Update on multimodal CT in stroke

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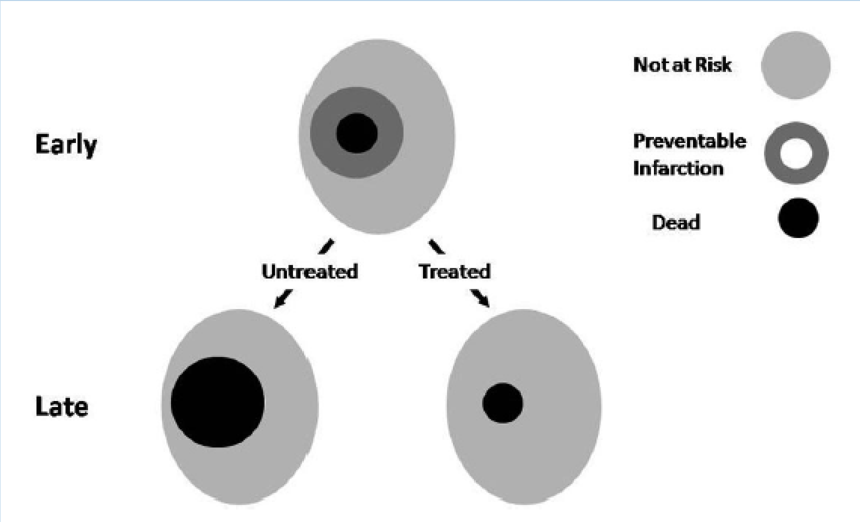
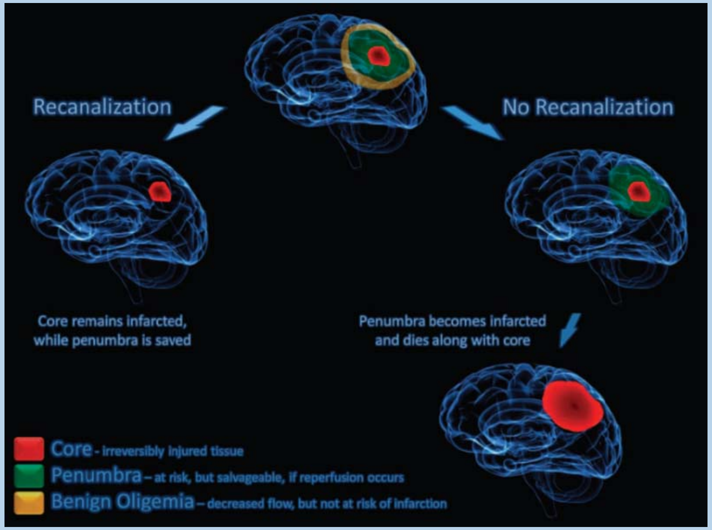
The target of reperfusion therapies





Powers WJ. Am J Neuroradiol 2008; 29: 1823-1825; Kidwell CS. Stroke 2013; 44: 570-578

the rescue of the ischemic penumbra

↓

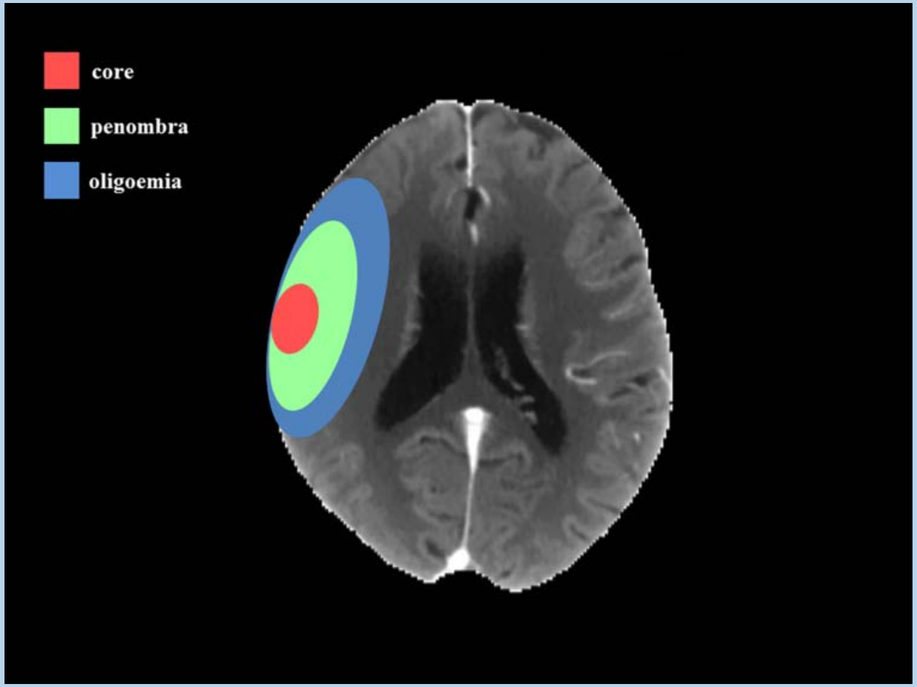
tissue at risk for infarction

Functional topography of ischemic area

- ***infarct core:***
critically hypoperfused, irreversibly damaged tissue located in the center of ischemic area

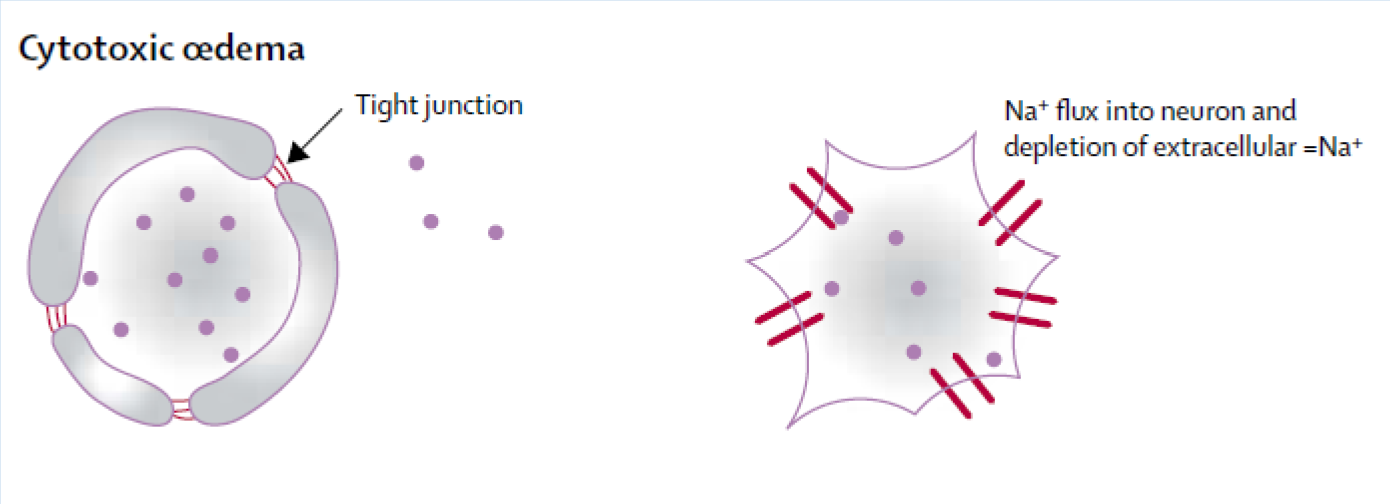
- ***ischemic penumbra:***
critically hypoperfused, reversibly damaged tissue located around the infarct core

- ***benign oligoemia:***
moderately hypoperfused tissue that recovers without reperfusion located peripheral to ischemic penumbra



Kidwell CS. Stroke 2003; 34: 2729-2735

Infarct core is not a viable tissue



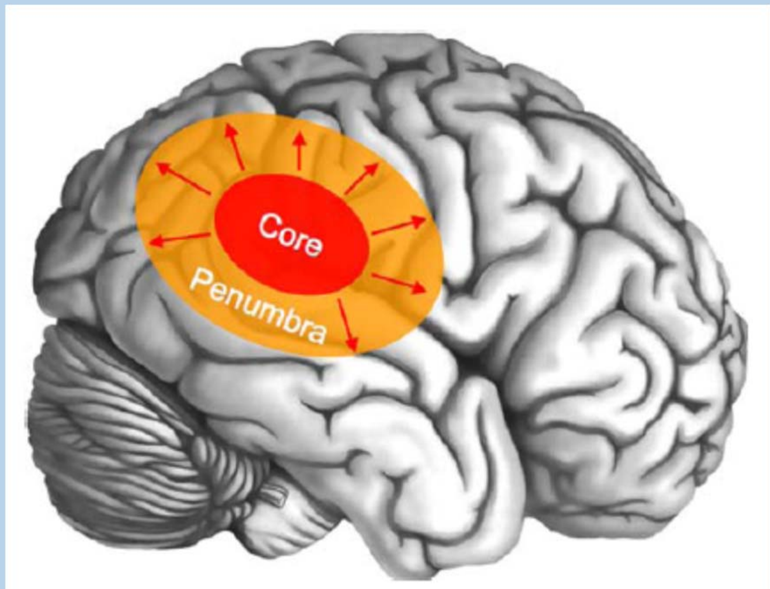
Simard JM et al. Lancet Neurol 2007; 6: 258-268

infarct core is characterized by *cytotoxic edema* = intracellular edema due to the influx of water from extracellular space into neurons promoted by ATP-dependent sodium/potassium pump failure

↓

cellular swelling and death

Ischemic penumbra is a viable tissue



Gonzalez RG. Am J Neuroradiol 2010; 27: 728-735; Heiss W-D. Cerebrovasc Dis 2011; 32: 307-320

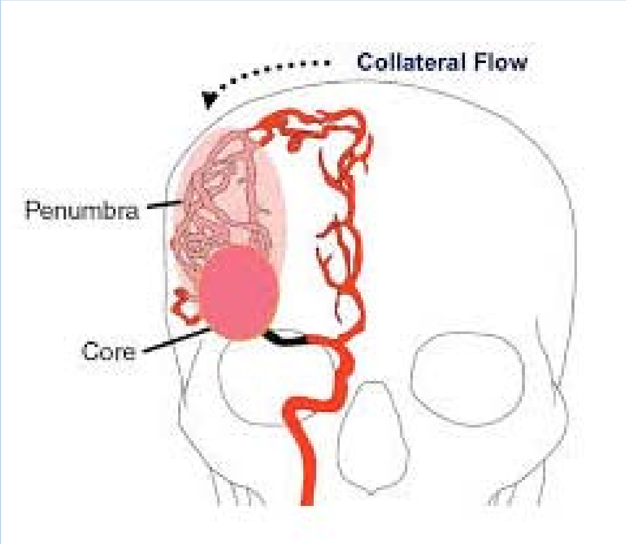
activation of hemodynamic and metabolic compensatory mechanisms:

- ***collateral circulation***
- ***cerebral autoregulation***

→ **hemodynamic**

- ***increasing metabolism*** → **metabolic**

Collaterals



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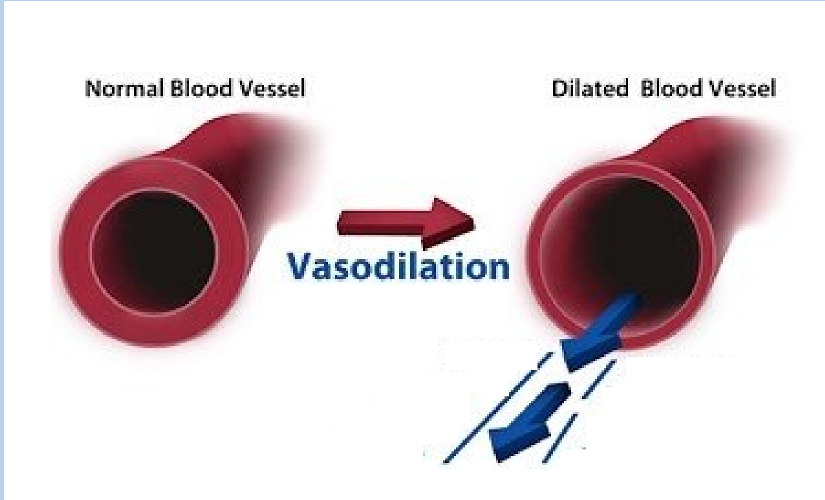


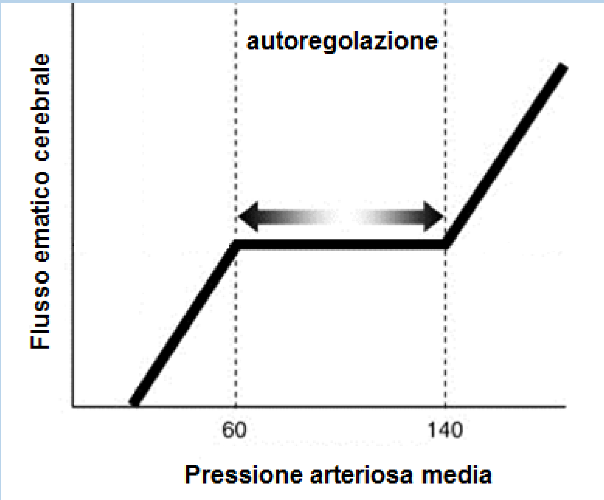
Pranevicius O et al. Stroke 2012; 43: 575-579; Goyal M et al. Radiology 2012; 266: 16-21; Bang O et al. Stroke 2015; 46: 3302-3309

opening of leptomeningeal collaterals = vasodilatation

↓

increase in blood supply at the level of penumbral tissue

Autoregulation



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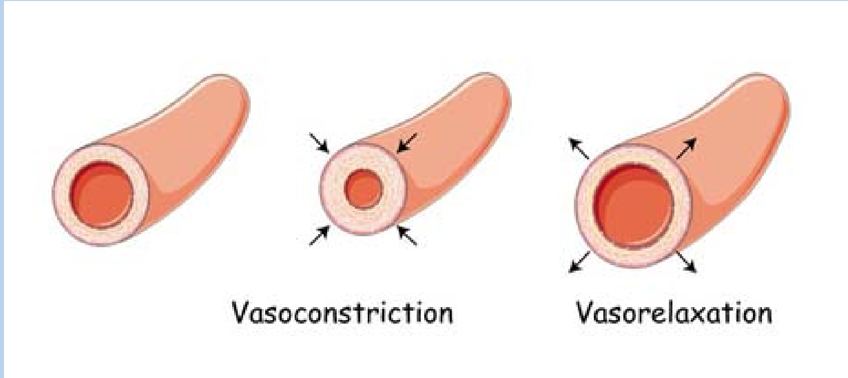


Markus HS. J Neurol Neurosurg Psychiatry 2004; 75: 353-361

autoregolatory response to a drop of cerebral blood flow is a reduction in cerebrovascular resistance

↓

vasodilatation = increase in penumbral blood supply

Metabolism

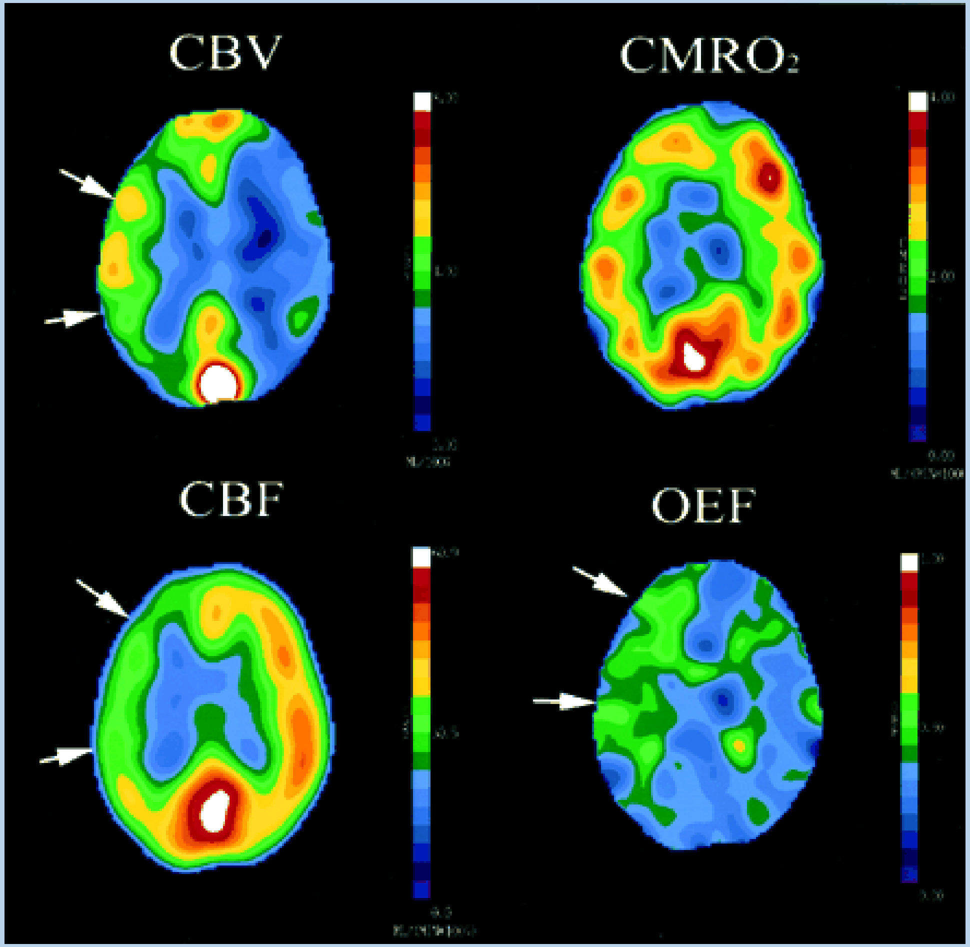
decrease in cerebral blood flow

↓

increase in cellular oxygen extraction fraction (OEF) in the penumbra

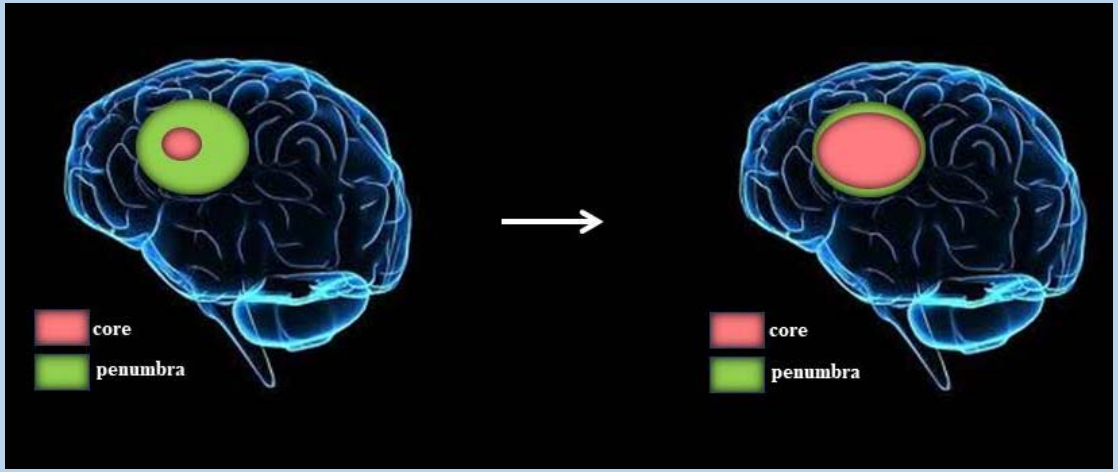
↓

cerebral metabolic rate of oxygen ($CMRO_2$) remains stable

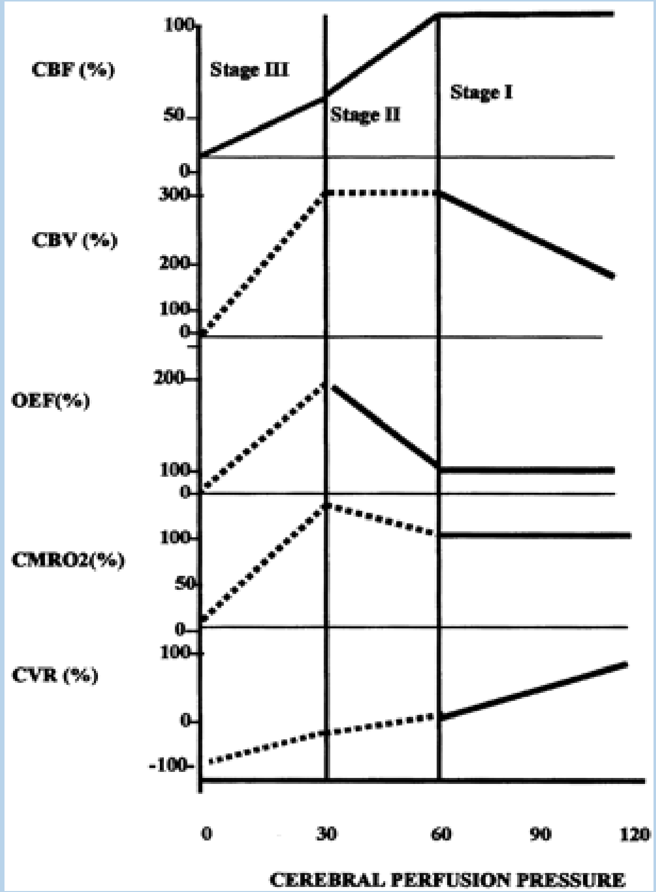


Heiss W-D. Cerebrovasc Dis 2011; 32: 307-320

Compensatory failure

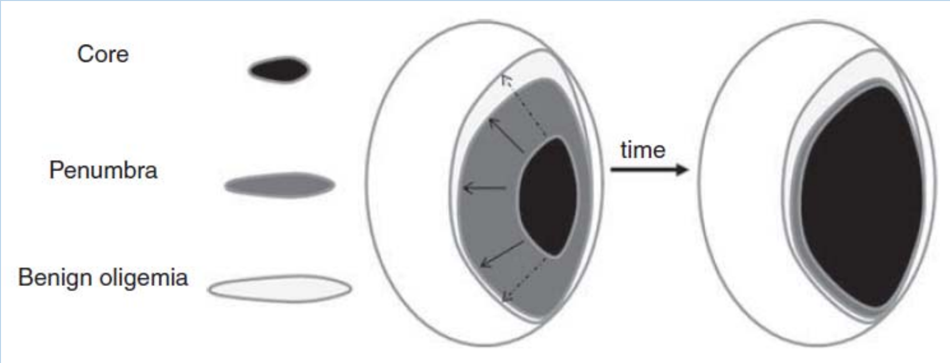


Markus HS. J Neurol Neurosurg Psychiatry 2004; 75: 353-361



compensatory mechanisms gradually exhaust and penumbra transforms into infarction

The fate of penumbra- time is brain



Farr TD, Wegener S. J Cereb Flow Metab 2010; 30: 703-717

Existence of the Diffusion-Perfusion Mismatch within 24 Hours after Onset of Acute Stroke: Dependence on Proximal Arterial Occlusion[1]

Radiology

Copen WA et al. Radiology 2009; 250: 878-886

Salvage of the PWI/DWI mismatch up to 48 h from stroke onset leads to favorable clinical outcome

H. Ma[1,3], P. Wright[1], L. Allport[2], T. G. Phan[3], L. Churilov[1], J. Ly[3], J. A. Zavala[1], S. Arakawa[1], B. Campbell[2], S. M Davis[2], and G. A. Donnan[1]*

Int J Stroke 2015; 10: 565-570

- **without reperfusion, infarct core expands into penumbra over time after 8-10 hours after symptom onset**

- **penumbra may exists after 24-48 hours post-ictus**

Therapeutic window

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke
A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Edward C. Jauch, MD, MS, FAHA, Chair; Jeffrey L. Saver, MD, FAHA, Vice Chair; Harold P. Adams, Jr, MD, FAHA; Askiel Bruno, MD, MS; J.J. (Buddy) Connors, MD; Bart M. Demaerschalk, MD, MSc; Pooja Khatri, MD, MSc, FAHA; Paul W. McMullan, Jr, MD, FAHA; Adnan I. Qureshi, MD, FAHA; Kenneth Rosenfield, MD, FAHA; Phillip A. Scott, MD, FAHA; Debbie R. Summers, RN, MSN, FAHA; David Z. Wang, DO, FAHA; Max Wintermark, MD; Howard Yonas, MD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology

Stroke 2013; 44: 870-947

AHA/ASA Guideline

2015 American Heart Association/American Stroke Association 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

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Endorsed by the American Association of Neurological Surgeons (AANS); Congress of Neurological Surgeons (CNS); AANS/CNS Cerebrovascular Section; American Society of Neuroradiology; and Society of Vascular and Interventional Neurology

William J. Powers, MD, FAHA, Chair; Colin P. Derdeyn, MD, FAHA, Vice Chair; José Biller, MD, FAHA; Christopher S. Coffey, PhD; Brian L. Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Karen C. Johnston, MD, MSc; S. Claiborne Johnston, MD, PhD, FAHA; Alexander A. Khalessi, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; James F. Meschia, MD, FAHA; Bruce Ovbiagele, MD, MSc, MAS, FAHA; Dileep R. Yavagal, MD, MBBS; on behalf of the American Heart Association Stroke Council

Stroke 2015;46: 3024-3039

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke
A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

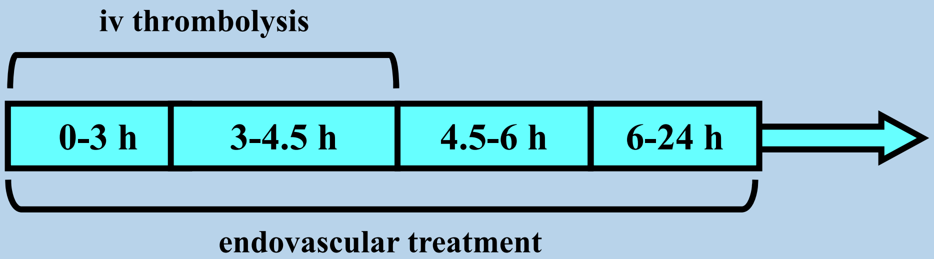
Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine and Neurocritical Care Society

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

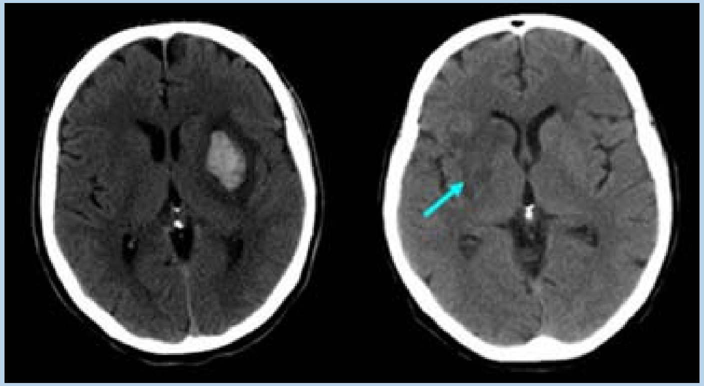
William J. Powers, MD, FAHA, Chair; Alejandro A. Rabinstein, MD, FAHA, Vice Chair; Teri Ackerson, BSN, RN; Opeolu M. Adeoye, MD, MS, FAHA; Nicholas C. Bambakidis, MD, FAHA; Kyra Becker, MD, FAHA; José Biller, MD, FAHA; Michael Brown, MD, MSc; Bart M. Demaerschalk, MD, MSc, FAHA; Brian Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; Thabele M. Leslie-Mazwi, MD; Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA; Phillip A. Scott, MD, MBA, FAHA; Kevin N. Sheth, MD, FAHA; Andrew M. Southerland, MD, MSc; Deborah V. Summers, MSN, RN, FAHA; David L. Tirschwell, MD, MSc, FAHA; on behalf of the American Heart Association Stroke Council

Stroke. 2018; 49: e46-e99

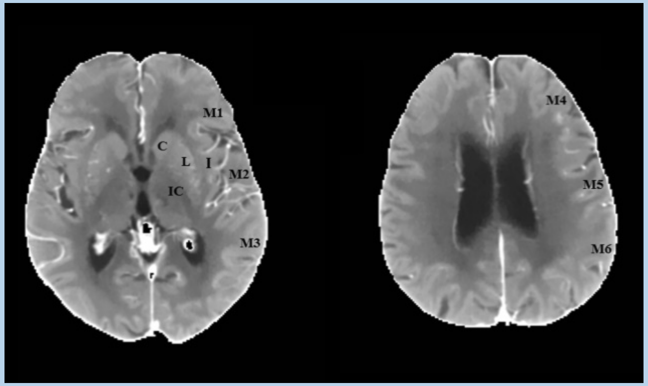


is currently quite restricted

Selection criteria ≤ 4.5 hours with NIHSS < 6



standard CT



ASPECTS

large vessel occlusion (LVO) unlikely

↓

intravenous thrombolysis

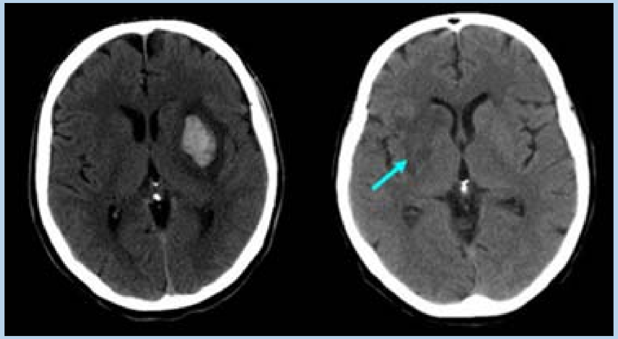
↓

standard CT

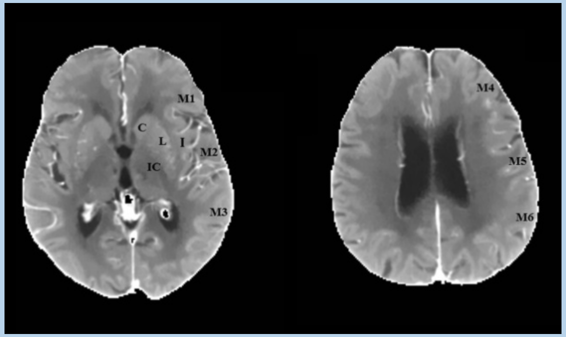
to exclude intracerebral hemorrhage (ICH) + to identify and quantify early ischemic changes (EIC)

iv thrombolysis if ASPECTS > 7

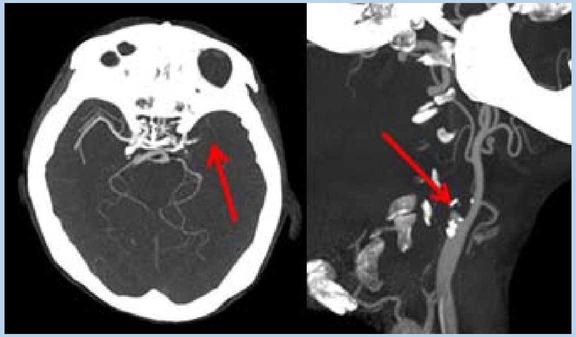
Selection criteria ≤ 6 hours with NIHSS ≥ 6



standard CT



ASPECTS



CTA

LVO very likely

↓

endovascular treatment with (≤ 4.5 hours) or without (4.5-6 hours) iv thrombolysis

↓

standard CT + CT Angiography (CTA)

to exclude ICH + to recognize and quantify EIC + to identify occlusion site

endovascular treatment if ASPECTS ≥ 6

Selection criteria 6-24 hours

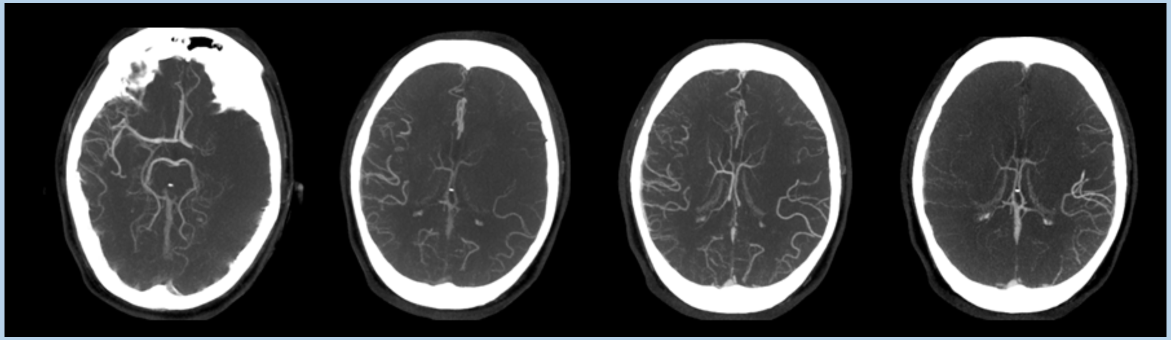
endovascular treatment

↓

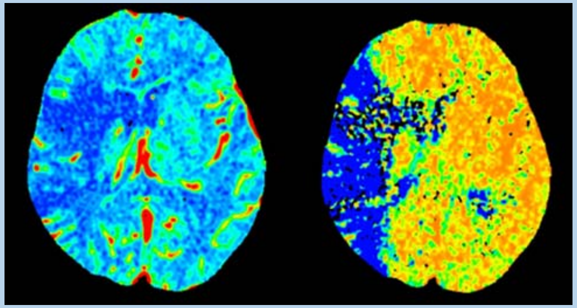
single-phase or multi-phase CTA
(collateral extent evaluation)

↓

CT Perfusion
(core and penumbra identification) → determinants of outcome

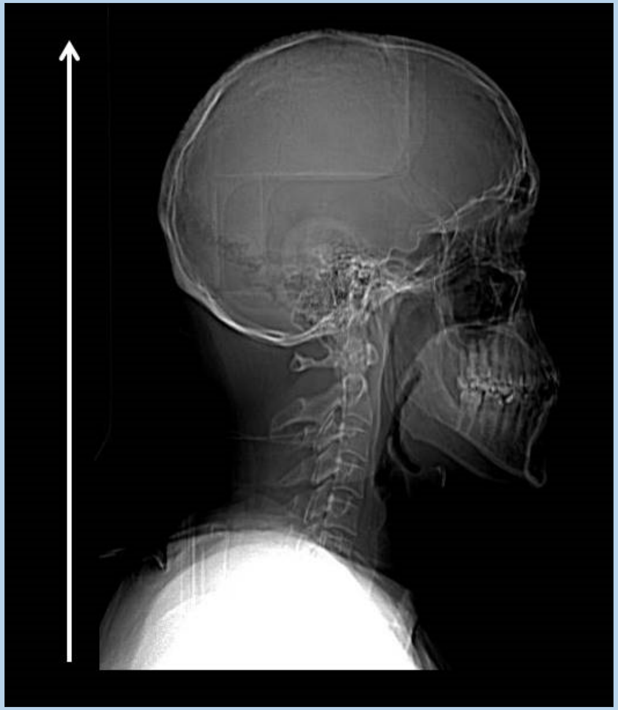


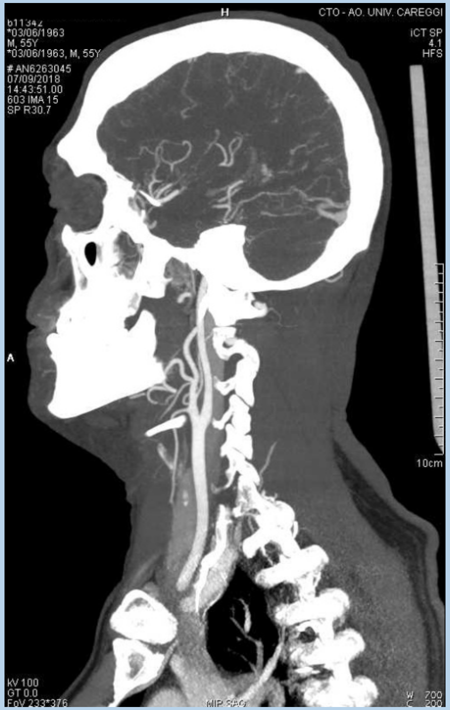
Single-phase CTA (sCTA) e multi-phase (mCTA)



CT Perfusion (CTP)

Single-phase CTA (sCTA)





Srinivasan A et al. Radiographics 2006; 26: S75-S95; Lövblad K-O, Baird AE. Neuroradiology 2010; 52: 175-187

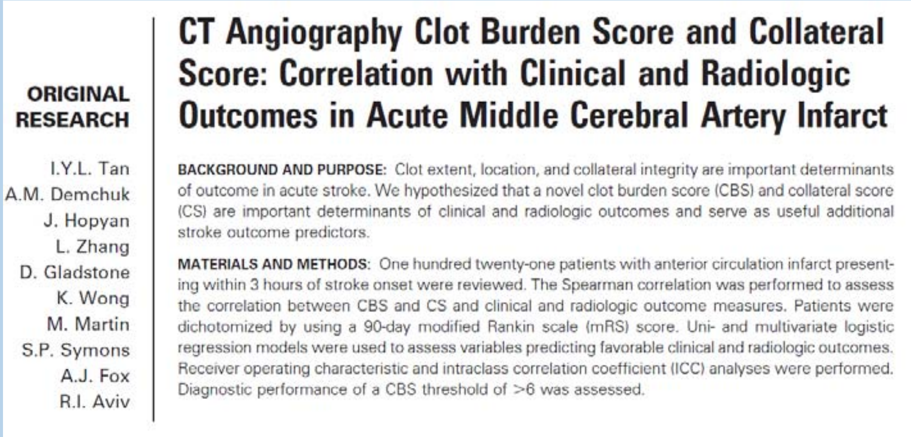
- **covers from the aortic arch or carotid bifurcation to vertex to explore extracranial and intracranial vessels**

- **is able to visualize only the arterial phase of vessel injection**

sCTA collateral score

• there are several classification of collaterals

• one of the most used is the classification proposed by Tan and colleagues:



ORIGINAL RESEARCH

I.Y.L. Tan
A.M. Demchuk
J. Hopyan
L. Zhang
D. Gladstone
K. Wong
M. Martin
S.P. Symons
A.J. Fox
R.I. Aviv

CT Angiography Clot Burden Score and Collateral Score: Correlation with Clinical and Radiologic Outcomes in Acute Middle Cerebral Artery Infarct

BACKGROUND AND PURPOSE: Clot extent, location, and collateral integrity are important determinants of outcome in acute stroke. We hypothesized that a novel clot burden score (CBS) and collateral score (CS) are important determinants of clinical and radiologic outcomes and serve as useful additional stroke outcome predictors.

MATERIALS AND METHODS: One hundred twenty-one patients with anterior circulation infarct presenting within 3 hours of stroke onset were reviewed. The Spearman correlation was performed to assess the correlation between CBS and CS and clinical and radiologic outcome measures. Patients were dichotomized by using a 90-day modified Rankin scale (mRS) score. Uni- and multivariate logistic regression models were used to assess variables predicting favorable clinical and radiologic outcomes. Receiver operating characteristic and intraclass correlation coefficient (ICC) analyses were performed. Diagnostic performance of a CBS threshold of >6 was assessed.

AJNR Am J Neuroradiol; 30: 525-531

- absence of collaterals (score = 0)

- collateral supply filling > 0% but ≤ 50% of the occluded territory (score = 1)

→ poor collaterals < 50%

- collateral supply filling > 50% but < 100% of the occluded territory (score = 2)

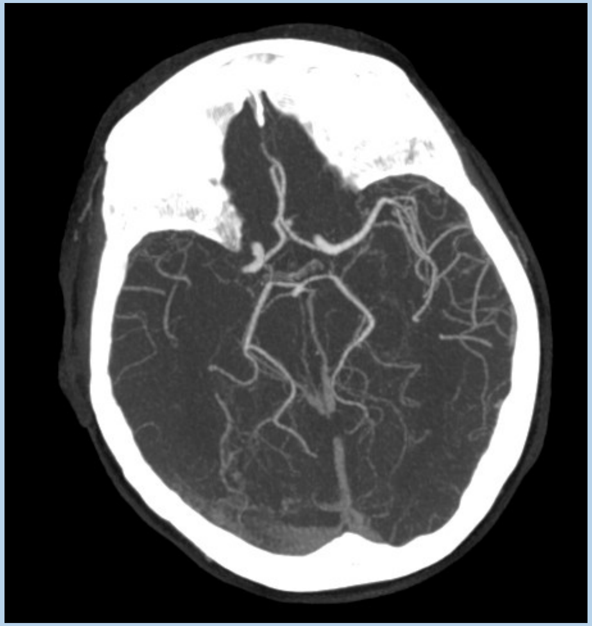
- collateral supply filling 100% of the occluded territory (score = 3)

→ good collaterals > 50%

sCTA collateral score

right MCA

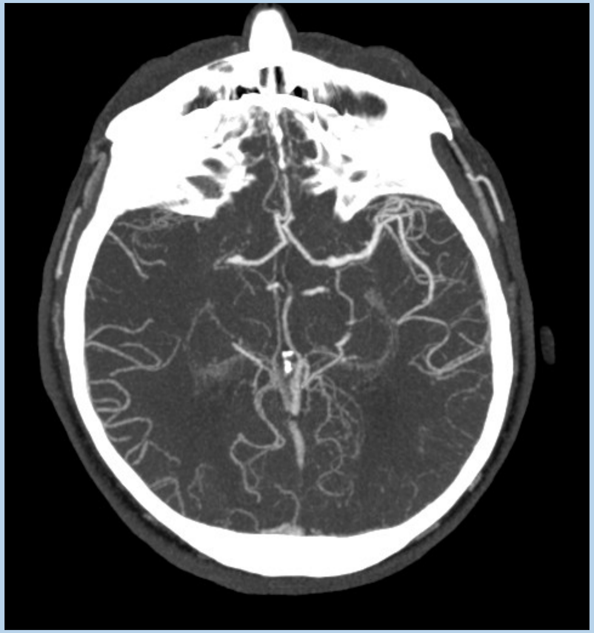
right MCA



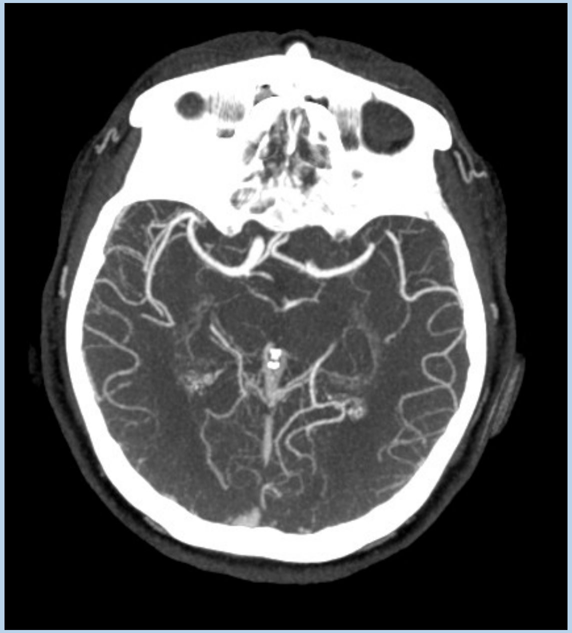
right MCA

collateral filling < 50% of occluded territory = poor collaterals

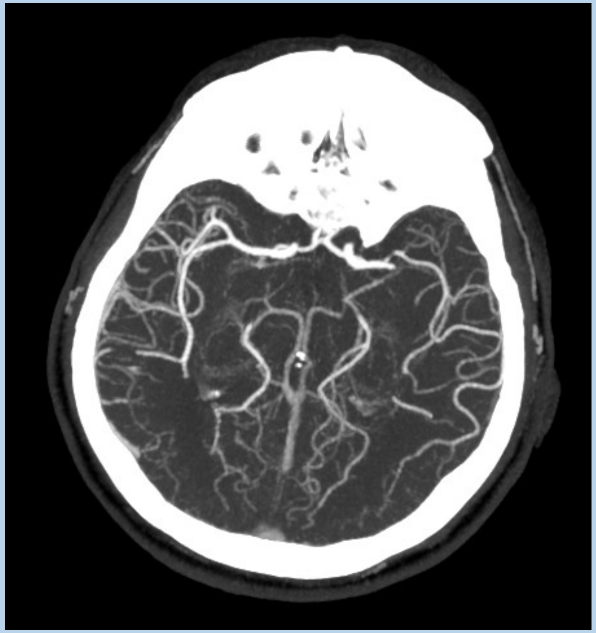
sCTA collateral score



right MCA



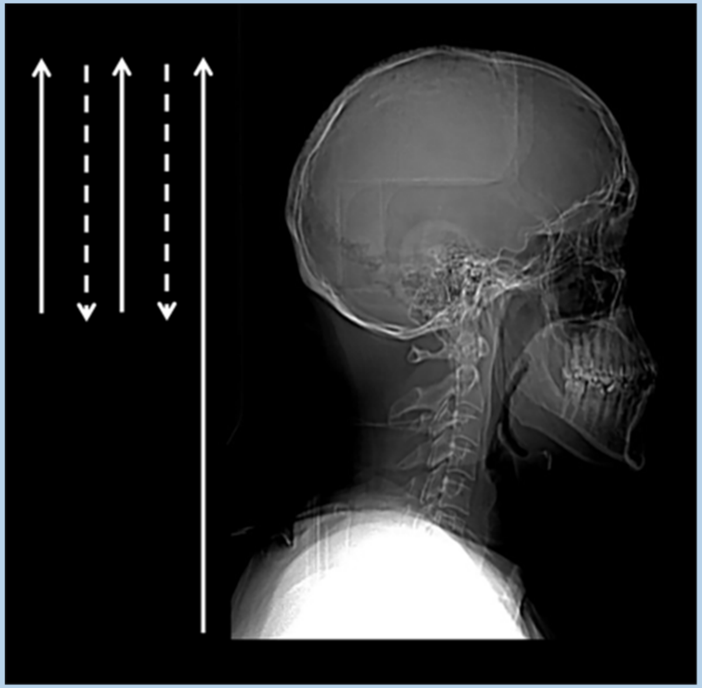
left MCA

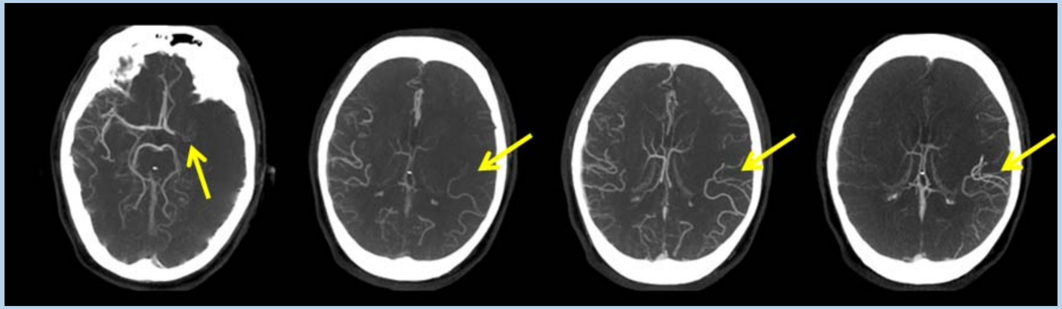


left MCA

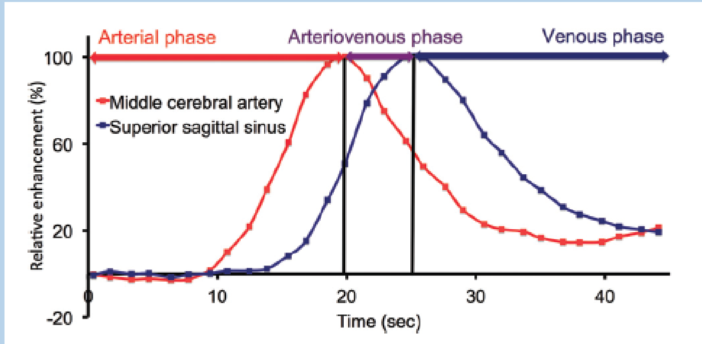
collateral filling > 50% of occluded territory = good collaterals

Multi-phase CTA (mCTA)





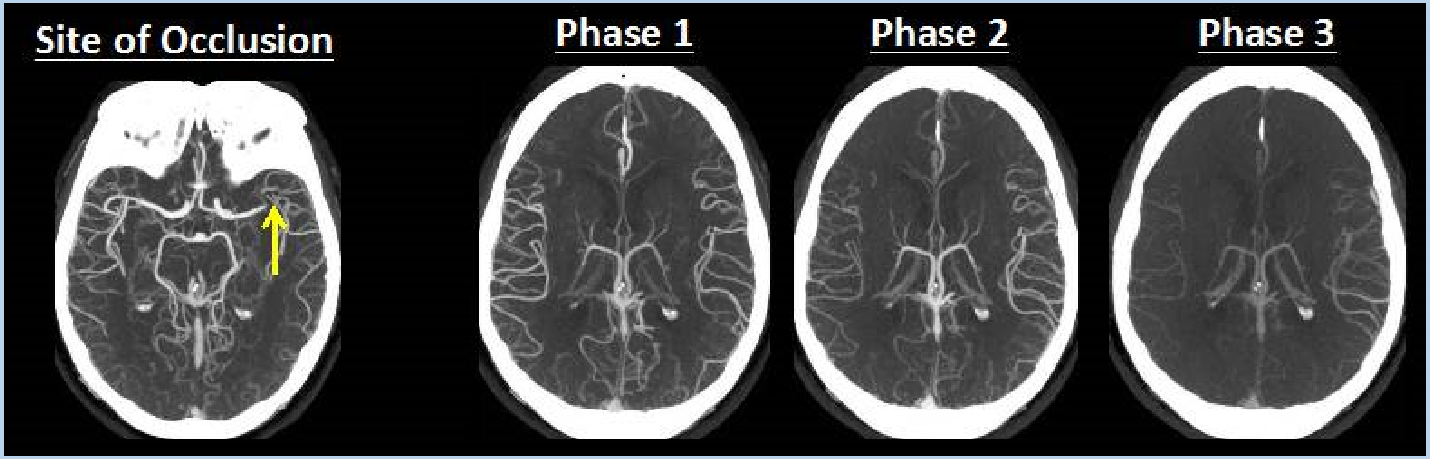
Menon BK et al. Radiology 2015; 275: 510-520



- is a three-phase technique = the first phase covers from aortic arch to vertex and the second and the third ones cover intracranial vessels

- is able to visualize not only early arterial but also delayed arterio-venous and venous phases of collateral filling like DSA

mCTA: collaterals



Impact of Collateral Status Evaluated by Dynamic Computed Tomographic Angiography on Clinical Outcome in Patients With Ischemic Stroke

Ido R. van den Wijngaard, MD; Jelis Boiten, MD, PhD; Ghislaine Holswilder, MSc; Ale Algra, MD, PhD; Diederik W.J. Dippel, MD, PhD; Birgitta K. Velthuis, MD, PhD; Marieke J.H. Wermer, MD, PhD*; Marianne A.A. van Walderveen, MD, PhD*

Stroke 2015; 46: 3398-3404

Assessment of Collateral Status by Dynamic CT Angiography in Acute MCA Stroke: Timing of Acquisition and Relationship with Final Infarct Volume

I.R. van den Wijngaard, G. Holswilder, M.J.H. Wermer, J. Boiten, A. Algra, D.W.J. Dippel, J.W. Dankbaar, B.K. Velthuis, A.M.M. Boers, C.B.L.M. Majoie, and M.A.A. van Walderveen

Am J Neuroradiol 2016; 37: 1231-1236

- **mCTA is superior to sCTA in collateral assessment**
- **is a strong predictor of clinical and radiological outcomes**

mCTA collateral score

- occluded side is compared to contralateral normal side
- poor collaterals:

  grade = 0
  grade = 1

- intermediate collaterals:

  grade = 2
  grade = 3

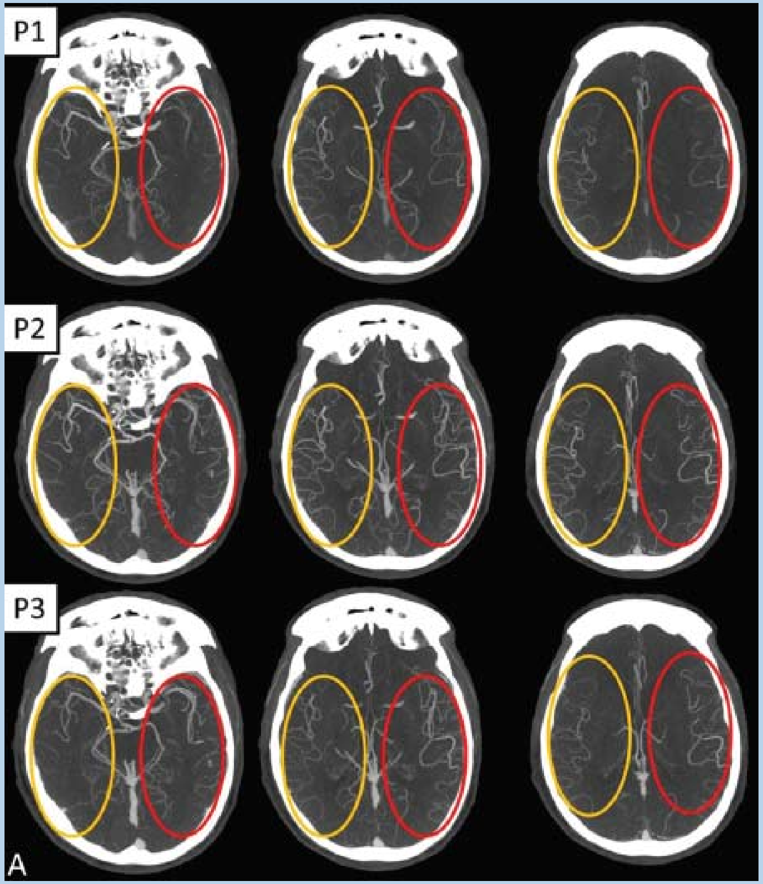
- good collaterals:

  grade = 4
  grade = 5

↓

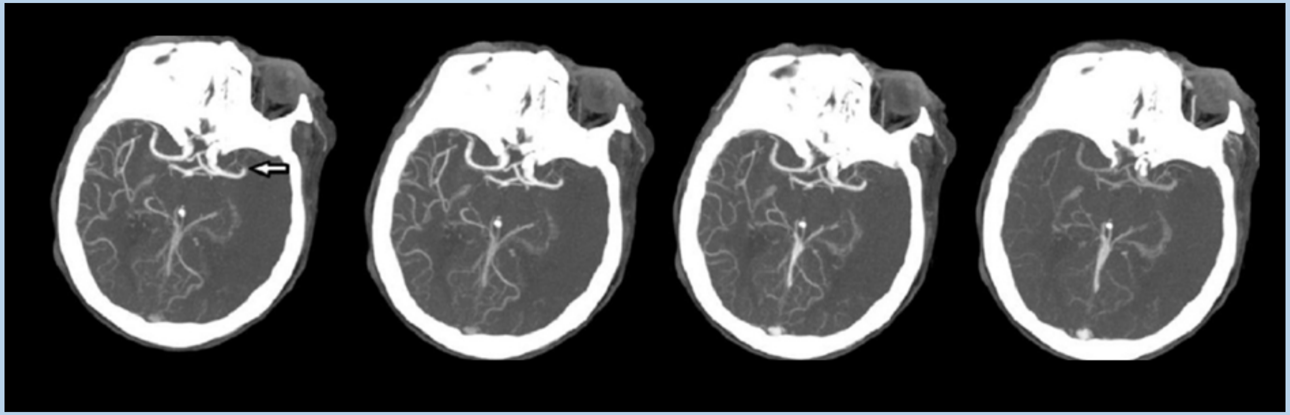
grades 0-3 = *poor collaterals*

grades 4-5 = *good collaterals*

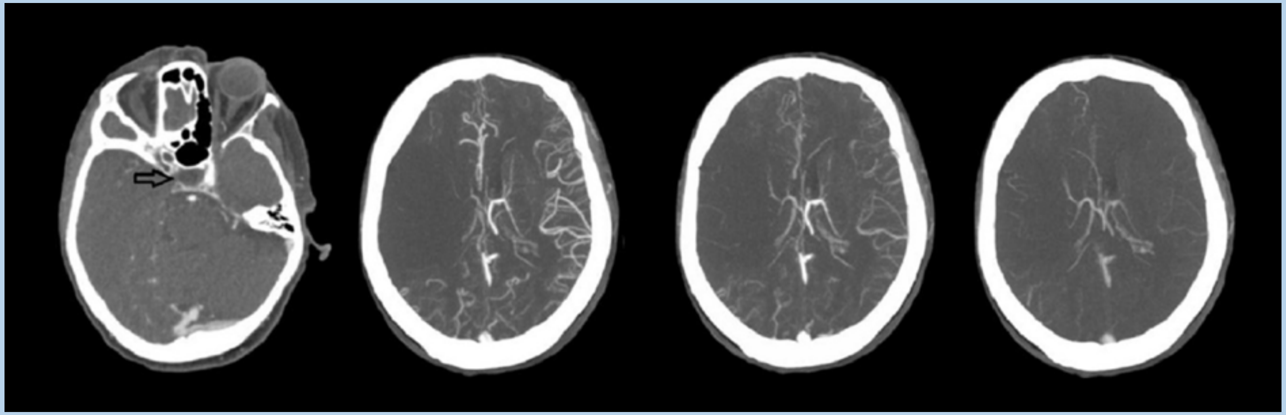


Menon BK et al. Radiology 2015; 275: 510-520
Zerna C et al. Am J Neuroradiol 2016; 37:978-984

mCTA poor collaterals

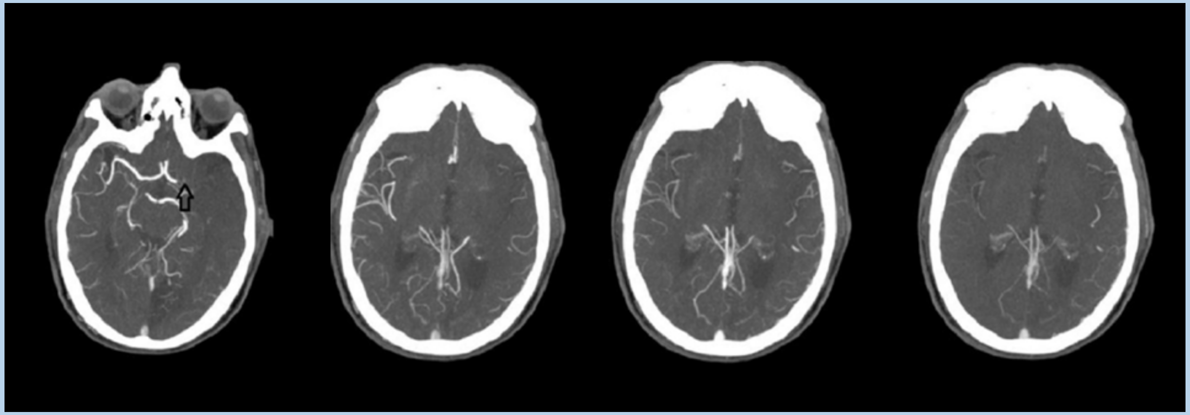


grade = 0
no vessels visible in any phase within the occluded territory (left MCA)

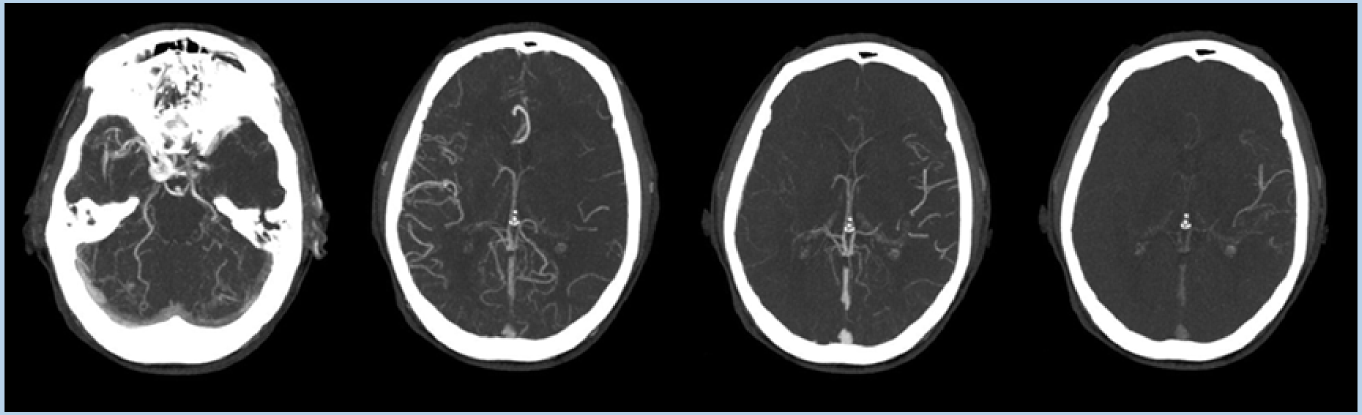


grade = 1
few vessels visible in any phase within the occluded territory (right MCA)

mCTA intermediate collaterals

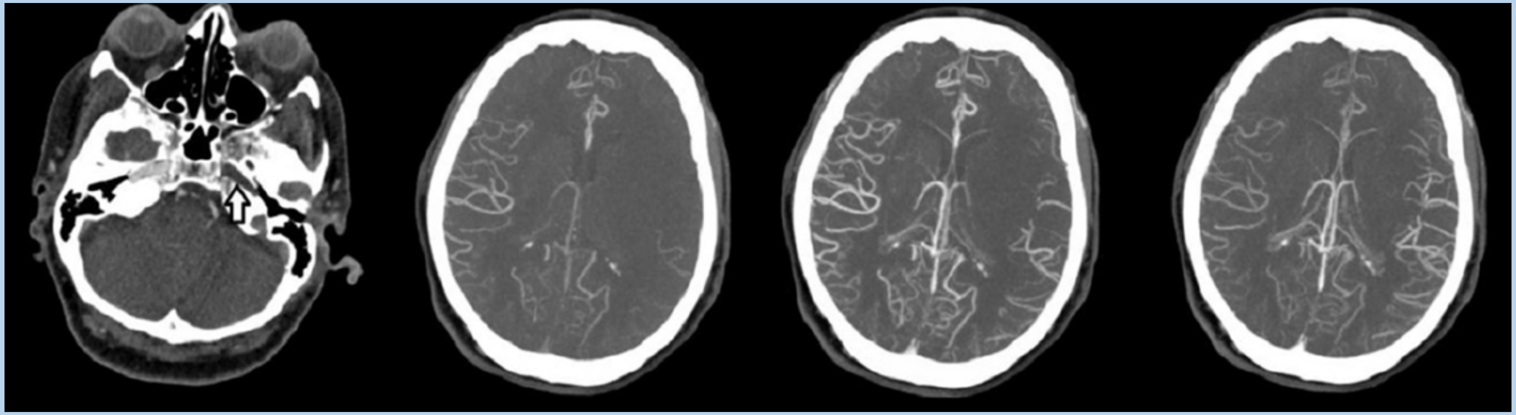


grade = 2
two phase delay with reduced filling extent within the occluded territory (left MCA)

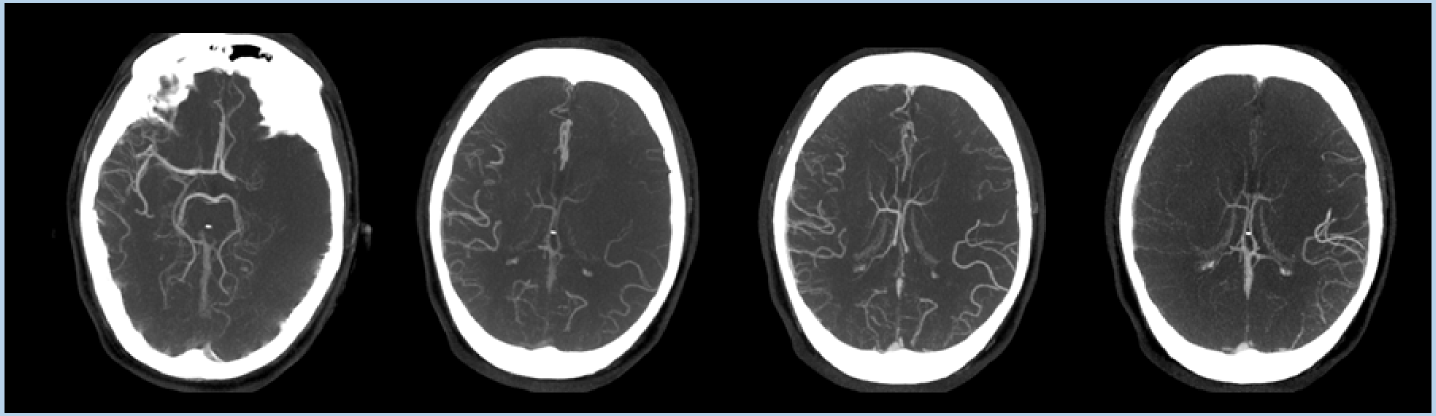


grade = 2
one phase delay with no vessels in some regions within the occluded territory (left MCA)

mCTA intermediate collaterals

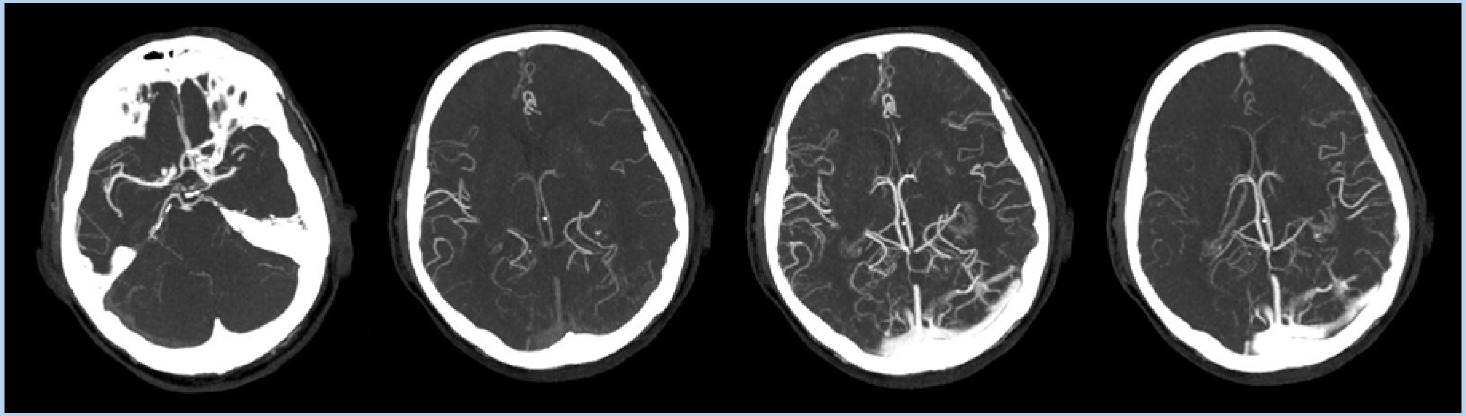


grade = 3
two phase delay with the same filling extent within the occluded territory (left MCA)



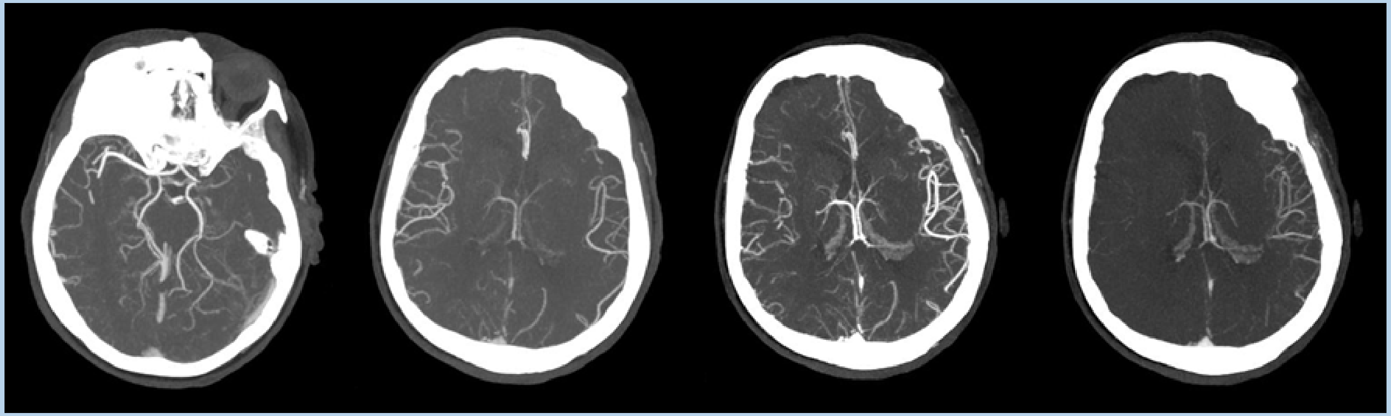
grade = 3
one phase delay with reduced filling extent within the occluded territory (left MCA)

mCTA good collaterals



grade = 4

one phase delay with the same filling extent within the occluded territory (left MCA)



grade = 5

no delay within the occluded territory (left MCA)

ESCAPE

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*

N Engl J Med 2015; 372:1019-1030

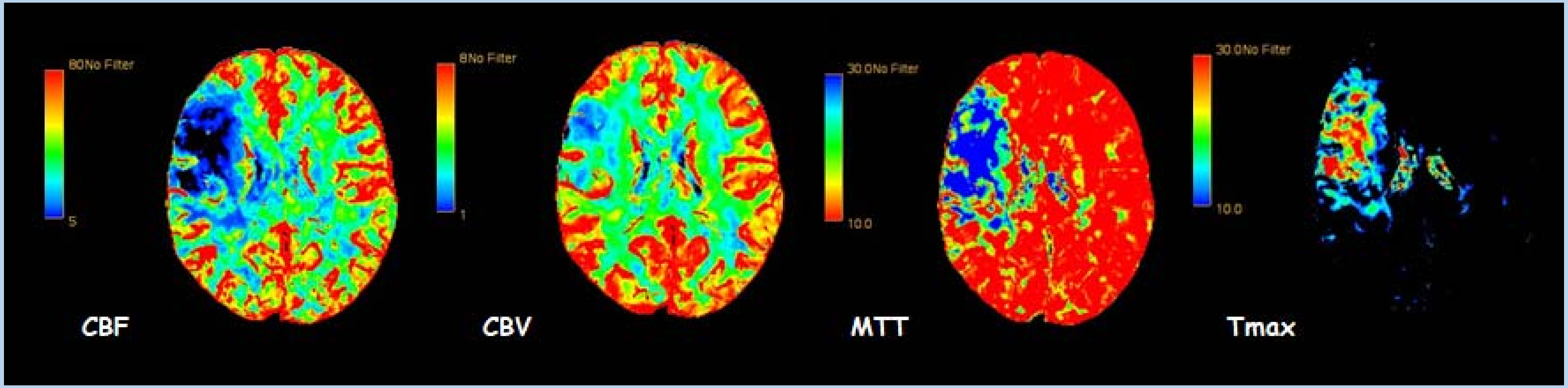
collateral assessment with mCTA was a good selection parameter

overall < 12 hours after onset | **most patients ≤ 6 hours after onset**

↓

good collaterals on mCTA = favorable prognosis

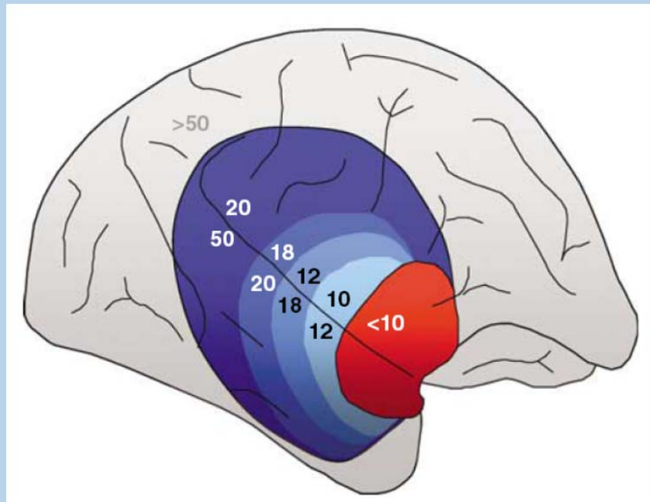
The role of CTP



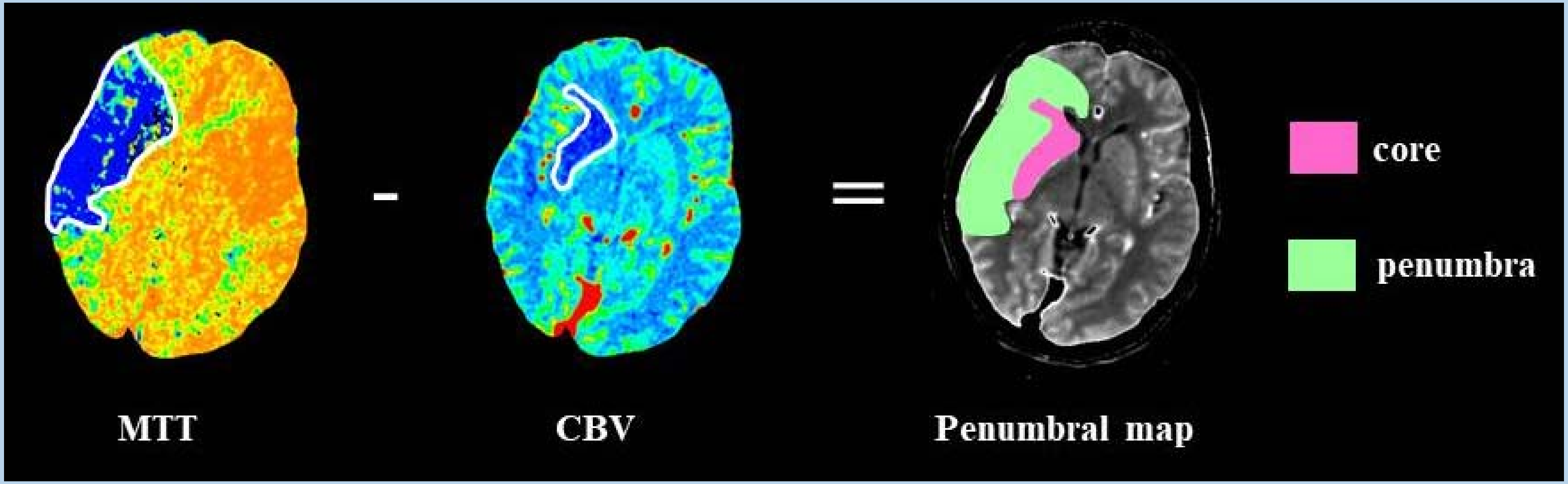
Leiva-Salinas C et al. Neuroimaging Clin N Am 2018; 28: 565-572; Campbell BCV, Parsons MV. Int J Stroke 2018; 13: 554-567

↓

to identify infarct core and ischemic penumbra →



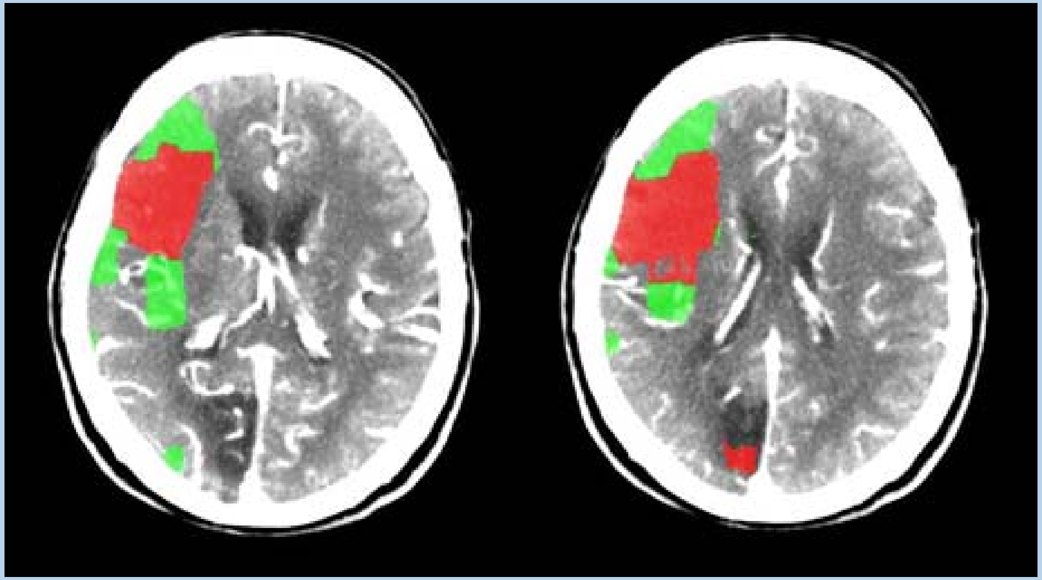
MTT - CBV mismatch



Wintermark M et al. Stroke 2006; 37: 979-985; Konstas AA et al. Am J Neuroradiol 2009; 30: 885-892
Sanelli PC et al. Am J Neuroradiol 2014; 35: 1045-1051

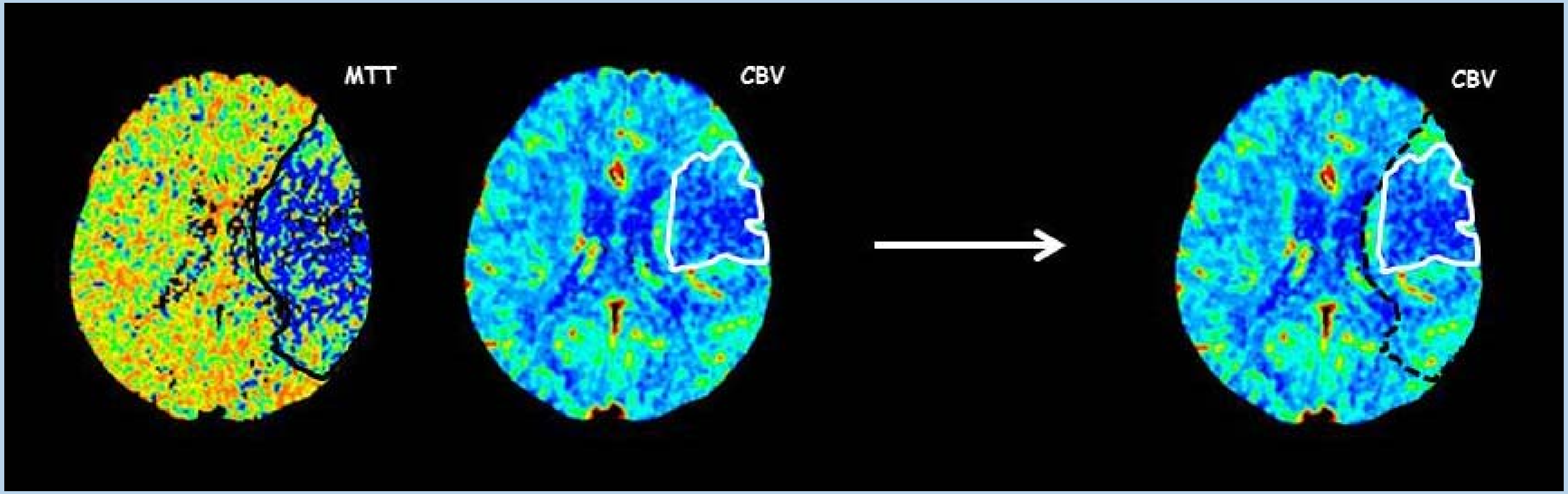
- **total hypoperfusion (core + penumbra) = MTT lesion extent**
- **infarct core = CBV lesion size**
- **ischemic penumbra = MTT lesion volume - CBV lesion volume**

MTT - CBV mismatch: threshold values



- total hypoperfusion = relative MTT (rMTT) > 145% compared to contralateral normal side
- infarct core = CBV < 2 ml/100gr

CBV as core



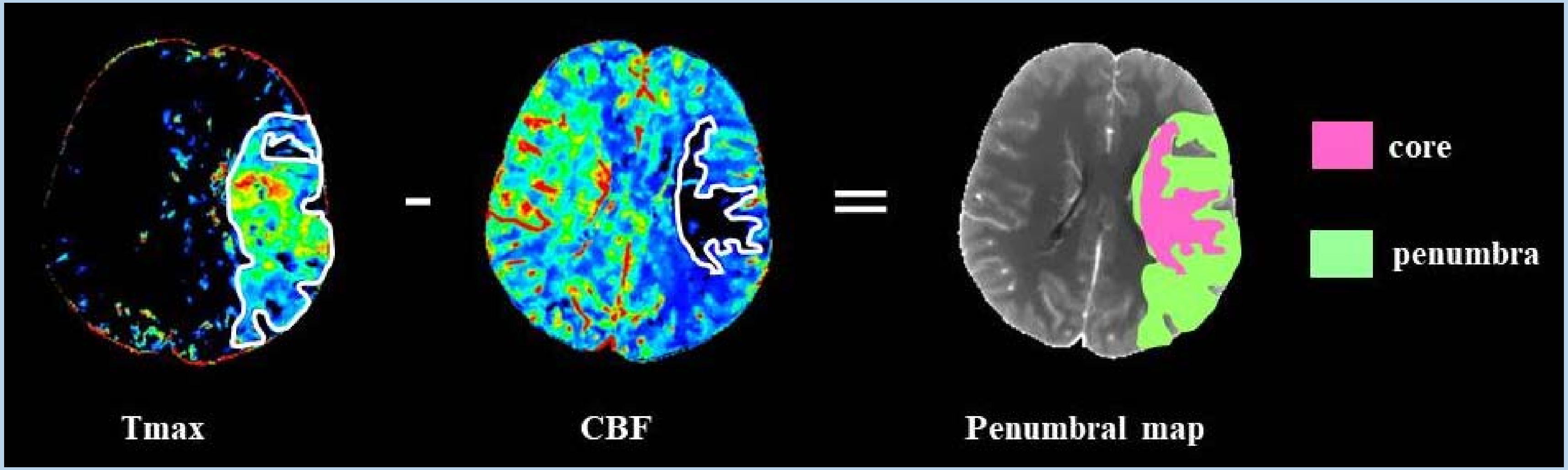
Heit JJ et al. Neuroimaging Clin N Am 2018; 28: 585-597

MTT - CBV mismatch is based on the assumption that CBV lesion size corresponds to infarct core

↓

on CBV map penumbra is not visible because the opening of collaterals in the penumbra region leads to vasodilatation = CBV normal or increased

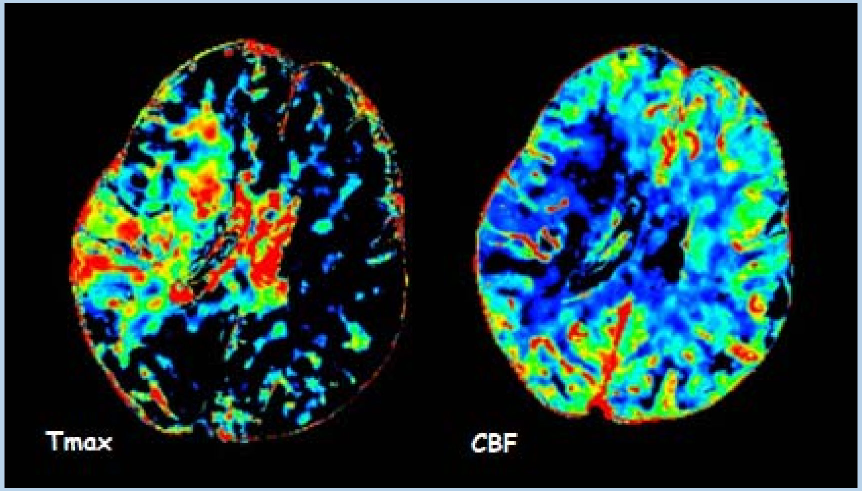
Tmax - CBF mismatch

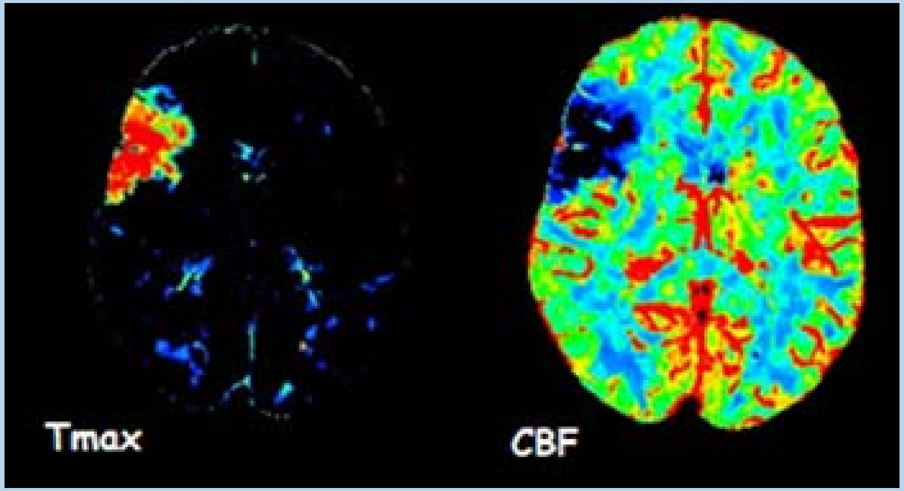


Campbell BCV et al. Stroke 2011; 42: 3435-3430; Bivard A et al. Brain 2011; 134: 3408-3416;
Campbell BCV et al. Stroke 2012; 43: 2648-2653; Bivard A et al. Radiology 2013; 267:543-550; Lin L et al. Radiology 2016; 279: 876-887

- **total hypoperfusion (core + penumbra) = Tmax lesion extent**
- **infarct core = CBF lesion size**
- **ischemic penumbra = Tmax lesion volume - CBF lesion volume**

Tmax - CBF mismatch: threshold values

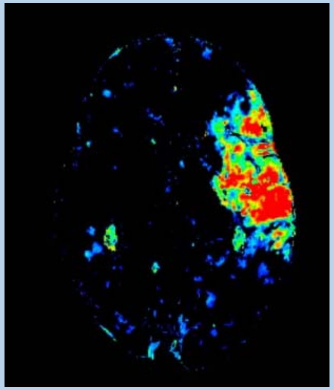




- **total hypoperfusion = Tmax > 6 sec**

- **infarct core = relative CBF (rCBF) < 30% compared to contralateral normal side**

Tmax and CBF maps



Tmax

Optimal Tmax Threshold for Predicting Penumbral Tissue in Acute Stroke

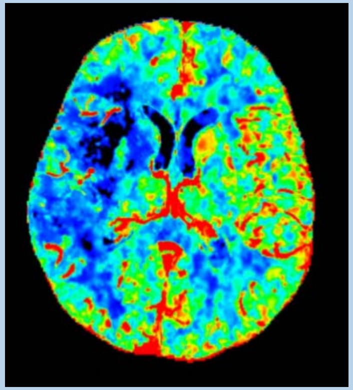
Jean-Marc Olivot, MD, PhD; Michael Mlynash, MD, MS; Vincent N. Thijs, MD, PhD; Stephanie Kemp, BS; Maarten G. Lansberg, MD, PhD; Lawrence Wechsler, MD; Roland Bammer, PhD; Michael P. Marks, MD; Gregory W. Albers, MD

Stroke 2009; 40: 469-475

Cerebral Blood Flow Is the Optimal CT Perfusion Parameter for Assessing Infarct Core

Bruce C.V. Campbell, MBBS, BMedSc, FRACP; Søren Christensen, PhD; Christopher R. Levi, MBBS, FRACP; Patricia M. Desmond, MBBS, MSc, MD, FRANZCR; Geoffrey A. Donnan, MD, FRACP; Stephen M. Davis, MD, FRACP; Mark W. Parsons, MBBS, PhD, FRACP

Stroke 2011; 42: 3435-3430

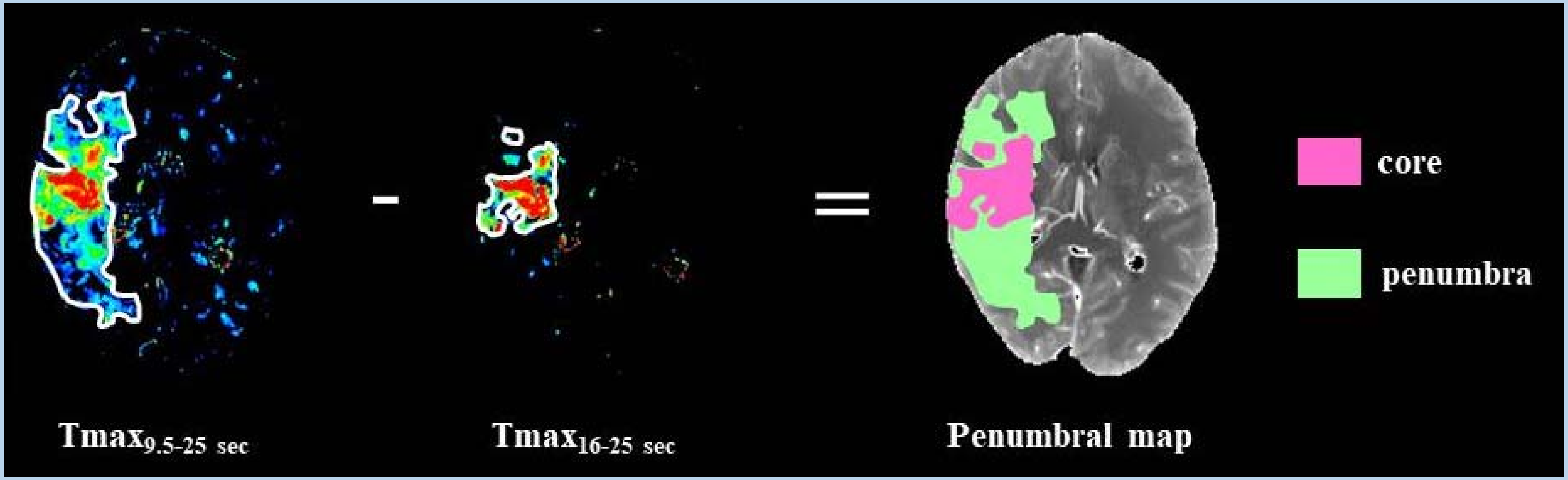


CBF

- **Tmax is better than MTT in delineating total hypoperfusion area (core + penumbra)**

- **CBF is superior to CBV in defining infarct core extent**

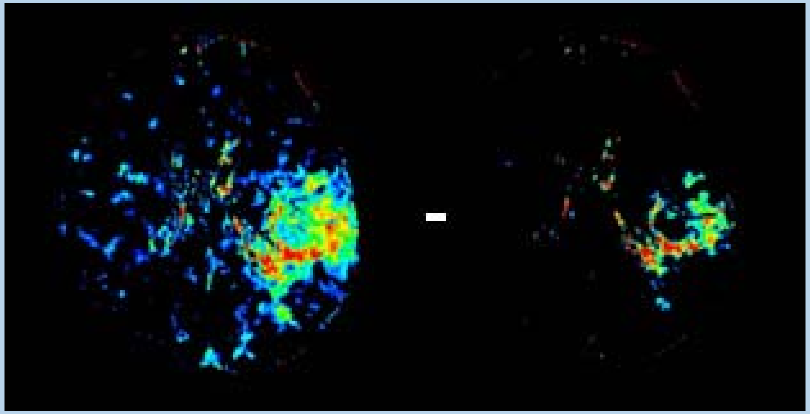
Tmax - Tmax mismatch



d'Esterre CD et al. Stroke 2015; 46: 3390-3397

- **total hypoperfusion (core + penumbra) = Tmax lesion extent with a threshold value > 9.5 sec**
- **infarct core = Tmax lesion size with a threshold value > 16 sec**
- **ischemic penumbra = Tmax lesion volume > 9.5 sec - Tmax lesion volume > 16 sec**

Tmax maps



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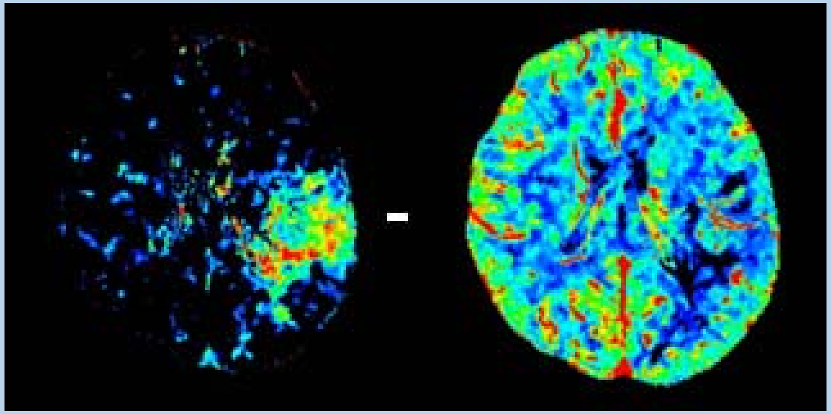


Tmax - Tmax **Tmax - CBF**

d'Esterre CD et al. Stroke 2015; 46: 3390-3397; Qiu W et al. Stroke 2019, Sep 4 [Epub ahead of print]

- **Tmax > 9.5 sec is better than Tmax > 6 sec in delineating total hypoperfusion area (core + penumbra)**

- **Tmax > 16 sec is superior to CBF in defining infarct core extent**

CTP in trials 2015-2018

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

Campbell BCV et al. N Engl J Med 2015; 372: 1009-1018
EXTEND-IA

Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke

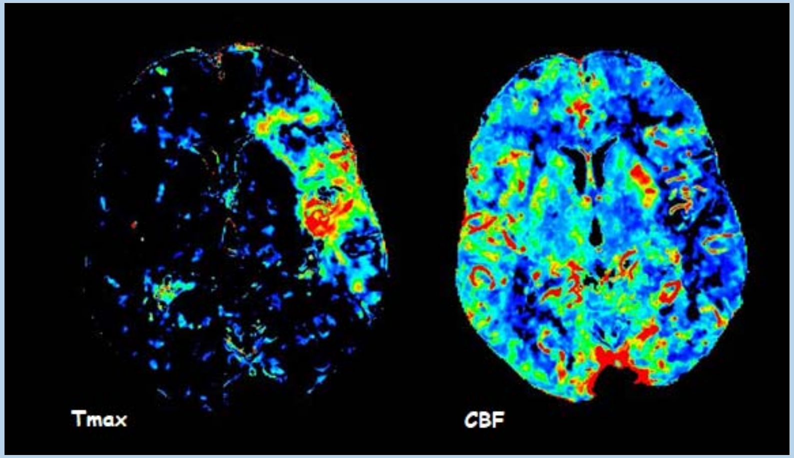
Saver JL et al. N Engl J Med 2015; 372: 2285-2295
SWIFT PRIME

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

Nogueira RG et al. N Engl J Med 2018; 378:11-21
DAWN

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

Albers GW et al. N Engl J Med 2018; 378: 708-718
DEFUSE 3



recent trials demonstrated that *Tmax - CBF mismatch* is the best for the selection of patients candidates for endovascular treatment (thrombectomy)

CTP selection criteria: target mismatch

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

Campbell BCV et al. N Engl J Med 2015; 372: 1009-1018

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↓

optimal selection criteria to achieve good outcome

6-24 hours after onset

DAWN; DEFUSE 3

≤ 4.5-6 hours after onset

SWIFT PRIME; EXTEND-IA

DEFUSE 3 Non-DAWN Patients

A Closer Look at Late Window Thrombectomy Selection

Thabele M. Leslie-Mazwi, MD; Scott Hamilton, PhD; Michael Mlynash, MD, MS; Aman B. Patel, MD; Lee H. Schwamm, MD; Maarten G. Lansberg, MD; Michael Marks, MD; Joshua A. Hirsch, MD; Gregory W. Albers, MD

Stroke 2019; 50: 618-625

↓

DEFUSE 3 criteria are more inclusive

↓

- **core volume < 70 ml**
- **penumbra volume > 15 ml**
- **mismatch ratio > 1.8 (total hypoperfusion/core)**

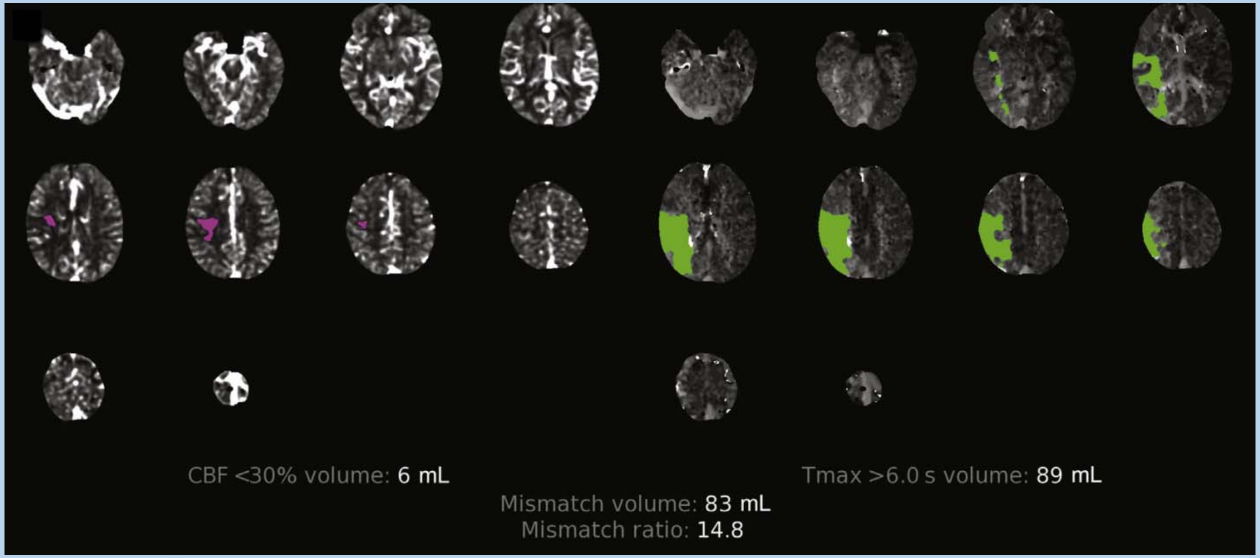
RAPID software

• **penumbral maps pixel per pixel**

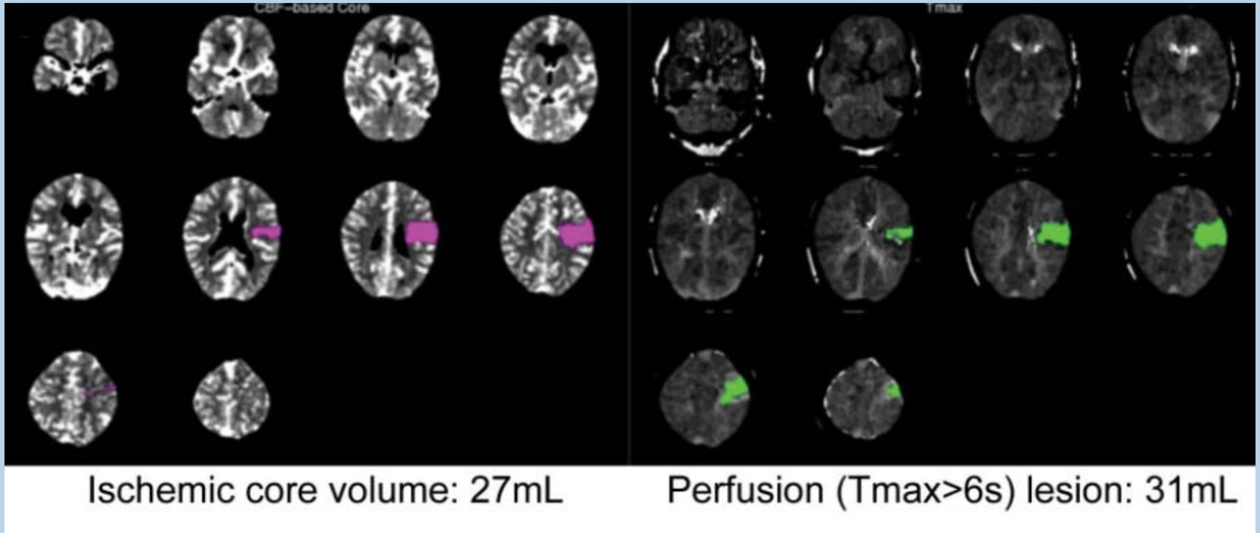
↓

• **target mismatch is automatically calculated according to the established threshold values:**

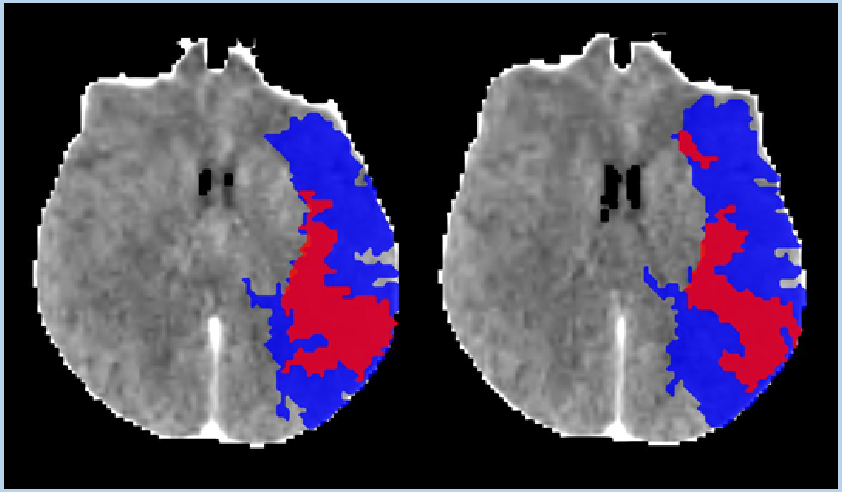
- ➢ **total hypoperfusion = Tmax > 6 sec**
- ➢ **infarct core = rCBF < 30%**



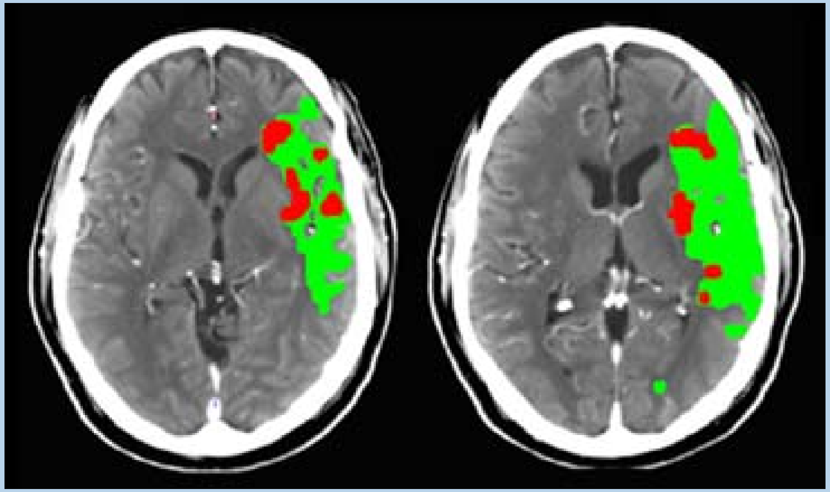
Lansberg MG et al. Lancet Neurol 2012; 11: 860-867
Campbell BCV et al. Int J Stroke 2015; 10: 51-54



OLEA and MIStar



OLEA CTP



MIStar CTP

OLEA CTP ↓

- **total hypoperfusion= Tmax > 6 sec**
- **infarct core = rCBF < 40%**

MIStar CTP ↓

- **total hypoperfusion = Delay Time > 3 sec**
- **infarct core = rCBF < 30%**

other software programs automatically calculating target mismatch exist

Patient selection remains a problem

Neuroradiology (2010) 52:341–343
DOI 10.1007/s00234-009-0636-2

INTERVENTION TO TREAT AND PREVENT STROKE

Poor clinical outcome despite successful arterial recanalization. What went wrong? How can we do better?

Mayank Goyal

ORIGINAL RESEARCH

Infarct growth despite full reperfusion in endovascular therapy for acute ischemic stroke

Diogo C Haussen,[1] Raul G Nogueira,[1] Mohamed Samy Elhammady,[2] Dileep R Yavagal,[2] Mohammad Ali Aziz-Sultan,[3] Jeremiah N Johnson,[2] Brandon G Gaynor,[2] Shyian Jen,[1] Seena Dehkharghani,[1] Eric C Peterson[2]

J Neurointerv Surg 2016; 8: 117-121

- **only 15-20% of AIS patients are eligible for reperfusion therapies**

- **many AIS patients (15-35%) do not achieve a good clinical outcome after recanalization (futile recanalization)**

- **an infarct growth has been found in 35% of AIS patients after full recanalization**

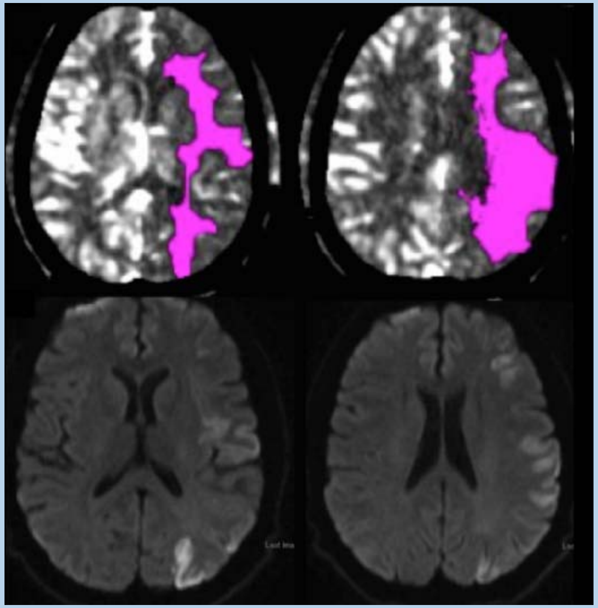
Inaccuracy of rCBF in core detection

Automated CT Perfusion Ischemic Core Volume and Noncontrast CT ASPECTS (Alberta Stroke Program Early CT Score)

Correlation and Clinical Outcome Prediction in Large Vessel Stroke

Diogo C. Haussen, MD; Seena Dehkharghani, MD; Srikant Rangaraju, MD; Leticia C. Rebello, MD; Mehdi Bouslama, MD; Jonathan A. Grossberg, MD; Aaron Anderson, MD; Samir Belagaje, MD; Michael Frankel, MD; Raul G. Nogueira, MD

Stroke 2016; 47: 2318-2322



Ghost Infarct Core and Admission Computed Tomography Perfusion: Redefining the Role of Neuroimaging in Acute Ischemic Stroke

Nuno Martins[d] Ana Aires[e, f] Beatriz Mendez[g] Sandra Boned[a, b] Marta Rubiera[a, b] Alejandro Tomasello[c] Pilar Coscojuela[c] David Hernandez[c] Marián Muchada[a, b] David Rodríguez-Luna[a, b] Noelia Rodríguez[a, b] Jesús M. Juega[a, b] Jorge Pagola[a, b] Carlos A. Molina[a, b] Marc Ribó[a, b]

Intervent Neurol 2018; 7: 513-521

- **rCBF < 30% can overestimate infarct core**

- **particularly in AIS patients who are imaged early (≤ 4.5 hours after onset) and successfully recanalized (TICI 3) in whom infarct core as defined by rCBF < 30% disappeared or was reduced in follow-up imaging (16% of cases)**

Tissue-dependent CTP thresholds

Thresholds for infarction vary between gray matter and white matter in acute ischemic stroke: A CT perfusion study

Chushuang Chen[1,2], Andrew Bivard[1,2], Longting Lin[1,2], Christopher R Levi[1,2], Neil J Spratt[1,2] and Mark W Parsons[1,2]

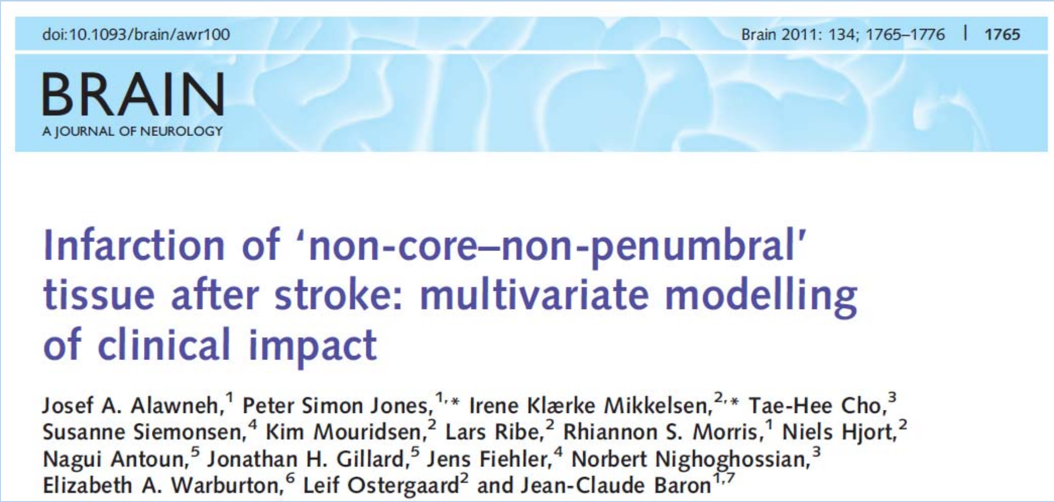
J Cereb Blood Flow Metab 2019; 39 :536-546

CTP thresholds are different in grey and white matter

↓

this variability is not considered by dedicated automated software

Oligoemia and infarct

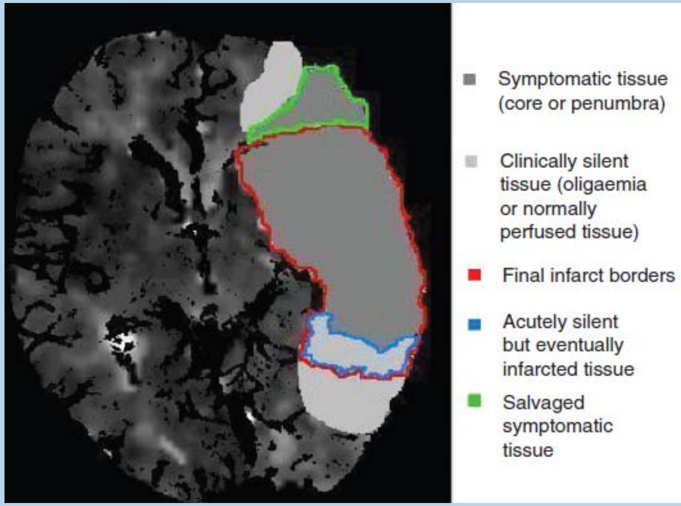


doi:10.1093/brain/awr100 Brain 2011: 134; 1765–1776 | 1765

BRAIN
A JOURNAL OF NEUROLOGY

Infarction of 'non-core–non-penumbral' tissue after stroke: multivariate modelling of clinical impact

Josef A. Alawneh,[1] Peter Simon Jones,[1,*] Irene Klærke Mikkelsen,[2,*] Tae-Hee Cho,[3] Susanne Siemonsen,[4] Kim Mouridsen,[2] Lars Ribe,[2] Rhiannon S. Morris,[1] Niels Hjort,[2] Nagui Antoun,[5] Jonathan H. Gillard,[5] Jens Fiehler,[4] Norbert Nighoghossian,[3] Elizabeth A. Warburton,[6] Leif Ostergaard[2] and Jean-Claude Baron[1,7]



in 10% of AIS patients oligoemic areas evolve into infarct

↓

vasogenic edema = adjacent tissue compressed and hypoperfused = infarct expansion?

Poor association between core and outcome

Large Volumes of Critically Hypoperfused Penumbral Tissue Do Not Preclude Good Outcomes After Complete Endovascular Reperfusion

Redefining Malignant Profile

Raul G. Nogueira, MD*; Diogo C. Haussen, MD*; Seena Dehkharghani, MD; Leticia C. Rebello, MD; Andrey Lima, MD; Meredith Bowen, BA; Samir Belagaje, MD; Aaron Anderson, MD; Michael Frankel, MD

Stroke 2016; 47: 94-98

Penumbral imaging and functional outcome in patients with anterior circulation ischaemic stroke treated with endovascular thrombectomy versus medical therapy: a meta-analysis of individual patient-level data

Bruce C V Campbell, Charles B L M Majoie, Gregory W Albers, Bijoy K Menon, Nawaf Yassi, Gagan Sharma, Wim H van Zwam, Robert J van Oostenbrugge, Andrew M Demchuk, Francis Guillemin, Philip White, Antoni Dávalos, Aad van der Lugt, Kenneth S Butcher, Aboubaker Cherifi, Henk A Marquering, Geoffrey Cloud, Juan M Macho Fernández, Jeremy Madigan, Catherine Oppenheim, Geoffrey A Donnan, Yvo B W E M Roos, Jai Shankar, Hester Lingsma, Alain Bonafé, Hélène Raoult, María Hernández-Pérez, Aditya Bharatha, Reza Jahan, Olav Jansen, Sébastien Richard, Elad I Levy, Olvert A Berkhemer, Marc Soudant, Lucia Aja, Stephen M Davis, Timo Krings, Marie Tisserand, Luis San Román, Alejandro Tomasello, Debbie Beumer, Scott Brown, David S Liebeskind, Serge Bracard, Keith W Muir*, Diederik W J Dippel*, Mayank Goyal*, Jeffrey L Saver*, Tudor G Jovin*, Michael D Hill*, Peter J Mitchell*, for the HERMES collaborators*

Lancet Neurol 2019; 18: 46-55

Endovascular Treatment for Patients With Acute Stroke Who Have a Large Ischemic Core and Large Mismatch Imaging Profile

Leticia C. Rebello, MD; Mehdi Bouslama, MD; Diogo C. Haussen, MD; Seena Dehkharghani, MD; Jonathan A. Grossberg, MD; Samir Belagaje, MD; Michael R. Frankel, MD; Raul G. Nogueira, MD

JAMA Neurol 2017; 74: 34-40

Mediation of the Relationship Between Endovascular Therapy and Functional Outcome by Follow-up Infarct Volume in Patients With Acute Ischemic Stroke

Anna M. M. Boers, PhD; Ivo G. H. Jansen, MD, PhD; Scott Brown, PhD; Hester F. Lingsma, PhD; Ludo F. M. Beenen, MD; Thomas G. Devlin, MD, PhD; Luis San Román, MD, PhD; Ji-Hoe Heo, MD, PhD; Marc Ribó, MD; Mohammed A. Almekhlafi, MD, FRCPC; David S. Liebeskind, MD; Jeanne Teitelbaum, MD; Patricia Cuadras, MD; Richard du Mesnil de Rochemont, MD, PhD; Marine Beaumont, PhD; Martin M. Brown, MD, FRCP; Albert J. Yoo, MD, PhD; Geoffrey A. Donnan, MD; Jean Louis Mas, MD; Catherine Oppenheim, PhD; Richard J. Dowling, MBBS; Thierry Moulin, MD, PhD; Nelly Agrinier, MD, PhD; Demetrius K. Lopes, MD; Lucía Aja Rodríguez, MD; Kars C. J. Compagne, MSc; Fahad S. Al-Ajlan, MD; Jeremy Madigan, MB ChB; Gregory W. Albers, MD; Sebastien Soize, MD; Jordi Blasco, MD, PhD; Stephen M. Davis, MD; Raul G. Nogueira, MD; Antoni Dávalos, MD, PhD; Bijoy K. Menon, MD; Aad van der Lugt, MD, PhD; Keith W. Muir, MD; Yvo B. W. E. M. Roos, MD, PhD; Phil White, MD, PhD; Peter J. Mitchell, MD; Andrew M. Demchuk, MD, FRCPC; Wim H. van Zwam, MD; Tudor G. Jovin, MD; Robert J. van Oostenbrugge, MD, PhD; Diederik W. J. Dippel, MD, PhD; Bruce C. V. Campbell, PhD, FRACP; Francis Guillemin, MD, PhD; Serge Bracard, PhD; Michael D. Hill, MD; Mayank Goyal, MD, FRCPC; Henk A. Marquering, PhD; Charles B. L. M. Majoie, MD, PhD

JAMA Neurol 2019; 76: 194-202

- **AIS patients with large CTP core can benefit from thrombectomy**

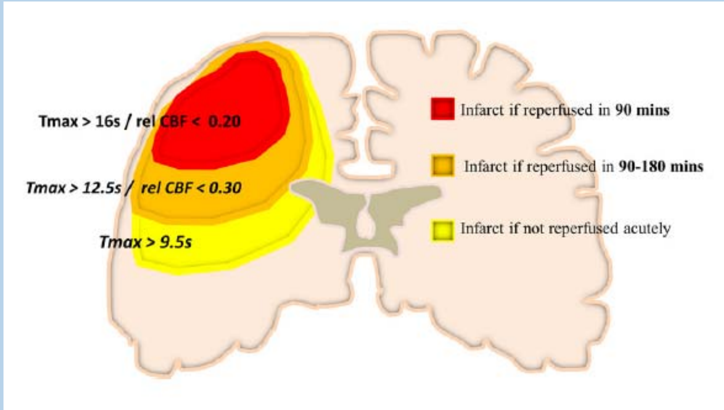
- **treatment benefit is not affected by CTP infarct core volume and is dependent from the final infarct volume only in 12% of cases**

CTP thresholds are time-dependent

Time-Dependent Computed Tomographic Perfusion Thresholds for Patients With Acute Ischemic Stroke

Christopher D. d'Esterre, PhD; Mari E. Boesen, MSc; Seong Hwan Ahn, MD; Pooneh Pordeli, PhD; Mohamed Najm, BSc; Priyanka Minhas, MD; Paniz Davari, MSc; Enrico Fainardi, MD; Marta Rubiera, MD; Alexander V. Khaw, MD; Andrea Zini, MD; Richard Frayne, PhD; Michael D. Hill, MD, MSc; Andrew M. Demchuk, MD; Tolulope T. Sajobi, PhD; Nils D. Forkert, PhD; Mayank Goyal, MD; Ting Y. Lee, PhD; Bijoy K. Menon, MD, MSc

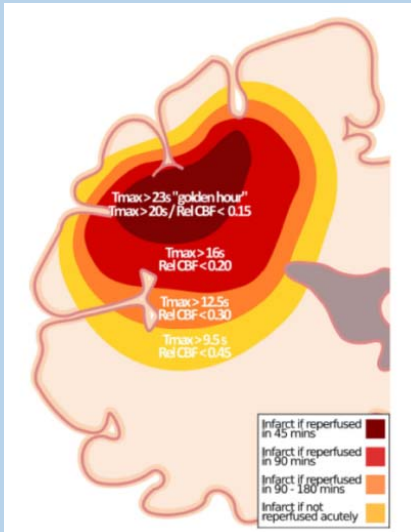
d'Esterre CD et al. Stroke 2015; 46: 3390-3397



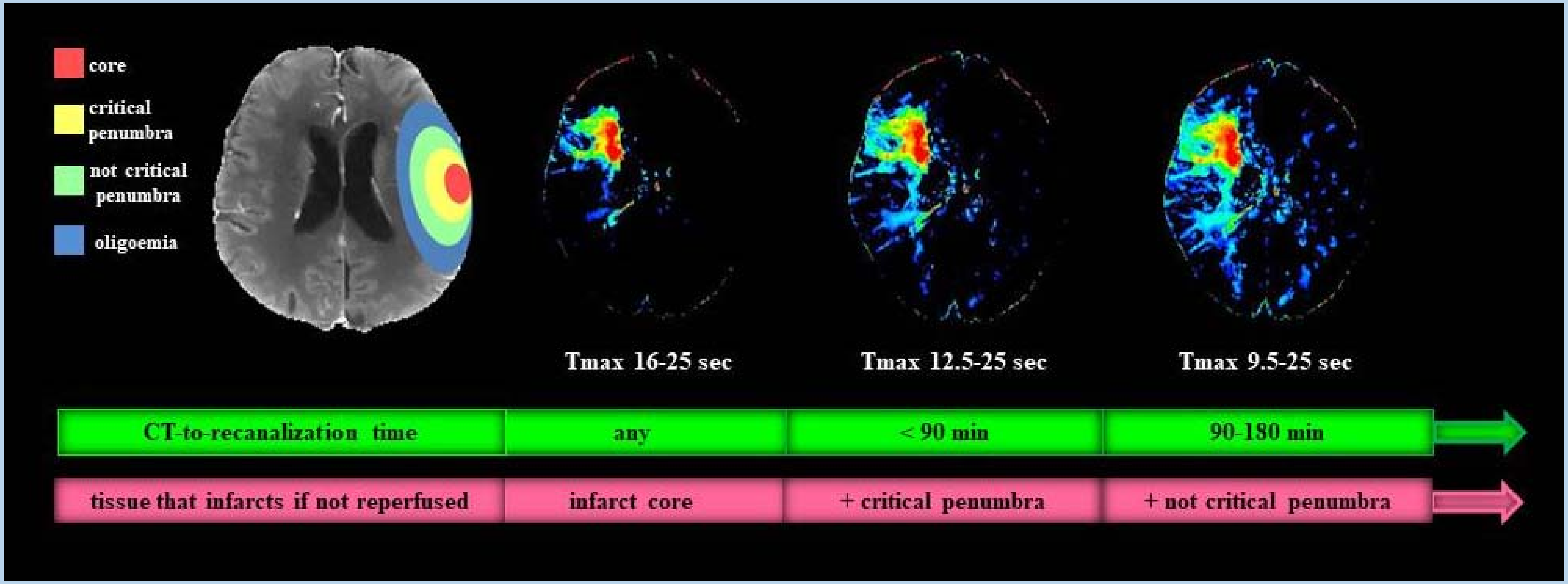
Defining CT Perfusion Thresholds for Infarction in the Golden Hour and With Ultra-Early Reperfusion

Mohamed Najm, Fahad S. Al-Ajlan, Mari E. Boesen, Lisa Hur, Chi Kyung Kim, Enrico Fainardi, Michael D. Hill, Andrew M. Demchuk, Mayank Goyal, Ting Y. Lee, Bijoy K. Menon

Can J Neurol Sci 2018; 45: 339-342



CTP thresholds are time-dependent



d'Esterre CD et al. Stroke 2015; 46: 3390-3397; Najm M et al. Can J Neurol Sci 2018; 45: 339-342

- **the amount of tissue that infarcts increases with the increasing of CT-to-recanalization time**

- **as CT-to-recanalization time is not predictable after baseline CT protocol, CTP thresholds are difficult to be identified at the time of the CT examination**

CTP thresholds change with time

Ischemic Core Thresholds Change with Time to Reperfusion: A Case Control Study

Andrew Bivard, PhD,[1] Tim Kleinig, PhD, FRACP,[2] Ferdinand Miteff, FRACP,[1] Kenneth Butcher, FRACP,[3] Longting Lin, PhD,[1] Christopher Levi, FRACP,[1] and Mark Parsons, PhD, FRACP[1]

Bivard A et al. Ann Neurol 2017; 82: 995-1003

The accuracy of ischemic core perfusion thresholds varies according to time to recanalization in stroke patients treated with mechanical thrombectomy: A comprehensive whole-brain computed tomography perfusion study

Laredo C et al. Cereb Blood Flow Metab. 2019, Jun 17 [Epub ahead of print]

Confirmatory Study of Time-Dependent Computed Tomographic Perfusion Thresholds for Use in Acute Ischemic Stroke

Wu Qiu, PhD; Hulin Kuang, PhD; Ting Y. Lee, PhD; Anna M. Boers, PhD; Scott Brown, PhD; Keith Muir, MD; Charles B.L.M. Majoie, MD; Diederik W.J. Dippel, MD; Phil White, MD; Francis Guillemin, MD; Peter J. Mitchell, MBBS; Antoni Dávalos, MD; Serge Bracard, MD; Bruce Campbell, PhD; Jeffrey L. Saver, MD; Tudor G. Jovin, MD; Michael D. Hill, MD; Andrew M. Demchuk, MD; Mayank Goyal, MD; Bijoy K. Menon, MD; for the HERMES collaborators

Stroke 2019, Sep 4 [Epub ahead of print]

this model has recently been confirmed

Overselection

Endovascular Treatment of Acute Stroke

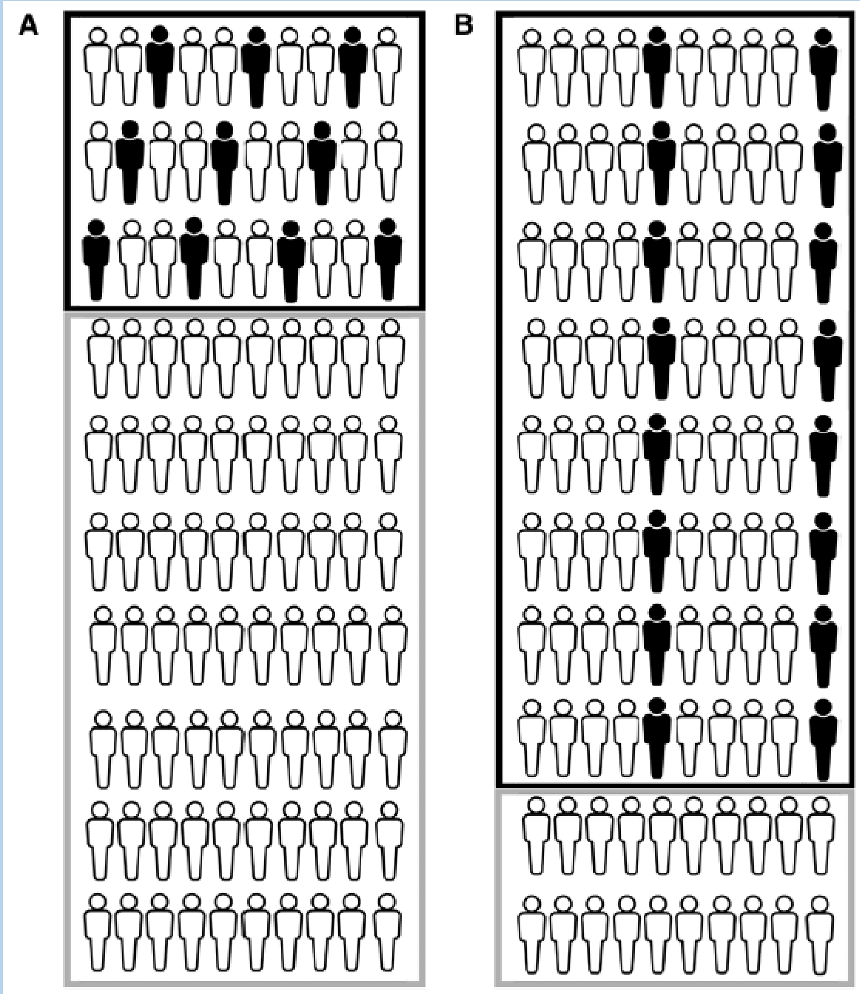
A Call for Individualized Patient Selection

Raul G. Nogueira, MD; Marc Ribó, MD

Stroke 2019; 50: 2612-2618

↓

advanced techniques are useful but can result in an overselection with a potential exclusion of some patients who could benefit from treatment



Independence from time

Response to endovascular reperfusion is not time-dependent in patients with salvageable tissue

Lansberg MG et al. Neurology 2015;85:708-714

Perfusion computed tomography in patients with stroke thrombolysis

Hiroyuki Kawano,[1] Andrew Bivard,[1] Longting Lin,[1] Henry Ma,[2] Xin Cheng,[3] Richard Aviv,[4] Billy O'Brien,[5] Kenneth Butcher,[6] Min Lou,[7] Jingfen Zhang,[8] Jim Jannes,[9] Qiang Dong,[3] Christopher R. Levi[1] and Mark W. Parsons[1]

Brain 2017; 140: 684-69114

Collateral response modulates the time–penumbra relationship in proximal arterial occlusions

Smriti Agarwal, MD, MRCP, Andrew Bivard, PhD, Elizabeth Warburton, DM, MRCP, Mark Parsons, PhD, FRACP, and Christopher Levi, MD, FRACP

Neurology® 2018;90:e316-e322.

penumbral salvage and favorable outcome

↓

are not dependent from time of onset but from the extent of ischemic penumbra and collaterals

Penumbra and collaterals are brain

Tissue is more important than time: insights into acute ischemic stroke from modern brain imaging

Andrew Bivard and Mark Parsons

Curr Opin Neurol 2018, 31:23-27

Collateral Clock Is More Important Than Time Clock for Tissue Fate

A Natural History Study of Acute Ischemic Strokes

Achala Vagal, MD, MS; Richard Aviv, MD; Heidi Sucharew, PhD; Mahati Reddy, MD; Qinghua Hou, MD; Patrik Michel, MD; Tudor Jovin, MD; Thomas Tomsick, MD; Max Wintermark, MD; Pooja Khatri, MD, MSc

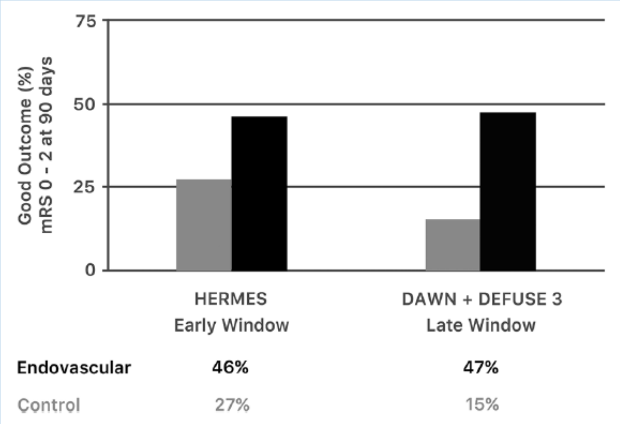
Stroke 2018; 49: 2102-2107

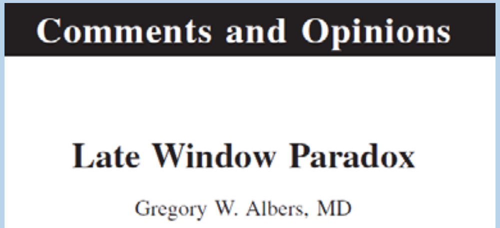
penumbra and collaterals are more important than time

↓

it is not important the time of onset, but the extent of penumbra and collateral circulation

Late time window paradox



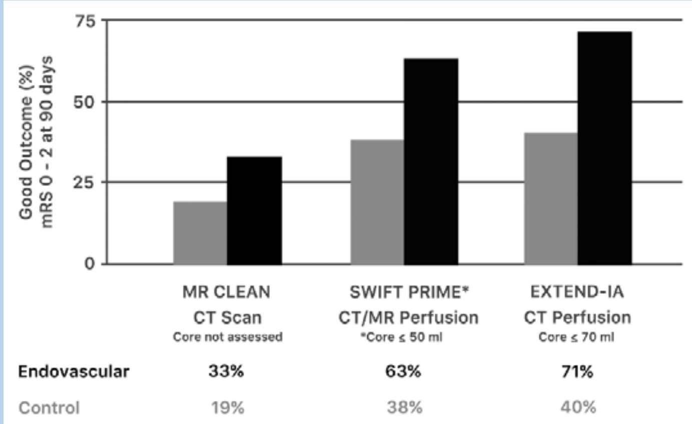


Comments and Opinions

Late Window Paradox

Gregory W. Albers, MD

Stroke 2018;49:768-771



HC1

- **the treatment effect is larger in the late than in early time windows**

- **in the early time window the treatment effect is greater when advanced imaging with CTP target mismatch automatically measured according with Tmax - rCBF mismatch threshold values is used for the selection**

Diapositiva 51

HC1 Hewlett-Packard Company; 14/10/2019

Advanced selection in early and late time window

Computed Tomographic Perfusion to Predict Response to Recanalization in Ischemic Stroke

Maarten G. Lansberg, MD, PhD,[1] Soren Christensen, PhD,[1] Stephanie Kemp,[1] Michael Mlynash, MD, MS,[1] Nishant Mishra, MD, PhD,[1] Christian Federau, MD,[1] Jenny P. Tsai, MD,[1] Sun Kim, MD,[1] Raul G. Nogueria, MD,[2] Tudor Jovin, MD,[3] Thomas G. Devlin, MD,[4] Naveed Akhtar, MD,[5] Dileep R. Yavagal, MD,[6] Diogo Haussen, MD,[2] Seena Dehkharghani, MD,[7] Roland Bammer, PhD,[8] Matus Straka, PhD,[9] Greg Zaharchuk, MD,[8] Michael P. Marks, MD,[8] and Gregory W. Albers, MD[1] for the CT Perfusion to Predict Response to Recanalization in Ischemic Stroke Project (CRISP) Investigators

Ann Neurol 2017; 81 :849-856

Computed Tomographic Perfusion Predicts Poor Outcomes in a Randomized Trial of Endovascular Therapy

Robert Wannamaker, BSc; Taurian Guinand, BSc; Bijoy K. Menon, MD; Andrew Demchuk, MD; Mayank Goyal, MD; Donald Frei, MD; Aditya Bharatha, MD; Tudor G. Jovin, MD; Jai Shankar, MD; Timo Krings, MD, PhD; Blaise Baxter, MD; Christine Holmstedt, DO; Richard Swartz, MD, PhD; Dar Dowlatshahi, MD, PhD; Richard Chan, MBBS; Donatella Tampieri, MD; Hana Choe, MD; Paul Burns, MD; Nina Gentile, MD; Jeremy Rempel, MD; Ashfaq Shuaib, MD; Brian Buck, MD, MSc; Andrew Bivard, PhD; Michael Hill, MD; Kenneth Butcher, MD, PhD

Stroke 2018; 49: 1426-1433

DEFUSE 3 CTP target mismatch
(core volume < 70 ml + penombra volume > 15 ml + mismatch ratio > 1.8)

↓

automatically measured according with Tmax - rCBF mismatch threshold values
(core = rCBF < 30%; total hypoperfusion = Tmax > 6 sec)

↓

elevated prognostic value for endovascular treatment ≤ 6 and > 6 hours after onset

Advanced selection in early and late time window

Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke

H. Ma, B.C.V. Campbell, M.W. Parsons, L. Churilov, C.R. Levi, C. Hsu, T.J. Kleinig, T. Wijeratne, S. Curtze, H.M. Dewey, F. Miteff, C.-H. Tsai, J.-T. Lee, T.G. Phan, N. Mahant, M.-C. Sun, M. Krause, J. Sturm, R. Grimley, C.-H. Chen, C.-J. Hu, A.A. Wong, D. Field, Y. Sun, P.A. Barber, A. Sabet, J. Jannes, J.-S. Jeng, B. Clissold, R. Markus, C.-H. Lin, L.-M. Lien, C.F. Bladin, S. Christensen, N. Yassi, G. Sharma, A. Bivard, P.M. Desmond, B. Yan, P.J. Mitchell, V. Thijs, L. Carey, A. Meretoja, S.M. Davis, and G.A. Donnan, for the EXTEND Investigators*

N Engl J Med 2019; 380: 1795-803

Extending thrombolysis to 4·5–9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data

Bruce C V Campbell*, Henry Ma*, Peter A Ringleb*, Mark W Parsons, Leonid Churilov, Martin Bendszus, Christopher R Levi, Chung Hsu, Timothy J Kleinig, Marc Fatar, Didier Leys, Carlos Molina, Tissa Wijeratne, Sami Curtze, Helen M Dewey, P Alan Barber, Kenneth S Butcher, Deidre A De Silva, Christopher F Bladin, Nawaf Yassi, Johannes A R Pfaff, Gagan Sharma, Andrew Bivard, Patricia M Desmond, Stefan Schwab, Peter D Schellinger, Bernard Yan, Peter J Mitchell, Joaquín Serena, Danilo Toni, Vincent Thijs, Werner Hacke†, Stephen M Davis†, Geoffrey A Donnan†, on behalf of the EXTEND, ECASS-4, and EPITHET Investigators‡

Lancet 2109; 13; 394: 139-147

CTP target mismatch
(core volume < 70 ml + penombra volume > 10 ml + mismatch ratio > 1.2)

↓

automatically measured according with Tmax - rCBF mismatch threshold values
(core = rCBF < 30%; total hypoperfusion = Tmax > 6 sec)

↓

good selection parameter for thrombolysis between 4.5 and 9 hours from onset

Time is brain dogma is still valid?

Neuroradiology (2019) 61:115–117
https://doi.org/10.1007/s00234-018-2122-1

EDITORIAL

Treatment of ischemic stroke beyond 3 hours: is time really brain?

Rüdiger von Kummer[1]

- **advanced techniques are very important in the selection of patients for reperfusion therapies**

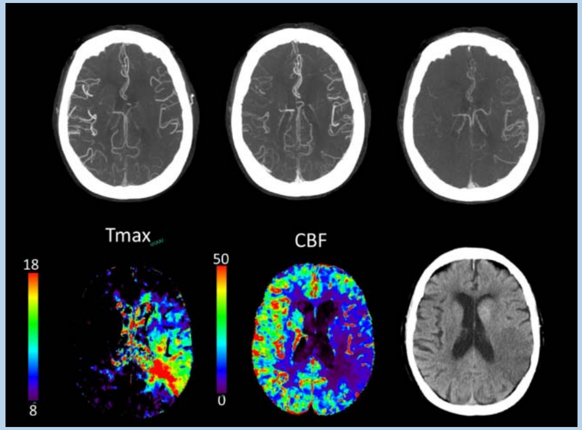
- **time of onset is not a sufficient reason to exclude LVO stroke patients from endovascular treatment**

mCTA and CTP association

Regional Comparison of Multiphase Computed Tomographic Angiography and Computed Tomographic Perfusion for Prediction of Tissue Fate in Ischemic Stroke

Christopher D. d'Esterre, PhD*; Anurag Trivedi*; Pooneh Pordeli, PhD; Mari Boesen, BSc; Shivanand Patil, MD; Seong Hwan Ahn, MD; Mohamed Najm, BSc; Enrico Fainardi, MD; Jai Jai Shiva Shankar, MD; Marta Rubiera, MD; Mohammed A. Almekhlafi, MD, MSc; Jennifer Mandzia, MD; Alexander V. Khaw, MD; Philip Barber, MD; Shelagh Coutts, MD; Michael D. Hill, MD; Andrew M. Demchuk, MD; Tolulope Sajobi, PhD; Nils D. Forkert, PhD; Mayank Goyal, MD; Ting-Yim Lee, PhD; Bijoy K. Menon, MD, MSc

Stroke 2017; 48: 939-945

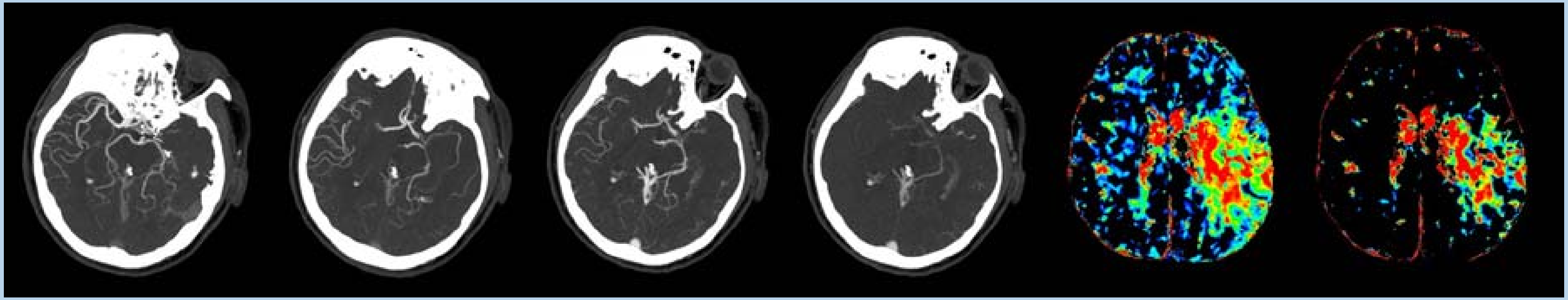


there is a high correlation between mCTA collateral extent and CTP core and penumbra assessment in predicting tissue fate

↓

mCTA collateral delay and Tmax perfusion delay present the same predictive value for final infarct volume = infarct core size

Delay is brain



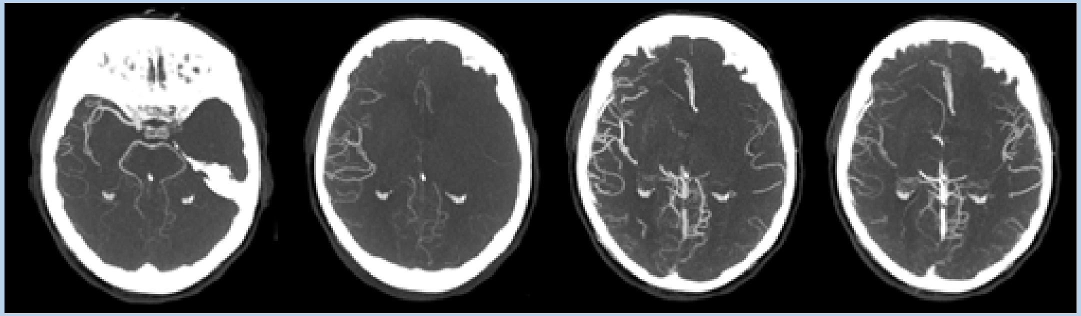
occlusione | mCTA 1° fase | mCTA 2° fase | mCTA 3° fase | Tmax$_{9.5\text{-}25sec}$ | Tmax$_{16\text{-}25sec}$

mCTA e CTP Tmax both express the delay in filling and perfusion of brain microcirculation

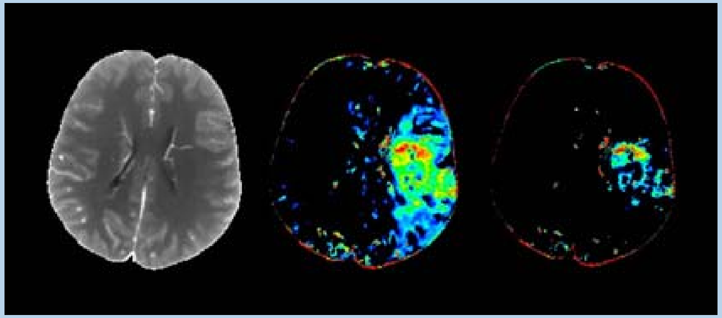
↓

maybe it could be not important the time of onset, but how much is the delay of capillary network injection

A combined mCTA/CTP selection



mCTA



CTP

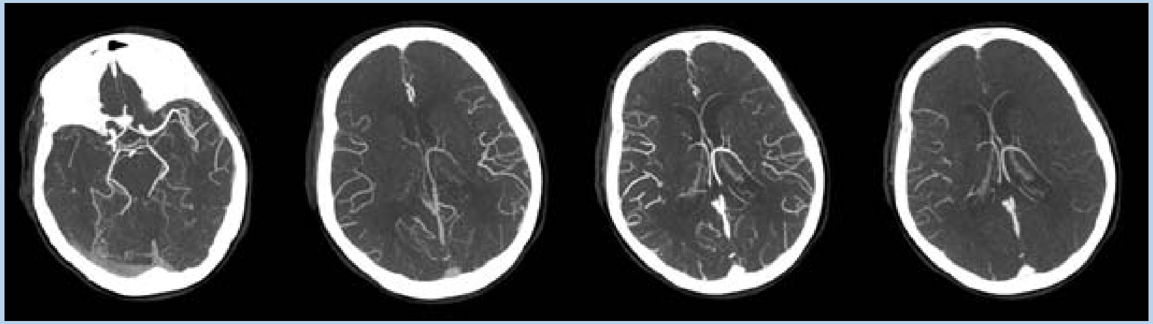
Vagal A et al. Stroke 2016; 47: 535-5338

overall these data suggest a potential selection strategy to improve patient selection

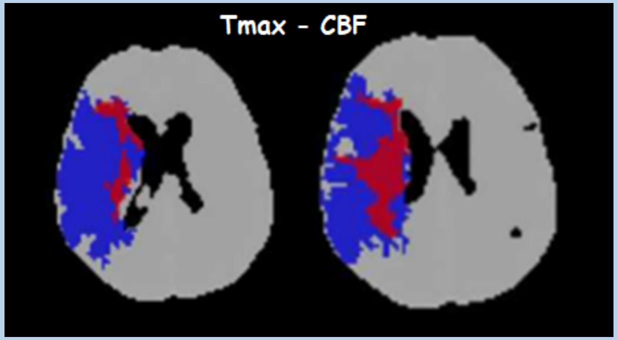
↓

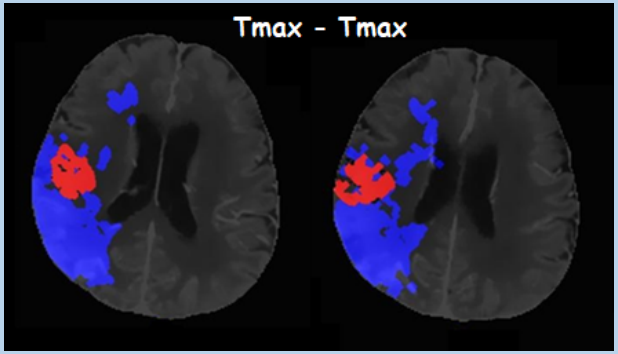
based on a combined analysis of mCTA and CTP results in which the information derived from both techniques are integrated

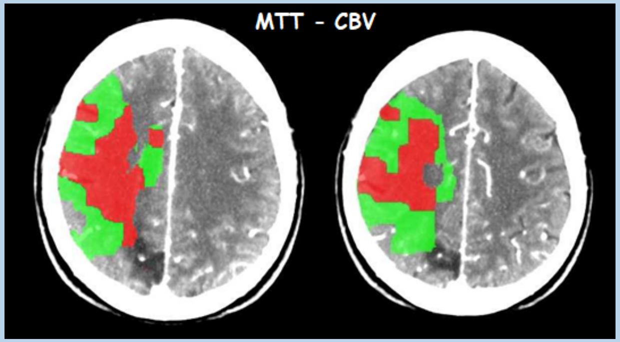
A combined mCTA/CTP selection



occlusion mCTA 1° phase mCTA 2° phase mCTA 3° phase







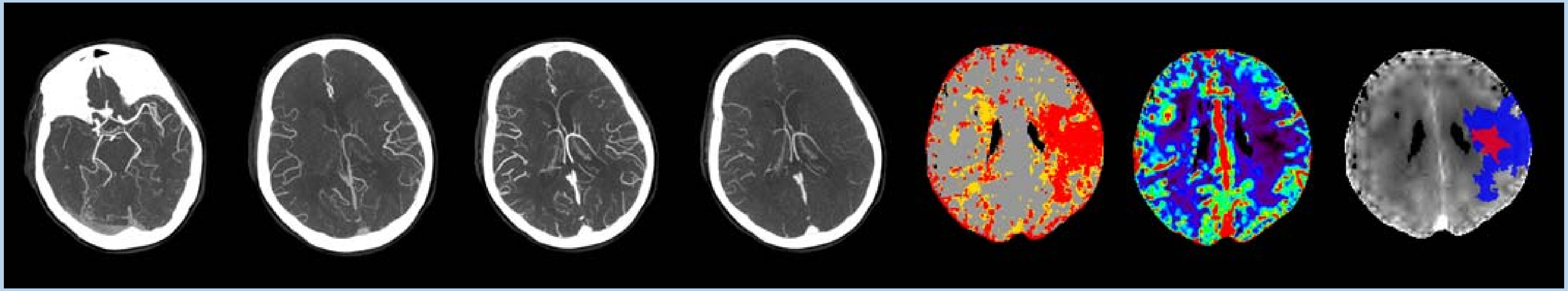
- **core e penumbra volumes are determined with dedicated automated software programs**

↓

CTP Tmax - CBF mismatch **is currently considered the method of choice**

Campbell BC, Parsons MW. Int J Stroke 2018; 13: 554-567; Leiva-Salinas C et al. Neuroimaging Clin N Am 2018; 28: 565-572

An integrated view



occlusion | 1° phase | 2° phase | 3° phase | Tmax | CBF | Penumbral map