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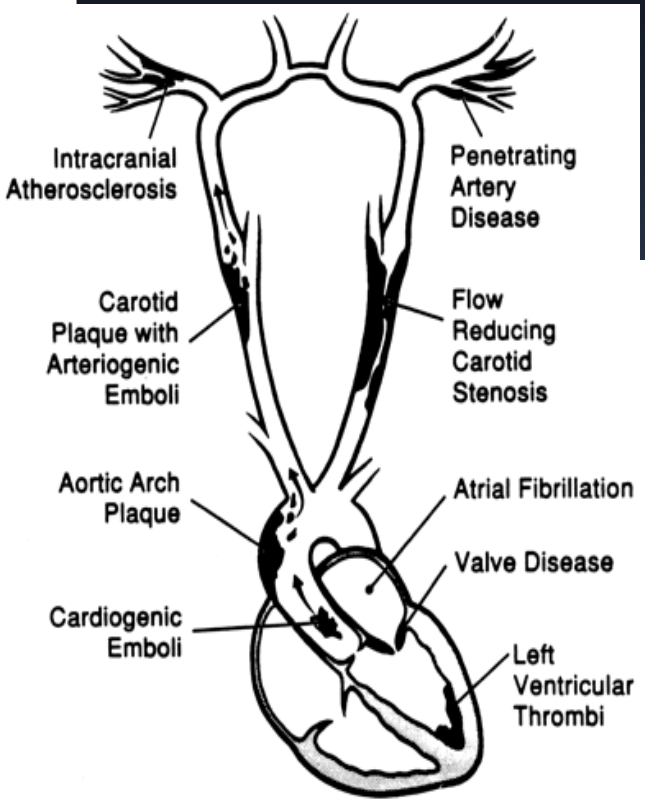
ACUTE STROKE TREATMENT: THROMBOLYSIS AND MECHANICAL CLOT RETRIEVAL

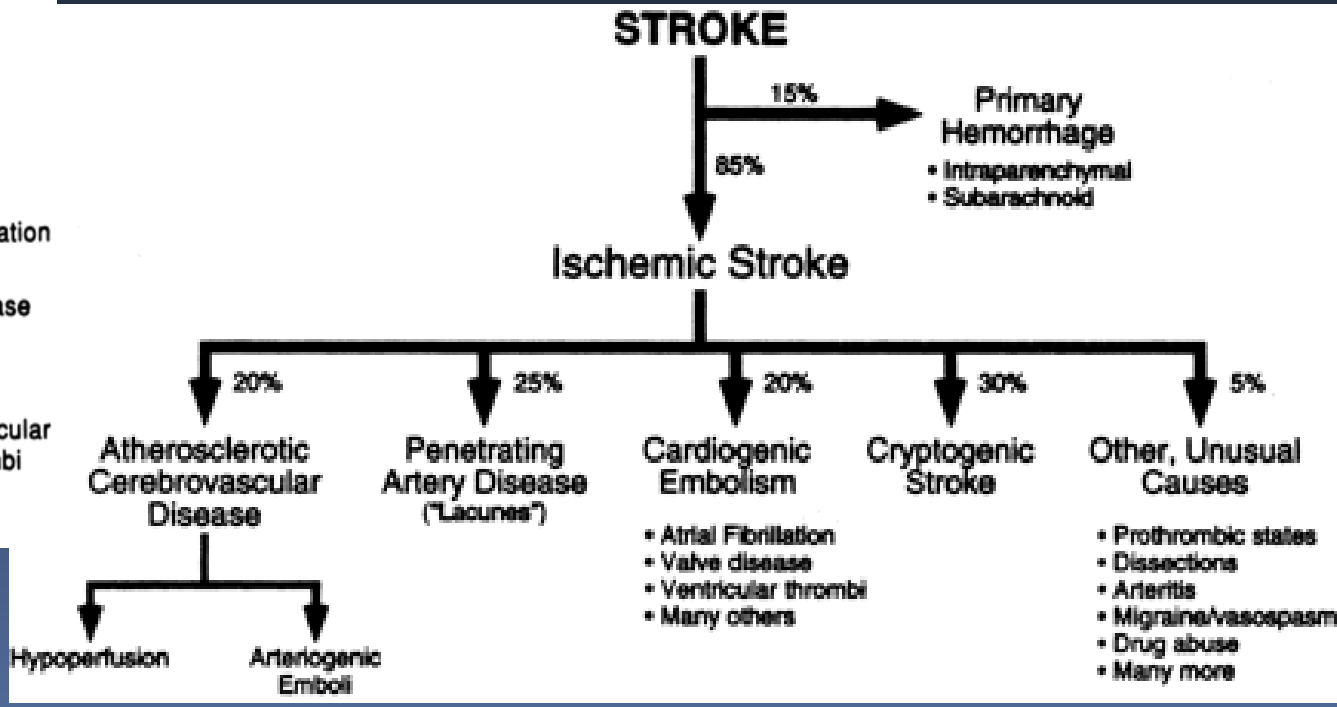
Disclosures

- Speakers Bureau BMS

Stroke is Heterogeneous



- Thrombi/Emboli of varying compositions



Will a Single Treatment or Modality Be Effective for All Stroke Subtypes and Stroke Patients?

Acute Stroke Treatment is Homogeneous

- Old
  - Diagnose, Prevent Medical Complications
- New
  - IV tPA- Only Approved Recanalization Tx
    - 0.9mg/kg, maximum 90mg
    - Same regimen for all stroke subtypes
    - Same regimen for all stroke severities
  - Aspirin
    - Mild effect on Outcomes- CAS & IST

Time is the Enemy

- The most critical factor that determines outcome is the **duration of ischemia**
  - Ischemia lasting < 5 minutes infrequently leads to infarction (irreversible cell death)
  - Ischemia lasting more than 15 minutes almost always results in infarction
- In humans the effective time window for minimizing injury is ≈ 1.5-3hrs
  - 6-24 hours in certain settings (e.g. vertebrobasilar ischemia)

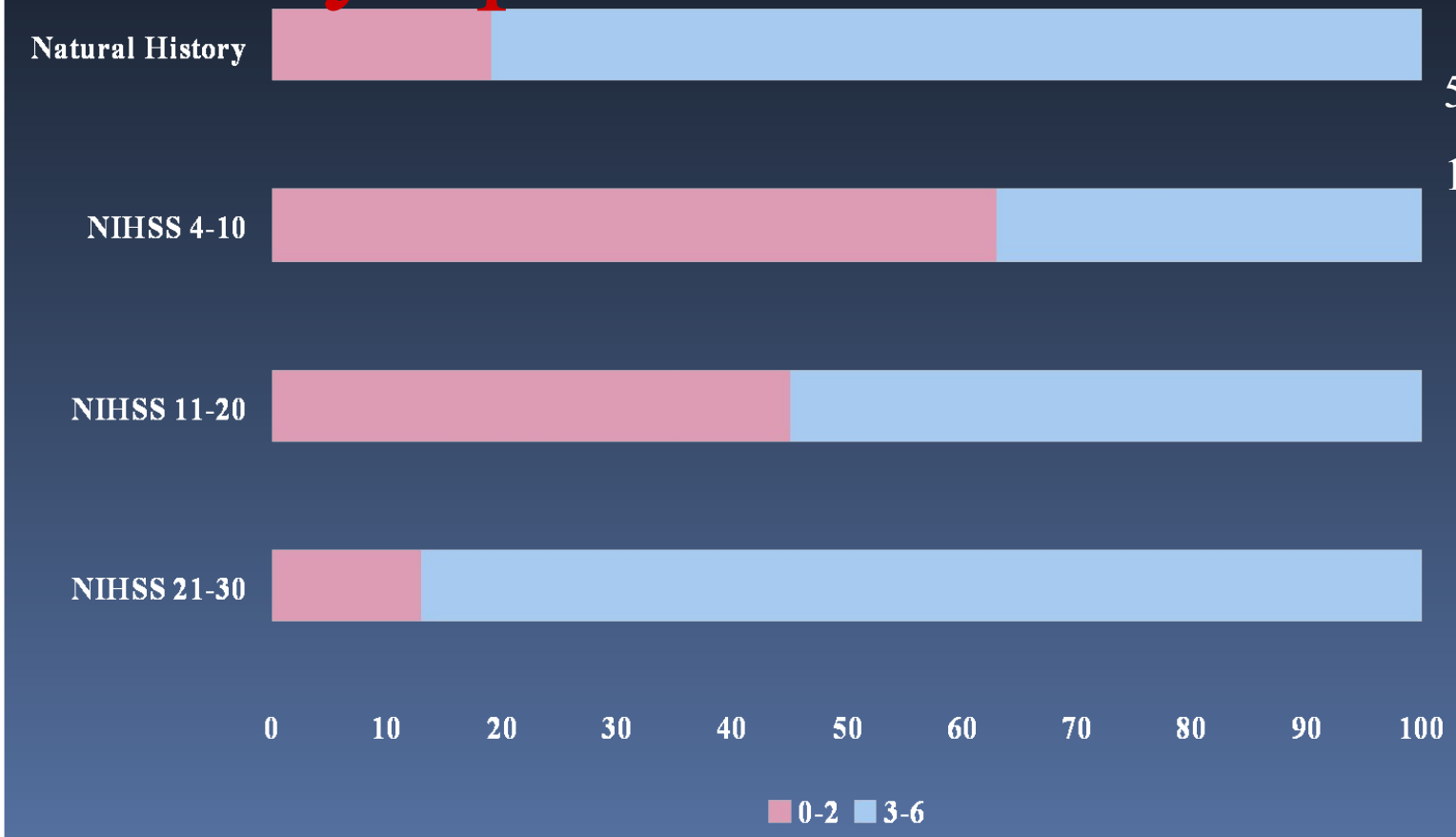
Intra-arterial Thrombolysis

The Prolyse in Acute Cerebral Thromboembolism Trial: PROACT II

- First and only randomized, controlled study of IA lysis (JAMA, February 1999)
  - Ischemic Stroke <6 hours duration
  - Angiographically proven MCA occlusion
  - Early infarct signs on initial CT <1/3 MCA territory
- 58% Relative benefit modified Rankin score of 2 or less (no or little disability), p=0.04
  - Absolute benefit 15% (40% Good outcome vs. 25%)
- Recanalization (TIMI 2 or 3) @ 2hrs
  - 66% vs. 18% in placebo
  - TIMI 3 rate for r-pro-UK 19%.

PROACT II Outcomes

Symptomatic ICH -10%



58% Relative

15% Absolute

Intra-Arterial Thrombolysis Clinical Practice

- Highly Varied
- Multiple Agents
  - tPA, Urokinase, Reteplase, etc.
- Multiple Large Series
  - Recanalization (TIMI 2 or 3): 40-70%
  - Good Clinical Outcome (mRankin 0-2): 18-60%

  Armold M Stroke 2007, Lee DH Korean J Radiol 2007, Kim D AJNR 2007, Tountopoulou A Neuroradiology 2008
- Metanalysis of 1,117 patients did not find any benefit for IA thrombolysis

  Mandava P Neurology 2007

IA Thrombolysis Limitations

- Use limited
  - Few interventionists trained
- Moderate Recanalization Efficacy
  - PROACT II
    - TIMI 3 19%
    - TIMI 2 or 3 67%
  - Up to 2hr for recanalization
- Only proven agent not available
  - r-pro-UK- same dose for every patient
- 10%-38% ICH

Multimodal Therapy

- 12 Patients
  - 4 Post-operative
- Age 65.7±12.1
- NIHSS 18.7±3.5
  - Range 15-25
- Sx Duration 3.6±2.2
  - Range 0.5-8hrs
- 5 MCA
- 6 Carotid Terminus
- 1 BA
- Etiology
  - 7 embolic
  - 5 Atherothrombotic

Endovascular Approach

Lysis	Lysis Result	2nd Intervention	Result	3rd Intervention	Result	4th Intervention	Result	5th Intervention	Result
Yes	TIMI 1	Angioplasty	TIMI 2 (Reoccl)	Reopro	TIMI 3	None			
IV full dose	TIMI 0	Angioplasty	TIMI 0	Snare	TIMI 0	Reopro	TIMI 2	ICA PTA	TIMI 3
No		Angioplasty	TIMI 2	Reopro	TIMI 3	None			
Yes	TIMI 1	Angioplasty	TIMI 1	Reopro	TIMI 3	Hypothermia	Good	None	
Yes	TIMI 2 (Reoccl)	Reopro	TIMI 2	Angioplasty	TIMI 2	None			
Yes	TIMI 0	Angioplasty	TIMI 2	Integrelin	TIMI 2	None			
Yes	TIMI 0	Reopro	TIMI 0	Angioplasty	TIMI 1	Angiojet (ICA)	TIMI 2	None	
Yes	TIMI 0	Reopro	TIMI 0	Angioplasty	TIMI 3	None			
Yes	TIMI 0	Mechanical Disruption	TIMI 1	Reopro	TIMI 3	None			
Yes	TIMI 0	Reopro	TIMI 0	Angioplasty	TIMI 0	Snare	TIMI 1 (ACA TIMI 3)	None	
Yes	TIMI 0	Angioplasty	TIMI 1	Reopro	TIMI 3	None			
Yes	TIMI 0	Angioplasty	TIMI 0	Reopro	TIMI 0	Snare	TIMI 3	None	

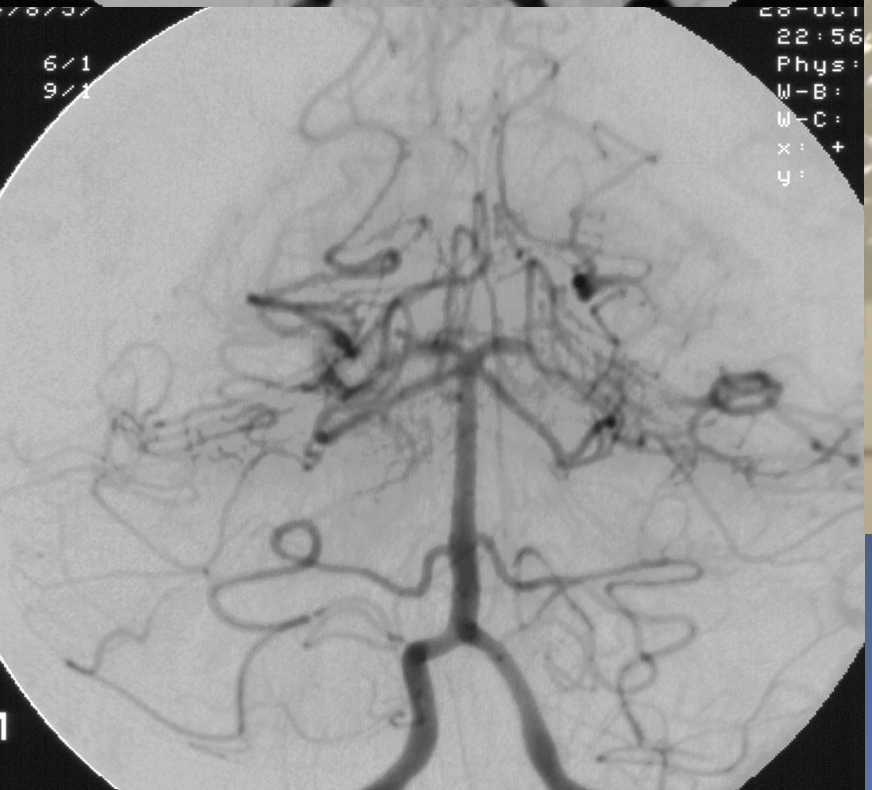
Clinical Outcome

- TIMI 2 or 3 92%
- >4 Point NIHSS Improvement 10/12 (83%)
  - Mean Improvement 11±6.8
  - Mean NIHSS @ D/C 7.7±8
  - No or Minimal Disability (Rankin≤2) 6/12 (50%)
- Mortality 2/12 (17%)
- ICH
  - Symptomatic 1/12 (8.3%)
  - Asymptomatic 1/12 (8.3%)

Mechanical Embolectomy

Mechanical Embolectomy With Commercially Available Snare

- Personal Experience
  - 9 Patients
  - All failed thrombolysis or contraindicated
  - 4/9 Complete clot removed in first pass
  - 3/9 Multiple passes for complete removal
  - 2/9 Partial clot removal
  - No complications
  - 4/9 Rapid Complete Recovery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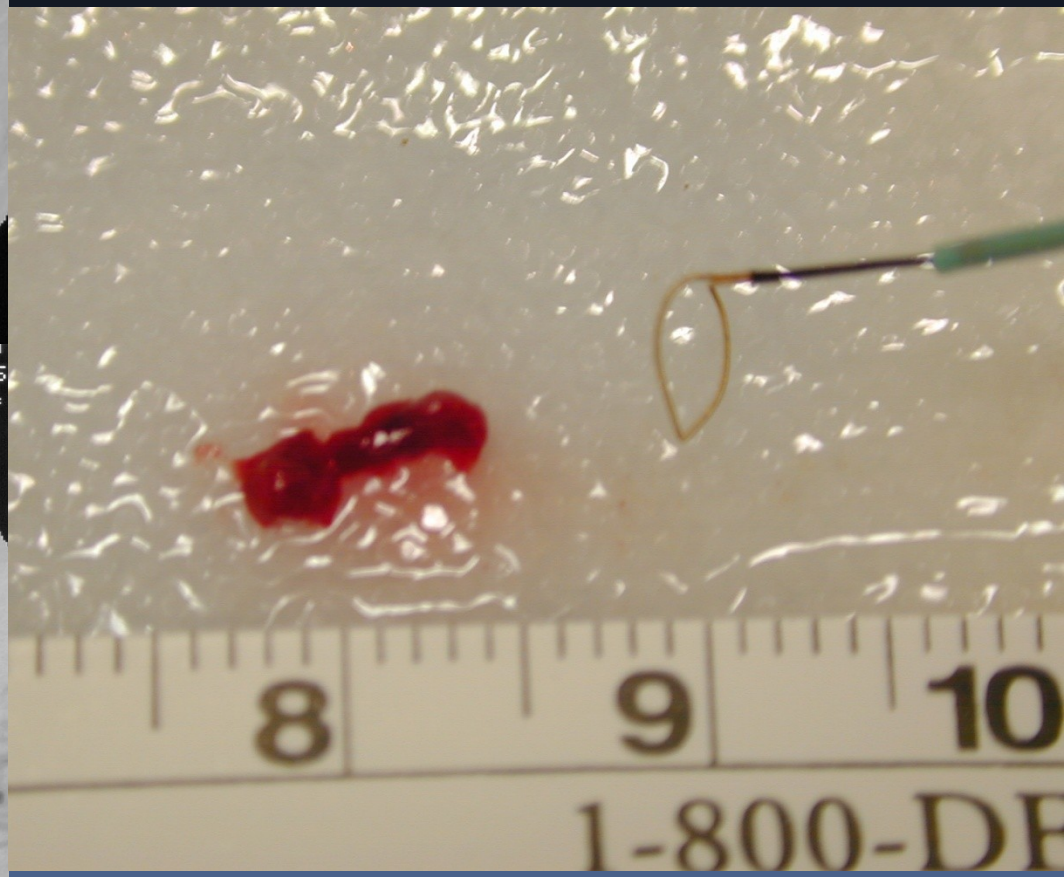
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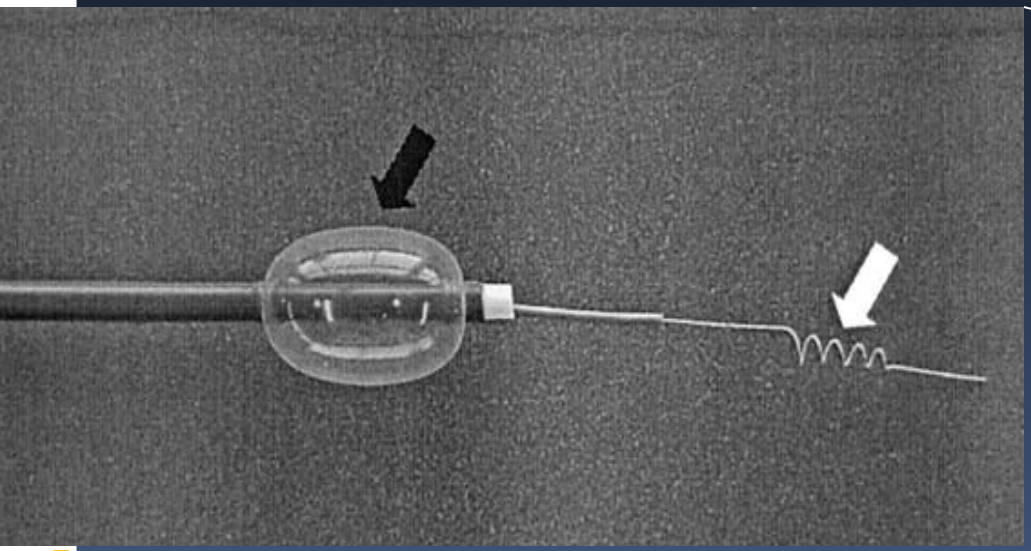
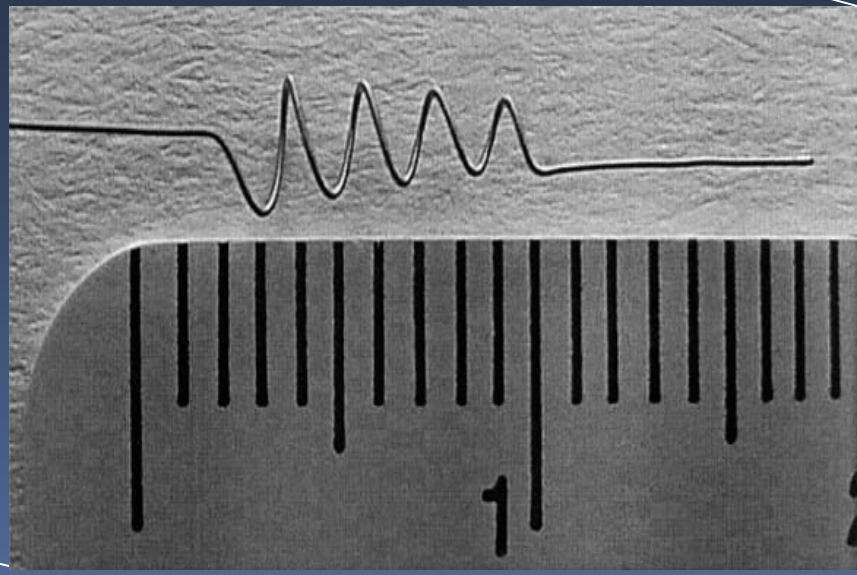
Concentric Retriever Device With Nitinol Coil N>250, ~45% Recanalization





Leary MC, et al. Ann Emerg Med. 2003 Jun;41(6):838-46

Merci Study

- Device deployed in 141/151 patients
- Mean NIHSS 20.1 (SD ± 6.6)
- Recanalization
  - Device only: 68 pts (48%)
  - + adjuvant: 85 (60%) pts.
- Symptomatic ICH
  - 7/90 pts (8%) with device only
  - 11/141 (8%) + adjuvant tx.
- MRS ≤ 2 at 90 days was 28% (36 of 130)

Stroke 2005;36(7):1432-1438

Multi Merci Trial N=164
L5 Retriever

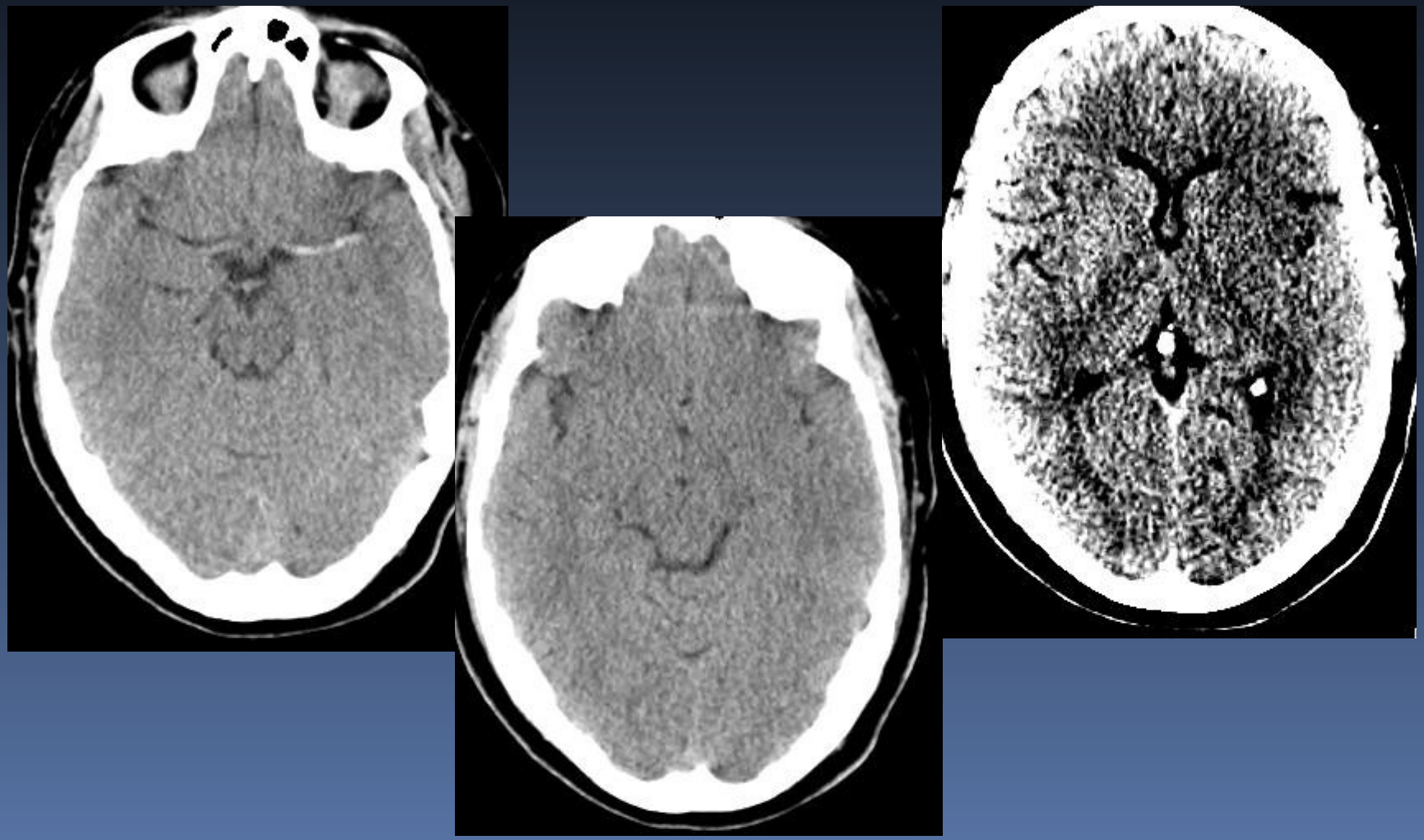
- Retriever revascularization 54.9% (90)
- Retriever +
  adjuvant revascularization 68.3%(112)
- Clinically significant complications 5.5% (9)
- Symptomatic ICH 9.8% (16)

International Stroke Conference 2007. San Francisco

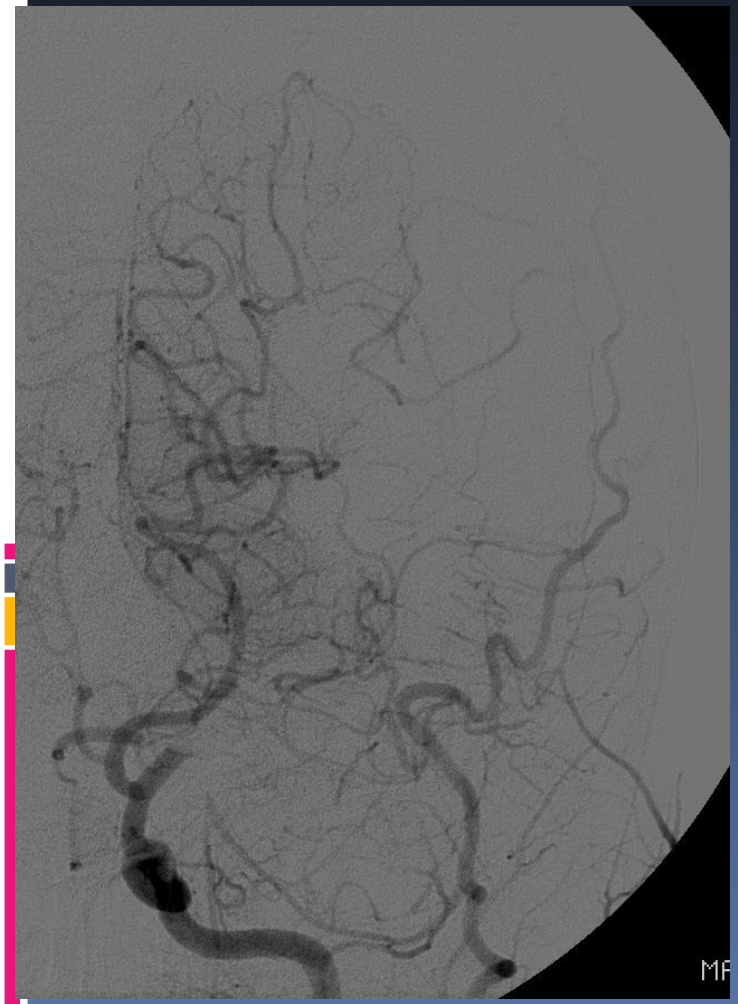
Illustrative Case 2: Mechanical Embolectomy

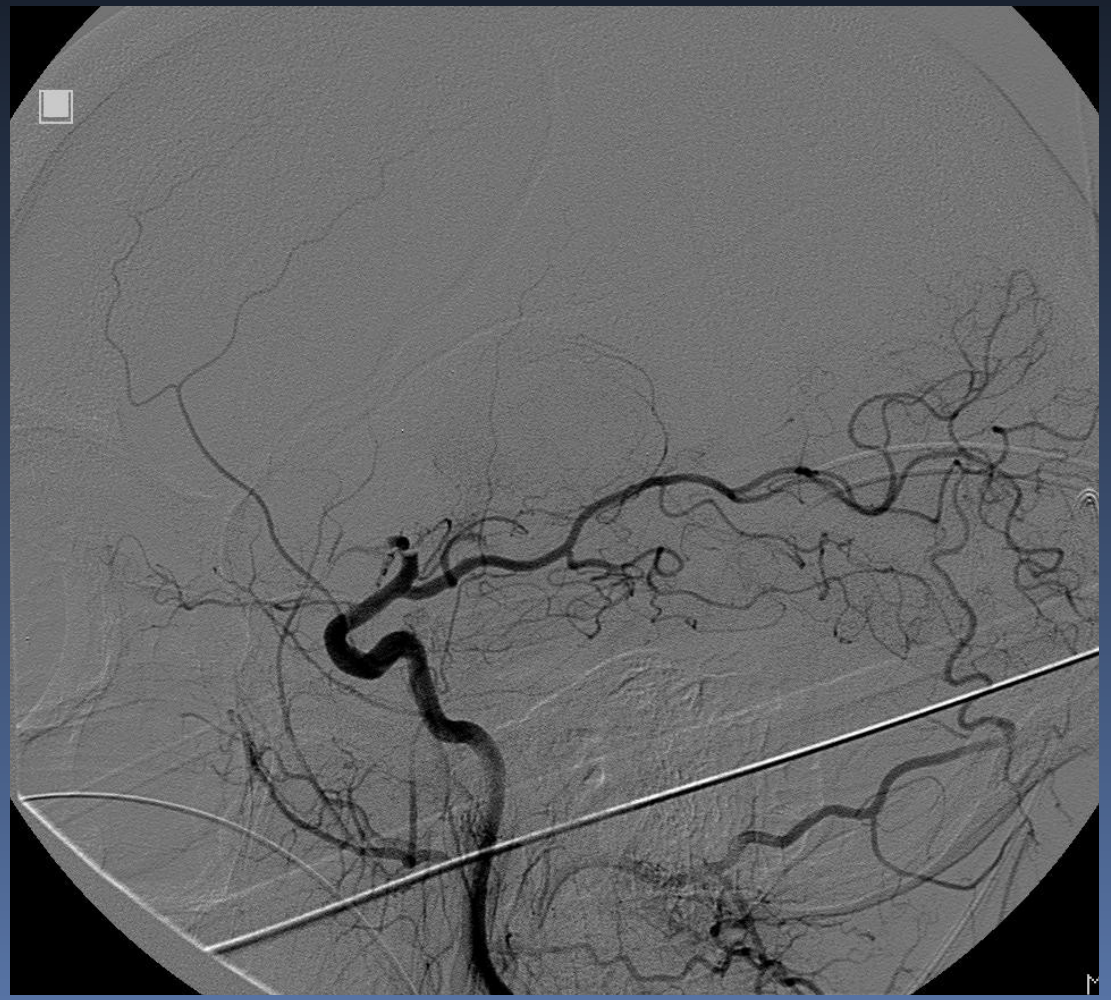
- 29 yo WF with no PMHx
- Found in AM with "confusion" and weakness
- In ED
  - Mute, following some commands
  - 1 hr later
    - Plegic on R

Initial CT Brain
12hrs after onset

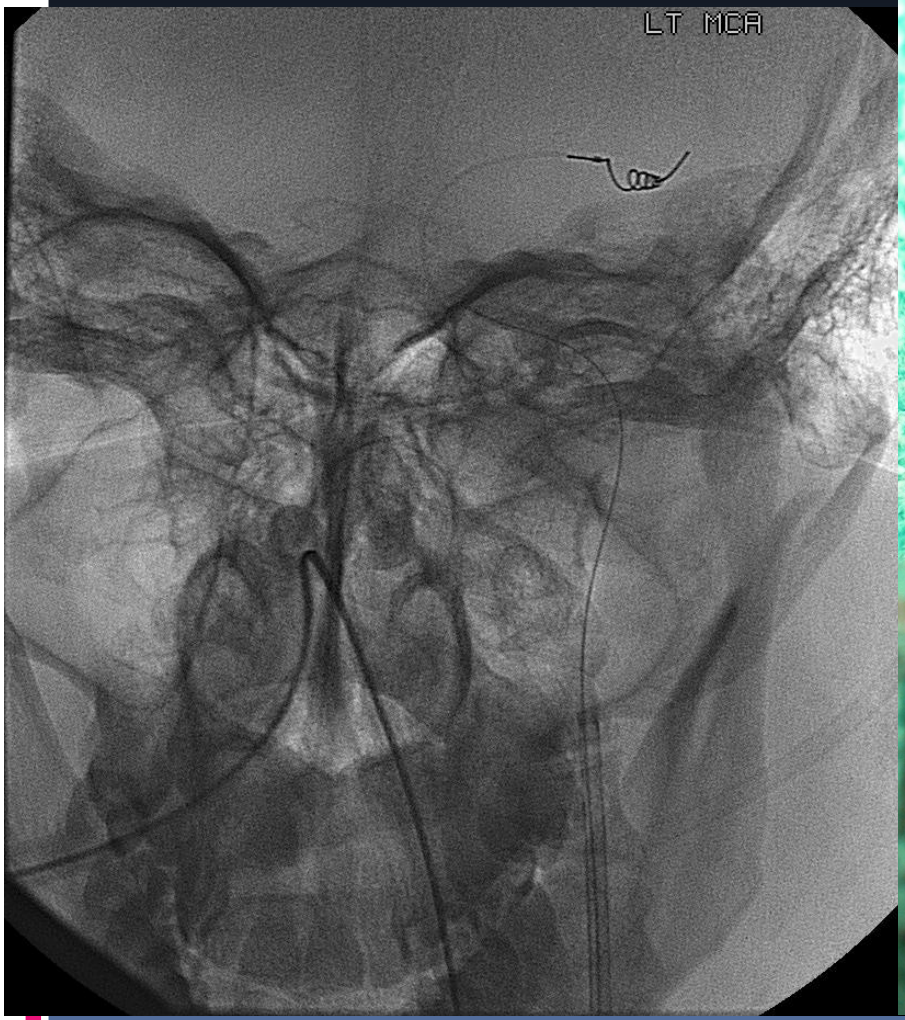


Cerebral Angiogram

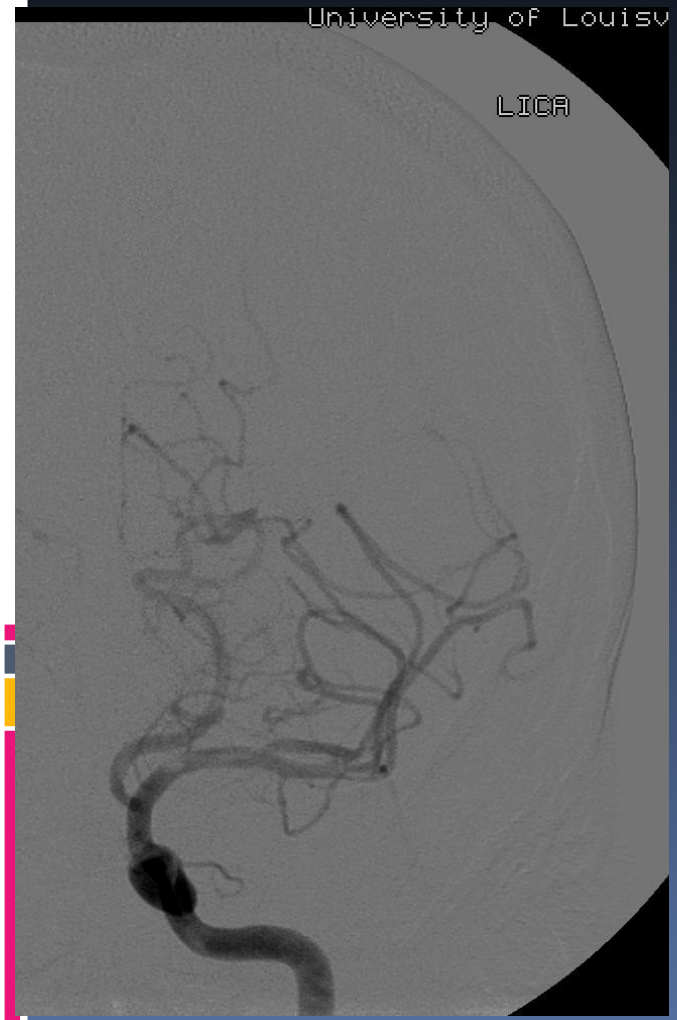




Embolectomy



Final Angiogram



Clinical Course

- Stabilized
- 1 Week later
  - D/C to Rehab
  - Following Commands
  - Moves R leg

Angioplasty for Acute Ischemic Stroke

- Nakano et al study of 34 Pts with MCA occlusion Tx with PTA alone
  - 91.2% Recanalization vs.. 64% in Historical controls Tx with tPA
  - ICH 2.9% vs.. 19.4%

- Ueda T et al Stroke 1998;29:2568-74
- Nakano et al Stroke 2002;33:2872-76
- Yoneyama et al AJNR 2002;23:277-81
  - Combined low dose tPA and PTA

Stenting for Acute Stroke

- Cleveland Clinic Experience 2000-2003
  - 9 consecutive Pts
    - PTA and Stenting
    - 7 Atherostenosis
    - 2 Cardioembolic Occlusion
    - No Thrombolytics or GPIIb/IIIa antagonists
  - Stroke duration 8-108hrs
  - Clopidogrel 300-600mg
  - ASA 325mg

Cleveland Clinic Results

Vessel	Initial NIHSS	Technical Success	D/C NIHSS
ICA/MCA	22	Yes	1
ICA/MCA	24	Yes	12
ICA/MCA	20	Yes	0
ICA/MCA	21	Yes	0
ICA Cavernous	18	Yes	5
MCA	24	Yes	3
ICA/MCA	17	Partial	17
ICA	14	Yes	2
MCA	22	Yes	12
Mean	20.2		5.8
Std Dev	3.3		6.3

Complications: None

Illustrative Case 3: Stenting for Acute Stroke

- 71 y.o. AAM
  - HTN, Cigs, Et-OH
- Presented 17 hours after onset of progressive
  - Aphasia
  - Right Homonymous Hemianopsia
  - Right sided Hemiparesis
- Initial NIHSS 17

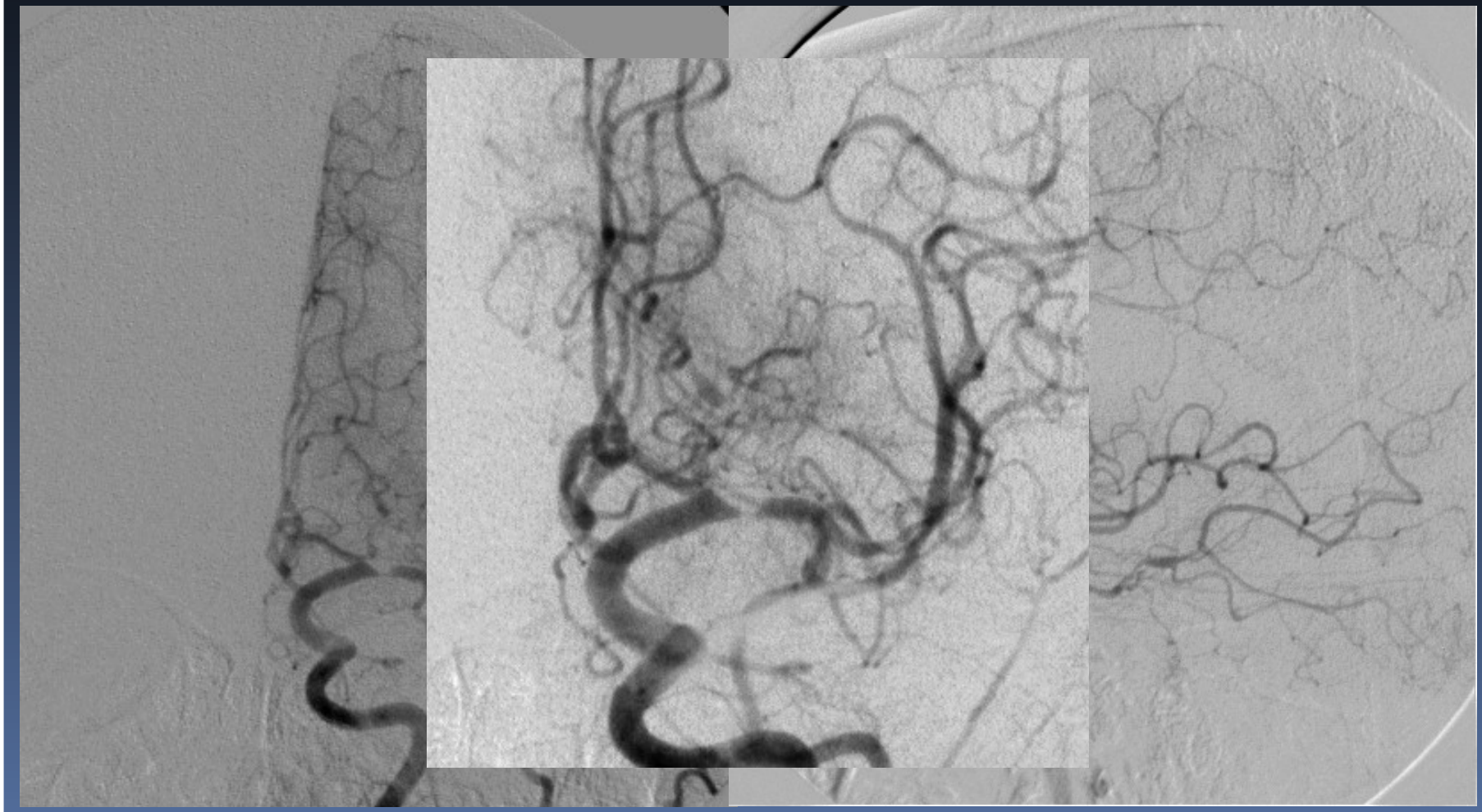
Clinical Course

- Initial CT
  - Normal
  - ? Subtle Early changes
- Admitted Pending MRI results
- Loaded with Plavix 300mg
- Fluid Bolus to elevate BP
- @ 24 hours NIHSS=24
  - Somnolent
  - Right Hemineglect

MRI

- Small deep DWI Lesion
- Large PWI Lesion
- M1 “Occlusion”

Angiogram



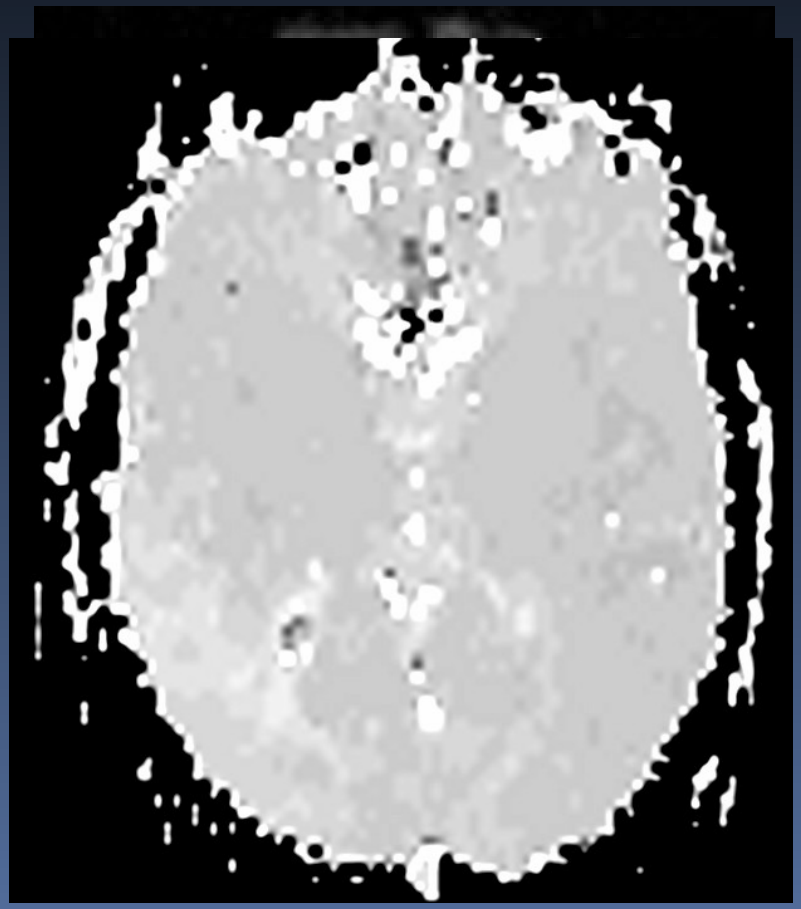
Endovascular Approach

- PTA to 8 ATM
- Marked Recoil post PTA
- 3X8mm Stent

Angiographic Result

Clinical Outcome

- Improvement began within 15 minutes
- 4 hours Post procedure NIHSS=6
- MRI Repeated
  - DWI Same
  - PWI Normal



- POD#2 NIHSS=3
- POD#3 D/C to Home

Conclusions

- A variety of endovascular Tx available with >3hr time window for Acute Stroke
  - Mechanical Embolectomy ideal when lytics contraindicated
- Stroke Tx is best when it can be individualized
  - Multimodal stroke treatment may be safest and most effective
- Patient selection critical
  - Clinical status
  - Size of infarct
  - Size of Penumbra

“A foolish consistency is the hobgoblin of little minds, adored by little statesmen and philosophers and divines.”

- Ralph Waldo Emerson