Revascularization in Acute Stroke

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TOSHIBA STROKE RESEARCH CENTER

Conflicts

- EKOS – med advisor
- Primus Medical – med advisor
- Sylva Medical - ?
- Toshiba Medical Systems - research grants

FIBRINOLYTICS (INTRAVENOUS)

tPA for acute ischemic stroke. NINDS trial

624 patients with ischemic stroke within 3 hours

Intravenous tPA (0.9 mg/kg)

vs

placebo

Follow-up
3 months

	tPA	placebo
Improvement at 24 h	47%	39%
Favorable outcome at 3 m (Rankin scale)	42%	27%
Intracerebral hemorrhage	6.4%	0.6%
Death at 3 m	17%	21%

FIBRINOLYTICS (INTRA-ARTERIAL)

Prolyse in Acute Cerebral Thromboembolism (PROACT) I

54 patients with occlusion of middle cerebral artery within 6 hours of onset

Intraarterial rPro UK (6mg)
vs
placebo

Follow-up
3 months

	prourokinase	placebo
Recanalization	58%	14.3%
Hemorrhagic transformation	15.4%	7.1%

FIBRINOLYTICS (INTRA-ARTERIAL)

Prolyse in Acute Cerebral Thromboembolism (PROACT) II

180 patients with occlusion of middle cerebral artery within 6 hours of onset

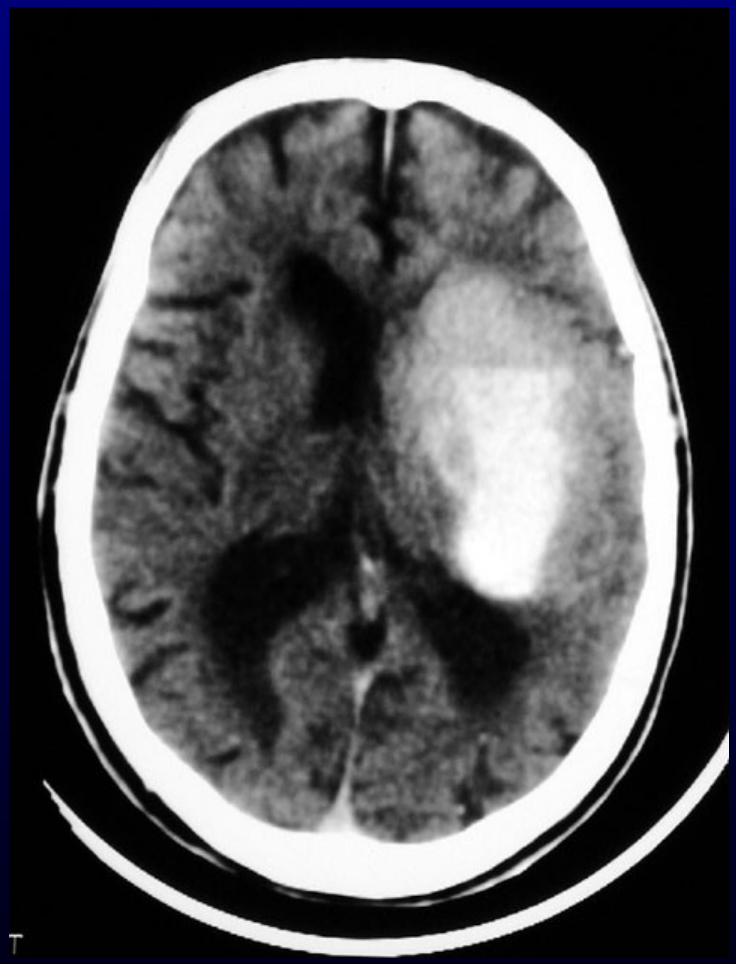
Intraarterial Prourokinase (9mg)
vs
placebo

Follow-up

3 months

	Prourokinase	Placebo
Recanalization	66%	18%
Hemorrhagic transformation	10%	2%
Favorable outcome	40%	25%

Time vs bleeding



Radiographic Evaluation

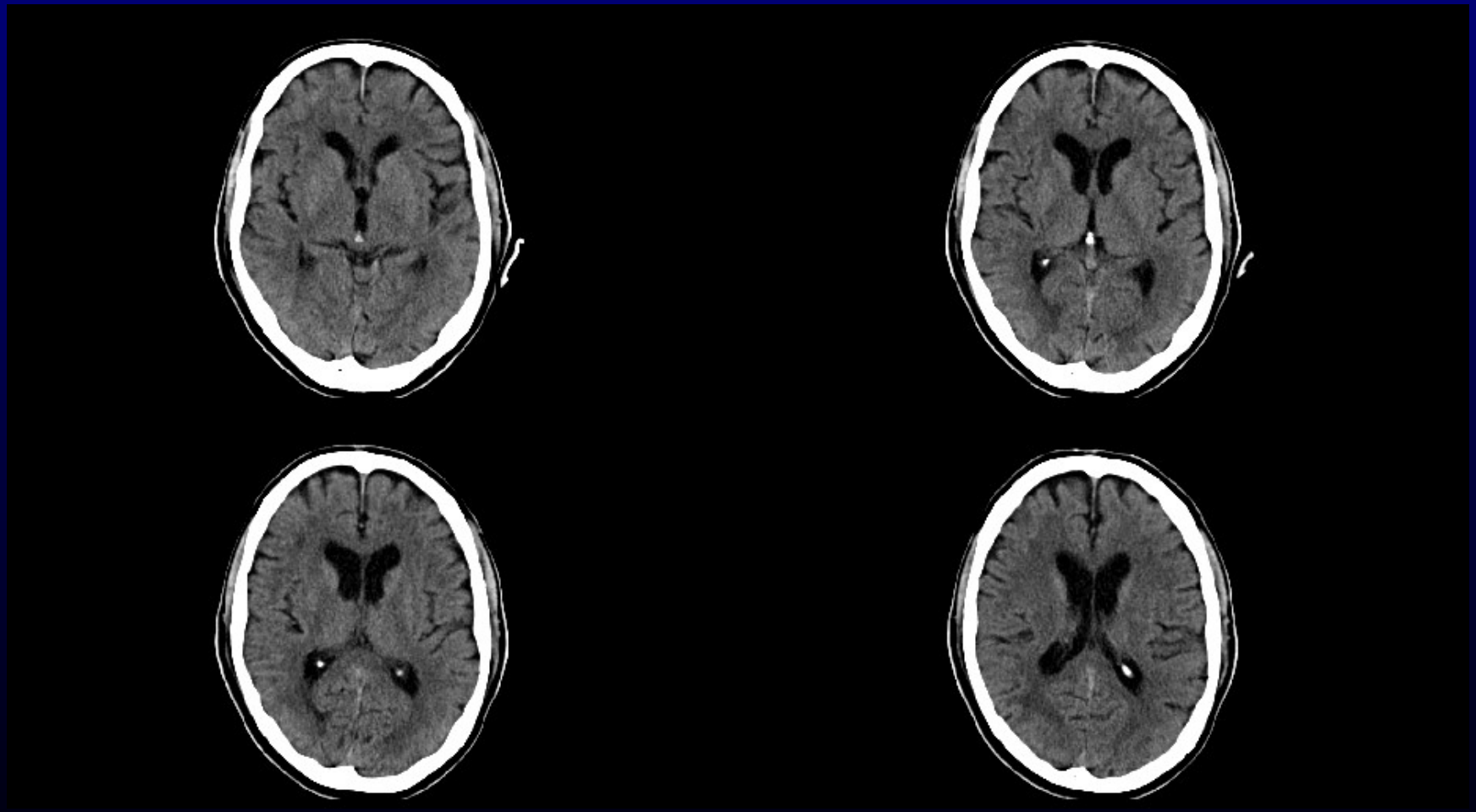
- **CT head**
  - **Rapid evaluation for ICH**
  - **Hypodenisty < 1/3 effected hemisphere**
- Cerebral perfusion
  - MRI diffusion perfusion
  - CT perfusion
  - CT angiogram

Triage

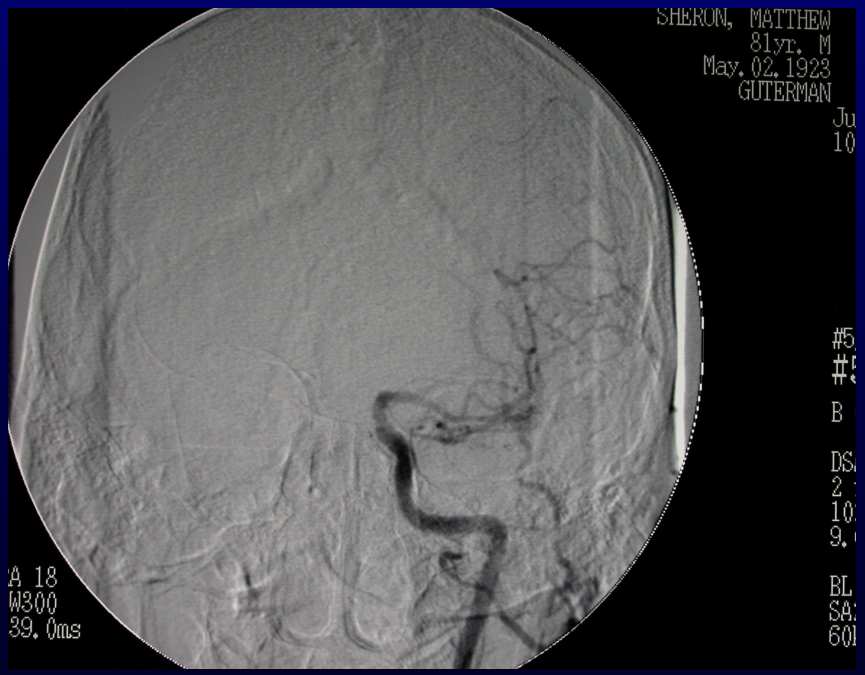
- **0-3 hrs NIHSS<10 IV tPA**
  - **Unless angular artery, speech**
- **0-3hurs NIHSS>10 IA lysis +/- mechanical**
- **3-6 IA lysis +/- mechanical**
- Over 6 hours guided by perfusion imaging
- Posterior circulation
  - Will treat up 12 – 24 hours
  - MRI dependant

CONFLICT
OF
KNOWLEDGE VS EVIDENCE

82 yo WM, NIHSS 18, Crescendo TIA, hemiparesis unchanged for 30 hours



Cerebral Angiogram



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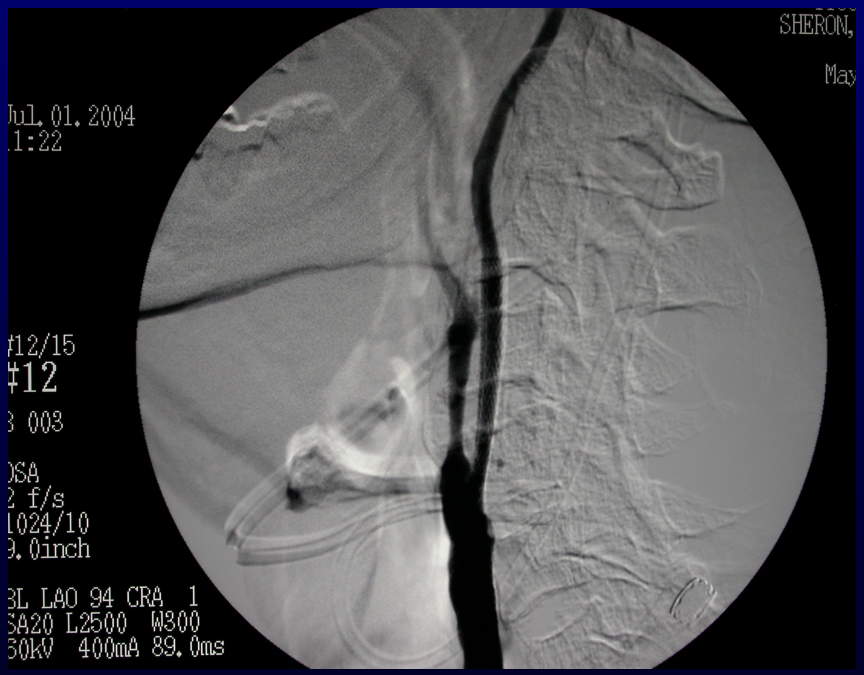
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1:22
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12
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SA20 L2500 W300
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GUTER
04
CRA 21
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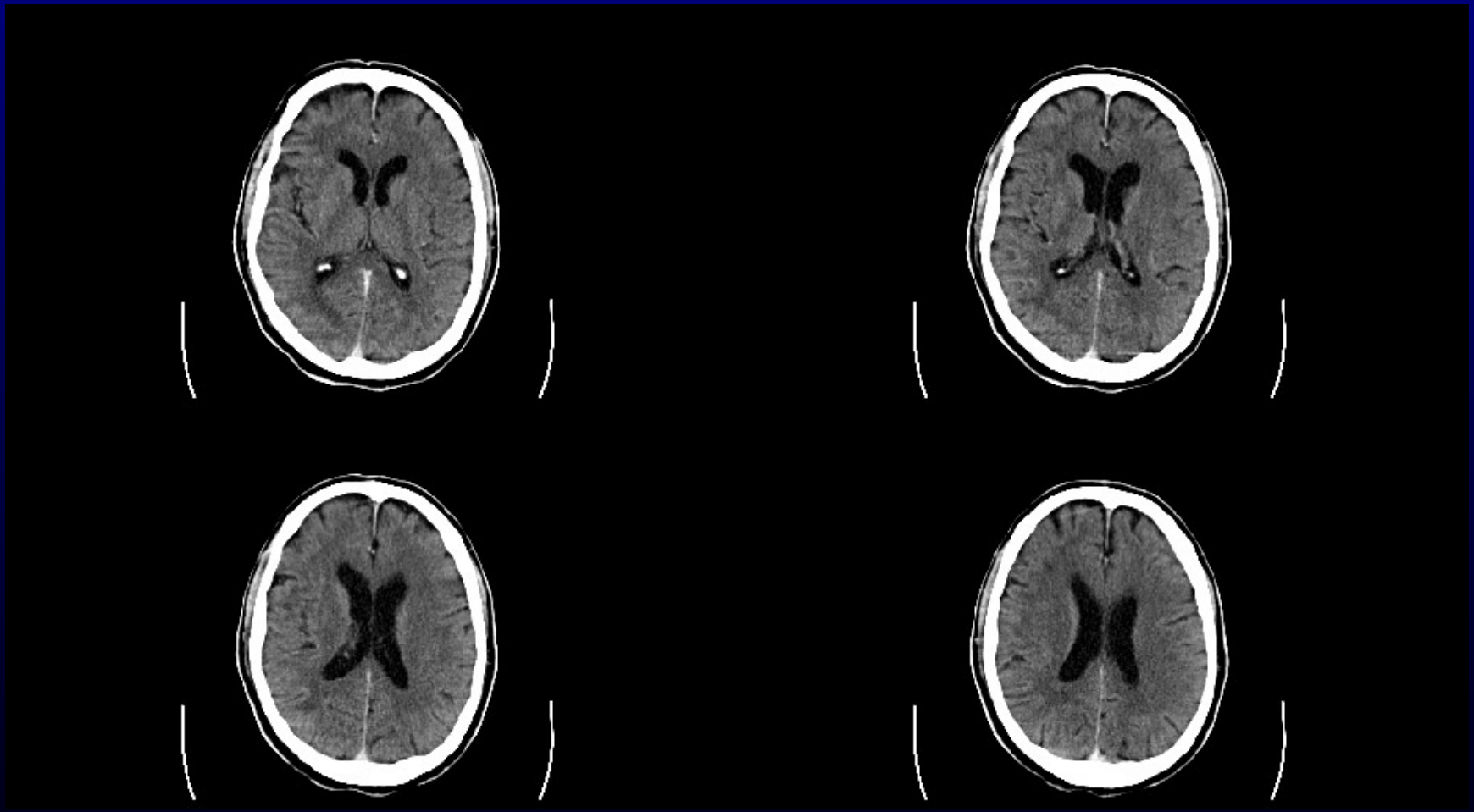
mA 81.0ms
7 / 16

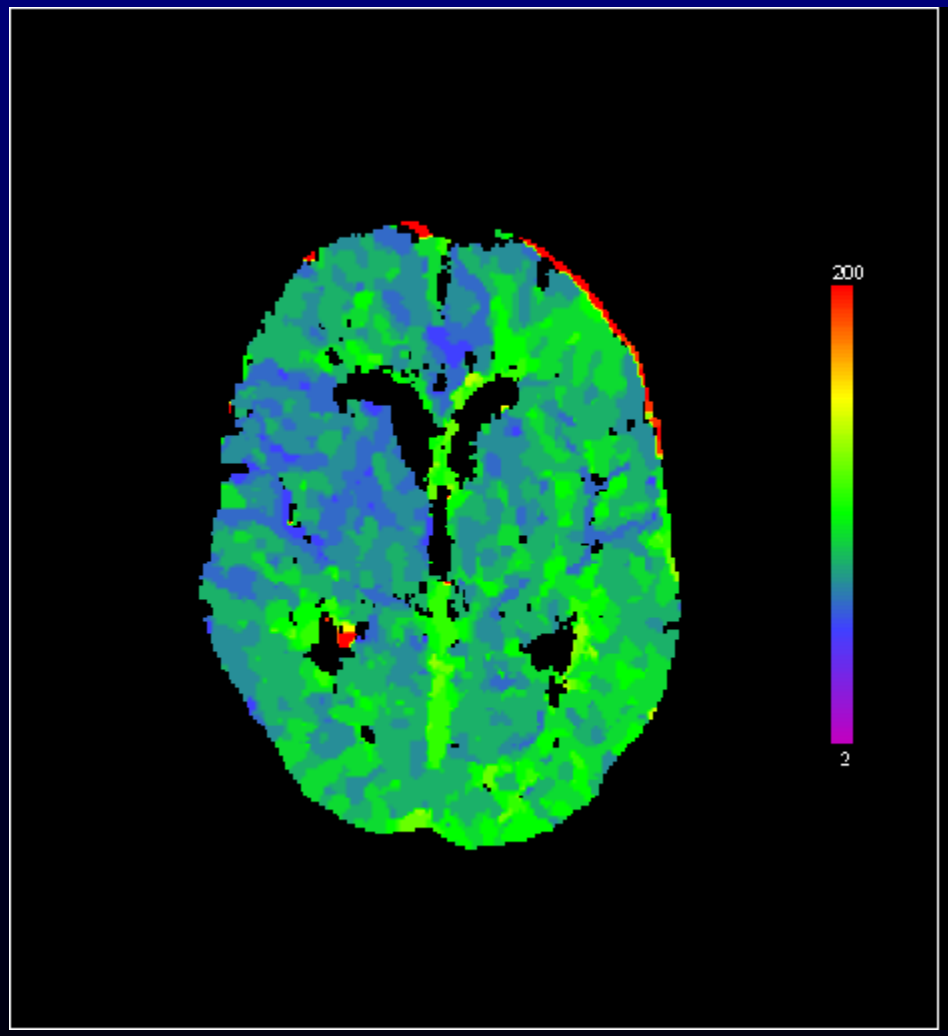
48 hours post

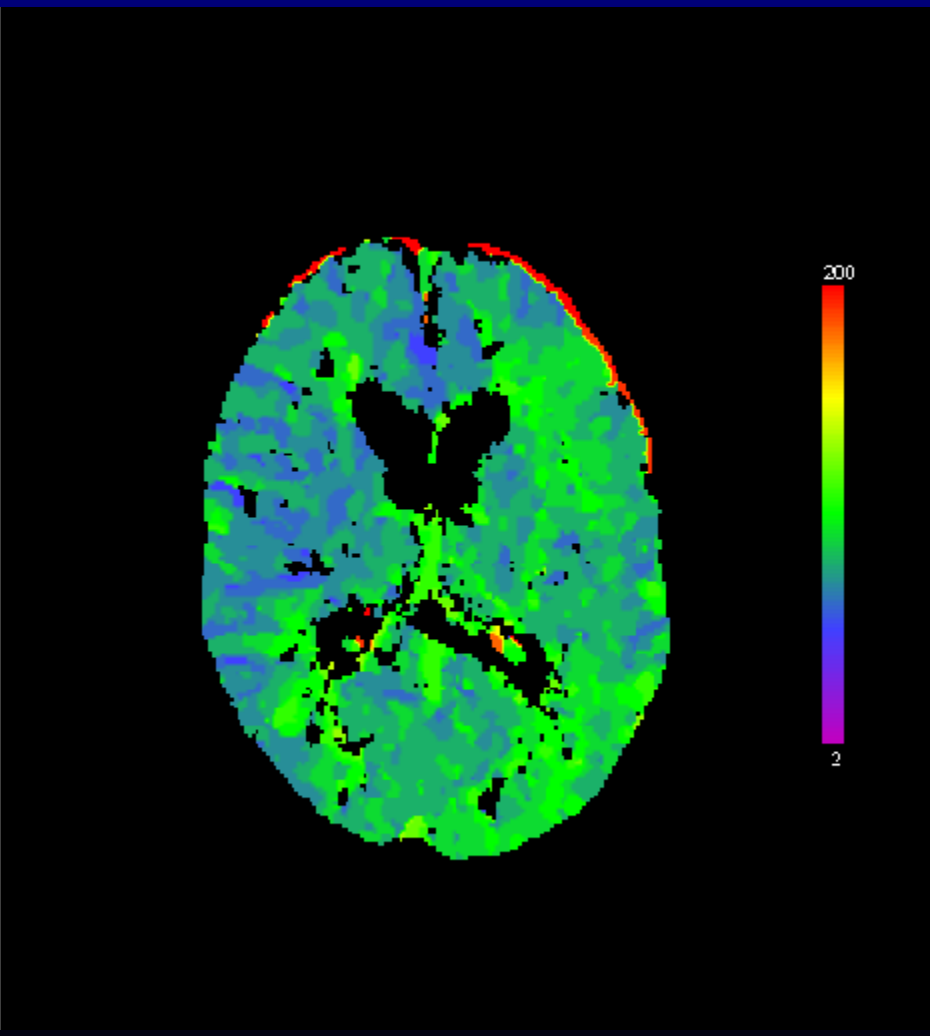


Outcome

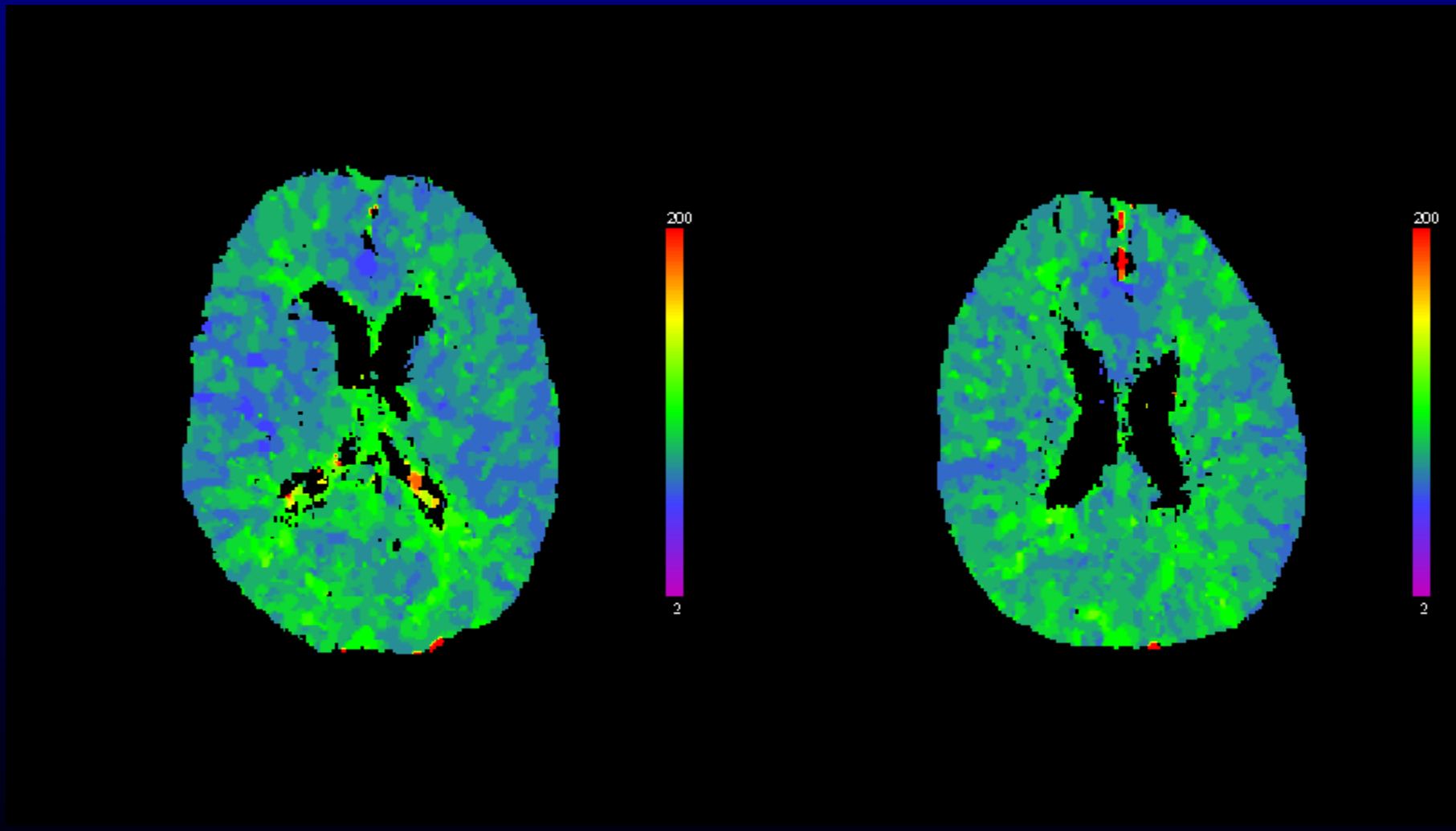
- Remarkable improvement
  - NIHSS 4 at 24h
  - NIHSS 1 at DC minimal speech problems

CT Perfusion PreRx



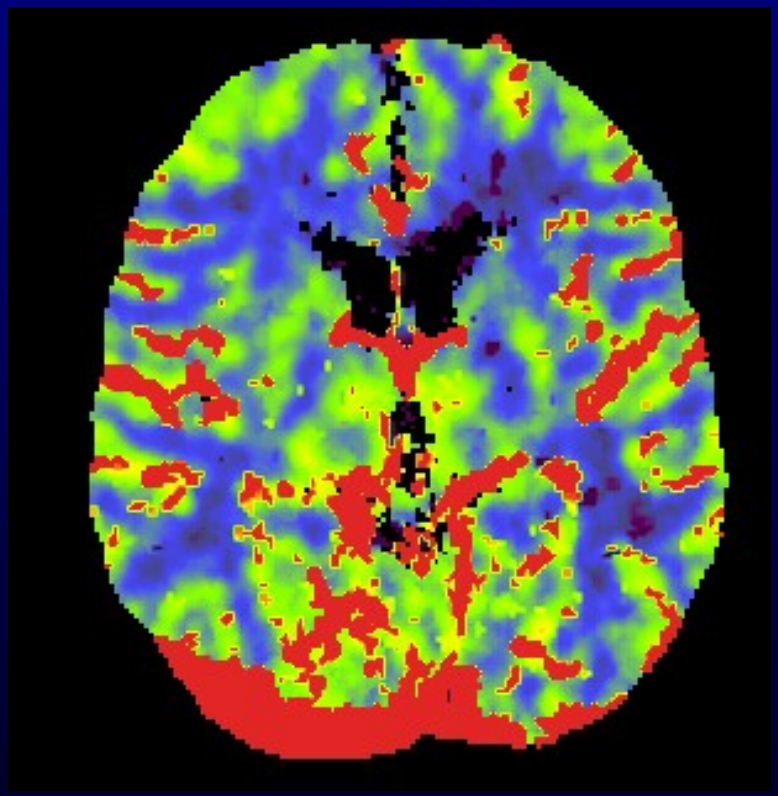


CT perfusion Post Rx

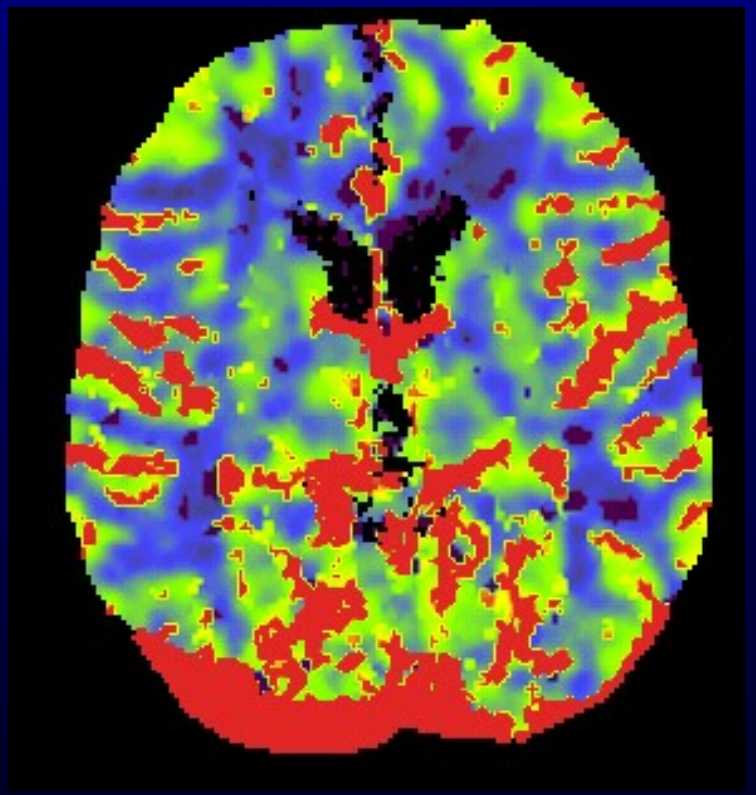


Don’t Try This at Home

CBF

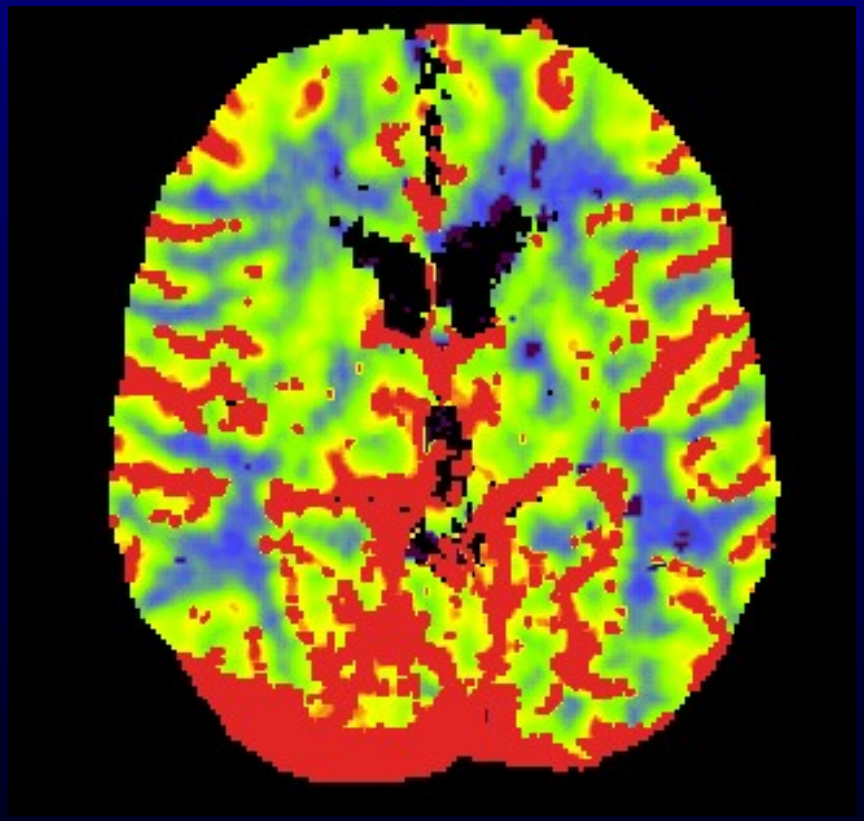


Pre Diamox

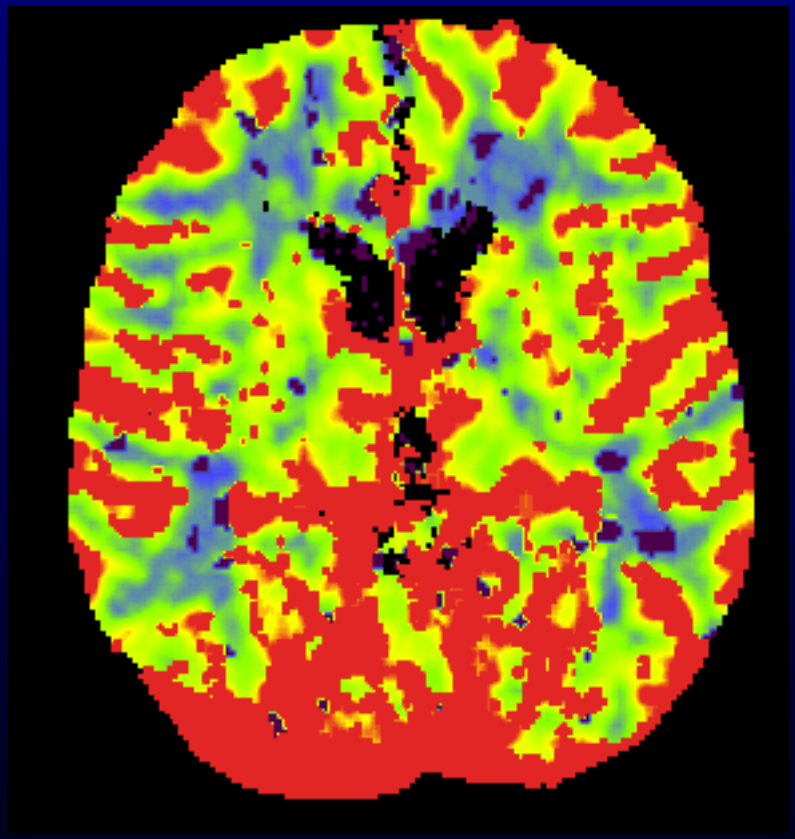


Post Diamox

CBV

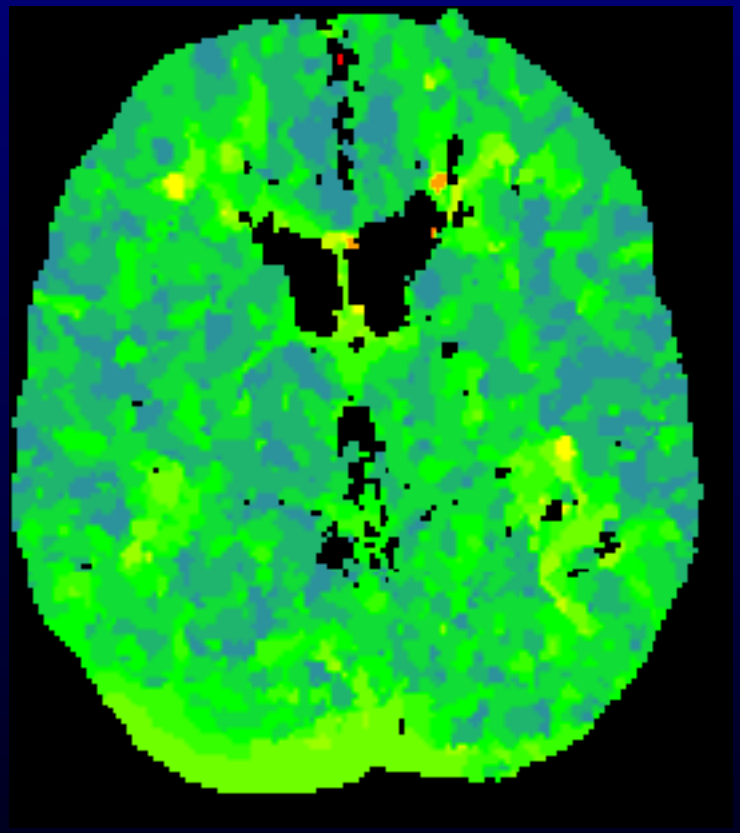


Pre Diamox

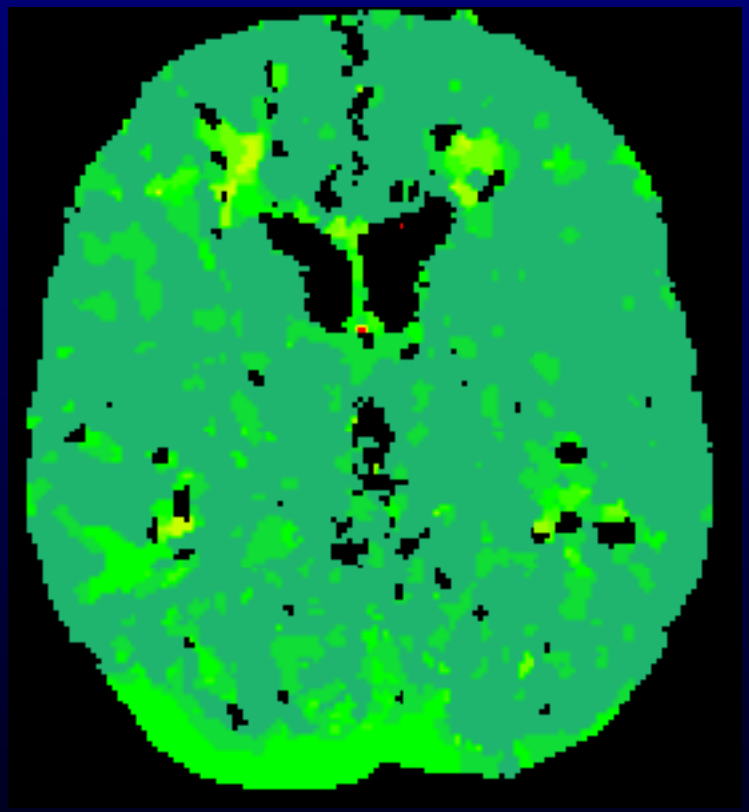


Post Diamox

TTP

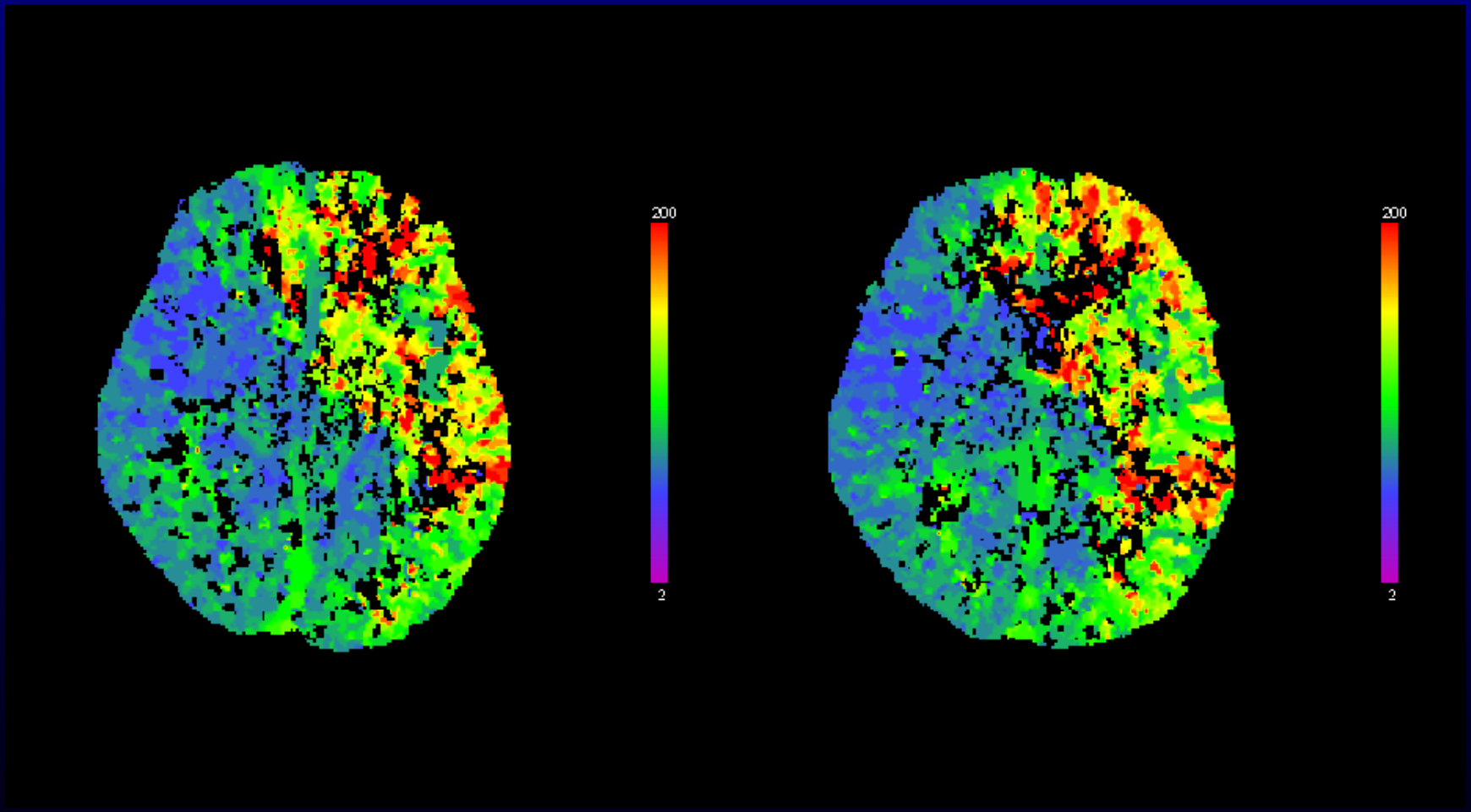


Pre Diamox

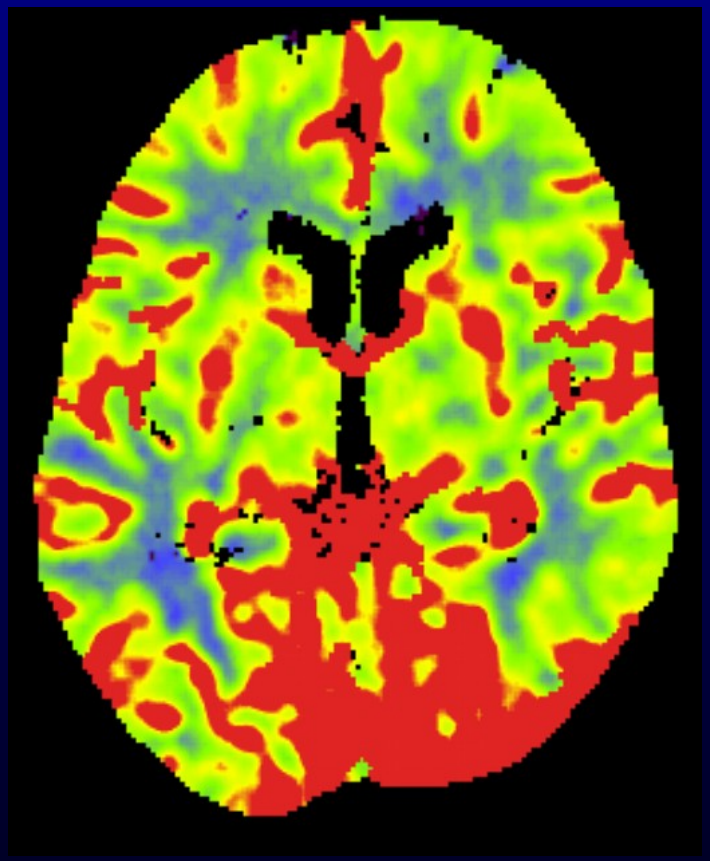


Post Diamox

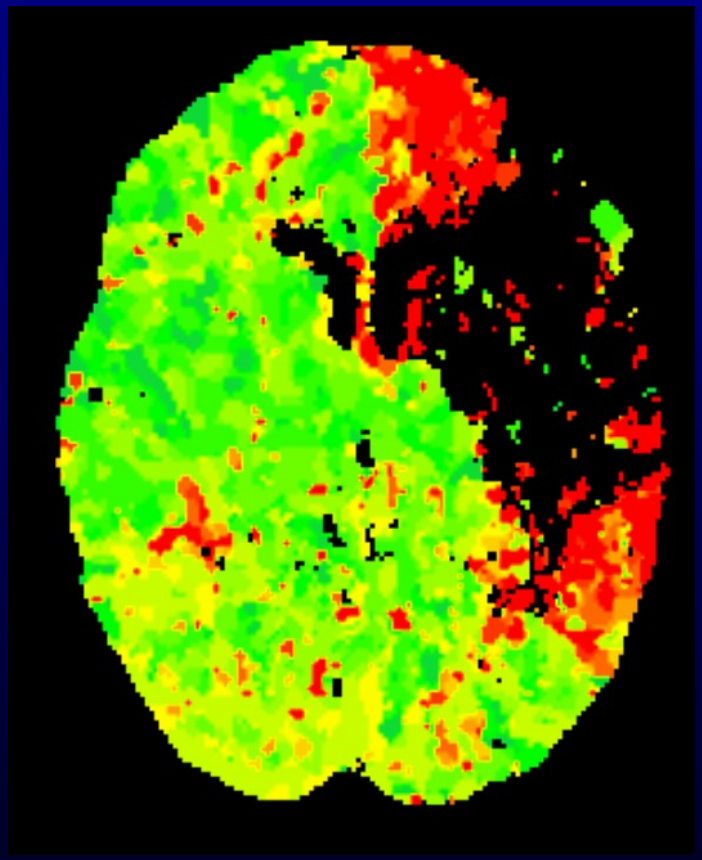
Hemispheric Ischemia



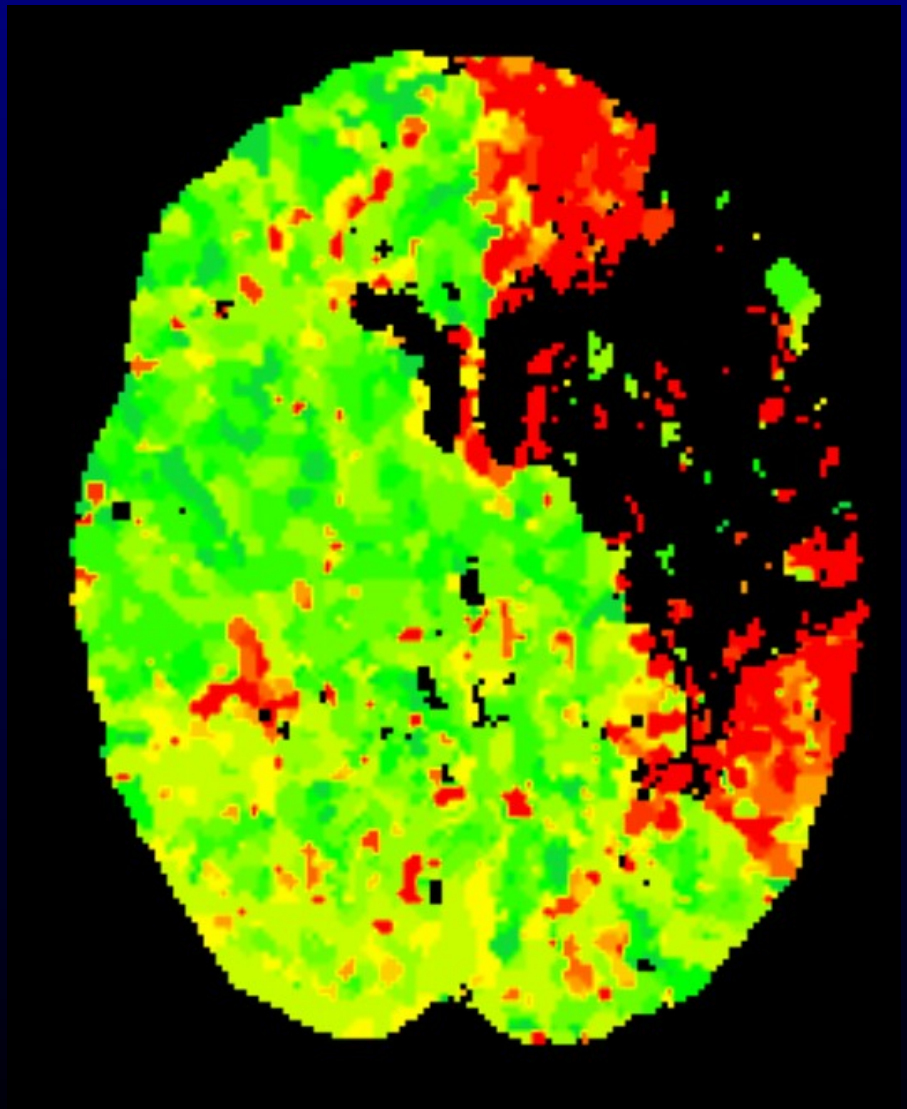
Successful Thrombolysis



Unsuccessful Thrombolysis



Pre Treatment

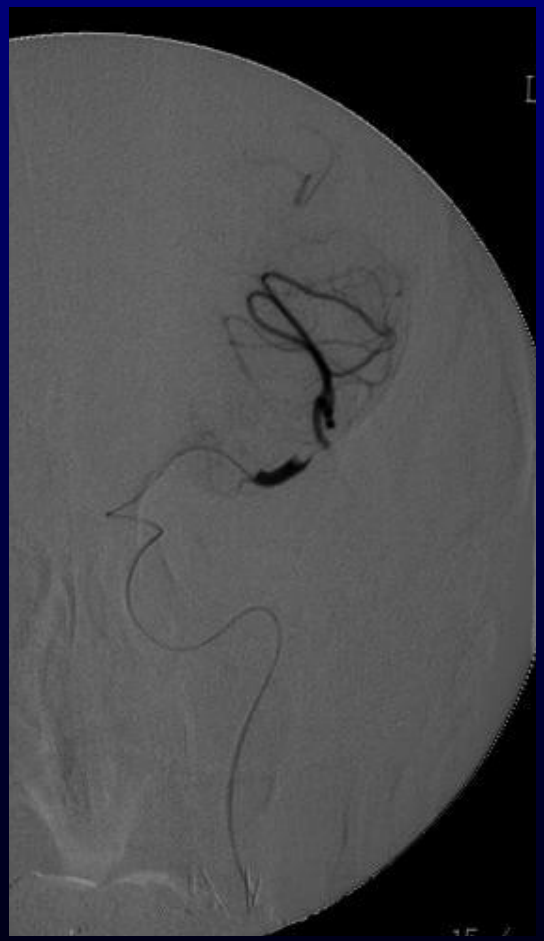


Technique

- Time is Brain
- Local anesthesia
- General anesthesia
- 6 F guide sheath is placed in the femoral artery
- Arch
- Selective angiogram

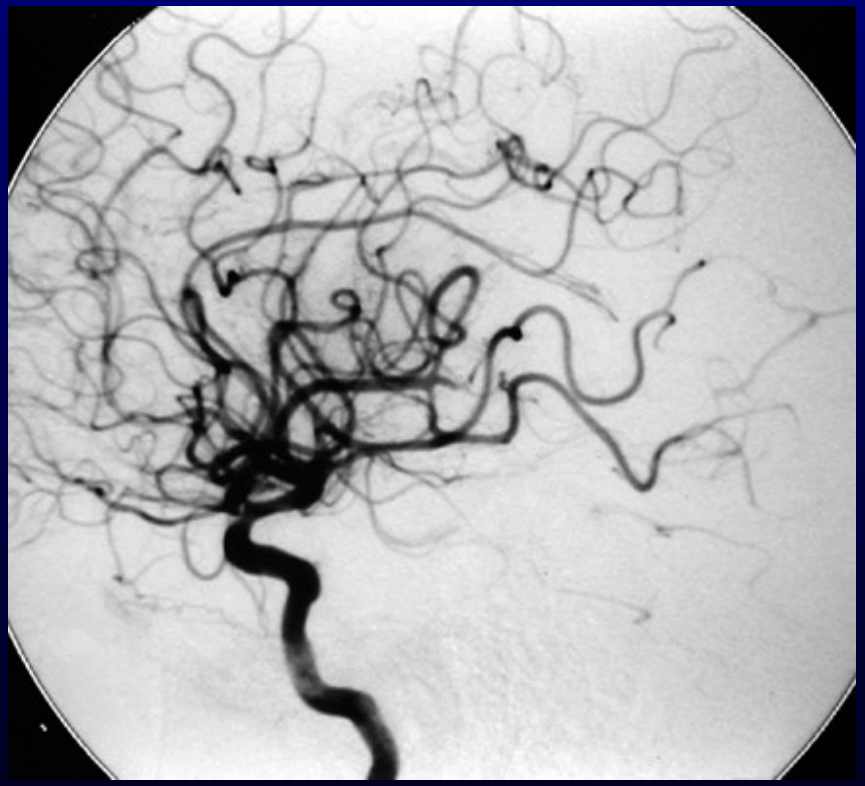
Technique (continued)

- Target SL-10
- A microcatheter angiogram
- Infusion thrombolytic of choice (retavase 1 U aliquot, max 4 U

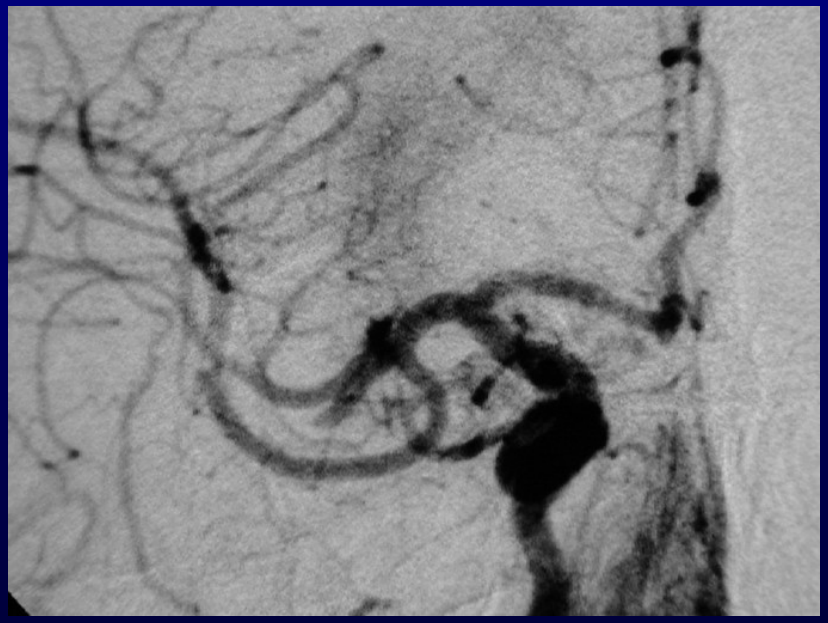


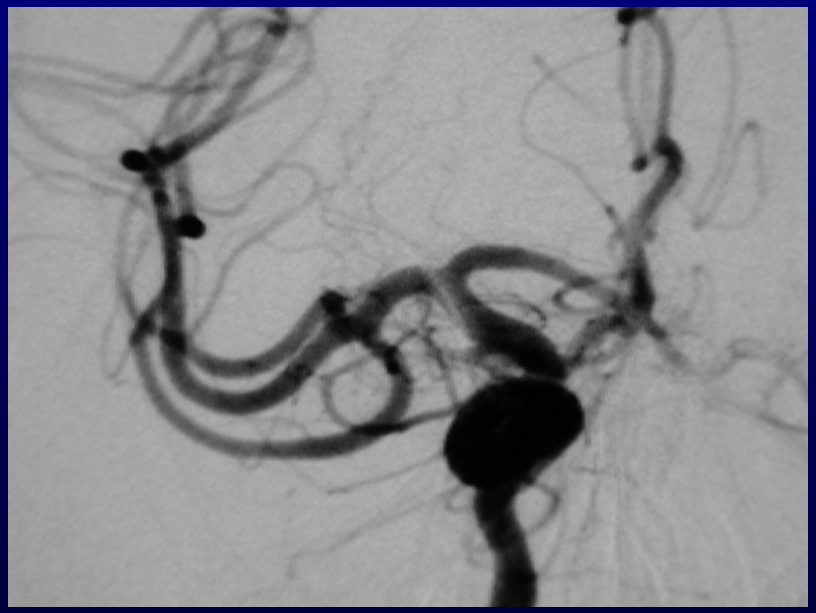
Be Patient, Let Drug Work

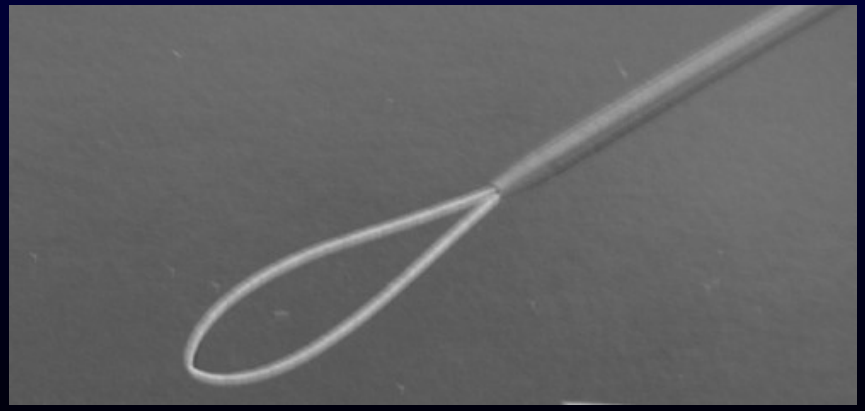
Can Take 60 min



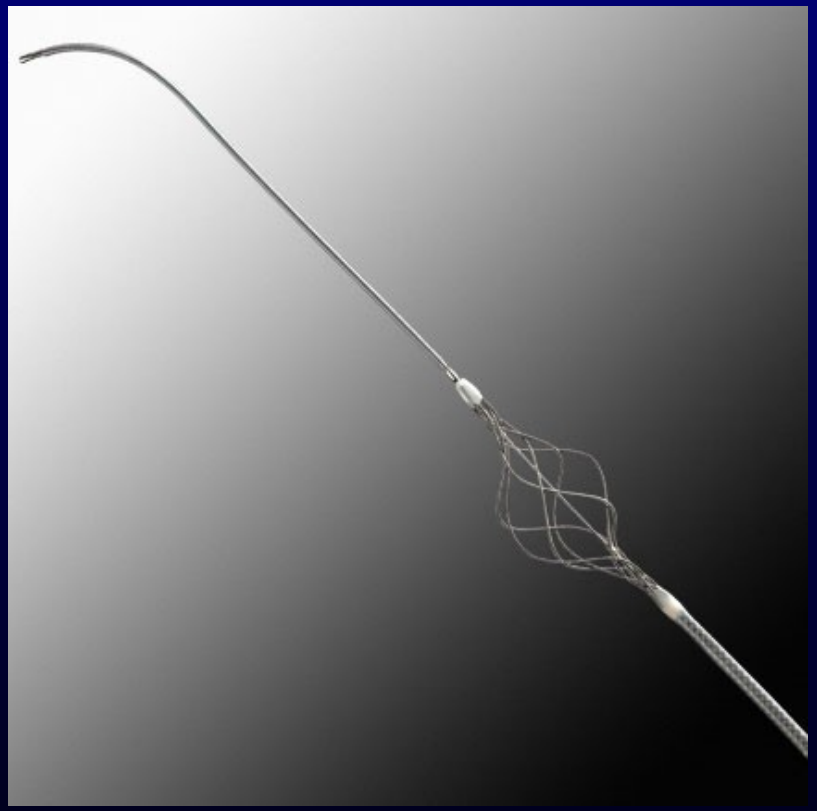
Can’t Wait - Snare



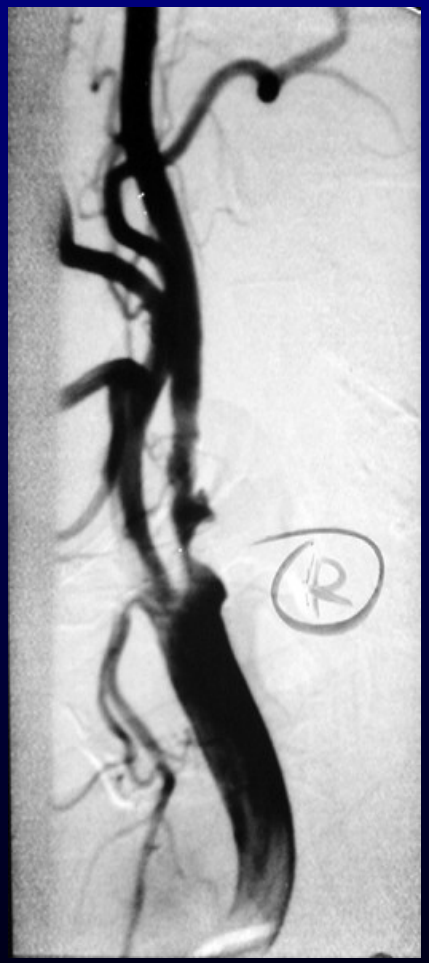




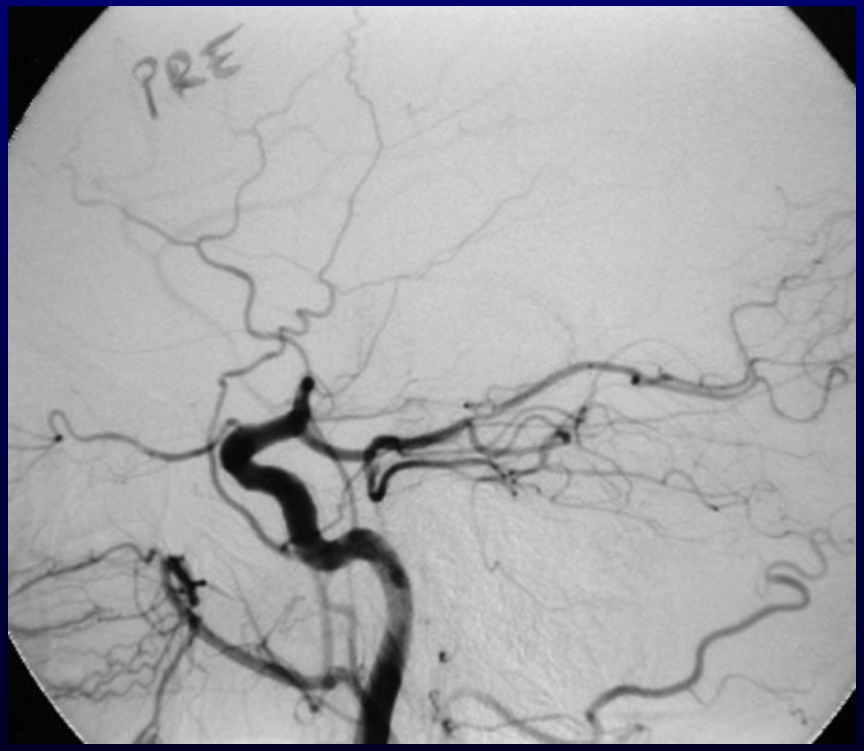
Target Coil Retriever



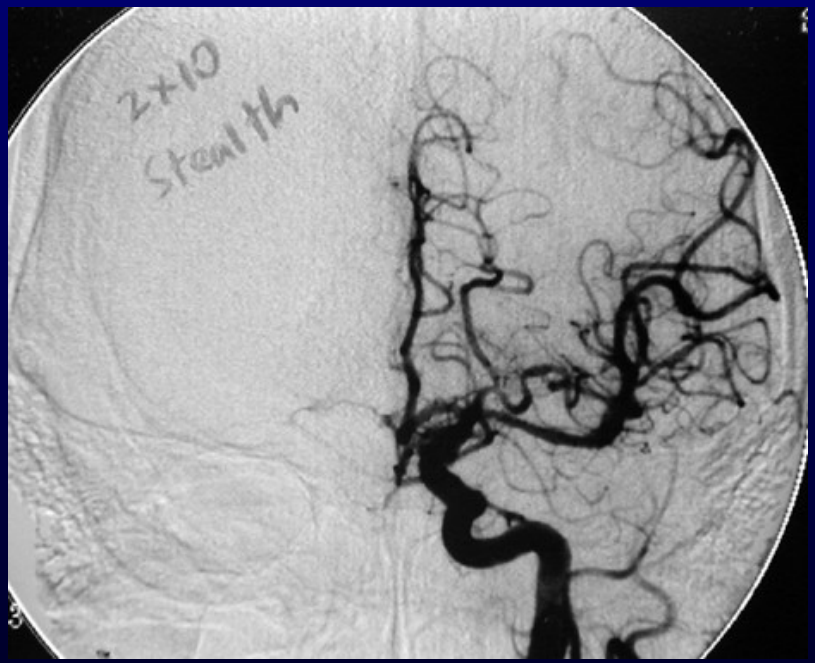
72 yr Black female
Acute Hemiplegia



72 yr female

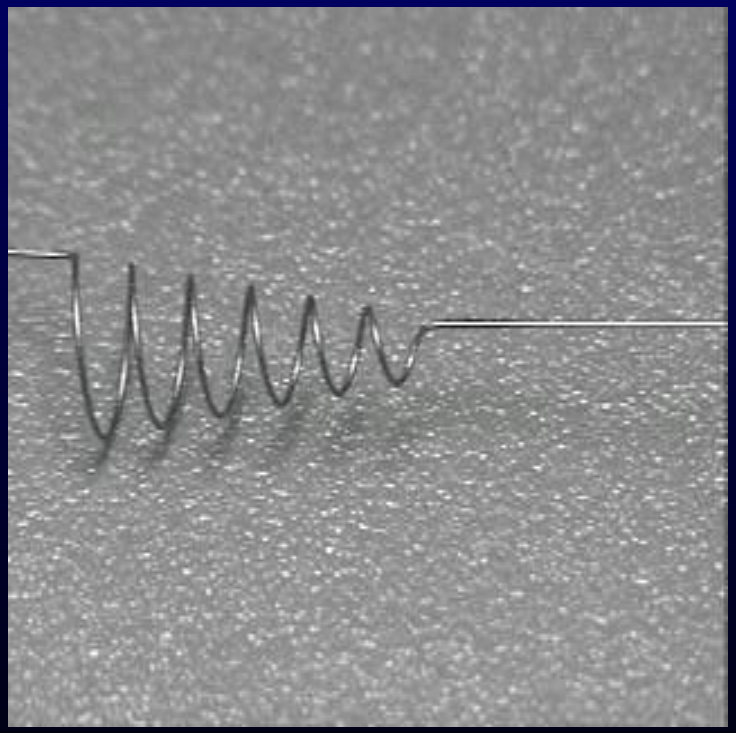


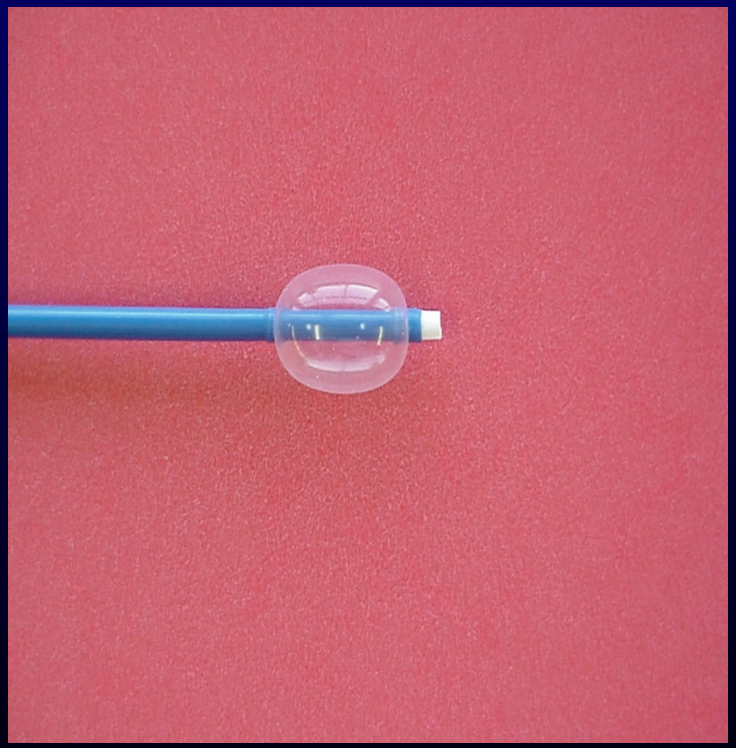
72 yr female post angioplasty



Concentric Retriever System

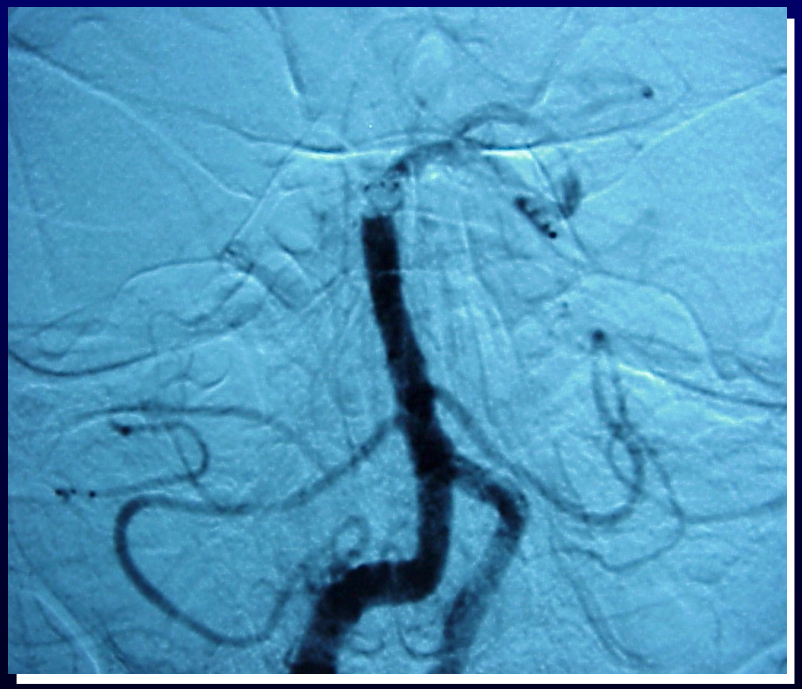
Thrombus Retriever X5

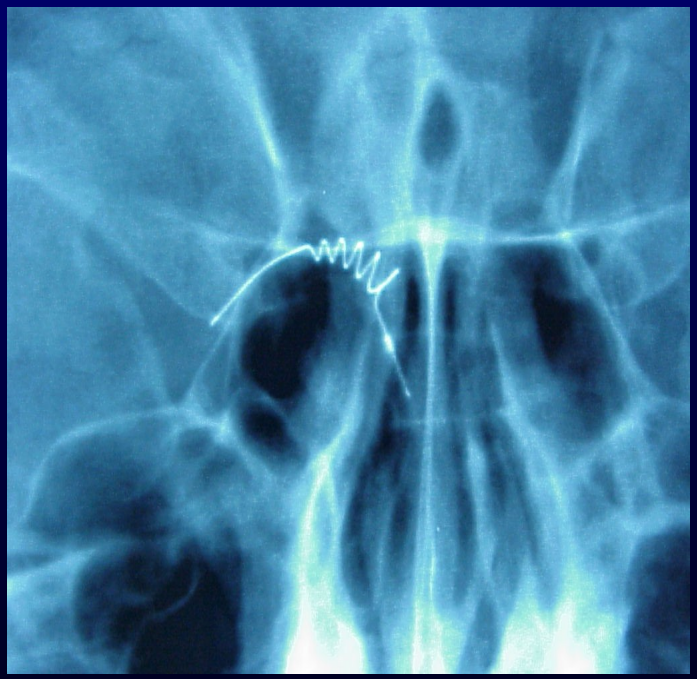




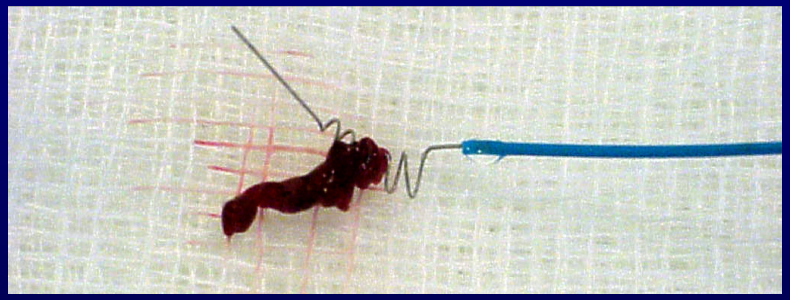
Basilar Case Study

31 year old male
Baseline NIHSS Score – 10
Symptom Onset to Treatment – 4h 30min





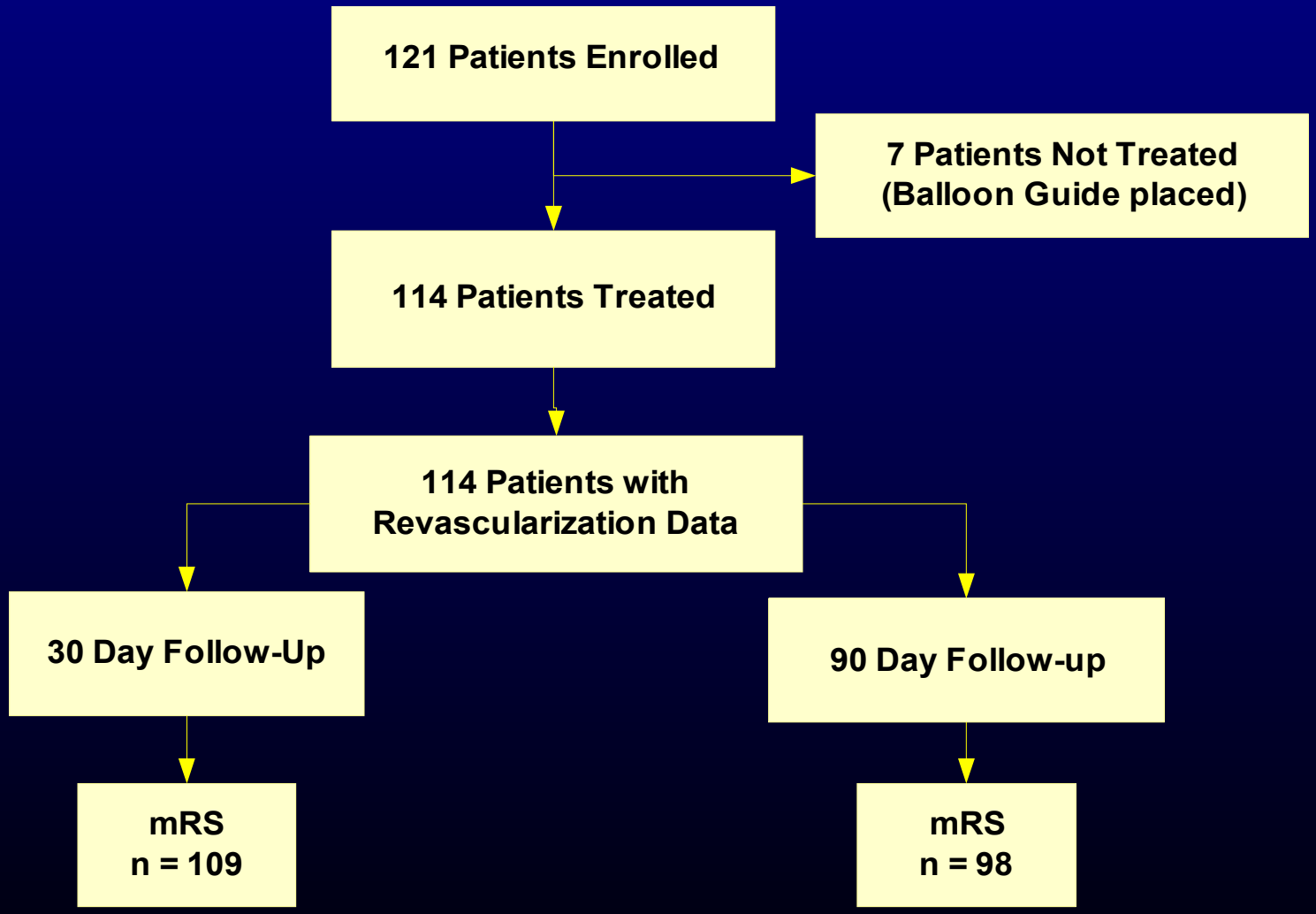
Basilar Case Study



NIHSSS 24 hours 0
30 days 0

mRS 90 days 0

MERCI® Trial Summary



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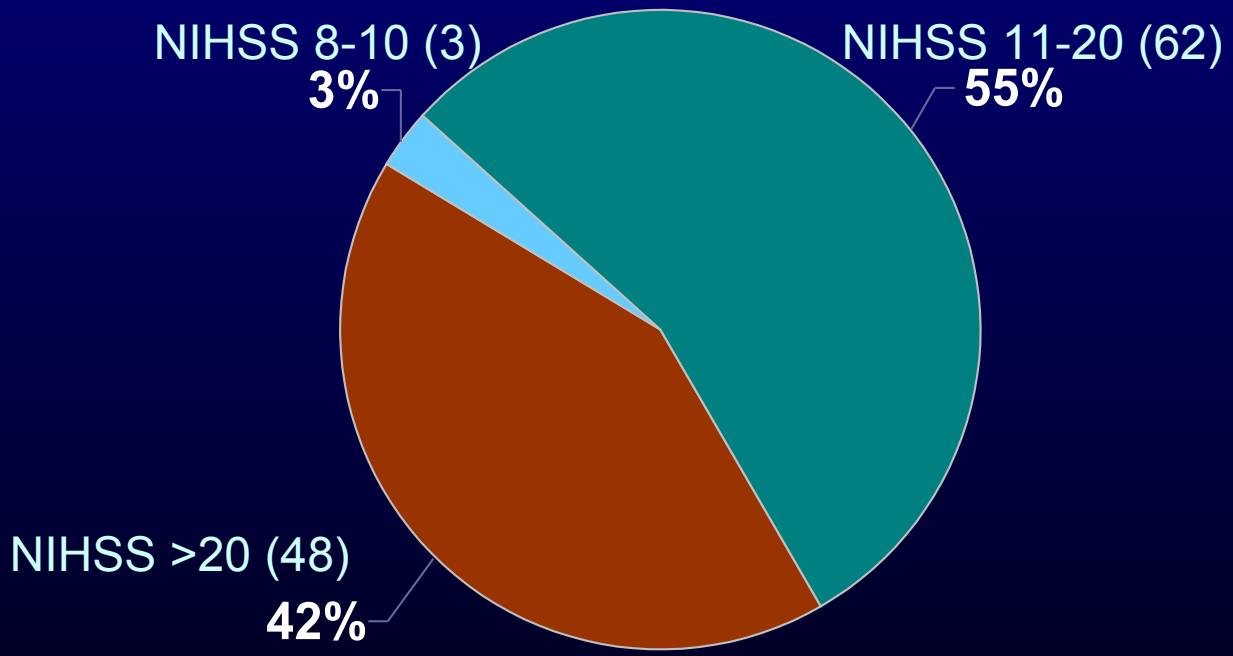
Baseline NIH Stroke Scale Scores

(n=113)*



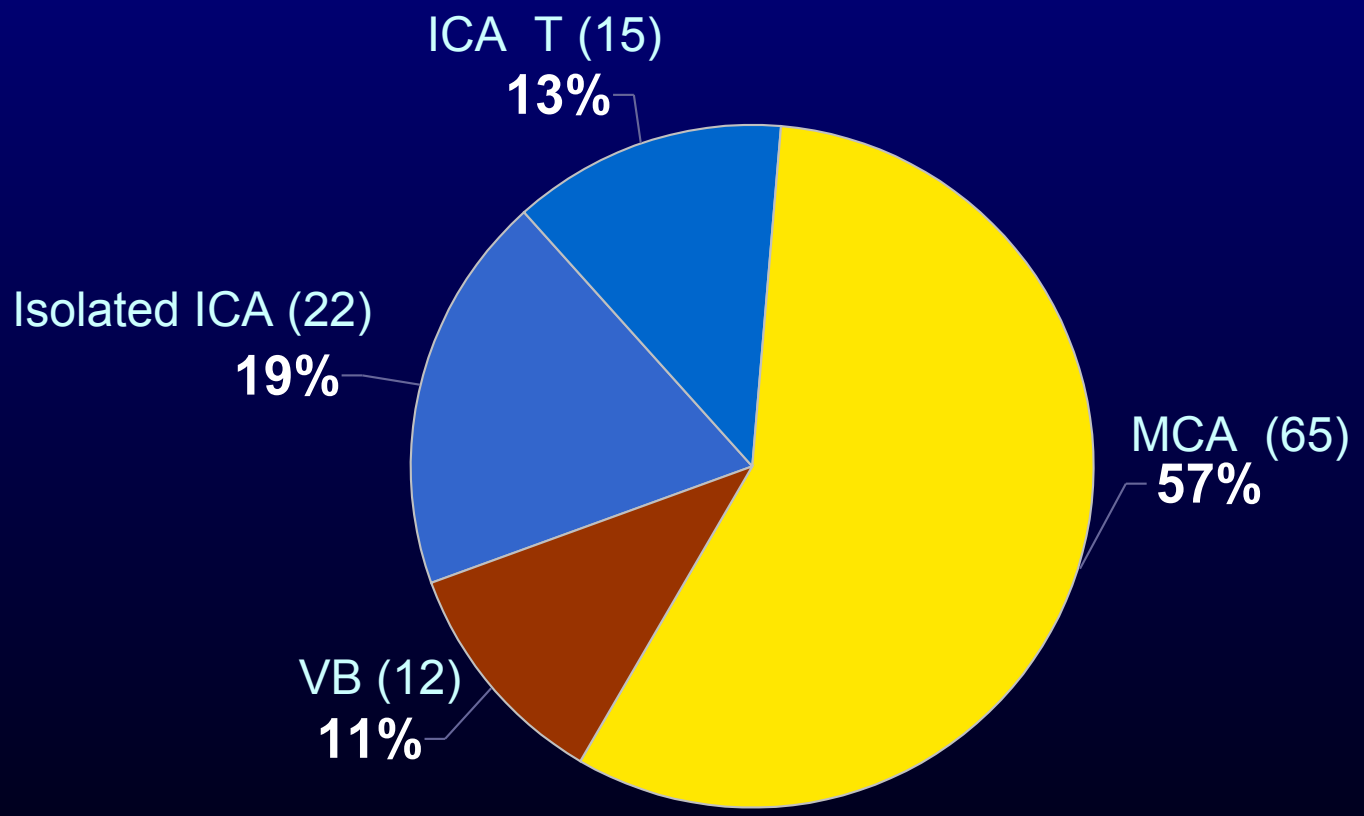
*Baseline NIHSS not recorded for 1 Patient

MERCI TRIAL

- Symptoms 0-8 hours
- Not just MCA and Vert (proact)
- Toughest lesions - carotid T

Occlusion Location/Vessels Treated

(n=114)



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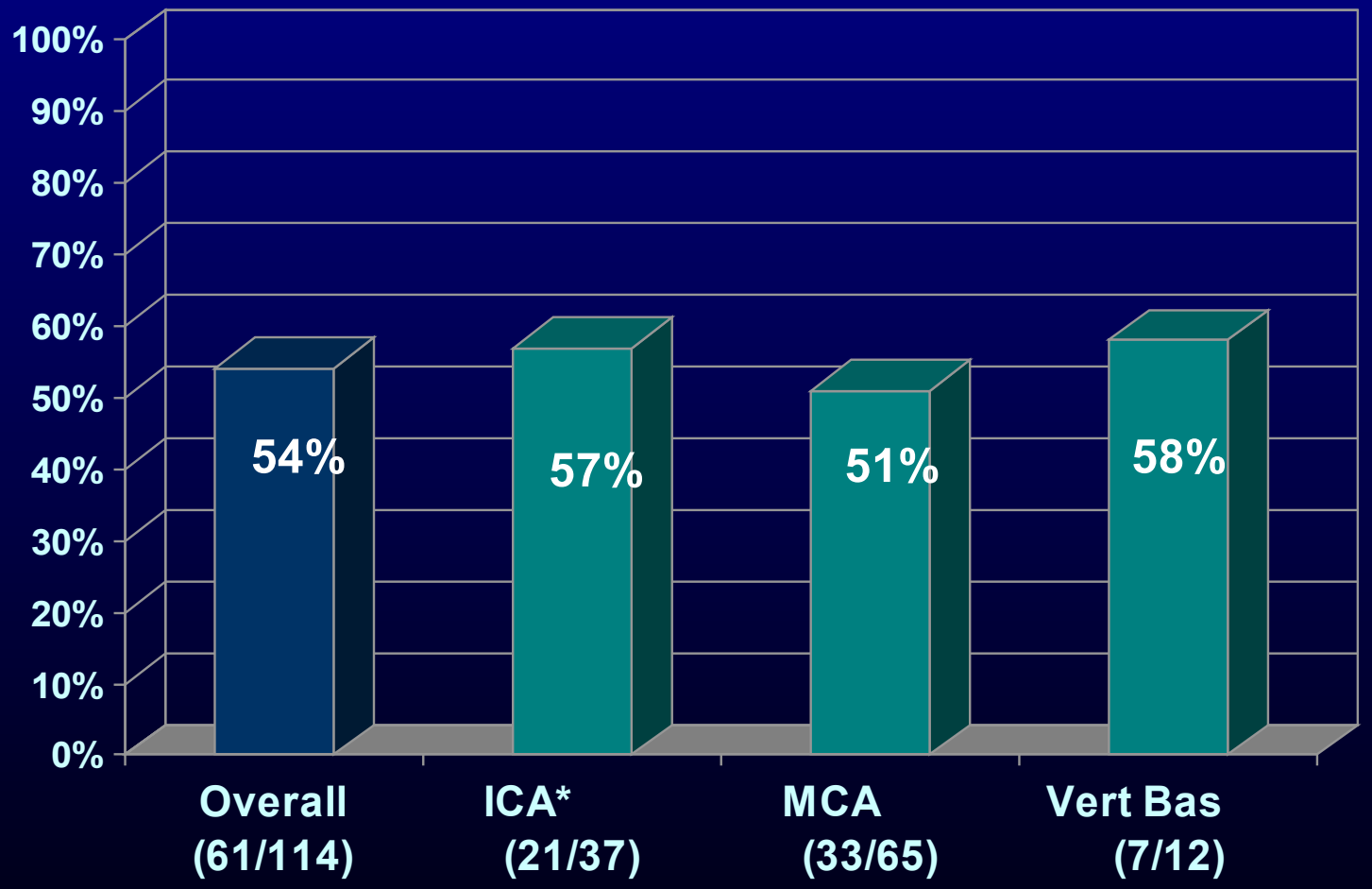
Successful Revascularization by Vessel



* ICA and ICA T (ICA/MCA/ACA) occlusions were combined into the ICA group

Device-Related Complications

3.5% (4/114)

Two Dissection/Vessel Perforation:

- Patient had evidence of a bleed on CT following treatment with the Retriever, snare and balloon angioplasty
- Patient had evidence of contrast extravasations on angiography following treatment with the Retriever
- **Merci Retriever tip detached in both patients**

Hemorrhage Rate Within 24 Hours

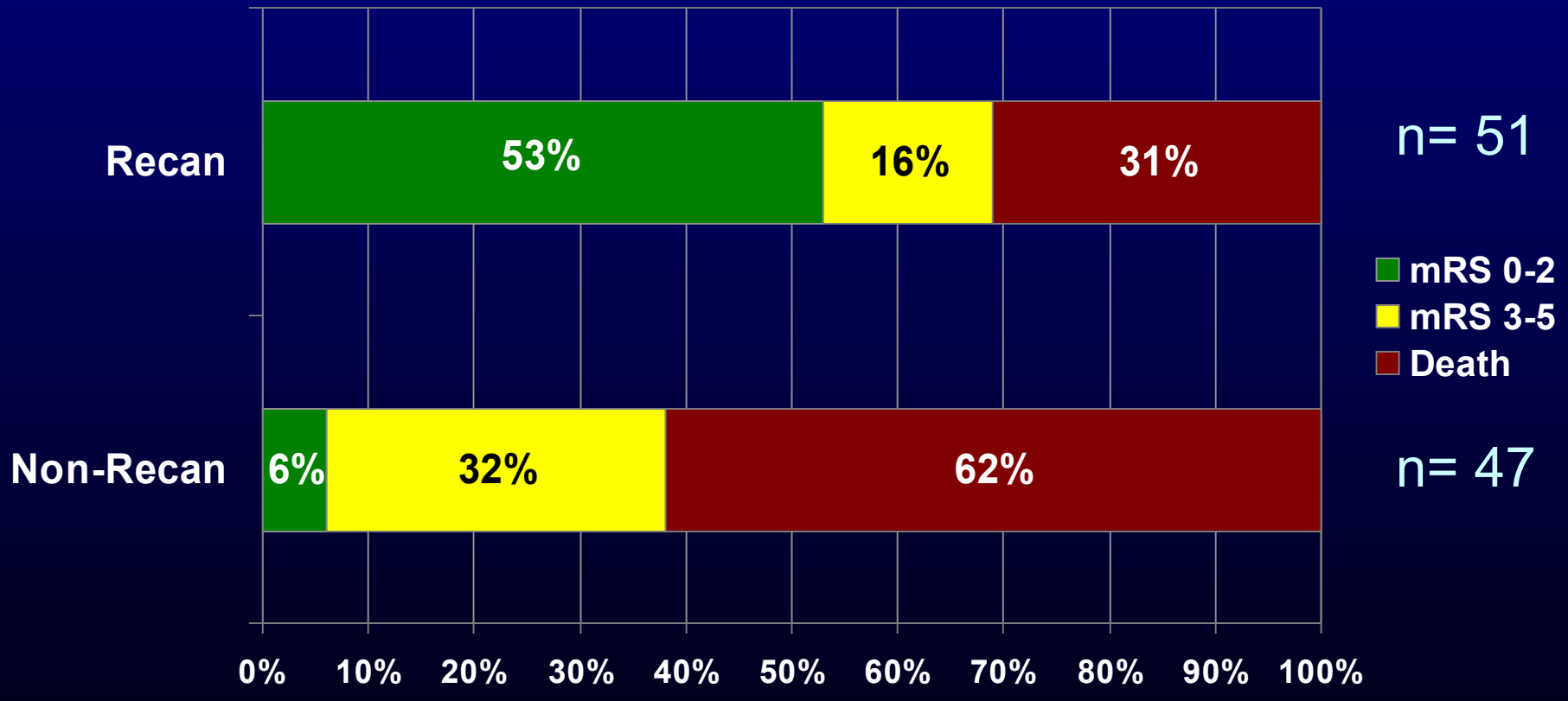
- Symptomatic Hemorrhage Rate — 8% (9/114)
  - Retriever Treatment Alone — 5% (5/97)
  - Retriever Plus (IA lytic/snare/etc.) — 24% (4/17)

- Symptomatic Hemorrhage by Clot Location
  - Middle Cerebral (n = 65) — 5% (3/65)
  - ICA/ICA-T (n=37) — 16% (6/37)
  - Vertebrobasilar (n=12) — 0%

- Asymptomatic Hemorrhage — 29% (33/114)

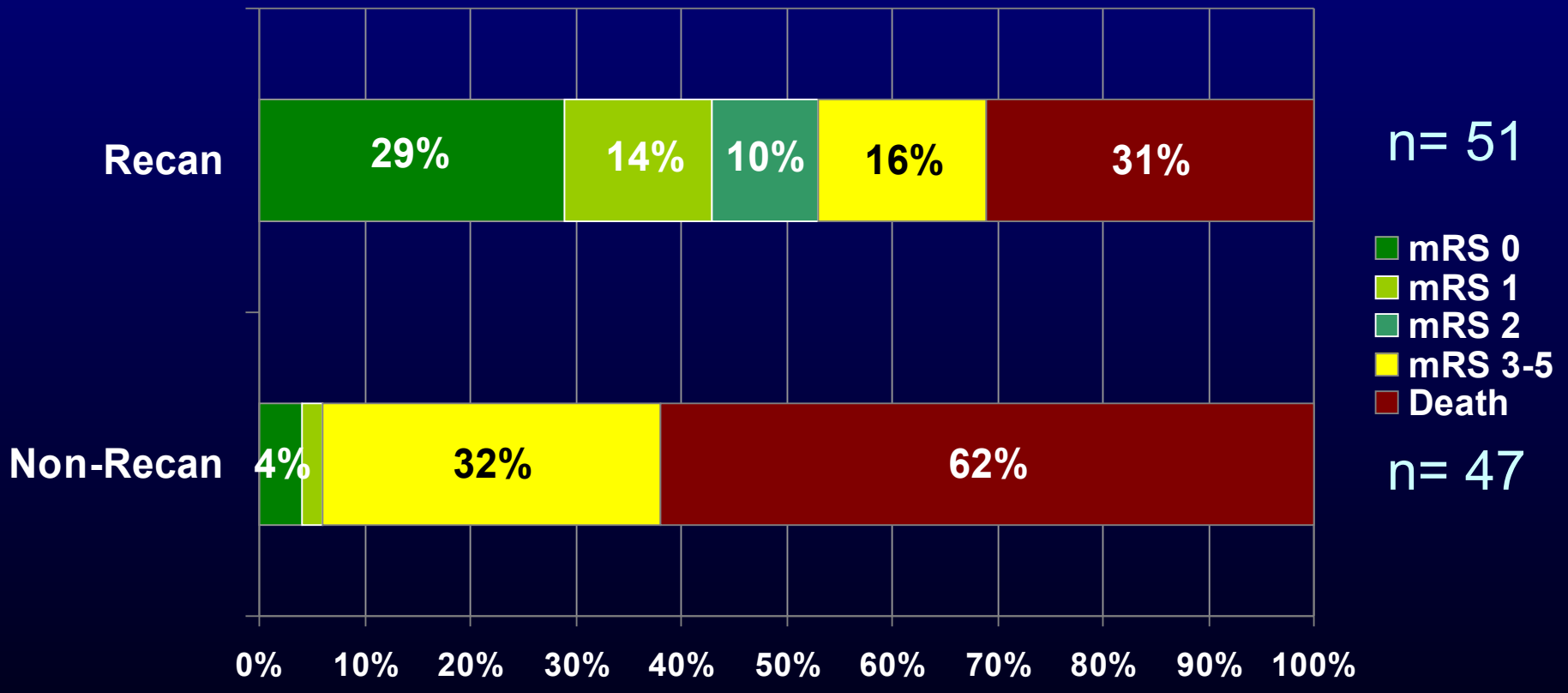
90-Day Modified Rankin Score

Revascularized vs. Unrevascularized



90-Day Modified Rankin Score

Revascularized vs. Unrevascularized



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MERCI® Primary Endpoints

	Revascularization*	Serious Complications (Device Related)
Total n=114	**53.5%** (61) $p < 0.0001^{\dagger}$ 95% Confidence Interval: 44.4% to 62.7%	**3.5%** (4)

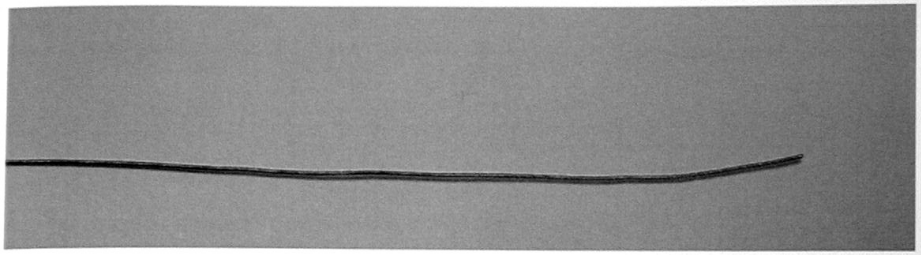
† p-value for showing superiority over a 18% success rate using the exact binomial test

* Revascularization defined as TIMI II/III flow achieved in the target vessel(s) with the Retriever alone (no adjunctive treatment).

Problems

- Rotate Device to Get it to engage clot
- Radial outward force

Primus

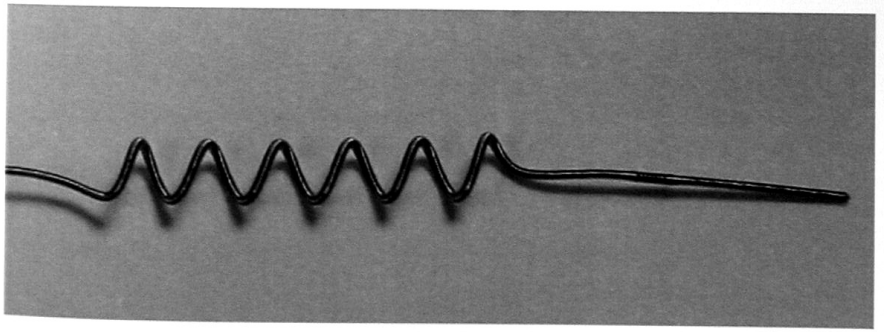


Device straightened

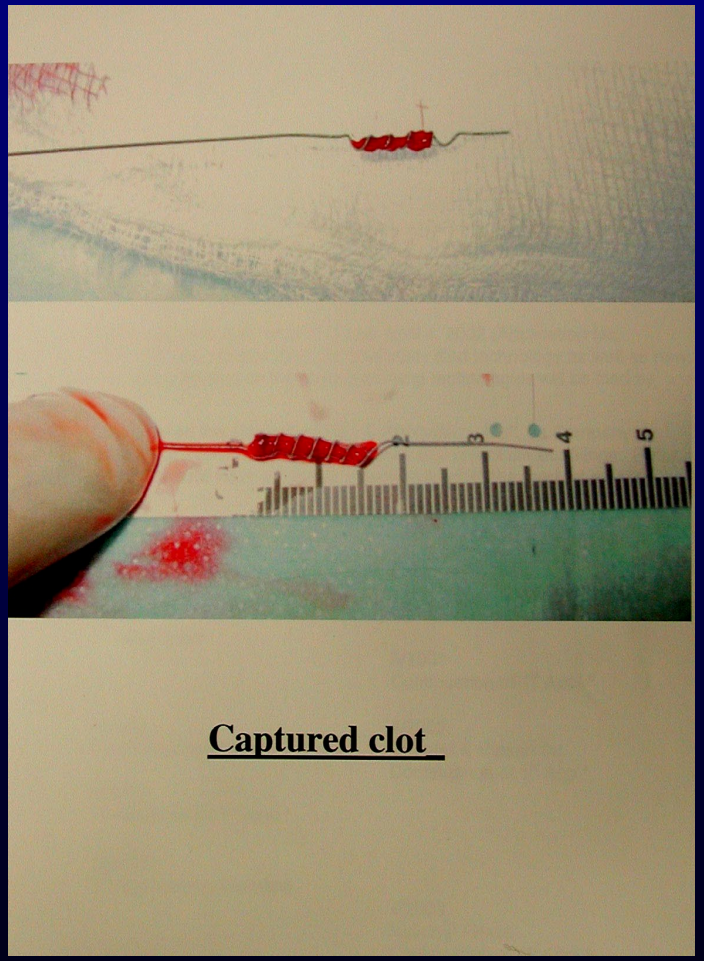
Actuated, for site access

Device deployed

Snare deployed for clot removal



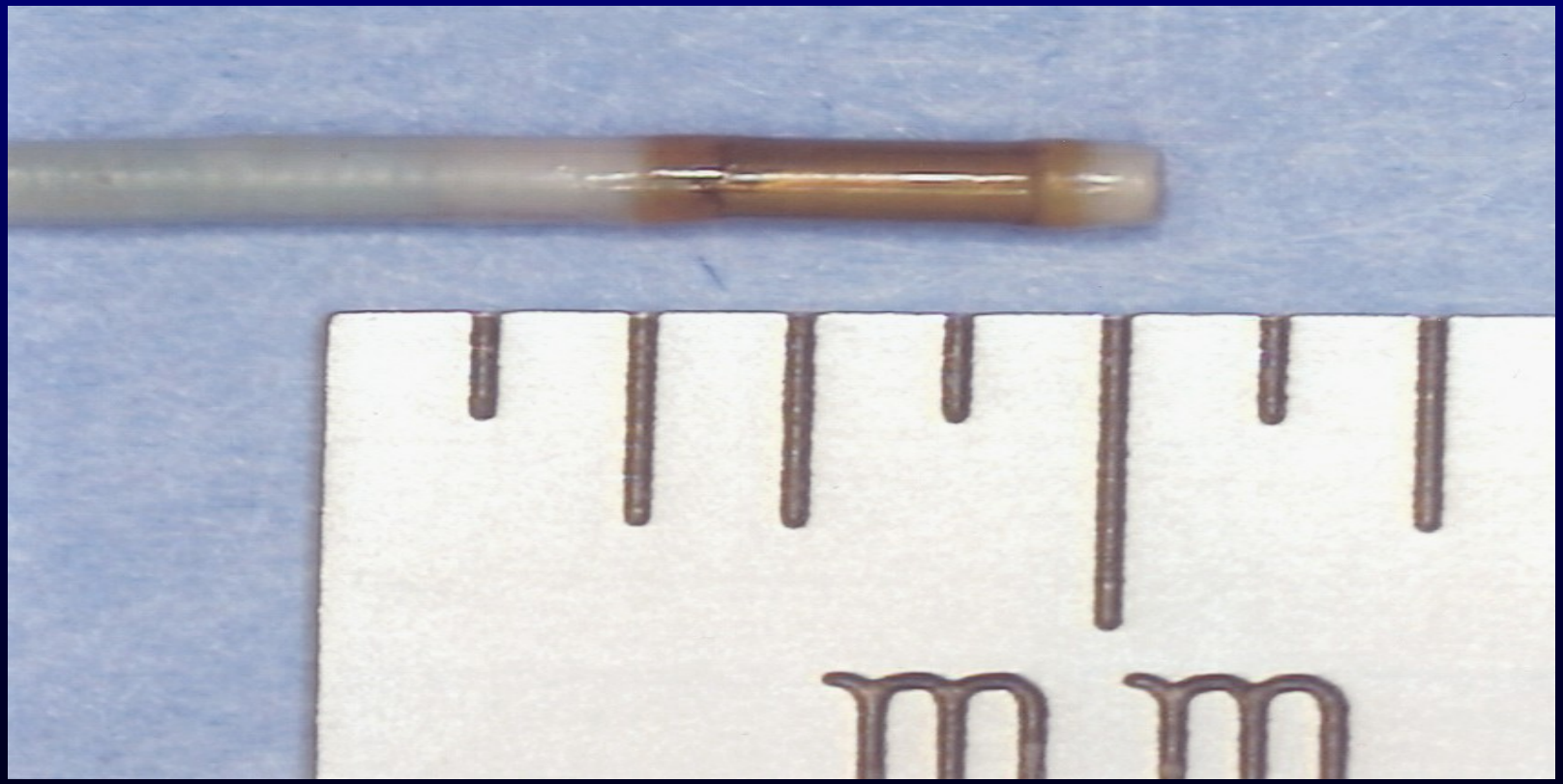
Primus



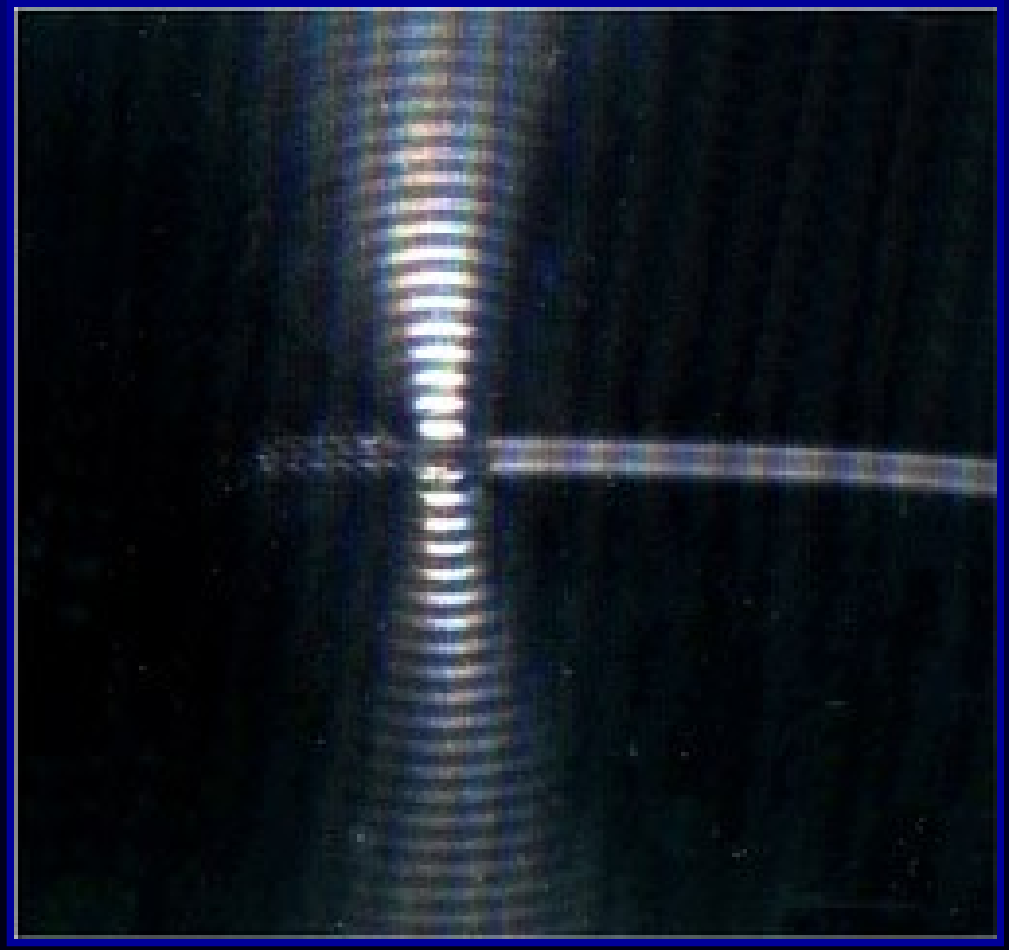
- Clot model invivo
- Not yet in humans
- Promising device
- Spring effect

TIME TO REVASCULARIZATION

The EKOS 2.5Fr SV Microcatheter Delivery Tip



EKOS Ultrasound Infusion Catheter_



Phase I Ischemic Stroke Clinical Data

- N = 30
- Anterior circulation < 6 hours
- Posterior circulation < 24 hours
- UK, rPA, tPA
- Results
  - No adverse events related to EKOS catheter
  - **Avg time to recan = 46min***

***Mahon, et.al, AJNR Mar 2003**

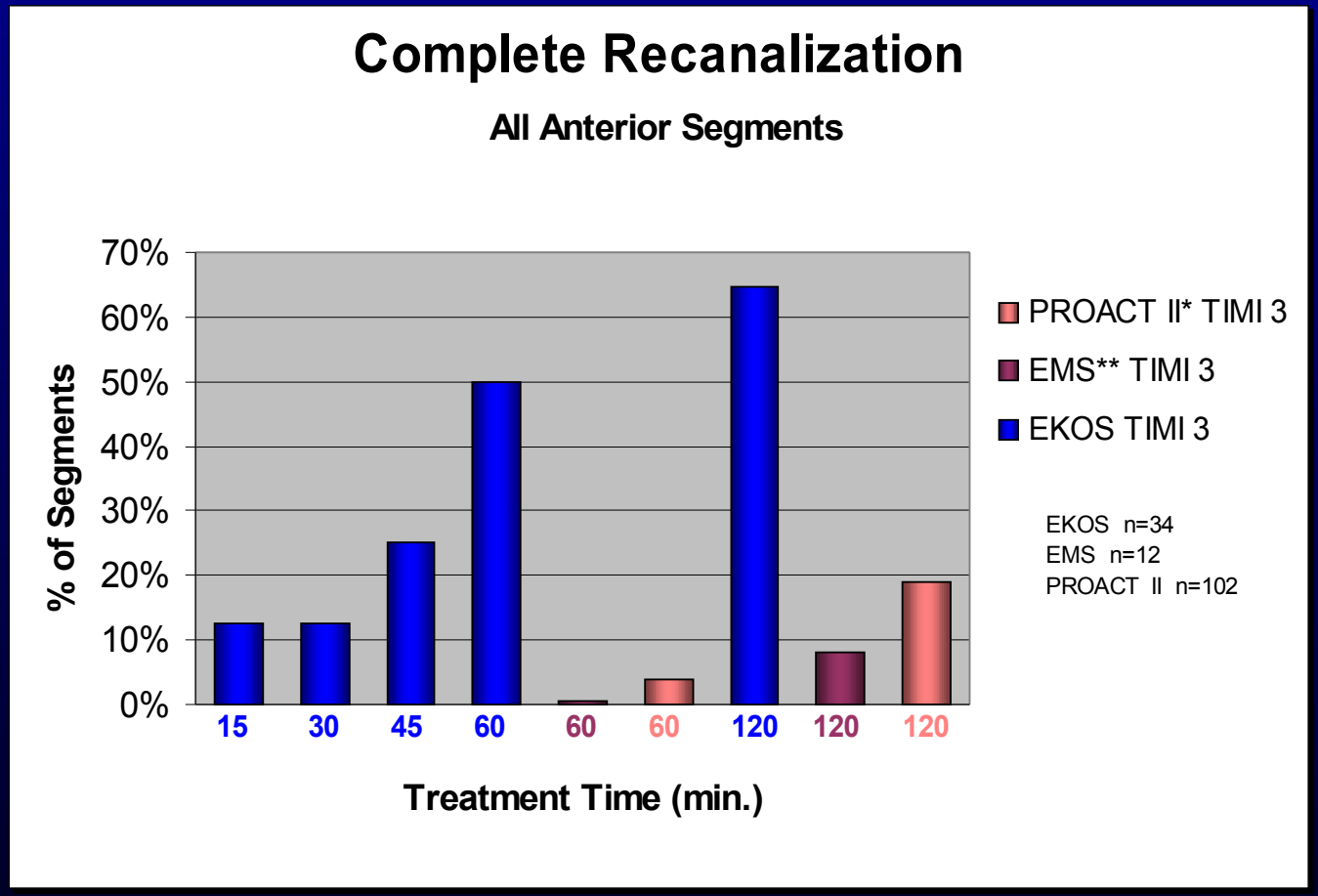
Recanalization Result

All MCA Occlusions	EKOS* 11 patients	PROACT II** 104 patients	EMS 10 patients
TIMI 3 @ 1 hr	27%	4%	10%*

*EKOS = All anterior occlusions

** PROACT II = MCA occlusions only

Complete Recanalization



* Furlan, et. al., JAMA, 1999; 282 (21):2003-11

** Lewandowski, et al, Emergency Management of Stroke (EMS), *Stroke*. 1999; 30:2598-2605

Comparisons of Carotid "T" Occlusion Results

	EKOS (7)	EMS(5)**
mRS ≤ 2 (good outcome)	29%	0%
NIHSS ≥ 50% decrease	**43%**	**0%***
Sx ICH	13%	20%
Mortality (7-10 days)*	25%	60%

* Lewandowski, et al, Emergency Management of Stroke (EMS), *Stroke*. 1999;30:2598-2605

1. IMS II (on-going): 0-3 h. window, comparable to NINDS
   - Expands 0-3 h. window market
   - IMS I Trial performed with standard microcatheter
   - Providing direct comparison for EKOS

IMS II Status

Sept 27, 2004

- 13 sites enrolling
  - Goal: 18 centers
- No. patients enrolled: **42**
  - No. IV only **14**
  - No. IA treated (67%) **28**
- Goal: 70

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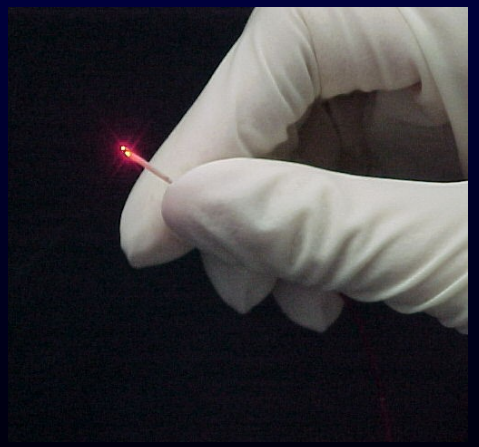
* Lewandowski, et al, Emergency Management of Stroke (EMS), *Stroke*. 1999;30:2598-2605

Early indicator of IMS II flow improvement Tomsick, et. al., 2004 World Stroke Conference

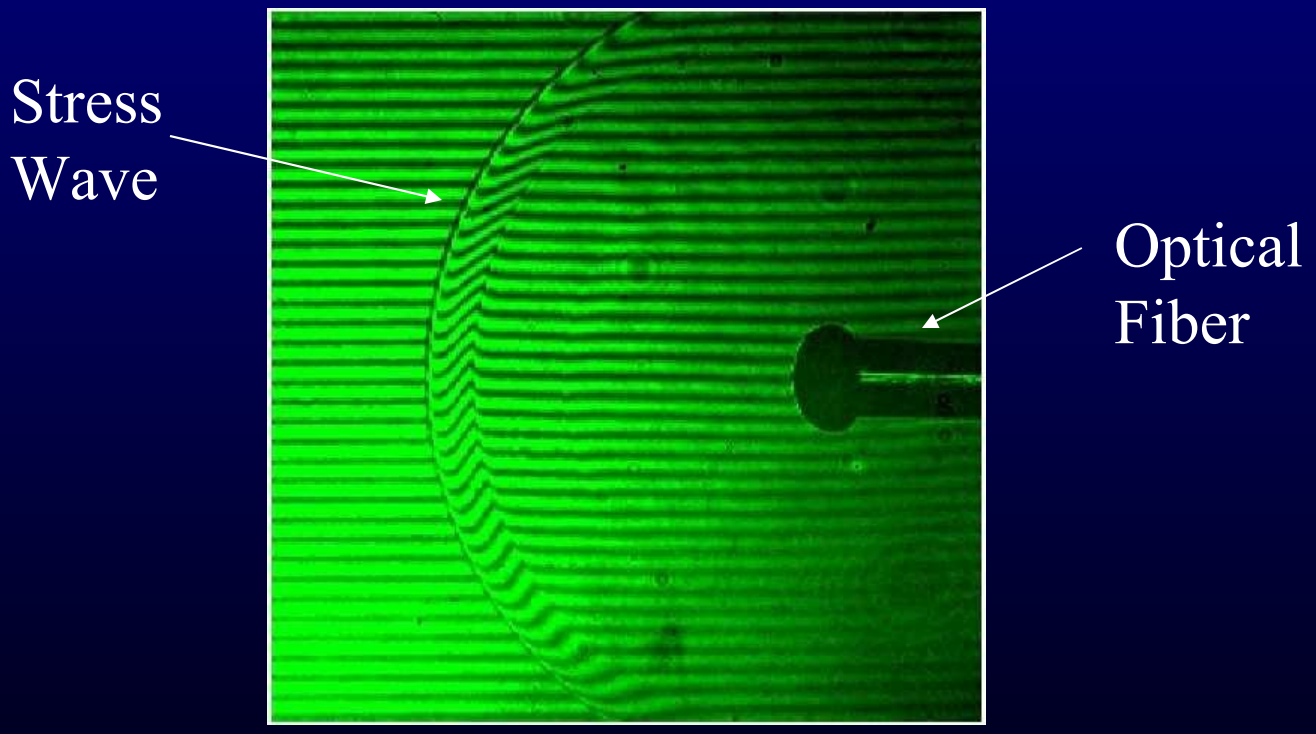
- Angiograms were performed every 15” during procedure to monitor for recanalization
- 62 available angiographic data points available for MicroLysus Catheter and 35 for standard microcatheter thrombolysis
  - **53% MicroLysus efficacy**
  - **34% standard catheter efficacy** (p=0.07)

EPAR Emulsiwire Microcatheter

- 3F windowed microcatheter
- Used with standard 0.014” guidewires
- Graded flexibility
- Wire reinforced proximal segment
- Highly flexible distal 3cm
- Hydrophilic coating



Transient Micro-bubble and Shockwave Generation



Conclusions

- Time is Brain
- Pharmacologic thrombolysis useful
- Mechanical adjuncts can help open vessels faster
- No reimbursement
- Labor intensive patients
- BUT REWARDING
- Team Approach most successful

WHO SHOULD DO THIS ?

- Different than coronary intervention, but close
- Dedicate your life to treatment cerebral ischemia

WELCOME TO THE FINAL FRONTIER