Acute Ischemic Stroke Imaging Innovations

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Disclosures

Microvention – consultant
Covidien/Medtronic – consultant and proctor
Penumbra - Consultant
Surpass Medical/Surpass – shareholder
InNeuroCo, Inc – shareholder
Medina Medical - shareholder

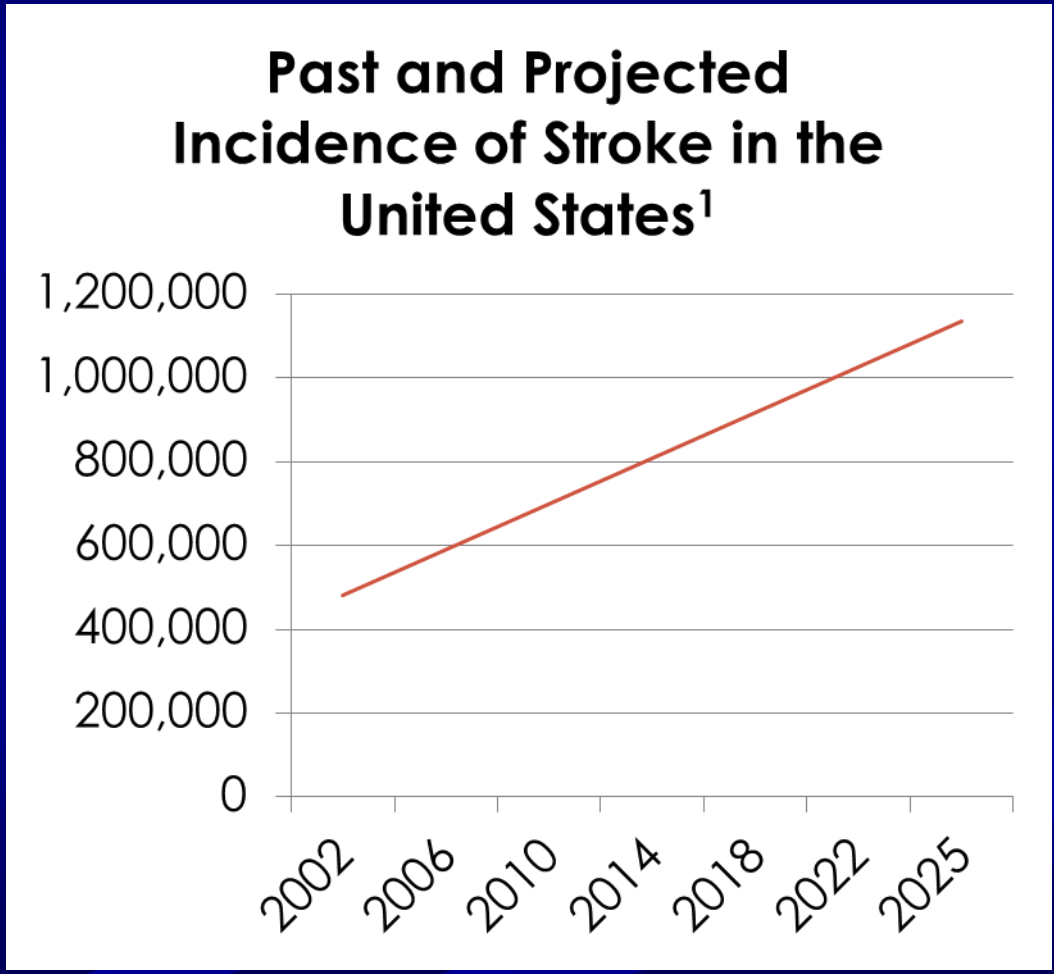
Stroke Statistics

- Stroke is important cause of death in the US
- 795,000 strokes/year in the US
- 25% death within 1 year after the initial stroke
- Near 50% of stroke victims will not regain functional independence
- Estimated costs: $68.9 billion in 2009

Lloyd-Jones D, et al: Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 119:e21-181, 2009

STROKE FUTURE

- Assuming no change in the age-specific rates of stroke, approximately 1.1 million Americans will suffer a stroke in 2025[1]



1. Broderick JP: William M. Feinberg Lecture: stroke therapy in the year 2025: burden, breakthroughs, and barriers to progress. **Stroke 35:205-211, 2004**

STROKE TYPES

Total Stroke
695, 000

Ischemic Stroke (85%)
590, 000

As many as 40% due to large vessel occlusion[1]
236, 000

Hemorrhagic Stroke (15%)
105, 000

1. Smith WS, Tsao JW, Billings ME, Johnston SC, Hemphill JC, 3rd, Bonovich DC, et al: Prognostic significance of angiographically confirmed large vessel intracranial occlusion in patients presenting with acute brain ischemia. **Neurocrit Care 4:14-17, 2006**

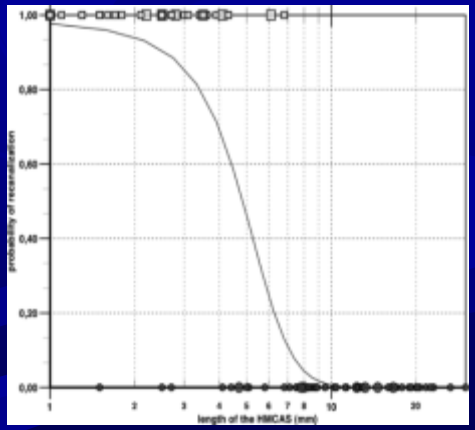
IV tPA Reperfusion Limitations

- Location
  - Vessel occlusion location prognostic of response*

Distal ICA	4.4%	M1-MCA	32.3%
M2-MCA	30.8%	Basilar	4.0%

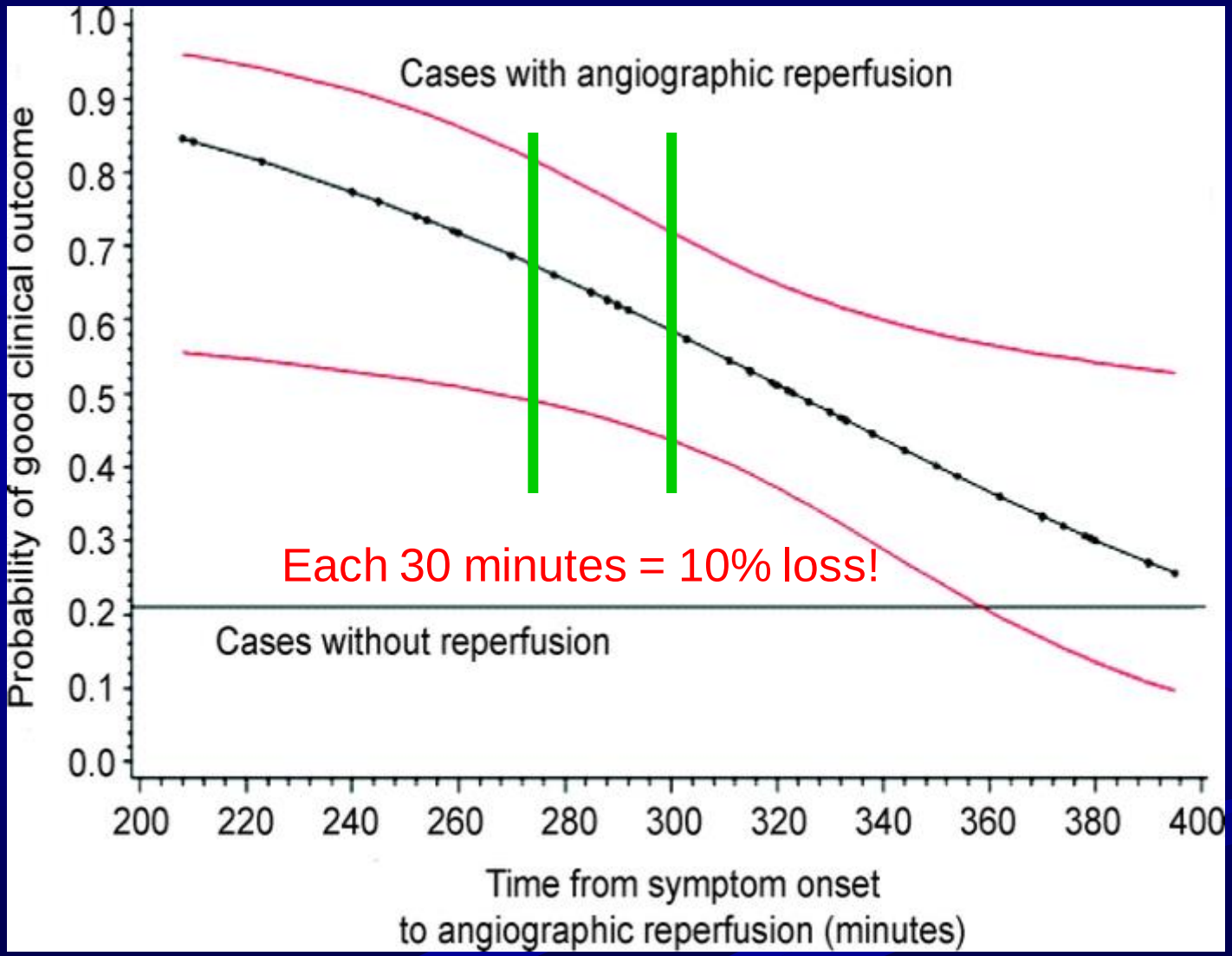
  - Reperfusion most predictive of outcome (RR 2.7)

- Clot size (<8mm)**
  - Reperfusion remains strongly predictive
    - Mean discharge mRS
      - Reperfused 1.9
      - No reperfusion 4.4



*Bhatia Stroke. 2010;41:2254-2258, **Riedel, Stroke. 2011;42:1775-1777

Timing Is Critical – IMS I & II



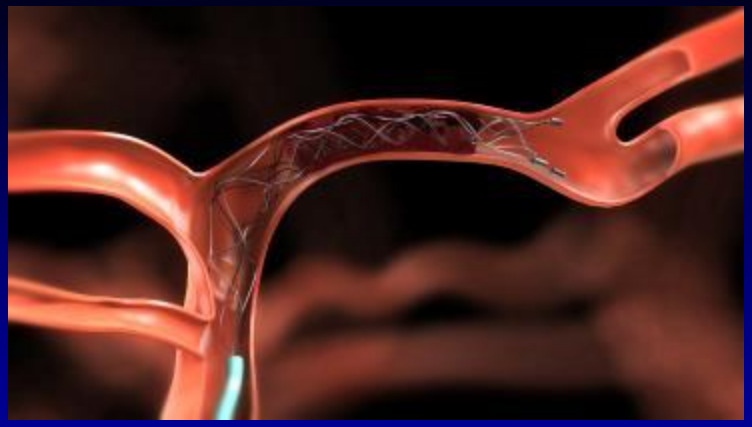
(Khatri. Neurology, 2009)

Advances in Stroke Treatment
Therapy for acute ischemic stroke

- "Standard" (…or old) imaging criteria
  - Standard imaging: no hemorrhage or extensive infarction
  - NINDS and ECASS III: IV tPA up to 3 or 4.5hs
- Changing perspective
  - A fixed time window is not physiologically based
  - Functional imaging can identify patients who might benefit from "delayed" treatment

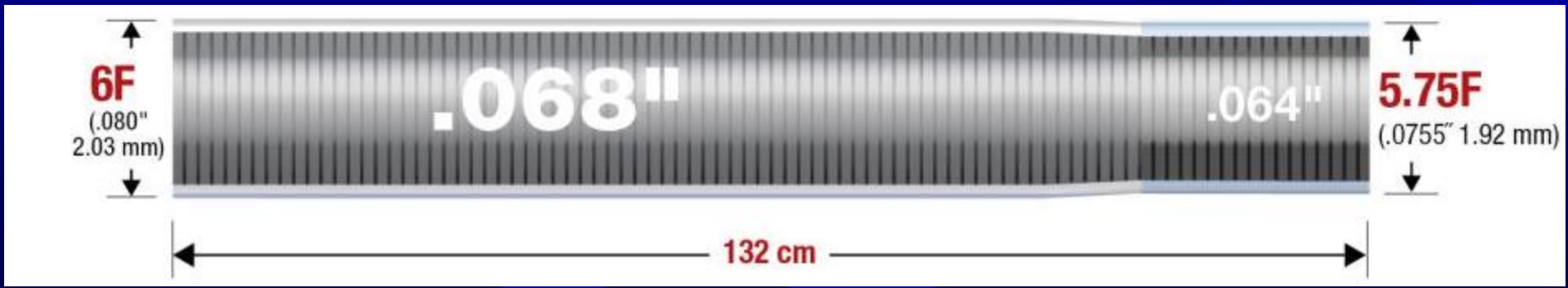
A NEW ERA

Solitaire



Trevo

Penumbra ACE™ 64




MR CLEAN
A Multicenter Randomized CLinical trial of Endovascular treatment for Acute Ischemic stroke in the Netherlands

ESCAPE

UNIVERSITY OF CALGARY
CUMMING SCHOOL OF MEDICINE

ESCAPE

Endovascular treatment for **S**mall **C**ore and **A**nterior circulation **P**roximal occlusion with **E**mphasis on minimizing CT to recanalization times

Michael D Hill, Mayank Goyal
on behalf of the ESCAPE Trial

Principal Inv
Michael D Hi
Mayank Goy
Andrew M D

EXTEND-IA

Extending the time for Thrombolysis in Emergency Neurological Deficits – Intra-Arterial

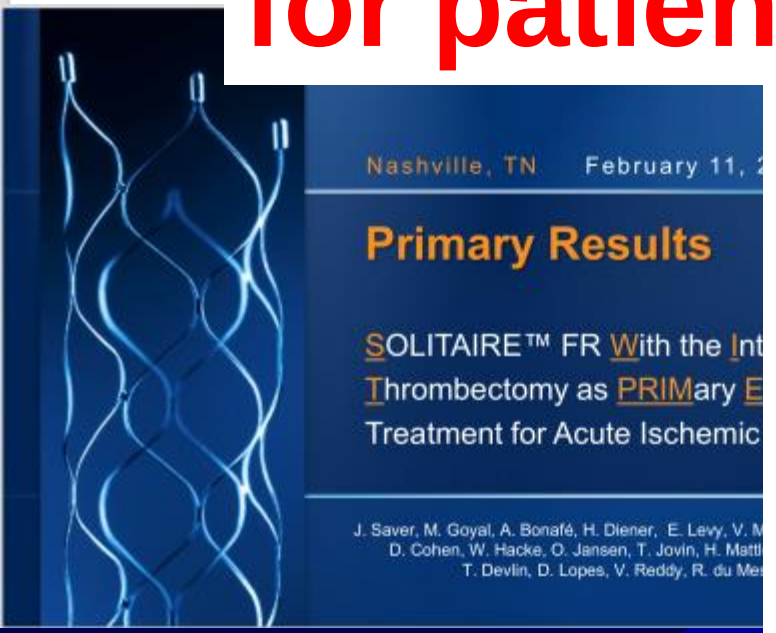
A randomized controlled trial of endovascular thrombectomy after standard dose intravenous t-PA within 4.5 hours of stroke onset utilizing dual target imaging selection

Bruce Campbell
Co-PI and Medical Coordinator

Peter Mitchell
Co-PI and Head of Neurointervention

Stephen Davis and Geoffrey Donnan

Imaging critical component for patient selection!



Nashville, TN February 11,

Primary Results

SOLITAIRE™ FR With the Int
Thrombectomy as PRIMary E
Treatment for Acute Ischemic

J. Saver, M. Goyal, A. Bonafé, H. Diener, E. Levy, V. M
D. Cohen, W. Hacke, O. Jansen, T. Jovin, H. Mattl
T. Devlin, D. Lopes, V. Reddy, R. du Me

ORIGINAL ARTICLE

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

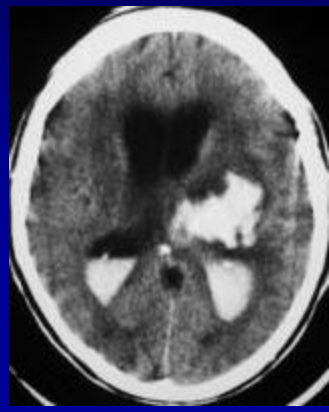
T.G. Jovin, A. Chamorro, E. Cobo, M.A. de Miquel, C.A. Molina, A. Rovira, L. San Román, J. Serena, S. Abilleira, M. Ribó, M. Millán, X. Urra, P. Cardona, E. López-Cancio, A. Tomasello, C. Castaño, J. Blasco, L. Aja, L. Dorado, H. Quesada, M. Rubiera, M. Hernández-Pérez, M. Goyal, A.M. Demchuk, R. von Kummer, M. Gallofré, and A. Dávalos, for the REVASCAT Trial Investigators*

ABSTRACT

Main Current AIS-LVO Trials

	Recanalization	90-day MRS 0-2 Interventional Arm	90-day MRS 0-2 Medical Arm
MR CLEAN	58.7%	32.6%	19.1%
ESCAPE	72.4%	53%	29.3%
EXTEND-IA	86%	71%	40%
SWIFT PRIME	88%	60.2%	35.5%

CT role: evaluation of acute stroke



- Exclude hemorrhage and “stroke” mimics
  - Hemorrhage, tumor, etc.
- If ischemic:
  - Exclude massive infarction
  - ASPECT Score
    - Very large infarcts do not do well even with early recanalization
  - Determine site of occlusion
- Assess potential for reversibility
  - Differentiate dead from viable but still “at risk” tissue - “Ischemic penumbra” with functional neuroimaging

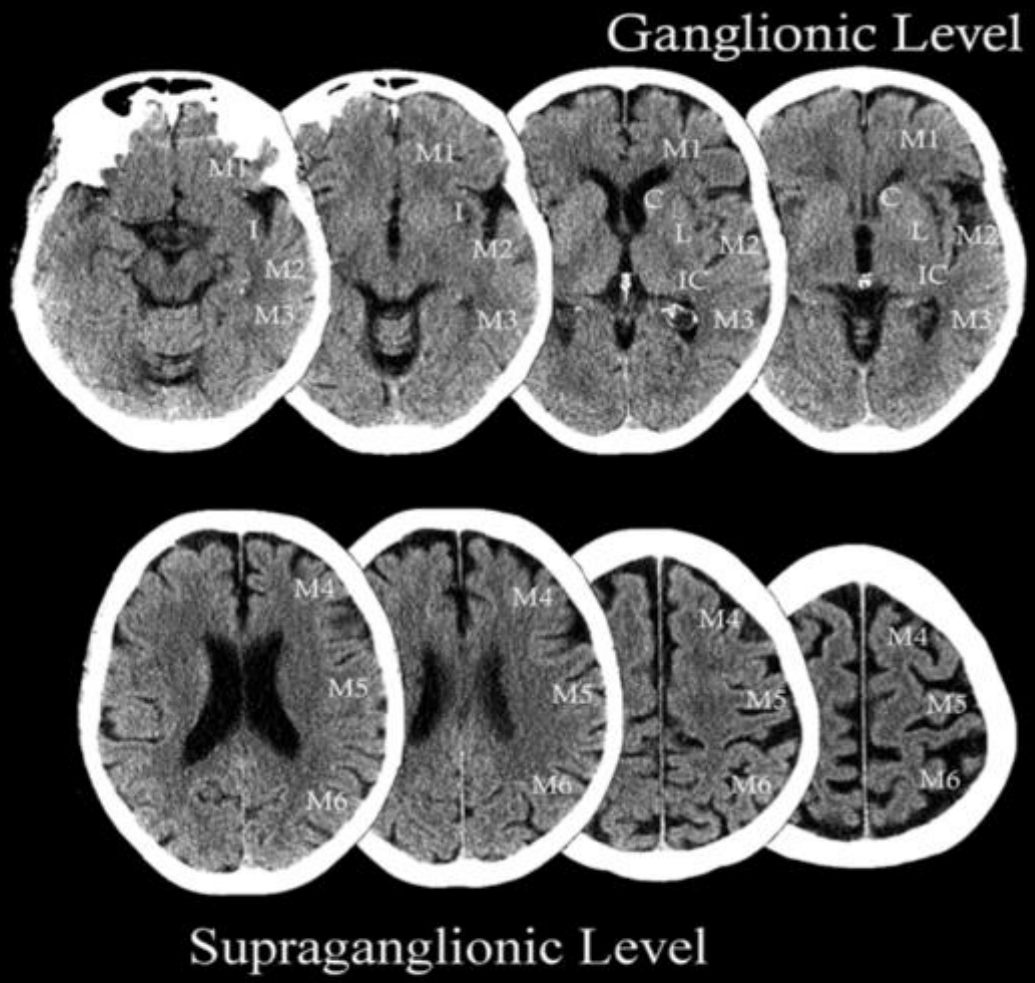
Infarct detection with CT: Early signs

- Hyperdense artery sign
  - Densest vessel visualized
- Loss of gray/white differentiation
  - Subtle but usually positive within 1-3 hours
  - Cortical band or insular ribbon sign
  - Obscuration of deep gray matter often the key - lentiform nucleus

CT sensitivity for detection of acute infarct in patients presenting in less than 6 hours after the onset is low (approximately 60%) - Horowitz SH. Stroke 1991

Imaging – ASPECTS

www.aspectsinstroke.com



Examine all the images at the ganglionic and supra-ganglionic levels.

Take off 1 pt from 10 for every region that is affected

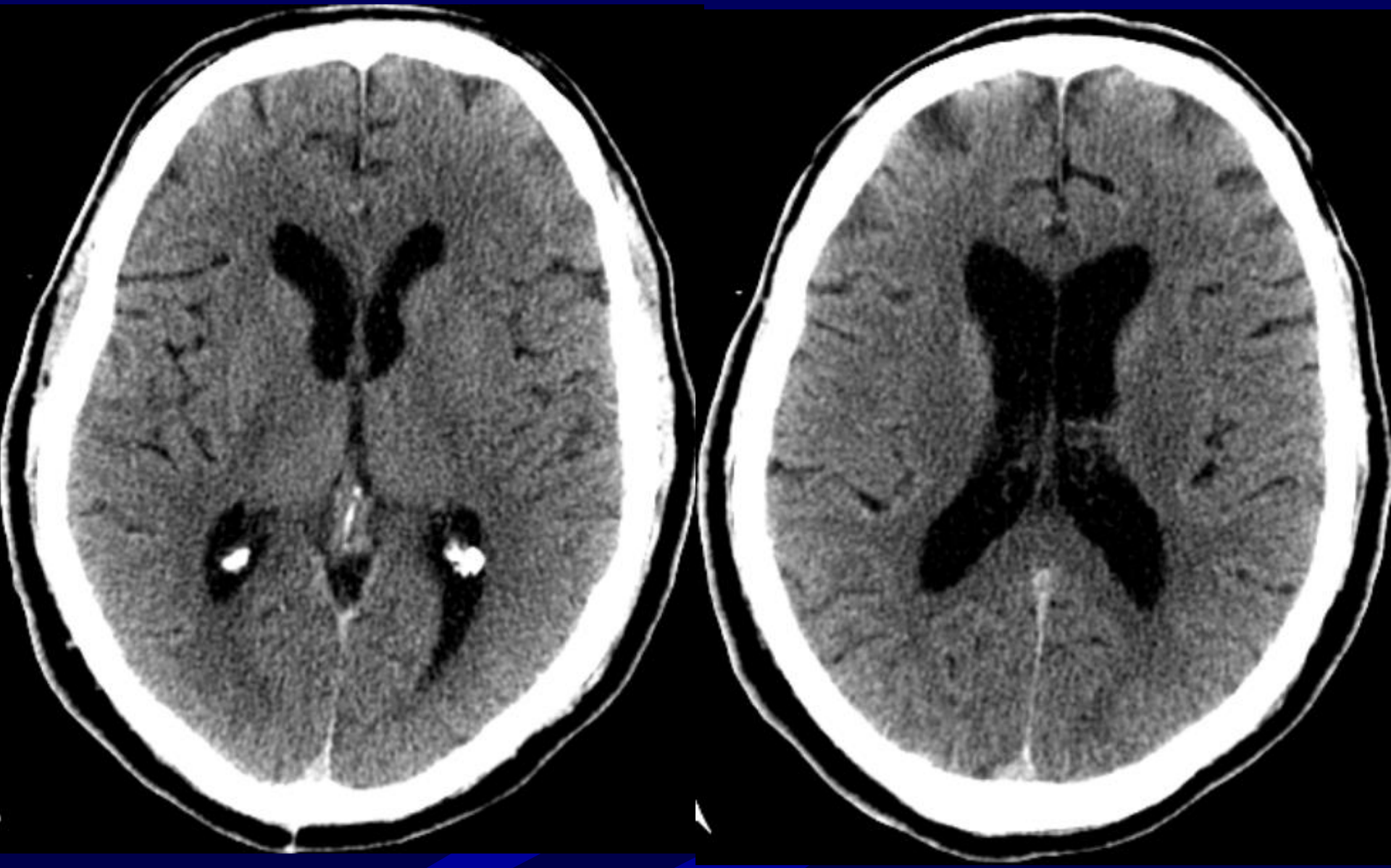
ASPECTS

8-10 Small core.

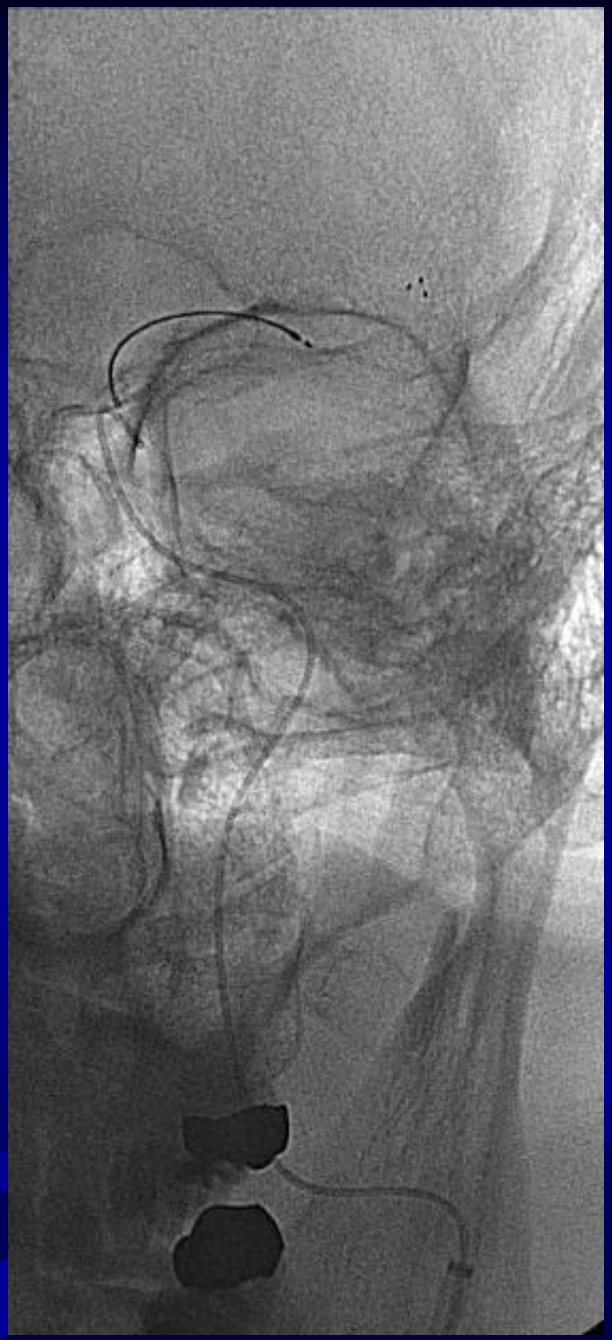
6-7 Moderate core.

0-5 Large core.

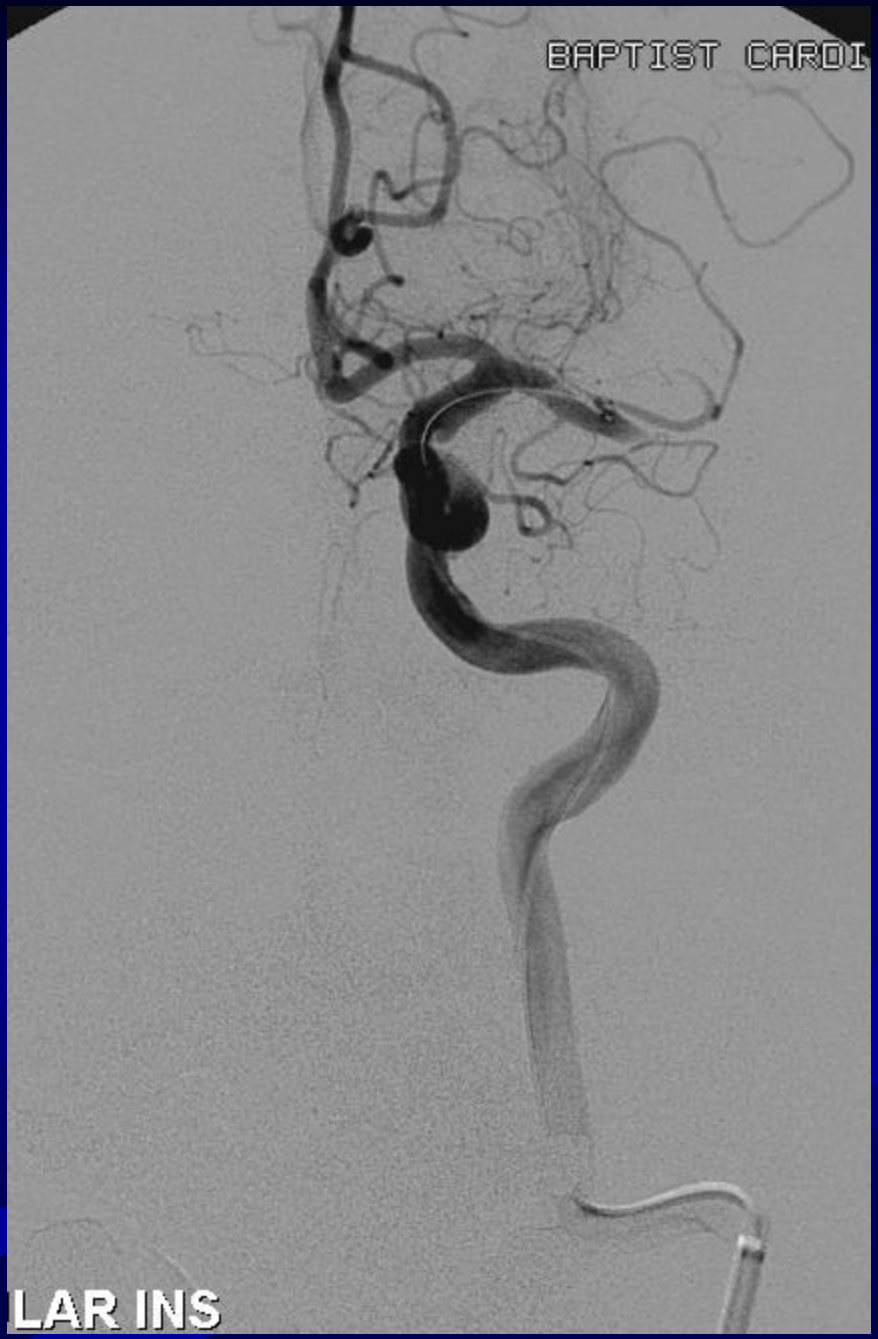
72M NIHSS 15

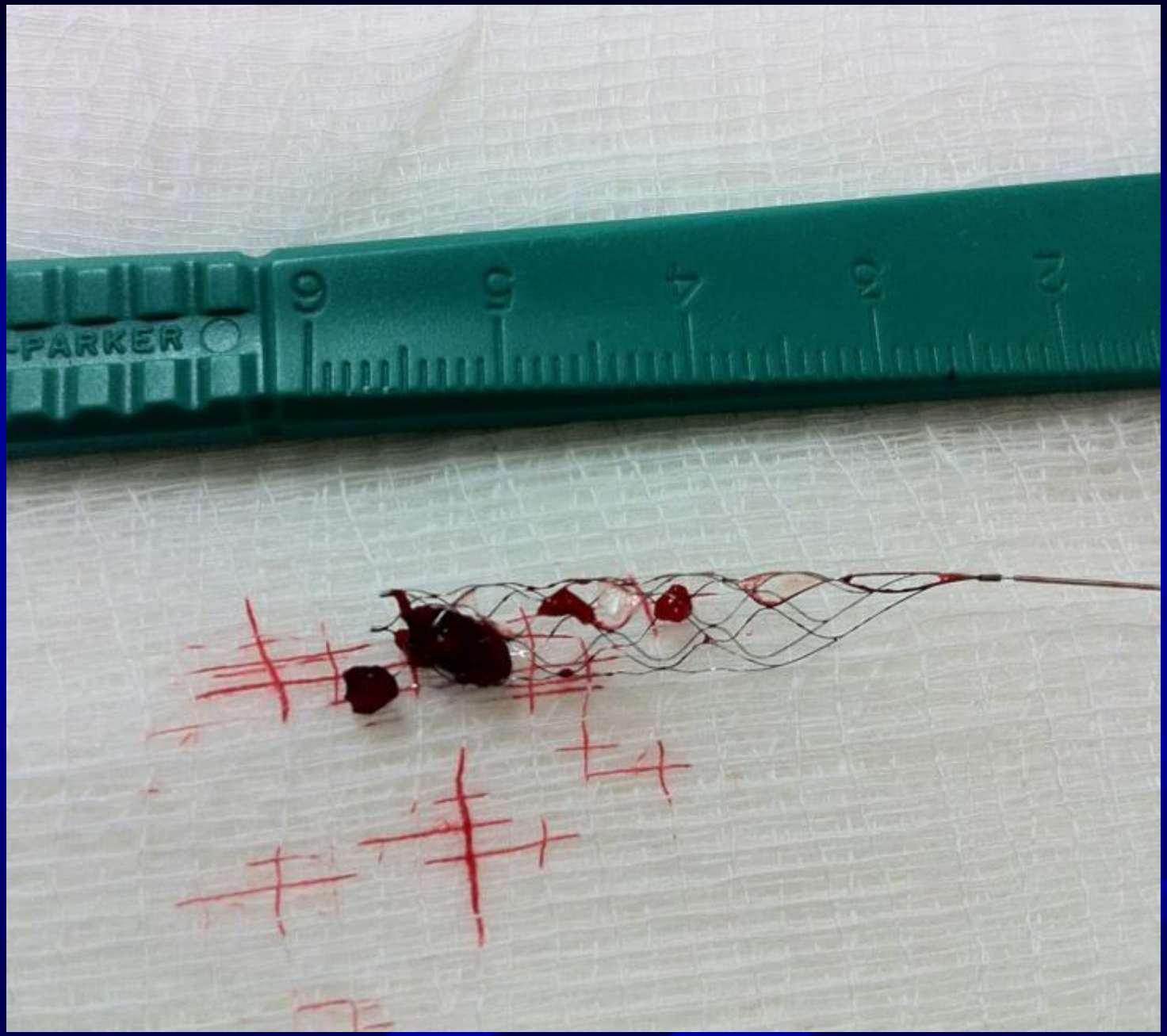



LAR INS

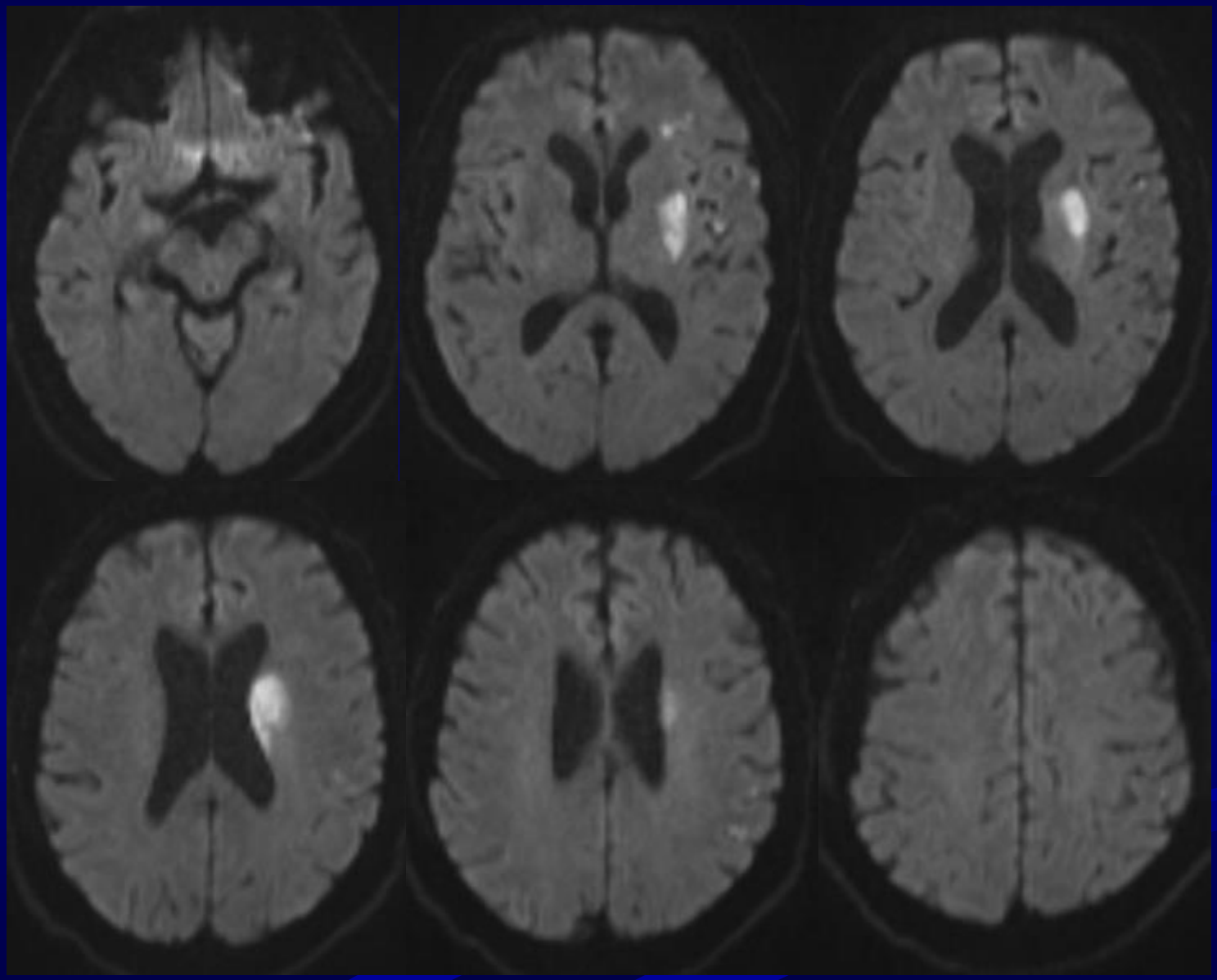



BAPTIST CARDI
LAR INS


BAPTIST CARDI
LAR INS

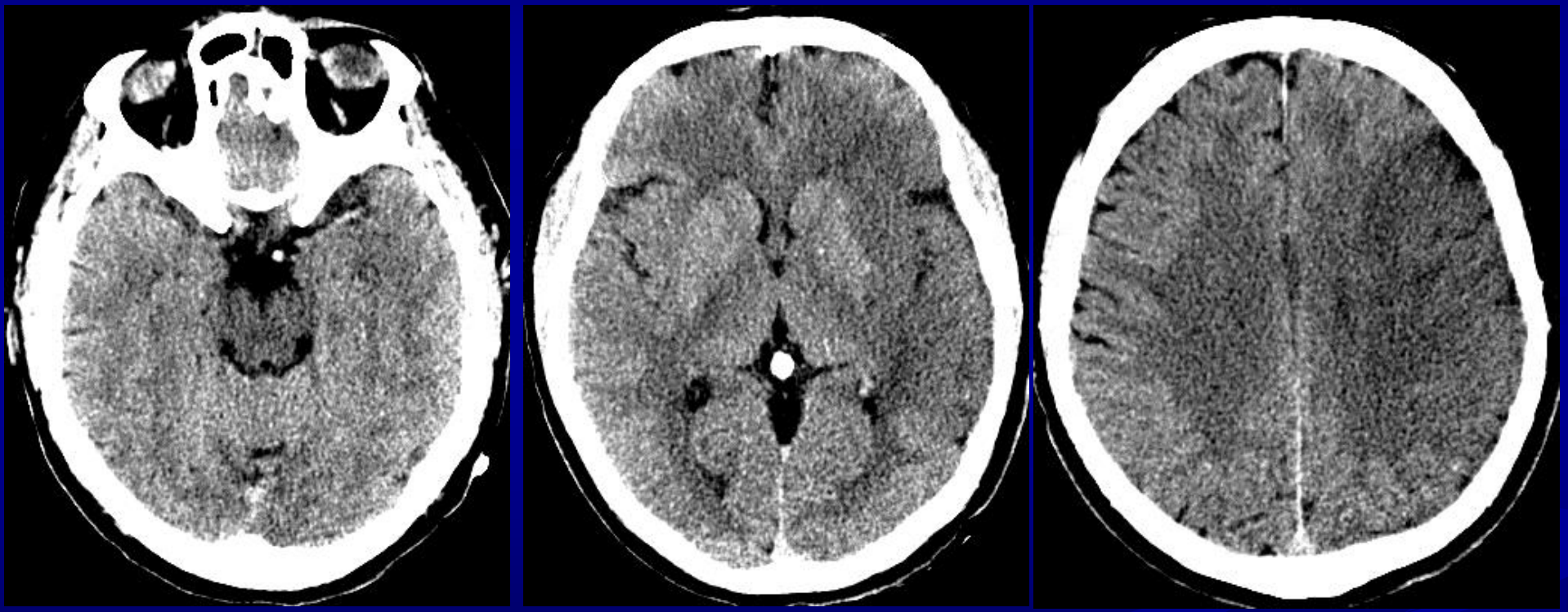

PARKER
6
5
4
3
2

24h post EVT NIHSS 1

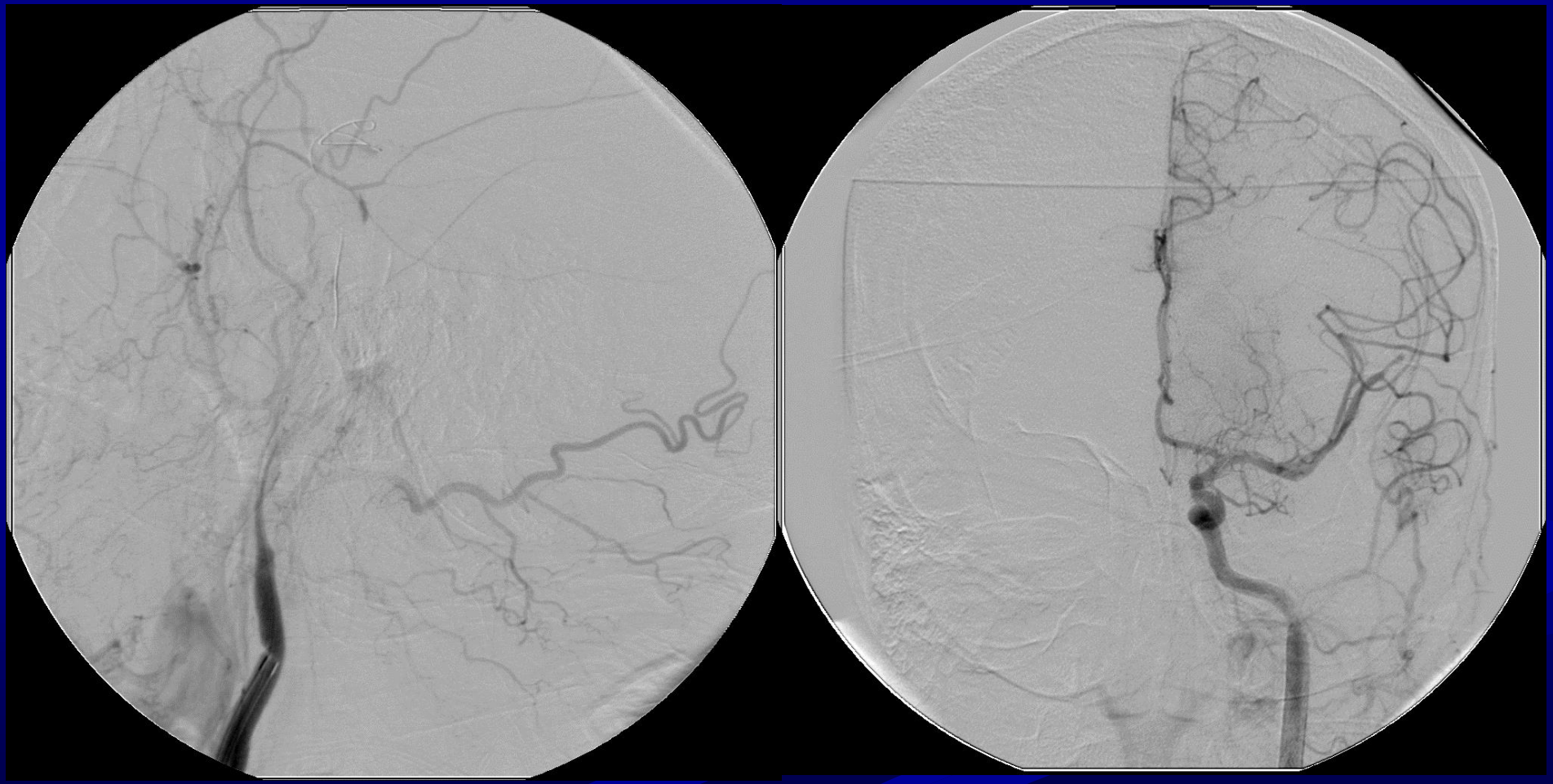


Should we go ahead???

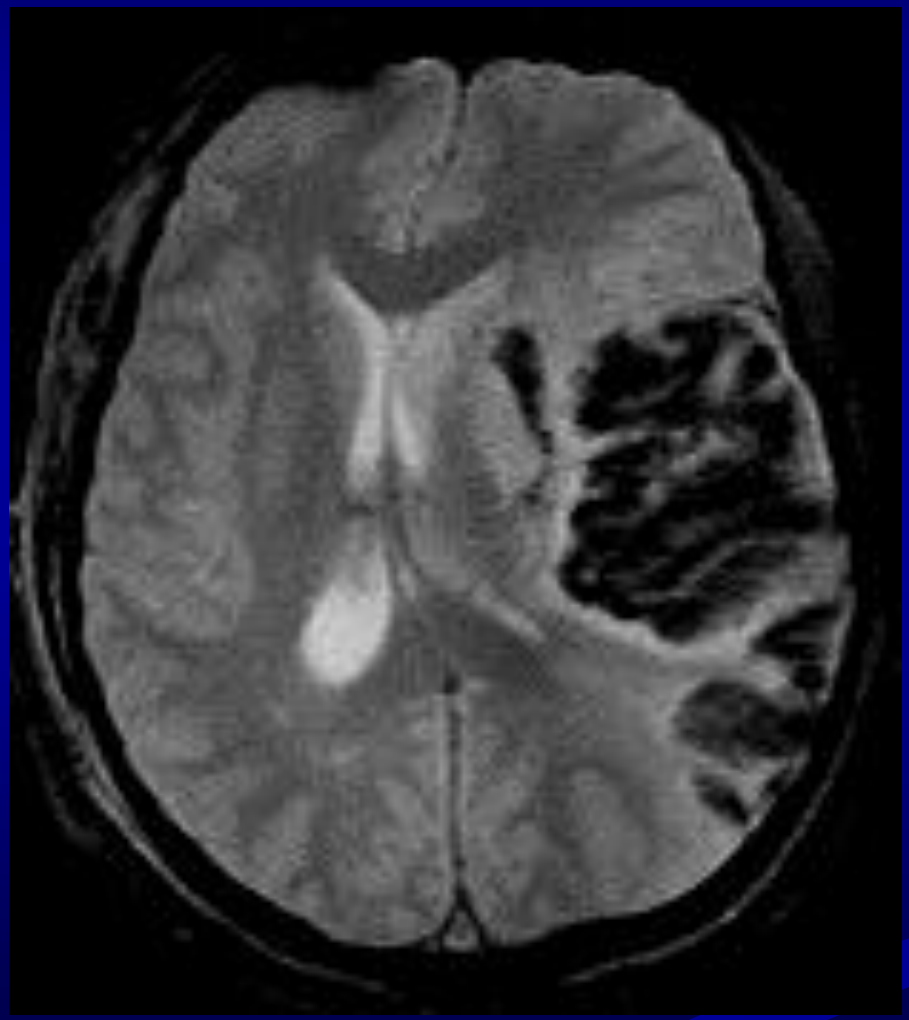
- 40yo M sudden onset of right sided hemiplegia during exercising

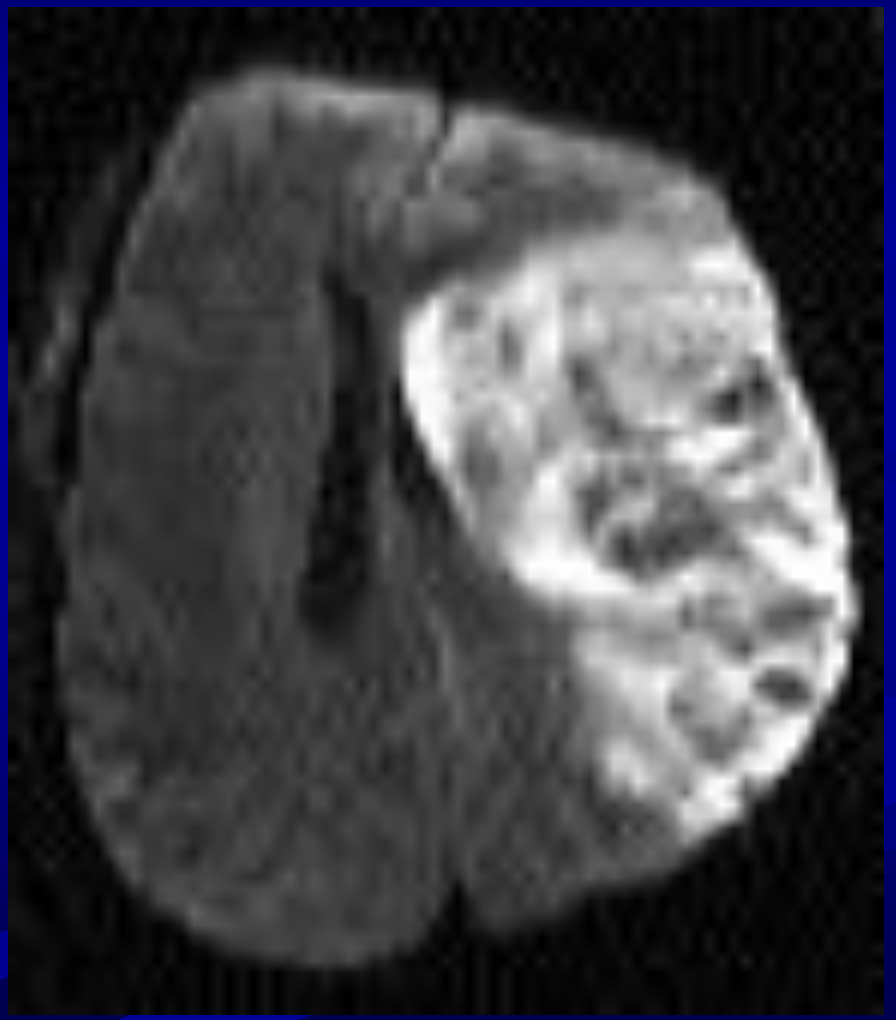


Should we go ahead???

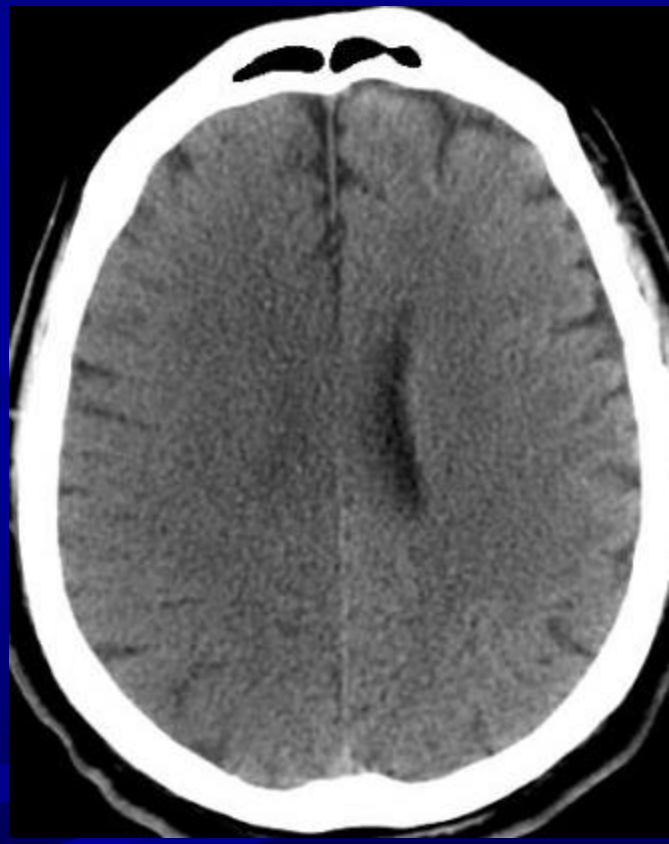


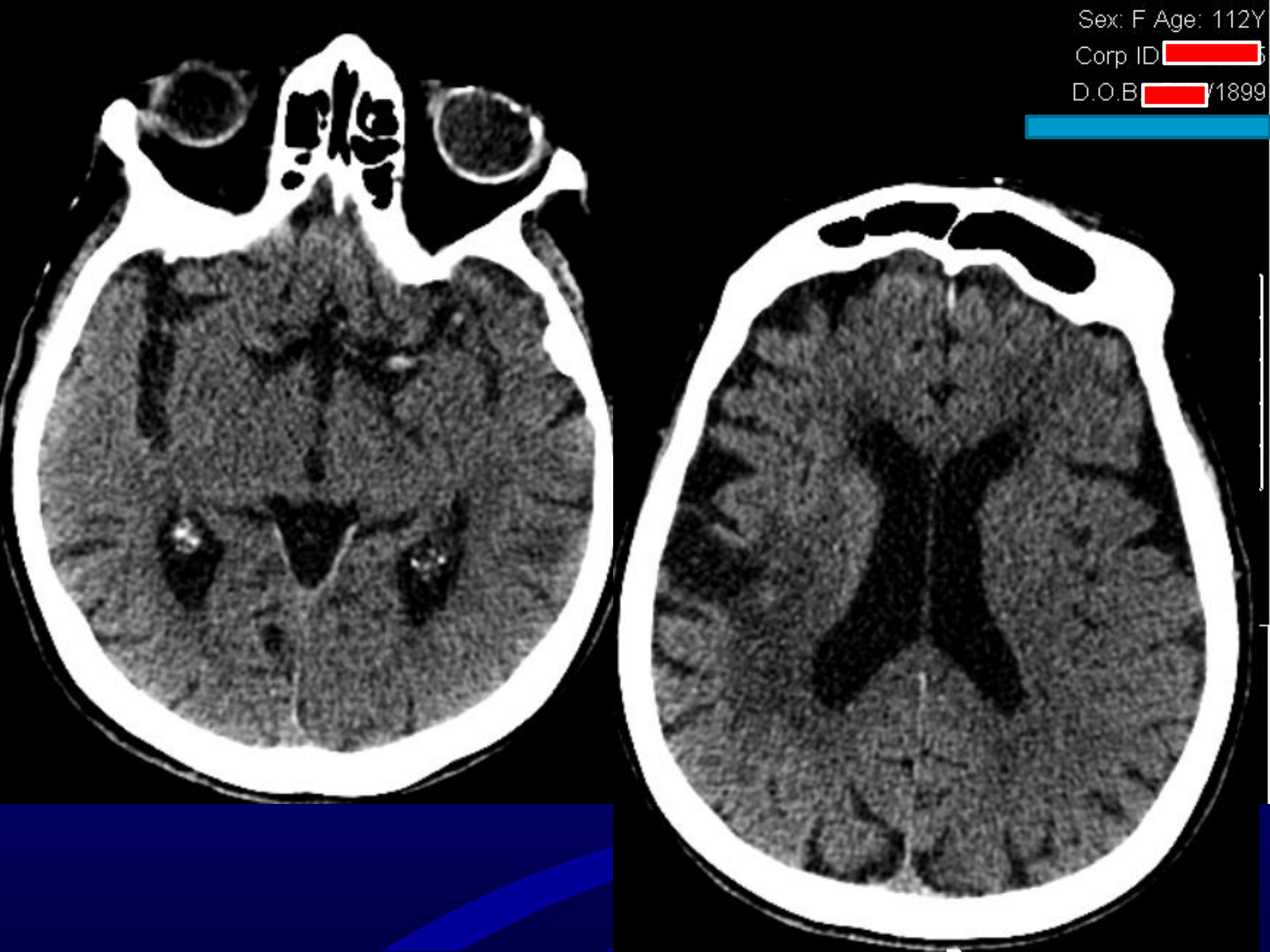
Should we go ahead???





When not to intervene? Ex. 1




Sex: F Age: 112Y
Corp ID [redacted]
D.O.B [redacted]/1899

44F presented left facial and left UE and LE weakness

3PM

6:25PM

MR of Hyperacute Infarction: standard sequences

- Standard sequences usually negative for parenchymal changes
  - No vasogenic edema (or mass effect)
  - No parenchymal enhancement
- Absent or slow arterial flow
  - “Flow voids” missing
  - Intravascular enhancement

The four P's

Systematic approach for stroke imaging

- Parenchyma: How much damage has occurred? – DWI or CTA-SI or CBV
- Pipes: What is the cause of stroke – MRA or CTA
- Perfusion: What is the status of hemodynamic compensatory mechanisms? – PWI or CTP
- Penumbra: How much tissue is still at risk?
  - PWI minus DWI or CBF minus CBV/CTA-SI

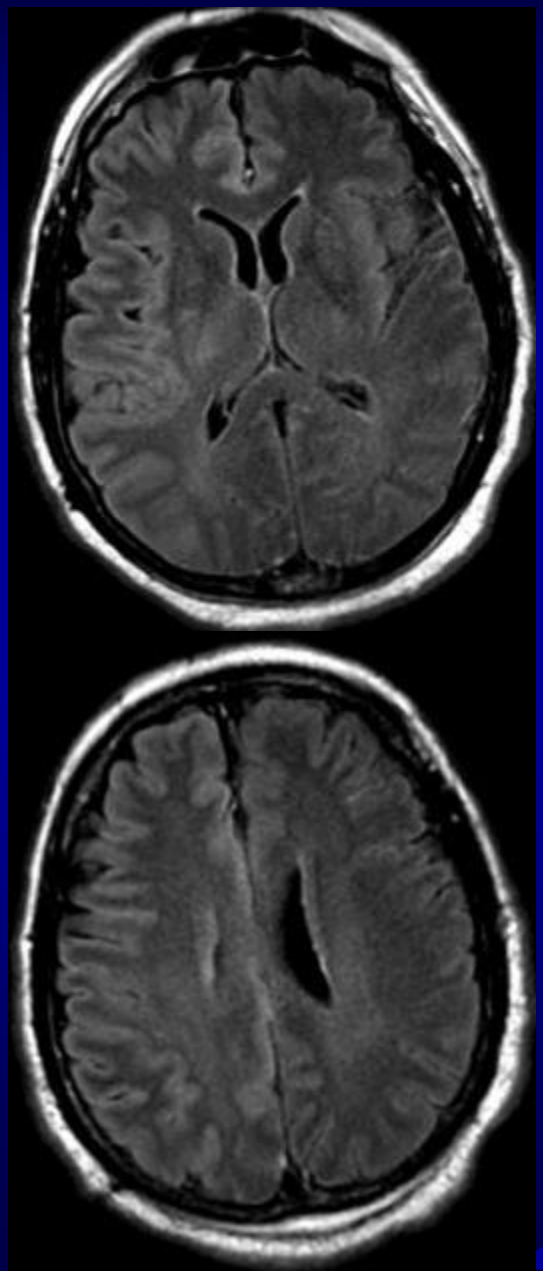
The four P's: Parenchyma
Diffusion Weighted Imaging (DWI)

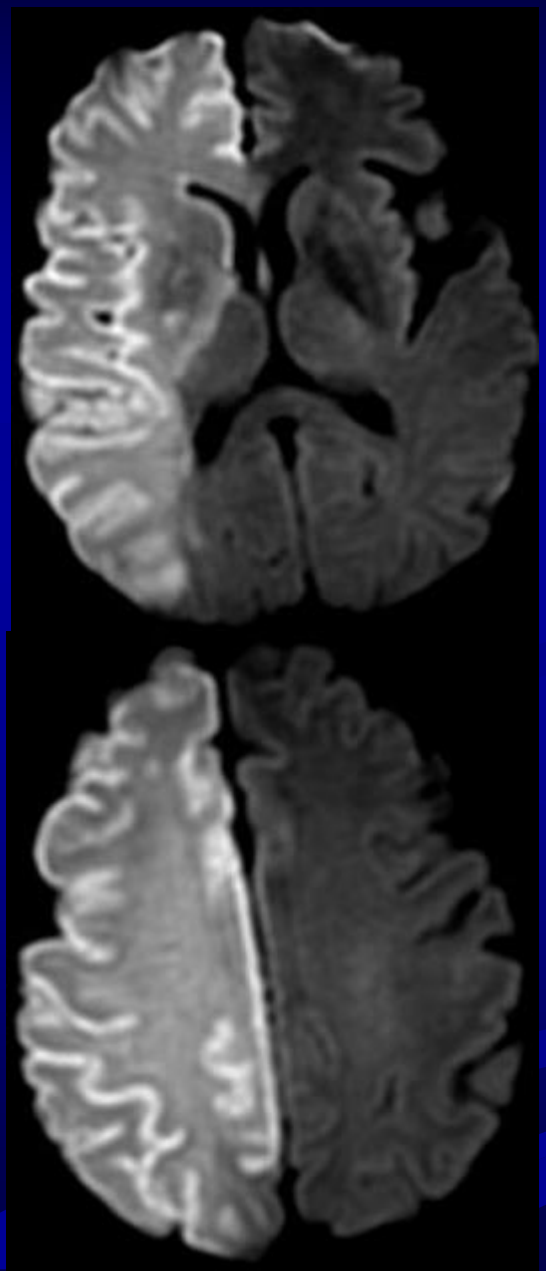
The most sensitive technique to identify the "core" of the infarct

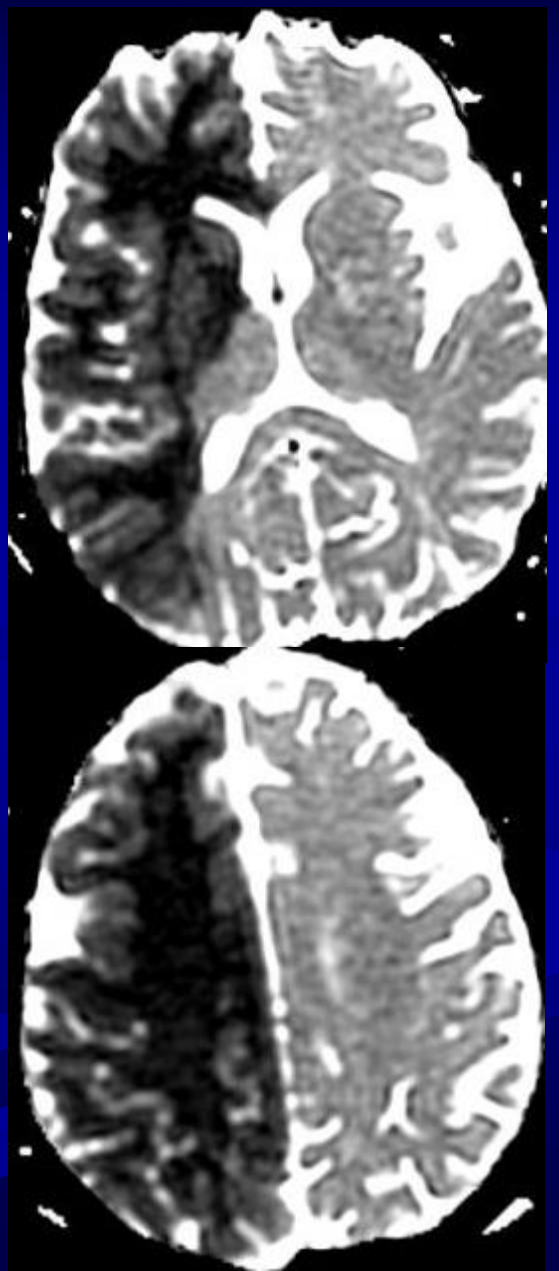
- Water shifts to intracellular space – cytotoxic edema and increased viscosity
- Intracellular "cytotoxic edema" results in slow Brownian motion of water - "diffusion restriction"

Gonzalez RG, et al. Radiology 1999
Perkins CJ, et al. Stroke 2001

65y F 2h after the onset







Reversible DWI Abnormalities

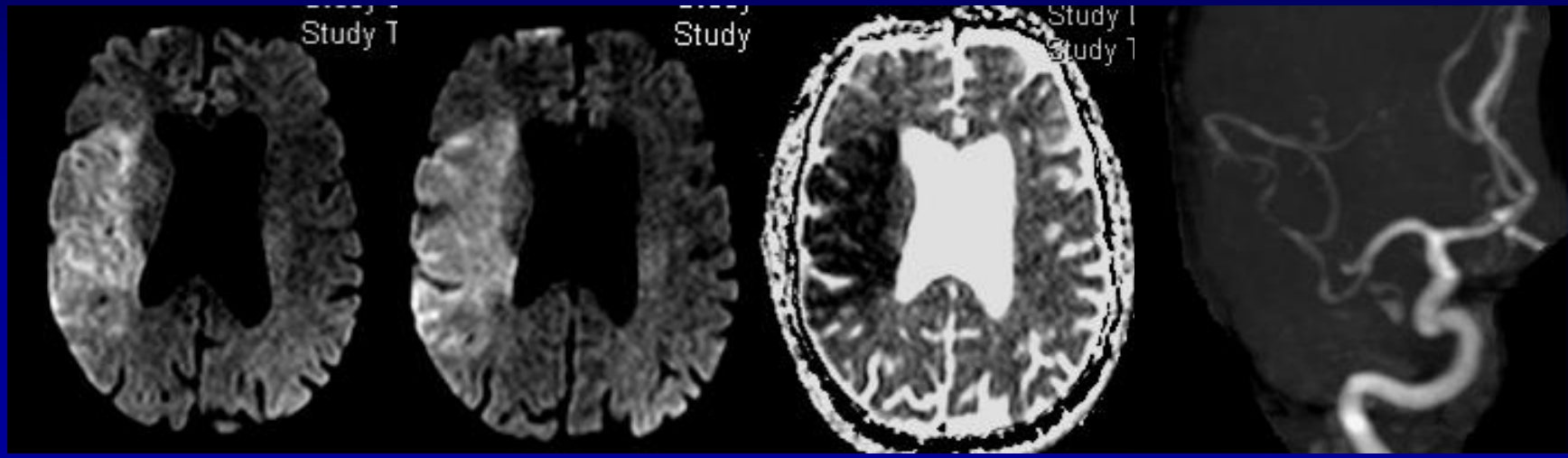
- Initial DWI abnormalities may resolve if occluded vessel is quickly reopened
- May see with other entities:
  - Post-ictal, Hemiplegic migraine, Transient global amnesia (TGA), venous hypertension, venous thrombosis, DAVF

Reversible DWI: Venous hypertension/ischemia

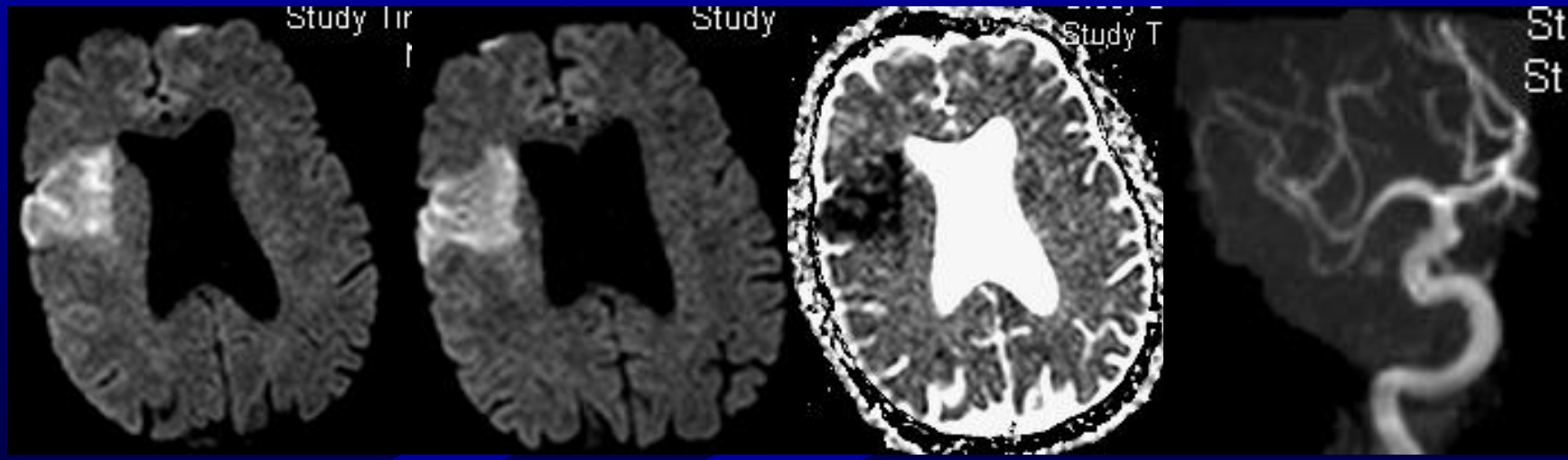
Patient with acute onset right sided weakness

Reversible DWI: arterial ischemia

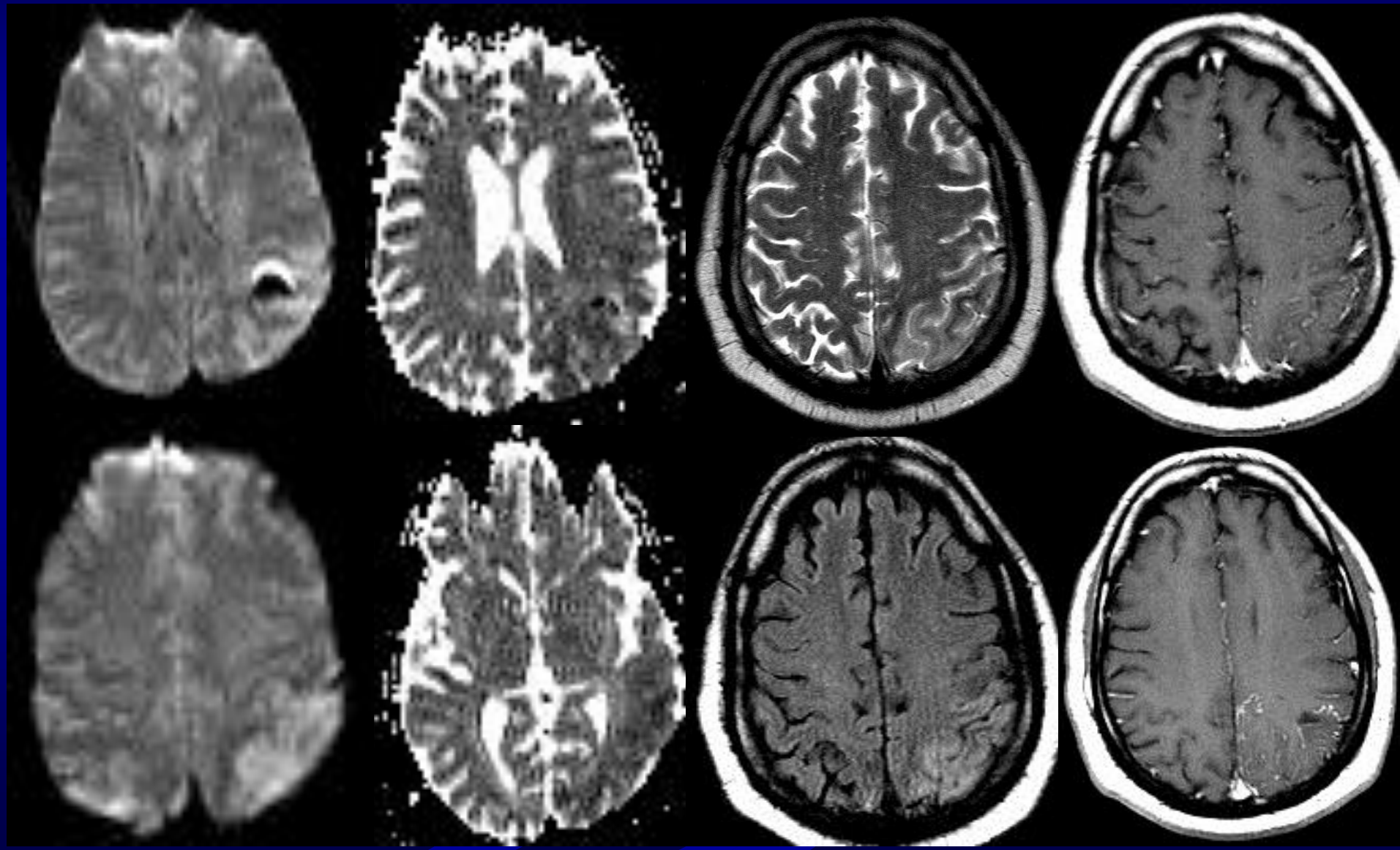
4pm



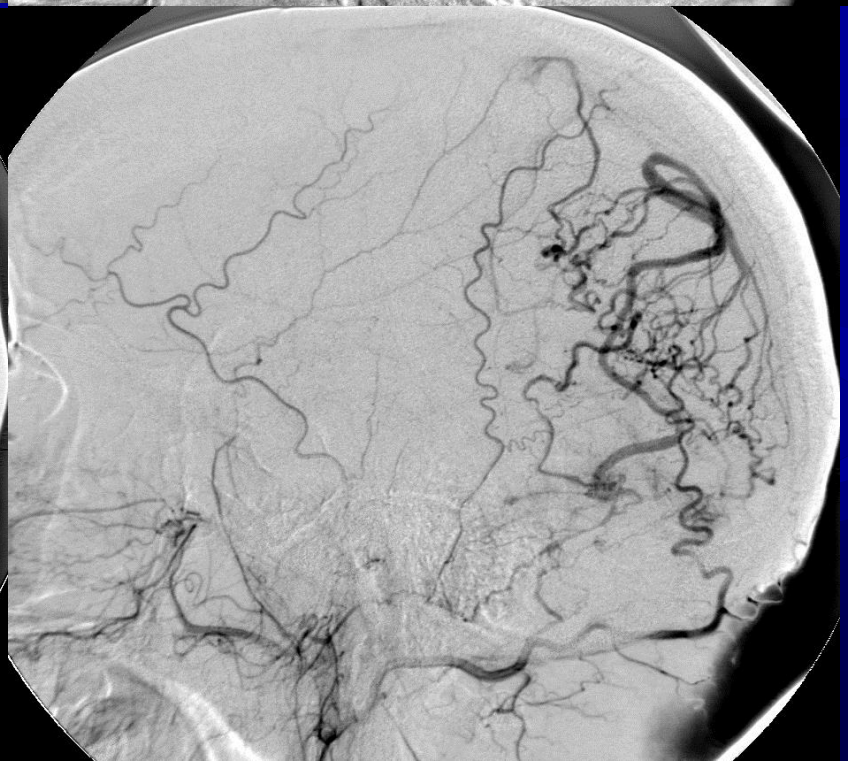
8pm



Reversible DWI: Venous ischemia

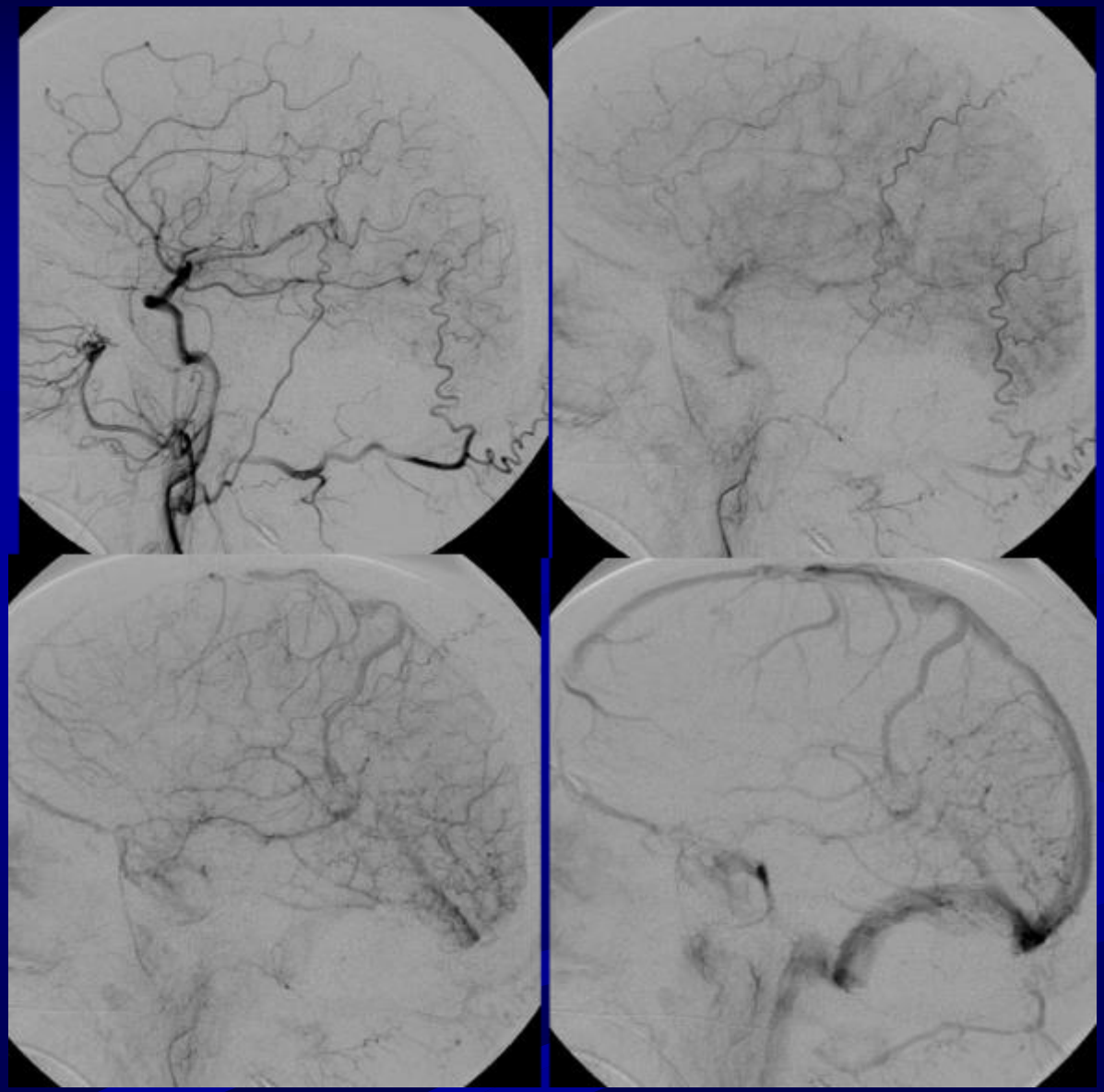




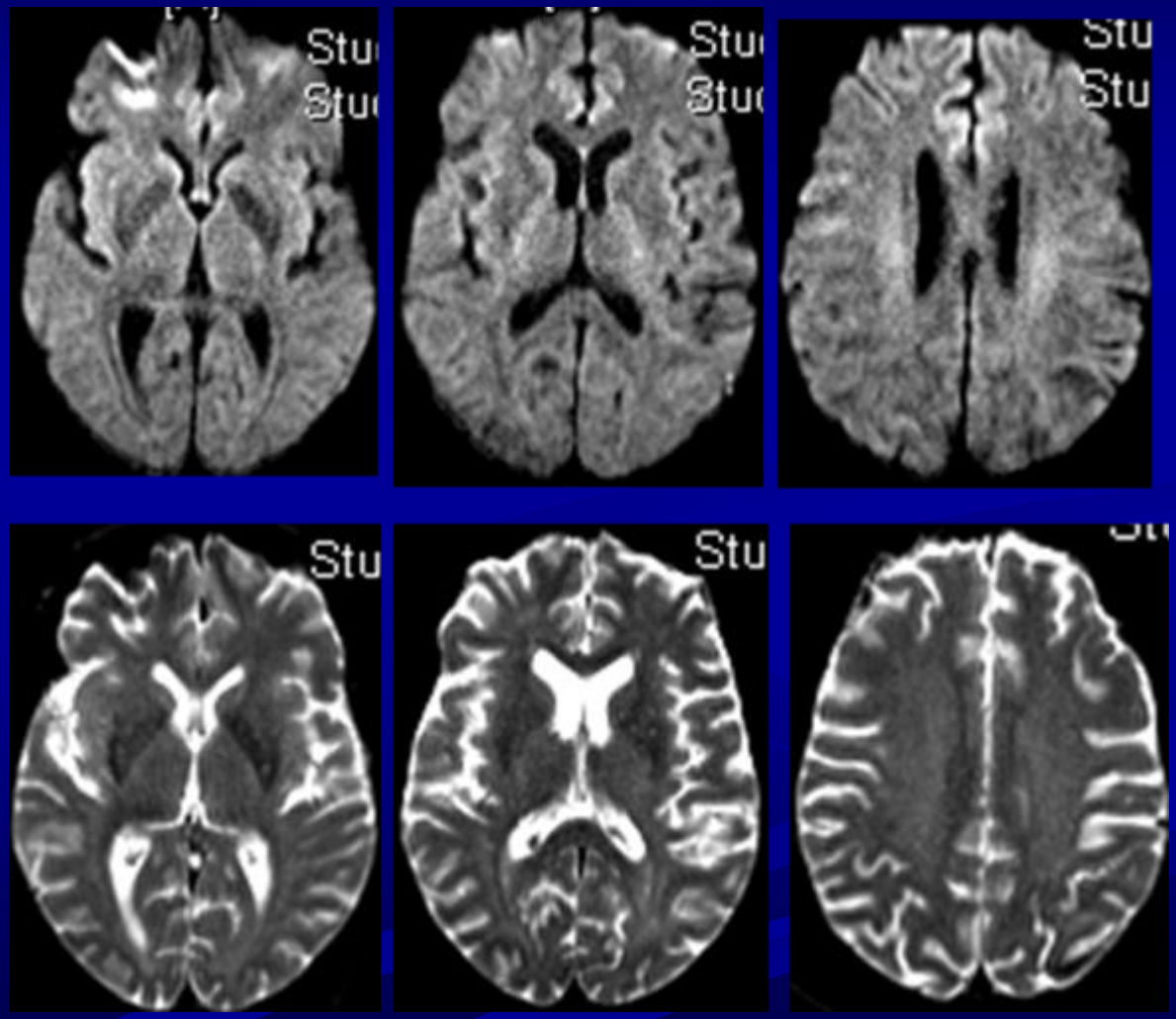



Post-embolization

LCCA injection



Follow-up imaging

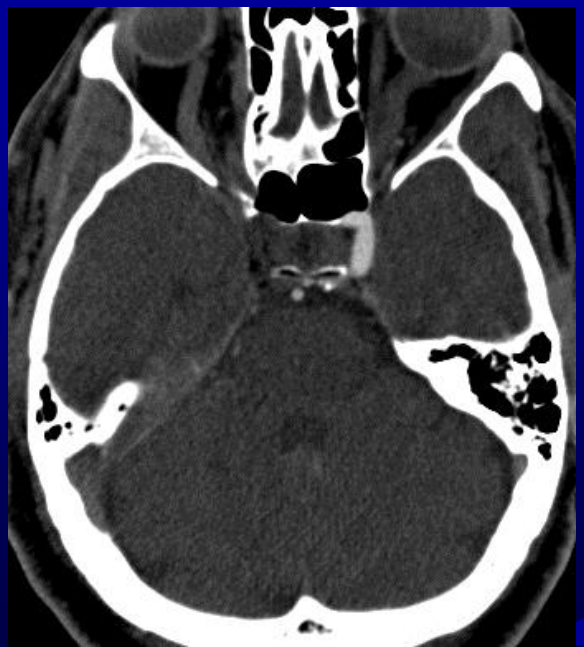


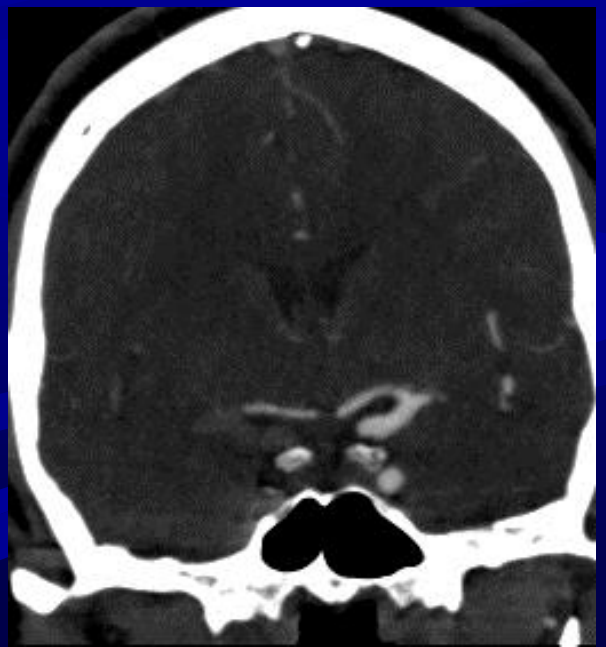
No evidence of infarction on CT or MRI

The four P's #2: Pipes

CTA and MRA

- Localization of vascular etiology is important
  - Source of emboli
  - Large vessel occlusions (ICA, M1, basilar) respond poorly to IV tPA
  - IA options defined by anatomy, collaterals

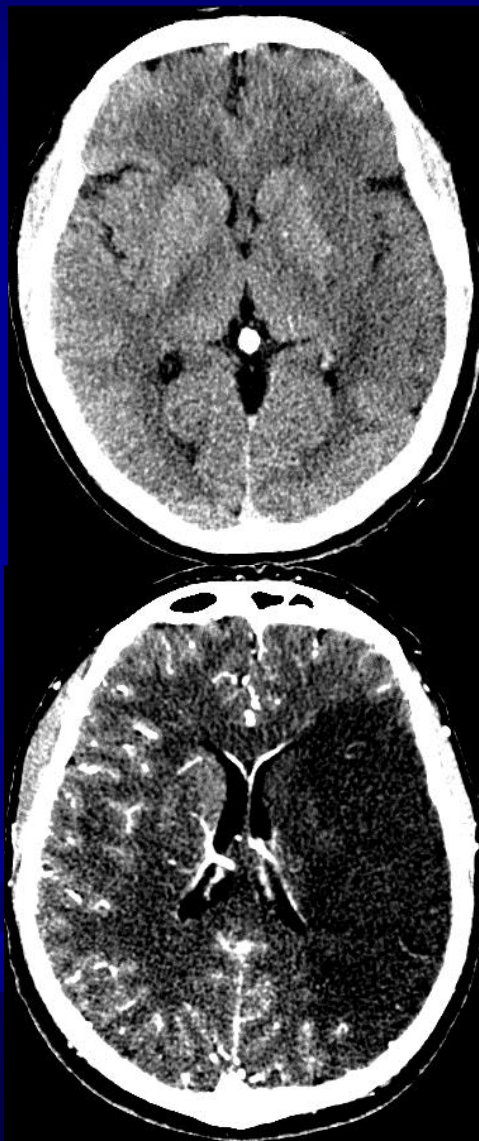




CTA source images for acute infarction

- NCCT and CTA source images compared (51 pts)
- Follow-up imaging to confirm infarct volume
- Results: 33 patients had an infarct
  - NCCT sensitivity: 48%
  - CTA source image sensitivity: 70%
- Conclusion: CTA source images more sensitive for early infarction and more accurate for prediction of final infarct volume

Camargo, et al: Radiology 244(2):541-548, August 2007



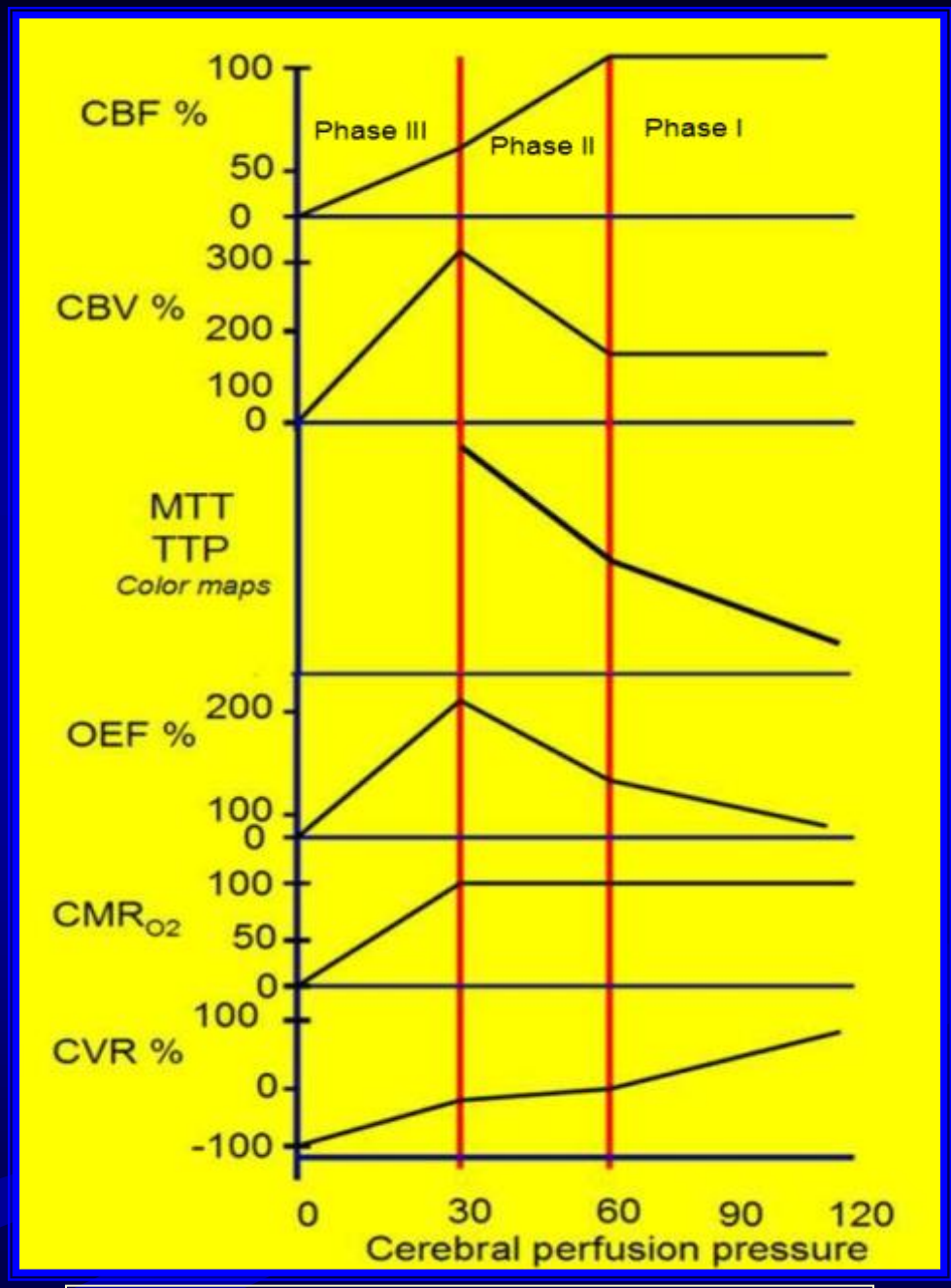
3rd "P": Perfusion
Location and severity of oligemia

- Goal: Evaluate capillary/tissue level hemodynamics in brain parenchyma
  - CBF – measure of the volume of blood perfusing an area of tissue per unit time
    - Neurological dysfunction - <18-20 ml/100gm/min
      - Potentially salvageable
    - Neurological dysfunction - <10 ml/100gm/min
      - Cell death within minutes

Autoregulation

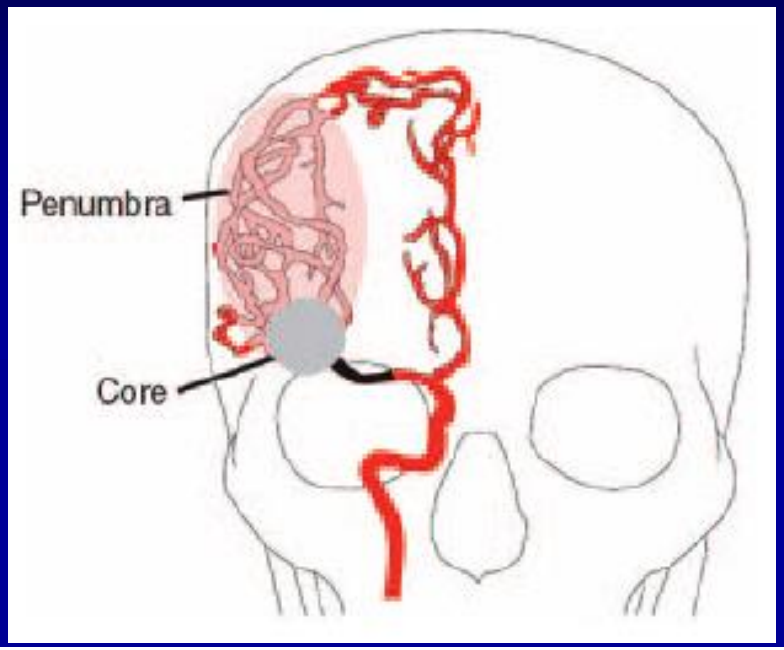
- Initial mechanism of autoregulation
  - Increasing oxygen extraction fraction (OEF)
- Primary mechanism of autoregulation
  - Vasodilatation
    - Decreases cerebral vascular resistance (CVR)
    - Increases cerebral blood volume (CBV)

$$CBF = \frac{CBV}{MTT}$$



Modified after: Powers WL. Ann Neurol. 1991;29:231–240.

The 4th "P": Penumbra - Tissue at risk



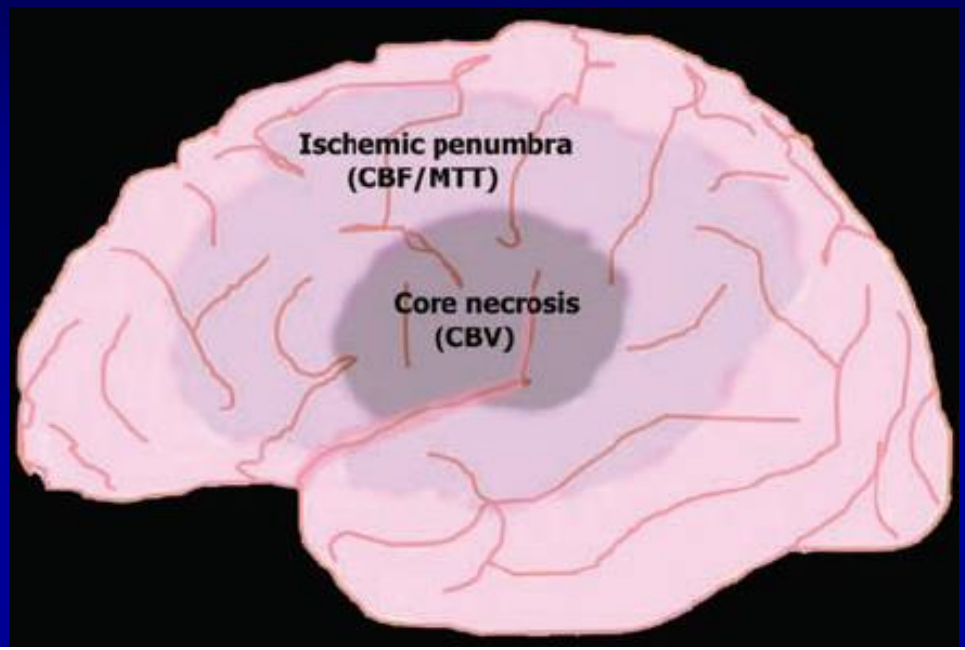
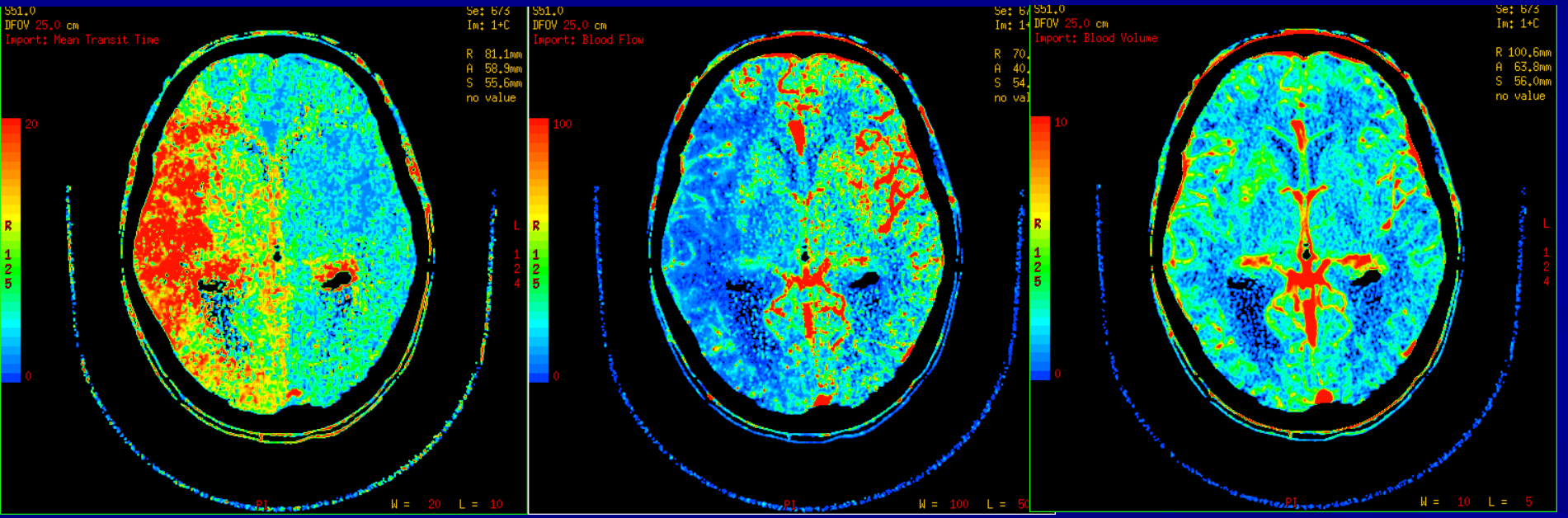


Table 4
Perfusion CT Analysis of Hyperacute Ischemic Stroke

	Analytic Tool			
Entity	MTT	CBF	CBV	Nonenhanced CT
Penumbra	Elevated (>145%)	Decreased	Normal or mildly increased	Normal findings or brain swelling
Infarct core	Elevated	Markedly decreased	Markedly decreased (<2.0 mL × 100 g^{-1})	Hypoattenuating parenchyma

Gonzalez. AJNR 2006; de Lucas et al. Radiographics 2008

Large Mismatch
Large penumbra

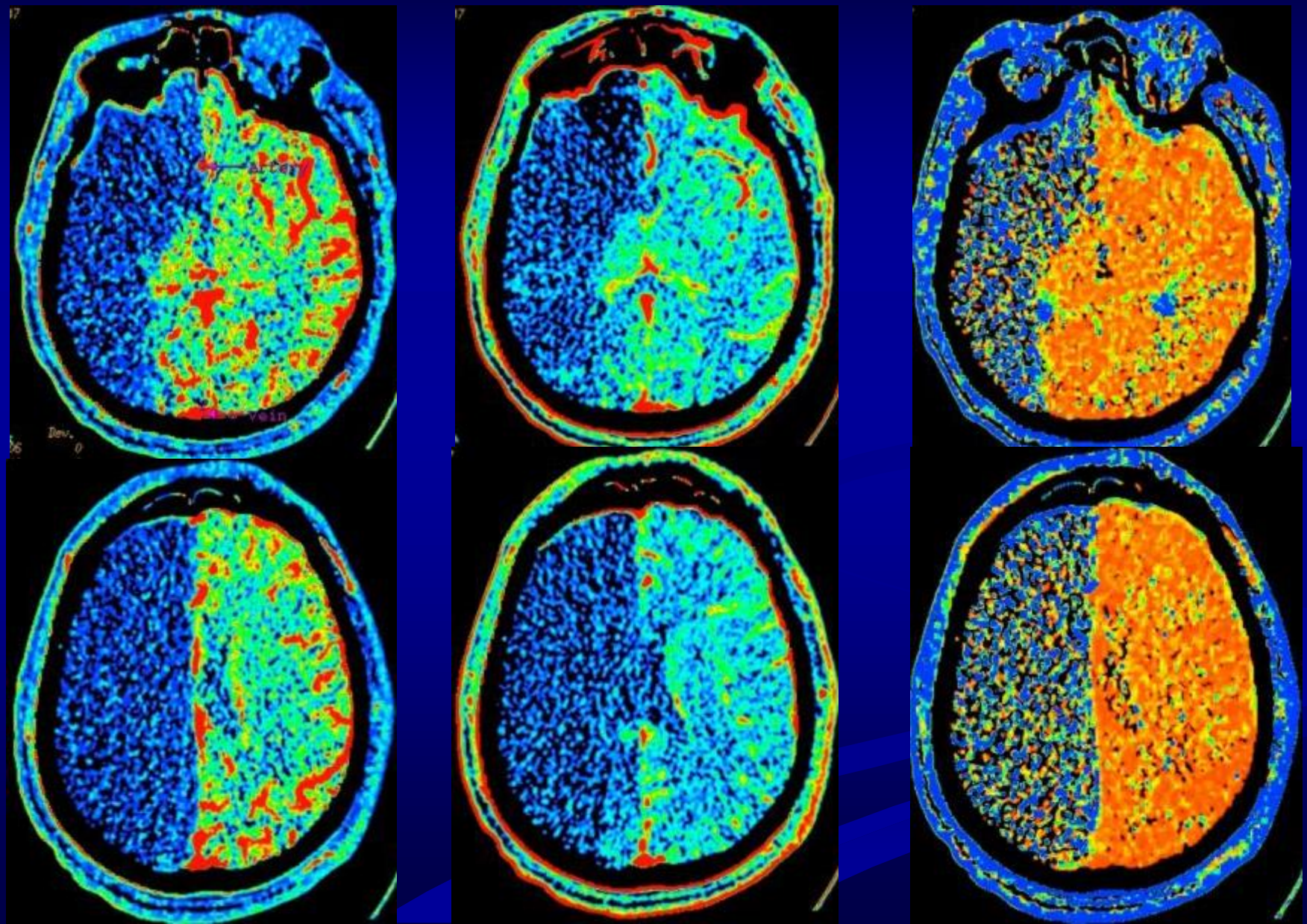


MTT

CBF

CBV

When not to intervene? Ex. 1



CT Perfusion: RAPID Processing

Stroke MRI/CTP

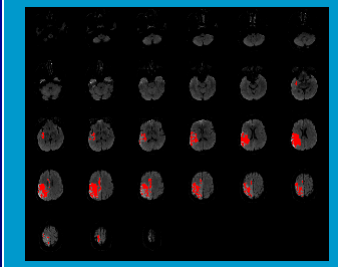
CT/MR tech pushes CTP/DWI & PWI to RAPID via DICOM

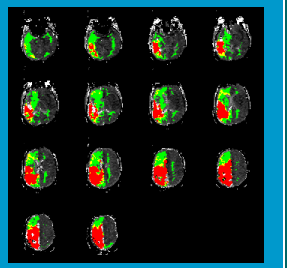
00:00:30

image arrival

00:04:30

RAPID image analysis complete





DWI lesion size is 72.88 cm3

PWI lesion size for TMax >= 4.01s is 305.95 cm3
PWI lesion size for TMax >= 6.01s is 159.24 cm3
PWI lesion size for TMax >= 8.01s is 125.86 cm3

Auto Image Analysis:

- motion & time correction
- AIF & VOF selection
- deconvolution & map generation
- *CTP or DWI and PWI lesion* segmentation
- Lesion volume calculation

auto-send via DICOM

00:05:00

Images on PACS

auto-send via secure e-mail

Courtesy Raul Nogueira, MD

RAPID for CT and MRI

Fast, standardized, fully automated, quantitative, thresholded mismatch

CT perfusion

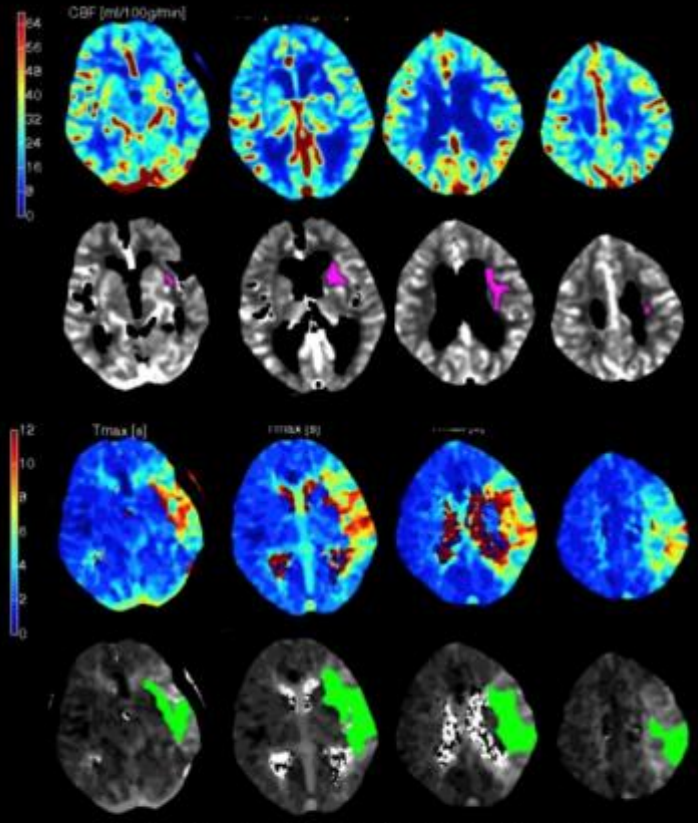
MRI

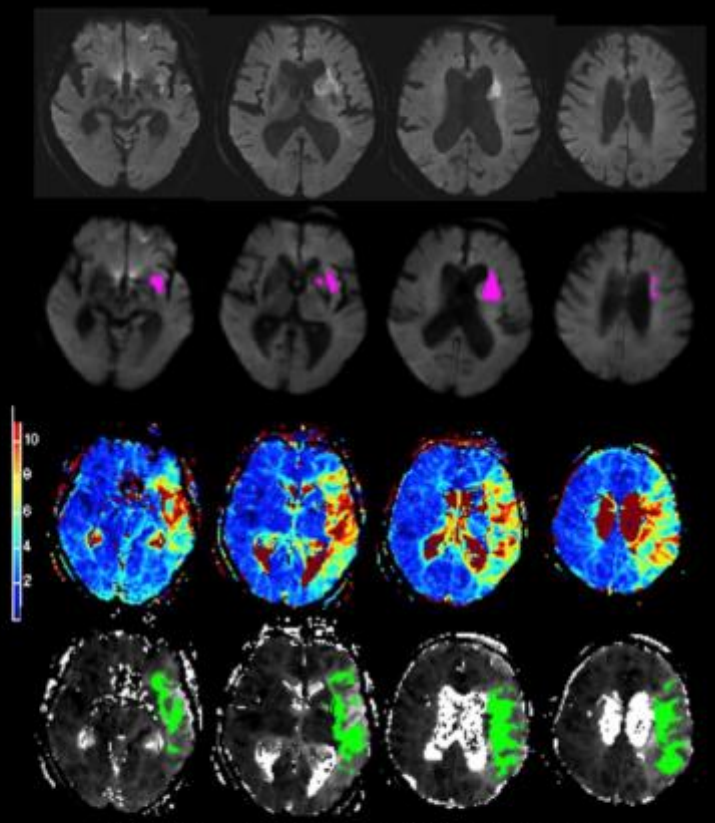
CT relCBF / Diffusion MRI

RAPID ischemic core segmentation CT relCBF<30%

Tmax

RAPID Tmax>6sec segmentation





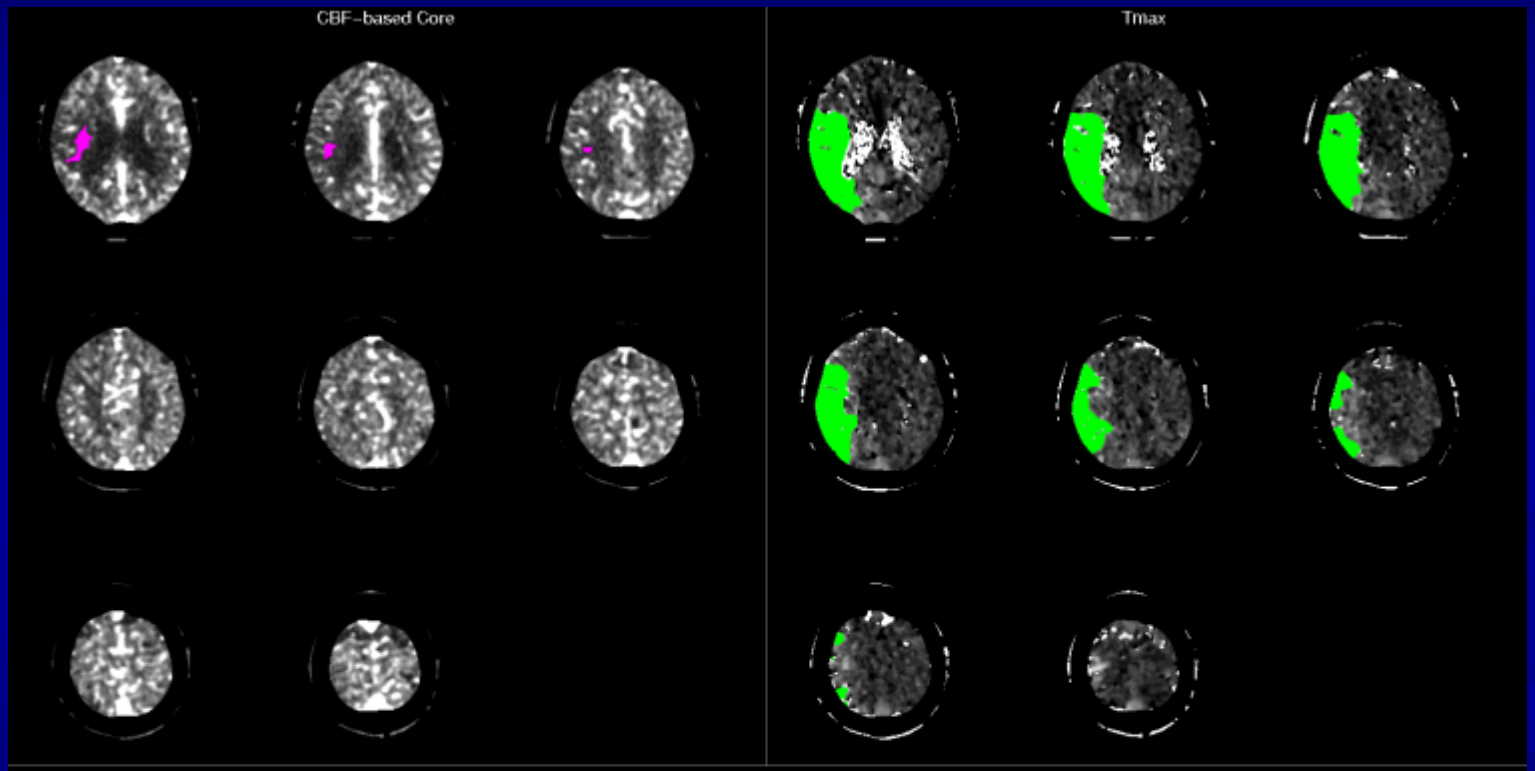
Ischemic core: 6mL Perfusion lesion: 58mL
Mismatch ratio = 9.7 Absolute mismatch = 52mL
→ Randomize patient

Ischemic core: 7mL Perfusion lesion: 55mL
Mismatch ratio = 7.6 Absolute mismatch = 48mL
→ Randomize patient

Straka et al JMRI 2010

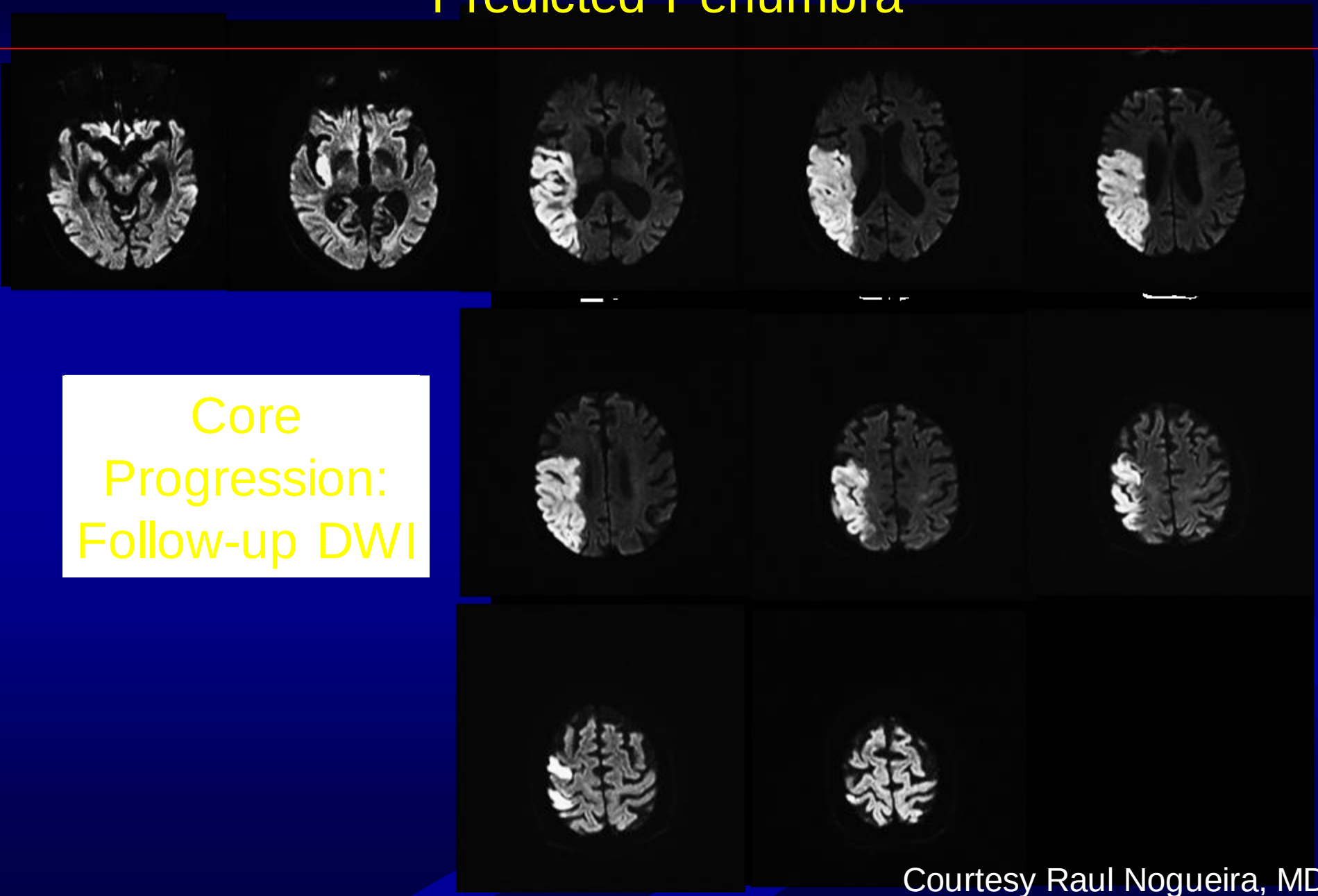
83 yo Man – NIHSS 14 – CTA Right M2 Cutoff – Not IV TPA Candidate – Patient/Family Declined IAT

RAPID: Prediction of Core and Penumbra



Courtesy Raul Nogueira, MD

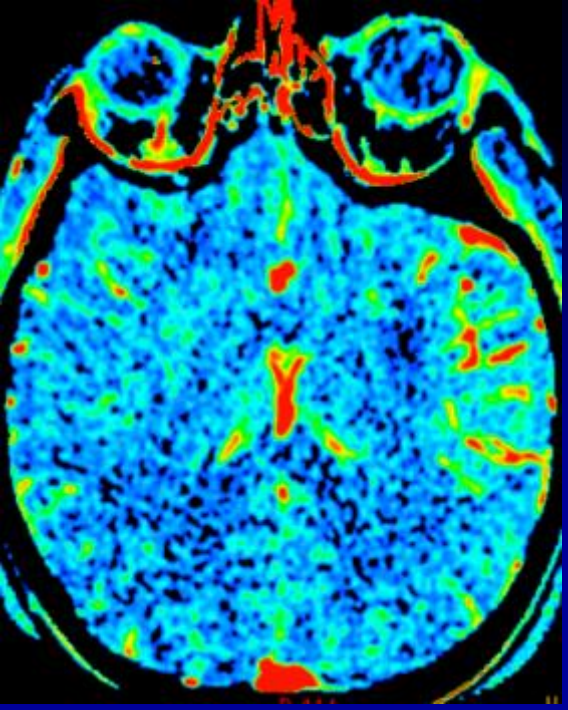
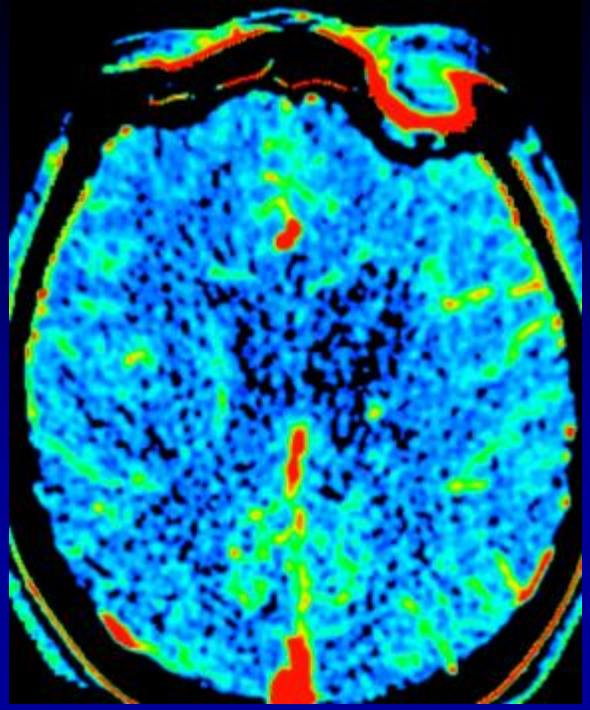
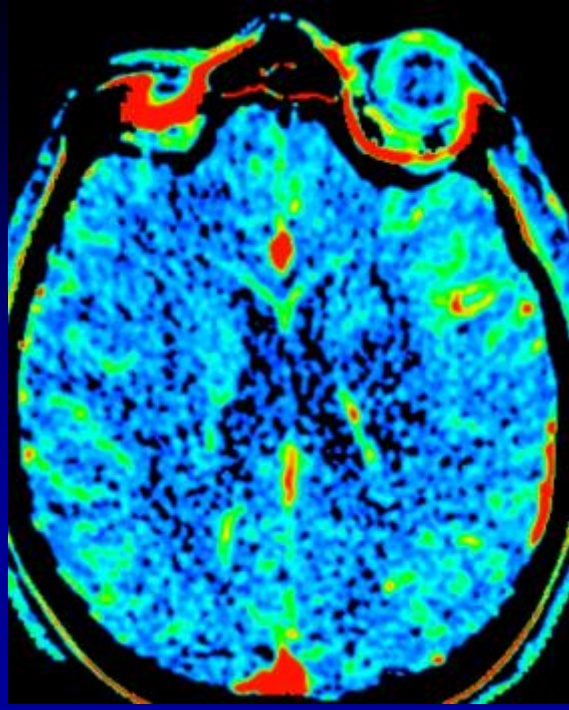
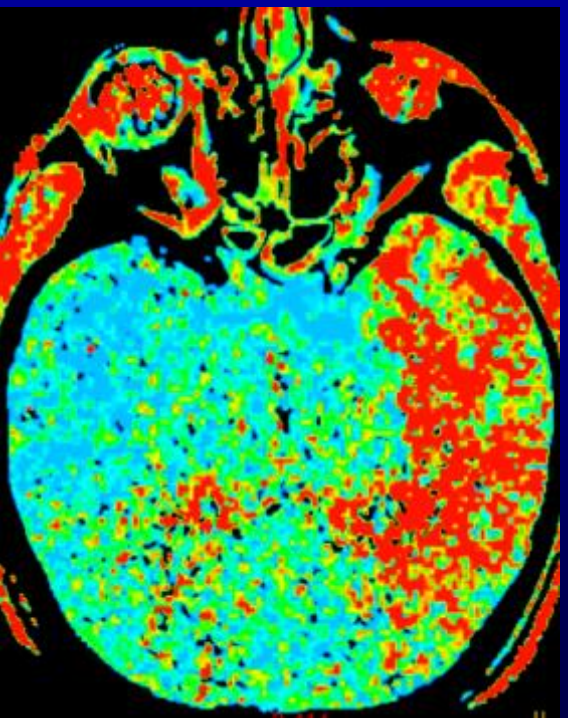
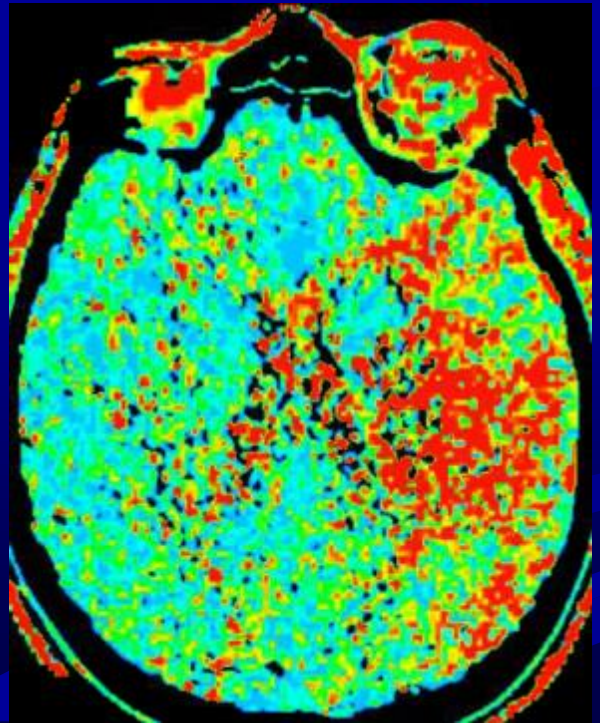
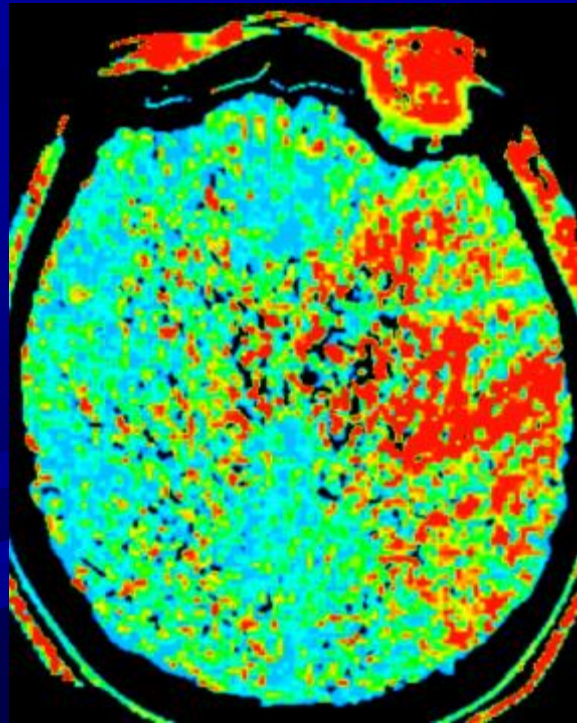
RAPID: Lack of Reperfusion and Core Progression in to Predicted Penumbra

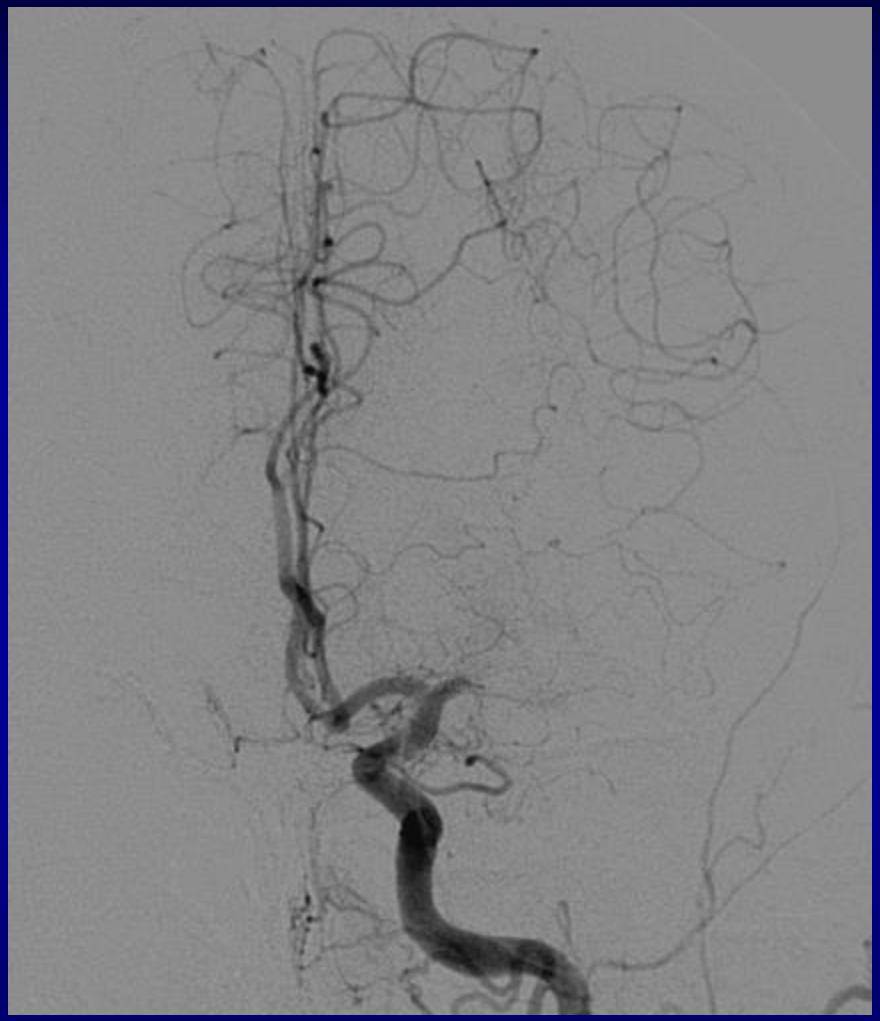


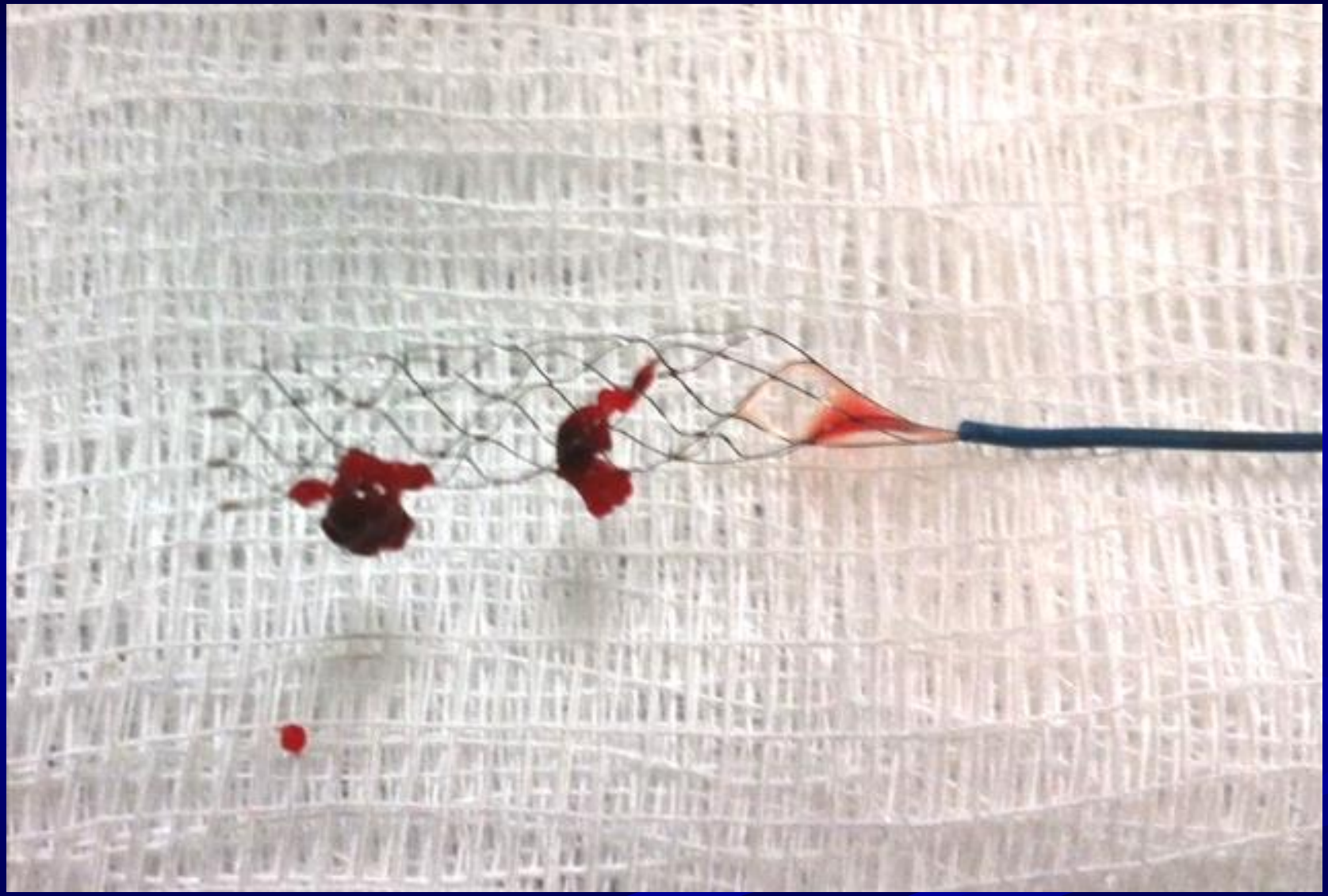
Core Progression: Follow-up DWI

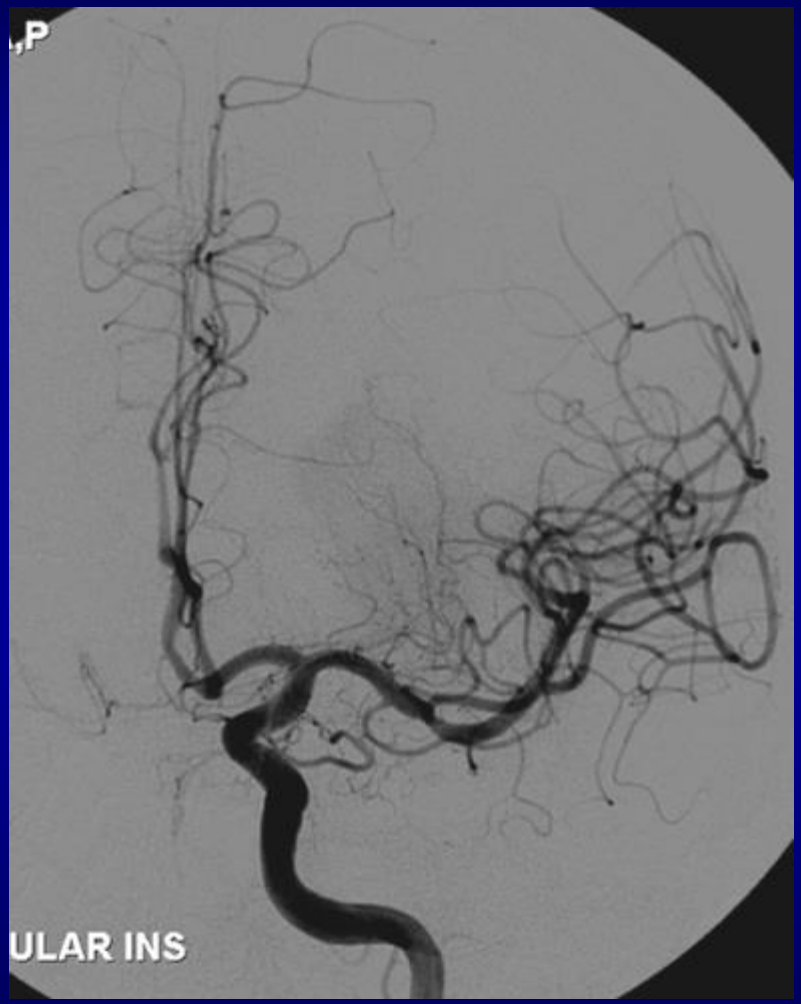
Courtesy Raul Nogueira, MD

81 yo wake up stroke at 5am – last seen normal at 11pm
Aphasia, right hemiparesis NIHSS 20



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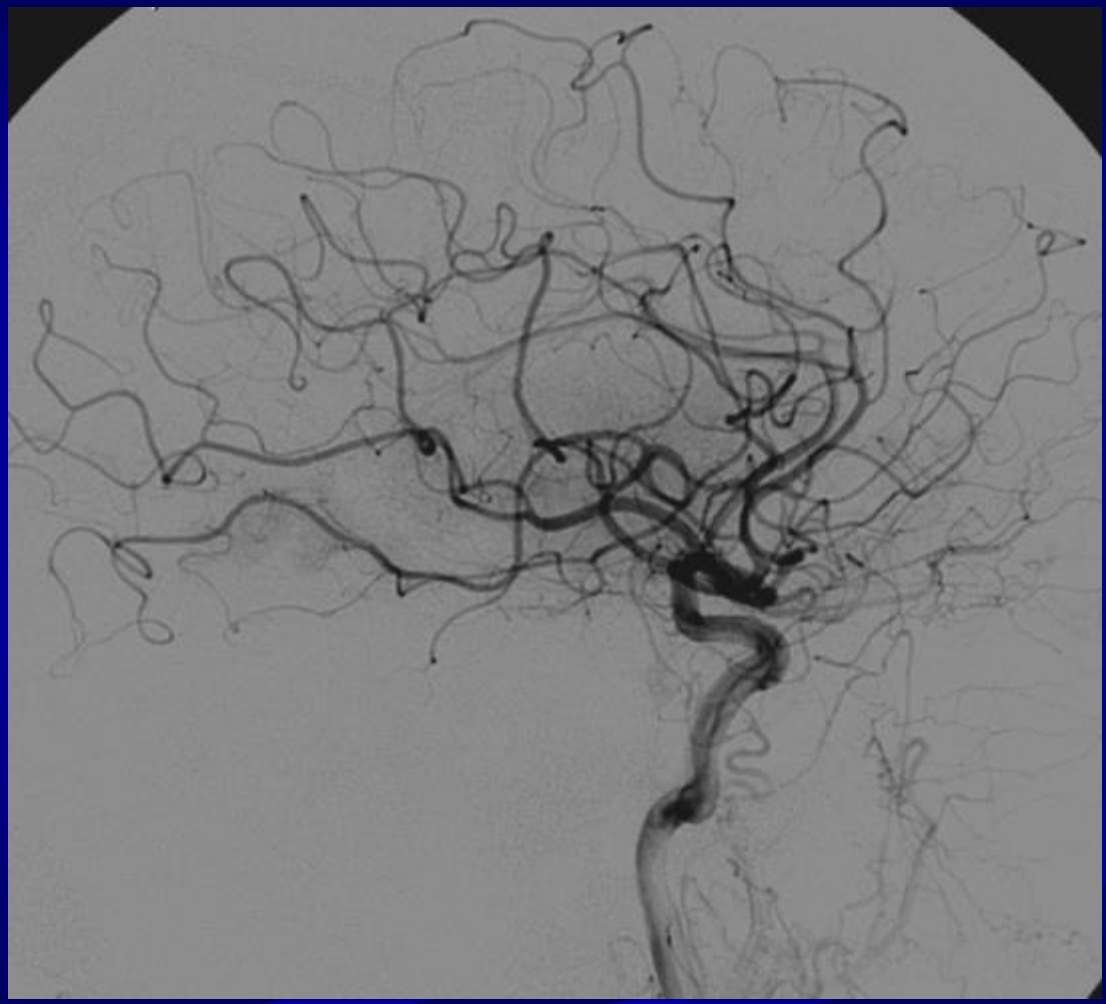
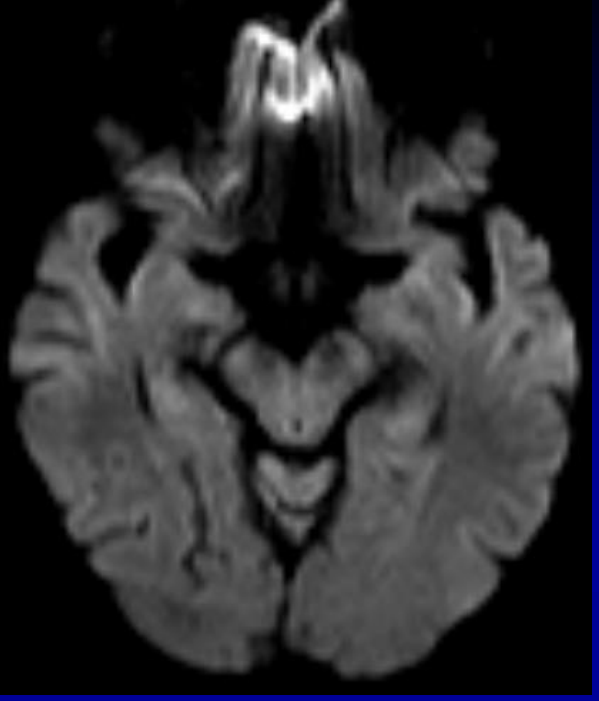
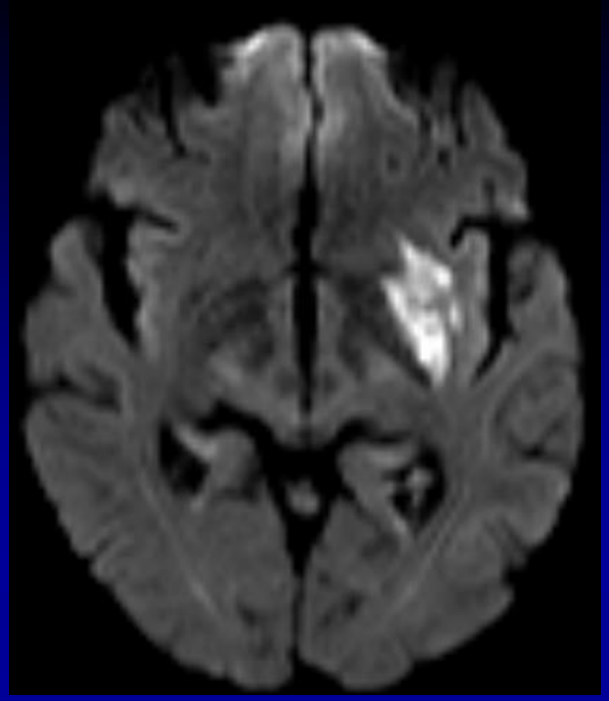
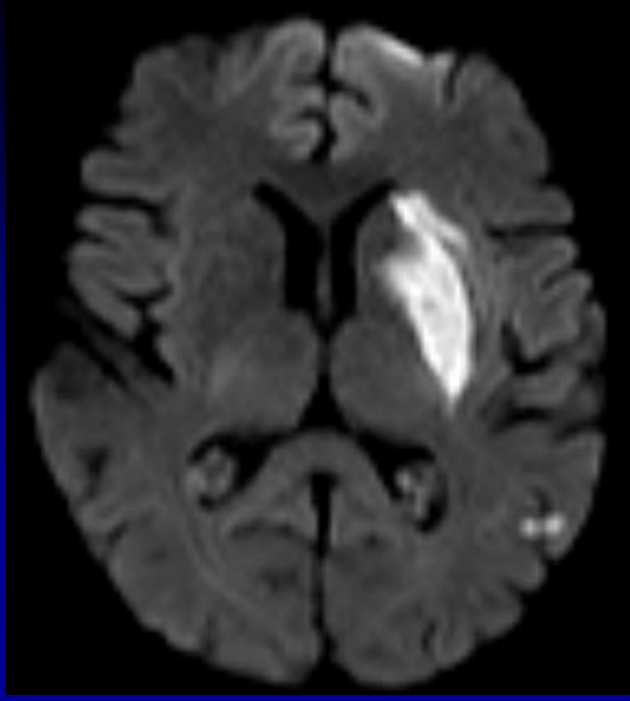
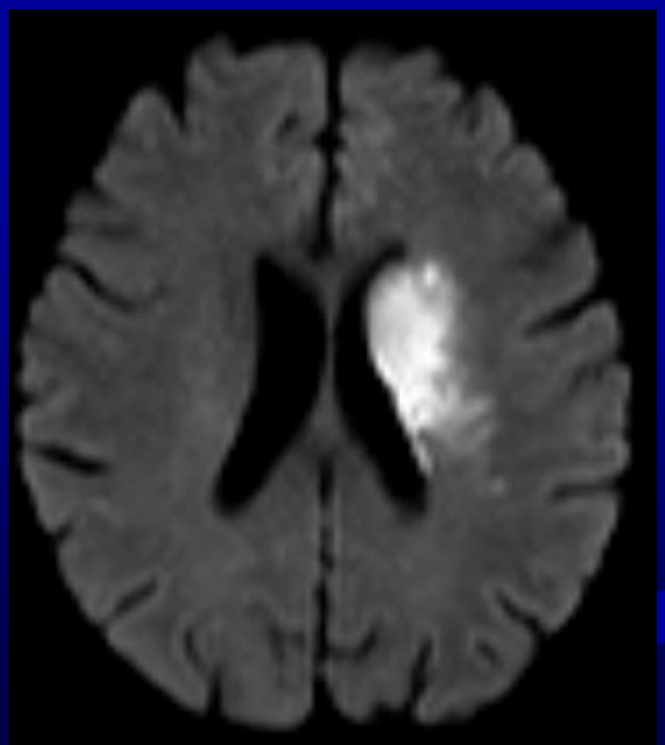
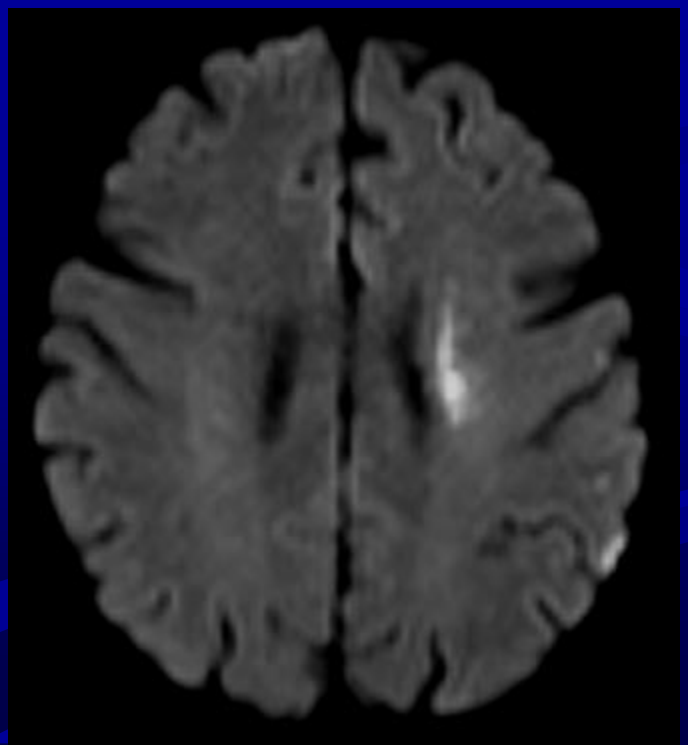
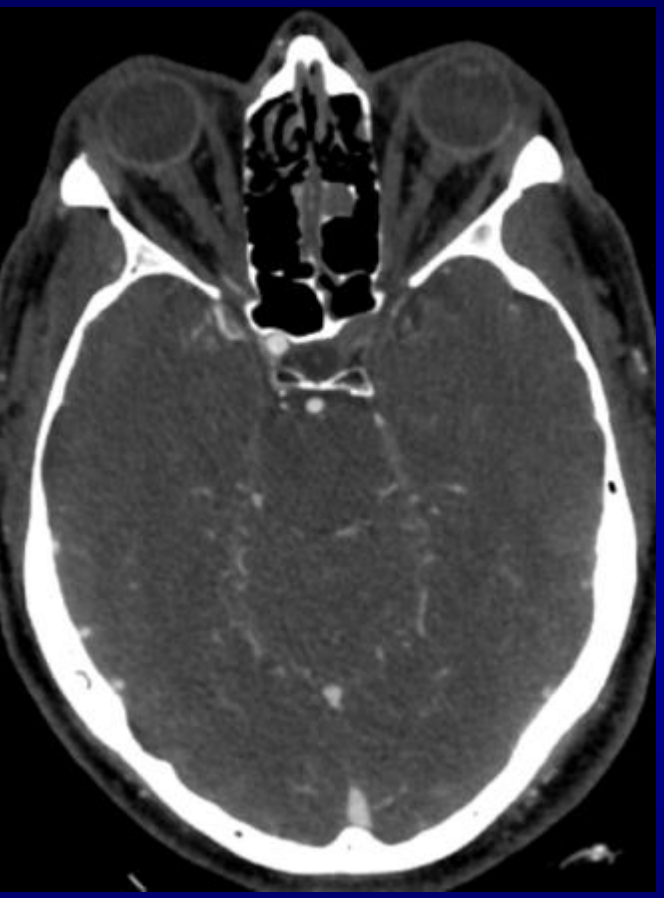


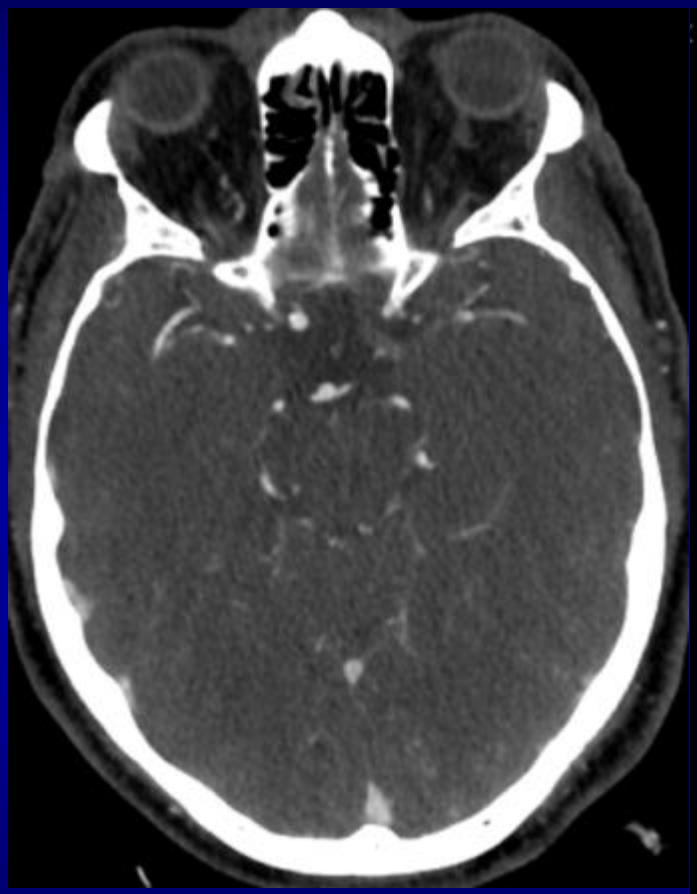






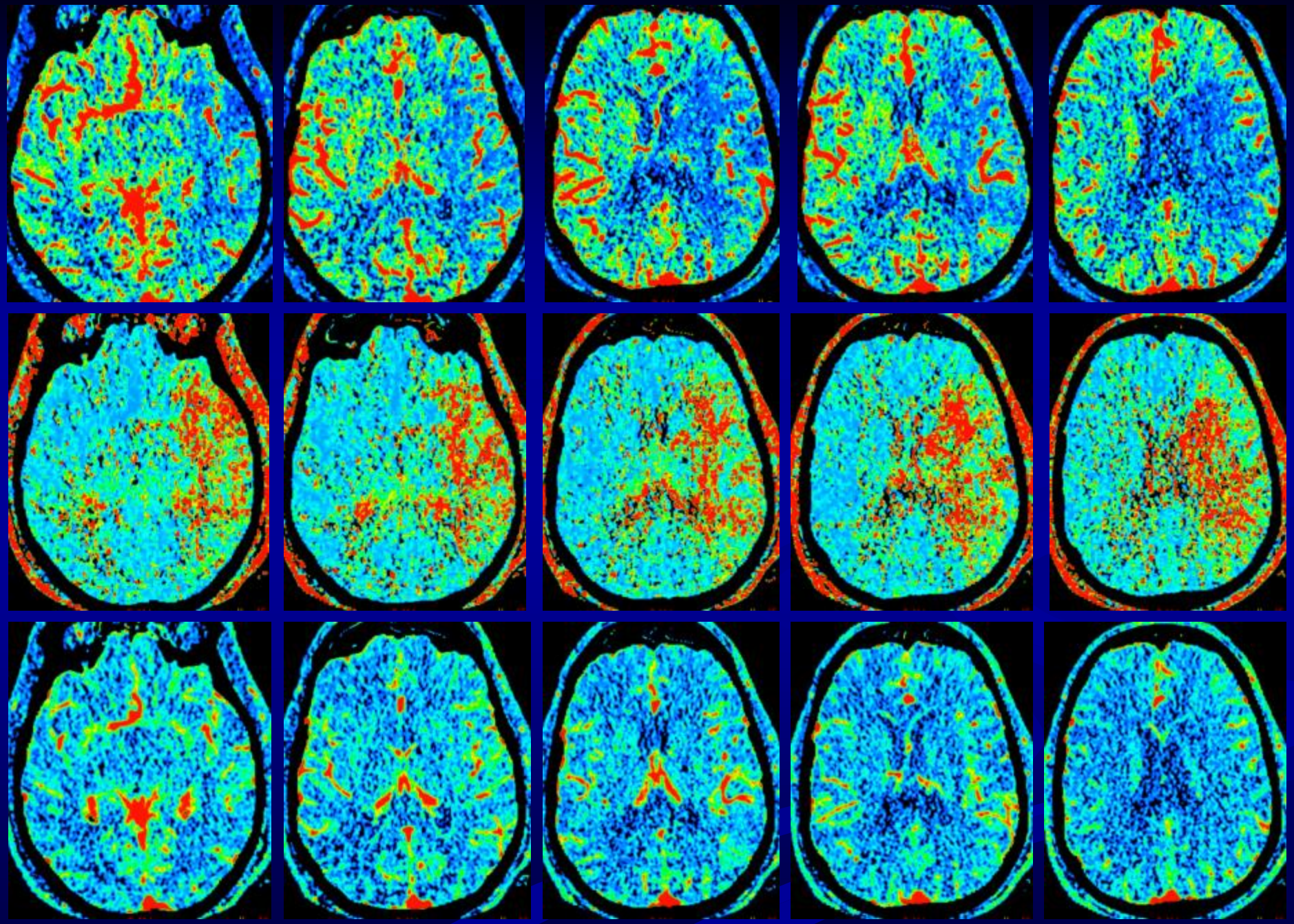
69M partial lung resection 2 days prior; heavy smoker, HTN

- 15h after last seen normal
- Arrived at OSH at 1:30pm
- Aphasic, right hemiplegia; NIHSS - 24
- Not considered for IV tPA
- CT/CTA/CTP ordered

CTA/CTP @ 2:30pm

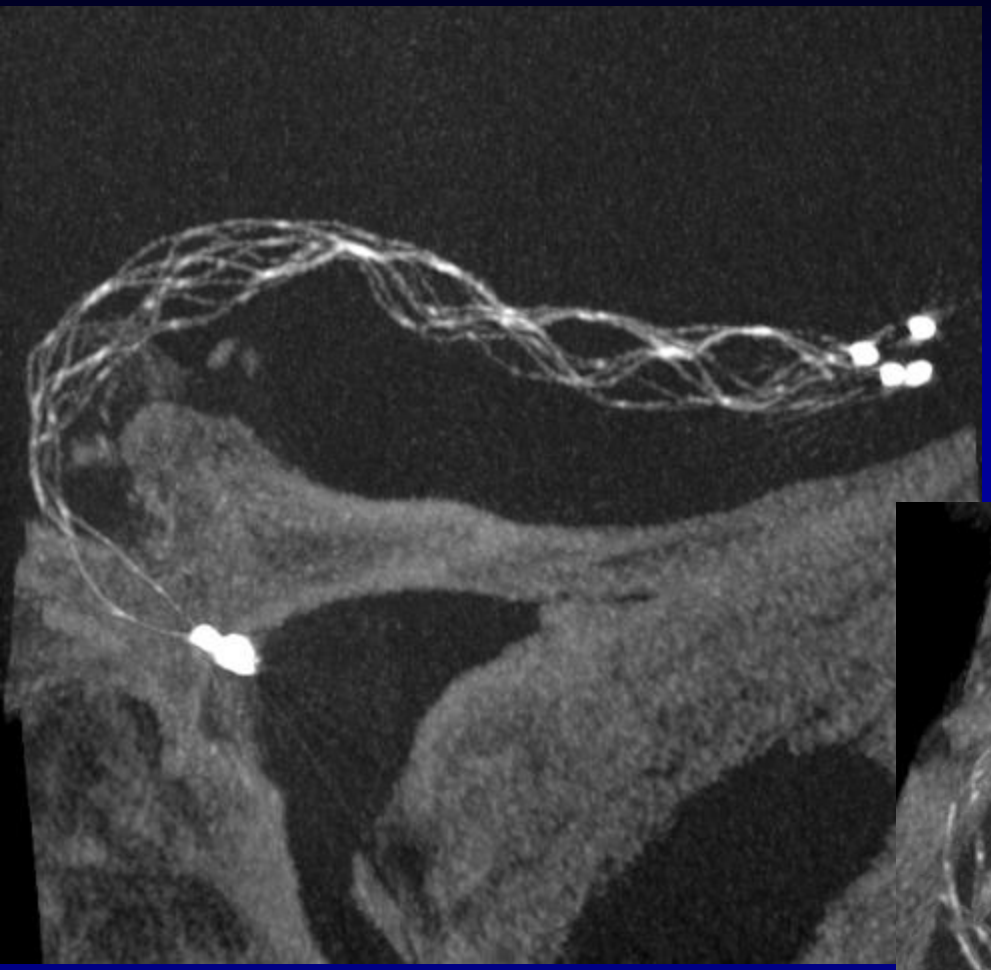




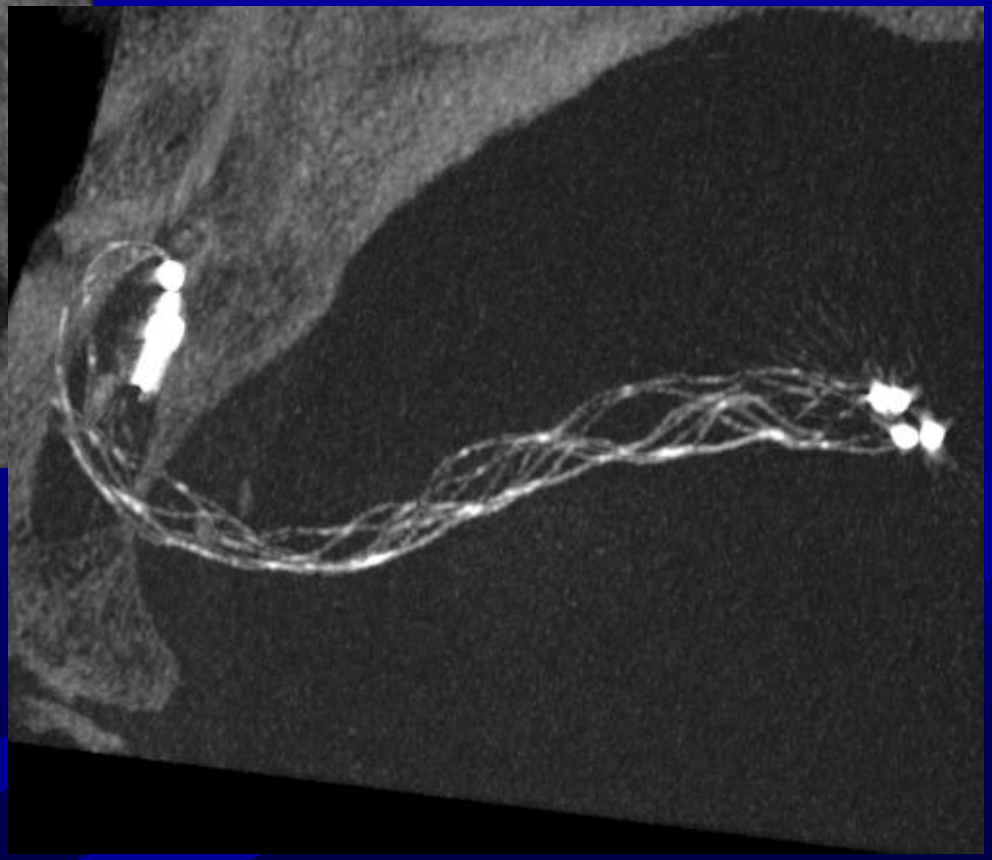


AP

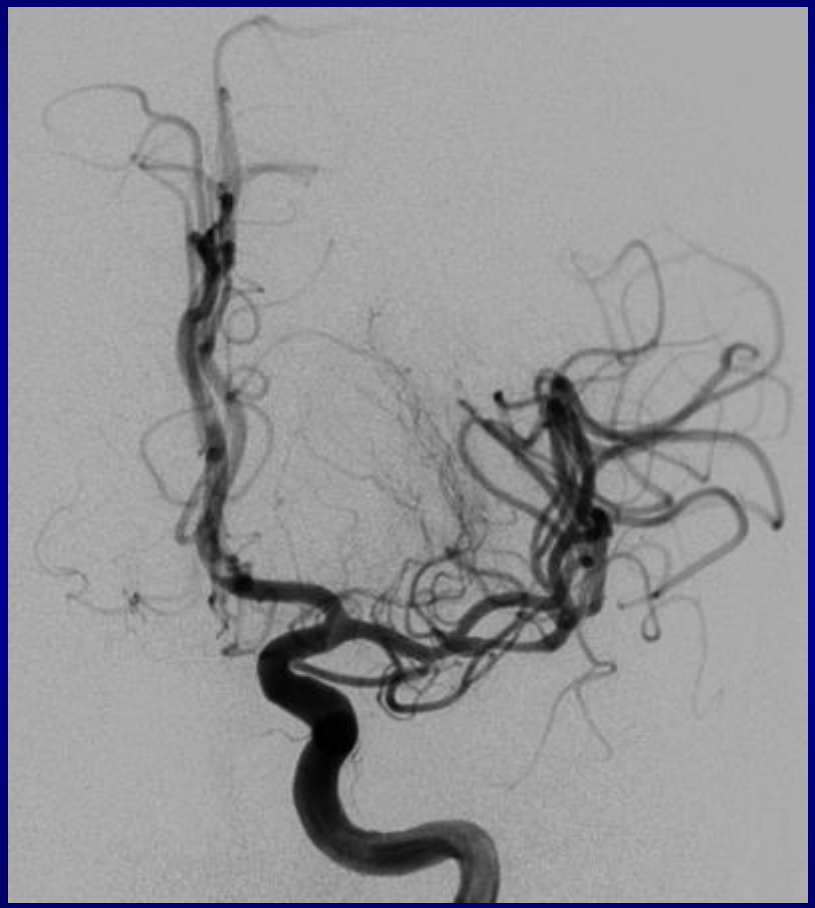
Lateral

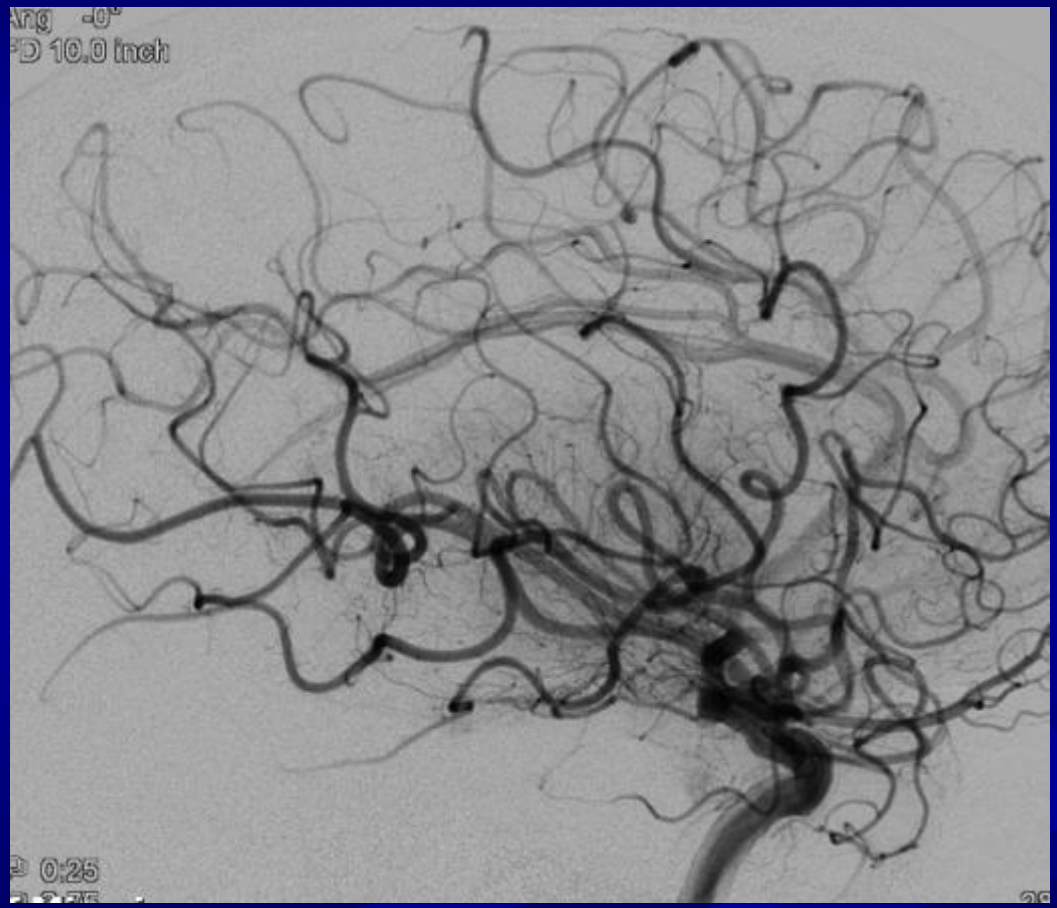


Stentretriever
6 x 30

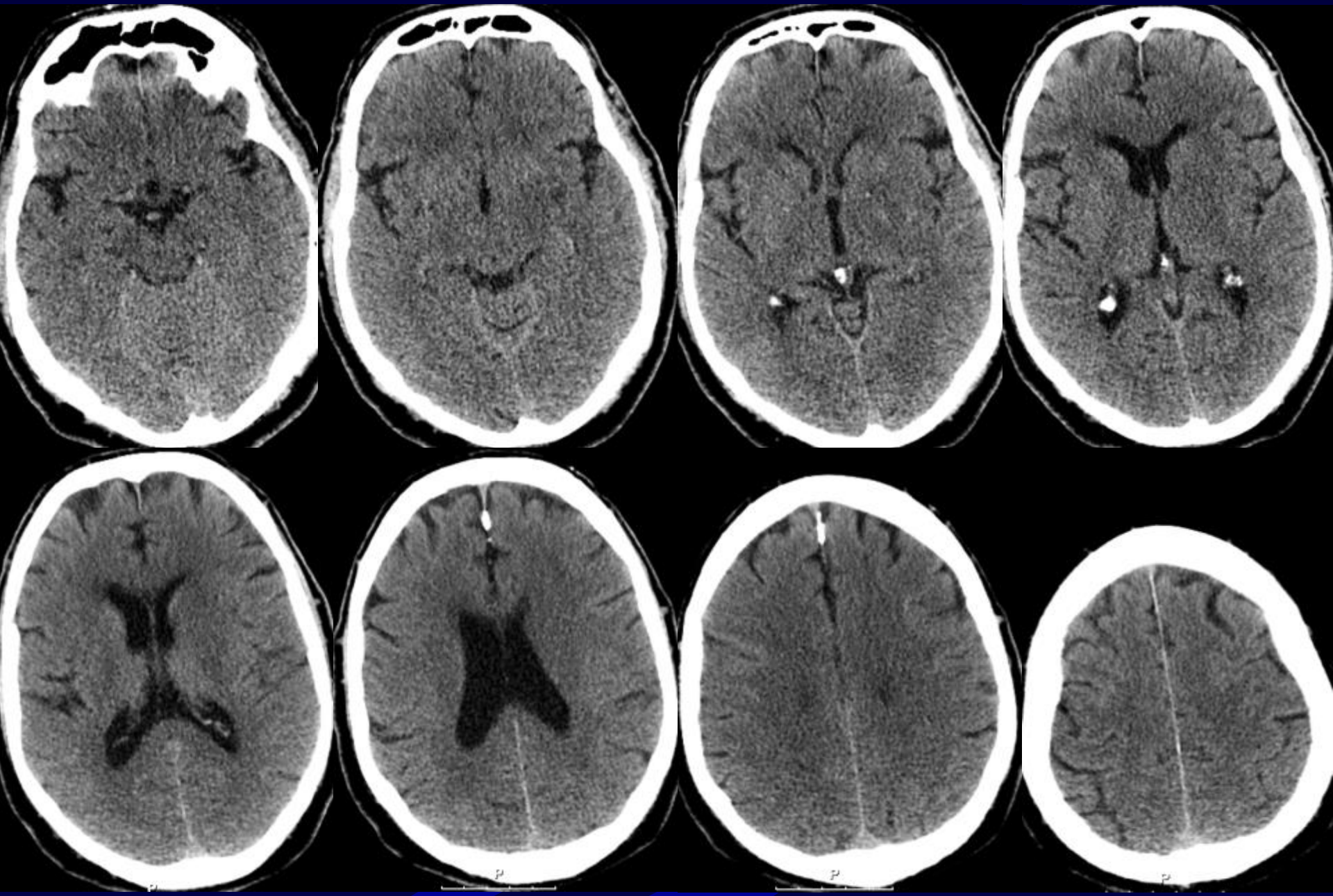


Angio final



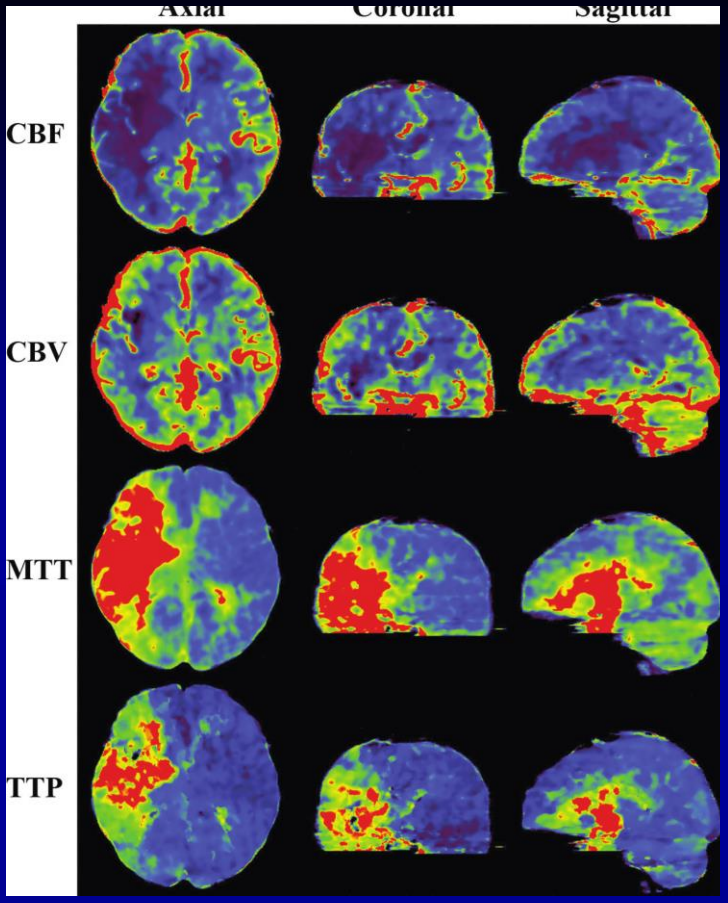


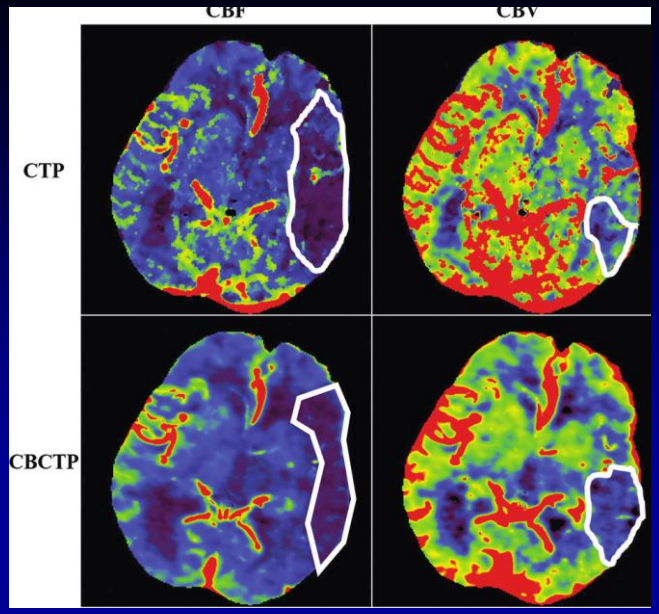
CT 48h post procedure – NIHSS 4



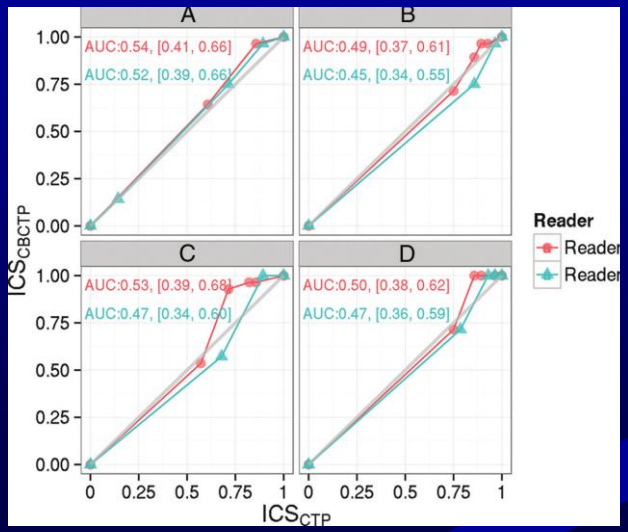
Future Imaging in Acute Stroke???

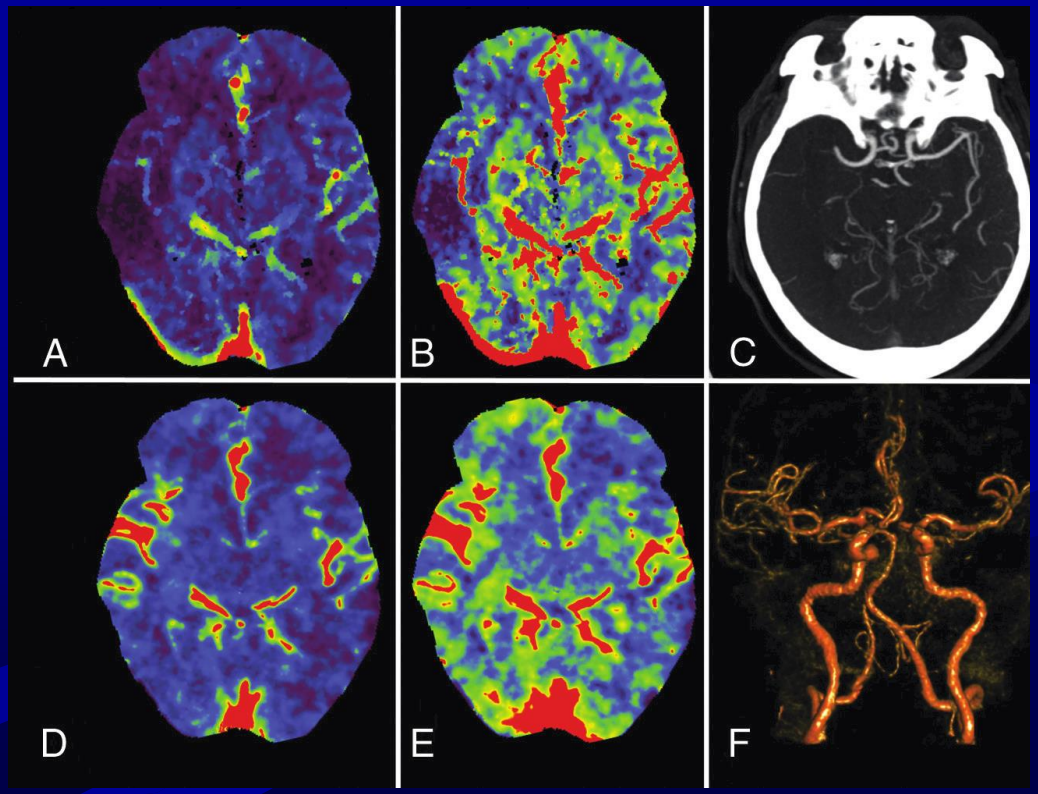
- Mobile CT or Stroke Units may plan an important role in pre-hospital patient selection
- Improvements in Cone Beam CT imaging will create a paradignm shift





Niu K, et al.
AJNR online
Feb 2016





Conclusions

- Therapeutic advances will require quantitative assessment of imaging data
- Off hours availability of expertise must be developed
- Functional imaging should be added to anatomical imaging for the assessment of acute stroke
- The future is bright…

"We are what we repeatedly do.
Excellence, then, is not an act,
but a habit."

Aristotle 384 BC-322 BC

Thank You!