

# Evaluation and Treatment of Wake-up Stroke in the DAWN Era: How Late Can We Intervene?

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**Mount  
Sinai**

# Disclosures

Affiliation/Financial Relationship

Grants/Trials

Consulting Fees/Honoraria

Stock Shareholder/Equity

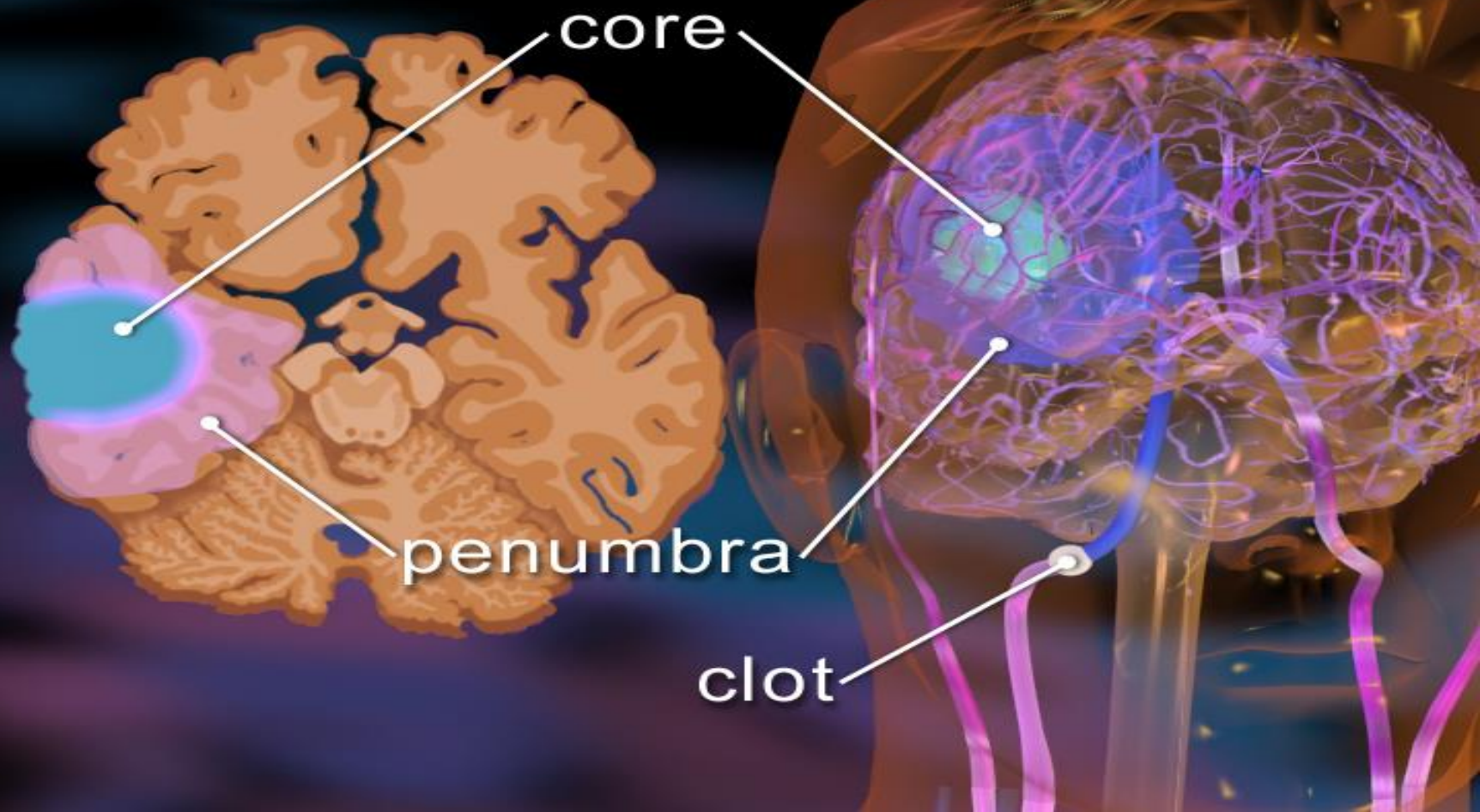
Company

- ▶ Stryker, Microvention
- ▶ Penumbra, Stryker
- ▶ Cerebrotech, Endostream, Synchron



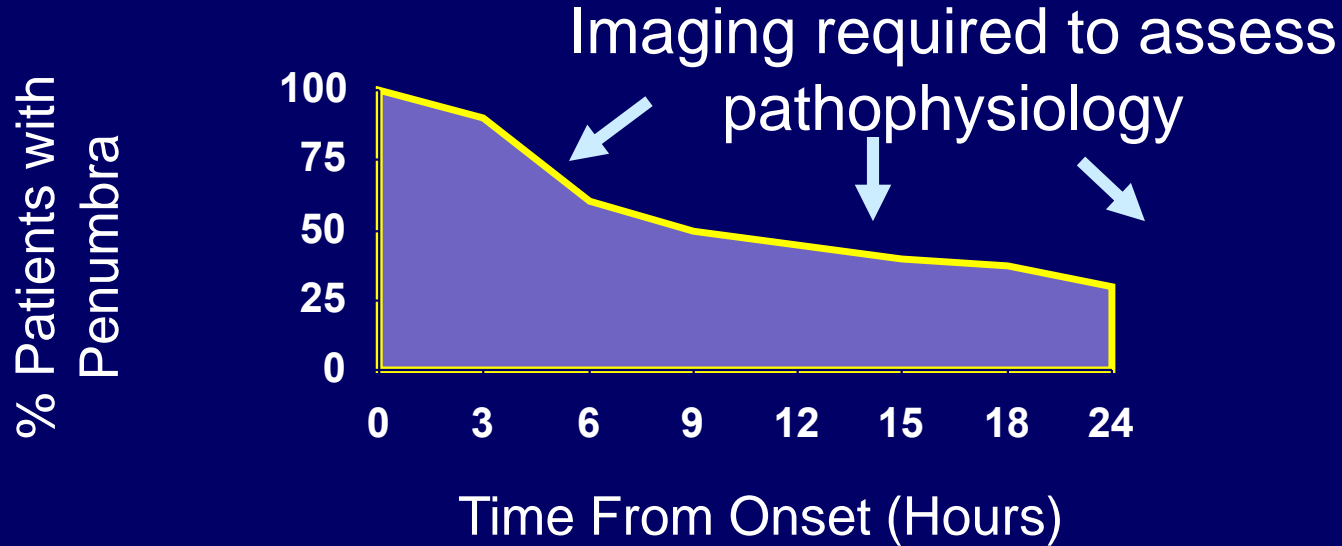
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# Acute Stroke



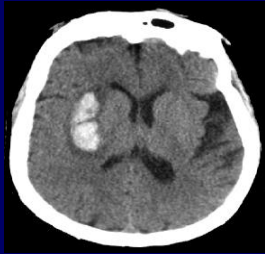
# Time vs. Tissue Window

Early time is surrogate marker for penumbra



# Imaging Approach – Multimodal CT

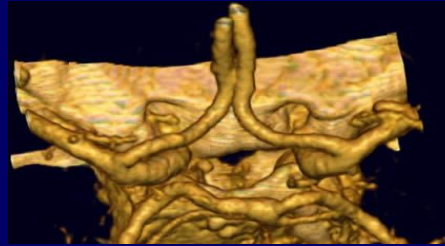
**Hemorrhage**



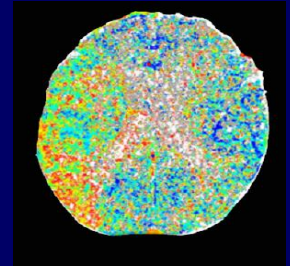
**Ischemic Injury**



**Vessel Status**



**Perfusion Status**



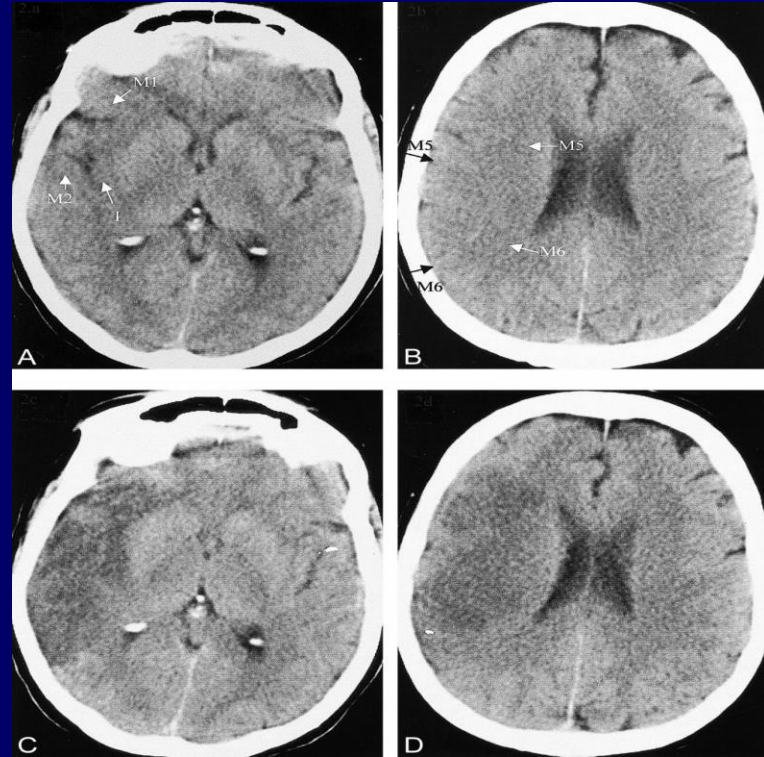
Identify Ischemic Penumbra



Optimize Therapy

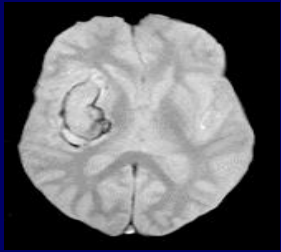
# ASPECTS Score

- ▶ Uses non-contrast CT
- ▶ Topographic scoring system for middle cerebral artery syndromes
- ▶ Meant to replace the 1/3 territory rule
- ▶ 1 to 10 points with scores <7 predicting poor outcome or hemorrhage



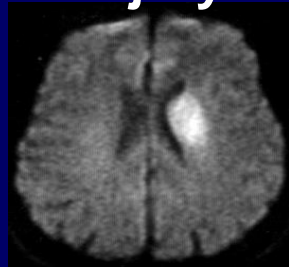
# Imaging Approach – Multimodal MR

**Hemorrhage**



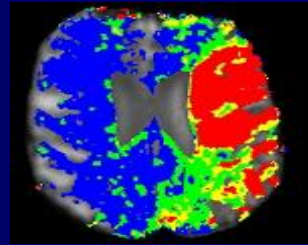
**GRE**

**Ischemic Injury**



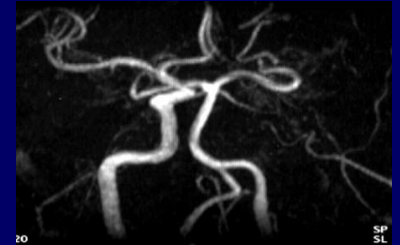
**DWI**

**Perfusion Status**



**PWI**

**Vessel Status**



**MRA**

Confirm Diagnosis



Optimize Safety

Identify Ischemic Penumbra



Optimize Therapy and Extend Time Window

# Positive Endovascular Trials

2015-2016

**MR CLEAN**

A Randomized Trial of Endovascular Treatment for Acute Ischemic Stroke

M. Goyal, A.M. ... T.T. Sajoo, MD, PhD, for the MR CLEAN Investigators\*

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

M. Goyal, A.M. ... T.T. Sajoo, MD, PhD, for the ESCAPE Trial Investigators\*

**ESCAPE**

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

B. C. ... T. W. ...

**EXTEND IA**

ORIGINAL ARTICLE

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

Har ... D. ...

**SWIFT PRIME**

Demétrio R. Lopes, M.D., Vivek R. Nandy, M.D., ... Oliver C. Singer, M.D., and Reza Jahan, M.D., for the SWIFT PRIME Investigators\*

ORIGINAL ARTICLE

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

T.G. ... R. von K ...

**REVASCAT**

Aspiration Thrombectomy After Intravenous Alteplase Versus Intravenous Alteplase Alone

J. Mocco, MD; ... Jawad Kirmani, MD; ...

**THERAPY**

Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial

Serge B. ... Francis Guillemin, on behalf of the THRACE Investigators\*

**THRACE**



**2015 AHA/ASA Focused Update of  
the 2013 Guidelines for the Early  
Management of Patients With Acute  
Ischemic Stroke Regarding  
Endovascular Treatment**



Patients should receive **endovascular therapy** with a stent retriever if they meet all the following criteria (*Class I*). (*New recommendation*):

- pre-stroke **Modified Rankin Scale score 0 to 1**
- acute ischemic stroke receiving **IV r-tPA within 4.5 hours** of onset according to guidelines from professional medical societies
- causative occlusion of the **ICA or proximal MCA**
- age  $\geq 18$  years
- **NIHSS score of  $\geq 6$**
- Alberta Stroke Program Early CT score (**ASPECTS**)  $\geq 6$
- treatment can be initiated (groin puncture) **within 6** ←
- hours of symptom onset**

# 2015 AHA/ASA Focused Update on Management of Acute Stroke Patients with Endovascular Therapy

- When treatment is initiated beyond 6 hours from symptom onset, the effectiveness of endovascular therapy is uncertain for patients with acute ischemic stroke who have causative occlusion of the ICA or proximal MCA (M1) (Class IIb; Level of Evidence C). **Additional randomized trial data are needed.** (New recommendation)

# AP

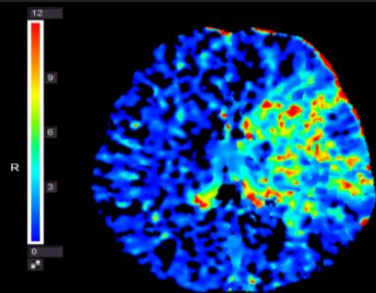
- ❑ 65 year old woman, history of HTN and smoking
- ❑ Works out every day, modified Rankin Score: 0
- ❑ She was seen well the day prior at 10:30 pm
- ❑ Symptom discovery at 10:00 am. Aphasia and right hemiplegia: NIHSS 16
- ❑ Presented to an outside hospital
- ❑ CT performed at 1217, CTA at 1406, called Sinai at 1500

# AP

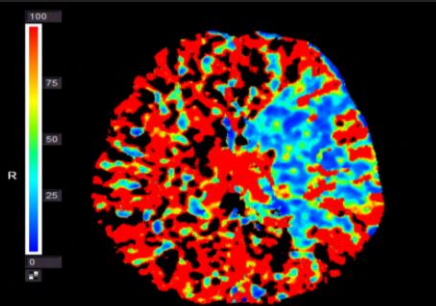
❓ Transferred

❓ Repeat imaging performed with CT Perfusion

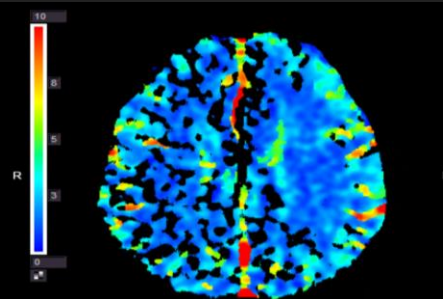
AP



MTT

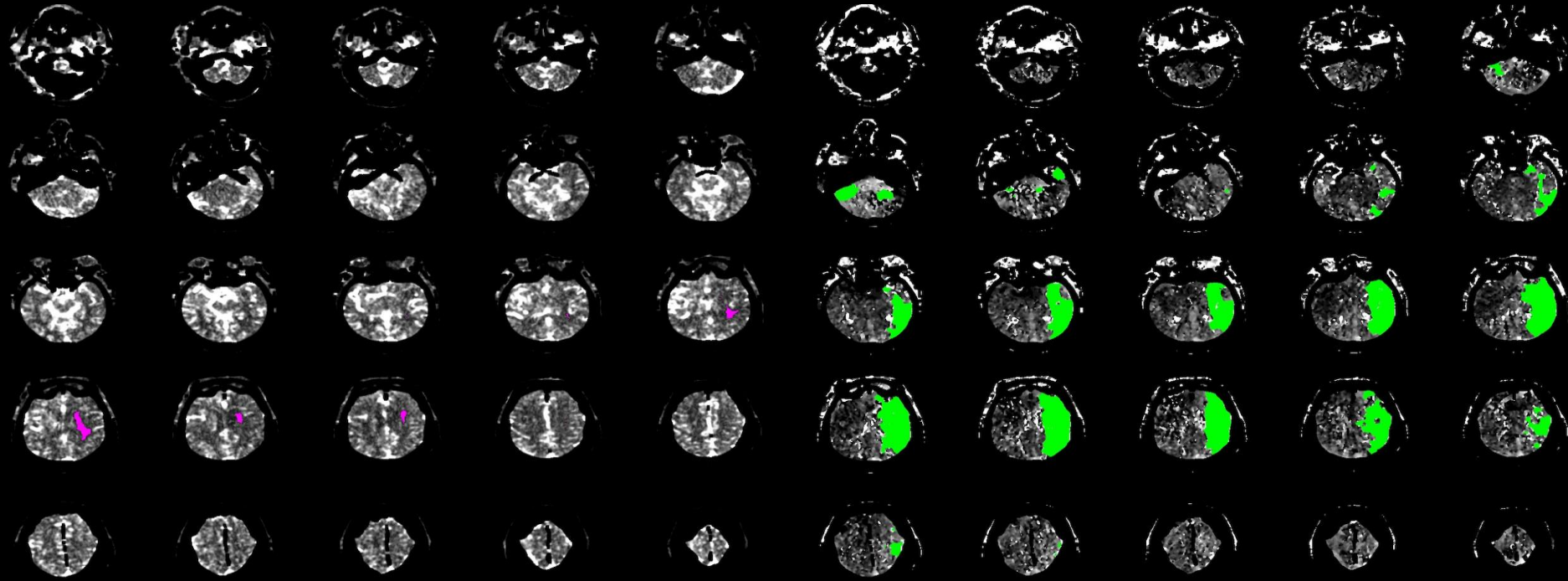


CBF



CBV

# Perfusion Imaging



**CBF (<30%) volume: 5.6 ml**

**Perfusion (Tmax>6.0s) volume: 187.4 ml**

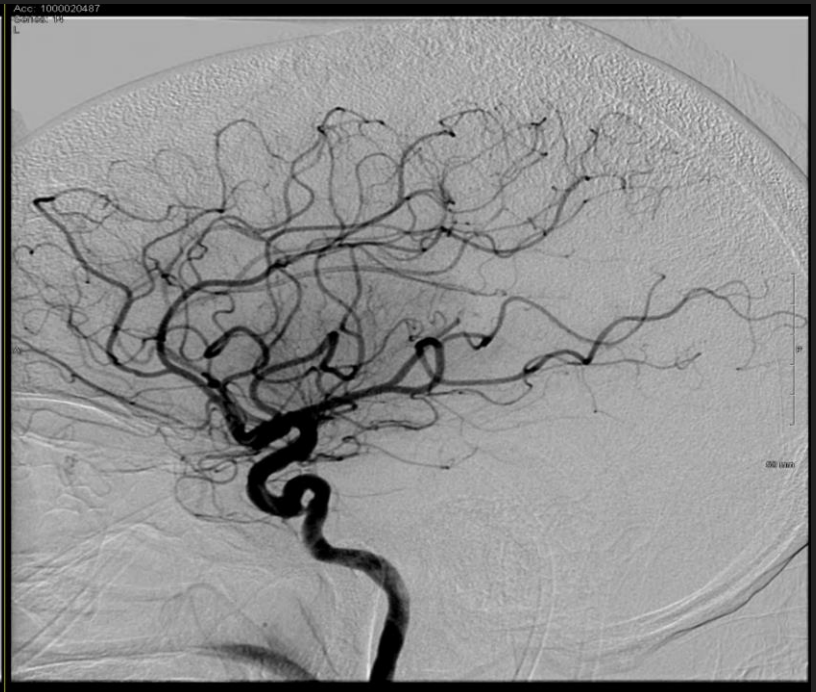
**Mismatch volume: 181.8 ml**

**Mismatch ratio: 33.5**

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FIRST RUN

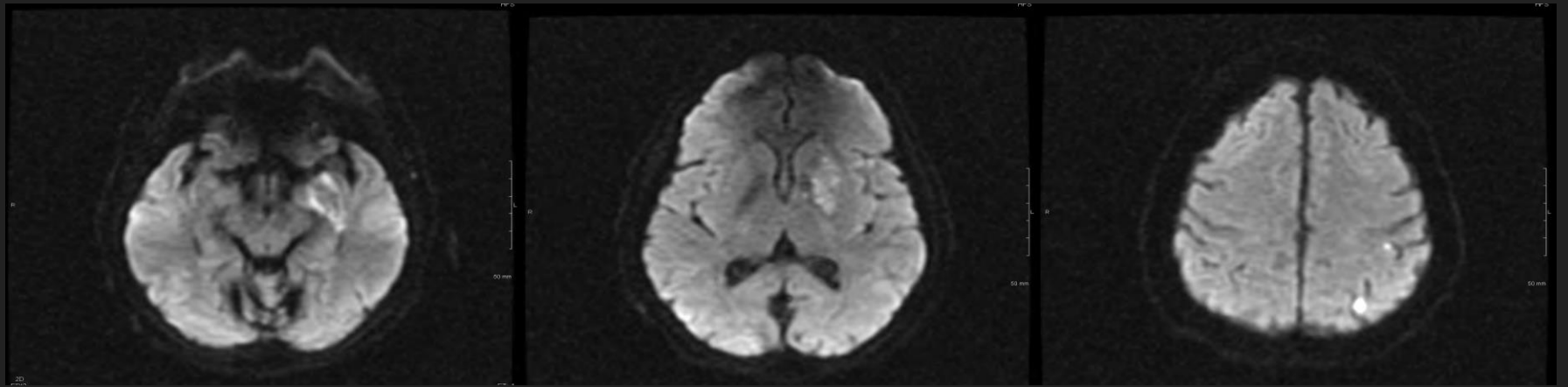


FIRST PASS USING STENTRIEVER - TICI 2B,  
GP TO RECAN: 28 MINUTES



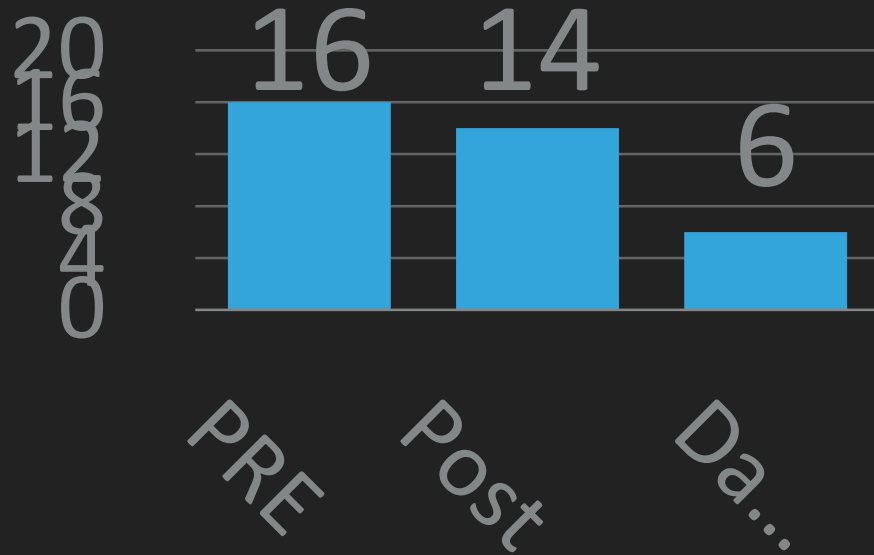


RETRIEVED CLOT



MRI - DWI

# NIHSS



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# OUTCOME

☐ Patient did well and recovered to 90 mRS of 1

# Extending the Time Window

- DEFUSE 3

defuse 3

- Prospective randomized Phase III multicenter controlled trial of patients with acute ischemic anterior circulation strokes due to large artery occlusion treated between **6-10** hours of stroke onset with endovascular thrombectomy therapy vs. control.

**HALTED**

positive

- 

- Prospective randomized Phase III multicenter controlled trial of patients with acute ischemic anterior circulation strokes due to large artery occlusion treated between **6-12** hours of stroke onset with endovascular thrombectomy therapy vs. control.

- DAWN

- A trial of wake up stroke **up to 24** hours
- **Halted for probable efficacy March 2017**
- **Data presented May 2017 European Stroke Organising Conference**

# DAWN Trial

- ▶ DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention
- ▶ To demonstrate superior clinical outcomes at 90 days with Trevo plus medical management compared to medical management alone in appropriately selected patients treated 6–24 hours after last seen well

# DAWN Trial

- ▶ Prospective, randomized (1:1), multi-center, Phase II/III (feasibility/pivotal), adaptive, population enrichment, blinded endpoint, controlled trial
- ▶ 50 sites (worldwide)
- ▶ 150 subjects (feasibility) up to 500 (pivotal) max
- ▶ Primary endpoint
  - Difference in average weighted mRS at 90 days between
- ▶ treatment and control in the enriched patient population

# DAWN – Imaging Criteria

- ▶ Occlusion of the intracranial ICA and/or MCA-M1 as evidenced by MRA or CTA
- ▶ Clinical Imaging Mismatch (CIM) defined as one of the following on RAPID MR-DWI or CTP-rCBF maps:
  - a. 0-20 cc core infarct and NIHSS  $\geq 10$  (and age  $\geq 80$  years old)
  - b. 0-30 cc core infarct and NIHSS  $\geq 10$  (and age  $< 80$  years old)
  - c. 31 cc to  $< 50$  cc core infarct and NIHSS  $\geq 20$  (and age  $< 80$  years old)



# DAWN Trial – Prelim Results

- ▶ Randomized control trial Trevo versus medical therapy
- ▶ **6 to 24** hours selected by perfusion imaging
- ▶ 206 patients enrolled, 107 Trevo
- ▶ 75% M1, 20% ICA, 3% M2

# Co-primary endpoints

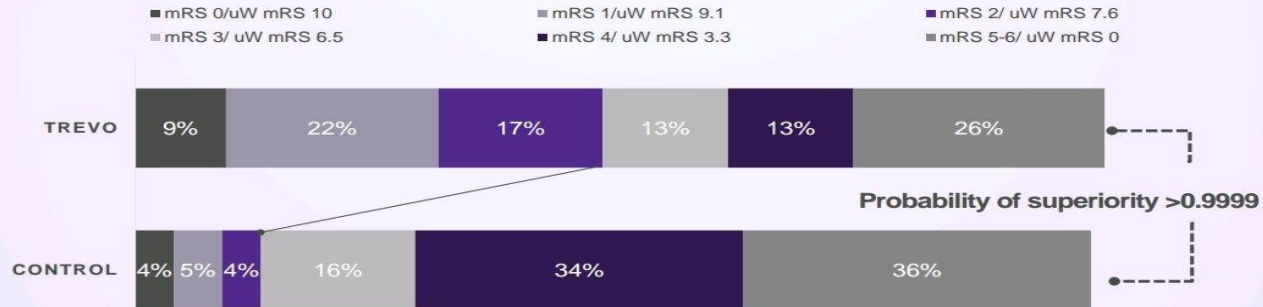
	Trevo	MM	Treatment benefit (95% CI)	Bayesian probability of superiority
Day 90 weighted mRS	5.5 ± 3.8	3.4 ± 3.1	2.1 (1.20, 3.12)	>0.9999*
Day 90 mRS (0-2)	48.6%	13.1%	35.5% (23.9%, 47.0%)	>0.9999*

**NNT for 90-day functional independence = 2.8**



\*Similar to  $p < 0.0001$

## Primary outcome



**73% relative risk reduction of dependency in ADL's**  
**NNT for any lower disability 2.0**



# DAWN Trial

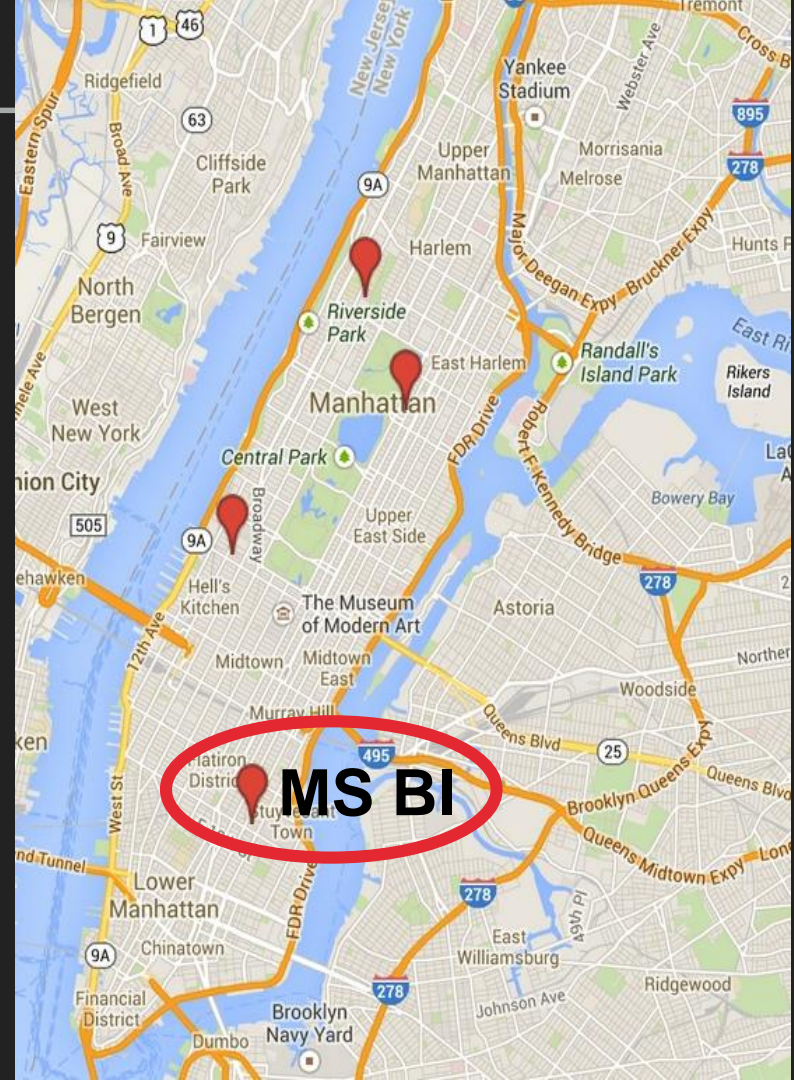
- ▶ Mean time from last well 13.4 +/- 4.1
- ▶ 64.5% vs. 47.5% wake up strokes
- ▶ Baseline core 8.8 cc
- ▶ Procedure: median of 56 minutes with 2 passes
- ▶ TIC1 2b or above 84%

# DEFUSE 3 and POSITIVE

- ▶ DEFUSE 3 to be presented at ISC
  - January 2018
  - Reportedly positive

# MSBI CASE

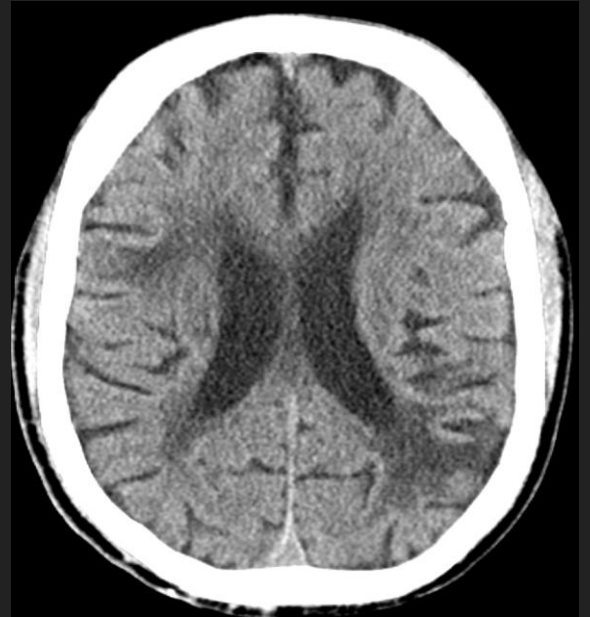
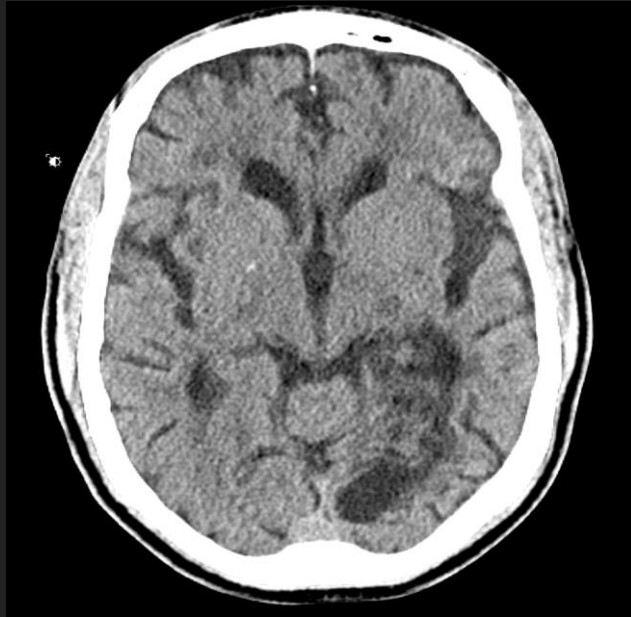
10/27/2017



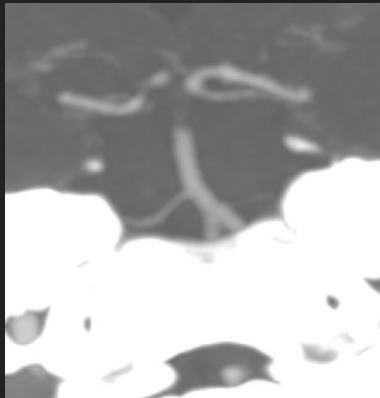
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# TIMELINE

- 63 M with HTN, DM, A-fib (only on ASA)
- LKW 10/26 @ 11:00 am
- DOS 10/27 @ ~7:00 am
- Stroke code: 9:16 am - lethargy, dysconjugate gaze and mild quadriparesis: NIHSS 14
- 30 mins into ED arrival: LOC worse, requiring intubation.



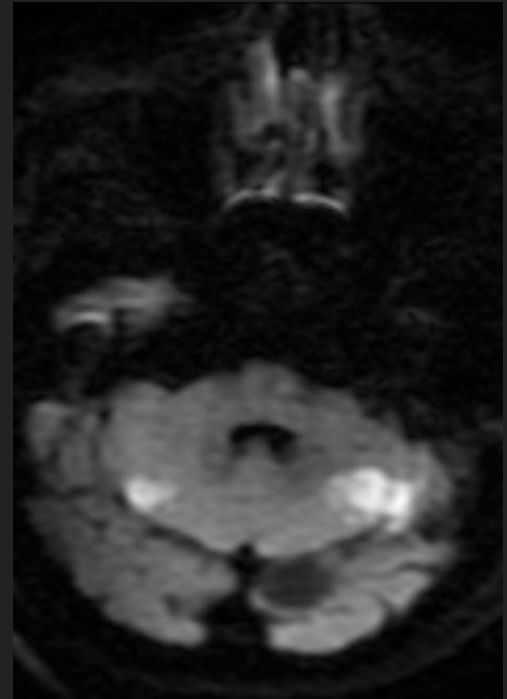
Baseline CT - 9:46 am



CTA - 11:34 am

MIST  
NOTIFICATION

11:42 am



MRI - 01:09 pm

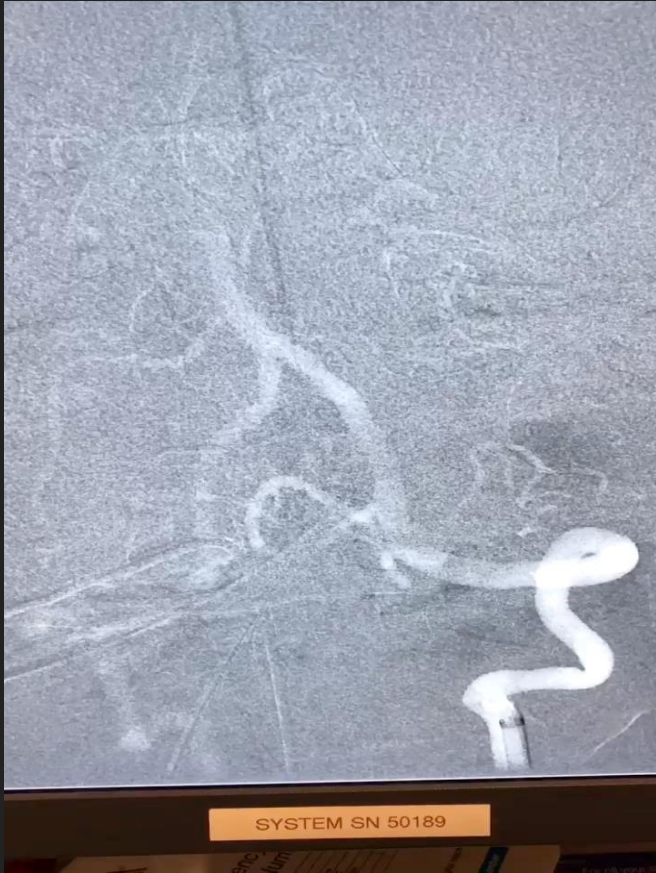




Distal Basilar Occlusion  
Via left VA injection



Status post single pass  
ADAPT thrombectomy



24 HOUR NIHSS 8

DISCHARGE NIHSS 0

# Conclusions

- ▶ Goal of endovascular stroke treatment is to restore flow into the salvageable penumbra
- ▶ The Time Window has been broken
- ▶ Entering age of the Tissue Window
- ▶ Advanced neuroimaging is required to select patients who are able to benefit from treatment beyond the 6 hours window

How late tissue edema occurs?

# Thank you!



**Mount  
Sinai**

# MOUNT SINAI NEUROENDOVASCULAR TEAM



Mocco



Fifi



De Leacy



Kellner



Oxley

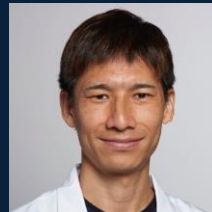


Singh



Berenstein

## Fellows



Shigematsu



Shoirah



Yaniv



Nouri