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Imaging Criteria for Selection of Acute Stroke Patients: Is ASPECTS enough?

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TOSHIBA STROKE & VASCULAR RESEARCH CENTER

Kaleida Health
Building a healthier future

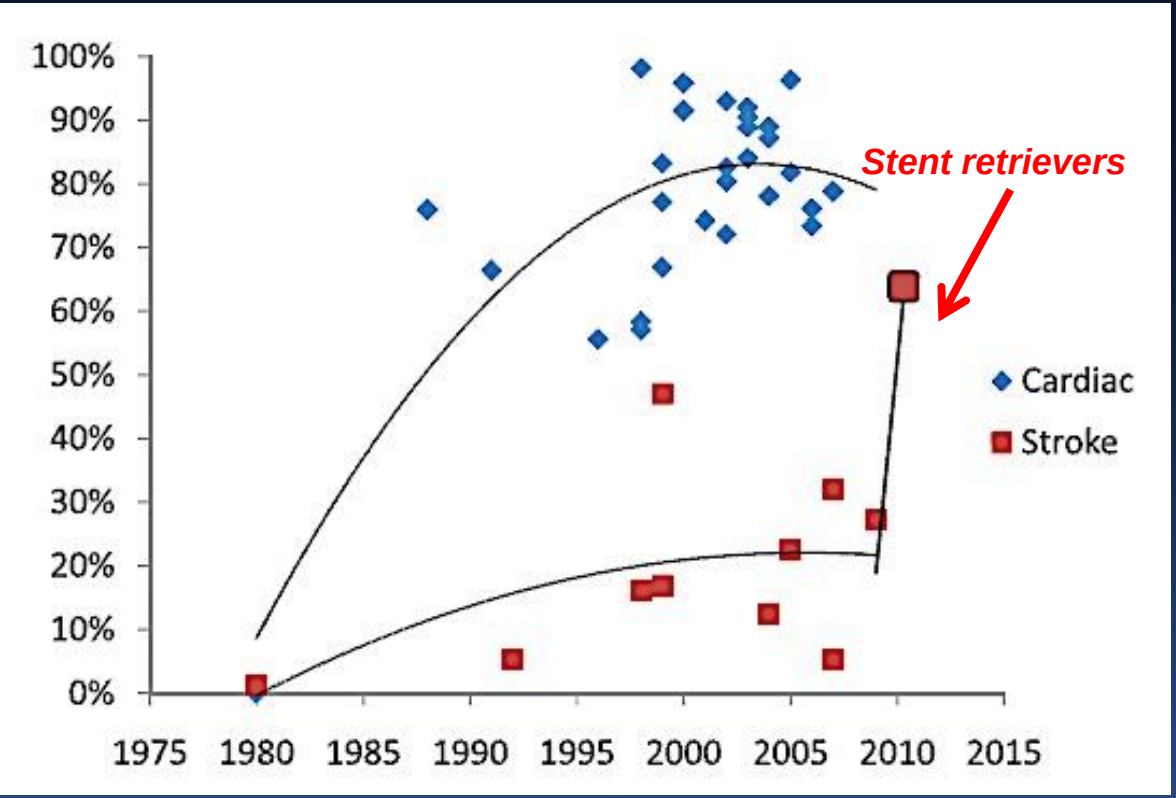
University at Buffalo
State University of New York

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

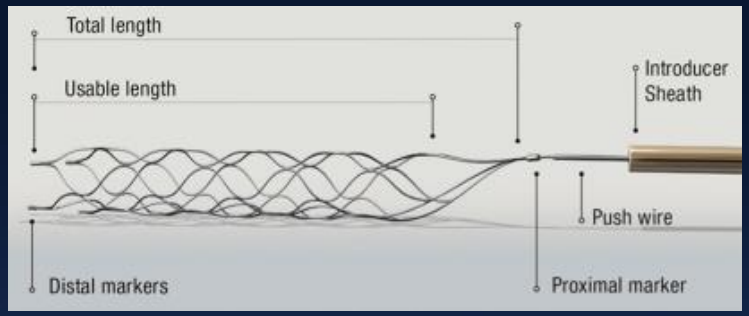
Affiliation/Financial Relationship	Company
	• Toshiba – Honorarium • Medtronic - Honorarium

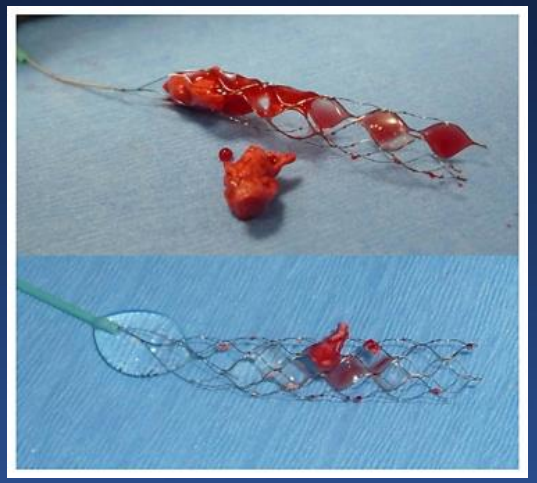
Improved Recanalization Rates with New Technology



Saver JL, Stroke 2013;44:270-277

What's a retrievable stent, anyway?





2015: Endovascular vs Best Medical Therapy

- 5 major studies evaluating the role of endovascular therapy in stroke treatment
  - MR CLEAN
  - EXTEND-IA
  - ESCAPE
  - SWIFT PRIME
  - REVASCAT
- EVT within 6 hrs, NIHSS >7
- ALL 5 trials stopped because of significant benefit in the Endovascular arms

	Nat Hx	NINDS	MR CLEAN	EXTEND-IA	ESCAPE	SWIFT PRIME	REVASCAT
# pts	178	333	500	70	315	196	206
Median NIHSS	16-20	14	17	13	16	17	17
TICI 2b-3			58.7%	86%	72.4%	88%	65.7%
sICH		6%	7.7%	0%	3.6%	0%	4.9%
mRS (0-2)	<5%	39%(vs 26%)	32.6%	72%	53%	60%	43.7%
Mortality	80%	17%	18.9%	9%	10.4%	9.2%	18.4%

Imaging Selection Criteria	MR CLEAN	EXTEND-IA	ESCAPE	SWIFT PRIME	REVASCAT
Small core	Not required	RAPID perfusion infarct <70 mL (relCBF<30% threshold)	ASPECTS score 6–10	ASPECTS score 6–10 on NCCT or DWI, RAPID perfusion infarct <50 mL (relCBF<30% threshold)	ASPECTS score >6 on NCCT, ASPECTS score >5 on DWI (NCCT ASPECTS >8 for age 80–85)
Penumbra	Not required	Target mismatch: RAPID perfusion ischemic core mismatch ratio >1.2, absolute mismatch >10 mL (T_{max}>6 s threshold)	Not required	Target mismatch: RAPID perfusion penumbra/ infarct ratio>1.8, penumbra absolute volume >15 mL (T_{max}>6 s threshold) -T_{max}>10 s Lesion ≤100 mL	Not required (clinical/core mismatch [NIHSS>5])
Collaterals	Not required	Not required	Adequate collateral circulation defined as some filling of 50% or greater of the ischemic territory pial circulation beyond occlusion on CT angiography (preferably multiphase CTA)	Not required	Not required
	32.6 % vs 19.1 %	***71% vs 40%***	***53% vs 29.3% 10.4%, vs. 19.0%***	***60.2% vs 35.5%***	***43.7% vs. 28.2%***

Why are these trials different than previous randomized trials of EVT vs BMM?

- Confirmation of large vessel occlusion before randomization
- Use of retrievable stents in the majority of patients

Update June 29 2015

- **Certain endovascular procedures have been demonstrated to provide clinical benefit in selected patients with acute ischemic stroke. Systems of care should be organized to facilitate the delivery of this care.**

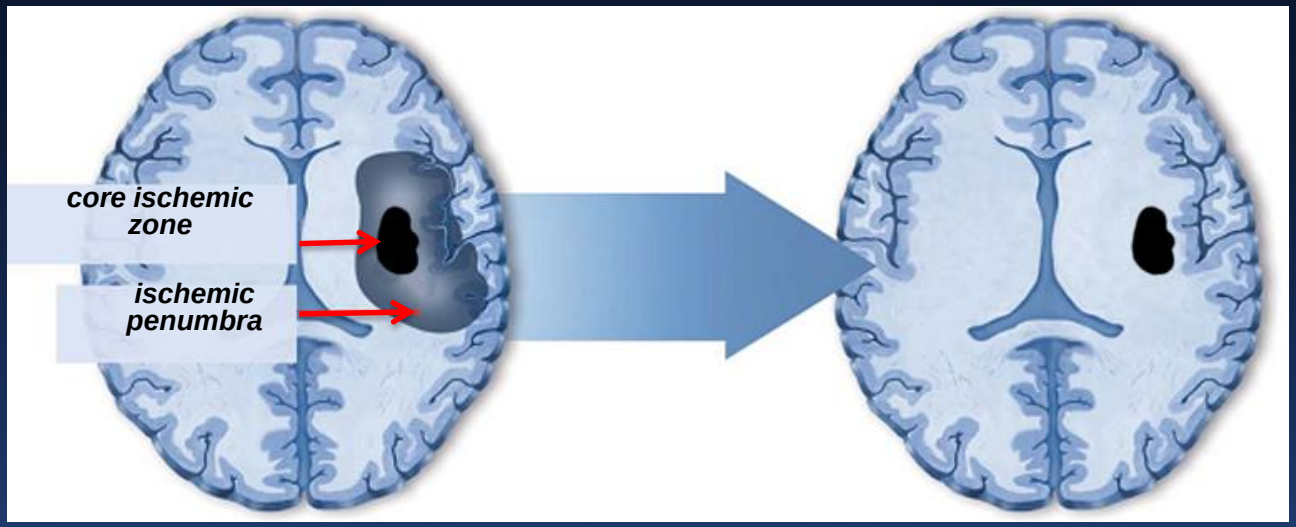
Stroke AHA/ASA Stroke Guidelines Focused Update

Future of Stroke Imaging

The greatest challenge is to show that advanced neuroimaging, used as a biomarker to select patients for reperfusion therapy (in an extended time window), improves patient outcomes

The Future of Stroke Imaging: What We Need and How to Get to It
Carlos Leiva-Salinas and Max Wintermark
Stroke 2010;41;S152-S153

Advanced Imaging



Advanced Imaging

- Dynamic Studies capturing one cycle of the full transit of a contrast bolus though the tissue
- Physiologic Imaging: Transit Time, Blood Flow, Blood Volume
  - Parenchyma (Capillary phase NOT large vessels)
  - Intravascular surrogate for Intracellular process (not biological, Xenon)

Imaging Strategies

- NCCT, ASPECTS (eASPECTS)
- Physiologic Imaging (CT Perfusion, MR Perfusion)
- Vascular Study to measure clot length (THERAPY)
- Collateral Imaging
- TCD
- Parametric Imaging

NCCT

- NCCT remains sufficient at identifying contraindications to fibrinolysis
  - Widespread, fast, low cost
- Rule out Hemorrhagic Stroke
- 6 hours before reliable changes, edema vs core?
- > 1/3 MCA EIC on NCCT predicts functional outcome and risk of ICH
  - Sensitivity 65%, Specificity 65%

Guidelines for the Early Management of Patients With AIS Stroke 2014

Schellinger, 2010, Neurology; Fiebach et al., 2002, Stroke

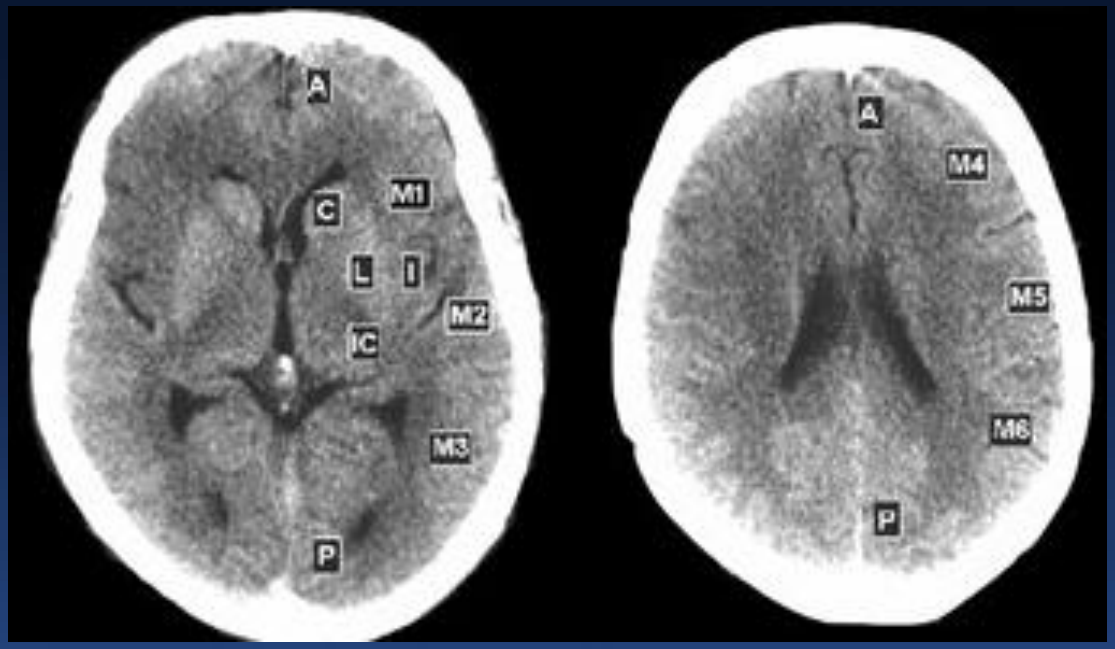
Alberta Stroke Program Early CT Score (ASPECTS)

- Standardize the detection and reporting of the extent of EIC on NCCT
- Scoring system of 1 or 0 for 10 predefined locations
- C- Caudate, I- Insularribbon, IC- Internal Capsule, L- Lentiform nucleus, and M1 to M6 MCA territories

http://www.aspectsinstroke.com

- < 8 is correlated with both poor functional outcome and sICH

ASPECTS



http://www.aspectsinstroke.com

MRI

- DWI – Diffusion Weighted Imaging
  - Sensitivity 90%, Specificity 95%
  - Within min of onset of sx
  - Small lesions
  - NOT all completed stroke (includes irreversible and reversible regions)
- GRE
  - Rule out ICH
- FLAIR
  - Importance to calculate Final Infarct Volume at 3-5 days

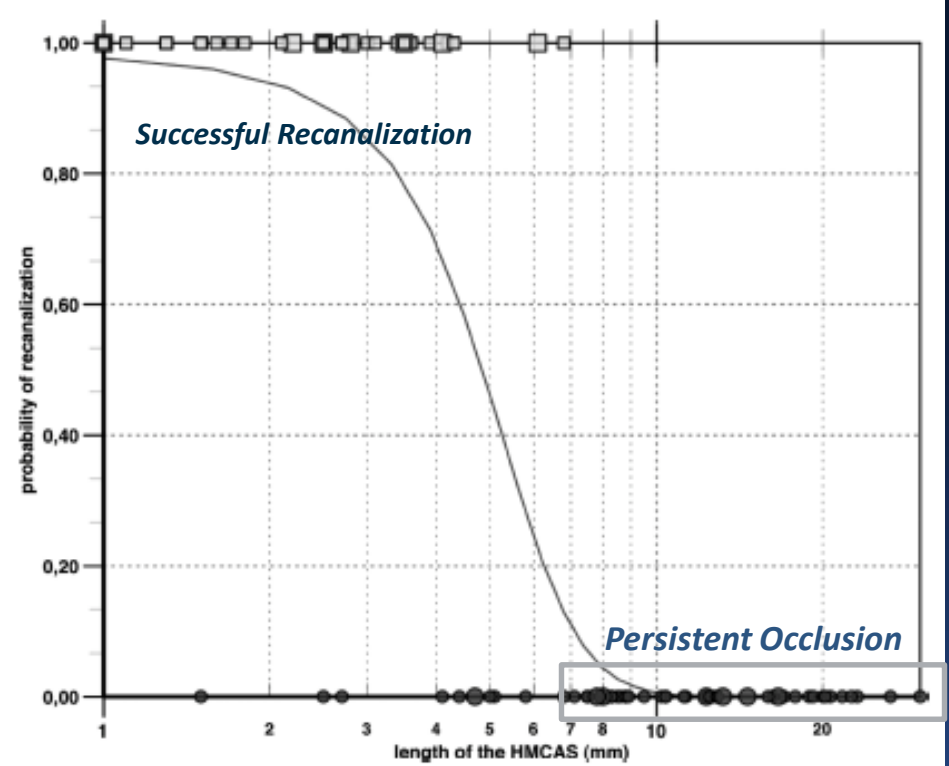
Schellinger, 2010, Neurology; Fiebach et al., 2002, Stroke

CTA/MRA

- Length of a clot within the MCA is inversely related to the success of recanalization with IV tPA
- Helps with identification of cause and can predict severity of stroke (Carotid)

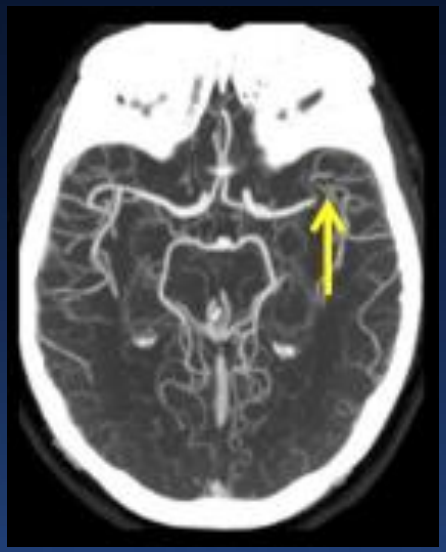
Stroke. 2011;42:1775–1777.

Impact of Clot Burden on Success Rate of IV tPA



Christian H. Riedel et. al. The Importance of Size: Successful Recanalization by Intravenous Thrombolysis in Acute Anterior Stroke Depends on Thrombus Length. Stroke, 2011;42:1775-1777

CTA Collaterals



http://www.aspectsinstroke.com

CONTRACTS & INSTALLATIONS

N.Y. stroke center installs Toshiba Aquilion One CT

Written by Editorial Staff
February 27, 2009
PRINT E-MAIL

FURTHER READING

City

- Buffalo
- Tustin

Company

- Toshiba America Medical Systems

Millard Fillmore Gates Circle Hospital in Buffalo, N.Y., has installed a Toshiba America Medical Systems' Aquilion One dynamic volume CT system at its Kaleida Health Stroke Center.

The Aquilion One can image the entire brain and show real-time brain function in less time than traditional multi-detector CT systems, according to Toshiba.

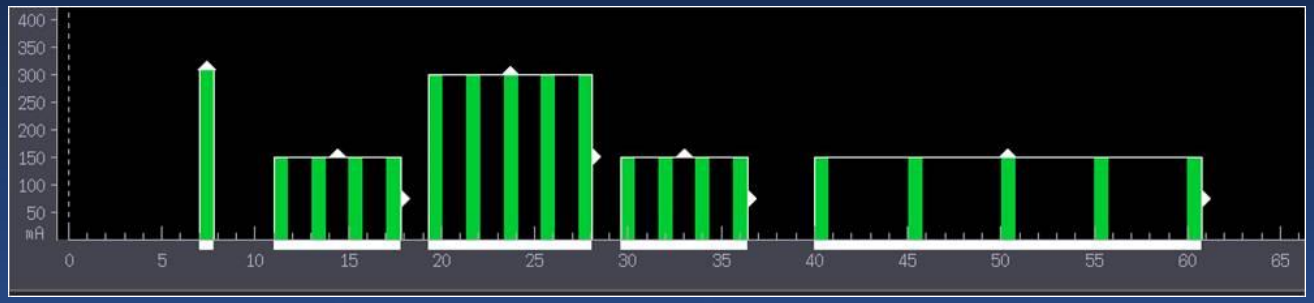
The 189-bed acute care medical center is home to a multi-disciplinary team trained in stroke care that comprises the hospital's Kaleida Health Stroke Center. It is the first stroke center in the United States to offer dynamic volume CT, the Tustin, Calif.-based Toshiba said.

Buffalo Protocol

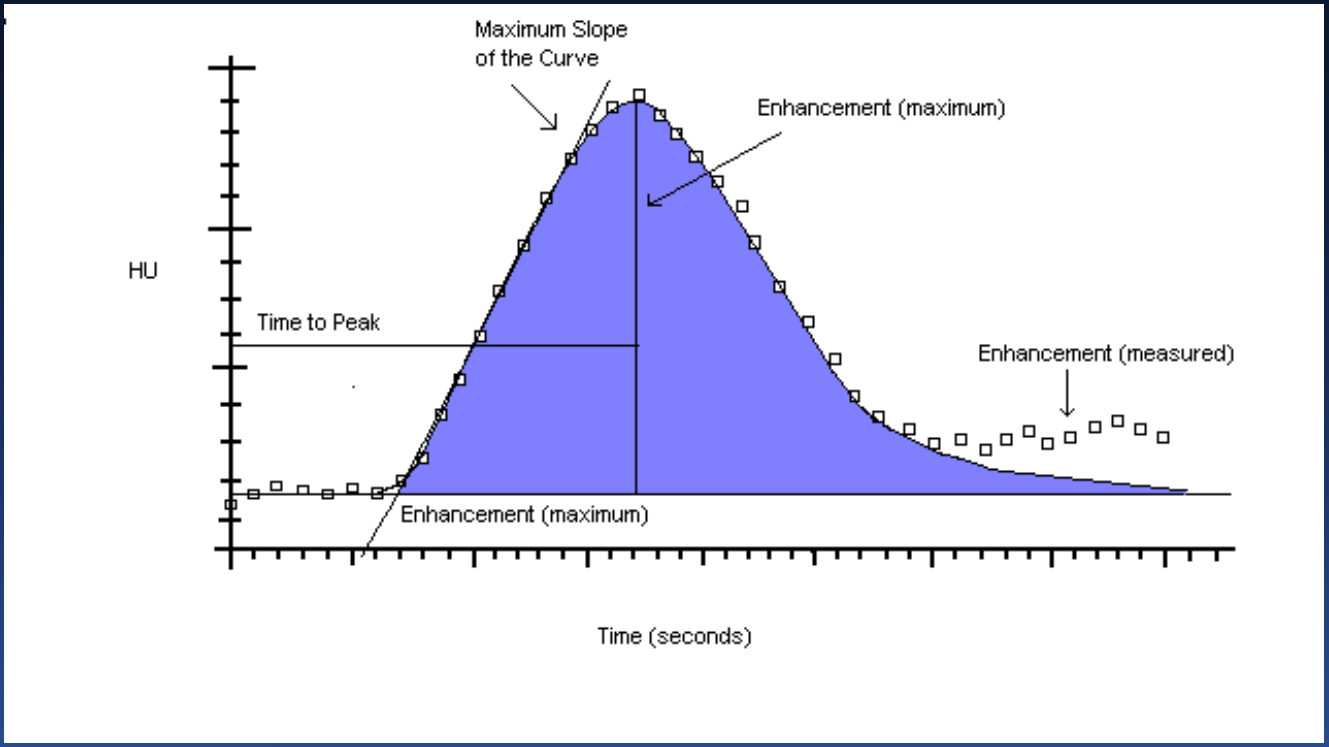
- NIHSS and CTSS (CTA head and neck and CTP)
  - Intervention based on perfusion parameters, clinical exam, and Time of Onset
  - MRI if no obvious deficit on CTP
- Post intervention CT/ LCI /MRI GRE
- CTP POD #1, NIHSS at 24hrs
- MRI at 3-5 days
- Discharge disposition, NIHSS and mRS
- CT or MRI at 1-3 months, mRS and NIHSS
- All patients collected in prospective registry

Aquilion One Protocol (1 min acquisition)

- CT Head w/o
- Perfusion
  - 50 cc at 5cc/s 19 volumes
    - 1 is mask



Time/Tissue Attenuation Curve



Perfusion Models (4 min processing time)

- Maximum Slope
- Deconvolution
  - Parametric R(t) has specific distribution
  - Non-parametric – R(t) is an unknown
    - Transform – Fourier
    - SVD
    - Delay Insensitive Deconvolution (SVD+)
- Bayesian

CT Perfusion Parameters

- CBF mL blood/100g brain tissue/min
- CBV mL blood/100g brain tissue
- Mean transit time (MTT)
- Time to peak (TTP)
- Delay Map

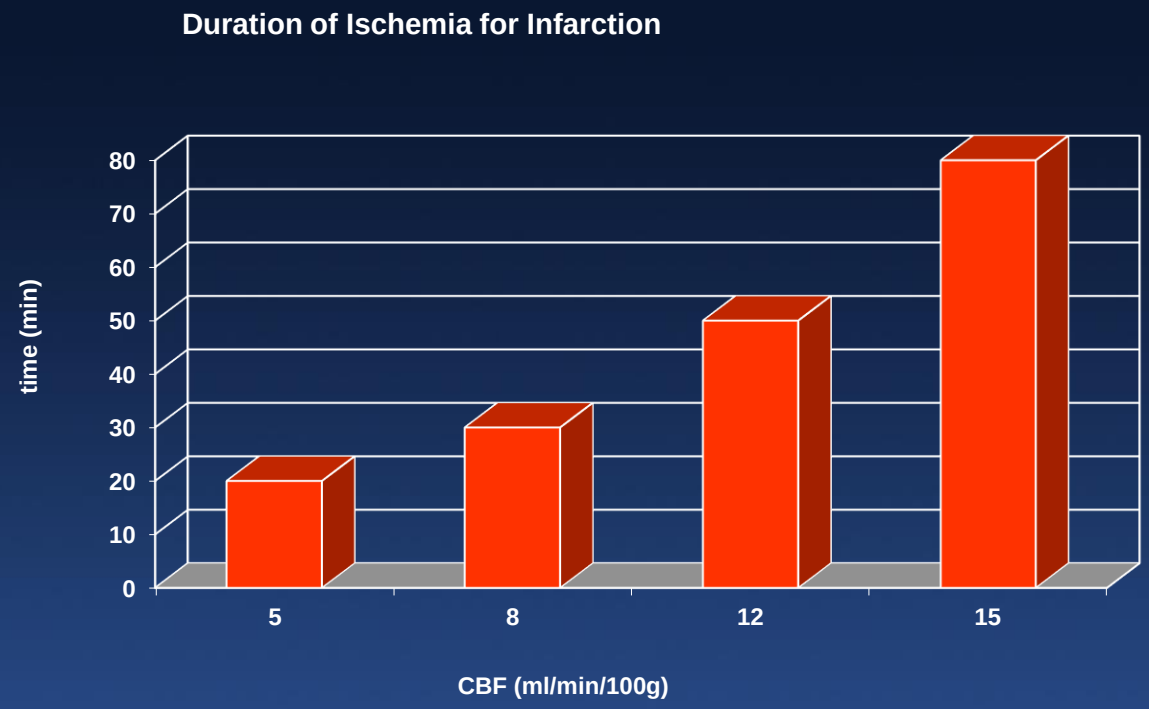
Condition	rTTP	rCBF	rCBV
None	Normal	Normal	Normal
Art stenosis/ occl with comp	Prolonged	Normal	Normal
Oligemic	Prolonged	> 60%	> 80%
Tissue at risk	Prolonged	> 30%	> 60%
Dead tissue	Strong prolonged	< 30%	< 30-40%

Tomandl, 2003; Mayer 2000; Koenig 2001

Cerebral Perfusion

- CBF = 50-60 mL/100 g/min, normal
- CBF = 35: protein synthesis ceases, oligemic stage, tissue can survive.
- CBF = 20: disturbance of synaptic transmission, loss of function (still viable)
- CBF = 10: irreversible cell death

Heiss and Rosner (1983)

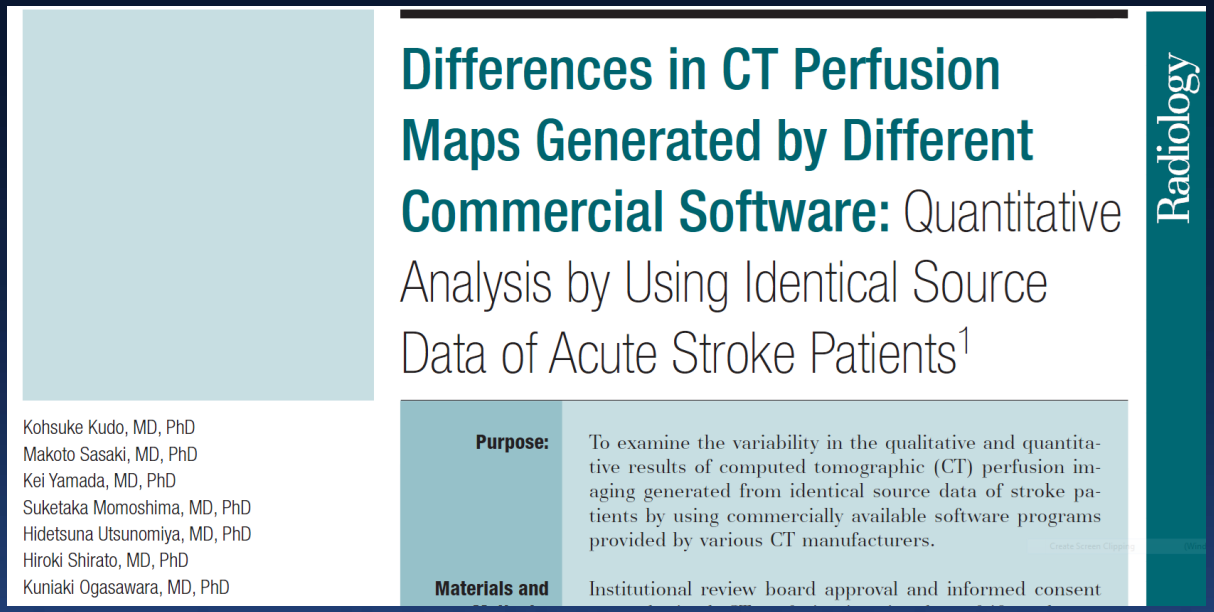


Time is Brain

- Reperfusion can lead to complete regeneration of neuronal function
- Infarct replaces penumbra at a rate that depends on degree of collateral circulation
- Different for different areas of tissue at risk
- Different for grey and white matter
- Different for each and every person being evaluated and potential treated!!!

- CTP at two different time points to assess Stroke Evolution

Reliability?



Differences in CT Perfusion Maps Generated by Different Commercial Software: Quantitative Analysis by Using Identical Source Data of Acute Stroke Patients[1]

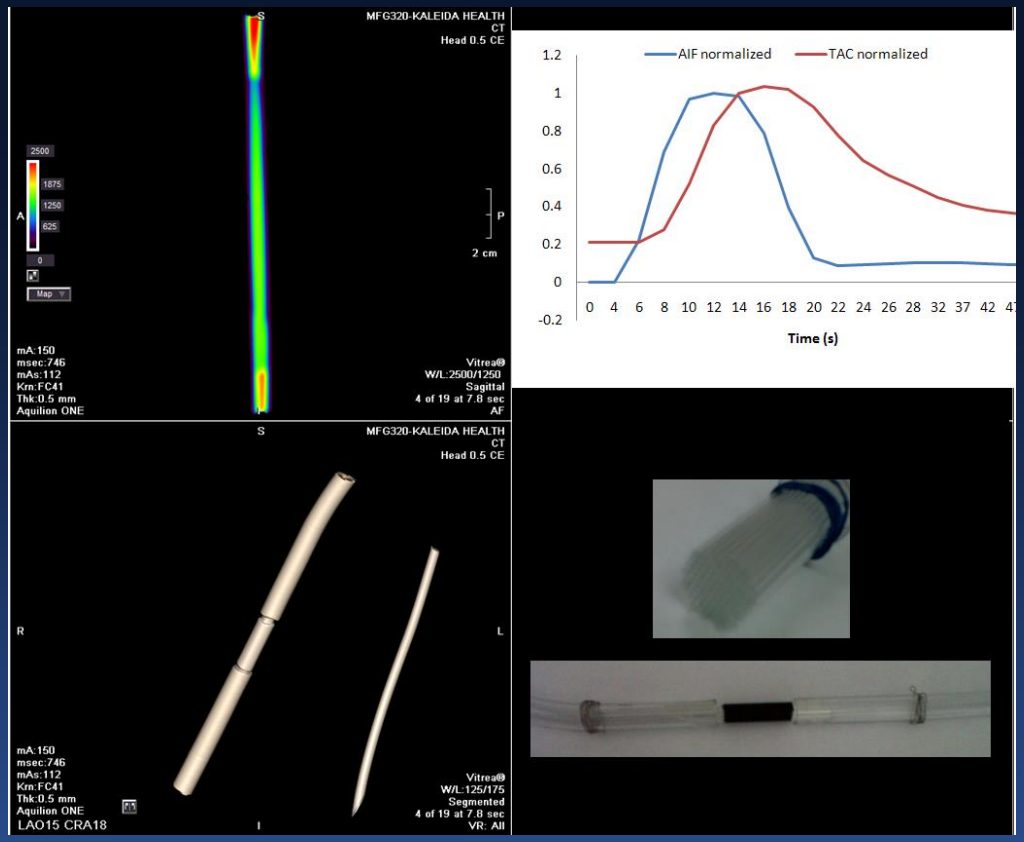
Kohsuke Kudo, MD, PhD
Makoto Sasaki, MD, PhD
Kei Yamada, MD, PhD
Suketaka Momoshima, MD, PhD
Hidetsuna Utsunomiya, MD, PhD
Hiroki Shirato, MD, PhD
Kuniaki Ogasawara, MD, PhD

Purpose: To examine the variability in the qualitative and quantitative results of computed tomographic (CT) perfusion imaging generated from identical source data of stroke patients by using commercially available software programs provided by various CT manufacturers.

Materials and Institutional review board approval and informed consent

Radiology

Radiology 254(1): jan 2010


MFG320-KALEIDA HEALTH
CT
Head 0.5 CE
2500
1875
1250
625
0
A
P
2 cm
Map
mA:150
msec:746
mAs:112
Krn:FC41
Thk:0.5 mm
Aquilion ONE
Vitrea
W/L:2500/1250
Sagittal
4 of 19 at 7.8 sec
AF
S
MFG320-KALEIDA HEALTH
CT
Head 0.5 CE
R
L
I
mA:150
msec:746
mAs:112
Krn:FC41
Thk:0.5 mm
Aquilion ONE
LAO15 CRA18
Vitrea
W/L:125/175
Segmented
4 of 19 at 7.8 sec
VR: All
AIF normalized
TAC normalized
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
0 4 6 8 10 12 14 16 18 20 22 24 26 28 32 37 42
Time (s)

Extend IA

- EVT within 6 hours of stroke onset.
- Advanced Imaging
  - Core (rCBF < 30%) < 70 mL
  - Penumbra (Tm > 6s)
  - Mismatch (> 1.2 and > 10mL larger than core)
    - Campbell *Stroke* 2012
- Mortality was higher in patients with an Core volume >70 mL as compared with those with a volume <70 mL, 35% (12/34) versus 9% (13/141), respectively (*P*<0.005)

EXTEND IA

- **Strong benefit for EVT if favorable mismatch and core <70 mL**
- **Near complete reperfusion (>90%) in target mismatch patients was strongly tied to favorable clinical outcome (regardless of the treatment strategy)**
- **Lack of reperfusion was associated with death or dependence in 70% of patients.**

SWIFT PRIME

- ASPECTS ≥6
- NIHSS >7
- EVT within 6 hrs
- Advanced Imaging:
  - Core < 50 ml (rCBF < 30%, Tm>10)
  - Penumbra (Tm >6)
  - Mismatch (>1.8 and > 15 mL larger than core)

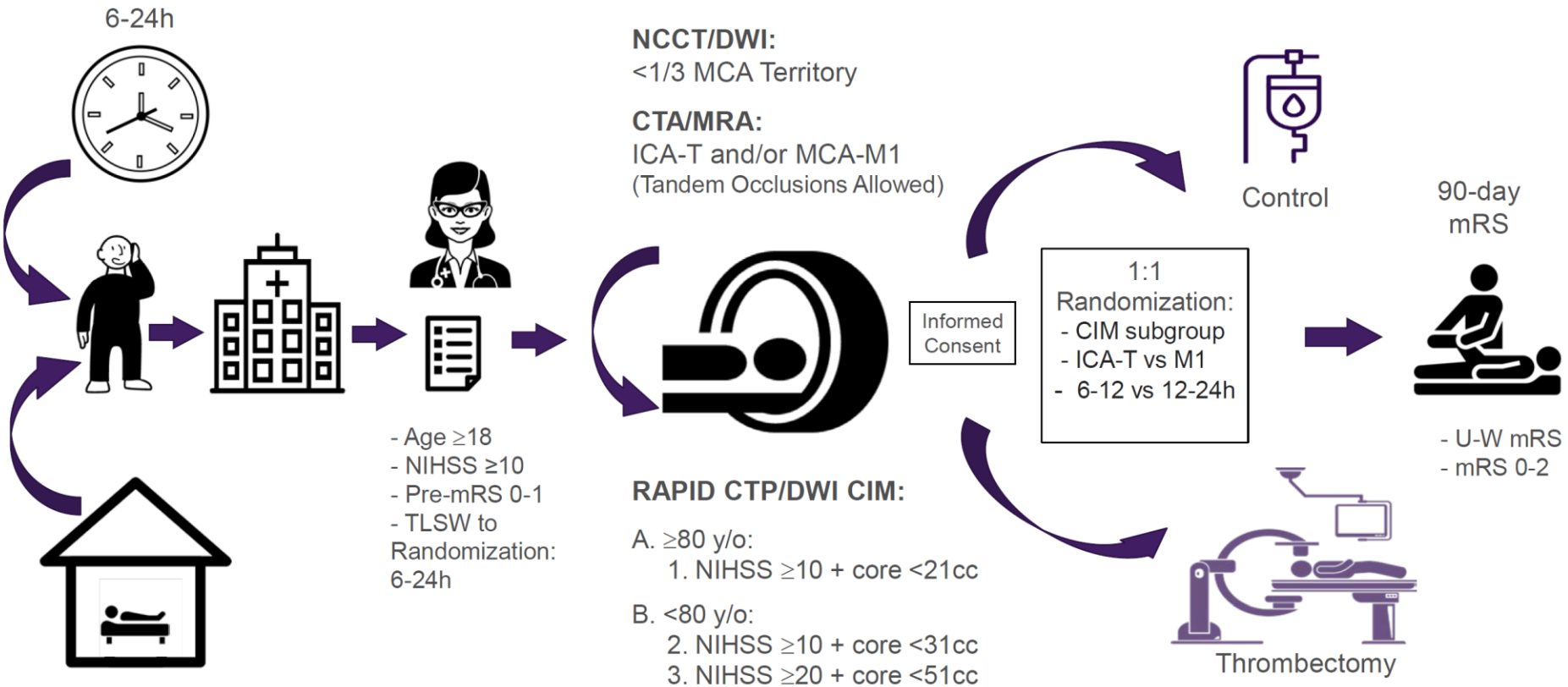
REVASCAT

- EVT within 8 hrs
- NCCT-based patient selection, only requiring ASPECTS score of ≥6
- Significant discrepancies were observed between the centralized core laboratory ASPECTS and the investigators' ASPECTS

ESCAPE

- ASPECTS > 5
- NIHSS > 5
- Mod to Good CS on CTA (> 50% filling)
- Favor EVT
  - ASPECTS and collateral scores were highly correlated
  - Higher Clot Burden (CBS) demonstrated more treatment effect

Study Methods: Workflow



Co-primary endpoints

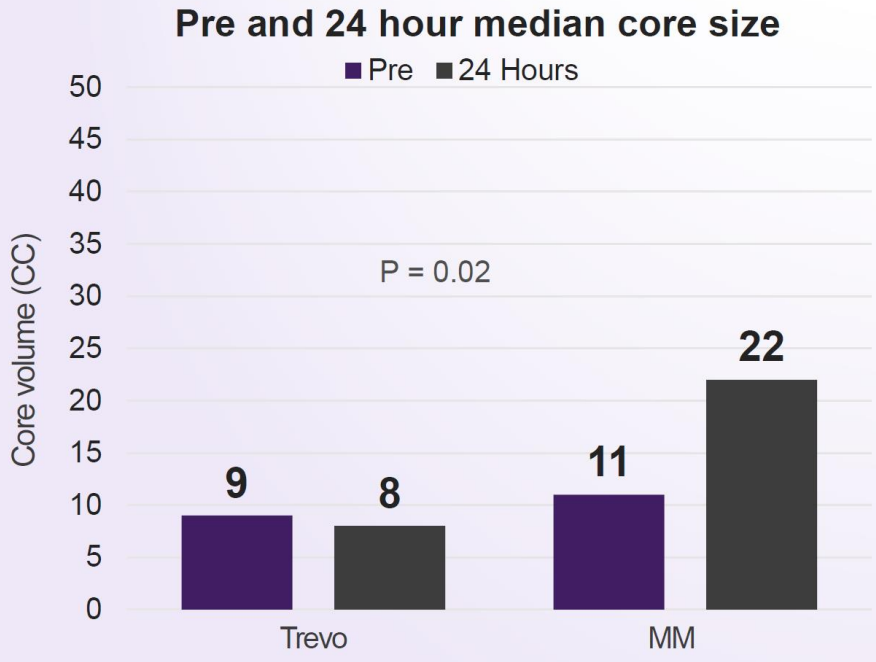
	Trevo	MM	Treatment benefit (95% CI)	Bayesian probability of superiority
Day 90 weighted mRS	5.5 ± 3.8	3.4 ± 3.1	2.1 (1.20, 3.12)	>0.9999*
Day 90 mRS (0-2)	48.6%	13.1%	35.5% (23.9%, 47.0%)	>0.9999*

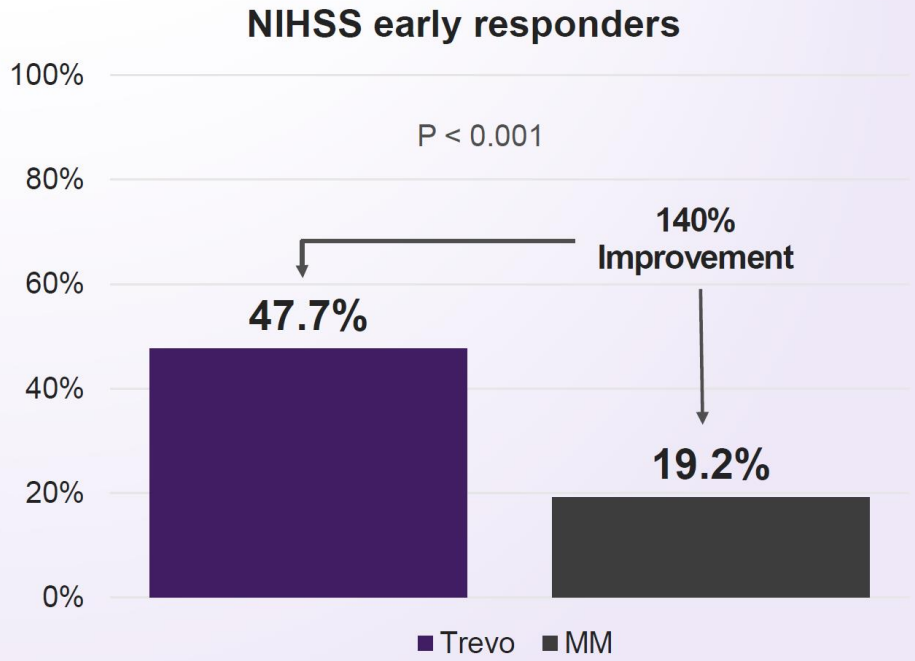
NNT for 90-day functional independence = 2.8

DAWN™ TRIAL

*Similar to p<0.0001

Secondary effectiveness endpoints





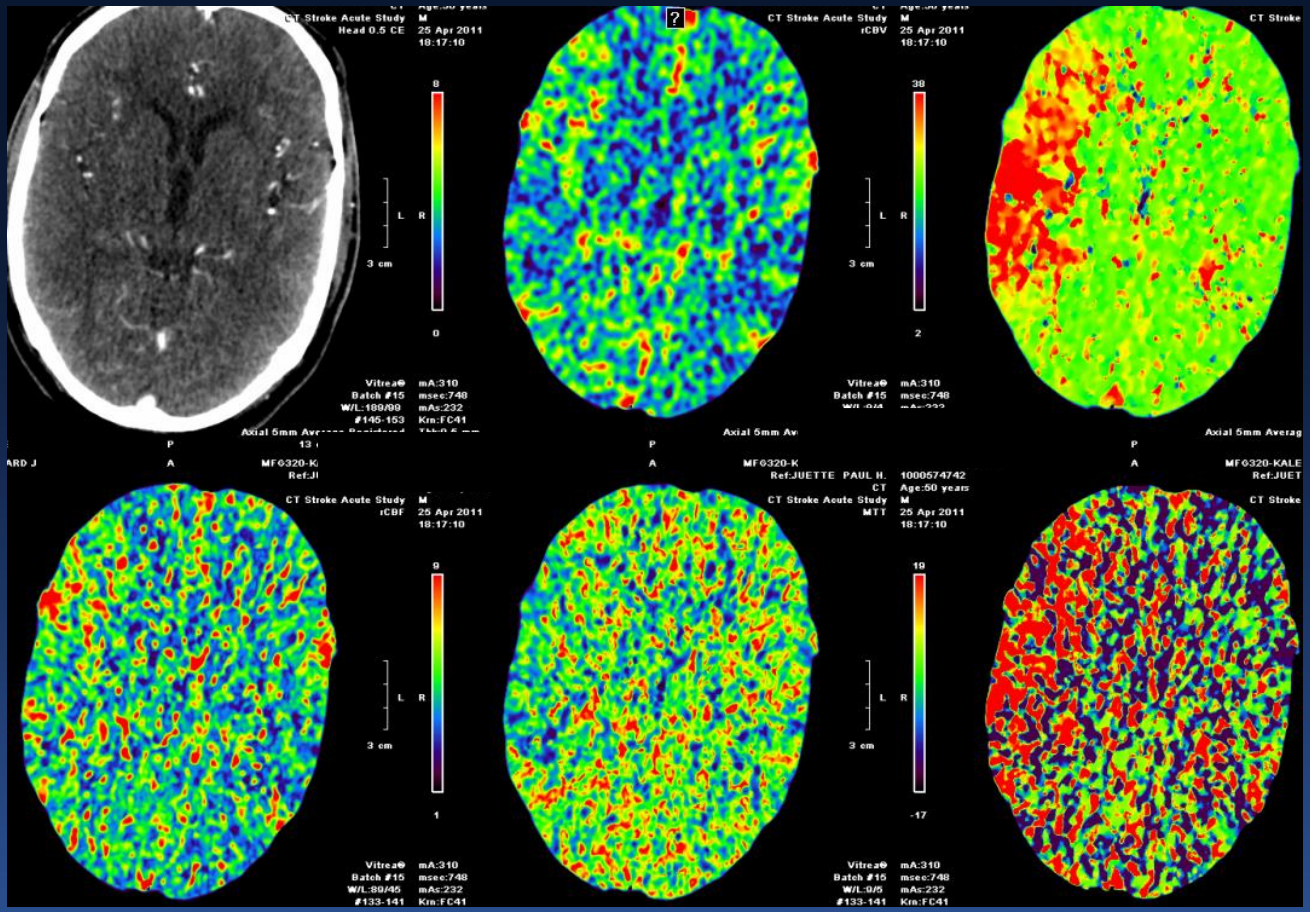
BUFFALO Decision Making for Acute Stroke Intervention

- Functional Imaging (SVD+)
  - Estimate of Penumbra by manual selection of ROI defined as rCBF of < 80% or significantly increased MTT (> 150%)
  - rCBV > 50% (CBV > 2 mL/100g)
- And
- Clinical Exam – NIHSS >7 unless receptive language
- Clinical Exam / Core assessment

Clinical History

- ***50 yo who woke up with with left hemiplegia, dysarthria, and facial droop.***
- ***NIHSS = 16.***

- ***PMH - Anxiety disorder, tobacco dependence, alcohol dependence***


CT Stroke Acute Study
Head 0.5 CE
25 Apr 2011
18:17:10
CT Stroke Acute Study
rCBV
25 Apr 2011
18:17:10
CT Stroke
Vitrea
Batch #15
W/L:189/99
#145-153
mA:310
msec:748
mAs:232
Krn:FC41
Axial 5mm Averag
MF6320-K
Ref:JUETTE PAUL H.
1000574742
CT
Age:50 years
CT Stroke Acute Study
rCBF
25 Apr 2011
18:17:10
CT Stroke Acute Study
MTT
25 Apr 2011
18:17:10
CT Stroke
Vitrea
Batch #15
W/L:89/45
#133-141
mA:310
msec:748
mAs:232
Krn:FC41
Vitrea
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W/L:9/5
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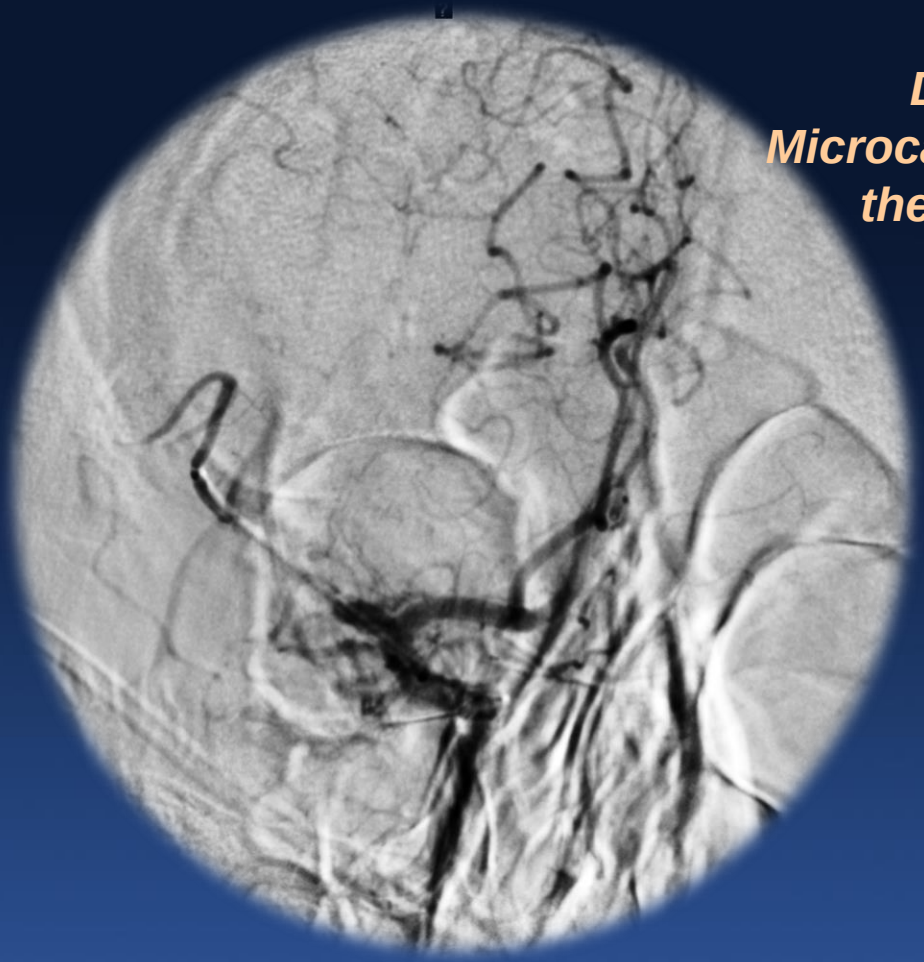
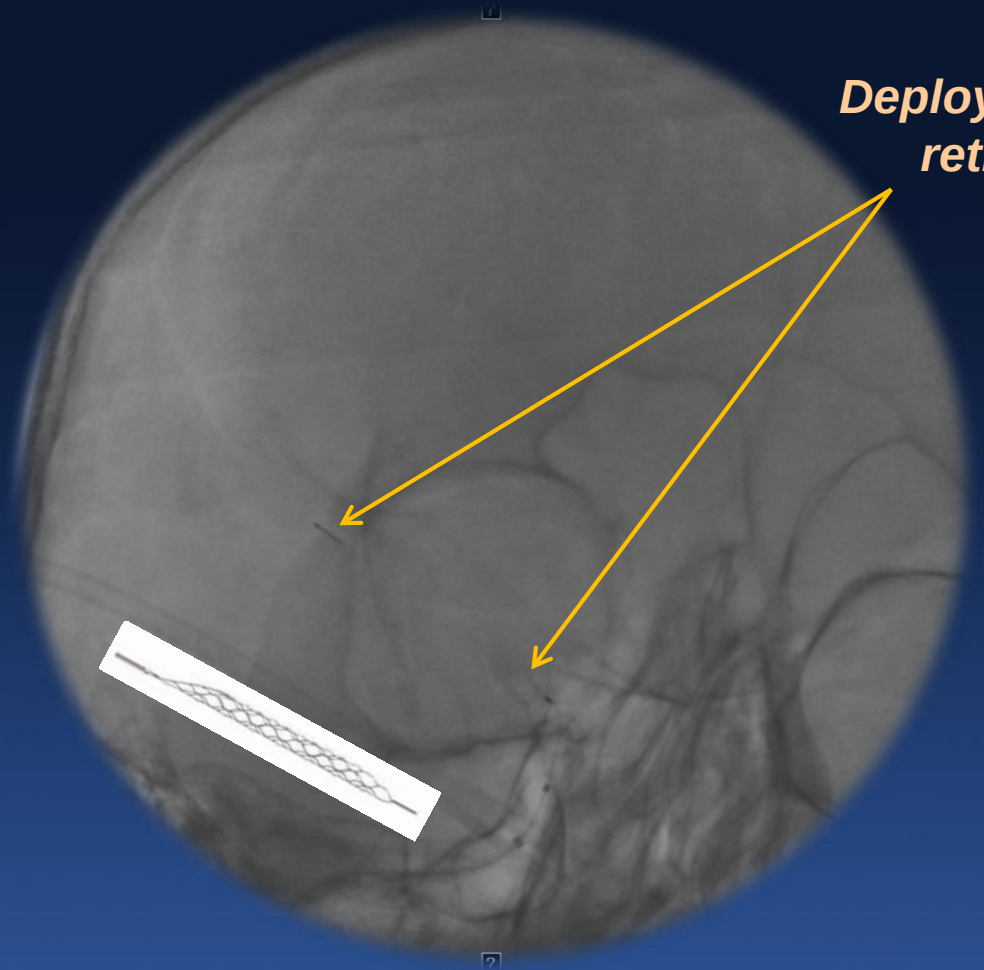
mA:310
msec:748
mAs:232
Krn:FC41

A: 3.4mm
A

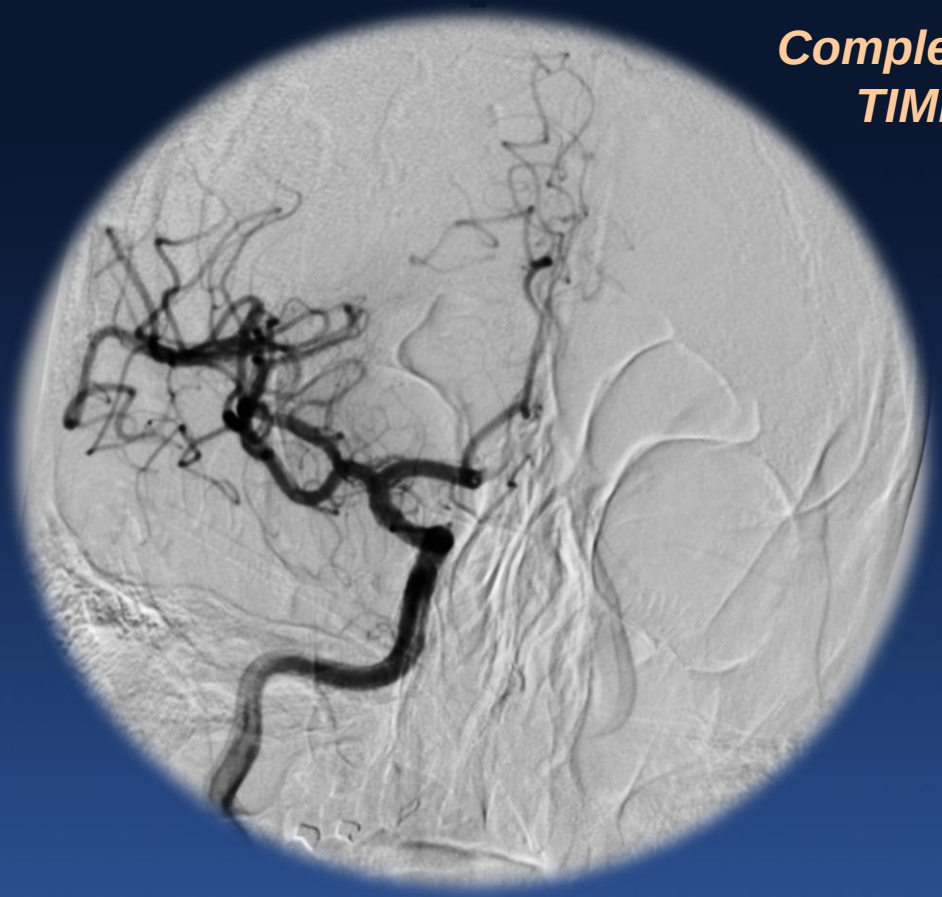


Dual Run
Microcatheter beyond the occlusion


Deployment of TREVO
retrieval device

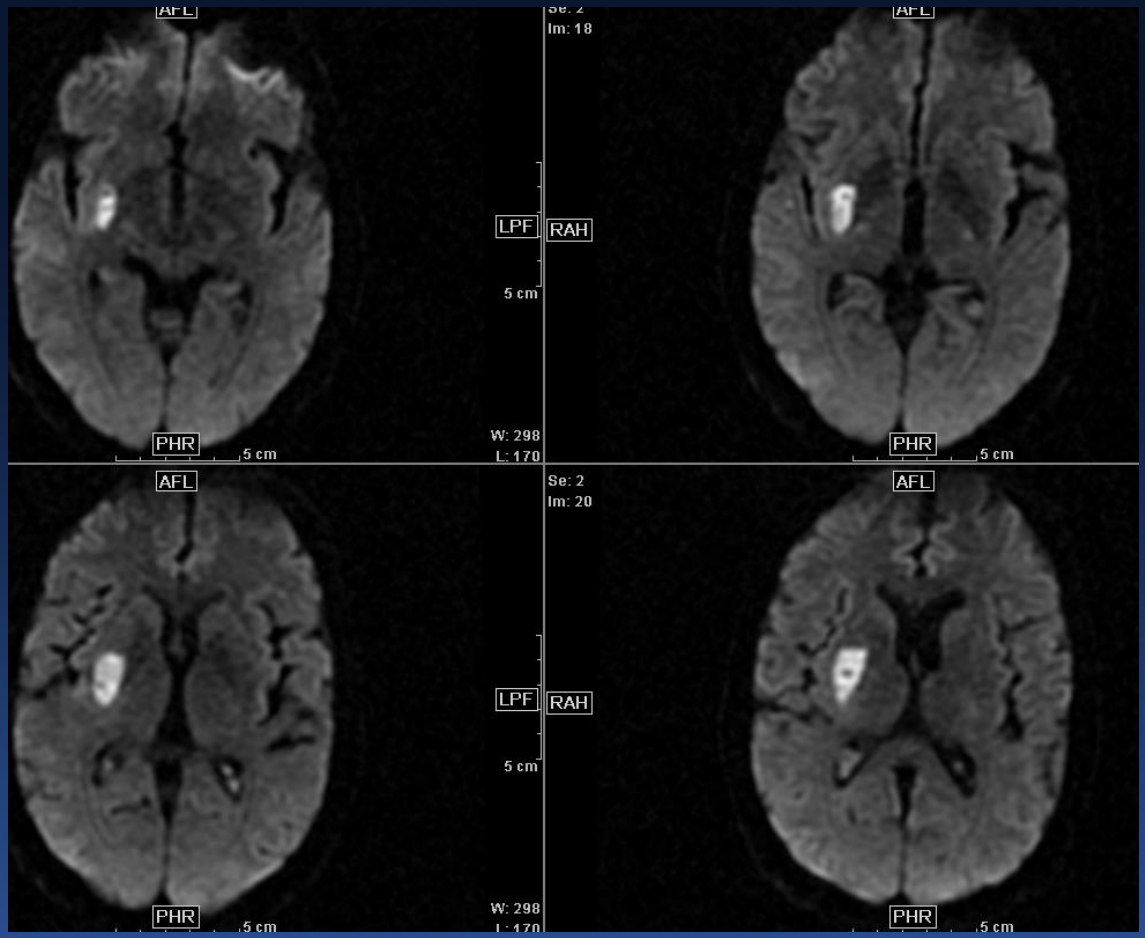
1st pull of the microcatheter with the retrieval device

Total intervention time ~20 min



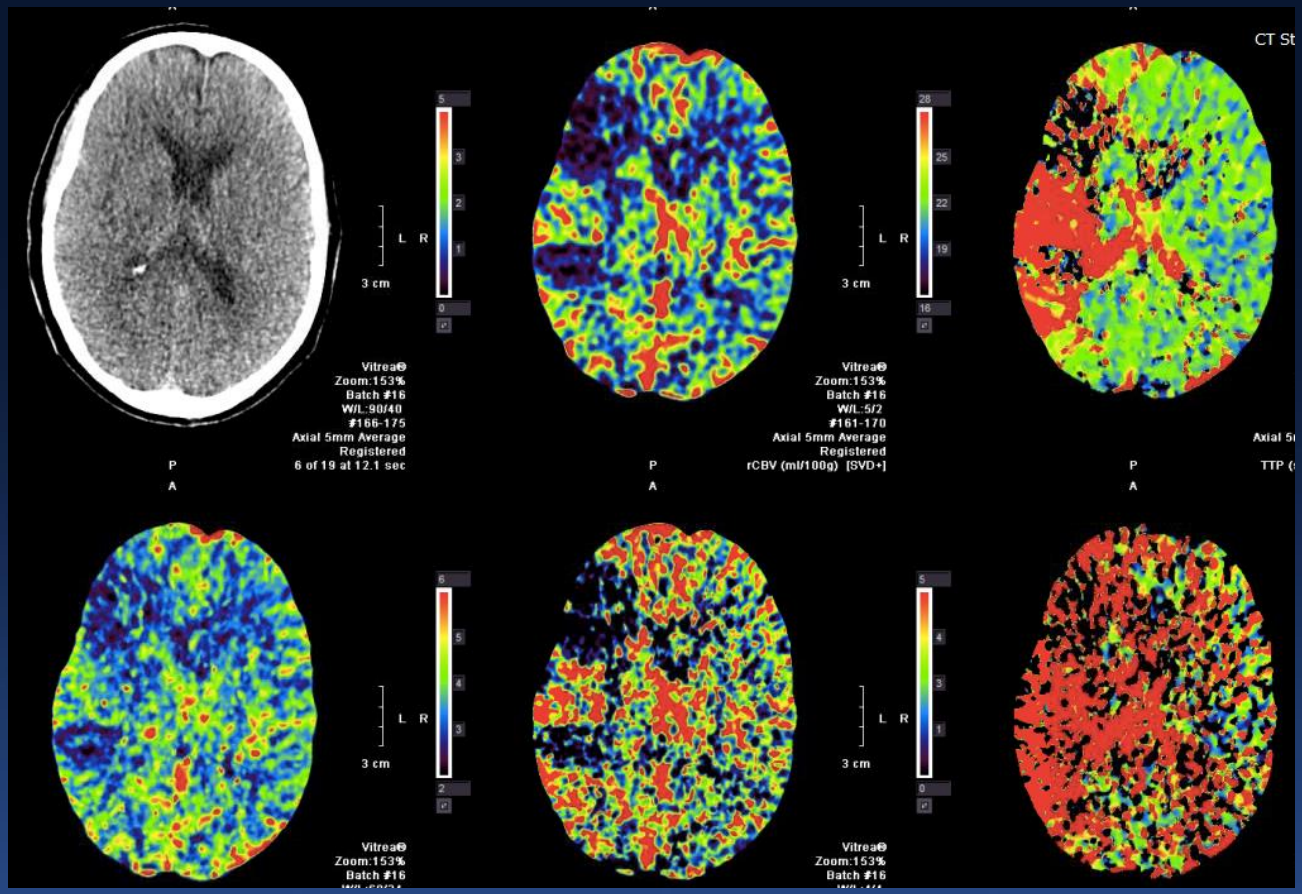
Complete recanalization
TIMI-3 after 1 pull

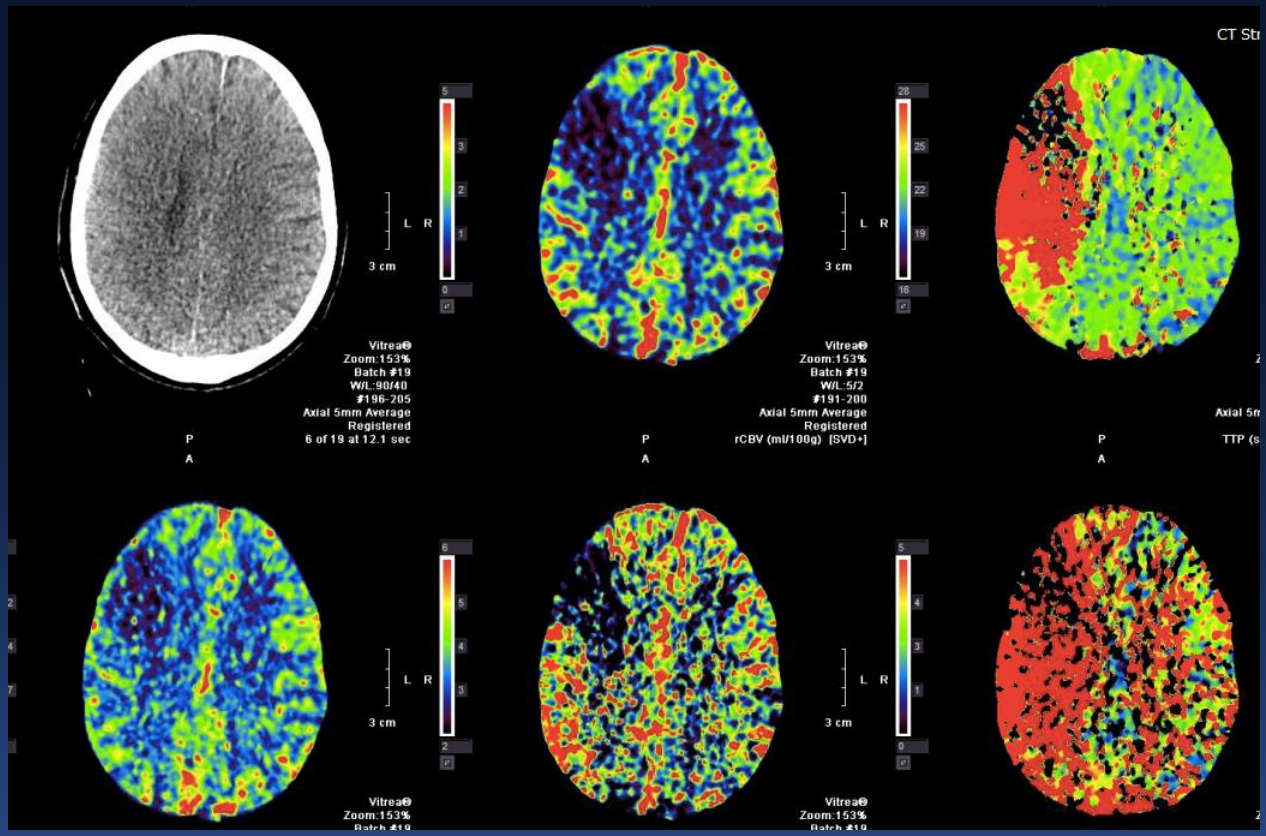
- *In the angio suite – the patient could lift his Rt arm antigravity, improved gaze, NIHSS 16 to 5 immediately*
- *POD#1 NIH -3*
- *POD#2– NIH -0*


AFL
Se: 2
Im: 18
LPF
RAH
5 cm
PHR
5 cm
W: 298
L: 170
AFL
PHR
5 cm
AFL
Se: 2
Im: 20
LPF
RAH
5 cm
PHR
5 cm
W: 298
L: 170
AFL
PHR
5 cm

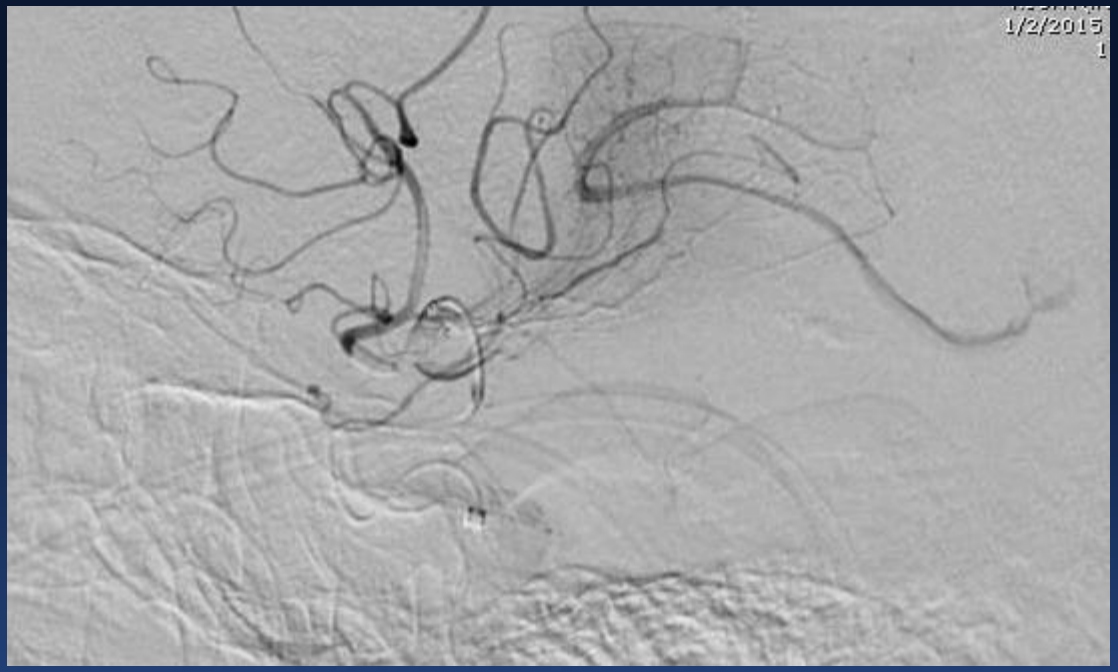
Clinical History

- 75 yo WM last seen normal at 10 pm, ? Issues at 2 am, awoke thrashing at 4 am with Right gaze preference and left HP
- NIHSS 18


CT St
L R
3 cm
Vitrea
Zoom:153%
Batch #16
W/L:90/40
#166-175
Axial 5mm Average
Registered
6 of 19 at 12.1 sec
W/L:5/2
#161-170
rCBV (ml/100g) [SVD+]
TTP
P
A


CT Str
3 cm
L R
Vitrea
Zoom:153%
Batch #19
W/L:90/40
#196-205
Axial 5mm Average
Registered
6 of 19 at 12.1 sec
P
A
3 cm
L R
Vitrea
Zoom:153%
Batch #19
W/L:5/2
#191-200
Axial 5mm Average
Registered
rCBV (ml/100g) [SVD+]
P
A
Axial 5m
TTP (s
P
A
3 cm
L R
Vitrea
Zoom:153%
3 cm
L R
Vitrea
Zoom:153%

Page: 21 of 23


1/2/2015
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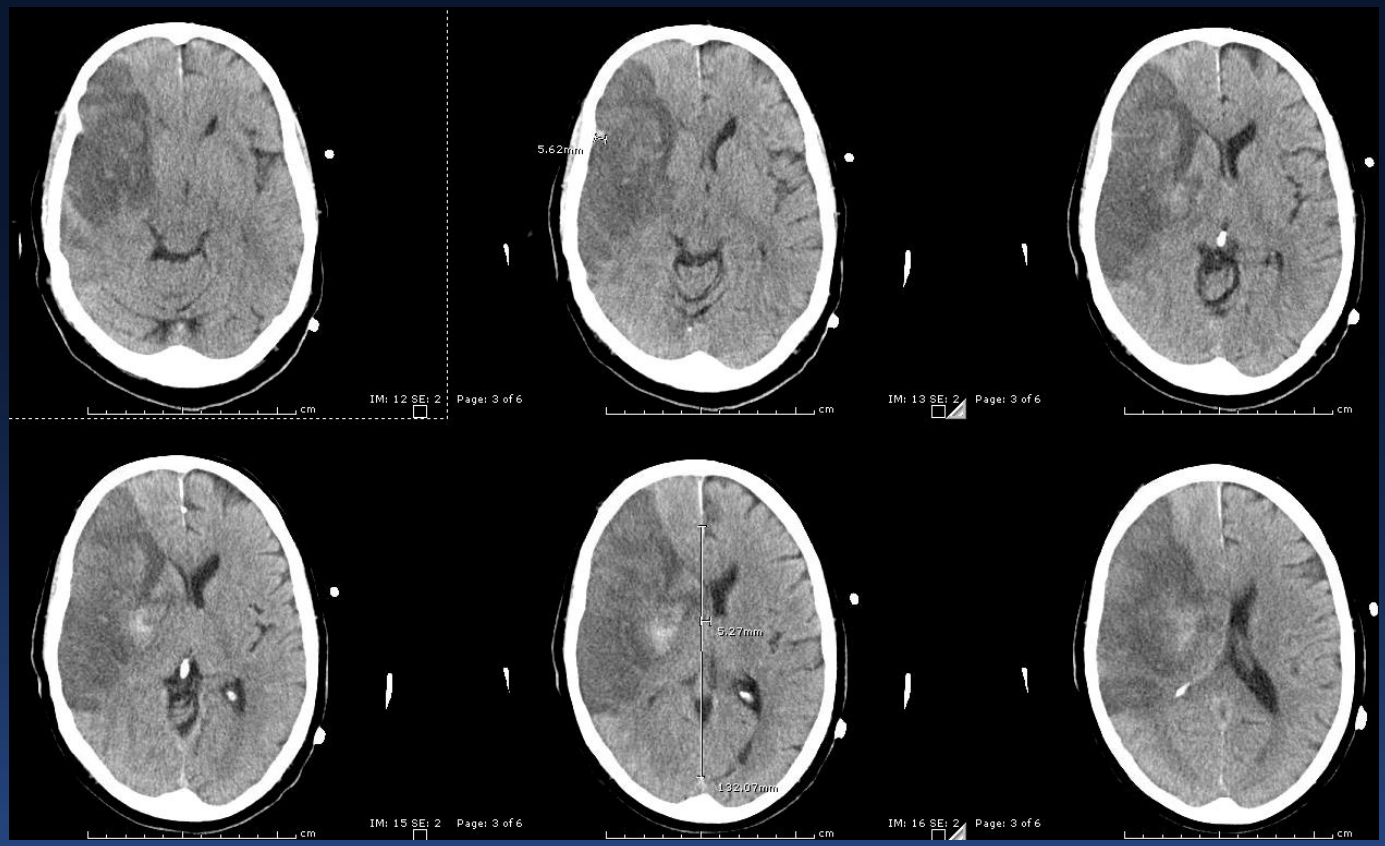
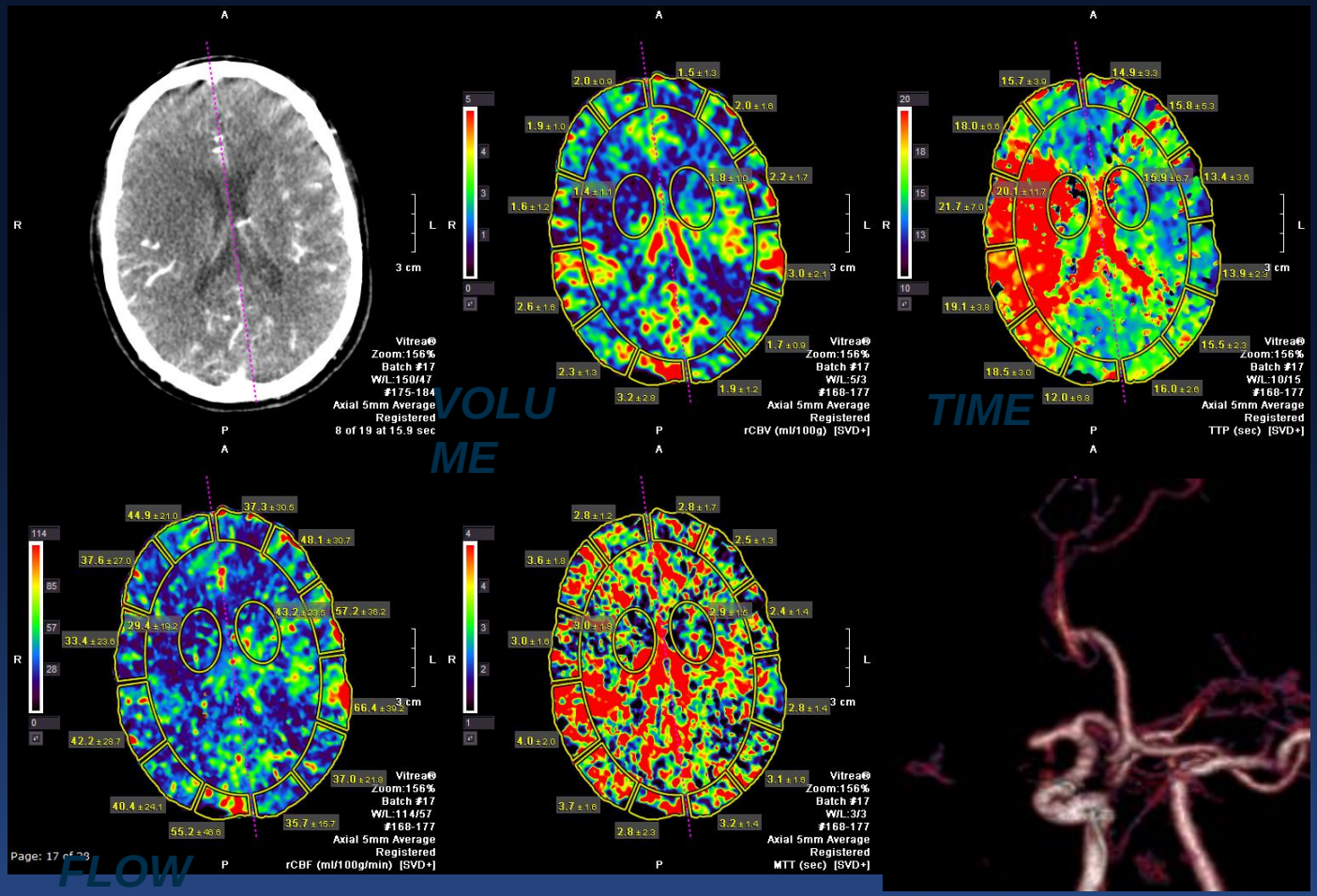
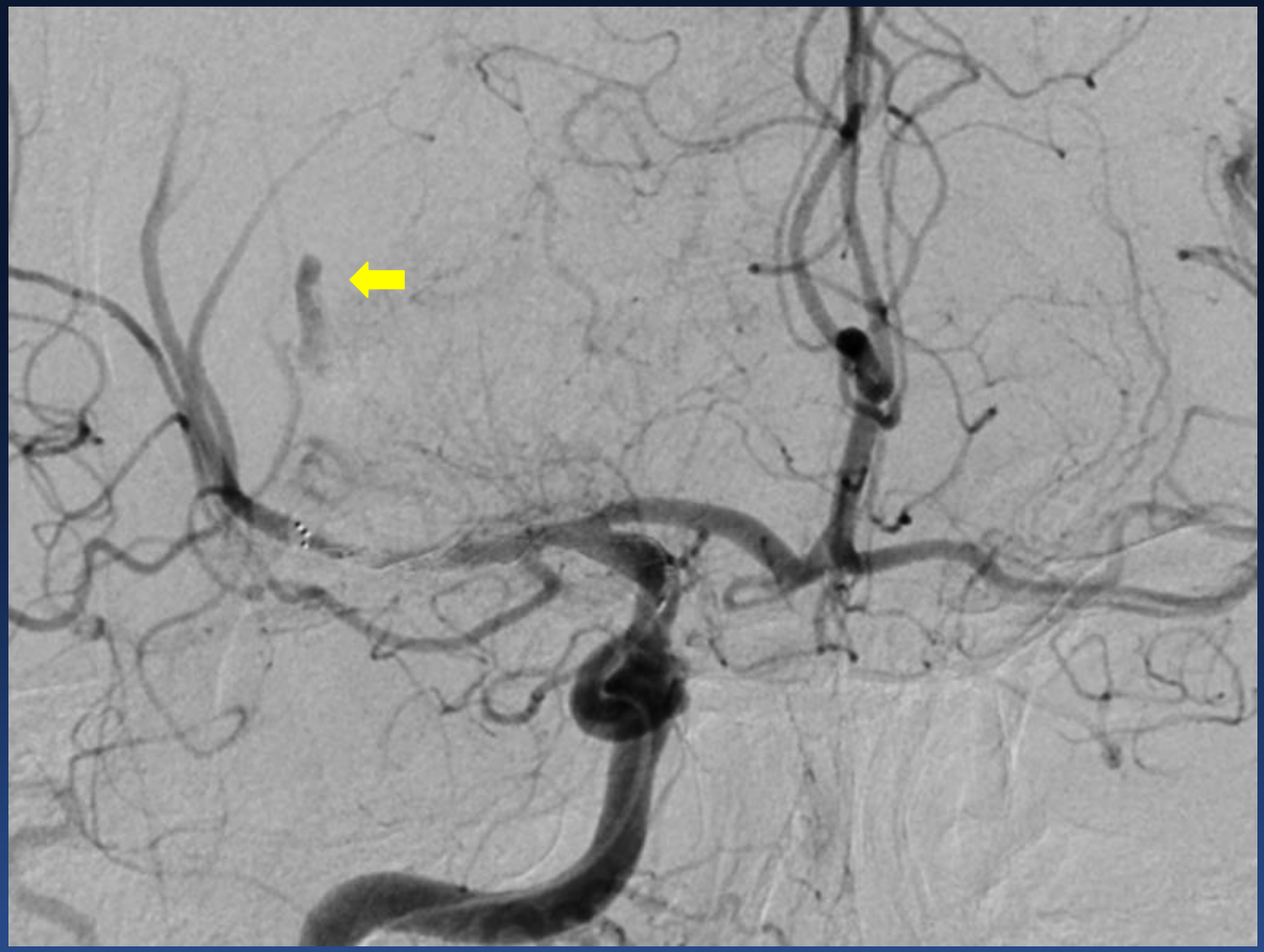
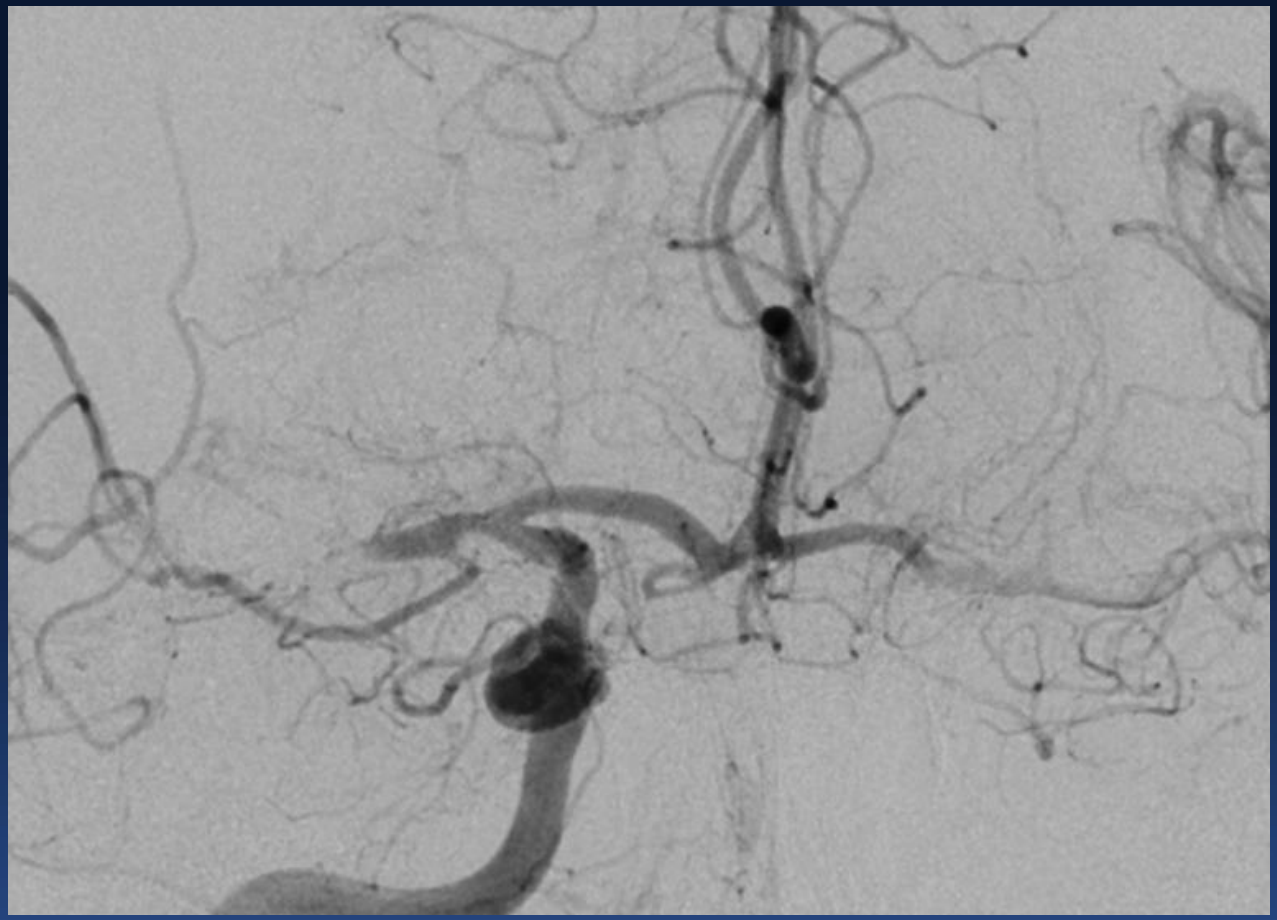

5.62mm
IM: 12 SE: 2
Page: 3 of 6
IM: 13 SE: 2
Page: 3 of 6
5.27mm
132.07mm
IM: 15 SE: 2
Page: 3 of 6
IM: 16 SE: 2
Page: 3 of 6


A
R
L
P
3 cm
Vitrea
Zoom:156%
Batch #17
W/L:150/47
#175-184
Axial 5mm Average
Registered
8 of 19 at 15.9 sec
VOLU
ME
W/L:5/3
#168-177
rCBV (ml/100g) [SVD+]
TIME
W/L:10/15
TTP (sec) [SVD+]
FLOW
W/L:114/57
rCBF (ml/100g/min) [SVD+]
W/L:3/3
MTT (sec) [SVD+]
Page: 17 of 28





Collateral Score Grading

- Best method is debated (Menon AJNR 2011)
- Tan ANJR 2009 method…
  - 0 for absent surface vasculature
  - 1 for 0 - 50% vasculature
  - 2 for 50 - 100% vasculature
  - 3 for normal or supra-normal surface vasculature of the MCA territory

Brain and Behavior

Open Access

Collateral state and the effect of endovascular reperfusion therapy on clinical outcome in ischemic stroke patients

Johannes C. Gerber[1], Marketa Petrova[2], Pawel Krukowski[1], Matthias Kuhn[3], Andrij Abramyuk[1], Ulf Bodechtel[4], Imanuel Dzialowski[5], Kay Engellandt[1], Hagen Kitzler[1], Lars-Peder Pallesen[4], Hauke Schneider[4], Ruediger von Kummer[1], Volker Puetz[4] & Jennifer Linn[1]

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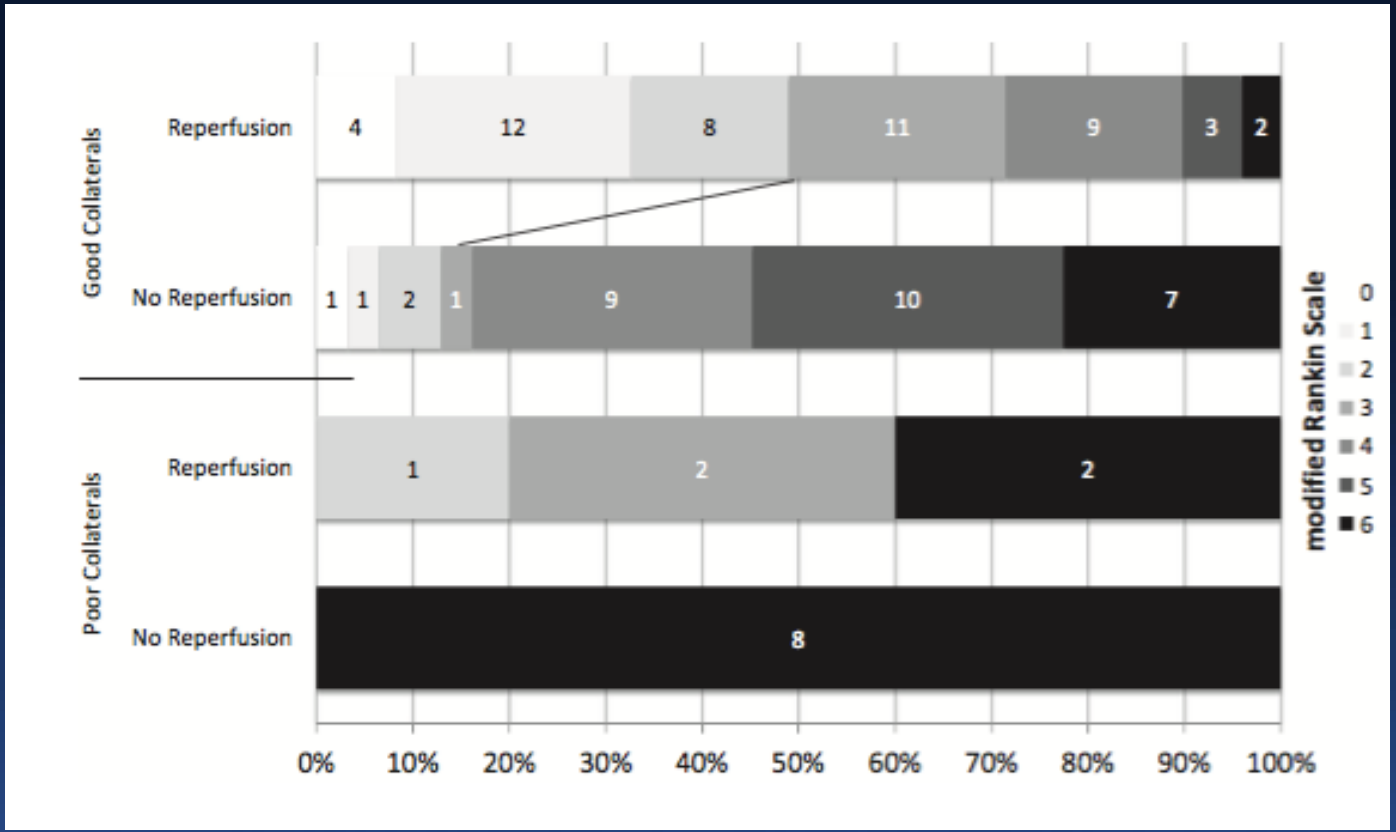
doi: 10.1002/brb3.513

Gerber 2016

- Retrospective review of 180 pts from 1/10-12/12
- Selection:
  - Imaging criteria: no ICH, < 1/3 on NCCT, CTA with large vessel
  - tPA when appropriate
  - ICA, M1, M2

Gerber 2016

- **Baseline characteristics**
  - **Median NIHSS 17 (1-34)**
  - **60% IVT bridging**
  - **88% of EVT were gen anesthesia**
  - **EVT: CAS (25%), Asp (51%), ST (39%) – half of which was combo asp, IA (3%), IA combo**
    - **EVT stopped at TICI 2b or 3 or after 2 hrs**
  - **Onset to angio (250 min), CT to angio (114 min)**
  - **90 day mRS <3 (31%)**
  - **90 day mRS = 6 (20%)**


Good Collaterals
Reperfusion
4
12
8
11
9
3
2
No Reperfusion
1
1
2
1
9
10
7
Poor Collaterals
Reperfusion
1
2
2
No Reperfusion
8
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
modified Rankin Scale
0
1
2
3
4
5
6

Dehkharghan AJNR 2016

- The objective of the study was to identify thresholds of NCCT- ASPECTS and CTA CS that best predict ischemic core volume threshold of <50mL quantified by CTP among patients with AIS.

Performance of CT ASPECTS and Collateral Score in Risk Stratification: Can Target Perfusion Profiles Be Predicted without Perfusion Imaging?

S. Dehkharghani, R. Bammer, M. Straka, M. Bowen, J.W. Allen, S. Rangaraju, J. Kang, T. Gleason, C. Brasher, and F. Nahab

Dehkharghan AJNR 2016

- Thresholds of NCCT-ASPECTS of 9 and CS of 3 with high specificity for finding patients with AIS with core volumes considered ideal for revascularization (<50 ml)
- Threshold of NCCT-ASPECTS of 6 and CS of 1 had a high specificity for identifying patients with AIS with core volumes that made them suboptimal candidates for revascularization (> 50 ml)
- ASPECTS and CS lack sensitivity to estimate true core volume.

Future Advanced Imaging Considerations

- Standardize definition of core, perfusion, mismatch, and CS
- Interrelationships and thresholds between different core measurements (ASPECTS, CBF, CBV) and FIV
- Define Futility Thresholds
- Validation of Semi automated methods across vendor platforms and modalities

Speed to reperfusion is Critical

- Even though physiologic imaging allows more people to be offered treatment at later time points, realize…
- IT IS STILL A RACE

- Streamlining Stroke triage from ambulance to CTP has helped tremendously

Need to Improve the Process

For each 1-hour increase in stroke onset to TICI 2b/3 reperfusion, odds of good clinical outcome decreased by 38%.

Menon et al. Stroke 2014

See. Diagnose. Treat.

SUMMARY

- We have established that endovascular treatment adds major benefit

- Challenge:
- Rapidly offer endovascular treatment to all eligible stroke patients with large vessel occlusions
- Use of Physiologic Imaging when avaialbe to increase eligibility for treatment and improve pt selection
- ASPECTS is reasonable surrogate when physiologic imaging is not available but may not appropriately represent volume of core
- Improve workflow efficiencies to decrease time from arrival to clot removal

- RESULT: Better Outcomes

Thank you!
Questions?