IMAGING IN ACUTE ISCHEMIC STROKE

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Acute Stroke Treatment: A TEAM Approach

- Workflow of a acute stroke treatment

  - Detection — Patient Education
  - Transfer to a stroke center — Ambulance
  - Medical evaluation — ER / Neurology
  - Imaging — Neuroradiology
  - Acute treatment — Neurology/INR
  - Post operative management — Stroke Unit
  - Rehabilitation — Rehab
  - Prevention — Neurology

Each chain is as strong as its weakest link

The standard of care until 2014: iv TPA

Intravenous Treatments

1995
NINDS, ECASS I

1998
ECASS II

2008
ECASS III

- Proven and Approved
- Initiation very fast
- Can be widely used up to 4.5 h
- More efficient on distal occlusions
- Better results when initiated before 90 minutes

Does IV r-tPA thrombolysis work irrespective of the location of the occlusion?

- with IV tPA, the chance of successful angiographic recanalization is low for proximal large artery occlusions
  - 9% for carotid occlusions
  - 35% for M1-MCA [M1 segment middle cerebral artery] occlusions
  - best for distal branch occlusions
    - 54% for M2-MCA occlusions
    - 66% for M3-MCA occlusions

del Zoppo, Ann of Neurol 1992

What could we do for the following patients?

- Contra-indications to IV r-tPA

- Arrival time after 4,5 hours

- Failed IV rt-PA
  - Persistent symptoms/occlusions
    - 81% Carotid occlusions
    - 70% of proximal M1 occlusions
    - Basilar occlusions

IV vs IA treatments

Intravenous Treatments

1995 NINDS, ECASS I

1998 ECASS II

2008 ECASS III

1997 PROACT

1998 PROACT II

2001 IMS I

2003 MERCI

2005 IMS II

2006 Multi Merci

2009 Penumbra

2011 Swift

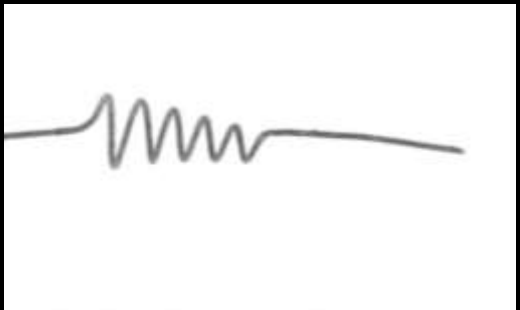
2013 IMS III, MR-Rescue/Synthesis/STar

Intra-arterial Treatments

- IA treatments: necessary but: no standard of care.

Intra-arterial treatment: First generation

Merci - ***Concentric***



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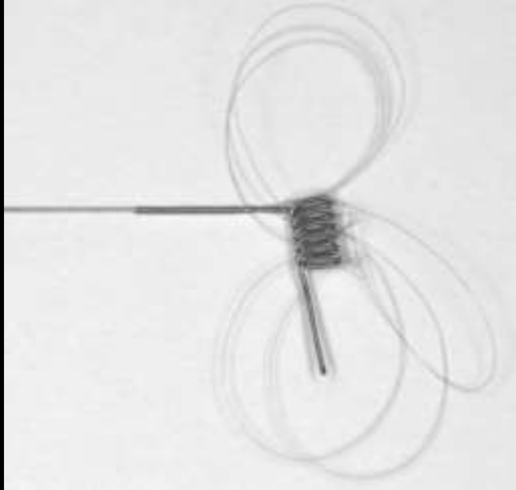


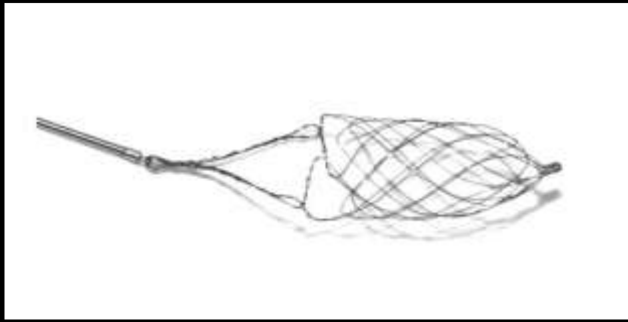
L-Type

Phenox

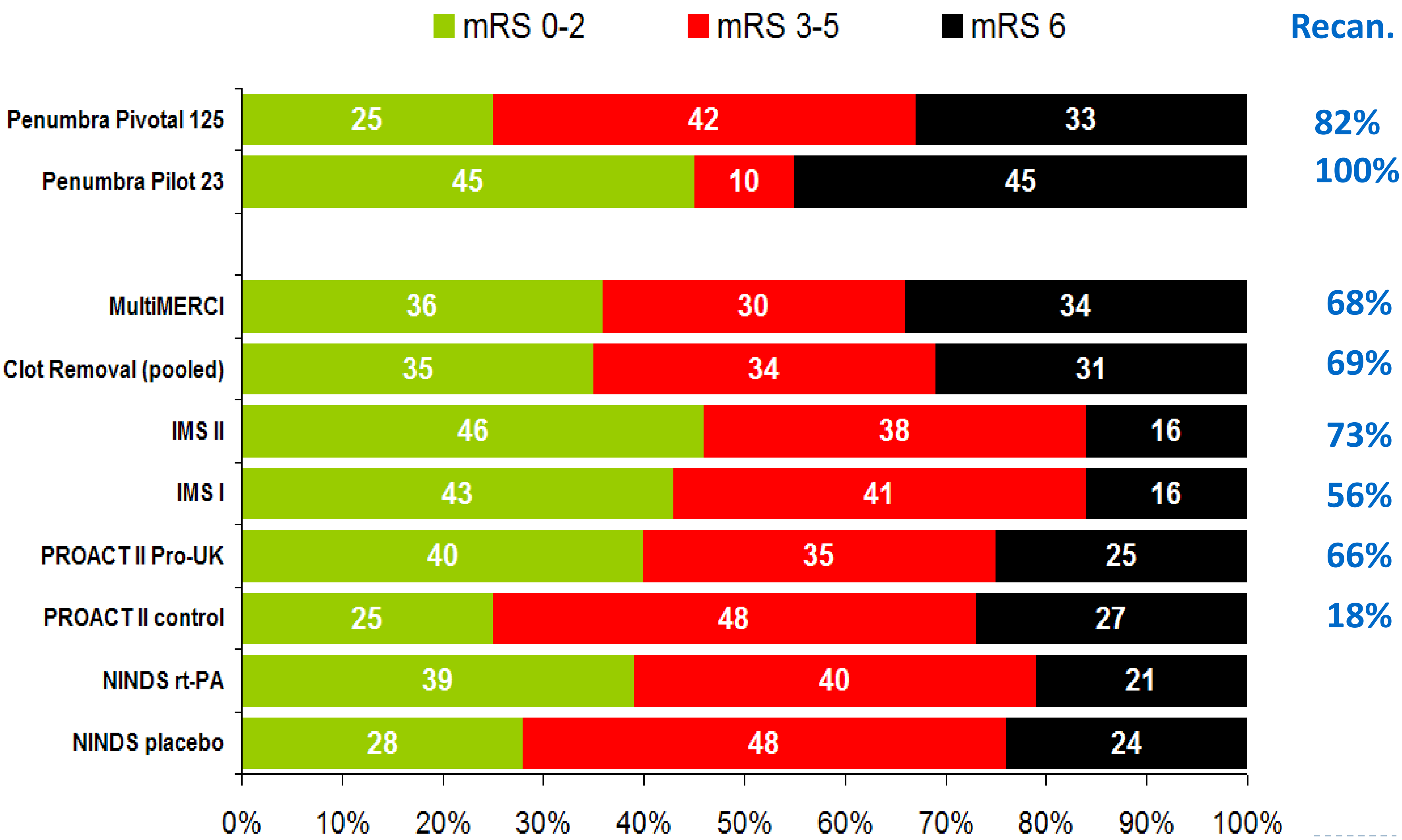
pCR

CRC

Catch - ***Balt***



Intra-arterial treatment: First generation



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 1, 2015 VOL. 372 NO. 1

A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

O.A. Berkhemer, P.S.S. Fransen, D. Beumer, L.A. van den Berg, H.F. Lingsma, A.J. Yoo, W.J. Schonewille, J.A. Vos, P.J. Nederkoorn, M.J.H. Wermer, M.A.A. van Walderveen, J. Staals, J. Hofmeijer, J.A. van Oostayen, G.J. Lycklama à Nijeholt, J. Boiten, P.A. Brouwer, B.J. Emmer, S.F. de Bruijn, L.C. van Dijk, L.J. Kappelle, R.H. Lo, J. van Dijk, J. de Vries, P.L.M. de Kort, W.J.J. van Rooij, J.S.P. van den Berg, B.A.A.M. van Hasselt, L.A.M. Aerden, R.J. Dallinga, M.C. Visser, J.C.J. Bot, P.C. Vroomen, O. Eshghi, T.H.C.M.L. Schreuder, R.J.J. Heijboer, K. Keizer, A.V. Tielbeek, H.M. den Hertog, D.G. Gerrits, R.M. van den Berg-Vos, G.B. Karas, E.W. Steyerberg, H.Z. Flach, H.A. Marquering, M.E.S. Sprengers, S.F.M. Jenniskens, L.F.M. Beenen, R. van den Berg, P.J. Koudstaal, W.H. van Zwam, Y.B.W.E.M. Roos, A. van der Lugt, R.J. van Oostenbrugge, C.B.L.M. Majoie, and D.W.J. Dippel, for the MR CLEAN Investigators*

MR CLEAN

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

M. Goyal, A.M. Demchuk, B.K. Menon, M. Eesa, J.L. Rempel, J. Thornton, D. Roy, T.G. Jovin, R.A. Willinsky, B.L. Sapkota, D. Dowlatshahi, D.F. Frei, N.R. Kamal, W.J. Montanera, A.Y. Poppe, K.J. Ryckborst, F.L. Silver, A. Shuaib, D. Tampieri, D. Williams, O.Y. Bang, B.W. Baxter, P.A. Burns, H. Choe, J.-H. Heo, C.A. Holmstedt, B. Jankowitz, M. Kelly, G. Linares, J.L. Mandzia, J. Shankar, S.-I. Sohn, R.H. Swartz, P.A. Barber, S.B. Coutts, E.E. Smith, W.F. Morrish, A. Weill, S. Subramaniam, A.P. Mitha, J.H. Wong, M.W. Lowerison, T.T. Sajobi, and M.D. Hill for the ESCAPE Trial Investigators*

ESCAPE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

B.C.V. Campbell, P.J. Mitchell, T.J. Kleinig, H.M. Dewey, L. Churilov, N. Yassi, B. Yan, R.J. Dowling, M.W. Parsons, T.J. Oxley, T.Y. Wu, M. Brooks, M.A. Simpson, F. Miteff, C.R. Levi, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfort, M. Priglinger, T. Ang, R. Scroop, P.A. Barber, B. McGuinness, T. Wijeratne, T.G. Phan, W. Chong, R.V. Chandra, C.F. Bladin, M. Badve, H. Rice, L. de Villiers, H. Ma, P.M. Desmond, G.A. Donnan, and S.M. Davis, for the EXTEND-IA Investigators*

EXTEND-IA

Nashville, TN February 11, 2015

Primary Results

SOLITAIRE™ FR With the Intention For Thrombectomy as PRIMary Endovascular Treatment for Acute Ischemic Stroke

J. Saver, M. Goyal, A. Bonafé, H. Diener, E. Levy, V. Mendes-Pereira, G. Albers, C. Cognard, D. Cohen, W. Hacke, O. Jansen, T. Jovin, H. Mattle, R. Nogueira, A. Siddiqui, D. Yavagal, T. Devlin, D. Lopes, V. Reddy, R. du Mesnil de Rochemont and R. Jahan for the **SWIFT PRIME Investigators**

SWIFTPRIME

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UNIVERSITY OF CALGARY
CUMMING SCHOOL OF MEDICINE

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Inclusion and exclusion criteria

- Acute ischemic stroke (NIHSS > 5)
- 12 hour window
- No upper age limit
- Good functional status

- CT head: ASPECTS > 5 (exclude large core)
- CTA: ICA + M1 or M1 or functional M1 (all M2s)
- CTA (preferably multiphase): moderate to good collaterals

NEJM, 2015

ESCAPE

Methods

- 22 centres in Canada (11), US (6), Korea (3), UK (1), Ireland (1)
- tPA given when patient eligible (no waiting for tPA response)
- Imaging must have shown: small core, proximal intracranial artery occlusion, moderate-good collaterals using CT, mCTA (use of MRI discouraged)
- Intensive quality improvement program with personalized site visits

NEJM, 2015

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Effect size for Intervention

common OR* ("shift") **3.1** (2.0-4.7)

[NNT ~ 3 for improvement on mRS]

mRS 0-2	**29.3% → 53.0%**	**NNT = 4** for independence
Death HR*	**19.0% → 10.4%**	**0.4** (0.2-0.8)

*Adjusted for age, sex, baseline NIHSS score, baseline ASPECTS score, IV alteplase use, baseline occlusion location

NEJM, 2015

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Conclusion

- Endovascular thrombectomy is a safe, highly effective procedure that saves lives and dramatically reduces disability WHEN:
  - Patients are carefully selected by imaging to identify proximal occlusions, and exclude large core and exclude patients with absent collaterals
  - Treatment is extremely fast with target first slice
    - imaging → to groin puncture < 60 min and
    - imaging → to reperfusion < 90 min
  - Safe effective technology (retrievable stents) is used

NEJM, 2015

The new Standard of Care

- Recommendations of the US Heart and Stroke Foundation
- Canadian Best Practice Guidelines

Current Best Practice Guidelines:
Patient with acute Neurological Deficit related to ischemic stroke

Rapid initiation of ivTPA

followed by mechanical thrombectomy

if

there is a large vessel occlusion

and tissue that can be saved

Current Best Practice Guidelines:
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Rapid Initiation of Treatment
TIME IS BRAIN

Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke				
	Neurons Lost	**Synapses Lost**	**Myelinated Fibers Lost**	**Accelerated Aging**
Per Stroke	1.2 billion	8.3 trillion	7140 km/4470 miles	36 yrs
Per Hour	120 billion	830 billion	714/447 miles	3.6 yrs
Per Minute	**1.9 million**	14 billion	12 km/7.5 miles	3.1 weeks
Per Second	32,000	230 million	200 meters/218 yards	8.7 hours

Modified from : Saver et al

Rapid Initiation of Treatment
TIME IS BRAIN

- Each hour in which treatment does not occur, the brain loses as many neurons as it does in almost 3.6 years of normal aging

- Rapid initiation of treatment is key!

1st Key Point in Imaging

Choose a fast Imaging Modality

SPEED in acute Stroke Imaging

CT

- Available 24/7

- No screening
- CT/CTA: 3min
- Postprocessing 24/7 5 min

Current Best Practice Guidelines:
Patient with acute Neurological Deficit related to ischemic stroke

Rapid initiation of ivTPA

followed by mechanical thrombectomy

if

there is a large vessel occlusion

and tissue that can be saved

Exclude Hemorrhage as the cause for the neurological deficit

2nd Key Point in Imaging

Choose an Imaging Modality that can exclude hemorrhage

UNENHANCED CT

Current Best Practice Guidelines:
Patient with acute Neurological Deficit related to ischemic stroke

Rapid initiation of ivTPA

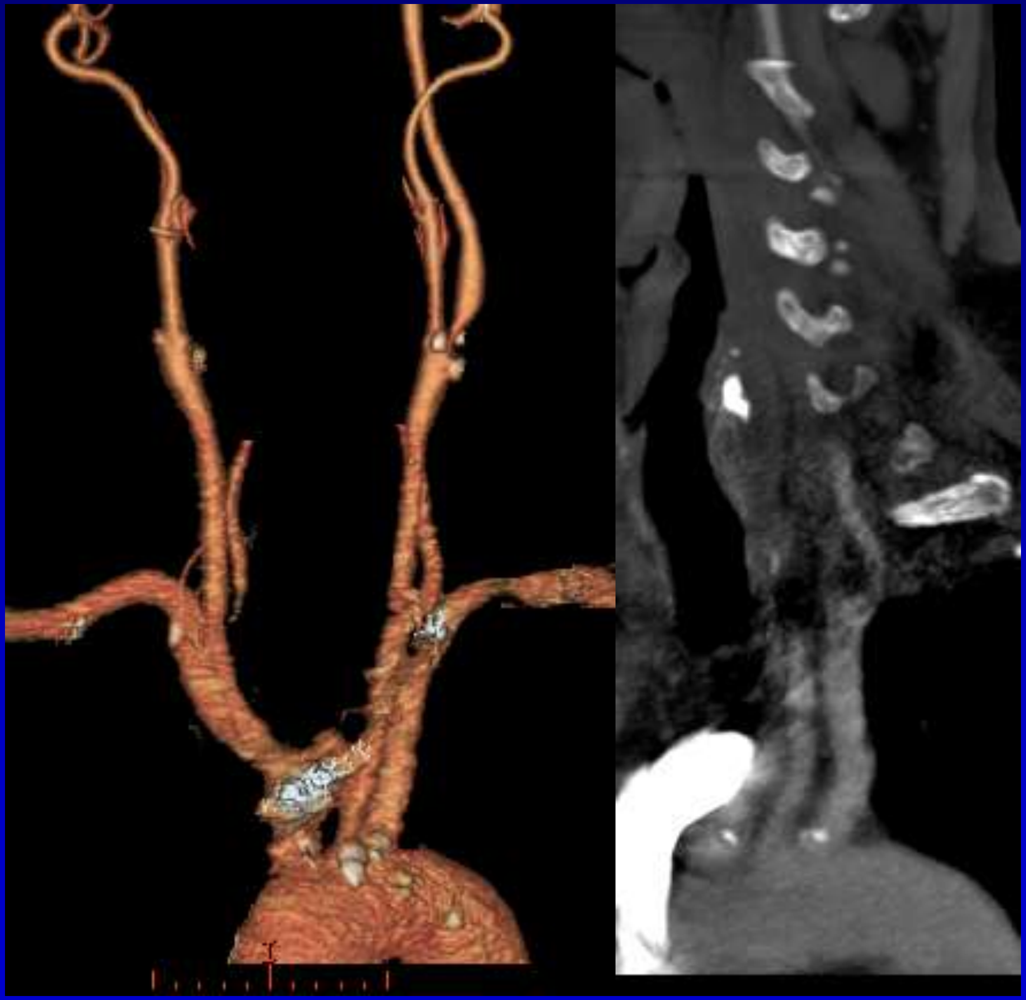
followed by mechanical thrombectomy

if

there is a large vessel occlusion

and tissue that can be saved

Determine if access to the clot is possible and safe

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18-Mar-2015
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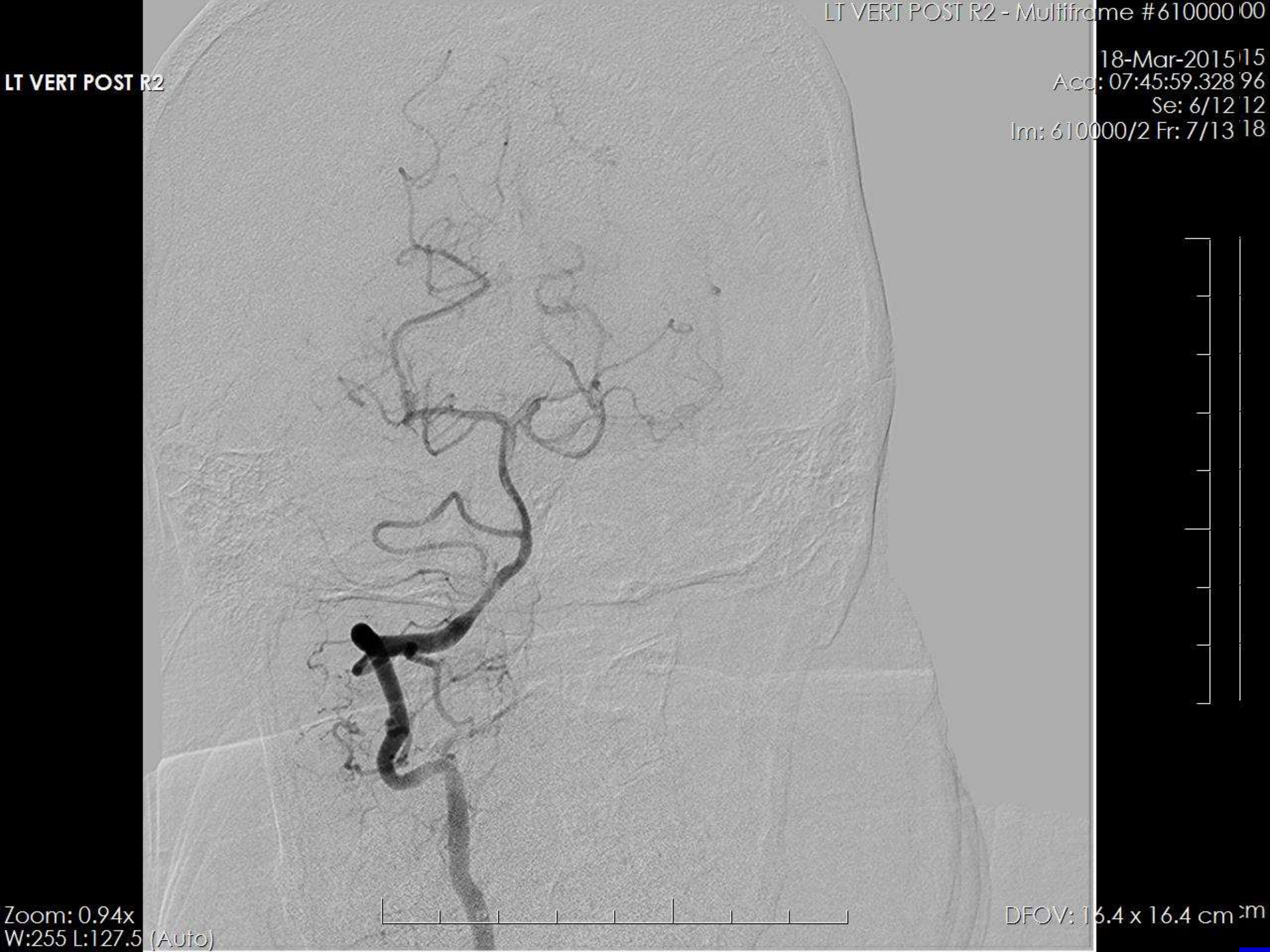
DFOV: 18.9 x 18.9 cm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Zoom: 0.94x
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DFOV: 16.4 x 16.4 cm

3rd Key Point in Imaging

Choose an Imaging Modality that can evaluate access to the site of occlusion

CTA Head and Neck including Arch

Current Best Practice Guidelines:
Patient with acute Neurological Deficit related to ischemic stroke

Rapid initiation of ivTPA

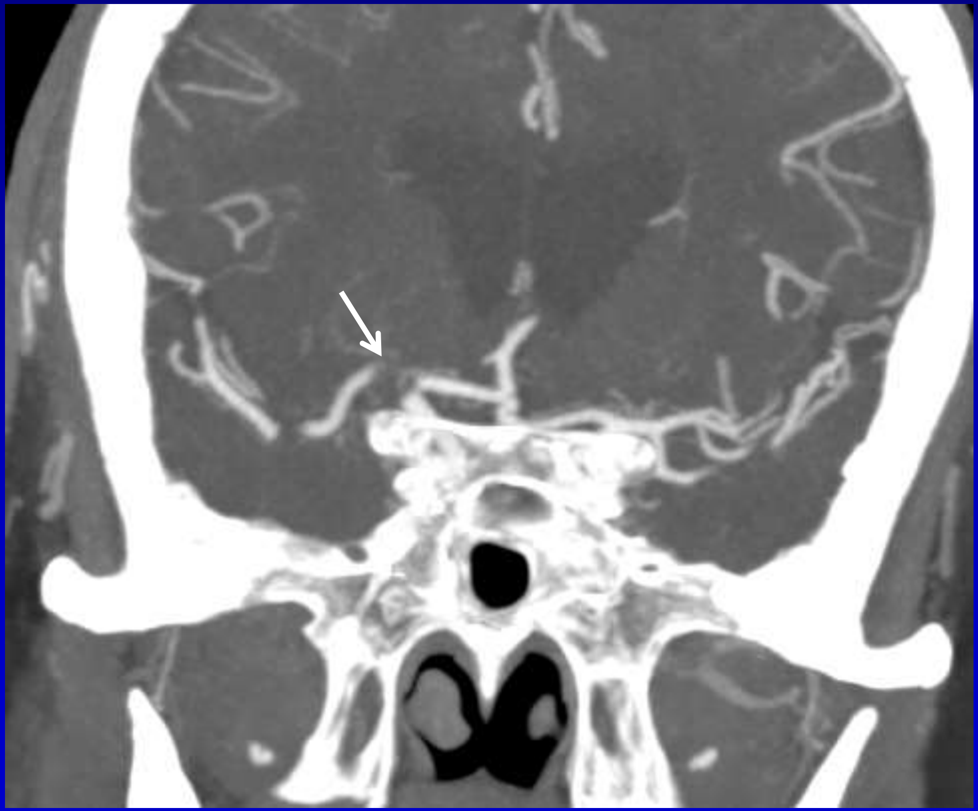
followed by mechanical thrombectomy

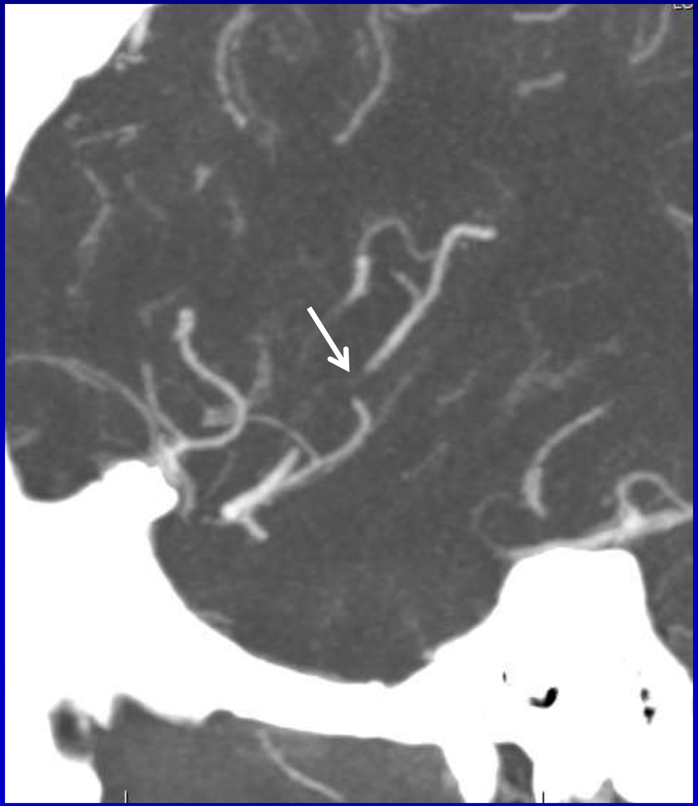
if

there is a large vessel occlusion

and tissue that can be saved

Determine site of occlusion: Large vessel (proximal) vs small vessel (distal)





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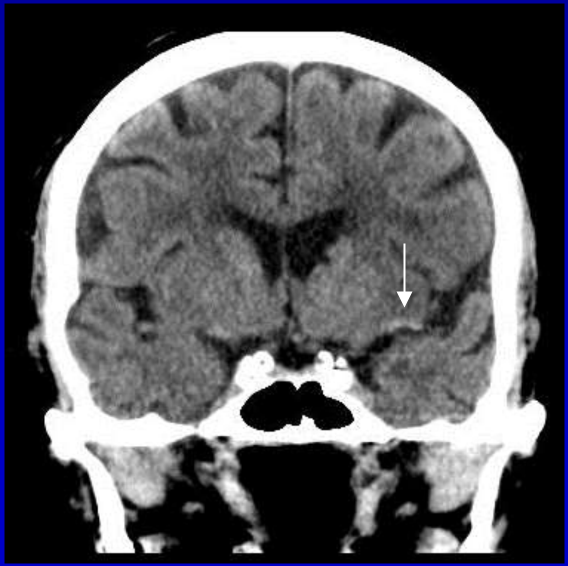
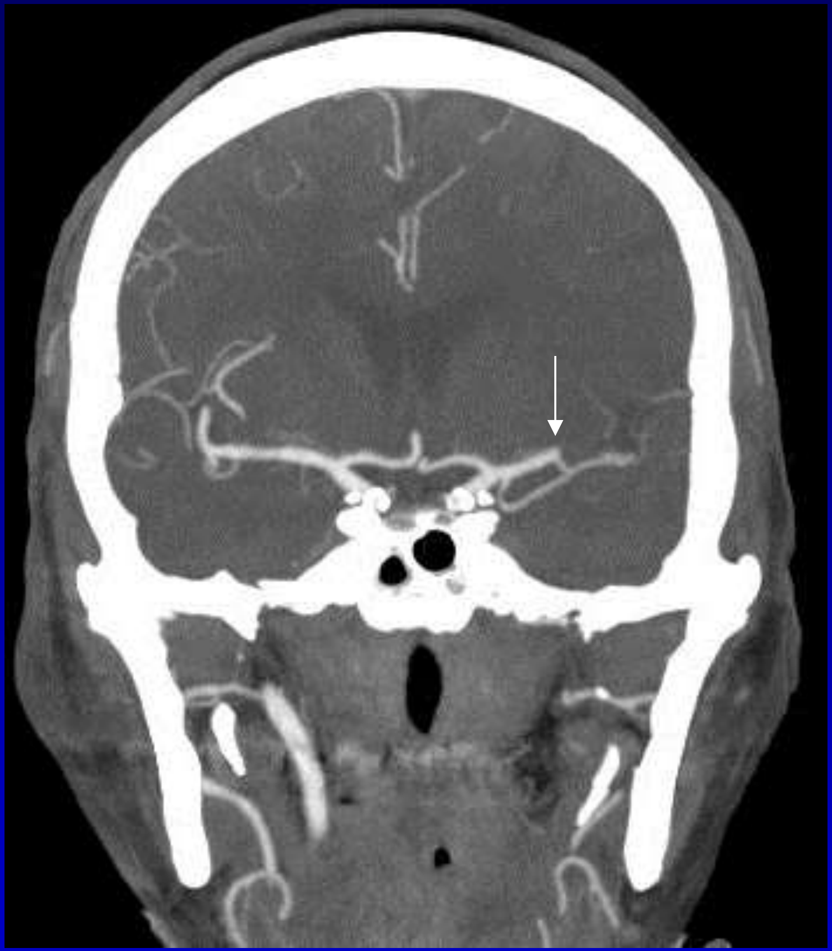




F 85 3 hrs post acute stroke right hemiplegia and aphasia

4^{th} Key Point in Imaging

Choose an Imaging Modality that can evaluate the site of occlusion

Unenhanced CT (Dense Vessel) and

CTA Head and Neck

with multiplanar reformats

Current Best Practice Guidelines:
Patient with acute Neurological Deficit related to ischemic stroke

Rapid initiation of ivTPA

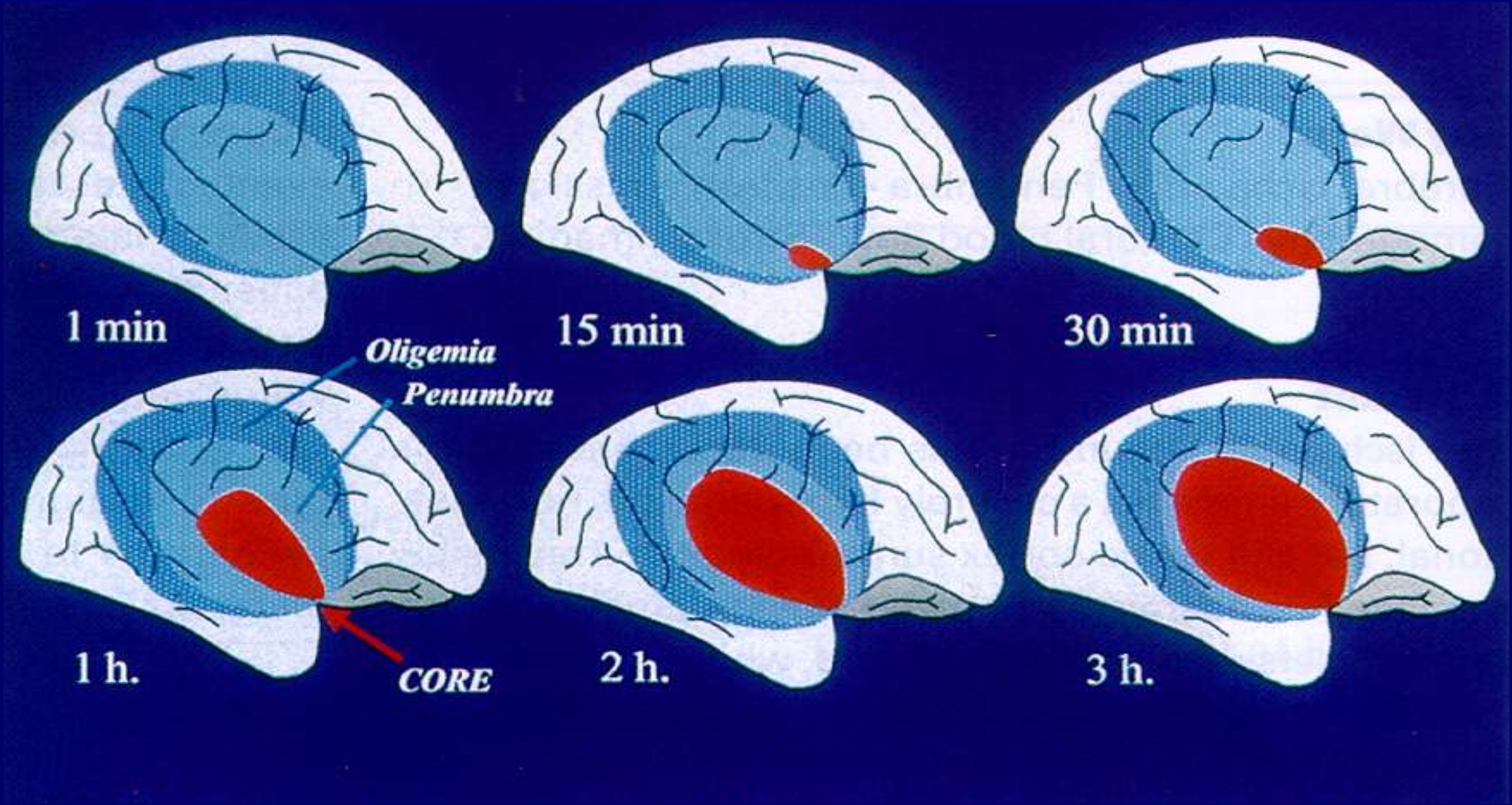
followed by mechanical thrombectomy

if

there is a large vessel occlusion

and tissue that can be saved

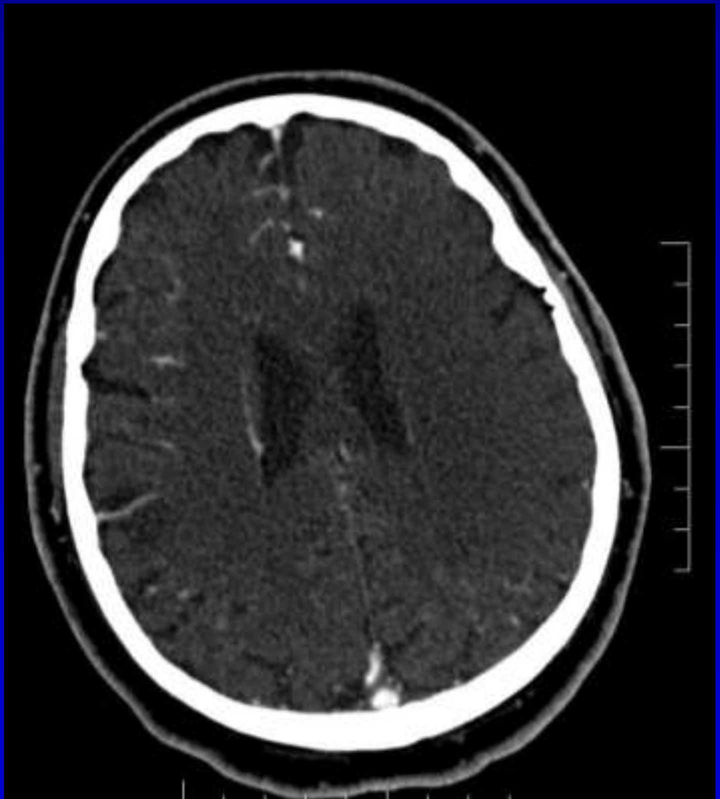
Determine how much tissue is irreversibly damaged and how much tissue is at risk



Baron, Cerebrovasc Diseas 1999

Determine how much tissue is irreversibly damaged and how much tissue is at risk

- Dead brain will not recover after recanalization
- Dead brain has a high risk for hemorhagic transformation



Ischemic Injury on CT

- Subtle decreased attenuation of grey matter
  - loss of grey - white differentiation
  - loss of cortical ribbon (look at insular cortex)
  - "disappearing basal ganglia"
- Early mass effect
  - sulcal effacement
  - shift

requires good quality CT with 5 mm sections

ASPECTS score

Alberta Stroke Program Early CT Score

Developed in Calgary, Alberta, Canada

A reproducible grading system to assess early ischemic changes on non-enahnced CT studies in patients with an acute ischemic stroke of the anterior circulation.

The MCA territory is divided into 10 areas.

Normal CT – ASPECTS 10

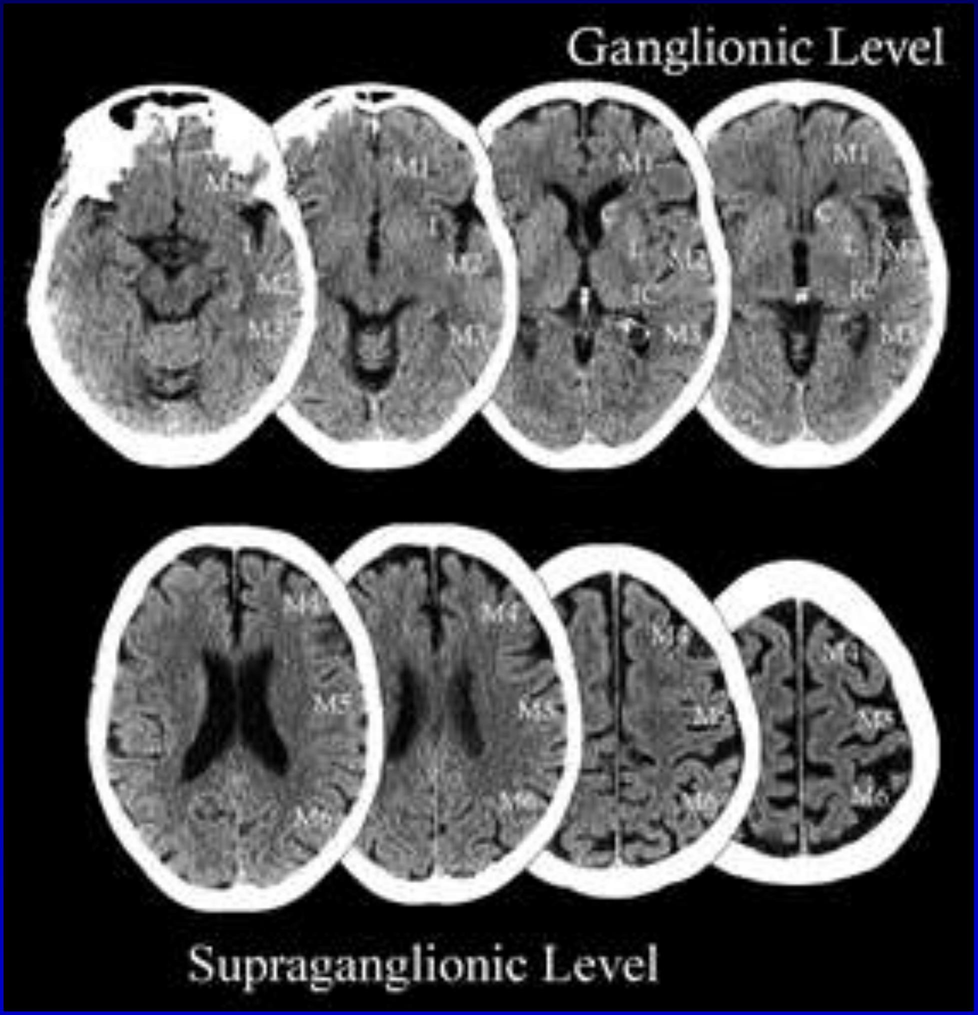
Every area with loss of gray-white matter differentiation reduces 1 from the score.

ASPECTS score

C	- Caudate nucleus
IC	- Internal capsule
L	- Lentiform nucleus
I	- Insular ribbon
M1	- Anterior MCA cortex
M2	- MCA cortex lateral to insular ribbon
M3	- Posterior MCA cortex
M4, M5, M6	- Anterior, lateral, posterior MCA territories immediately superior to M1, M2 and M3 rostral to basal ganglia.

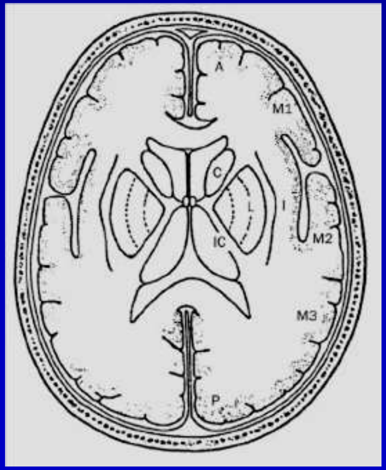
Subcortical structures are allotted 3 points (C, L, and IC).

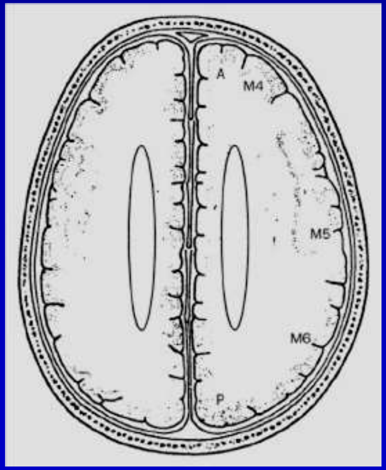
MCA cortex is allotted 7 points (IC, M1, M2, M3, M4, M5 and M6).



A normal CT scan received an ASPECTS of 10 points.

A score of 0 indicated diffuse ischemic involvement throughout the MCA territory





Pexmann et al; AJNR 22:1534–42, 2001
Aviv et al. AJNR 28:1975-80, 2007

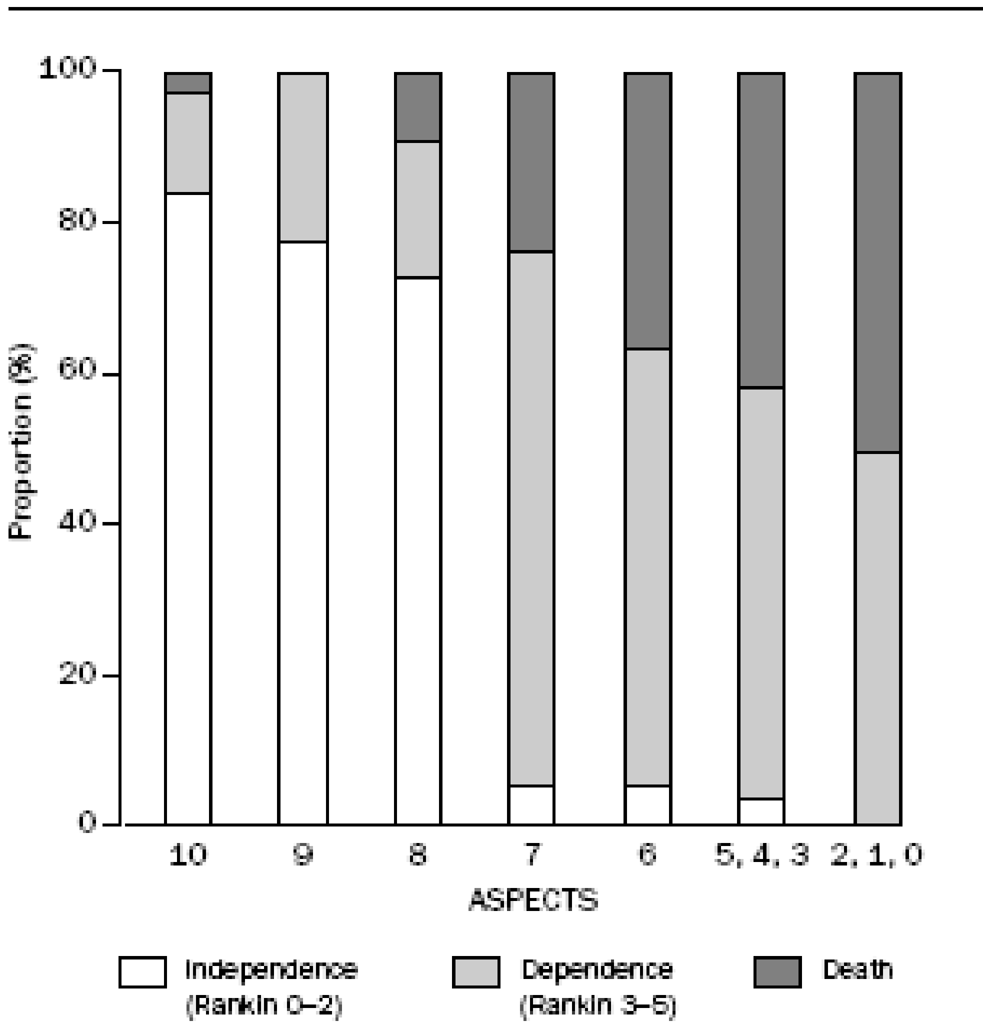


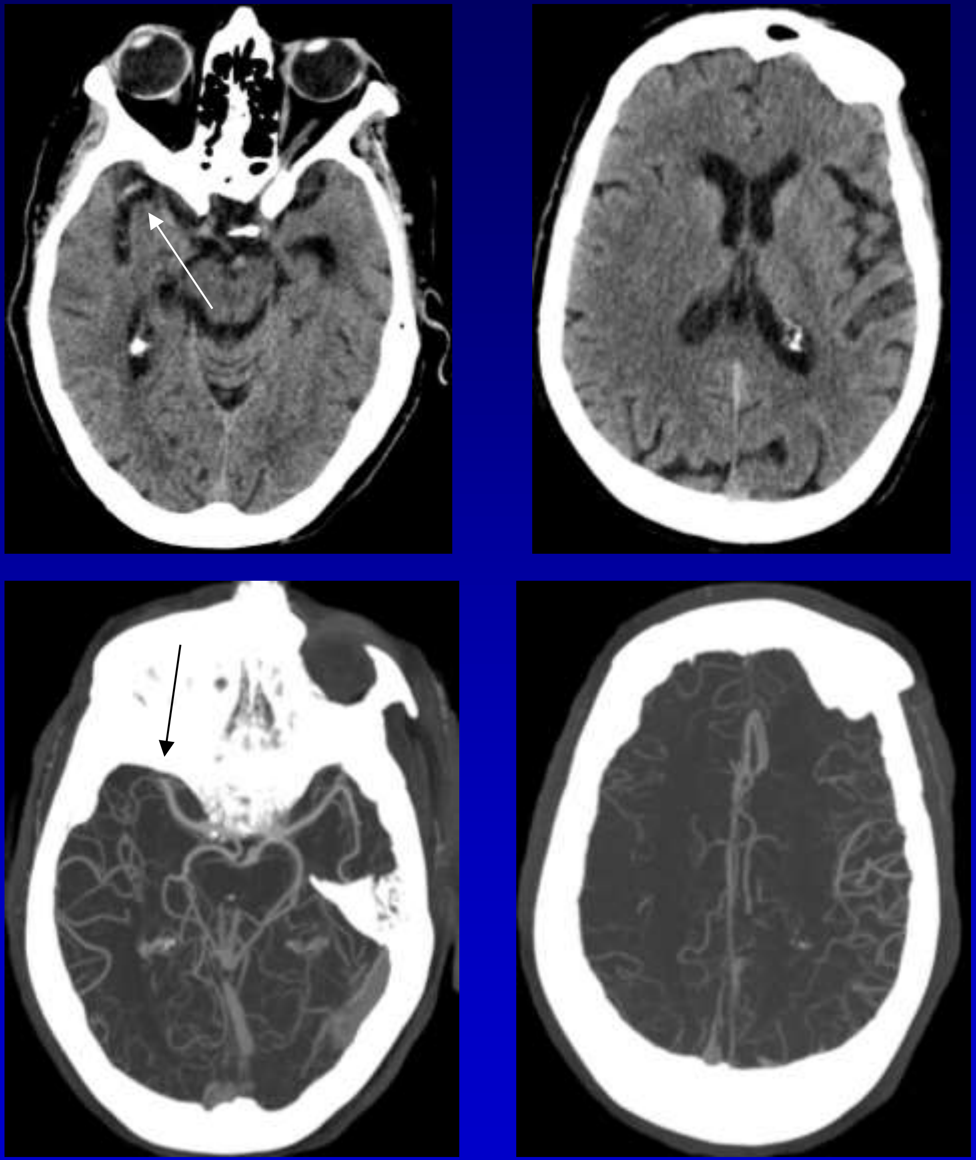
Figure 2: **ASPECTS and functional outcome**

ASPECTS Score

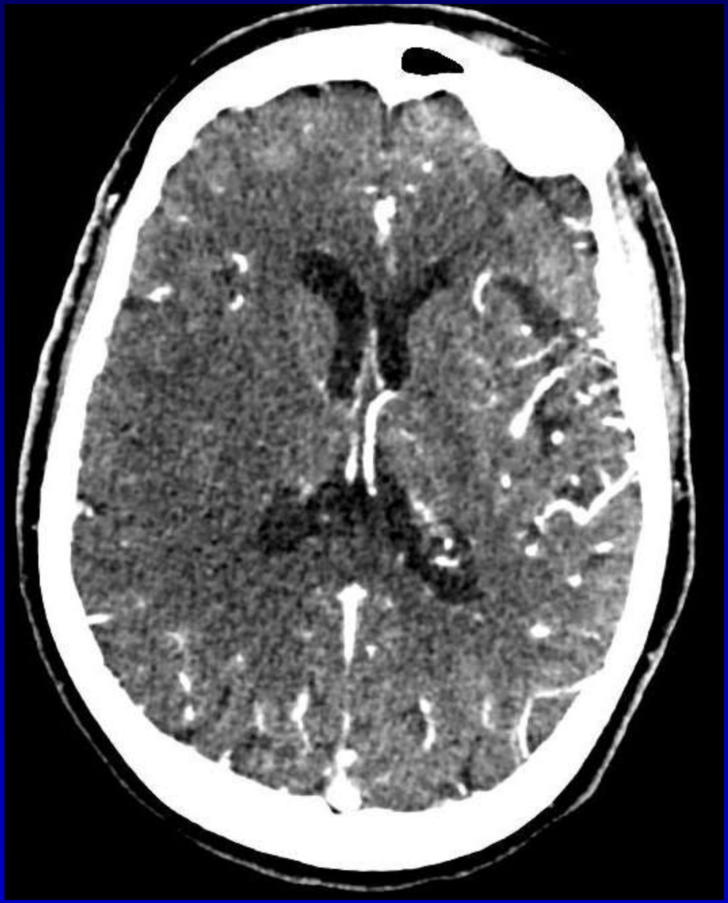
Barber et al. Lancet 355: 1670-1674, 2000

ASPECTS score of >7 corresponds to hypoattenuation of < 1/3 of the MCA territory

84 F 6 hrs post onset acute stroke



"collapse CTA view"

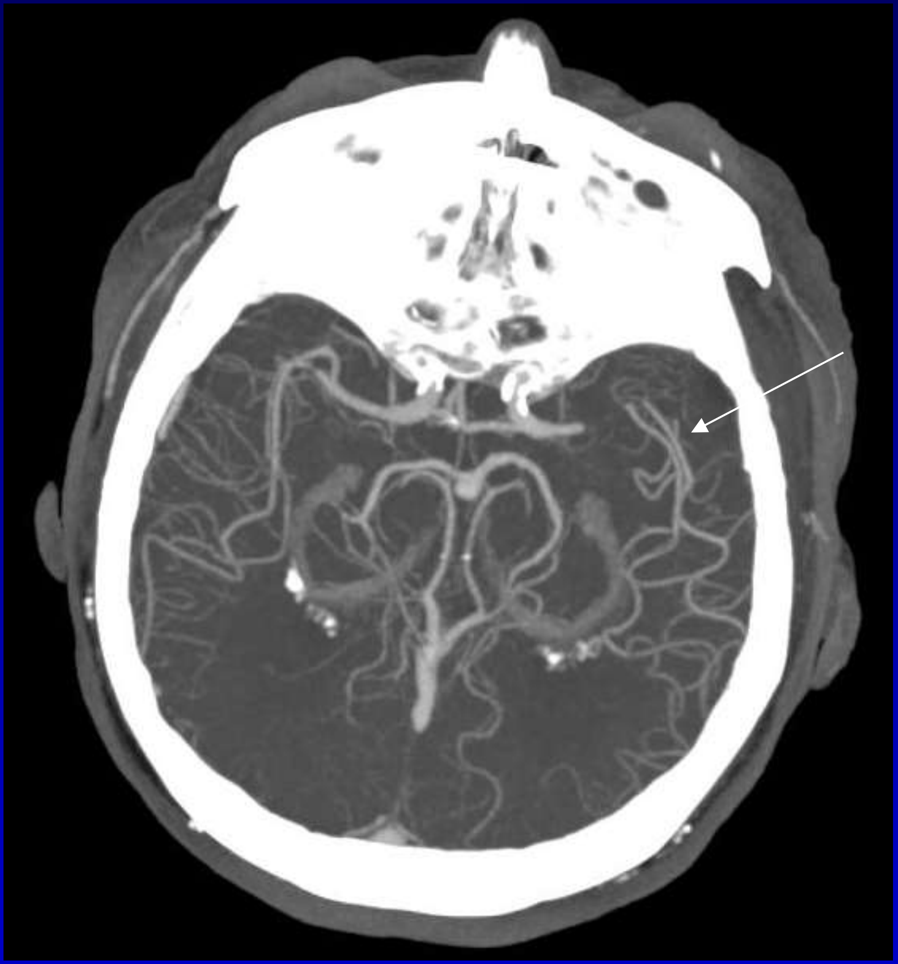


CTA source images

Ta

first pass

second pass, 10 sec delay

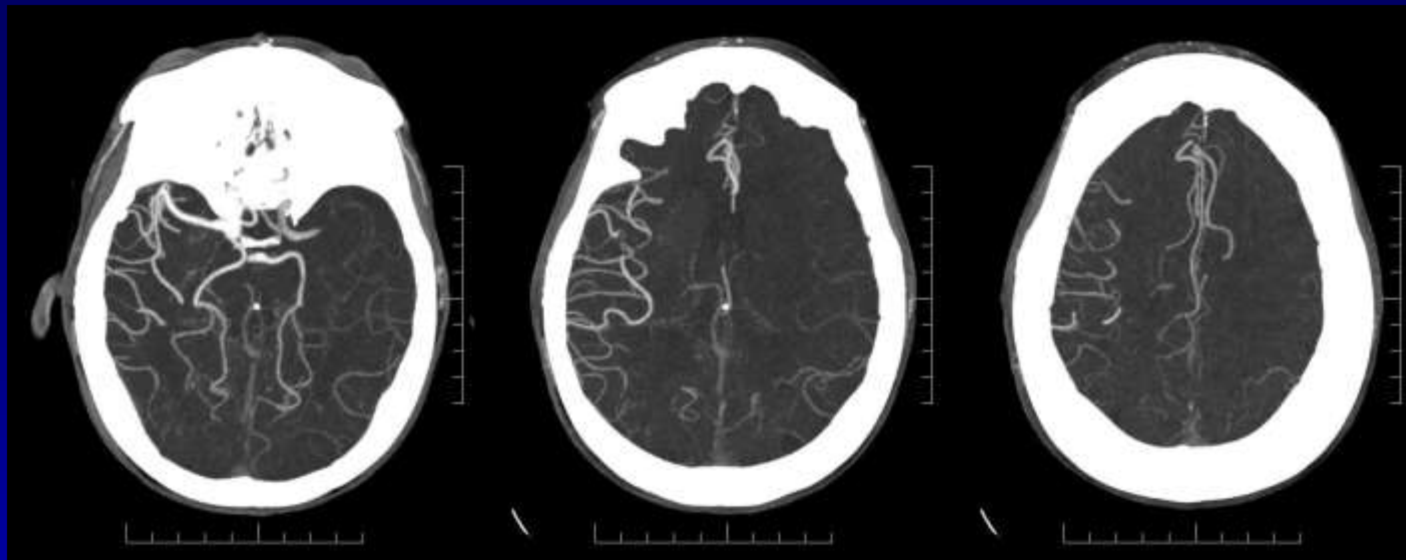


The role of delayed vascular imaging

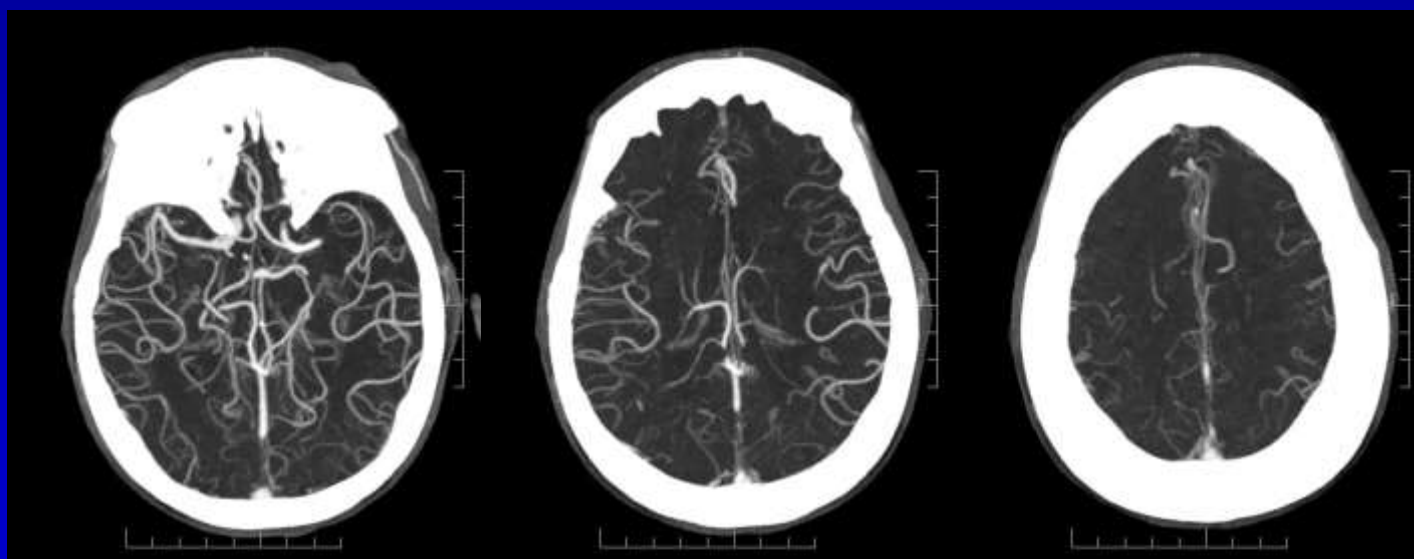
second pass, 10 second delay

Assessing Leptomeningeal Collaterals

Arterial



Delay



Single phase CT – can underestimate the filling of leptomeningeal collateral and can mislabel a patient with sufficient collaterals as insufficient

Is Collateral Flow Associated with…

...Baseline NIHSS?

Baseline NIHSS score Correlates with Collateral score:

Miteff et al, Brain 2009; 132:2231-38

***Significant difference in median acute NIHSS between good and reduced collateral groups* (NIHSS 16 vs 18 *P*=0.012).** Left and right hemisphere strokes equally distributed between groups

Menon et al, AJNR 2011;32:1640-45

In multivariable analysis ***poor collaterals score was associated with higher baseline NIHSS score*** (OR 1.1 per 1 point increase in NIHSS *P*=0.04)

Is Collateral Flow Associated with…

…Baseline ASPECTS score?

Lima et al, Stroke 2010; 41:2316-22

Patients with "equal" or "greater" collaterals had higher baseline ASPECTS than those with "less" collaterals (*P*=0.02)

…Baseline DWI volume?

Souza et al, AJNR 2012;33:1331-36

Admission DWI lesion volume was an independent variable associated with collateral score on multivariable analysis (*P*<0.001)

Is Collateral Flow Associated with…

…Final infarct volume?

Tan et al, AJNR 2009;30:525-31

Collateral score was associated with final infarct size on multivariate linear regression analysis (*P*=0.04). Collateral score predicts final infarct size but does not independently predict clinical outcome.

…Follow up CT ASPECTS score?

Menon et al, AJNR 2011;32:1640-45

Better collateral status showed strong correlation with higher follow up CT ASPECTS score (Spearman *r*=0.58 *P*<0.001)

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UHN Toronto Western Hospital

Is Collateral Flow Associated with…

…Hemorrhage?

AJNR 2009;30:165-170

ORIGINAL RESEARCH

Predictors of Hemorrhage Following Intra-Arterial Thrombolysis for Acute Ischemic Stroke: The Role of Pial Collateral Formation

G.A. Christoforidis
C. Karakasis
Y. Mohammad
L.P. Caragine
M. Yang
A.P. Slivka

BACKGROUND AND PURPOSE: The extent of pial collateral formation during acute ischemic stroke has been shown to influence outcomes. This study examines whether angiographic assessment of pial collateral formation is predictive of hemorrhagic transformation following intra-arterial thrombolysis (IAT) for acute ischemic stroke.

MATERIALS AND METHODS: Rates of any hemorrhage and significant hemorrhage (>25 mL) were reviewed in 104 consecutive patients who underwent IAT following acute ischemic stroke. The influence of the anatomic extent of pial collateral formation on the rates of hemorrhage and significant hemorrhage relative to known predictors for hemorrhagic transformation (presenting systolic blood pressure, blood glucose level, platelet level, and National Institutes of Health Stroke Scale [NIHSS] score, history of diabetes, time to treatment, age, sex, occlusion site, and extent of reperfusion) was analyzed by using logistic regression models.

RESULTS: Rates of any hemorrhage and significant hemorrhage were 25.2% (26/104) and 9.7% (10/104), respectively. The rate of significant hemorrhage was 25.0% (8/32) in patients with poor pial collaterals and 2.78% (2/72) in those with good pial collaterals ($P = .0004$, Pearson correlation). The rate of any hemorrhage was also significantly higher in patients with poor pial collaterals (40.6% versus 18.1%; $P = .0142$, Pearson correlation). Logistic regression analyses revealed that pial collateral formation (odds ratio [OR] = 3.04), history of diabetes (OR = 4.83), platelets <200,000/μL (OR = 2.95), and time to treatment <3 hours (OR = 12.0) were statistically significant predictors of hemorrhage, whereas pial collateral formation (OR = 13.1) and platelets <200,000/μL (OR = 8.1) were statistically significant predictors of significant hemorrhage.

CONCLUSIONS: Poor pial collateral formation is associated with higher incidence and larger size of hemorrhage following IAT.

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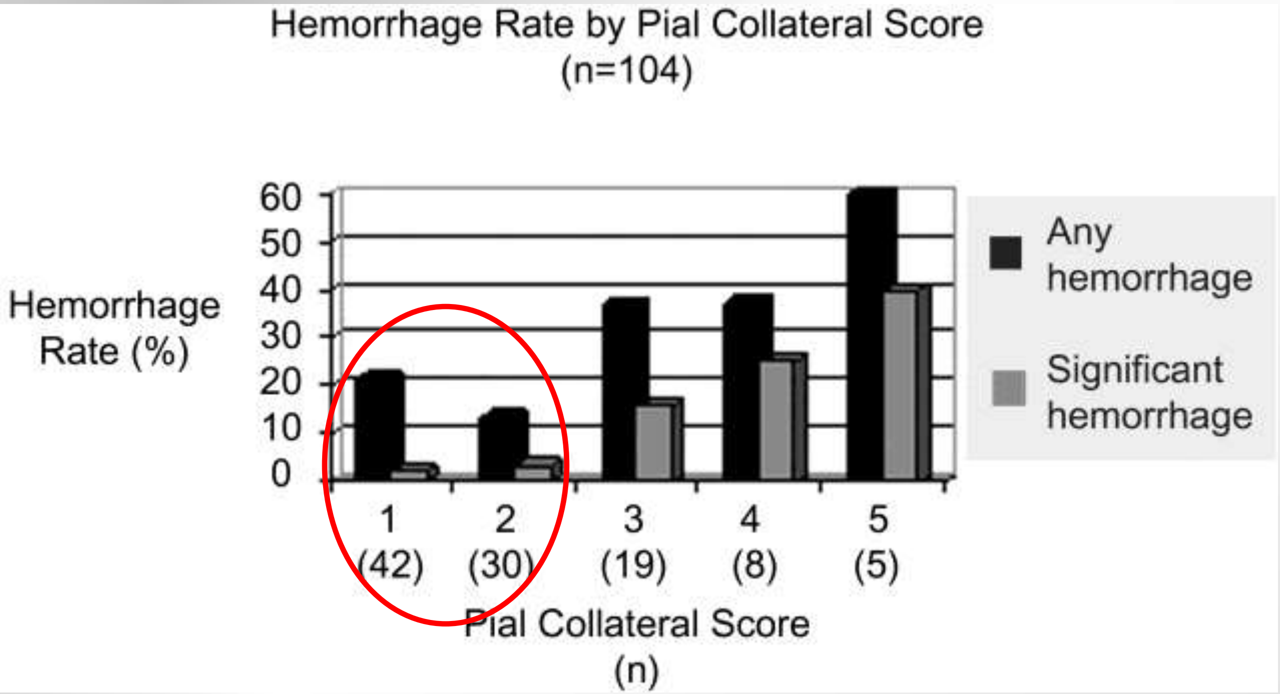


Grades 1-2: Good collaterals.
Grades 3-5: Poor collaterals

Christoforidis G et al. AJNR Am J Neuroradiol 2009;30:165-170

Clinical factors found to be predictive of hemorrhage were: poor pial collateral formation (OR 3.03, *P*=0.342), platelets <200,000/μL (OR 2.95 *P*=0.403), diabetes (OR 4.82 *P*=0.01), and time to treatment > 3 hours (OR 12.0 *P*=0.033)

Multivariable analysis identified only **poor pial collateral formation as a statistically significant predictor for symptomatic hemorrhage** (OR 6.8, *P*=0.0286)

Is Collateral Flow Associated with…

…Clinical Outcome?

Miteff et al, Brain 2009; 132:2231-38

In multivariable analysis ***good collateral status was an independent predictor of good outcome*** (mRS 0-2 at 3 months)

Menon et al, AJNR 2011;32:1640-45

In multivariable analysis collateral score was an independent predictor of good clinical outcome (mRS 0-2 at 3 months)

(OR 16.7 for Good vs Poor collateral score; OR 9.2 for Medium vs Poor collateral score)

Lima et al, Stroke 2010; 41:2316-22

Pattern of leptomeningeal collaterals was significantly associated with good outcome (mRS 0-2 at 6 months) OR 1.93 P=0.03

Interventional Cohort

- Nambiar et al AJNR 2014; 35:884-90

RECANALIZED PATIENTS	NON-RECANALIZED PATIENTS
Infarct growth significantly lower in good collateral group compared to intermediate or poor groups (*P*=0.05)	No significant difference in infarct growth stratified by collateral status (*P*=0.09)
Higher good clinical outcome among patients with good collateral status (*P*=0.04)	No significant difference in in good clinical outcome stratified by collateral status (*P*=0.67)

Recanalized patients

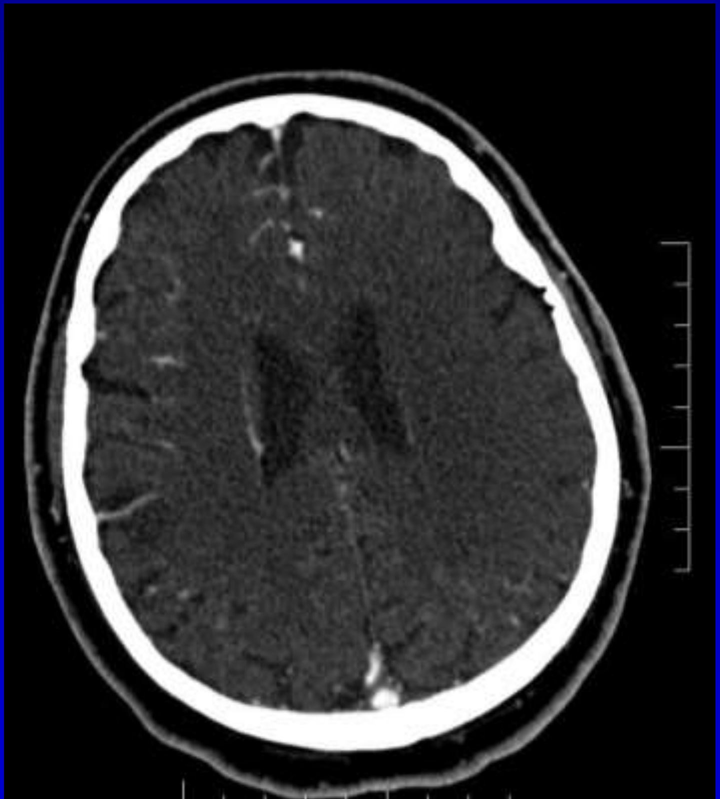
Collateral status	mRS 0-2
Good	*100%*
Intermediate:	*58.8%*
Poor	*33.3%*

Non-recanalized patients

Collateral status	mRS 0-2
Good	*30.8%*
Intermediate:	*17.6%*
Poor	*18.2%*

Determine how much tissue is irreversibly damaged and how much tissue is at risk

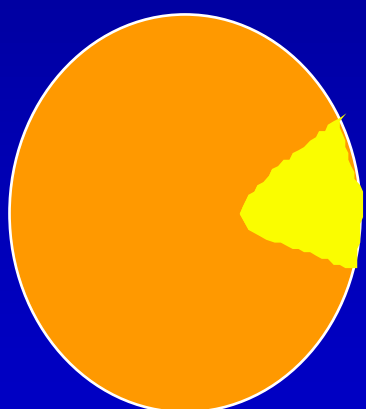
- Futility of Treatment if there is no tissue that can be saved
- Potential harm of both ivTPA and Thrombectomy



Mismatch Concepts

Mismatch between dead tissue and Clinical Findings

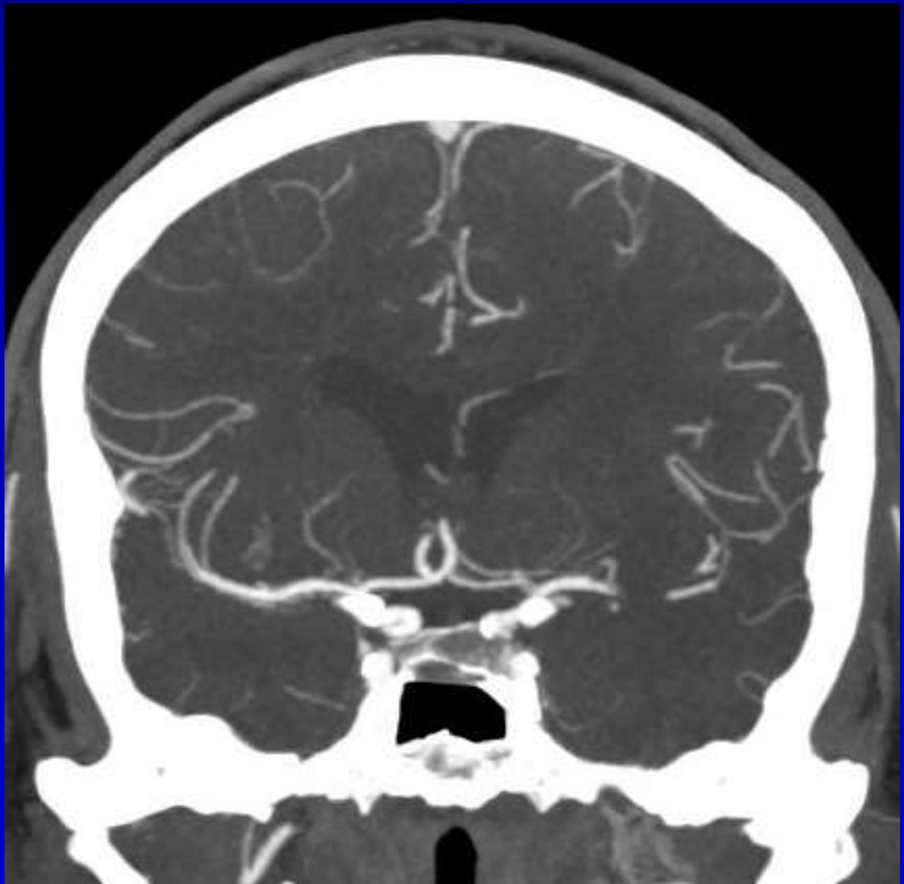
Dead Tissue



Coll Score CTA

Mismatch Concepts

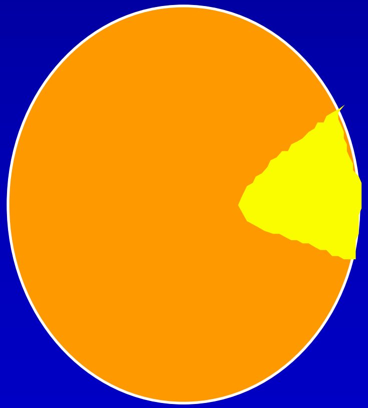
Mismatch between dead tissue and Clinical Findings



Mismatch Concepts

Mismatch between dead tissue and Angiography

Dead Tissue

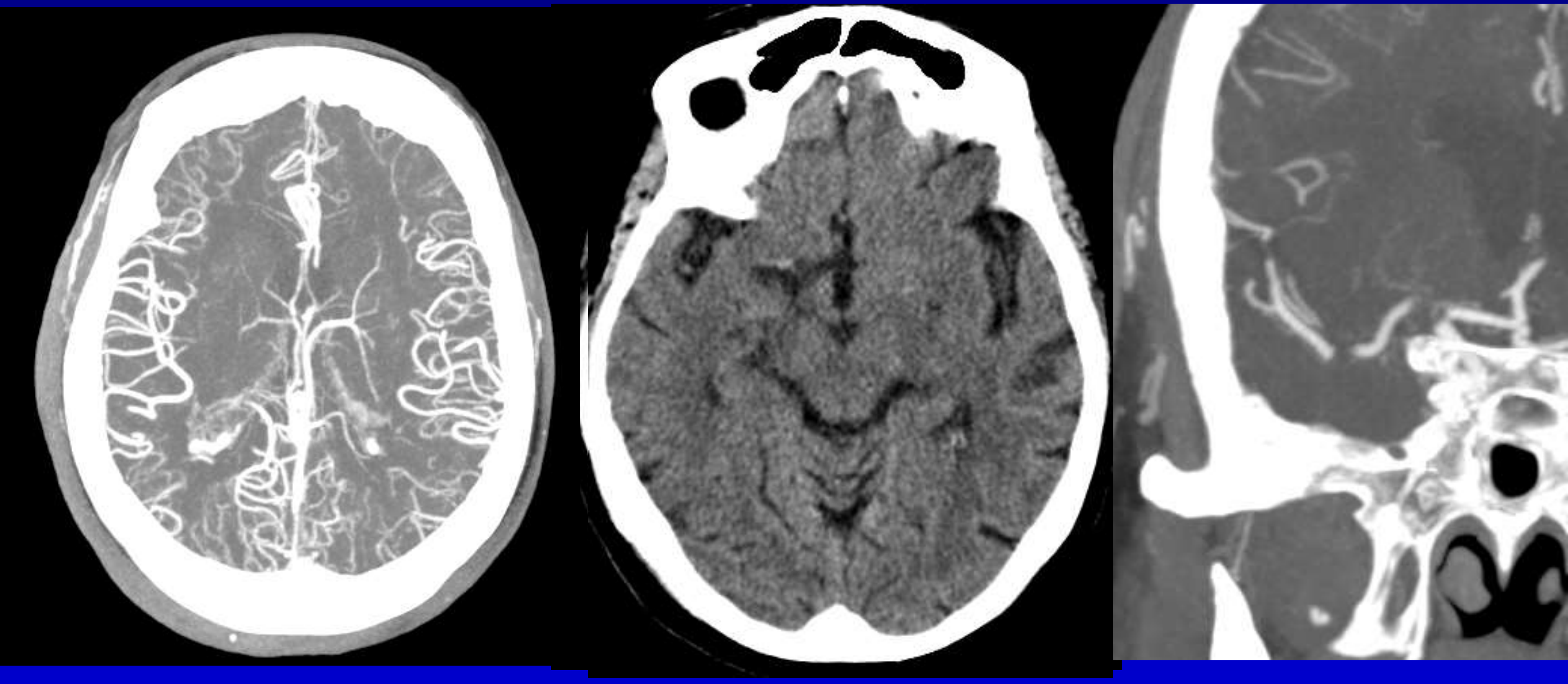


Coll Score CTA

CTA

Mismatch Concepts

Mismatch between dead tissue and Angiography



5th Key Point in Imaging

Choose an Imaging Modality that can evaluate

a) whether brain tissue is still “alive”
   - Unenhanced CT: ASPECTS
   - first pass CTA rawdata and collateral score (delayed CTA)

b) whether brain tissue is “at risk”
   - Mismatch CTA vs delayed CTA

Key Points in acute Stroke Imaging

Choose an Imaging Modality that

- is the fastest in your hospital setting
- can exclude hemorrhage
- can evaluate access to the site of occlusion
- can determine the site of occlusion
- can evaluate whether treatment makes sense:
  - Is brain tissue still "alive"
  - Is brain tissue "at risk"

- CT
- Plain CT
- CTA Head and Neck

- Multiplanar reformats
- CT Aspects
- CTA First pass
- CTA Second Pass (Collaterals)
- Mismatch

Questions?

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