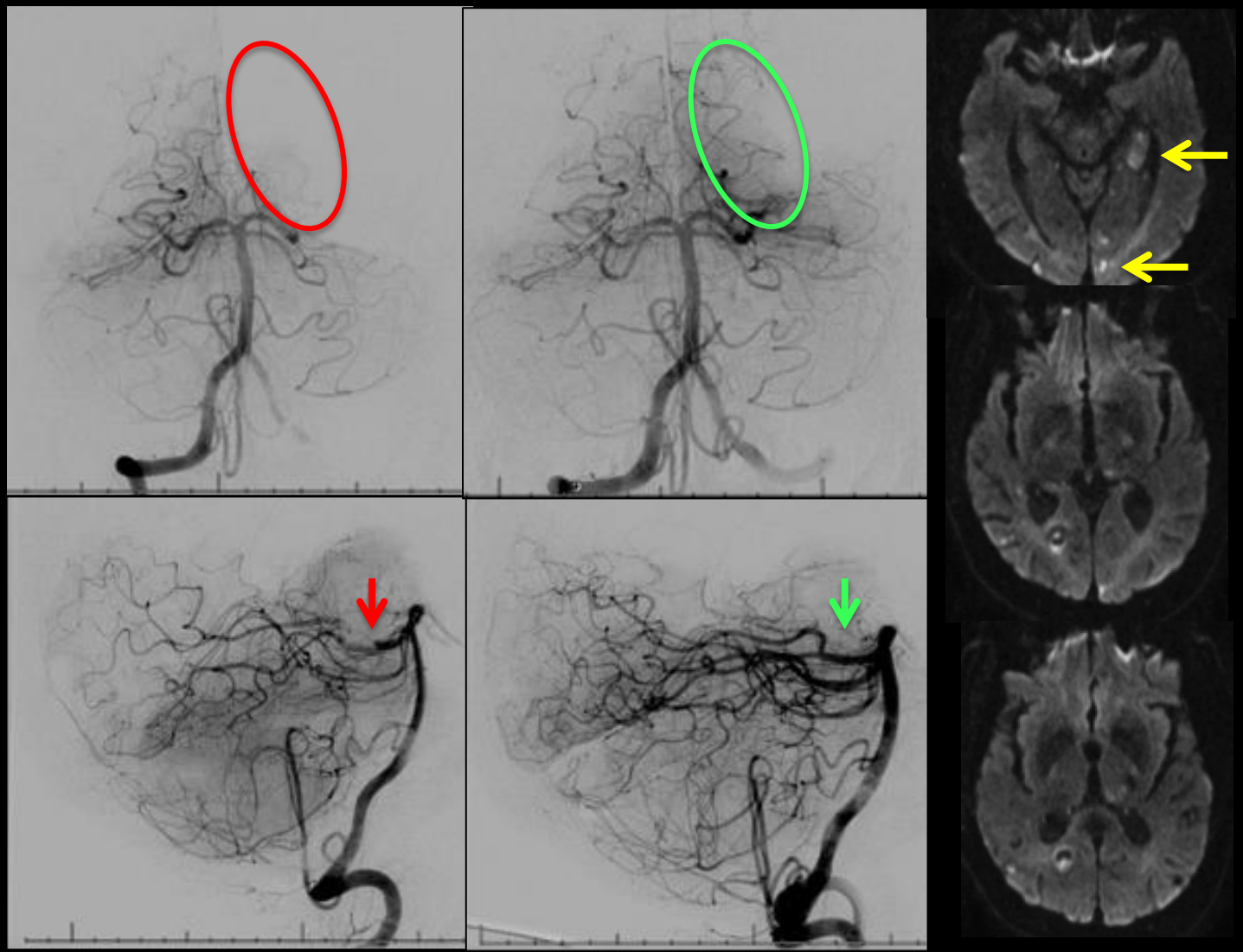


Scenario #1: 80 y/o fully-independent retired accountant. He no longer drives due to OD macular degeneration.

Scenario #2: 55 y/o truck driver and only breadwinner for his family.

# D. Individualized Disability

Left PCA-P2 Occlusion. Complete RHH. Normal CT – Should We Treat?



# Should We Treat M3, ACA, PCA Occlusions?

Just because we can do it…
it doesn't mean we should always do it…

- Smaller, thinner, and more tortuous vessels = higher risk
- Smaller tissue territory at risk = lower benefit
- Likely particularly dangerous in the distal superior division branches due to multiple branching points and greater tortuousity
- Intra-arterial lytic may be a consideration
- Vasospasm prevention with IA Nicardipine or Milrinone

A very reasonable option for territories of high eloquence in particular if poor angiographic collateral flow or non-recovery with intraprocedural neurological exam.

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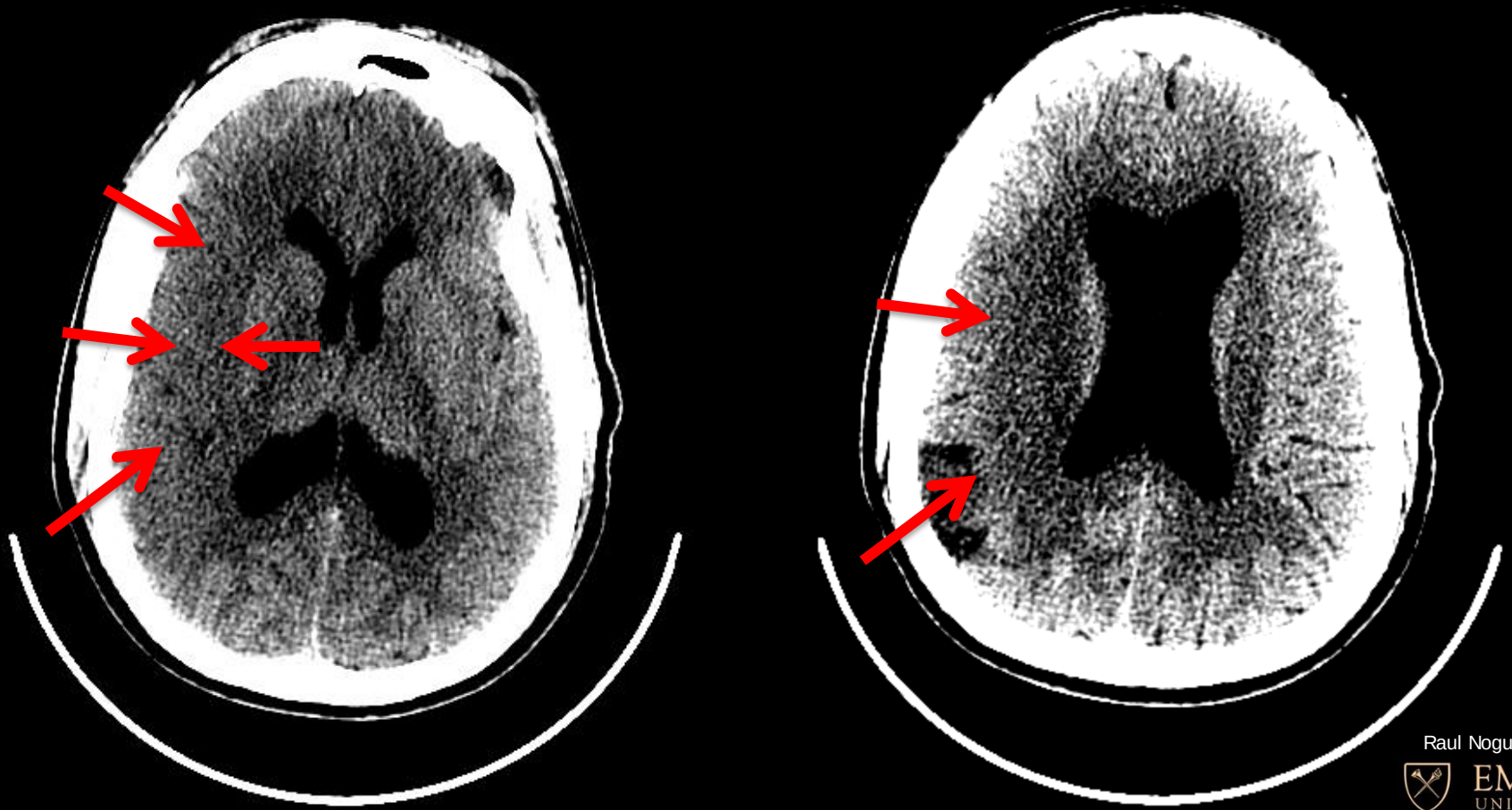
# Baseline Infarct Volume: How Big is too Big?

# How Much is Too Much (Infarct Core)?

- 39 y/o man p/w RMCA sd. NIHSS=18.
- Some improvement after IV tPA
- NCCT: ASPECTS = 4
- CTA: Right MCA-M1 Occlusion



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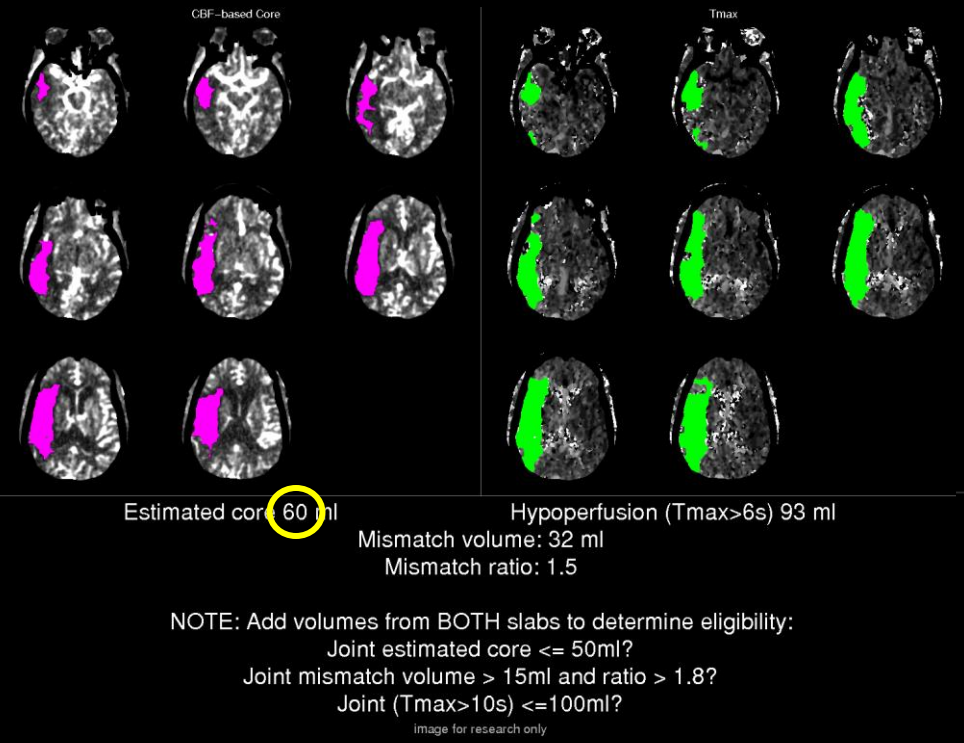
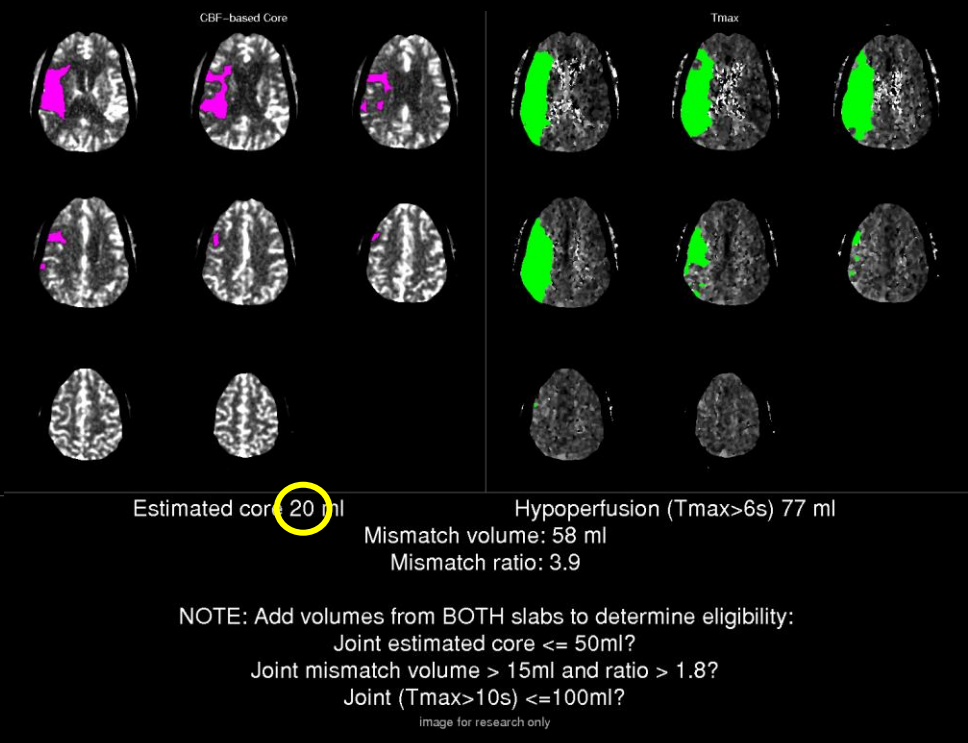
# How Much is Too Much (Infarct Core)?

## Core=80cc but Hypoperfusion=170cc: Mismatch 90cc; Ratio > 2:1




Baseline ASPECTS 4
Baseline Core Volume = 80

→

Not a candidate based on most of the RCT's or AHA Guidelines

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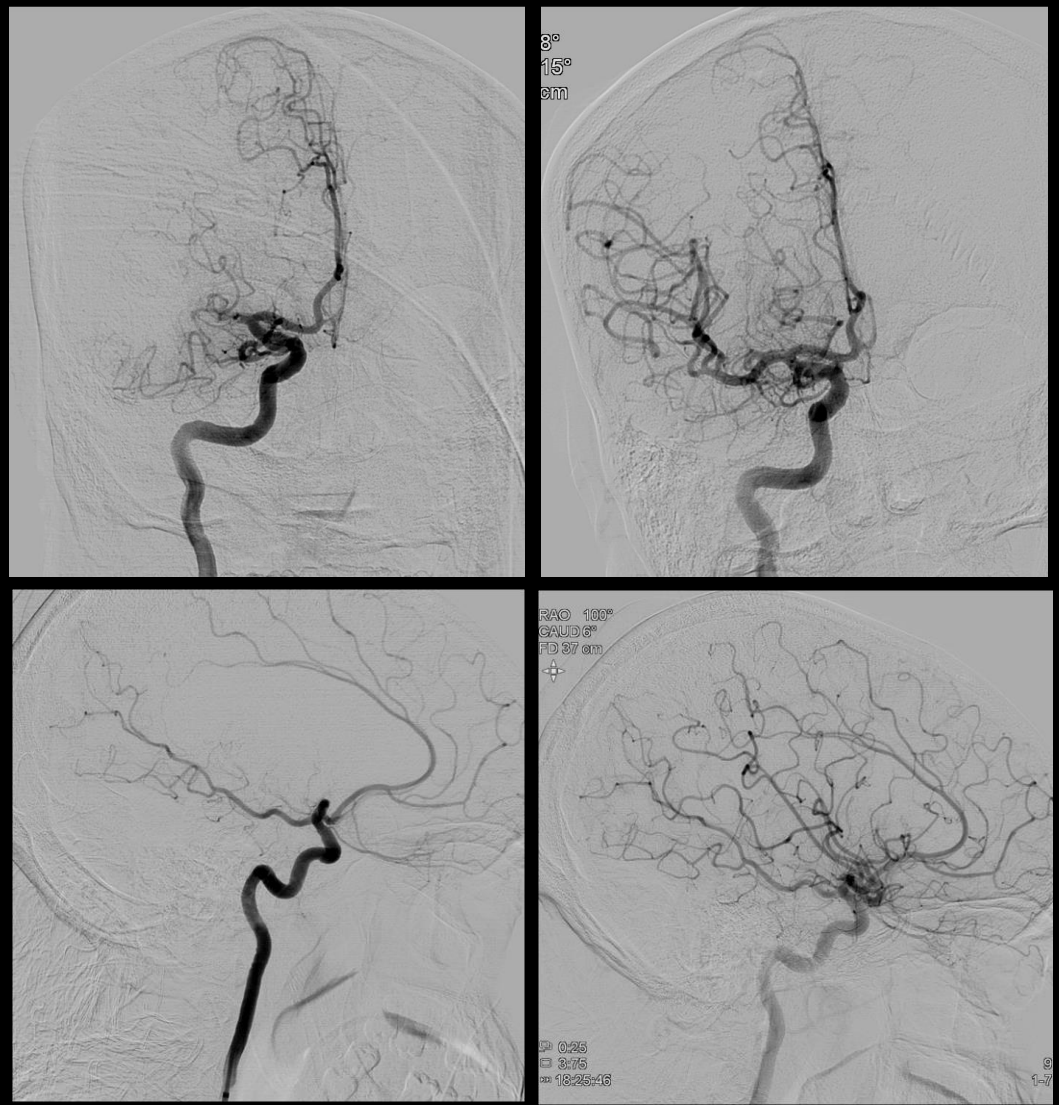
# How Much is Too Much (Infarct Core)?

Treated with Mechanical Thrombectomy: mTICI 3

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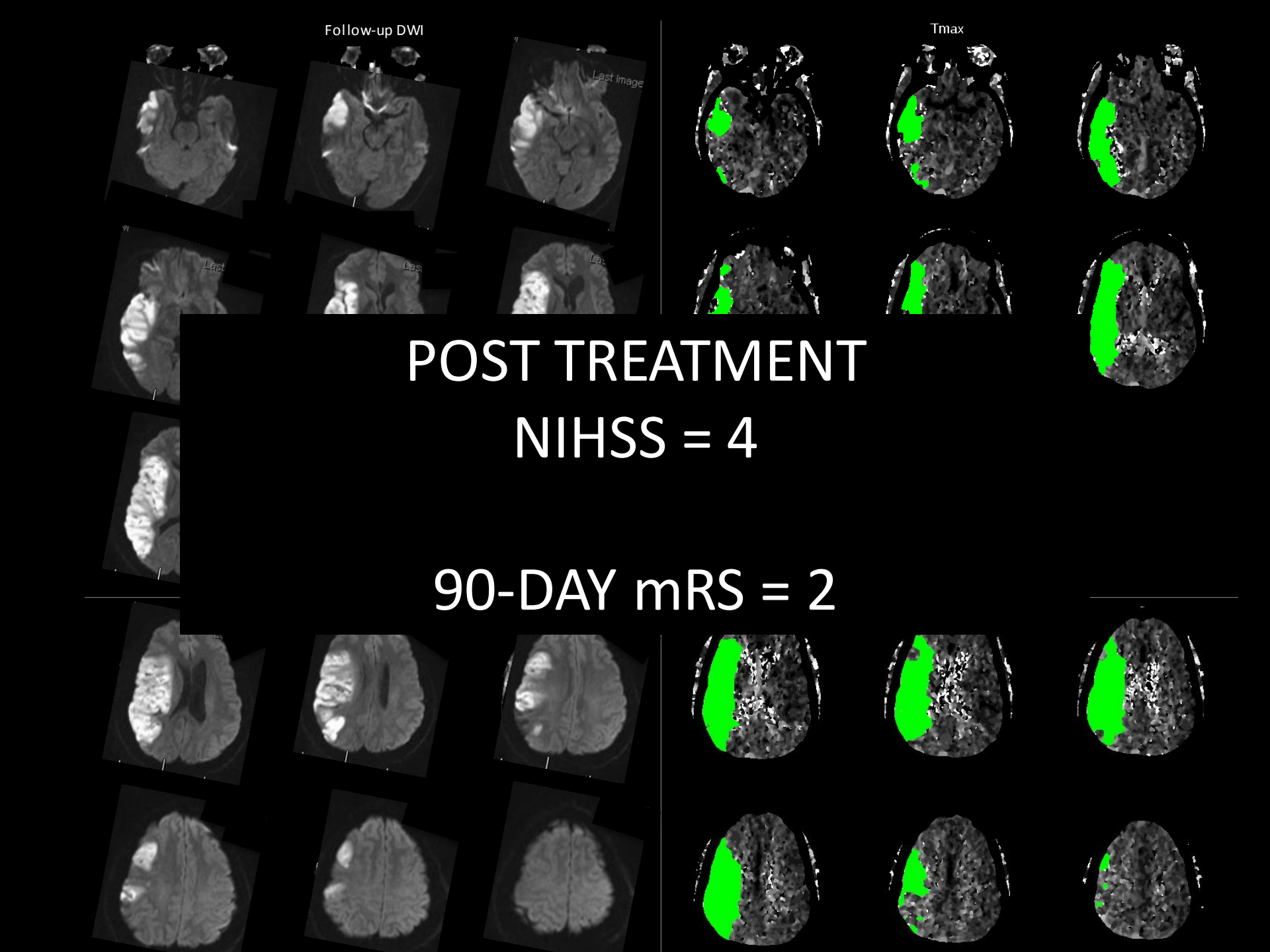



POST TREATMENT

NIHSS = 4

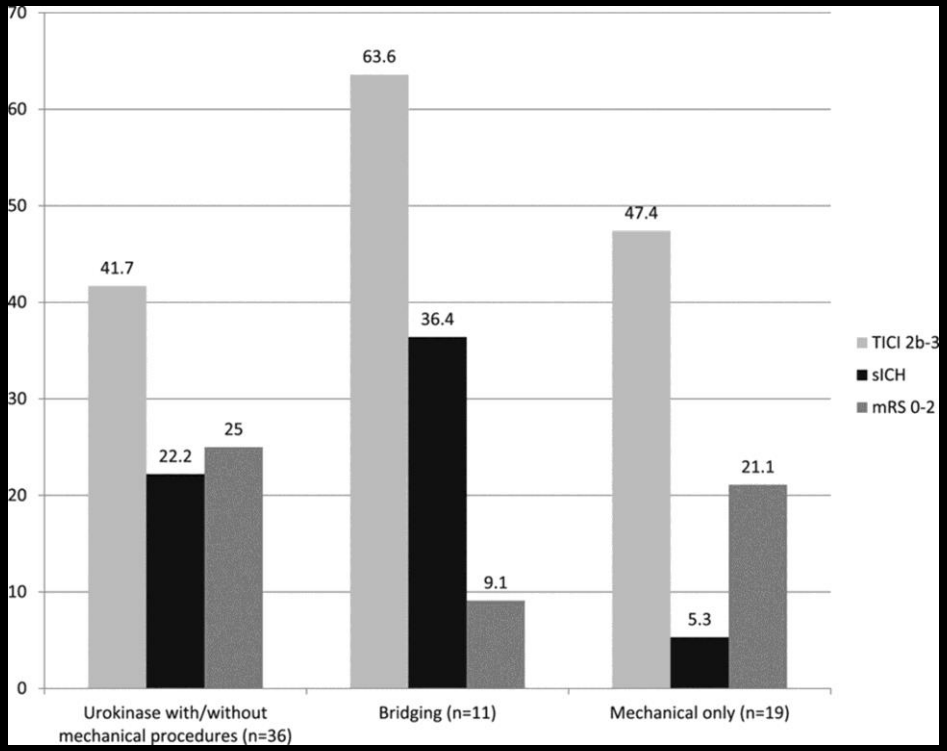
90-DAY mRS = 2

# Endovascular Therapy with DWI> 70 mL

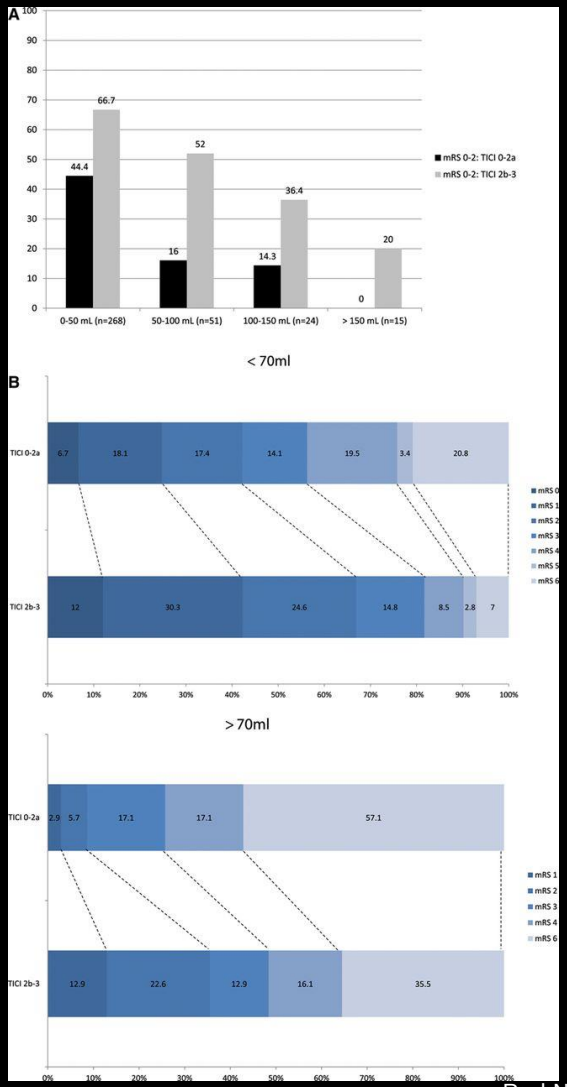
- 372 ICA/MCA pts with baseline DWI
- Baseline DWI volume = independent predictor of unfavorable outcome, survival, and SICH (P<0.001 each)
- DWI lesions >70 mL (n=105) mRS 0–2:

TICI 2b-3: 35.5% (11/31) vs. TICI 0-2a: 8.6% (3/35 ), P=0.014

- TICI 2b-3, Age, and DWI volume = independent predictors of outcome
- SICH = 19.7% (13/66) - a trend for reduced risk with avoidance of thrombolytic agents




mRS 0–2 vs. DWI Volume vs. TICI

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Marc D. Gilgen et al. Stroke. 2015;46:2510-2516

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# How Much is Too Much (Infarct Core)?

It depends on our goals:

- Functional Independence (90-day mRS 0-2):
  - ASPECTS >7 (Hill et al., Stroke 2003)
  - Volume <30-40 mL (less if age >80) (Zaidi S, Nogueira RG, Jovin TG et al. Stroke.2013)
  - Little chance if Volume > 70 mL (Yoo AJ et al, Stroke 2009)

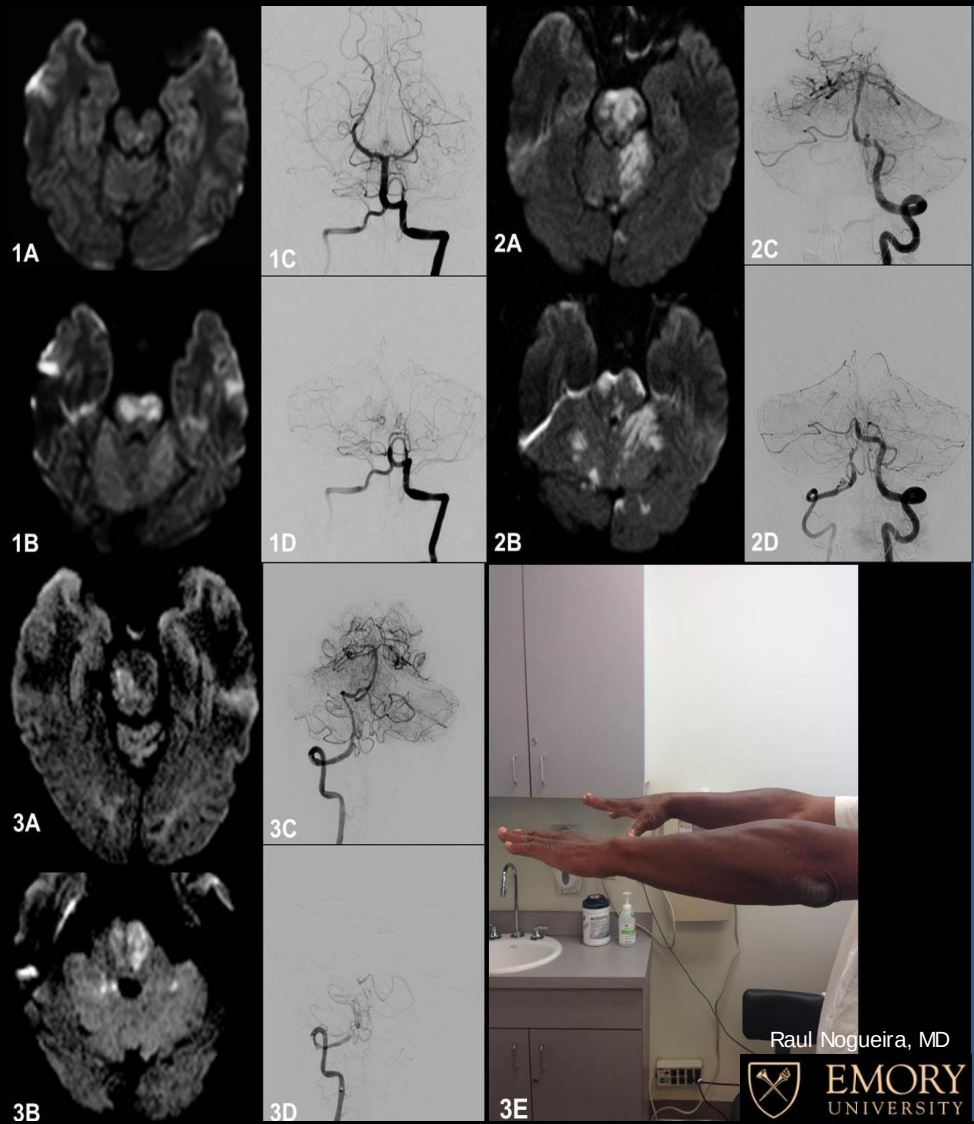
- mRS Shift – every mL brain volume likely matters…
  - ASPECTS 5-7 likely reasonable
  - Volumes 50-100 mL likely reasonable

- Prevent hemicraniectomy or death
  - Can we carefully consider Volumes >100 mL/ >1/3 MCA Territory?
  - The risks is SICH/Edema >100 ML (Albers GW et al, Ann Neurol 2006)

# Basilar Occlusion, Core, and Outcomes

## Full Functional Independence Following Endovascular Treatment for Basilar Artery Occlusion Despite Extensive Bilateral Pontine Infarcts on DWI: Refuting at Sell-Fulfilling Prophecy.

- 3 out of 40 BAO pts who had extensive bilateral pontine DWI changes and achieved 90-day mRS 0-2
- Patient #1: 18 year-old man with embolic BAO due to a PFO. 90-day mRS=0
- Patients #2 (age 73) and #3 (age 56) had atherosclerotic occlusions that required adjunctive intracranial stenting and angioplasty, respectively. 90-day mRS 1 and 2, respectively

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# Time From Onset to Treatment: Time is Essential but Is It the Only Variable in the Equation?

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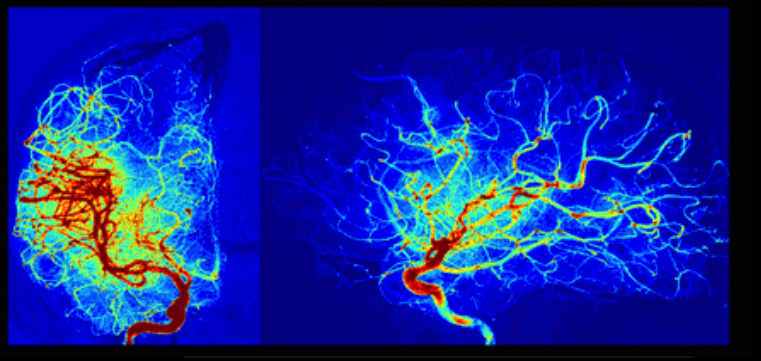
# Outcomes After Reperfusion

$$\text{Outcomes} = \frac{1}{\text{Time}}$$



↑ Time to Reperfusion = ↓ Good Clinical Outcome

12% RR ↓ for every 30-min delay

Khatri P et al. Lancet Neurol. 2014;13(6):567-74

↑ Time to Treatment = ↑ Basal Ganglia ICH

11% RR ↑ for every 10-min delay

Raychev R et al. ISC 2012

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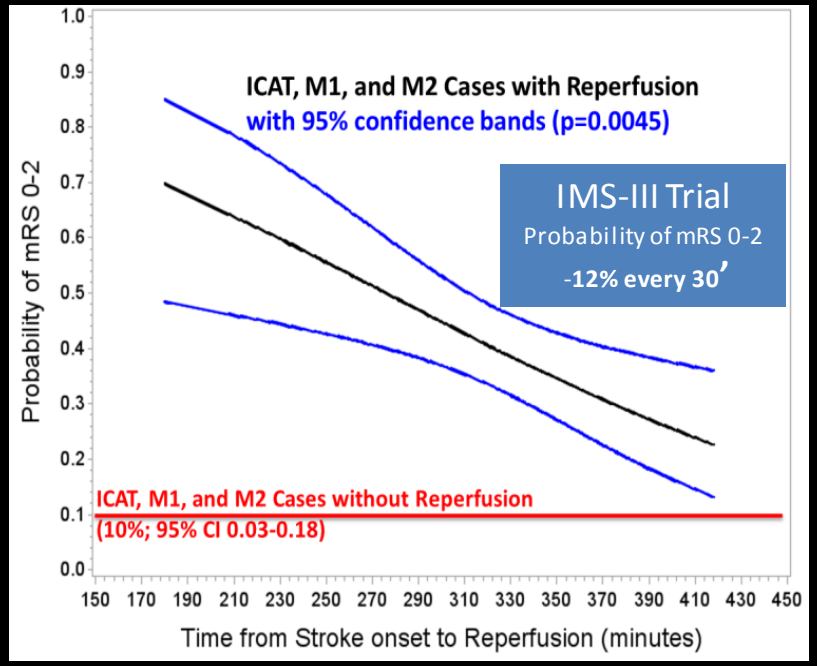
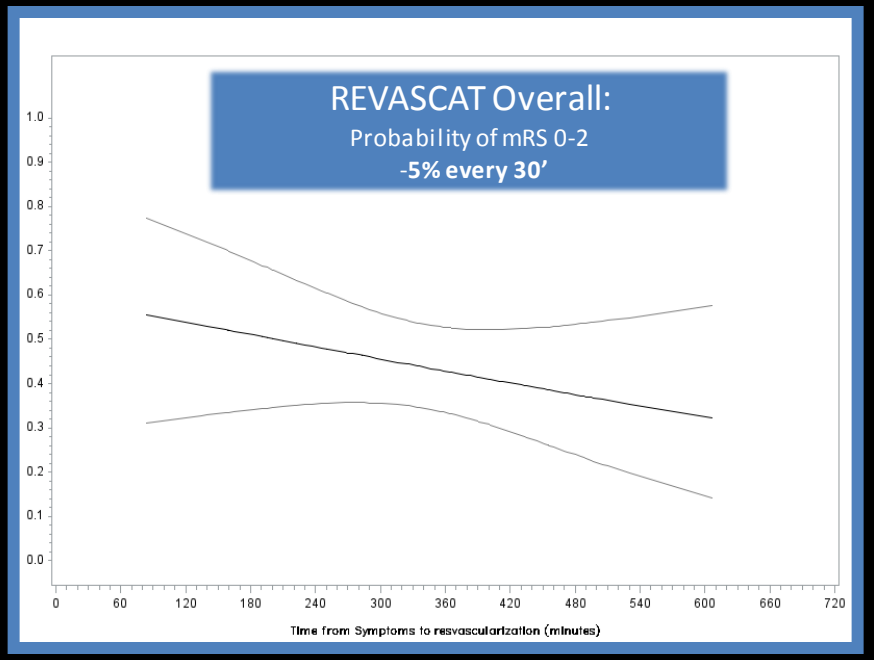
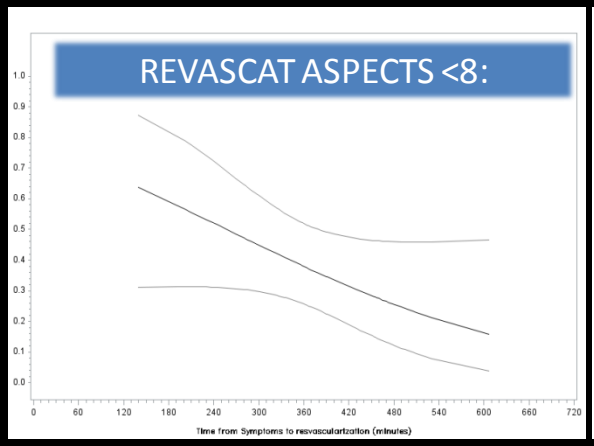
# The Faster The Better But It Ends at 6 Hours?

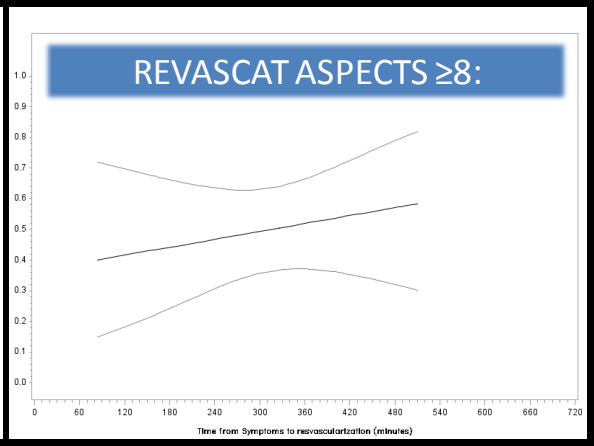



Positive RCTs Time Window:

- 0-6 hours except for:
  - REVASCAT 6-8h (n=20)
  - ESCAPE 6-12h (n=49)




High ASPECTS = Better Collaterals

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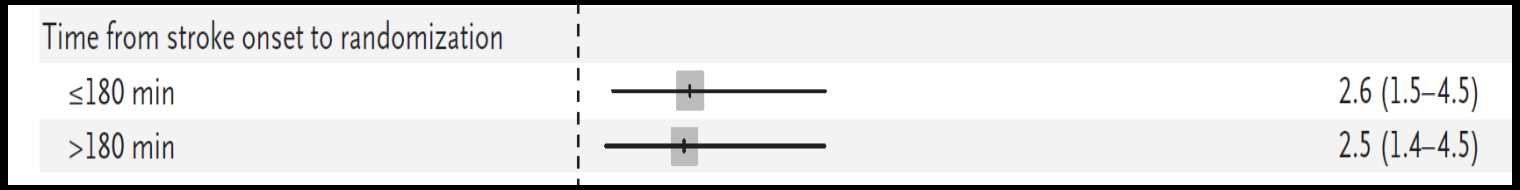
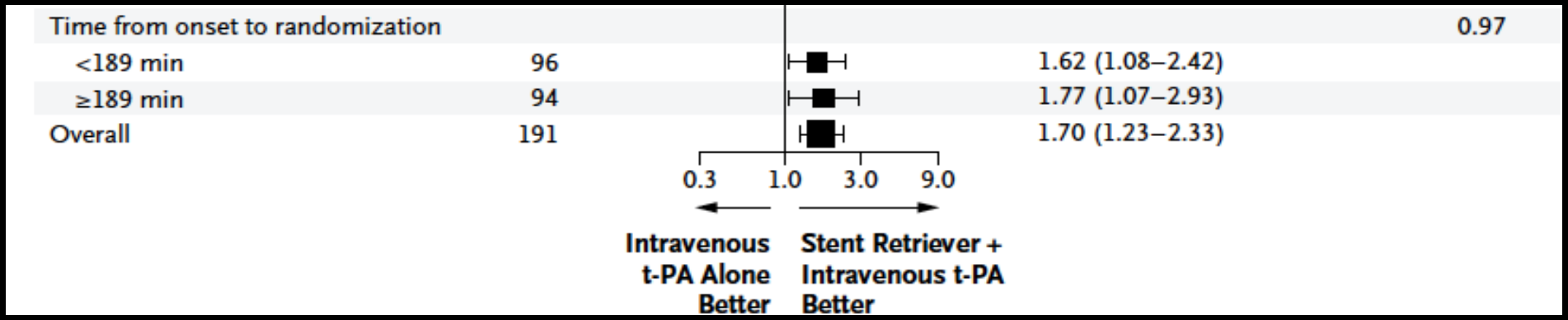
# Subgroup Analyses: TIME

## MR CLEAN


## ESCAPE




## SWIFT PRIME



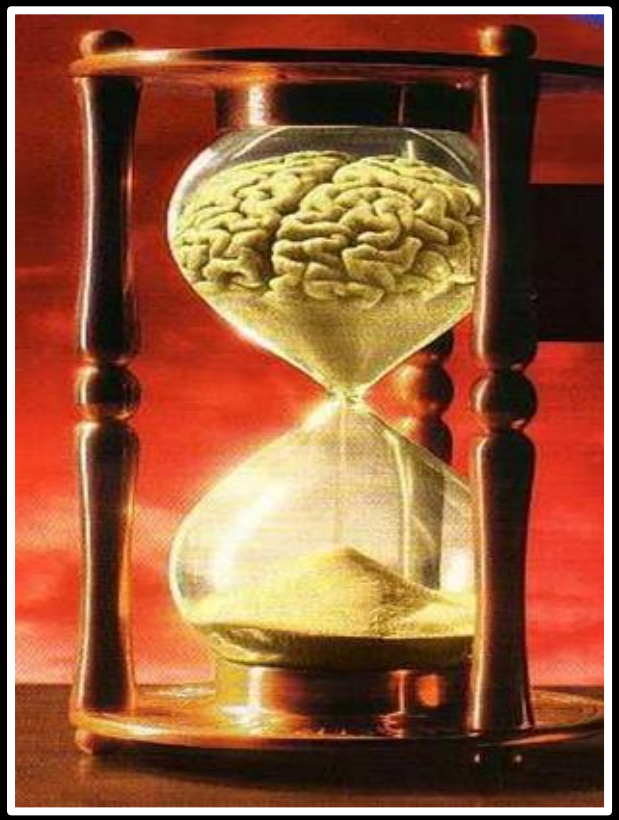
# How Variable is the Infarct Growth Rate?

*"In patients experiencing a typical large vessel acute ischemic stroke, 120 million neurons are lost each hour."*

*Jeff Saver, 2006*

Essential and Valid Concept but an Over simplistic View:

The Brain is not a clock! We need to move from time based to physiology-based decisions!

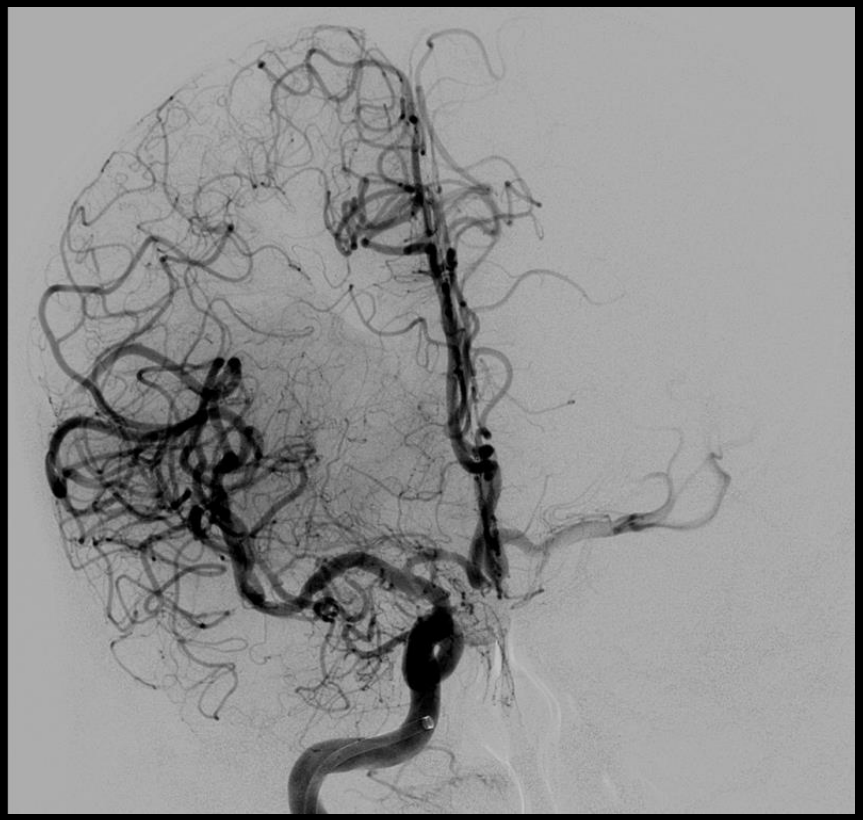


Saver Time Is Brain—Quantified. *Stroke*. 2006;37(1):10.

# Collateral Flow
# Understanding the Right Equation…

# Times is Brain: an Oversimplistic Concept!

## Outcomes = Collaterals/Time



Collaterals buy Time….

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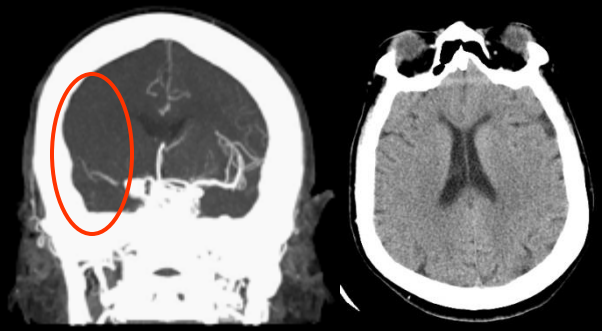
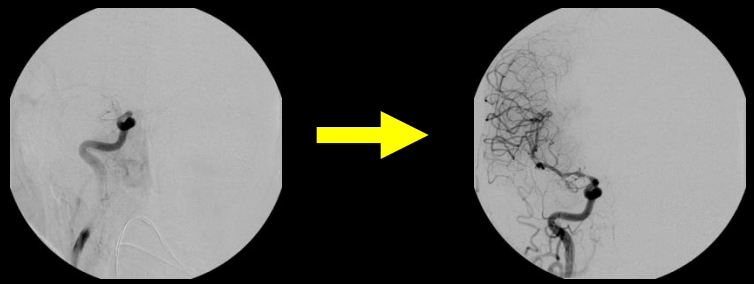
# Collaterals vs. Time:

- 69 y/o F NIHSS: 23
- Head CTA/Head CT

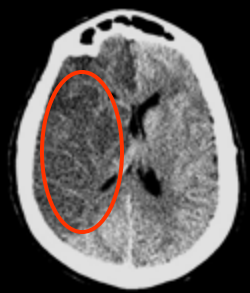


- Time to Reperfusion (TICI 3): <3h

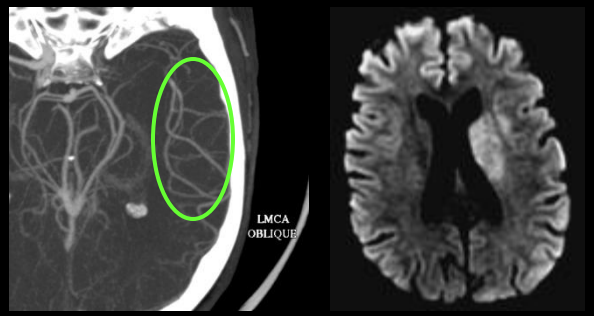


- 90-Day mRS: 4

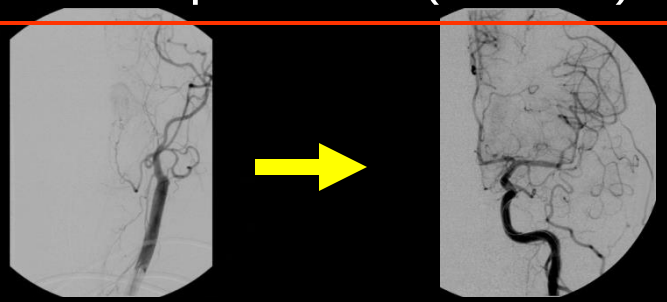
Post-Rx CT



- 67 y/o F NIHSS: 20
- Head CTA/Brain MRI

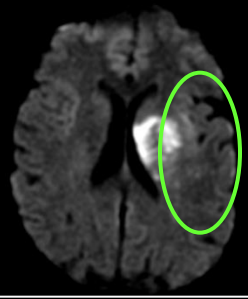



- Time to Reperfusion (TICI 2b): >12h



- 90-Day mRS: 2 (NIHSS: 4)

Post-Rx MRI



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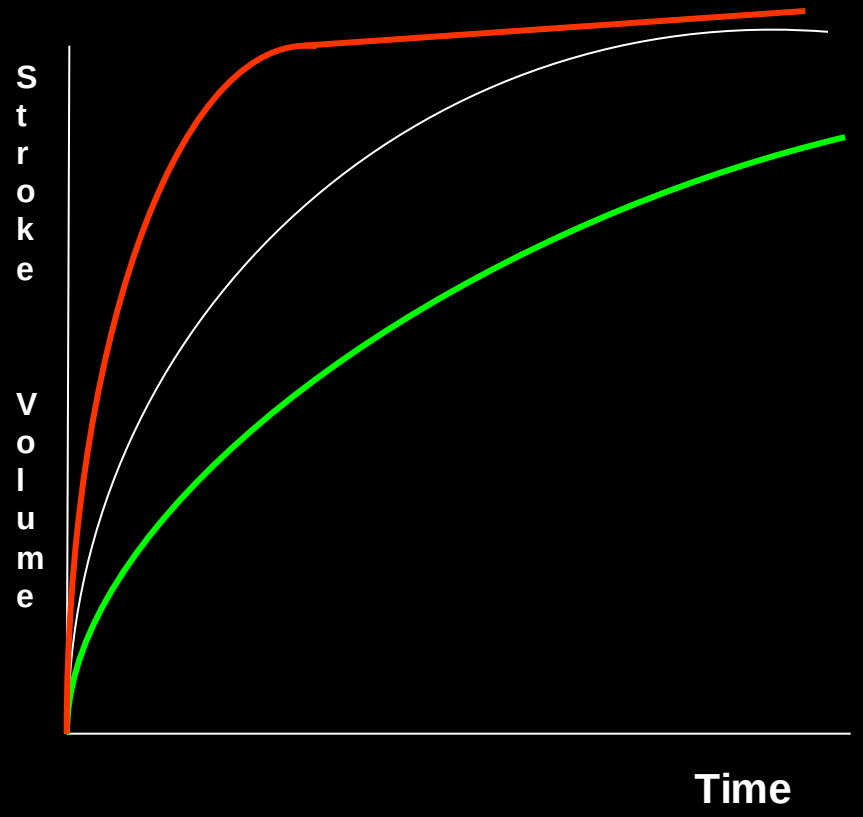
# Different Brains Have Different Time Profiles!

The pace of stroke progression appears to be highly variable and is likely dependent of multiple factors other than the duration and intensity of ischemia including:

- Collateral flow (via Circle of Willis and/or leptomeningeal collaterals)
- Ischemic preconditioning
- Cerebral perfusion pressure
- Cerebral blood volume
- Serum glucose
- Body temperature
- Oxygen delivery capacity

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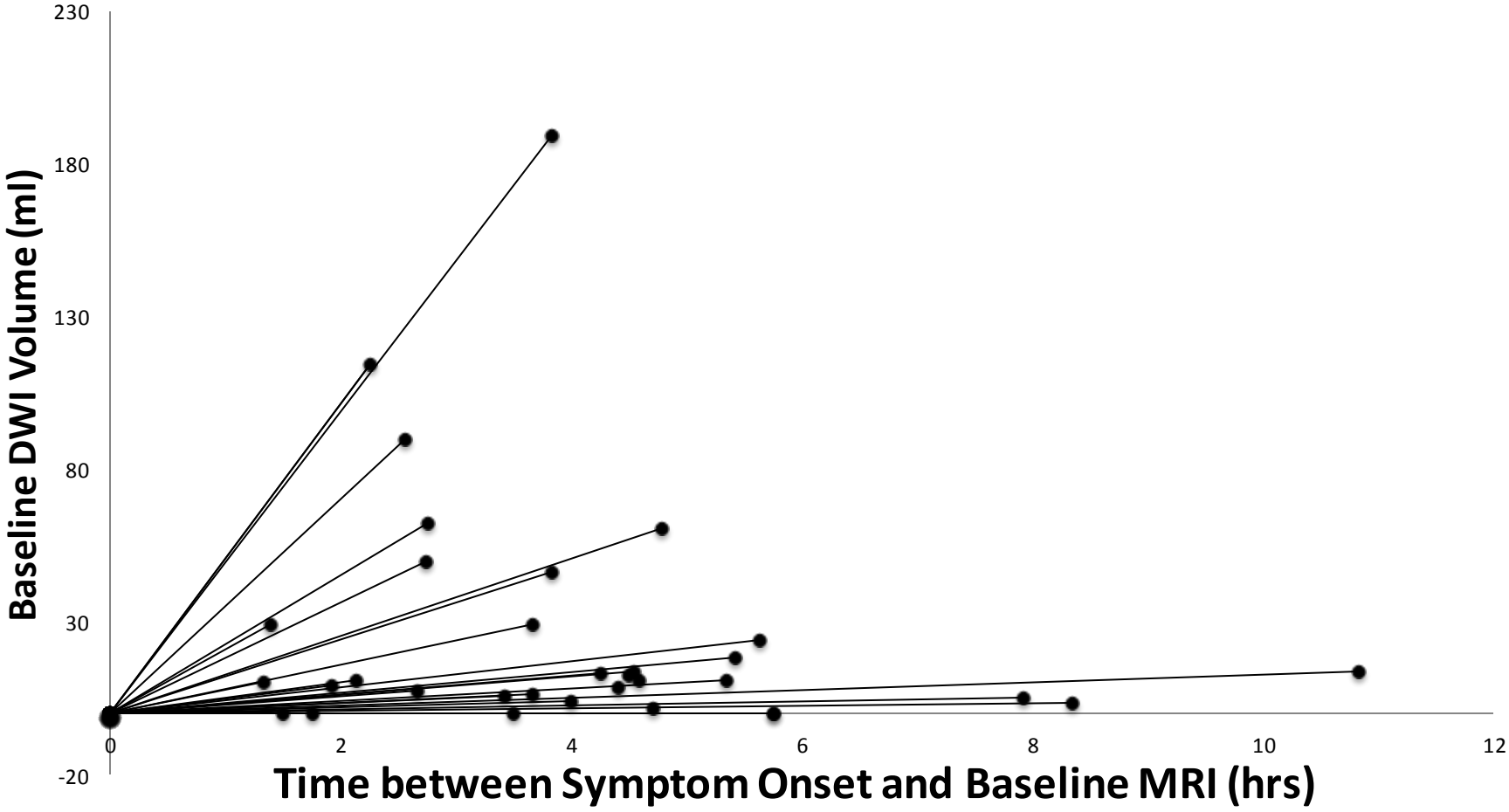
# DEFUSE-2: High Variation in DWI Volumes over Time



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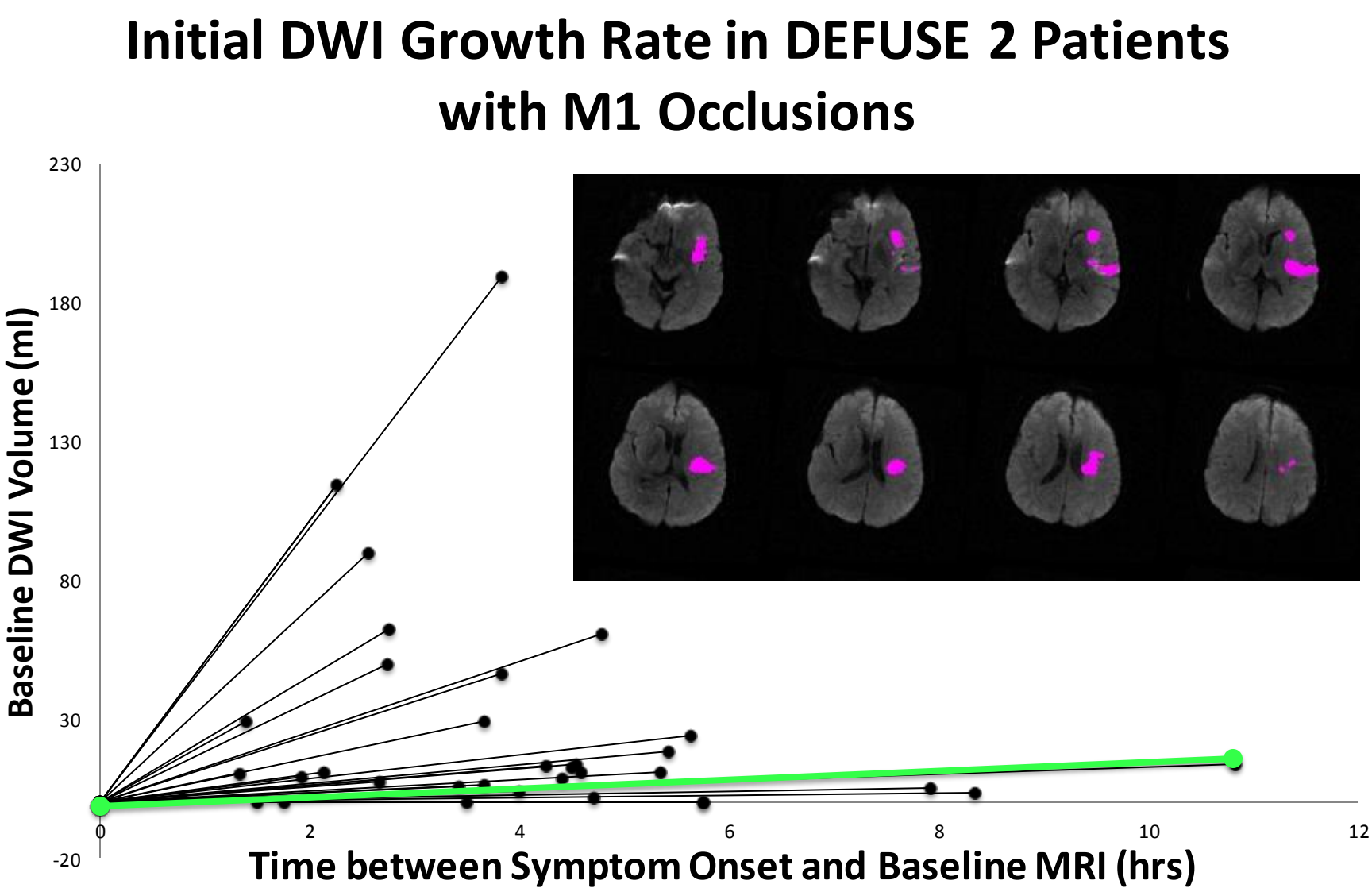

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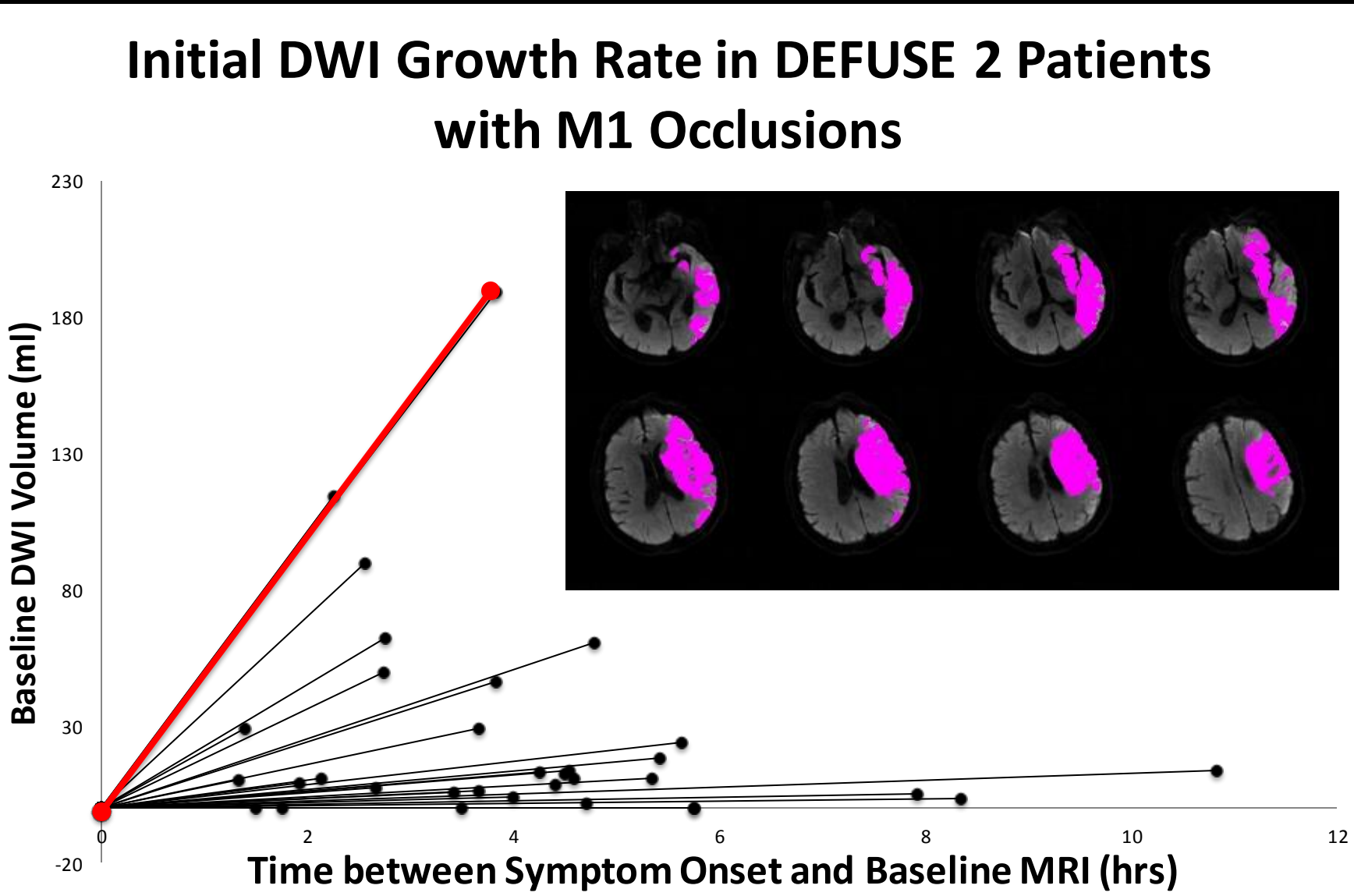

# Refining the Therapeutic Window for Acute Reperfusion Therapy

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# Oct/31/2014: Acute Left MCA-M1 Occlusion: Age 74 NIHSS 26

Stroke Onset: 3PM - IV tPA: 4:48PM - CTP:4:53PM – No IAT (<2h onset)

Early Time

but

Poor Collaterals

=

Poor Outcome

FAST PROGRESSOR!

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# Oct/31/2014: Acute Left ICA/M1 Occlusion: Age 75 NIHSS 24

Last Seen Well: 8PM – No IV tPA - CTP: 11:40AM – IAT: 11:55AM (~16h LSW)

Late Time

but

Good Collaterals

=

Good Outcome

SLOW PROGRESSOR!

Raul Nogueira, MD

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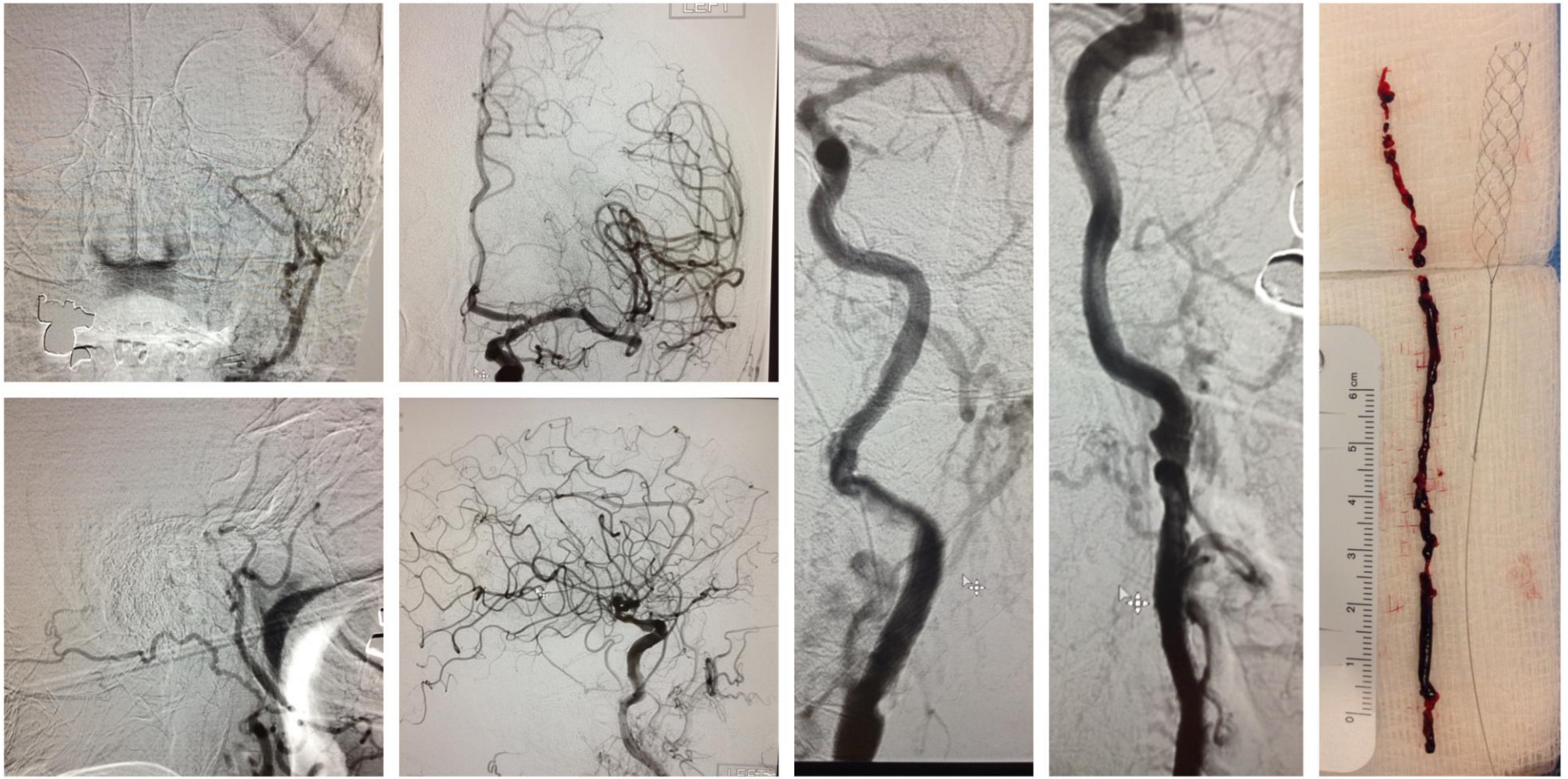
# Oct/31/2014: Acute Left ICA/M1 Occlusion: Age 75 NIHSS 24

Last Seen Well: 8PM – No IV tPA - CTP: 11:40AM – IAT: 11:55AM (~16h LSW)

IAT: 9F BCG + PTAS + 1 Pass Stentriever with Navien 072



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# Time, Stroke Severity, Penunbral Tissue and Collaterals

## Imaging-Based Endovascular Therapy for Acute Ischemic Stroke due to Proximal Intracranial Anterior Circulation Occlusion Treated Beyond 8 Hours From Time Last Seen Well

OUTCOMES = COLLATERALS

TIME


present beyond this timeframe. We sought to assess safety, procedural, and clinical outcomes of MRI or CT perfusion imaging-based endovascular therapy in patients with anterior circulation stroke treated beyond 8 hours from time last seen well.

***Methods***—We conducted a multicenter retrospective review of consecutive patients meeting the following criteria: (1) acute proximal intracranial anterior circulation occlusion; (2) endovascular treatment initiated >8 hours from time last seen well; and (3) treatment selection based on MRI or CT perfusion imaging.

***Results***—Two hundred thirty-seven patients were identified (mean age, 63.8±16 years; mean baseline National Institutes of Health Stroke Scale, 15±5.5; mean time last seen well to treatment, 15±11.2 hours; male gender, 46%). Successful revascularization was achieved in 175 of 237 (73.84%) patients. Parenchymal hematoma occurred in 21 of 237 (8.86%) patients. The 90-day mortality rate was 21.5% (51 of 237). The rate of good outcomes was 45% (100 of 223) in the 223 patients with available modified Rankin Scale data at 90 days or time of hospital discharge. In multivariate analyses, age (OR, 0.96; 95% CI, 0.94 to 0.98; $P=0.002$), admission National Institutes of Health Stroke Scale (OR, 0.93; 0.87 to 0.98; $P=0.016$), and successful revascularization (OR, 4.32; 1.99 to 9.39; $P<0.0001$) were identified as independent predictors of good outcomes.

***Conclusions***—Endovascular therapy can be instituted with acceptable safety beyond 8 hours from time last seen well when selection is based on advanced neuroimaging. Successful revascularization is significantly associated with higher rates of good outcomes. The benefit of this approach compared with standard medical therapy should be assessed in a prospective randomized trial. (***Stroke*. 2011;42:2206-2211.**)

# The Time vs. Collateral Flow Interaction Will it be the Future?

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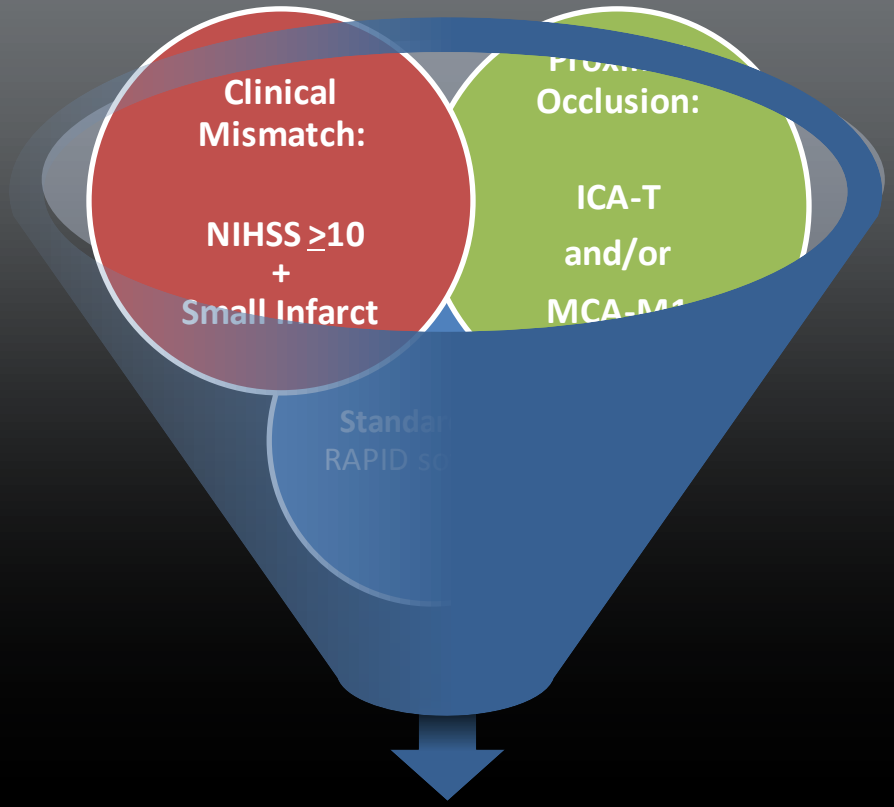
# DAWN™ Clinical Trial

**Goal: To identify the Target Mismatch Patient in the 6-24h Window (including Wake-Up Strokes)**




Randomization

Balanced re: CIM subgroup, time and occlusion location

# DAWN™ Breaking News

March 2, 2016

## Grady enrolled their 19th Subject!

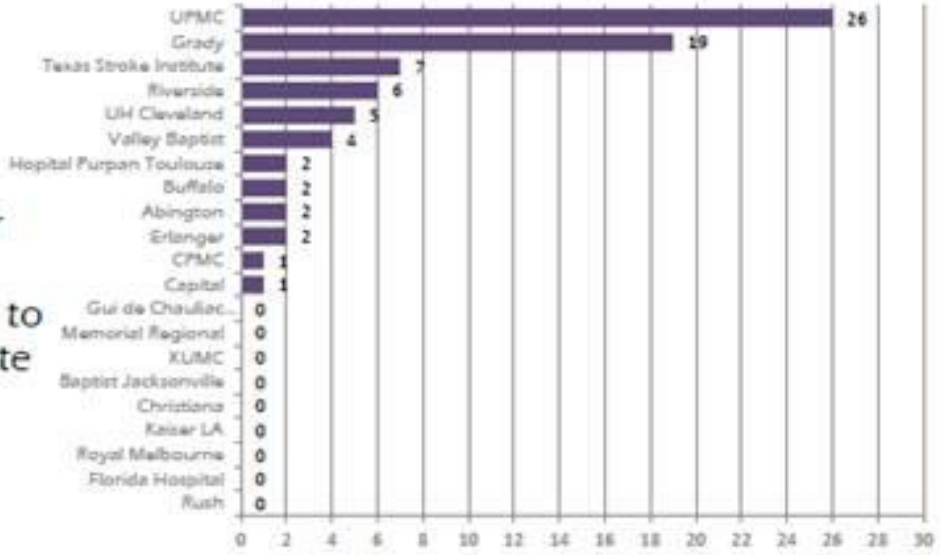
Site: Grady Hospital/Emory University
PI: Raul Nogueira, MD/Diogo Haussen, MD
Primary RC: Shannon Doppelheuer, CCRC

### Congratulations and Thank You!

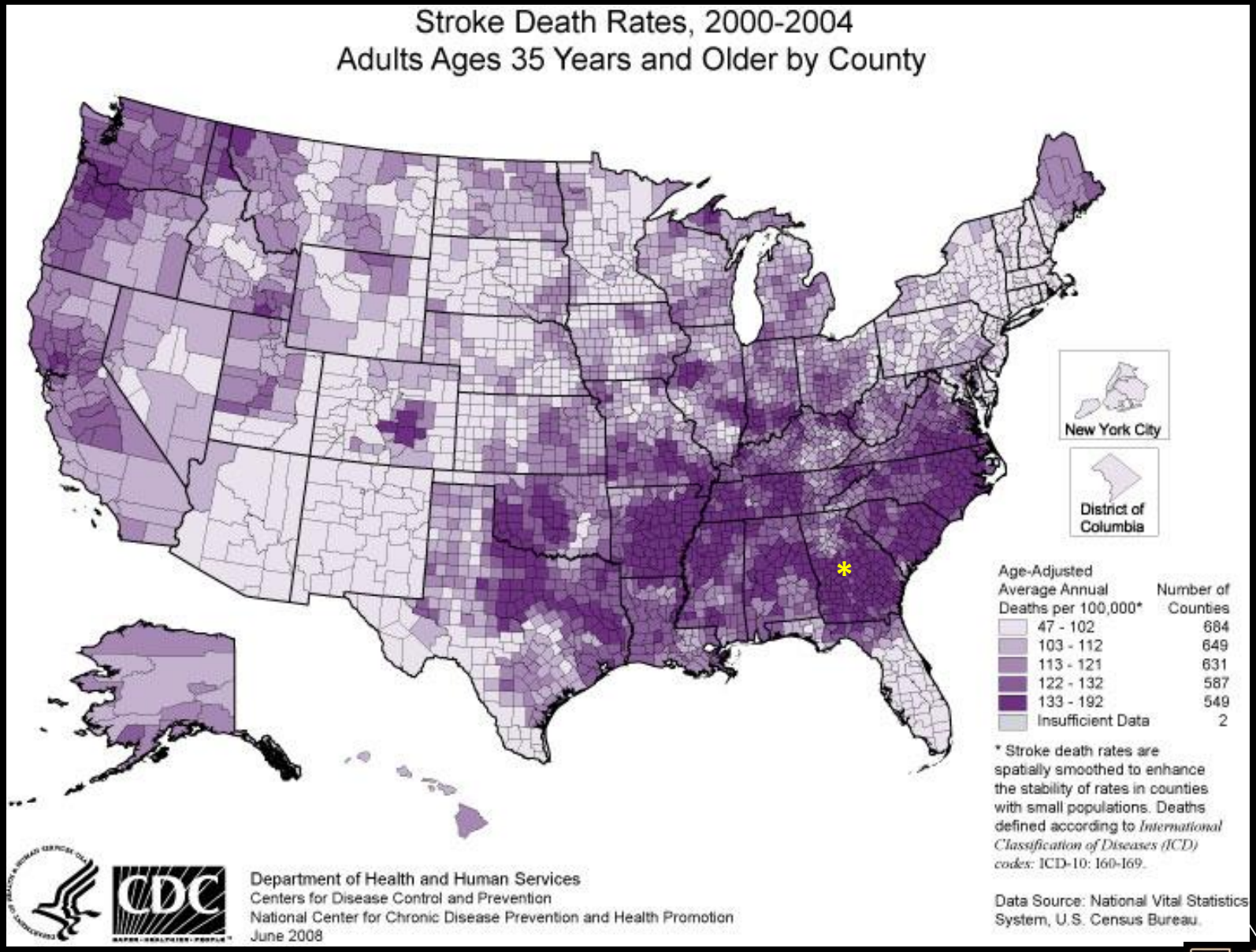
We acknowledge that this study involves the efforts and support of many individuals. We thank each and every team member for his or her efforts in screening and identifying this subject for enrollment into this important trial to expand treatment options for wake-up and late presenting AIS patients!

*The Stryker NV DAWN Clinical Study Team*

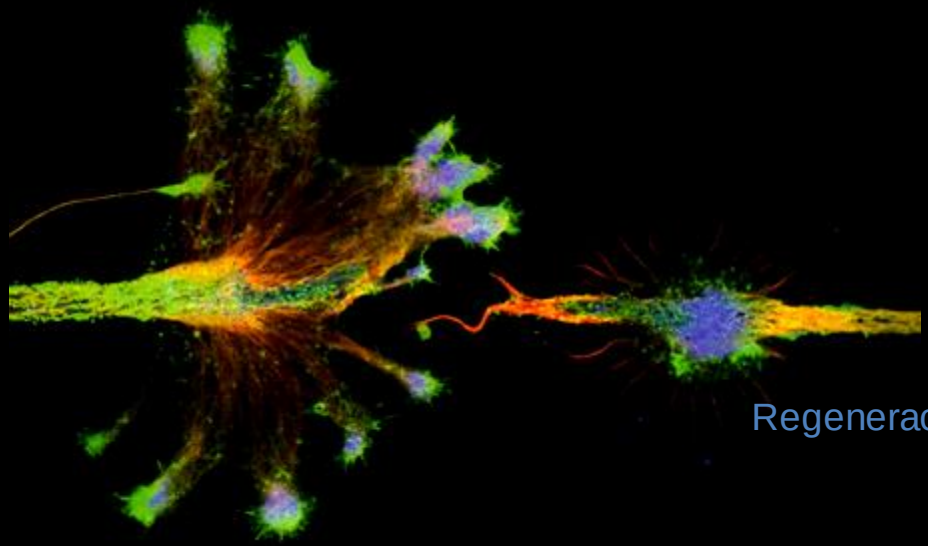
**77 Total Subjects Enrolled**



# We live in the Stroke Belt and now we can make a greater difference!



It's a beautiful day
Skeptics fall, you feel like
It's a beautiful day
Don't let that clot get away



Regeneracion, Pasajes Neuronales, 2006

Thank you for your attention!

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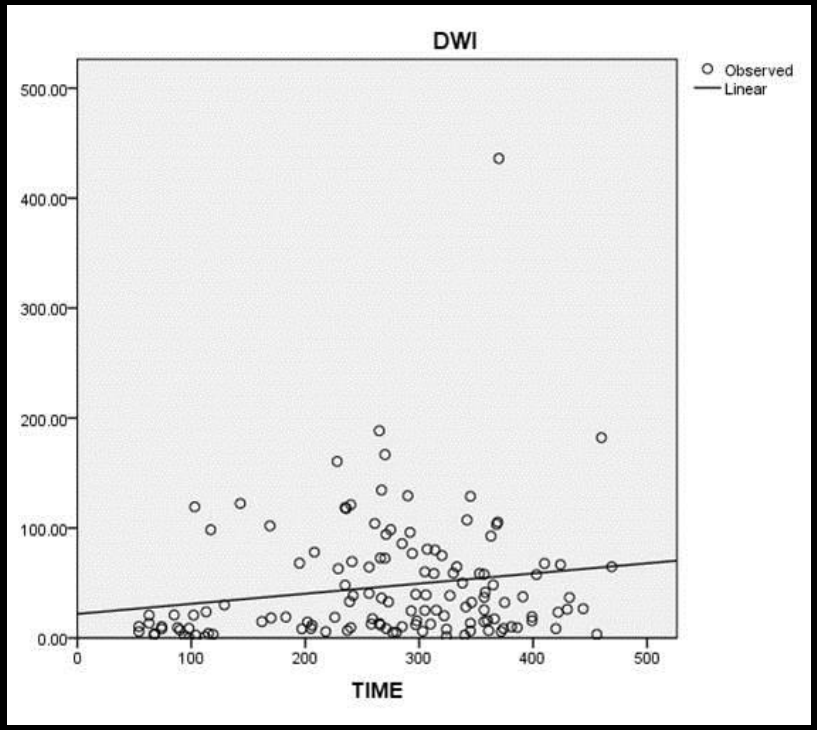
# Temporal Distribution of Stroke Volumes and Clinical-Diffusion Mismatch in Proximal Arterial Occlusions

- 132 consecutive pts with bNIHSS ≥8 + PAO + DWI ≤8 hours from stroke onset:
- Age, 66±16.8 years; 57% females;
- Baseline NIHSS 17.5±5.3;
- Occlusion site:
  - MCA-M1: 64%
  - Intracranial-ICA: 29%
  - Tandem, 5%
- TSO to DWI, 269.5±105.48 min
- DWI volume: 46.7±54.8 cc (range, 0.19-436.1) and 63 (46.7%) patients had Clinical-DWI Mismatch
- No significant changes in age, gender, bNIHSS, or occlusion site amongst the different time quartiles.
- Median infarct volume (cc) increased (quartile #1=8.5; #2=30.1; #3=38.5; #4=29.4) and the chances of having a CDM decreased (p<0.0001) across the different time quartiles.




Nogueira RG et al. ISC 2012

- Poor correlation between DWI volume and TSO to MRI (R-square=0.031, Figure)
- Significant proportion of the patients still had a CDM at later time epochs:
  - #1=91.1%[20/22];
  - #2=47.8%[11/23];
  - #3=34.4% [21/61];
  - #4=42.3%[11/26]).

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# DWI Volumes over Time and Collateral Flow

91 pts: ICA, M1, M2 occlusions + MRI <6 hours (23%: 0-3h; 76% 3-6h).

- Median infarct volume: 24.7 vs. 29.4 mL, *P* = 0.906
- % pts infarct volumes >70 mL: 23.8% vs. 22.8%, *P =0*.928
- No association between time from onset to MRI and infarct volumes (AUC 0.509)
- Independent predictors of infarct volume:
  - CTA collaterals (50% of the territory) (aOR, 0.192; 95% CI, 0.04 – 0.9; *P* .046)
  - CTA ASPECTS (aOR, 0.464; 95% CI, 0.3– 0.8; *P* .003)
  - Hyperlipidemia (adjusted OR, 11.0; 95% CI, 1.4–88.0; *P=0*.023)
  - NOT time from stroke onset to imaging

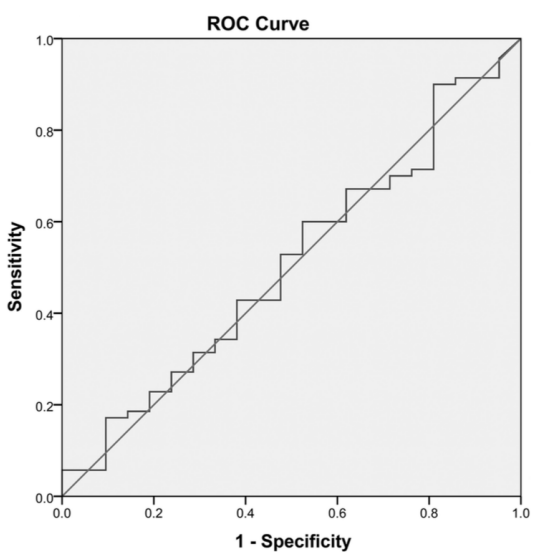



**FIG 3.** Receiver operating characteristic curve demonstrating no association between the time from LSW to MR imaging (0–3 hours versus 3–6 hours) and DWI infarct volume.

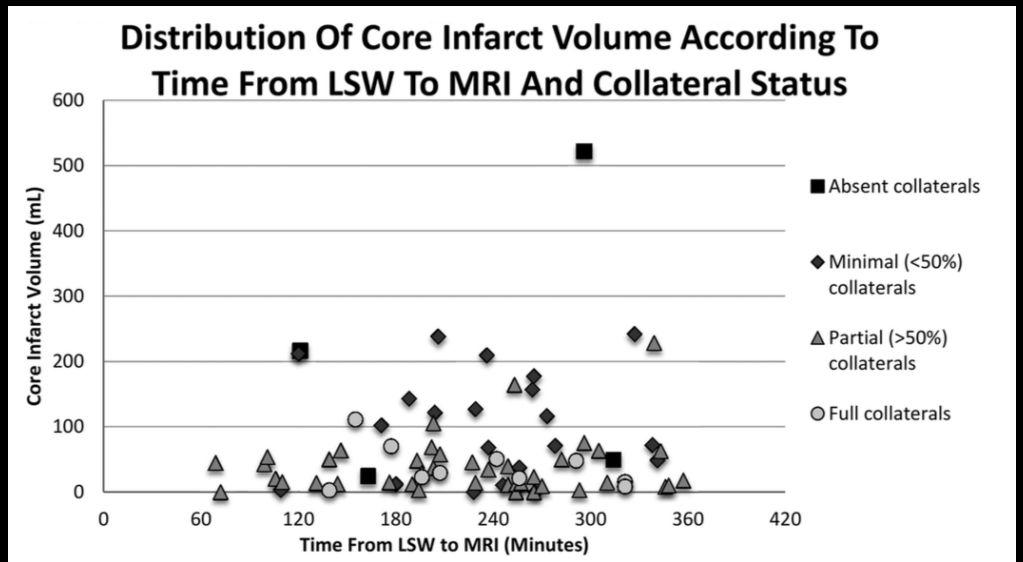
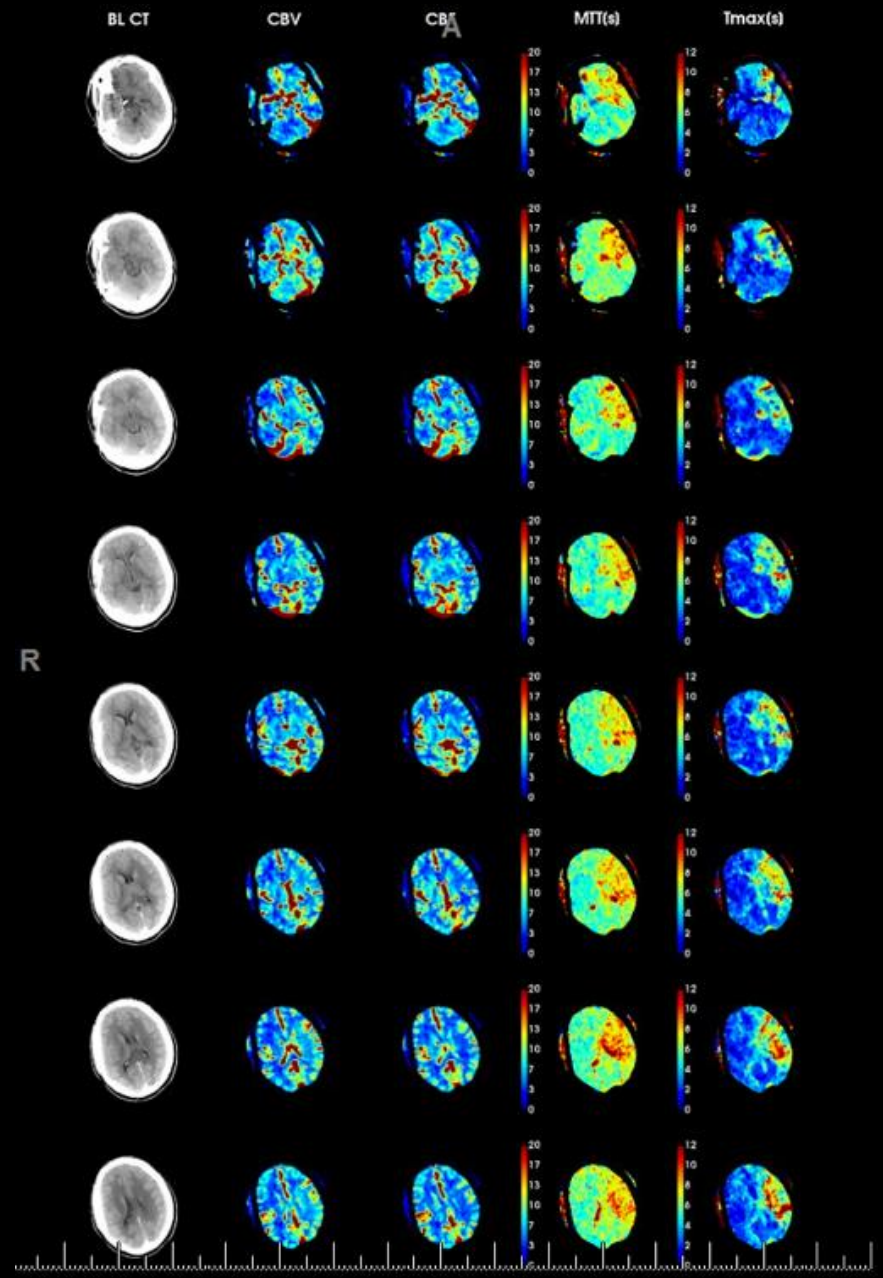
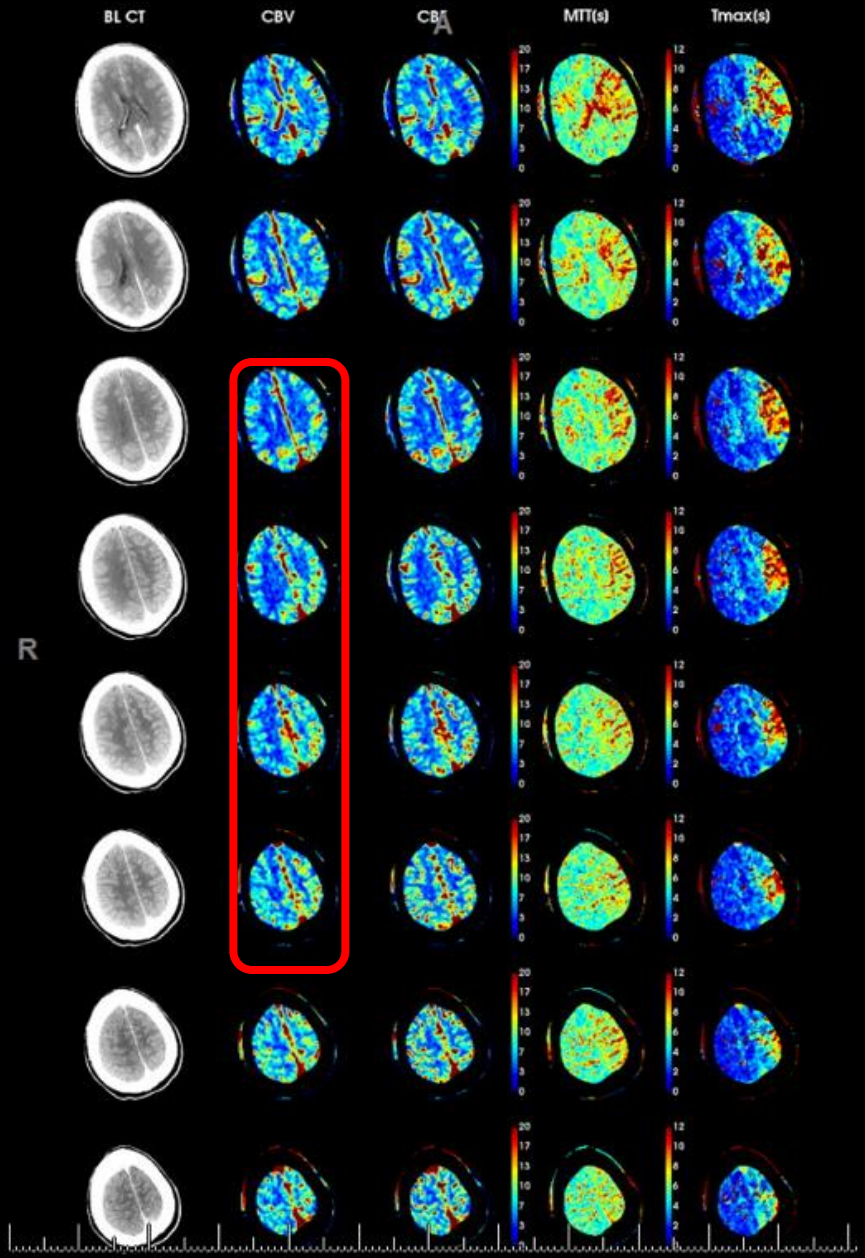



**FIG 2.** Distribution of DWI infarct volume of each patient according to the time from last seen well to MR imaging and collateral status.

Cheng-Ching E et al. AJNR 36:1272–76 Jul 2015

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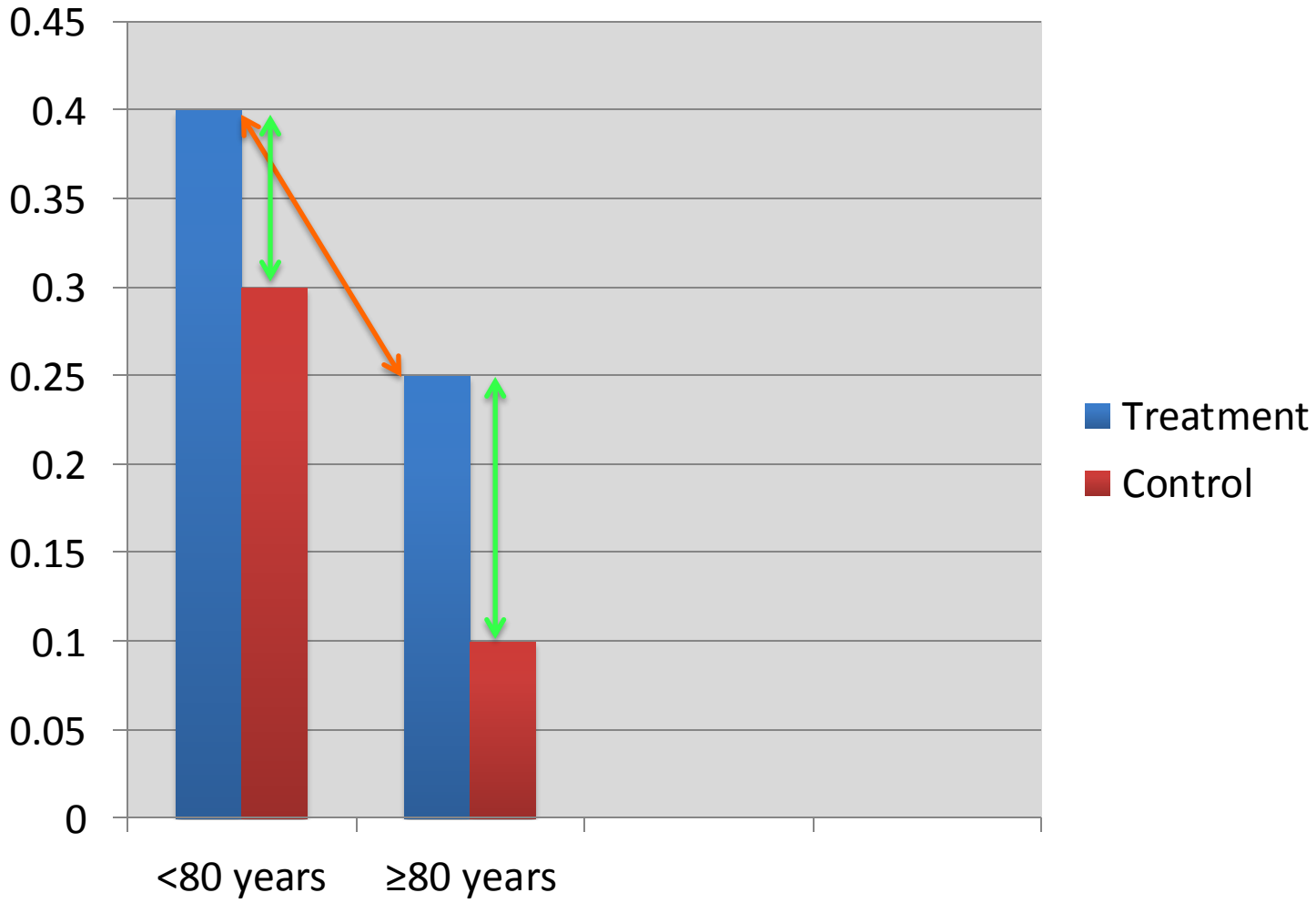
# IAT in the Elderly Revisited:

## Hypothetical Outcomes in Young vs. Elderly: Absolute Benefit vs. Treatment Effect Size

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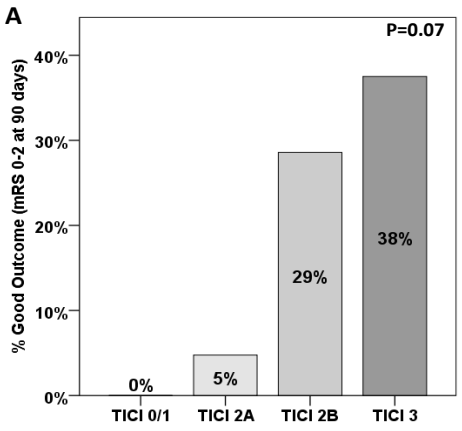
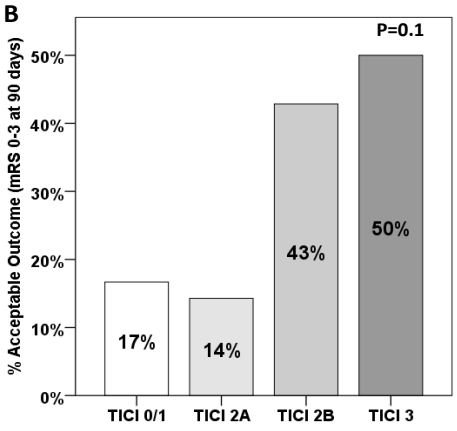
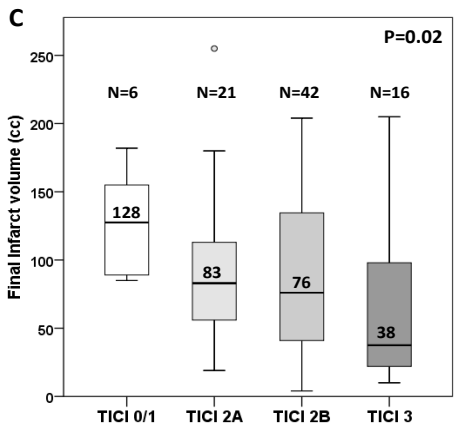
# Endovascular Therapy in ASPECTS 5-7

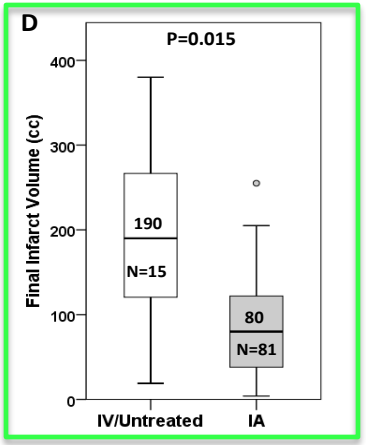
- LVOS with ASPECTS 5-7 treated with IAT (n=86) or medical therapy alone (± IV t-PA; n=15) at two centers from 2009-2012
- Age (67±14 vs. 67±19yrs) and bNIHSS (20±5 vs. 20±6) similar in IAT vs. Medical.
- IAT: mTICI≥2B=67%; ICH: Symptomatic=10%; Asymptomatic=36%
- IAT 90-day Outcomes: mRS≤2=20%; mRS≤3=33%; Death=43%
- Successful IAT reperfusion = smaller FIV (p=0.015) and higher rates of good (p=0.02) and acceptable (p=0.03) outcomes.
- Strong trend towards a higher hemicraniectomy requirement in medical vs. endovascular pts (20% vs. 6%, p=0.06) despite similar in-hospital mortality.
- Median FIV significant lower with IAT vs. medical therapy (80ml[IQR, 38-122] vs. 190ml[121-267], p=0.015).

Noorian A et al. Interventional Neurology. In Press



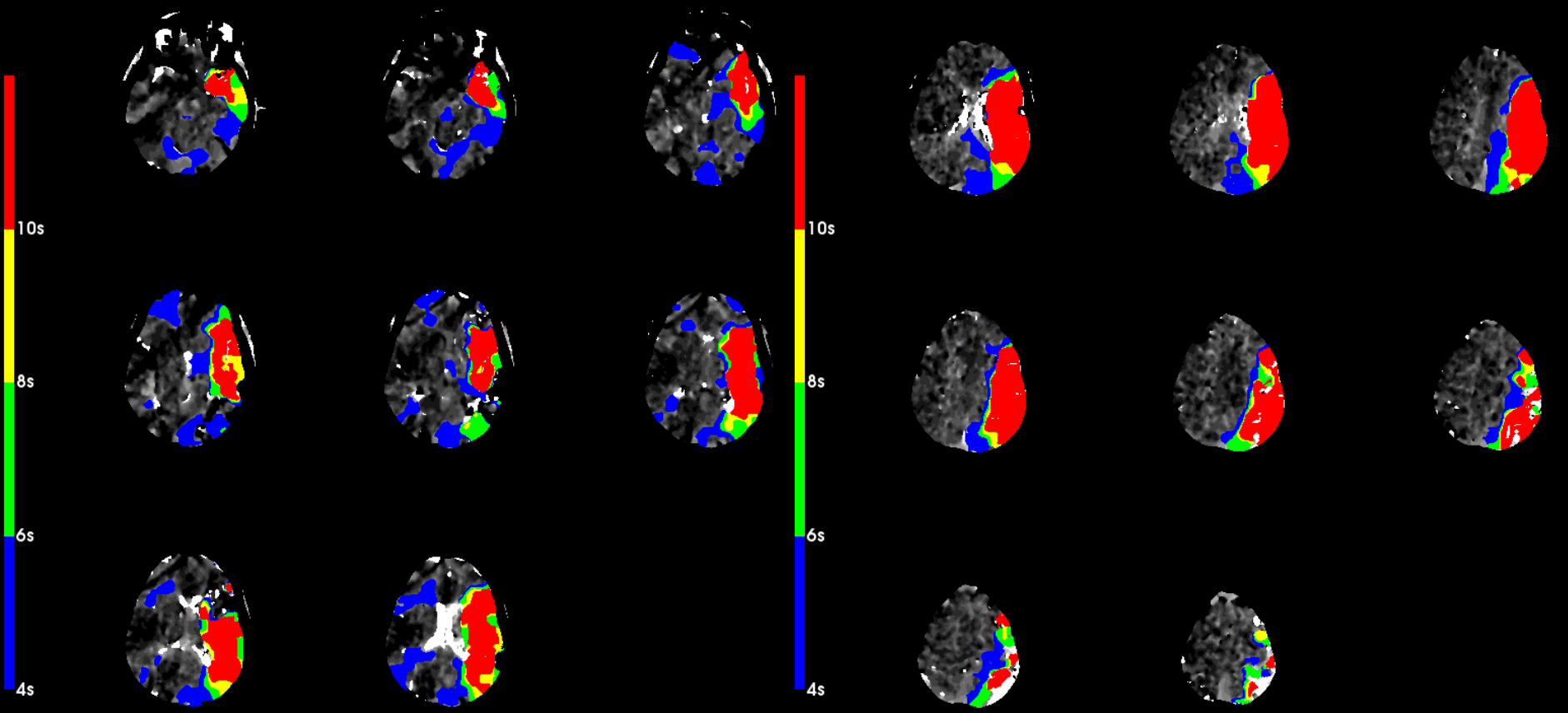



# Oct/31/2014: Acute Left MCA-M1 Occlusion: Age 74 NIHSS 26

Stroke Onset: 3PM - IV tPA: 4:48PM - CTP:4:53PM – No IAT (<2h onset)

## Tmax MAPS = Collateral Strength = Time to Reperfuse




Perfusion (Tmax>10.0s) volume: 72.3 ml
Perfusion (Tmax>8.0s) volume: 85.3 ml
Perfusion (Tmax>6.0s) volume: 107.9 ml
Perfusion (Tmax>4.0s) volume: 192.1 ml

Perfusion (Tmax>10.0s) volume: 91.8 ml
Perfusion (Tmax>8.0s) volume: 101.4 ml
Perfusion (Tmax>6.0s) volume: 118.6 ml
Perfusion (Tmax>4.0s) volume: 156.7

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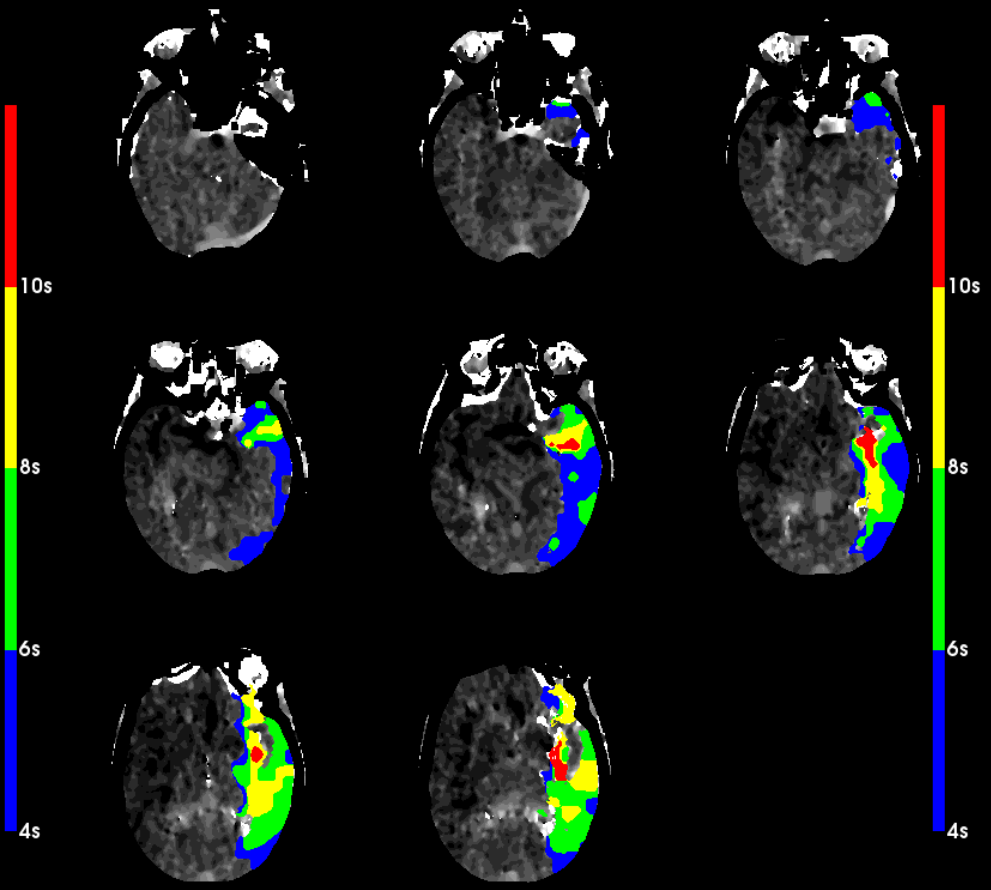
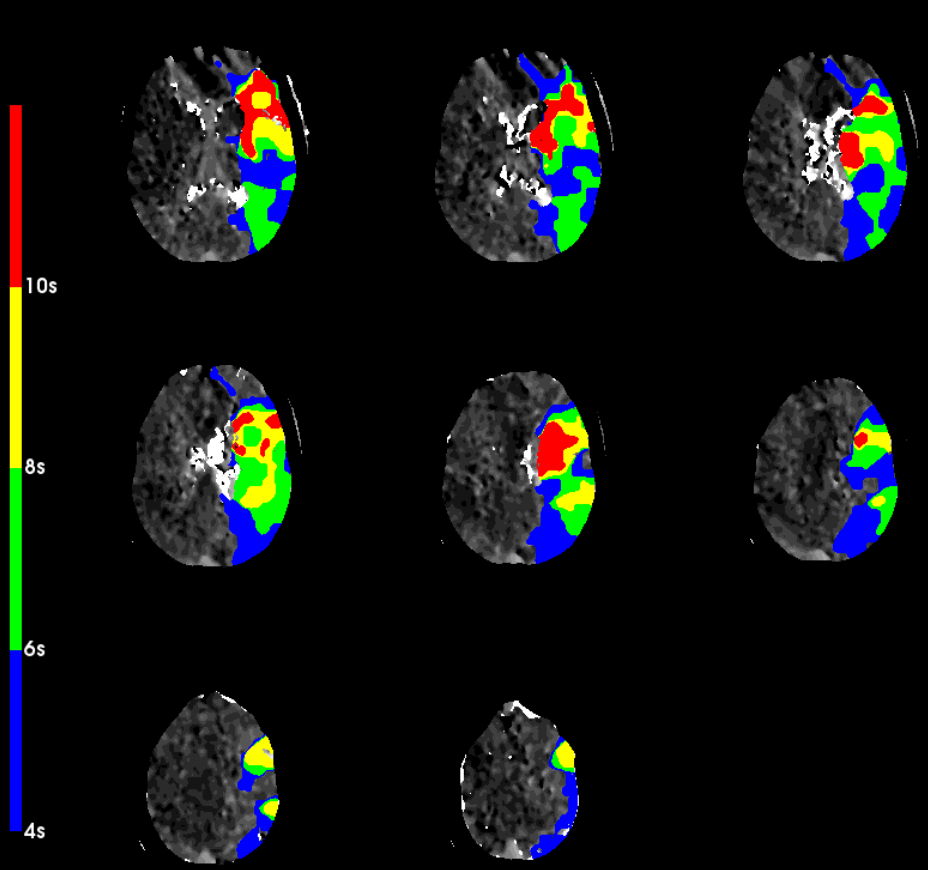
# Oct/31/2014: Acute Left ICA/M1 Occlusion: Age 75 NIHSS 24

Last Seen Well: 8PM – No IV tPA - CTP: 11:40AM – IAT: 11:55AM (~16h LSW)

## Tmax MAPS = Collateral Strength = Time to Reperfuse




Perfusion (Tmax>10.0s) volume: 3.0 ml
Perfusion (Tmax>8.0s) volume: 17.3 ml
Perfusion (Tmax>6.0s) volume: 43.6 ml
Perfusion (Tmax>4.0s) volume: 75.2 ml

Perfusion (Tmax>10.0s) volume: 16.8 ml
Perfusion (Tmax>8.0s) volume: 38.6 ml
Perfusion (Tmax>6.0s) volume: 78.5 ml
Perfusion (Tmax>4.0s) volume: 133.9 ml

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