Stanford Stroke Center

DEFUSE 3

Greg Albers, MD

Director, Stanford Stroke Center

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DEFUSE 3

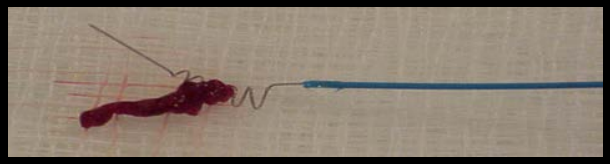
Greg Albers, MD

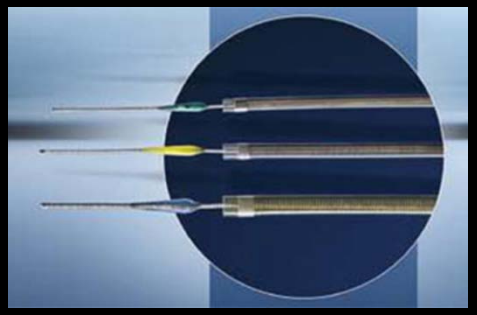
Disclosures: Equity interest and Consultant, RAPID (iSchemaView)

Steering Committee and Core Lab, SWIFT PRIME (Covidien)

THROMBECTOMY DEVICES

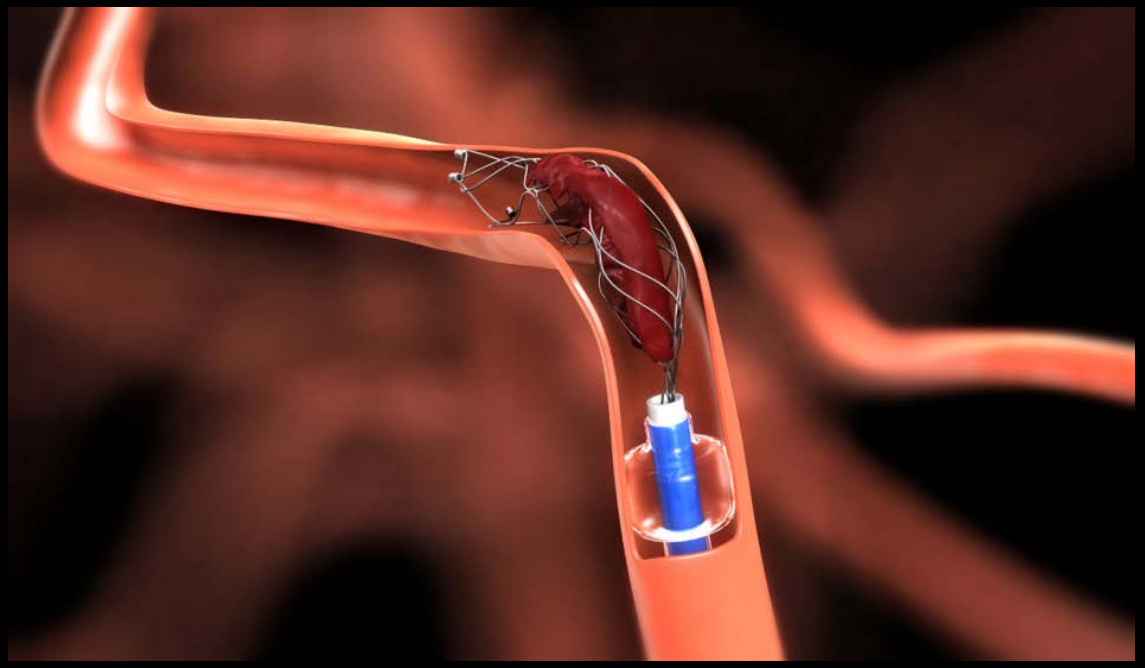
First generation





Second generation

(stent retrievers)



RECENT RANDOMIZED CLINICAL TRIALS OF ENDOVASCULAR THERAPY

- Stent-retriever + IV tPA vs. IV tPA alone
- Fast endovascular treatment (< 6 hrs)
- Large vessel occlusions (ICA / MCA M1)
- Moderate/Severe deficits (NIHSS 17)
- High rates of reperfusion (TICI 2b/3 of 59-88%)
- NEJM publications (all 5)

MR CLEAN REVASCAT ESCAPE SWIFT PRIME EXTEND-IA

New AHA Guidelines 2015

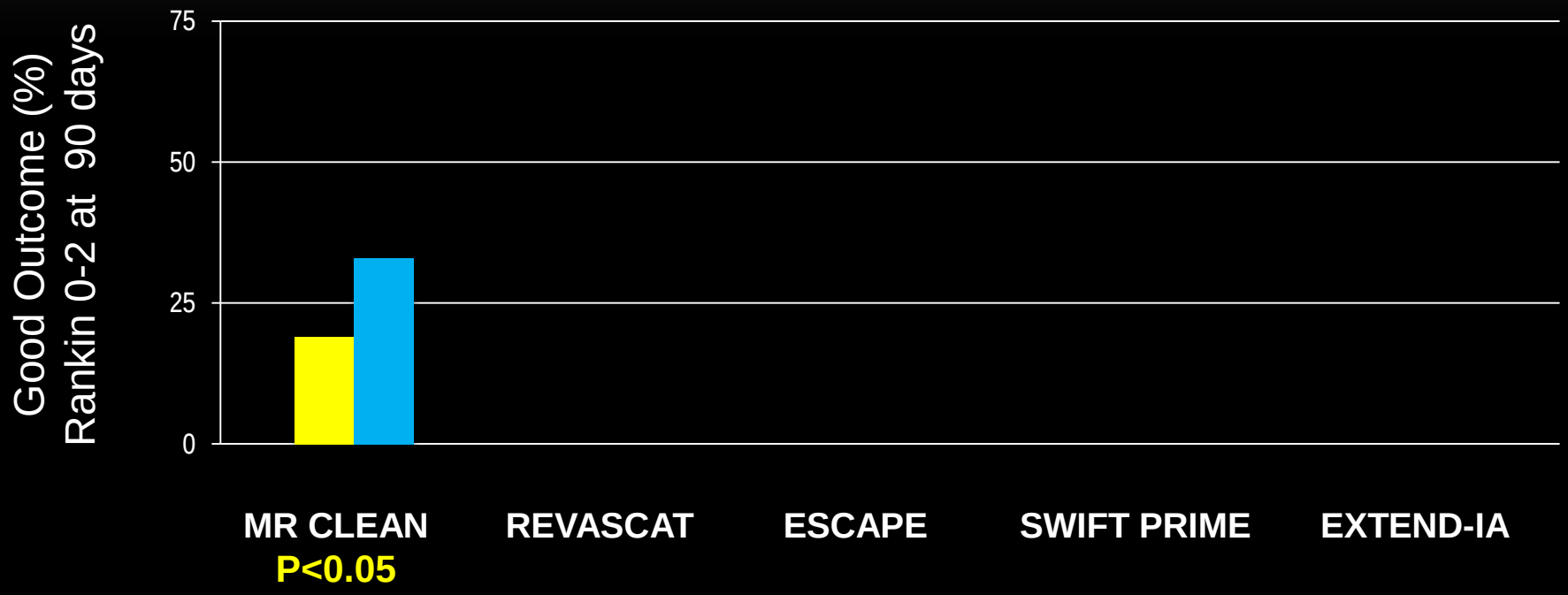
Endovascular therapy with a stent retriever is recommended (Class 1 Level A)

- **Proximal MCA or ICA occlusion**
- **Within 6 hours of symptom onset**

We have a New Standard of Care for Stroke!

RECENT RANDOMIZED CLINICAL TRIALS OF ENDOVASCULAR THERAPY

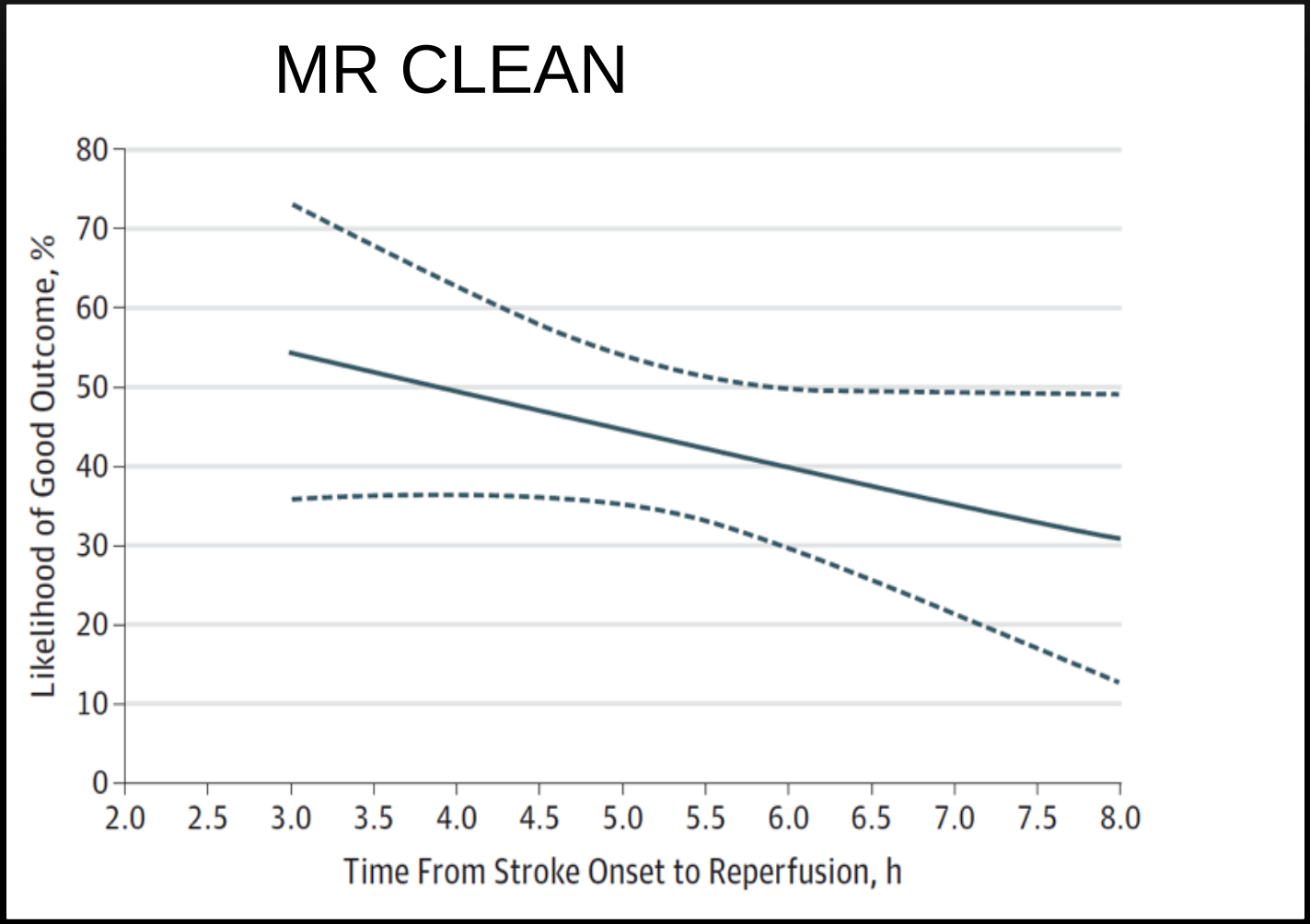
RECENT RANDOMIZED CLINICAL TRIALS OF ENDOVASCULAR THERAPY



Endo-vascular **33%**

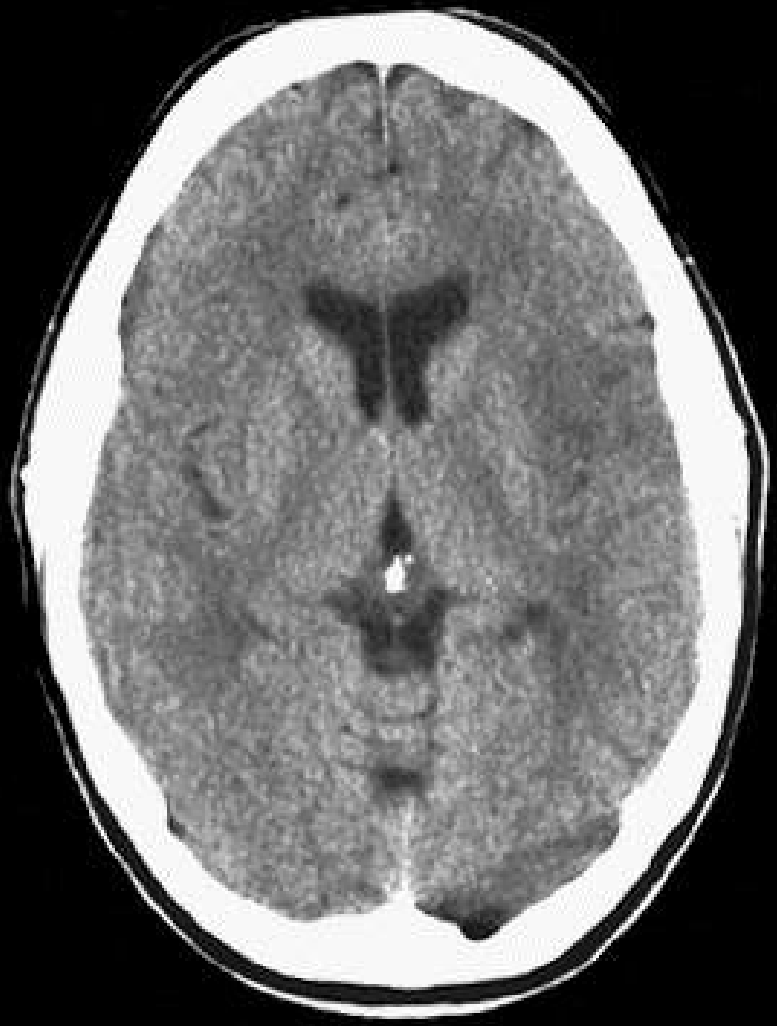
Control 19%

GOOD OUTCOME RATES FOLLOWING ENDOVASCULAR REPERFUSION

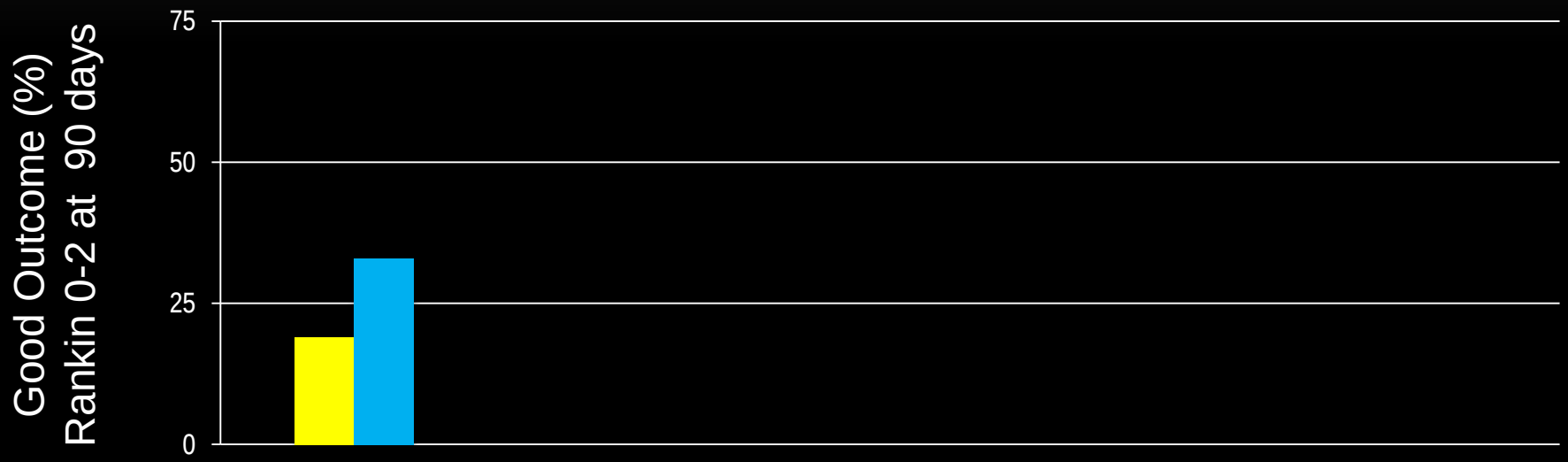


Fransen P., et al. JAMA Neurol. 2015

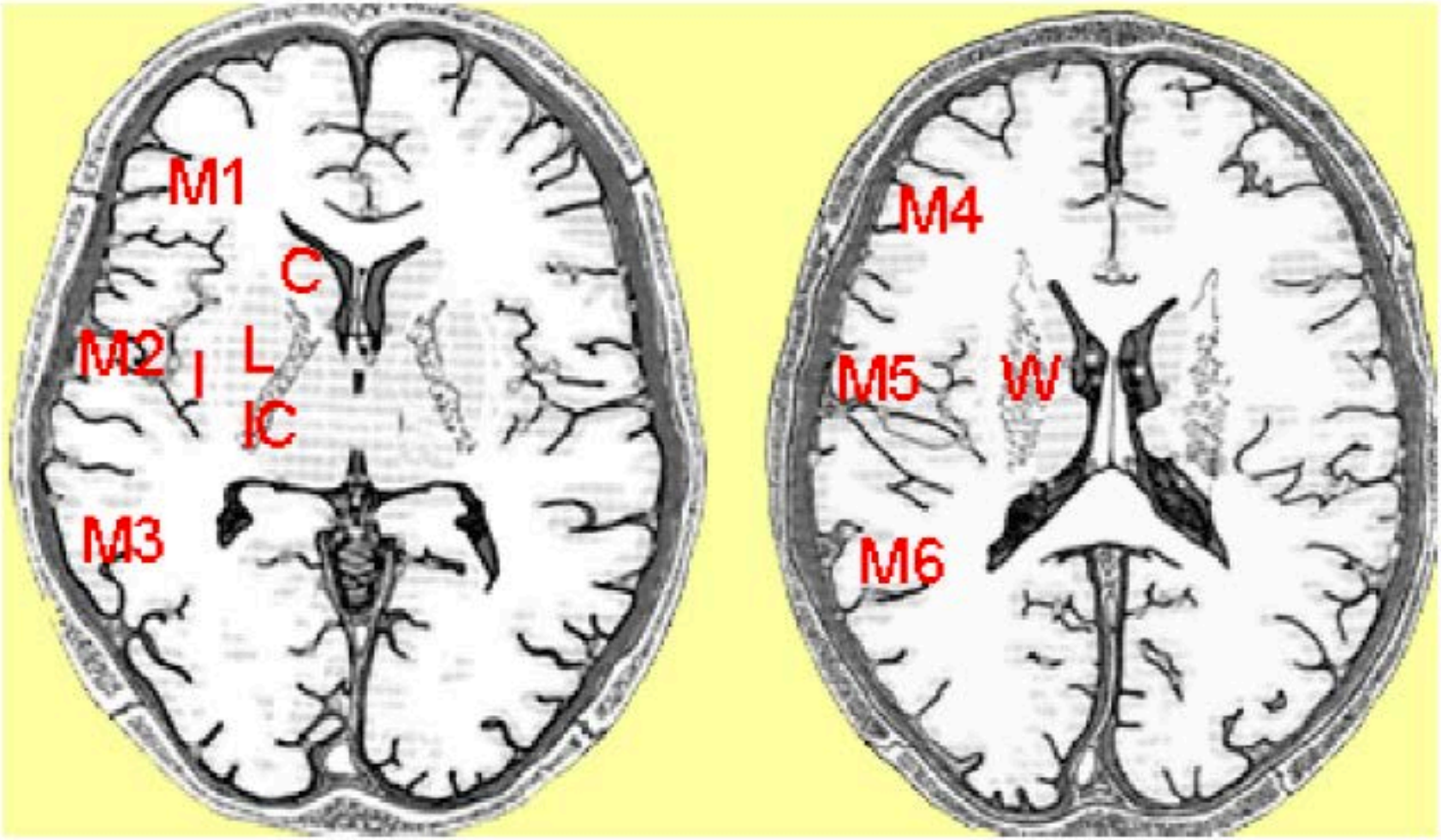
Non contrast CT scan



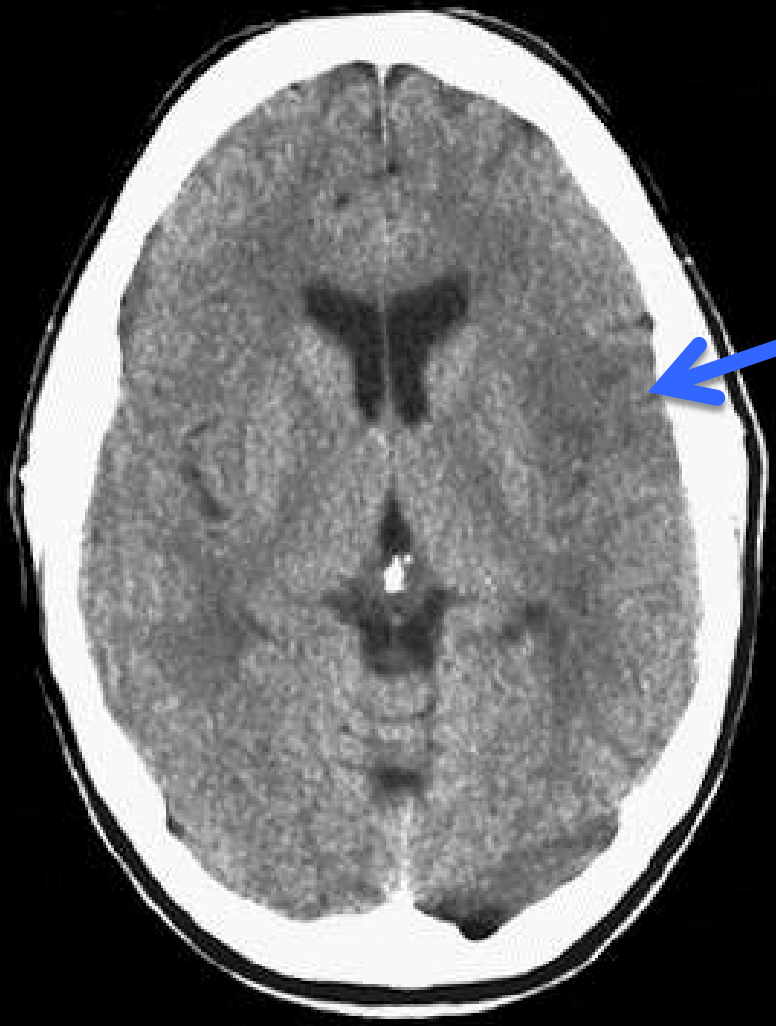
RECENT RANDOMIZED CLINICAL TRIALS OF ENDOVASCULAR THERAPY



ASPECT SCORE



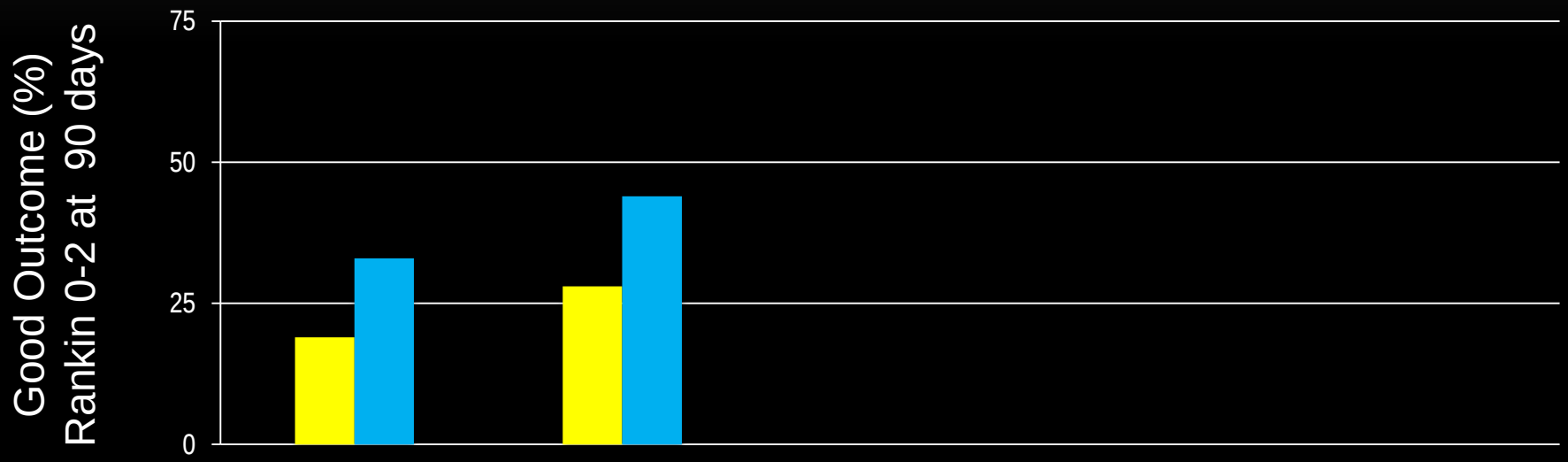
CT scan: early signs of stroke
ASPECTS SCORE



M2 + I

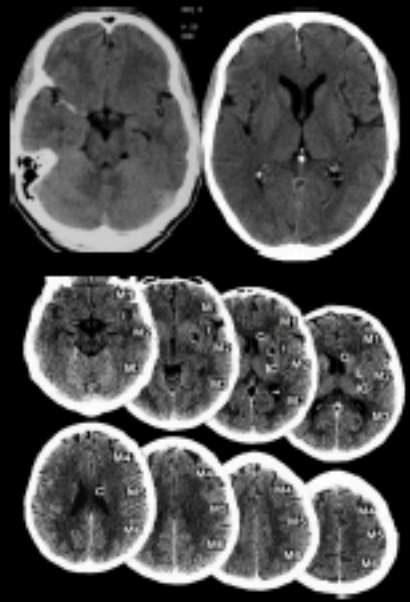
ASPECTS = 8

NEW RANDOMIZED CLINICAL TRIALS OF ENDOVASCULAR THERAPY

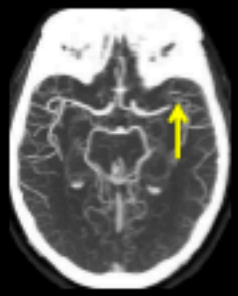


	MR CLEAN P<0.05 CT	REVASCAT P<0.05 ASPECTS	ESCAPE ASPECTS + Collaterals	SWIFT PRIME	EXTEND-IA
Endo-vascular	**33%**	**44%**			
Control	19%	28%			

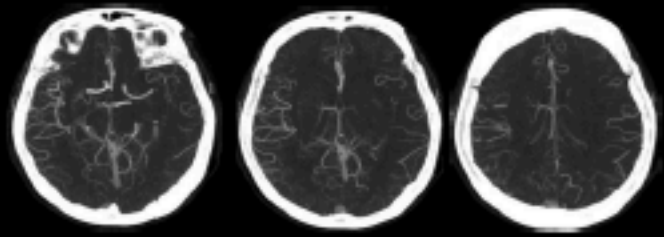
ESCAPE Imaging Selection Criteria:
Good scan, proximal occlusion, mod/good collaterals



NCCT ASPECTS 6-10



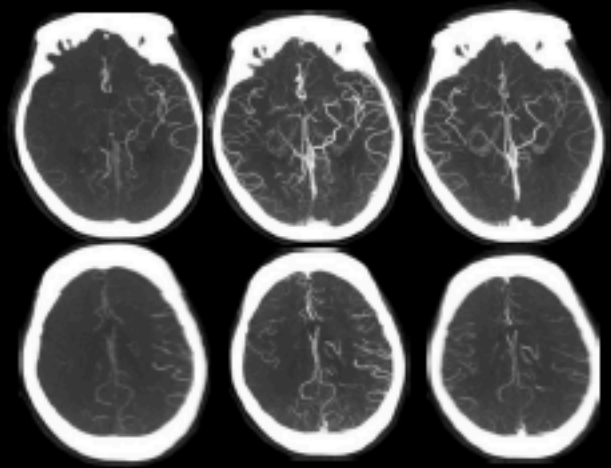
CTA: ICA T or M1 occl



Single phase CTA: mod/good collaterals

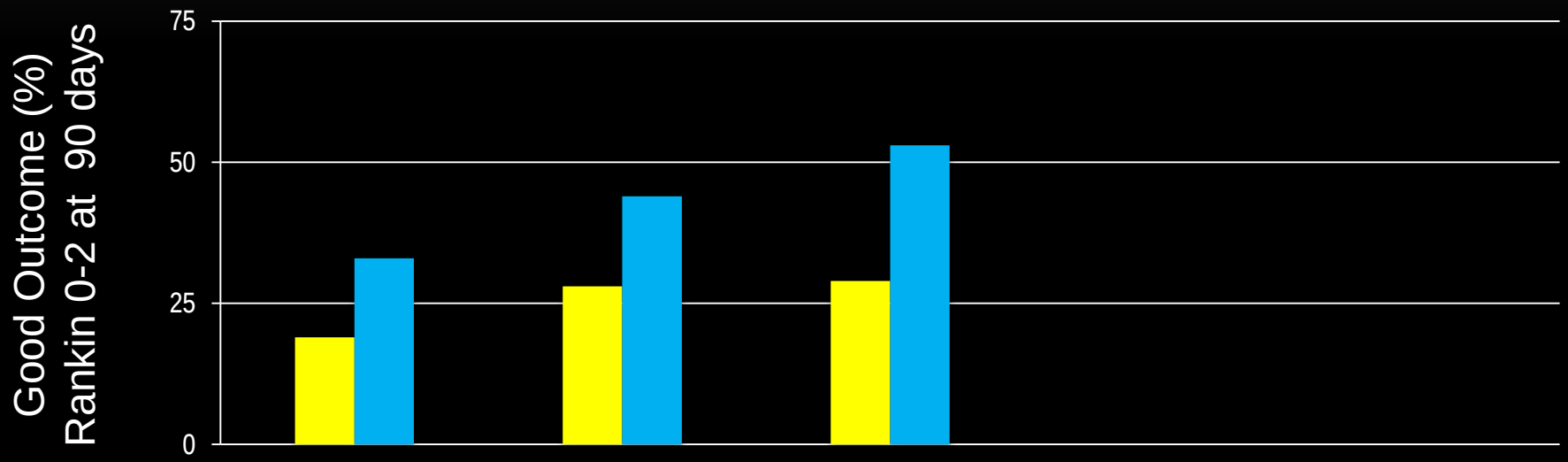
or

1st 2nd 3rd phase



Multiphase CTA: mod/good collaterals

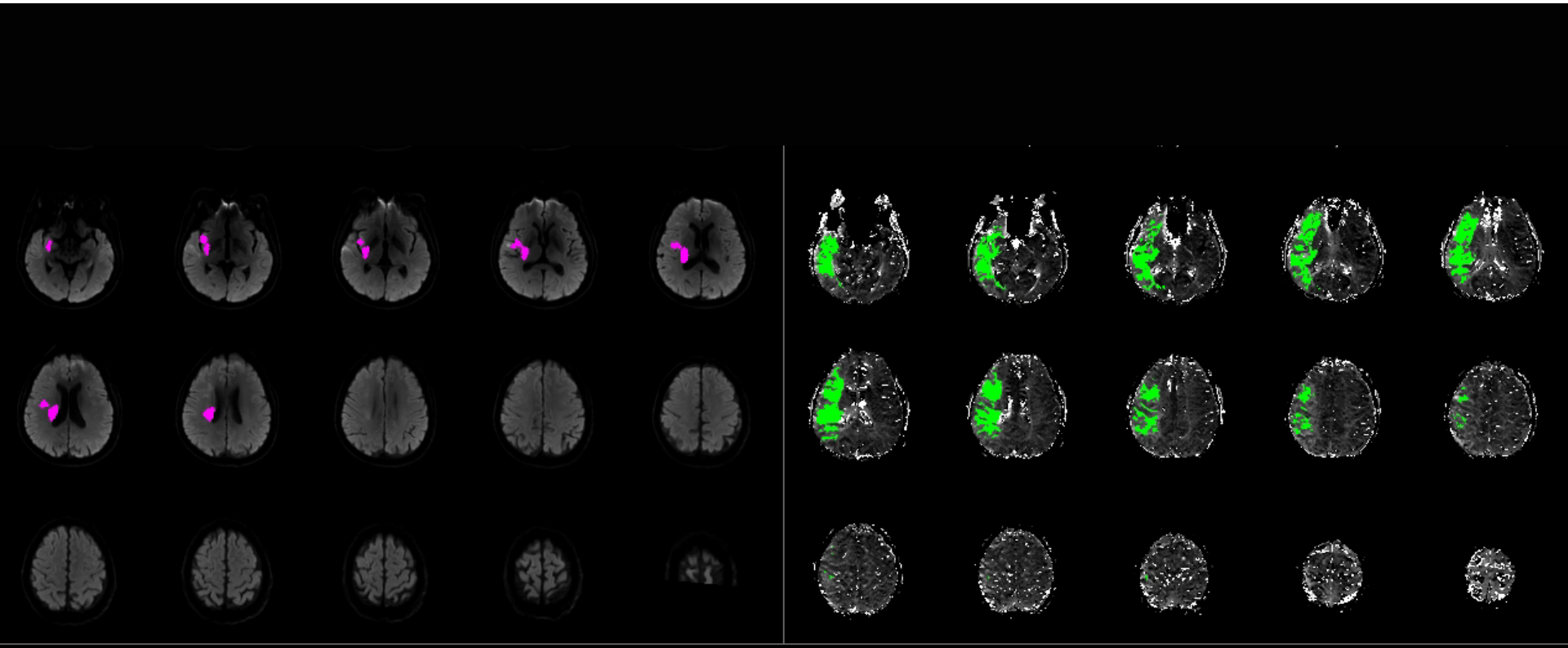
RECENT RANDOMIZED CLINICAL TRIALS OF ENDOVASCULAR THERAPY



	MR CLEAN P<0.05 CT	REVASCAT P<0.05 ASPECTS	ESCAPE P<0.001 Collaterals	SWIFT PRIME CTP and MRI Target mismatch	EXTEND-IA
Endo-vascular	**33%**	**44%**	**53%**		
Control	19%	28%	29%		

RAPID MRI Target mismatch

Mismatch map: directly compare volumes of DWI and hypoperfusion



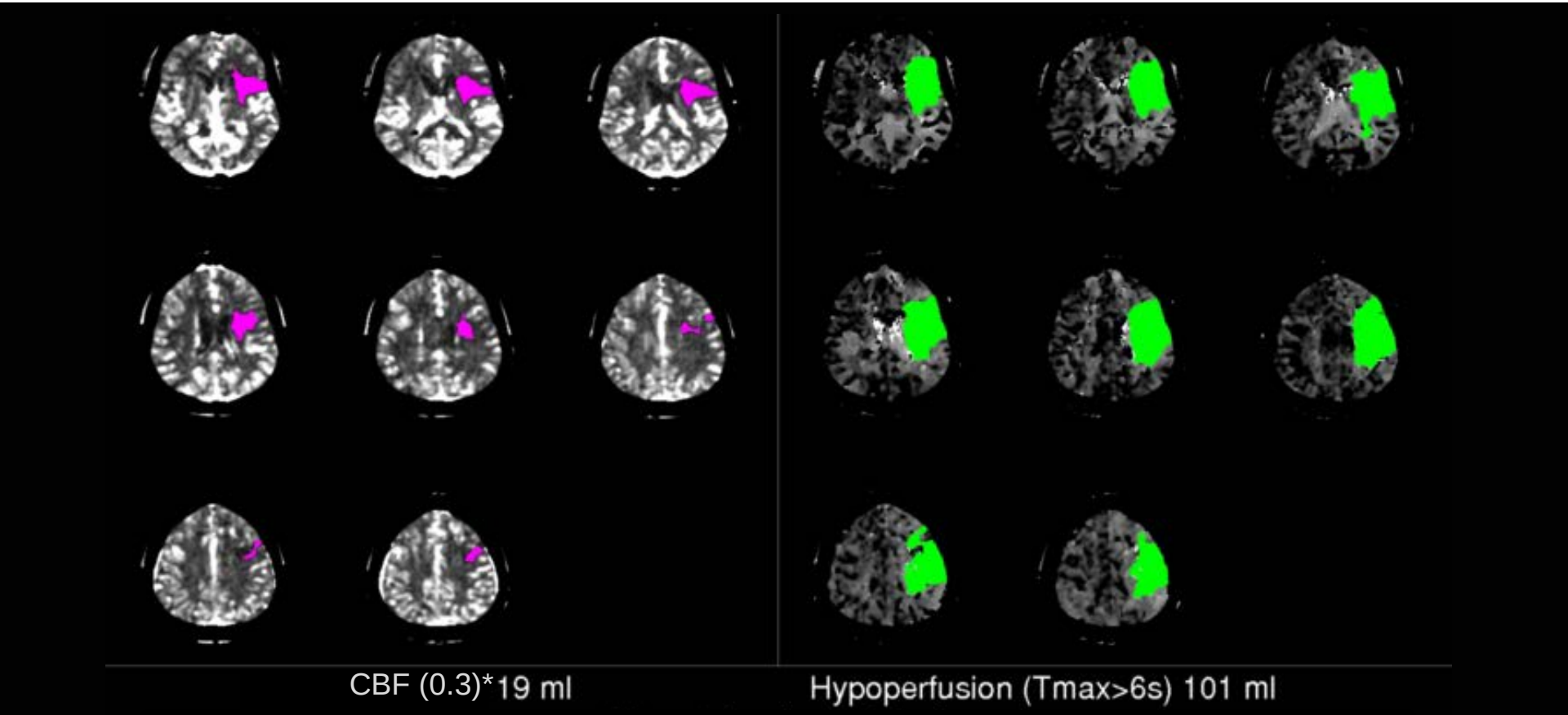
DWI (ADC<620) volume 10 ml

Perfusion (Tmax>6s) volume 76 ml

Mismatch volume: 66 ml
Mismatch ratio: 7.6

RAPID CTP Target mismatch

Mismatch map: directly compare volumes of ischemic core & critical hypoperfusion

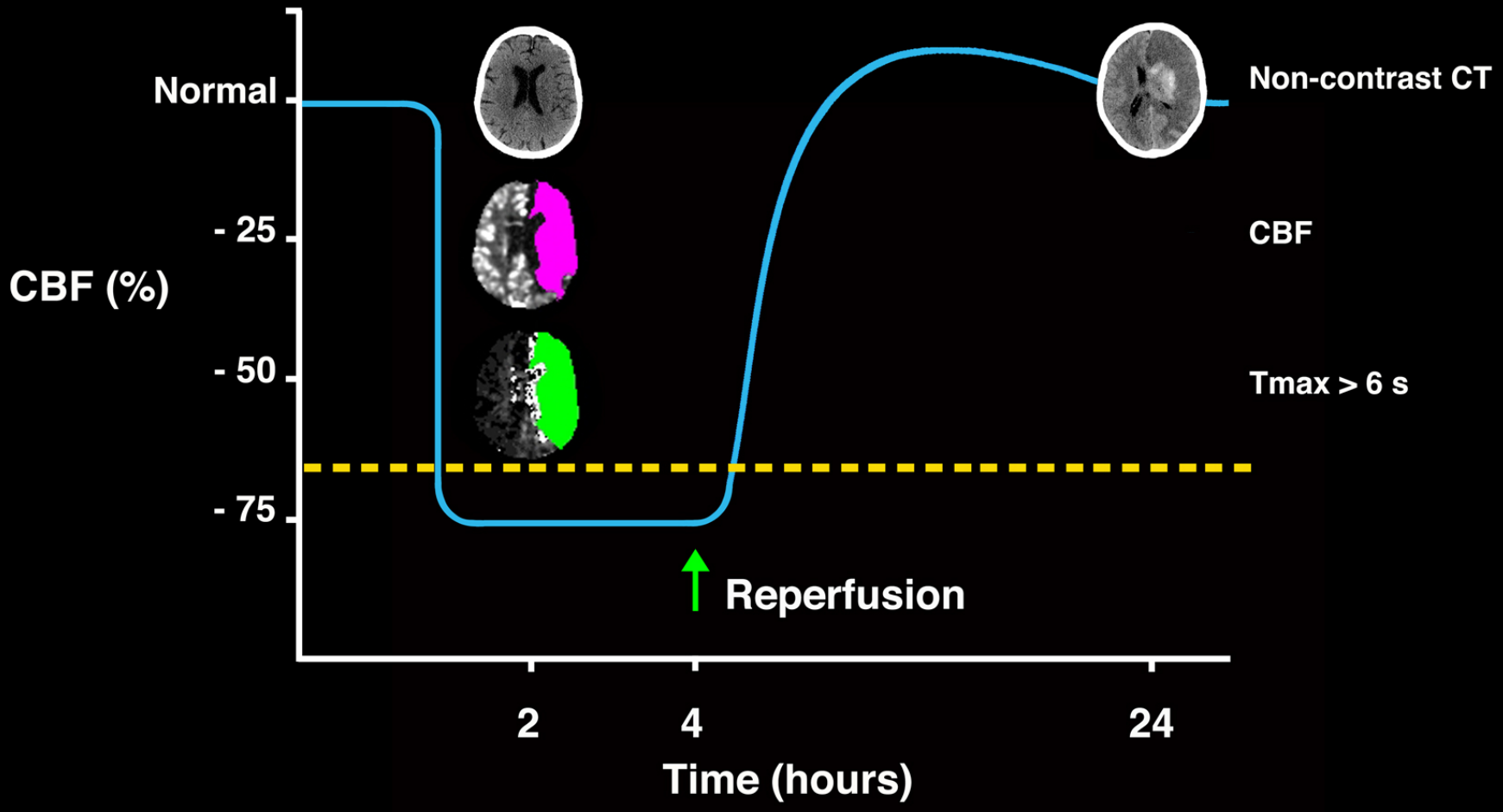


*tissue with >70% reduction in CBF predicts DWI lesion volume; median absolute error, 9 ml

Cereda et al. JCBFM 2015

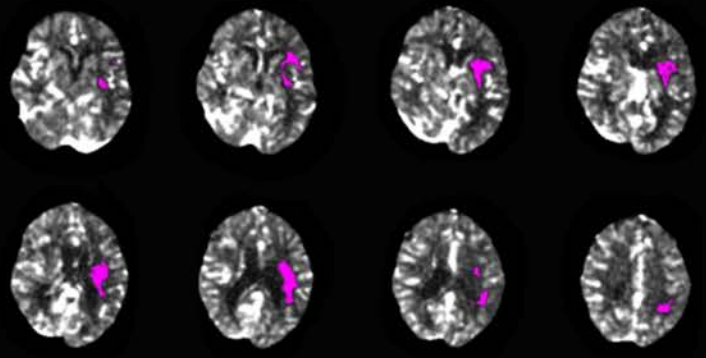
STROKE EVOLUTION

Large ischemic core

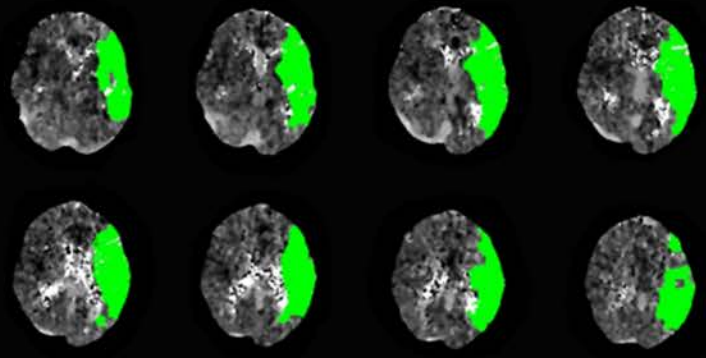


SWIFT PRIME CASE: SMALL CORE WITH COMEPLETE REPEFUSION

Baseline CTP

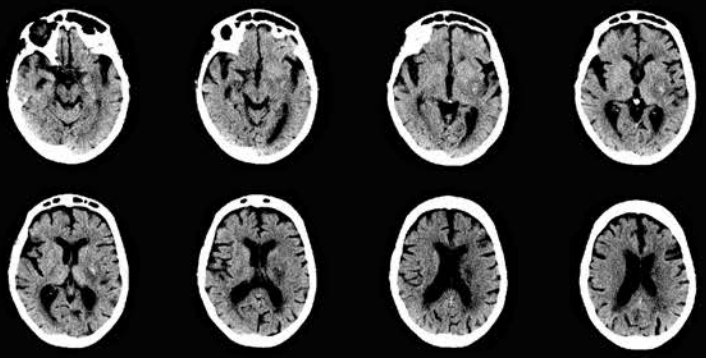


CBF (< 30%): 11 ml

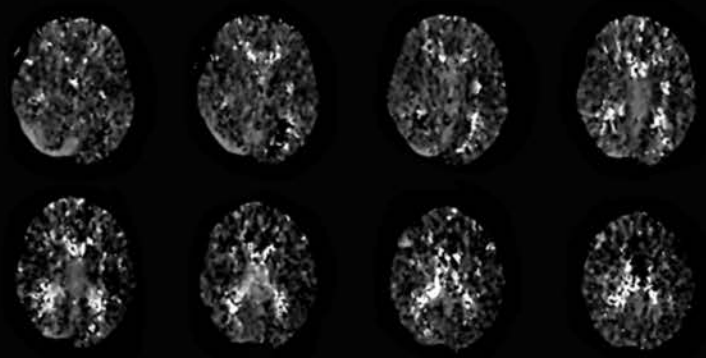


Perfusion (Tmax>6s) volume: 151 ml

24 h Follow Up CT/CTP



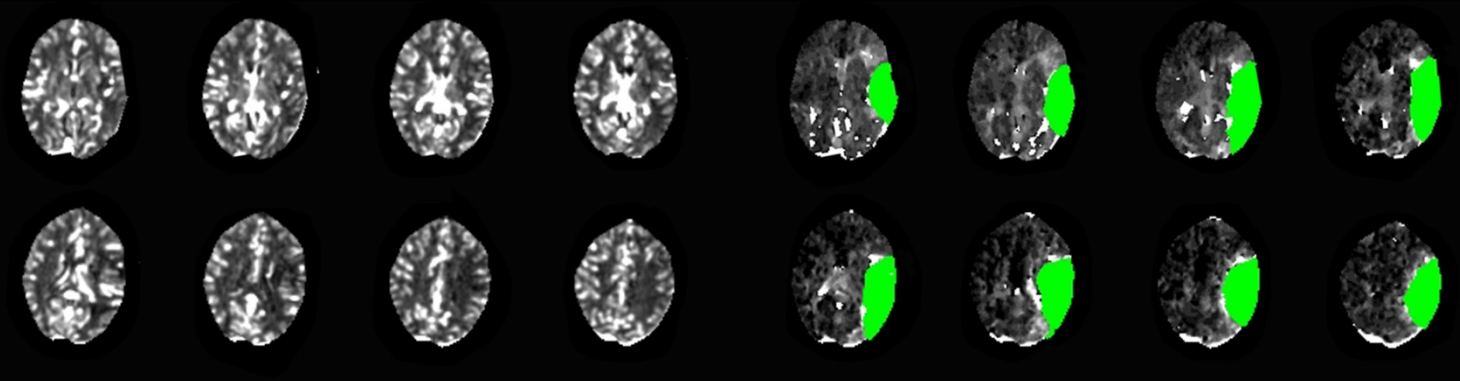
Infarct volume: 12 ml



100% Reperfusion

NO CORE WITH COMPLETE REPERFUSION

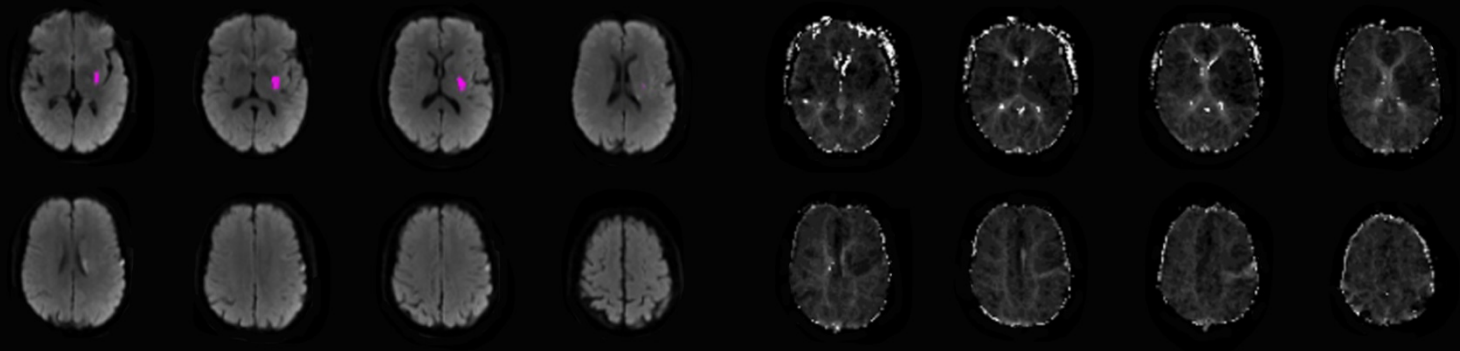
Baseline CTP



CBF (0.3 threshold) 0 ml

Hypoperfusion (Tmax>6s) 135 ml

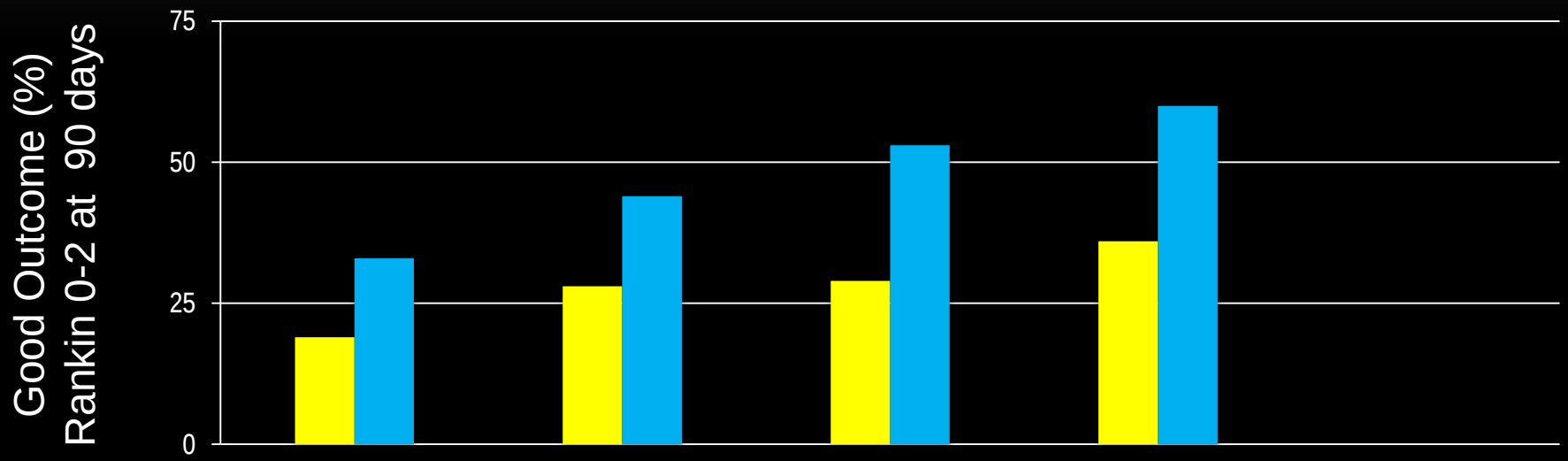
27 h Follow Up MRI



Infarct Volume 1 ml

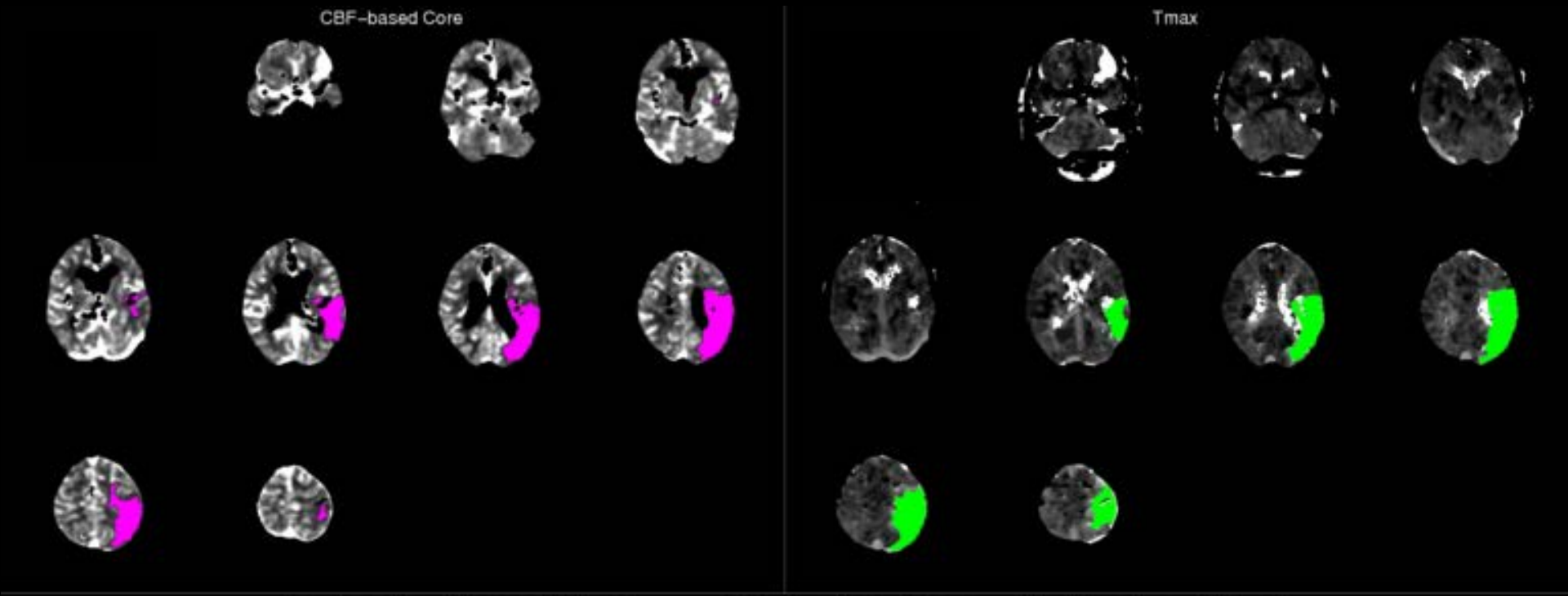
100% Reperfusion

RECENT RANDOMIZED CLINICAL TRIALS OF ENDOVASCULAR THERAPY



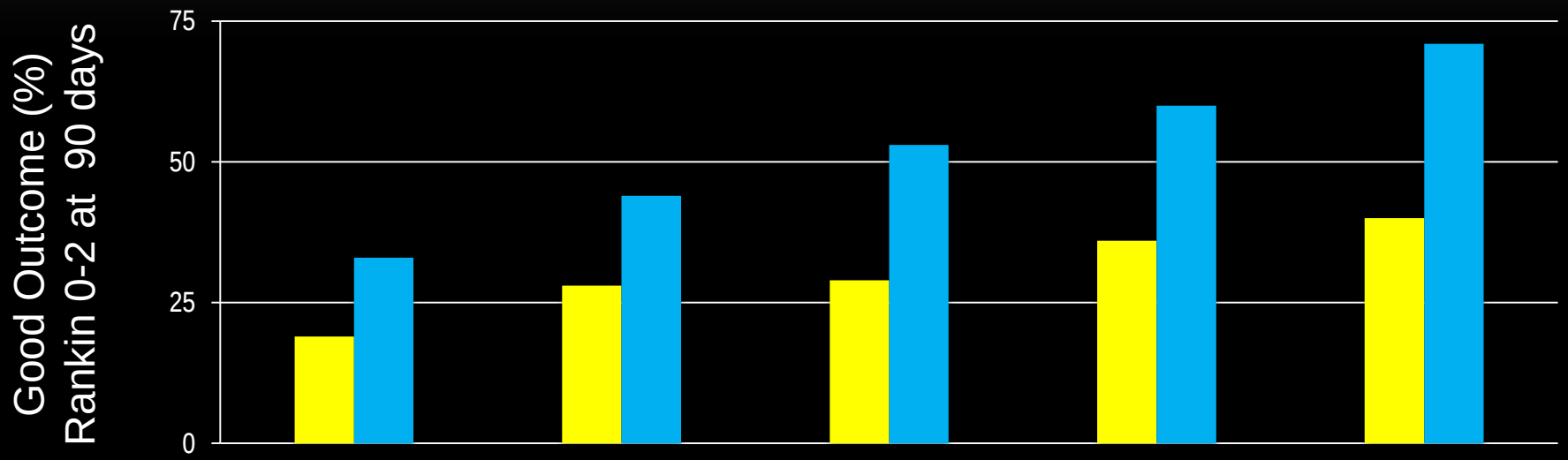
	MR CLEAN P<0.05 CT	REVASCAT P<0.05 ASPECTS	ESCAPE P<0.001 Collaterals	SWIFT PRIME P<0.001 CTP/MRI (90%)	EXTEND-IA CTP (100%)
Endo-vascular	**33%**	**44%**	**53%**	**60%**	
Control	19%	28%	29%	36%	

EXTEND-IA: Ischemic Core >70 ml



Ischemic Core: 73 ml Perfusion (Tmax>6s) lesion: 88 ml
Mismatch ratio: 1.2 Absolute Mismatch Difference: 16 ml
Mismatch > 1.2: YES
Absolute mismatch > 10 ml: YES
Ischemic Core < 70 ml: NO
Randomize patient: NO

RECENT RANDOMIZED CLINICAL TRIALS OF ENDOVASCULAR THERAPY



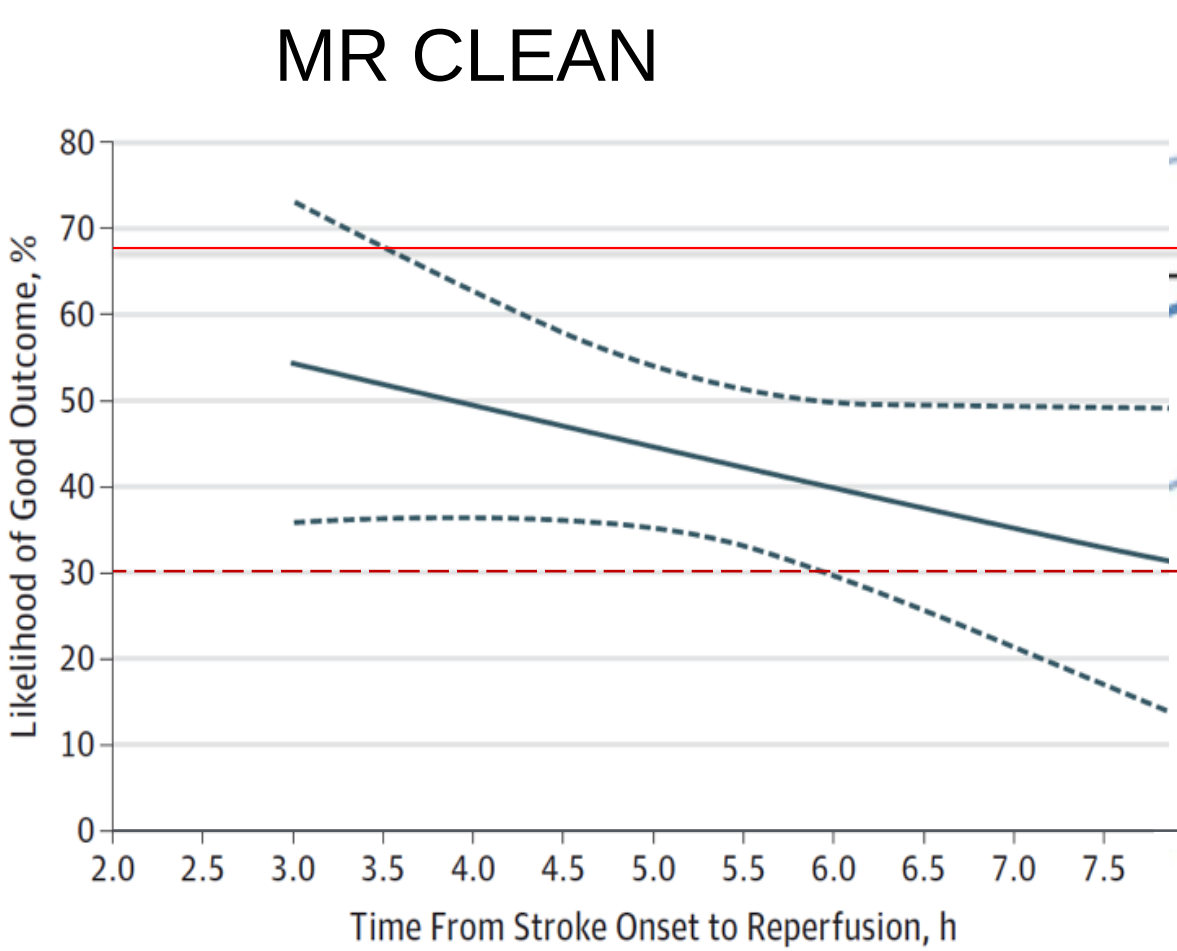
	MR CLEAN P<0.05 CT	REVASCAT P<0.05 ASPECTS	ESCAPE P<0.001 Collaterals	SWIFT PRIME P<0.001 CTP/MRI 90%	EXTEND-IA P<0.01 CTP 100%
Endo-vascular	**33%**	**44%**	**53%**	**60%**	**71%**
Control	19%	28%	29%	36%	40%

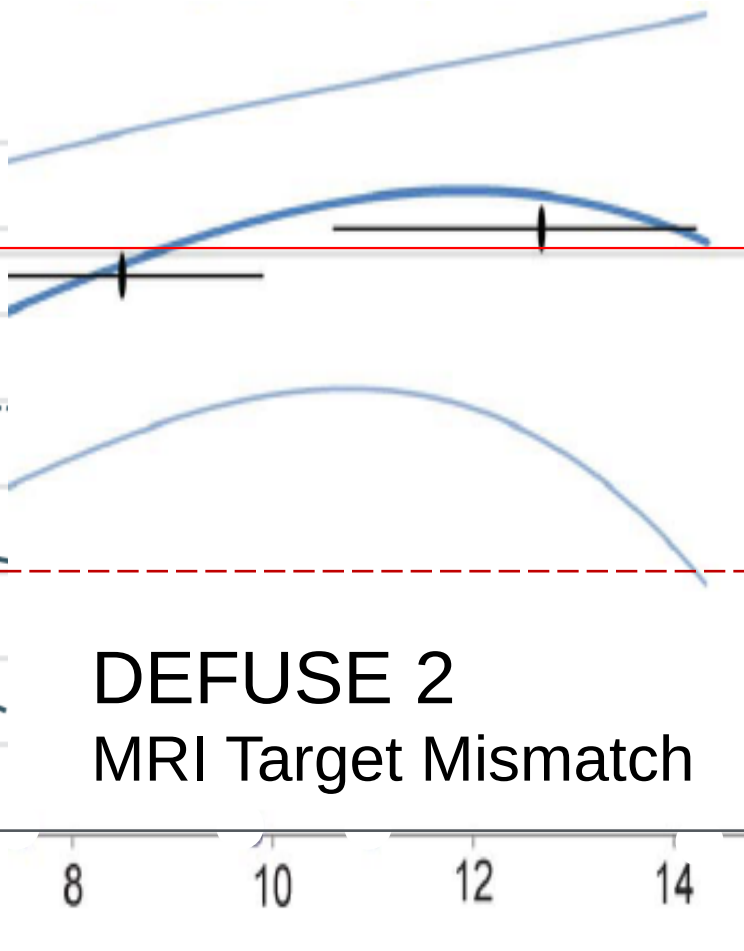
FUTURE DIRECTIONS

EXTENDING THE WINDOW FOR REPERFUSION THERAPY WITH ADVANCED IMAGING:

- Endovascular therapy
  - DEFUSE 3 (6-16 hours) — CTP or MR (Target mismatch)
  - DAWN (6-24 hours) — CTP or MR (small core)
  - POSITIVE (6-12 hours) — CTP or MR (local criteria)
- Intravenous thrombolysis
  - EXTEND (4.5-9 hours) — CTP or MR (Target mismatch)
  - ECASS 4 (4.5-9 hours) — MRI (local mismatch criteria)

GOOD OUTCOME RATES FOLLOWING ENDOVASCULAR REPERFUSION



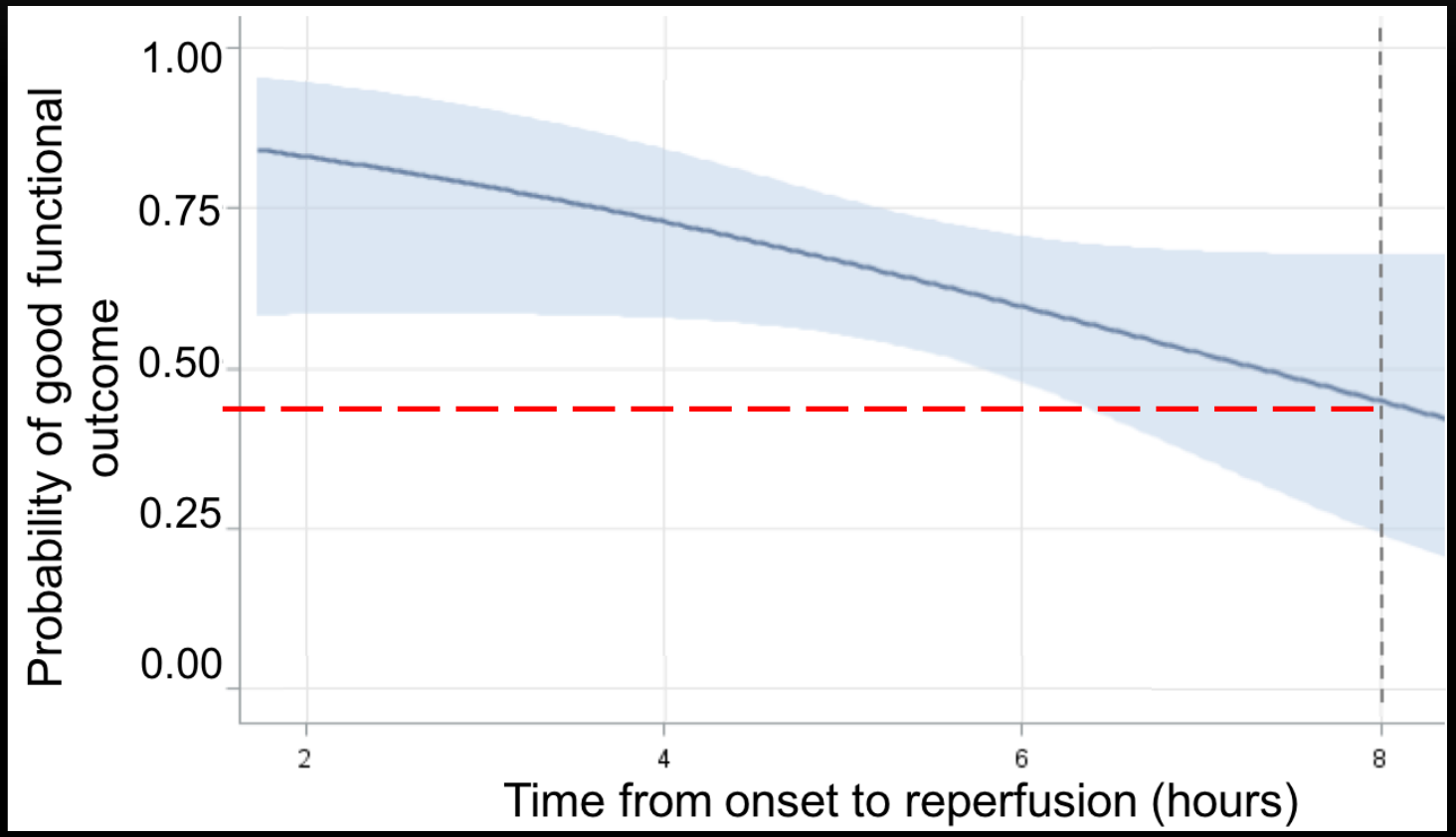


Fransen P., et al. JAMA Neurol. 2015

Lansberg M., et al. Neurology. 2015

CRISP: CT PERFUSION STUDY

ALL REPERFUSED PATIENTS (N=164)



p=0.08

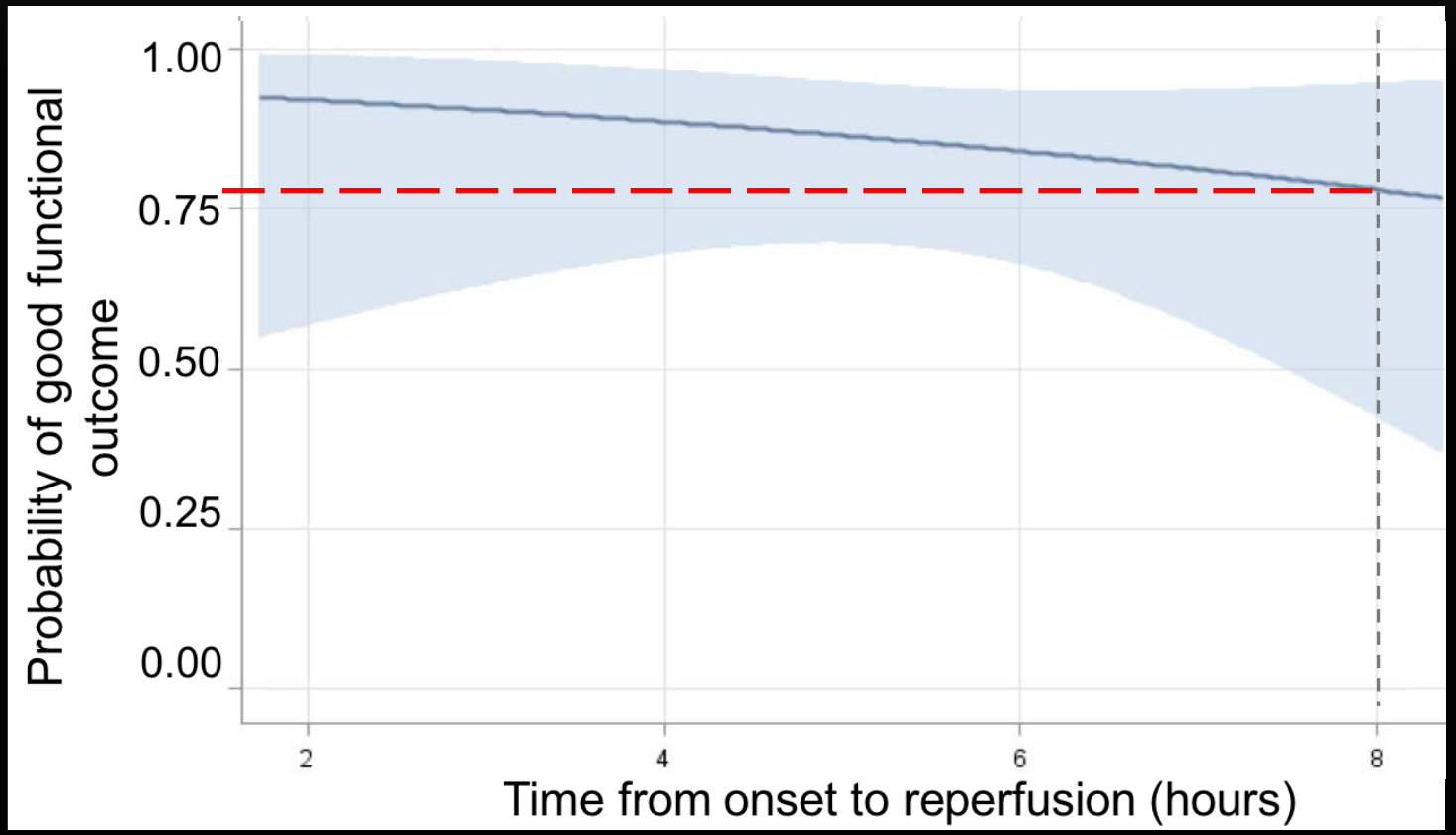
95% C.I.

Lansberg, et al. ISC 2016

Tsai, et al. ISC 2016

CRISP:

REPERFUSED CTP TARGET MISMATCH (N=111)



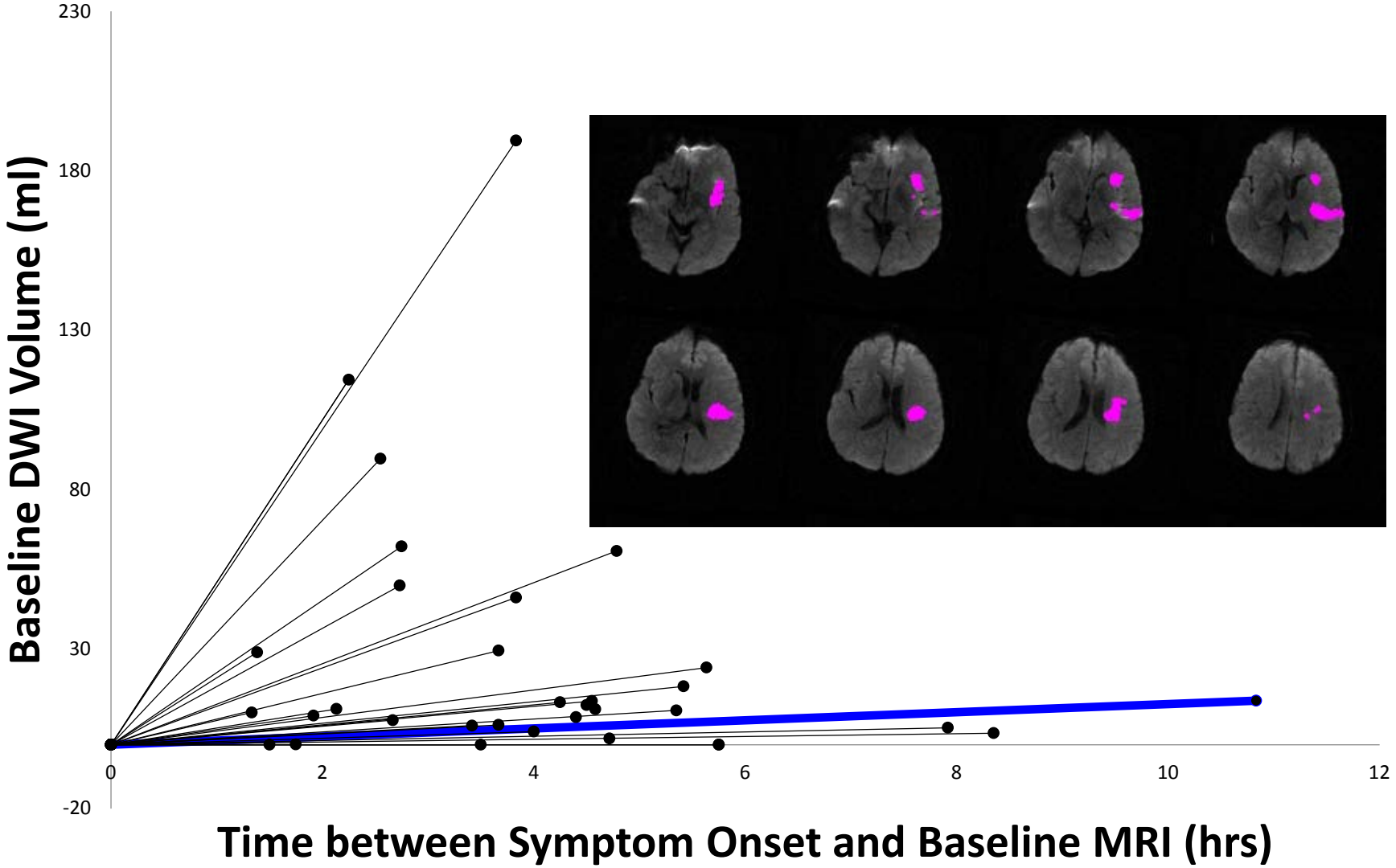
p=0.47

95% C.I.

Tsai, et al. ISC 2016

DEFUSE 2

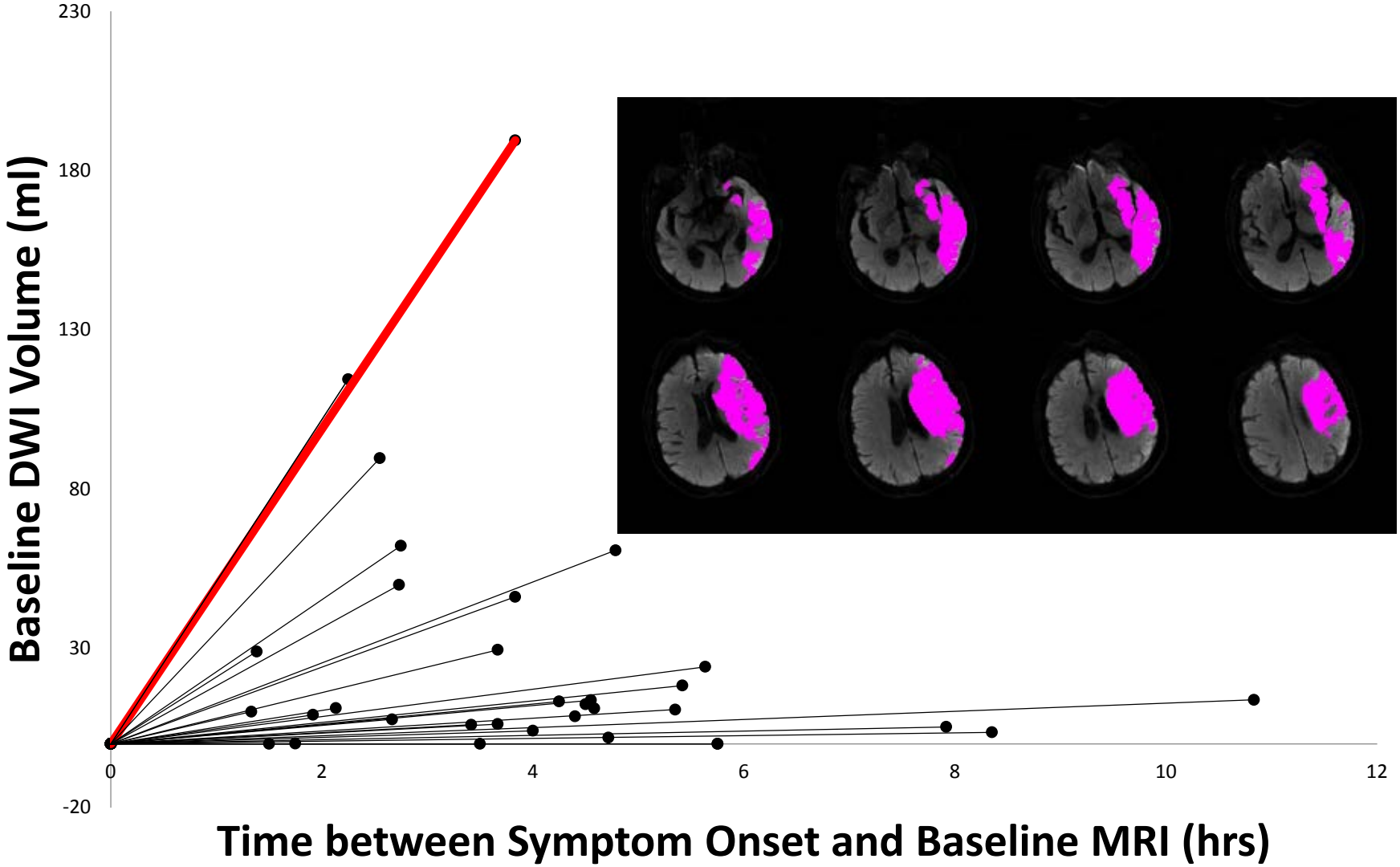
Initial Growth Rate: Known Onset & M1 Occlusion



Wheeler HM, et al. Int J Stroke. 2015

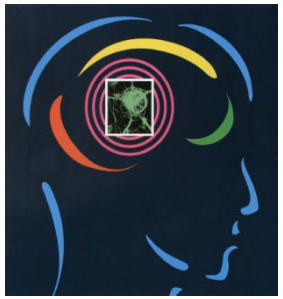
DEFUSE 2

Initial Growth Rate: Known Onset & M1 Occlusion



Wheeler HM, et al. Int J Stroke. 2015

Stanford MEDICINE



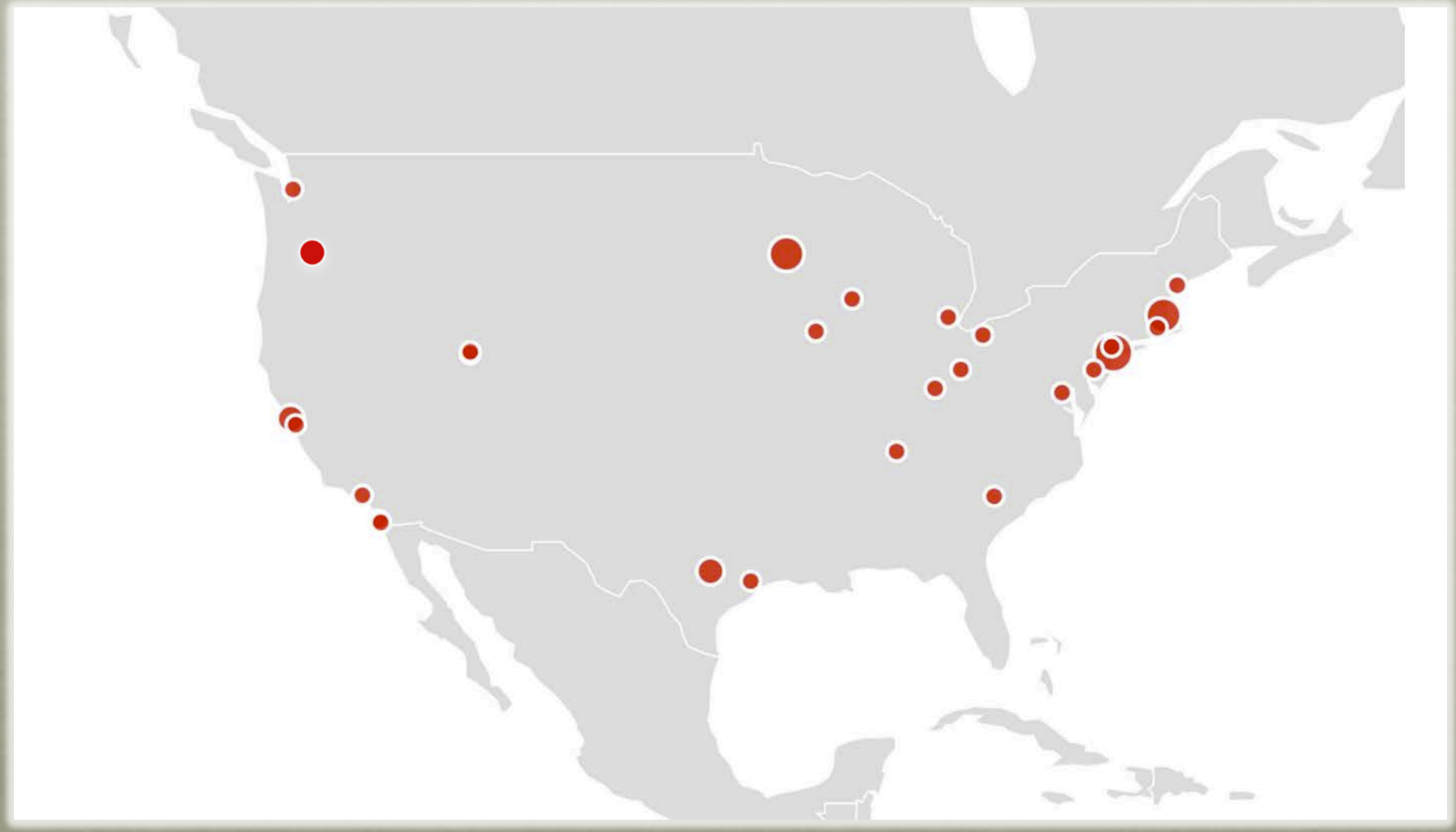
defuse·3

NIH StrokeNet

PREVENTION | TREATMENT | RECOVERY

Funded by a Grant from the National Institutes of Health

DEFUSE 3 Sites



DEFUSE 3: Study Design

- Prospective, Randomized, Open-treatment, Blinded Endpoint, Adaptive trial
- 476 patients at 45 sites
- 1:1 randomization: endovascular vs. medical therapy

6-16 hours after stroke onset

Clinical Inclusion Criteria

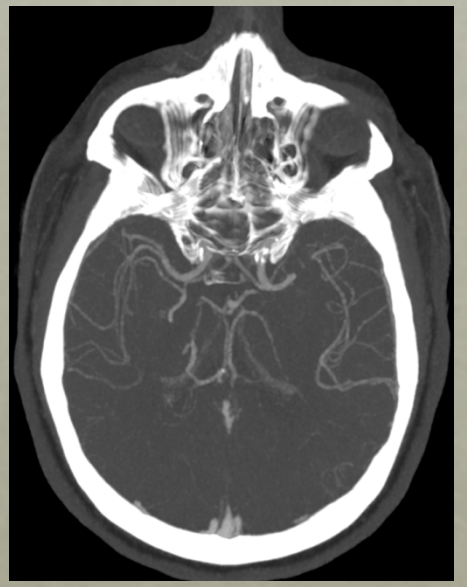
- Signs and symptoms consistent with an acute anterior circulation stroke
- Age 18-90 years
- Baseline NIHSSS ≥ 6 immediately prior to randomization
- Endovascular treatment (femoral puncture) between 6-16 hours of stroke onset (onset is defined as time last known well)
- Pre-stroke mRS score 0-2 (= functionally fully independent for all ADLs)
- Patient or Legally Authorized Representative has signed Informed Consent

Clinical Exclusion Criteria

- Other serious, advanced, or terminal illness or life expectancy <6 months
- Pre-existing neurological /psychiatric disease that would confound evaluations
- Pregnancy
- Unable to undergo a contrast brain perfusion scan with either MRI or CT
- Known allergy to iodine that precludes an endovascular procedure
- Treated with tPA >4.5 hrs after last known well (ECASS III criteria apply if 3-4.5)
- Known hereditary or acquired hemorrhagic diathesis, coagulation factor deficiency; oral anticoagulant with INR > 3 (recent use of new oral anticoagulants ok if eGFR > 30 ml/min)

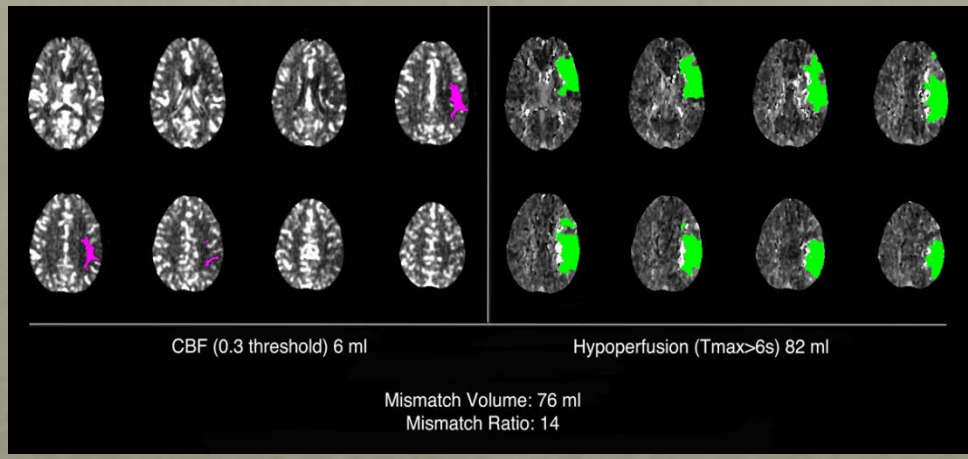
DEFUSE 3: Neuroimaging Criteria

1) MRA / CTA demonstrates
   - M1 segment MCA occlusion, or
   - ICA occlusion (cervical or intracranial; with or without tandem MCA lesions)



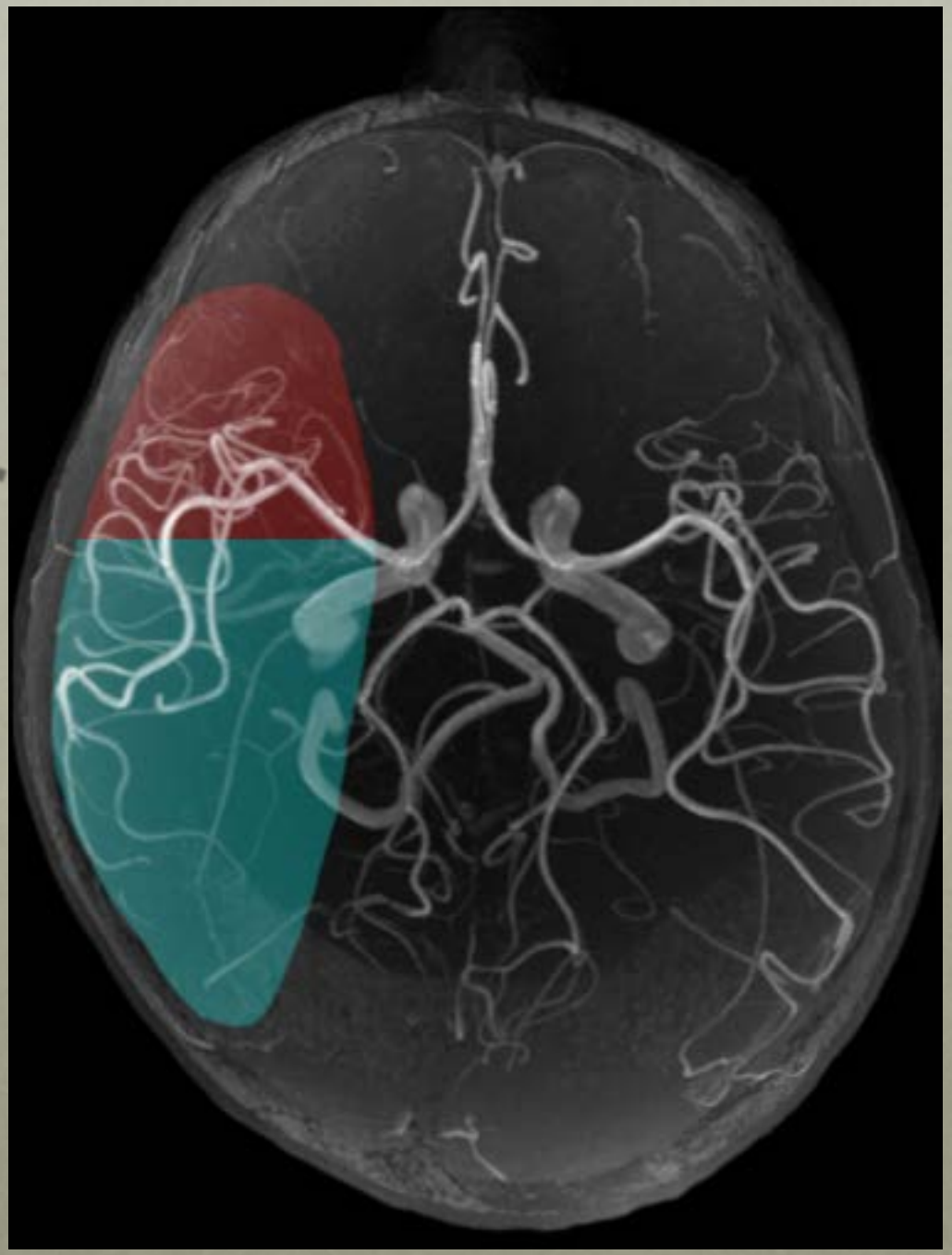
AND

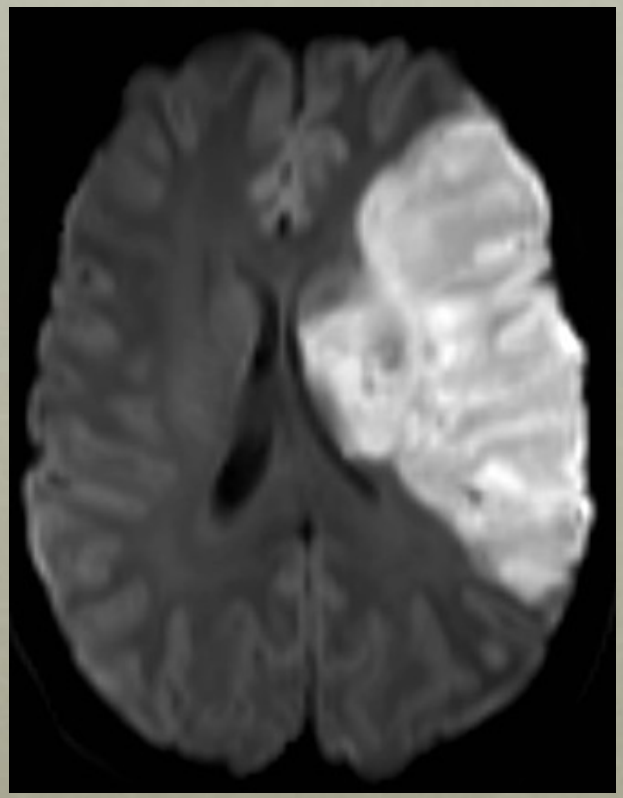
2) Target Mismatch Profile on CT perfusion or MRI (RAPID)
   - Ischemic core < 70 mL
   - Mismatch ratio ≥ 1.8
   - Mismatch ≥ 15 mL

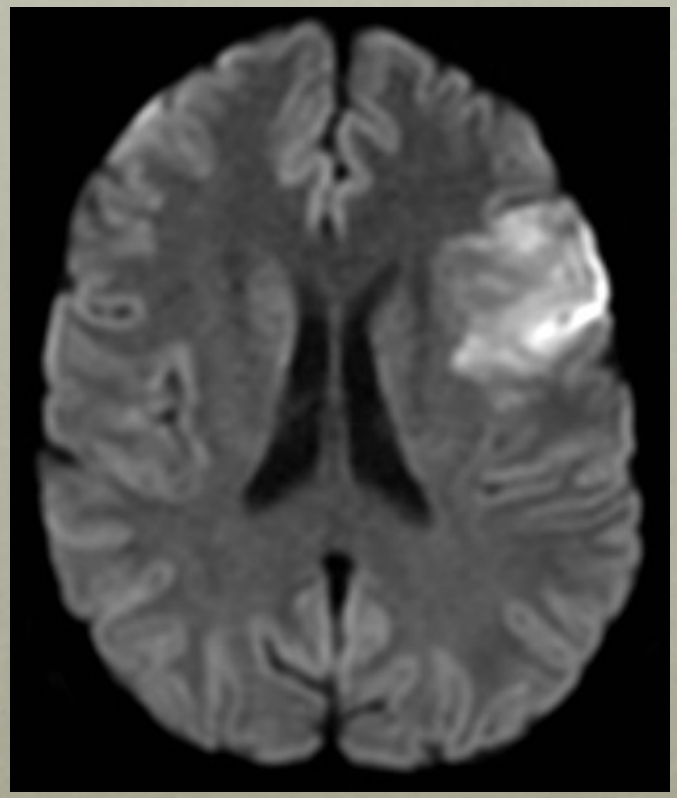


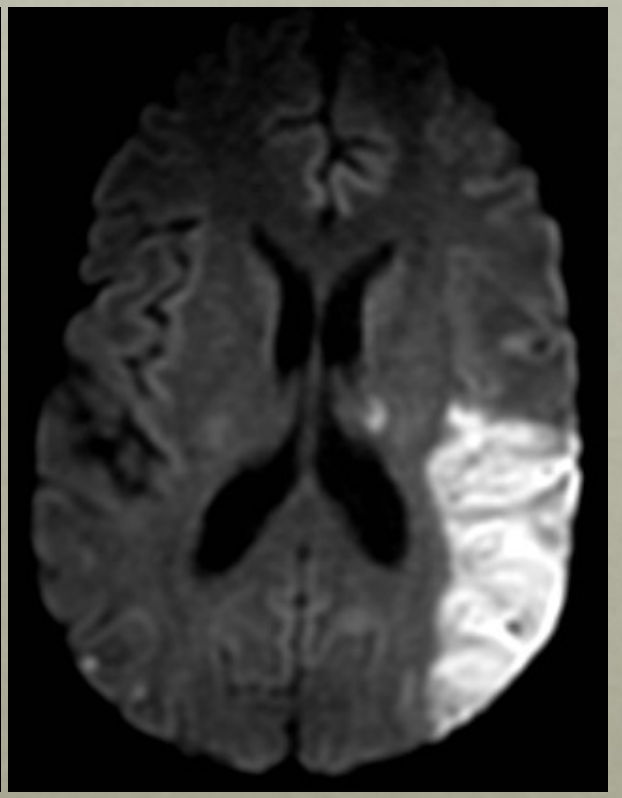
M2
Superior

M2
Inferior





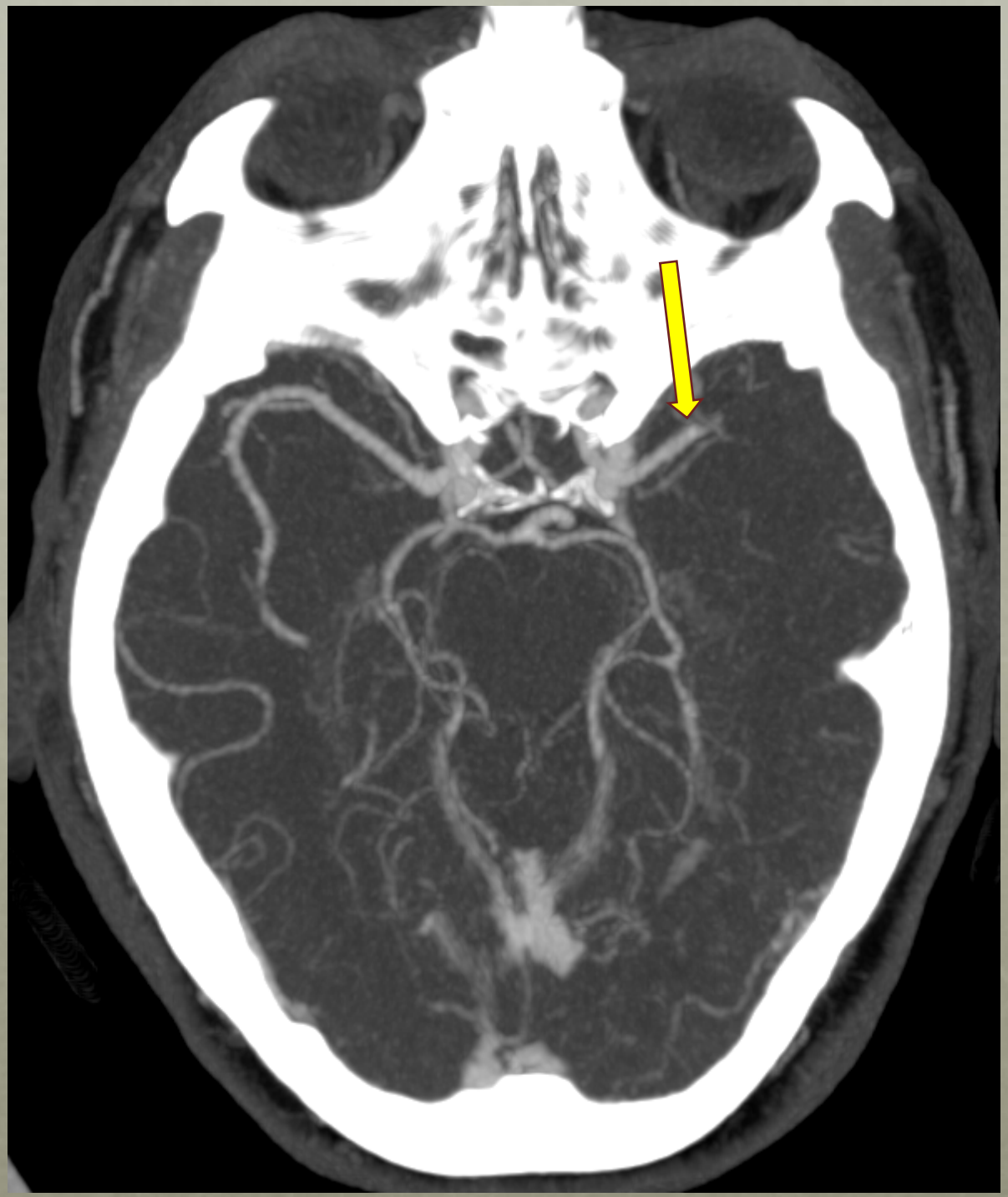




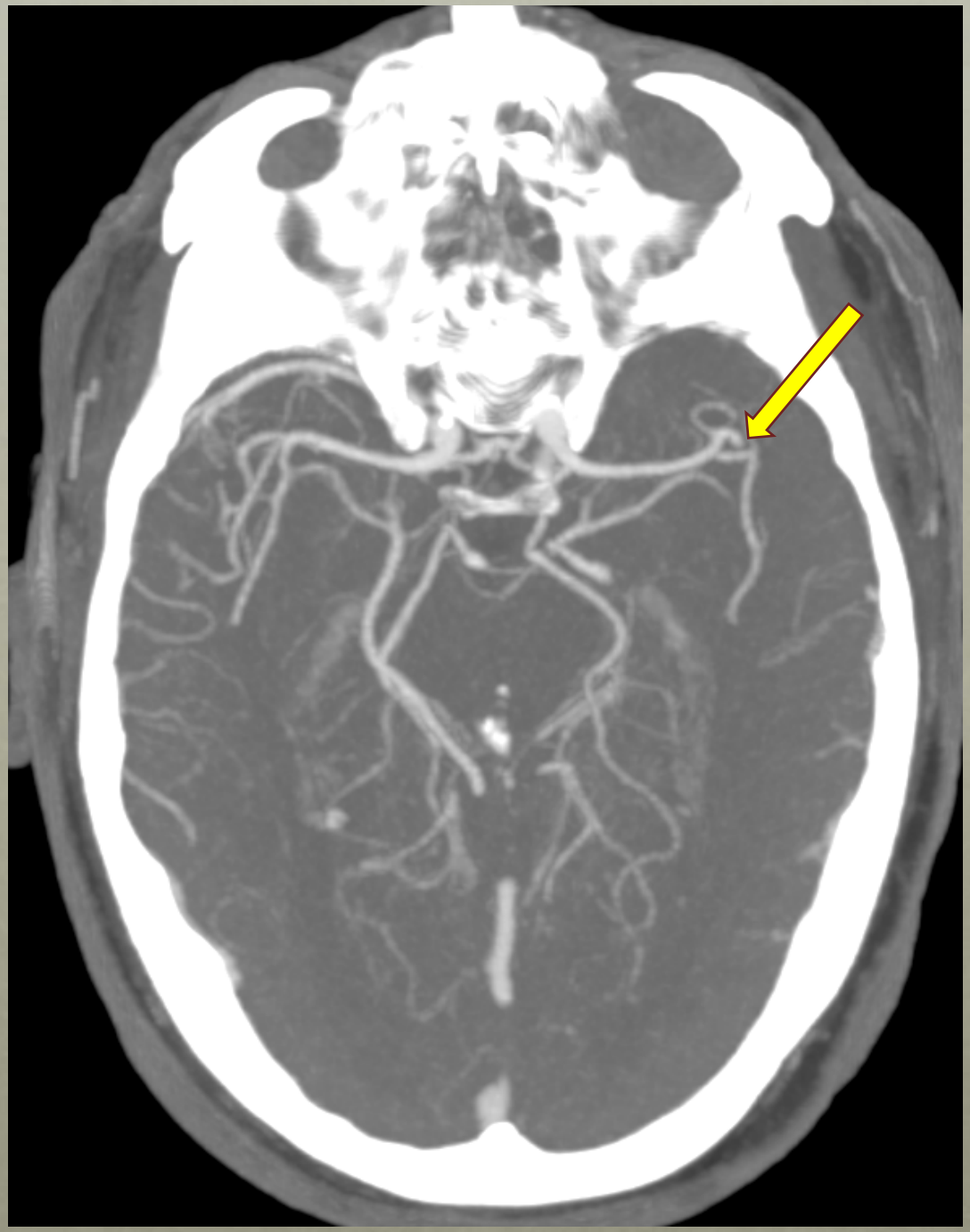
M1

M2 Superior

M2 Inferior

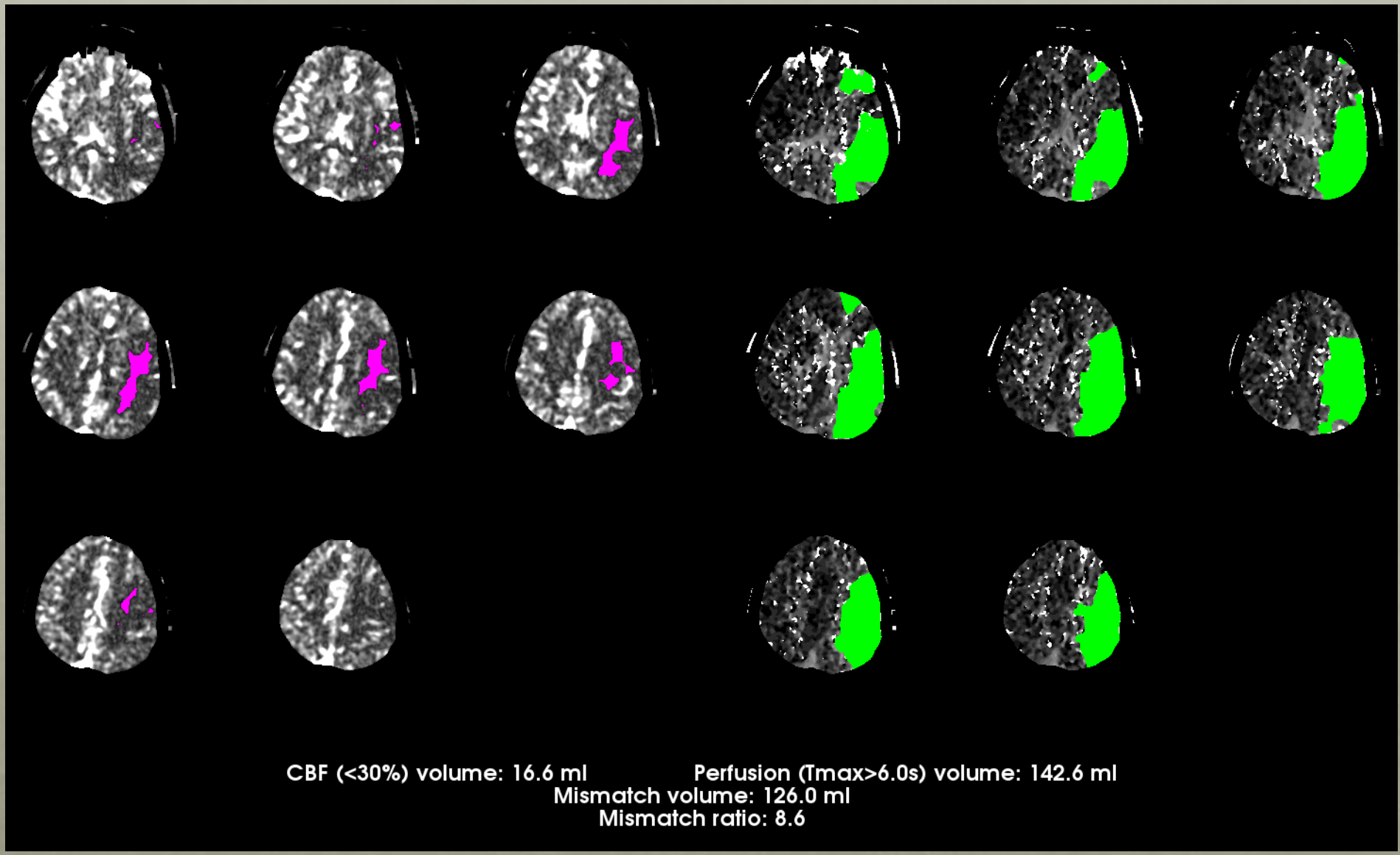


Axial MIP from CTA- Left MCA M1 Occlusion in the horizontal segment of the MCA, prior to the genu **Qualifies for randomization**



Axial MIP from CTA- Left MCA M2 Occlusion just distal to the genu

Does not qualify for randomization


CBF (<30%) volume: 16.6 ml
Perfusion (Tmax>6.0s) volume: 142.6 ml
Mismatch volume: 126.0 ml
Mismatch ratio: 8.6

May 6, 2016; Stanford site
64 yo with L sided paralysis
7.5 hours after onset

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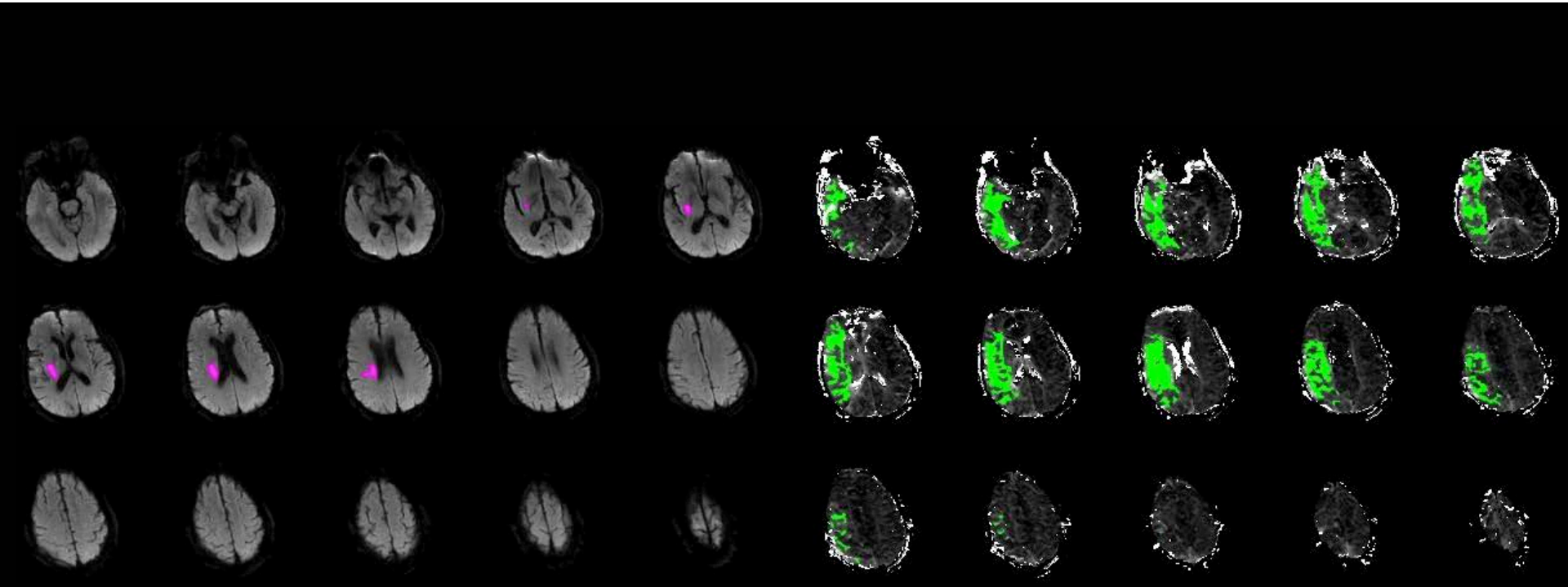


DWI (ADC<630) volume: 5.9 ml

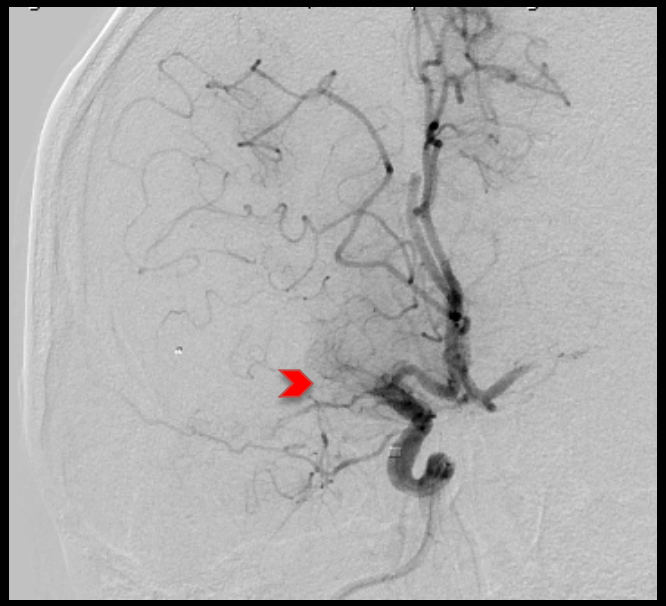
Perfusion (Tmax >6s) volume: 108.6 ml

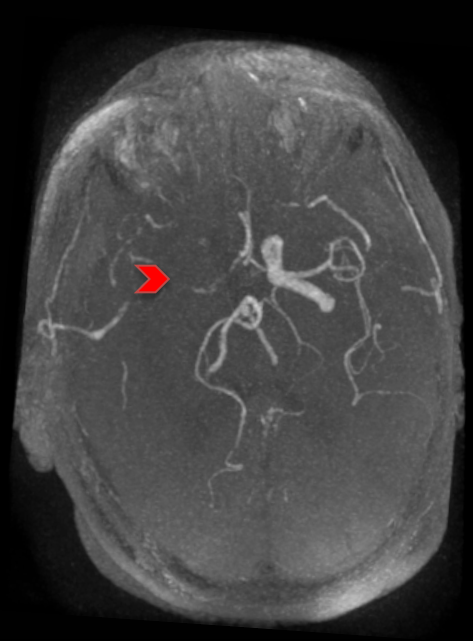
Mismatch volume: 102.7 ml

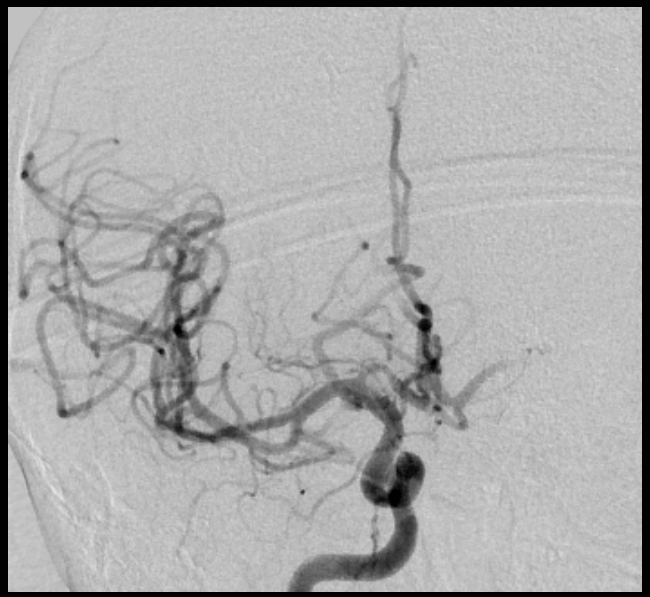
Mismatch ratio: 18.4 ml

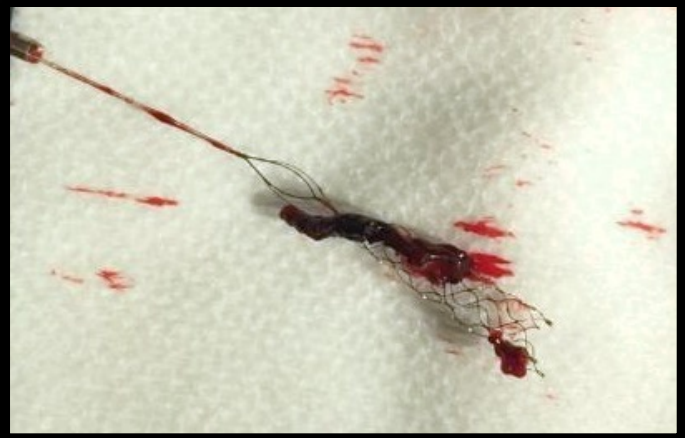
May 6, 2016; Stanford site
64 yo with L sided paralysis
7.5 hours after onset

defuse·3









Conclusions

- Endovascular therapy within 6 hrs of onset for patients with MCA M1 or ICA occlusions is highly effective and safe using modern stent-retrievers
- Optimal patient selection and prompt triage to endovascular centers is essential
- Patients with small ischemic core lesions who achieve complete reperfusion have exceptional clinical outcomes
- Infarct growth rates are highly variable (tissue vs. time)
- Future studies will clarify the role of endovascular therapy in extended time windows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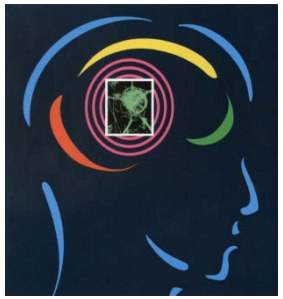

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NIH StrokeNet

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