

INTERVENTIONAL THERAPY OF ACUTE STROKE: CURRENT INDICATIONS, TOOLS AND OUTCOMES

Alex Abou-Chebl, MD
Associate Professor of Neurology
Director of Interventional Neurology
Director of Vascular and Interventional Neurology Fellowships
University of Louisville School of Medicine



Disclosures

- Speakers Bureau BMS/Sanofi
 - Consultant Codman (J&J)
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Challenge for Neurology

- Quickly recanalize without increasing the risk of ICH
 - Cerebral vessels thin and fragile
 - Catastrophic
- Reperfusion injury
- Distal embolization

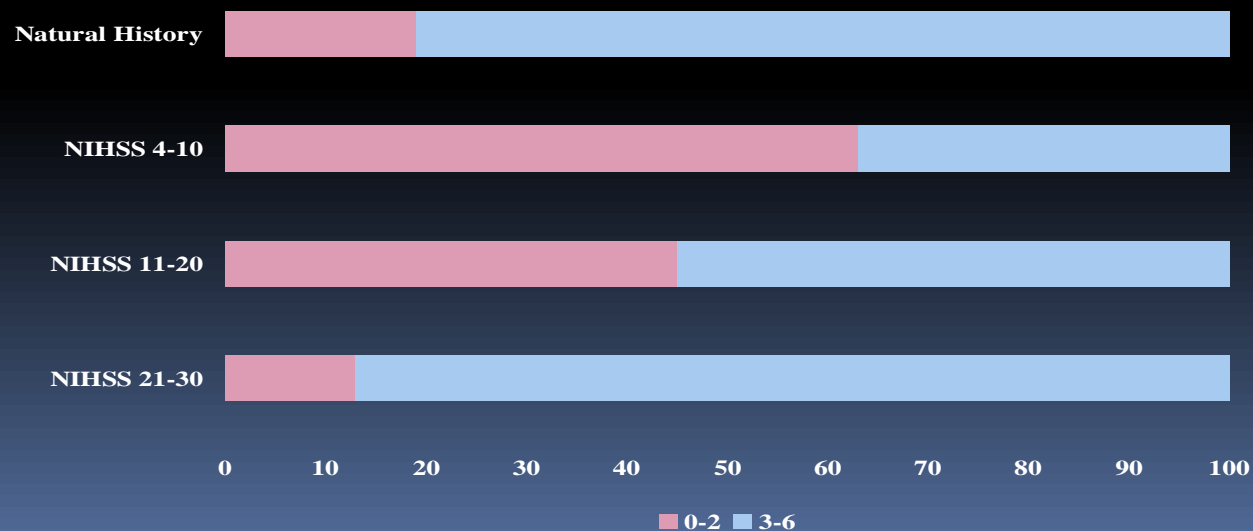
Current Practice

- Effective time window for minimizing injury is
 - <3hrs with IV Lysis unselected- NINDS tPA Trial, ATLANTIS, etc.
 - 3-4.5hrs selected- ECASS 3 Trial
- Time window for IA lysis accepted to be <6hrs- PROACT II Trial
- Based heavily on pharmacological thrombolytic therapy
 - 6-37% risk of ICH
- Without benefit of modern imaging modalities to assess the ischemic penumbra
- Few patients present <6hrs
 - 58% >6hrs
- Some territories more resistant, e.g. BA occlusion
- Some patients can not receive thrombolytics
- There is a need to Tx beyond 6hours

The Prolyse in Acute Cerebral Thromboembolism Trial: PROACT II

Furlan A, et.al.JAMA, February 1999

- Only randomized, controlled study of IA lysis
 - Ischemic Stroke <6 hours duration
 - Angiographically proven MCA occlusion
 - Early infarct signs on initial CT <1/3 MCA territory
- 58% Relative (15% Absolute) Benefit
- sICH 10%

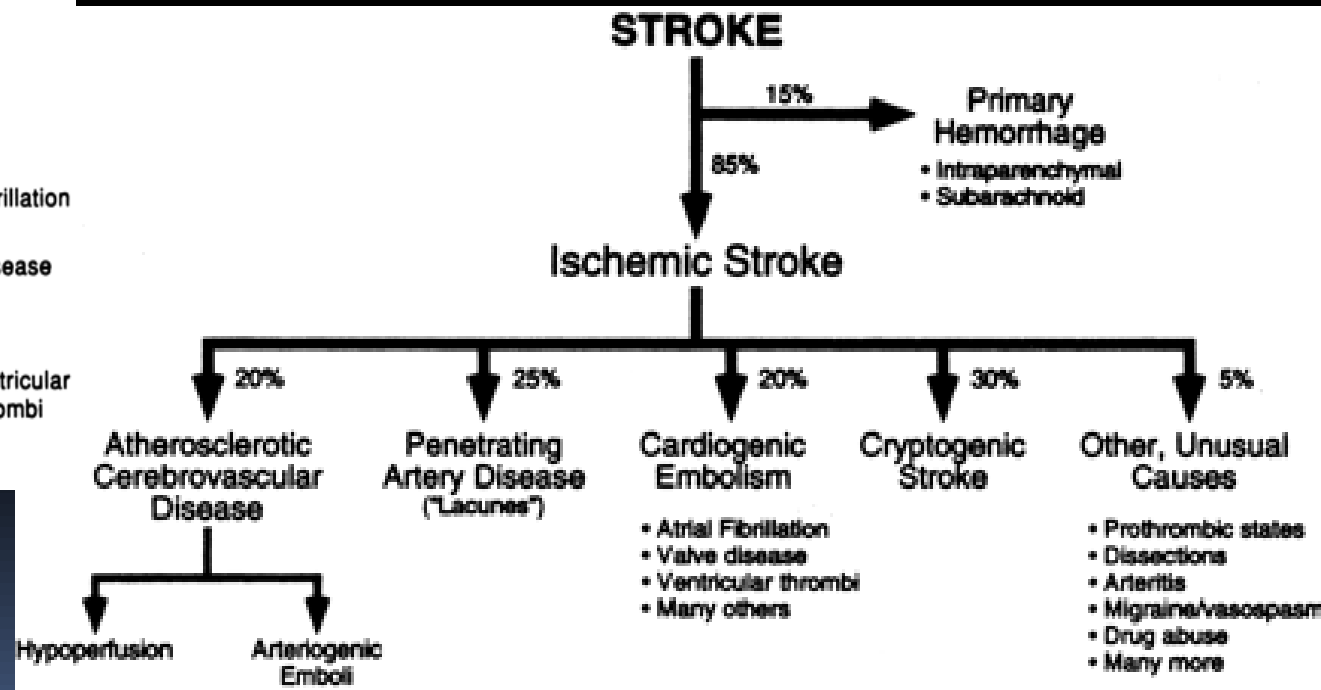
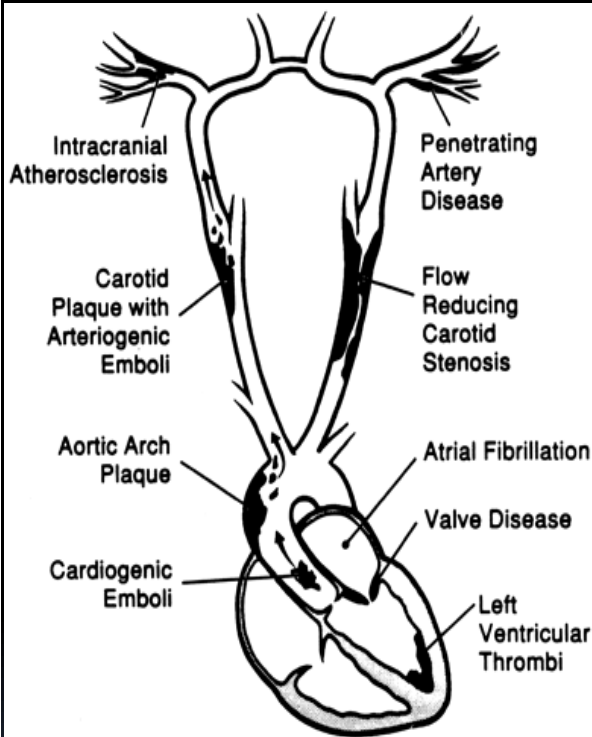


Thrombolysis Limitations

- IV tPA
 - <5% Ischemic strokes treated
 - <3-4.5hr window
 - Same for All Pts.
 - Multiple Exclusions
 - Modest Clinical Efficacy
 - 6% ICH
- IA Thrombolysis
 - Moderate Recanalization Efficacy
 - TIMI₃ 19%
 - Up to 2hr for recanalization
 - Only proven agent (r-pro-UK) not available
 - 10%-38% ICH

Stroke is Heterogeneous

- Thrombi/Emboli of varying compositions



Multimodal Treatment Tailored for Each Patient

- 12 Patients
- NIHSS 18.7 ± 3.5 (Range 15-25)
- Sx Duration 3.6 ± 2.2 (Range 0.5-8hrs)
- Occlusion- 5 MCA, 6 Carotid Terminus, 1 BA

Lysis	Lysis Result	2nd Intervention	Result	3rd Intervention	Result	4th Intervention	Result	5th Intervention	Result
Yes	TIMI 1	Angioplasty	TIMI 2 (Reoccl)	Reopro	TIMI 3	None			
IV full dose	TIMI 0	Angioplasty	TIMI 0	Snare	TIMI 0	Reopro	TIMI 2	ICA PTA	TIMI 3
No		Angioplasty	TIMI 2	Reopro	TIMI 3	None			
Yes	TIMI 1	Angioplasty	TIMI 1	Reopro	TIMI 3	Hypothermia	Good	None	
Yes	TIMI 2 (Reoccl)	Reopro	TIMI 2	Angioplasty	TIMI 2	None			
Yes	TIMI 0	Angioplasty	TIMI 2	Integrelin	TIMI 2	None			
Yes	TIMI 0	Reopro	TIMI 0	Angioplasty	TIMI 1	Angiojet (ICA)	TIMI 2	None	
Yes	TIMI 0	Reopro	TIMI 0	Angioplasty	TIMI 3	None			
Yes	TIMI 0	Mechanical Disruption	TIMI 1	Reopro	TIMI 3	None			
Yes	TIMI 0	Reopro	TIMI 0	Angioplasty	TIMI 0	Snare	TIMI 1 (ACA)	TIMI 3) None	
Yes	TIMI 0	Angioplasty	TIMI 1	Reopro	TIMI 3	None			
Yes	TIMI 0	Angioplasty	TIMI 0	Reopro	TIMI 0	Snare	TIMI 3	None	

- Mortality 2/12 (17%)
- sICH 1/12 (8.3%)
- D/C No or Min. Disability (Rankin ≤ 2) 6/12 (50%)

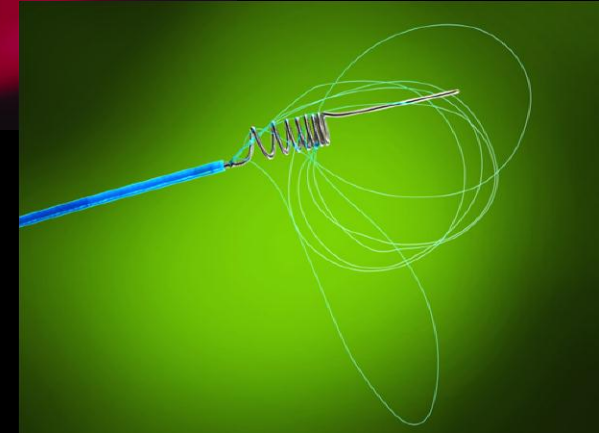
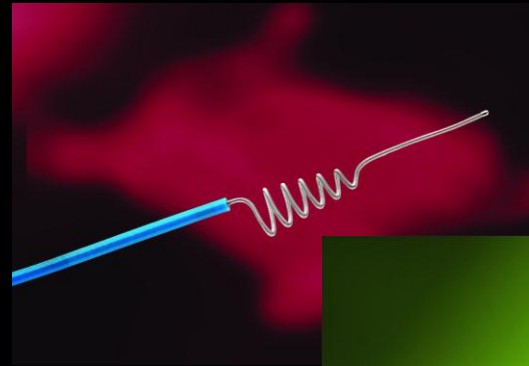


Mechanical Embolectomy

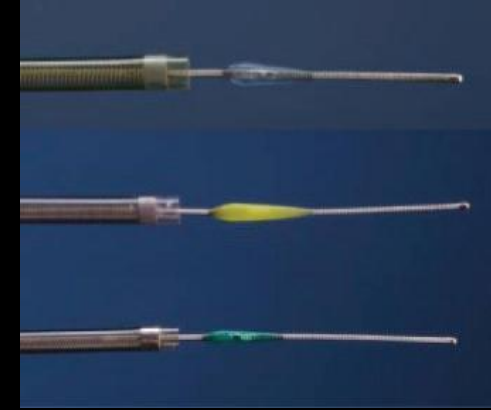
Merci Registry

N=1000

- Median NIHSS 17
- 29% Iv tPA
- Mean time from onset 6.33 ± 6.56
 - 16.9% >8hrs
- Recanalization 80.1%
- Good outcome 31.6%
 - Recanalization best predictor of outcome
 - >79yrs old 50% lower outcomes
 - 70% good outcome if NIHSS<16
 - 10% good outcome if NIHSS>25
- sICH 7%
- Reimer M. ISC, Los Angeles 2011



Penumbra POST Results



Median Time From Symptom Onset To Arterial Puncture	4.5 hours
Median Revascularization Time	48 minutes

	PS alone (n=32)	PS + IA tPA (n=80)	PS + IV tPA (n=50)	
Revascularization	78%	89%	80%	
Symptomatic ICH	3%	9%	8%	7.2%
90 Day Mortality	25%	20%	23%	22%
90 Day mRS ≤ 2	36%	49%	32%	40%



What About PCI for the Brain?



Angioplasty/Stenting for AIS

- 34 Pts with MCA occlusion Tx with PTA alone
 - 91.2% Recan. vs. 64% tPA Historical controls
 - ICH 2.9% vs. 19.4%

Ueda T et al Stroke 1998;29:2568-74, Nakano et al Stroke 2002;33:2872-76

- Jovin TG et al. Stroke 2005
 - 25 ICA occlusions- stroke/fluctuating Sx
 - 92% Recanalized with carotid stenting
- Levi et al conducted 20 pt pilot study of AIS
 - Wingspan™ achieved nearly complete recan.

Stenting for AIS

Abou-Chebl A, Vora N, Yadav J. J Neuroimaging 2008

	Vessel	Initial NIHSS	Technical Success	D/C NIHSS
□ 7 Atherostenosis	ICA/MCA	22	Yes	1
□ 2 Cardioembolic	ICA/MCA	24	Yes	12
□ No Thrombolytics	ICA/MCA	20	Yes	0
□ Stroke duration 8-10hrs	ICA/MCA	21	Yes	0
□ Clopidogrel 300-600mg ASA 325mg	ICA Cavernous	18	Yes	5
	MCA	24	Yes	3
	ICA/MCA	17	Partial	17
	ICA	14	Yes	2
	MCA	22	Yes	12
	Mean	20.2		5.8
	Std Dev	3.3		6.3
Complications: None				

35yo WM 48hr NIHSS=18

Smokes, Brother MI age 35

LVA



RVA



Post-Penumbra & Stenting 2 Co-Cr Coronary Stents





Intraprocedural Management



Conscious Sedation Versus General Anesthesia During Endovascular Therapy for Acute Anterior Circulation Stroke

Preliminary Results From a Retrospective, Multicenter Study

Alex Abou-Chebl, MD; Ridwan Lin, MD; Muhammad Shazam Hussain, MD; Tudor G. Jovin, MD; Elad I. Levy, MD; David S. Liebeskind, MD; Albert J. Yoo, MD; Daniel P. Hsu, MD; Marilyn M. Rymer, MD; Ashis H. Tayal, MD; Osama O. Zaidat, MD, MS; Sabareesh K. Natarajan, MD, MS; Raul G. Nogueira, MD; Ashish Nanda, MD; Melissa Tian, RN; Qing Hao, MD, PhD; Junaid S. Kalia, MD; Thanh N. Nguyen, MD; Michael Chen, MD; Rishi Gupta, MD

- N=980
- GA 44%
 - Poor outcome OR 2.33 (1.63-3.44), $p < 0.0001$
 - Death OR 1.68 (1.23-2.3), $p < 0.0001$
- sICH 9.2%
- No increase in wire perforation with local
- Conscious sedation or no sedation is safer

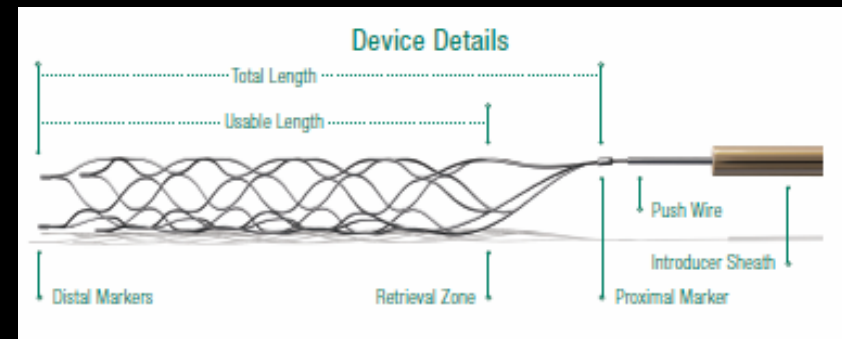


Stent-Triever



SWIFT Trial of Solitaire™ FR

- Randomized vs. Merci
- Planned 200pts.
- Age 22-85
- NIH- 8-29
- <8hrs duration
- Maximum 3 passes
- Success TIMI 2/3 without sICH
- Core Lab blinded



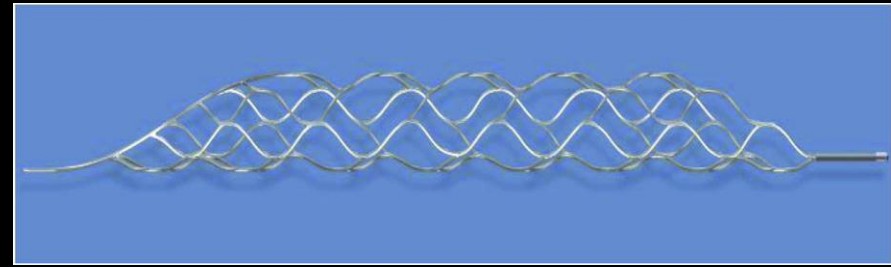
SWIFT Trial Results

- Stopped Early by DSMB N=144

- 31 roll in, 113 randomized- 55 Merci, 58 Solitaire

	Solitaire™	Merci™
■ sICH	1.7	10.9
■ Recan. no ICH	61	24% (OR 4.87, p=0.0001)
■ Recanalization	83.3%	48.1% p=0.00002
■ 90 day mRS<3	58.2	33.3 (OR 2.78, p=0.02)
■ Mortality	17.2	38.2 p=0.0001

TREVO 2



- Randomized Trevo™ vs. Merci™
- N=178 88 90
- NIHSS 19 18
- Time to Tx 4.7hrs 4.2hrs

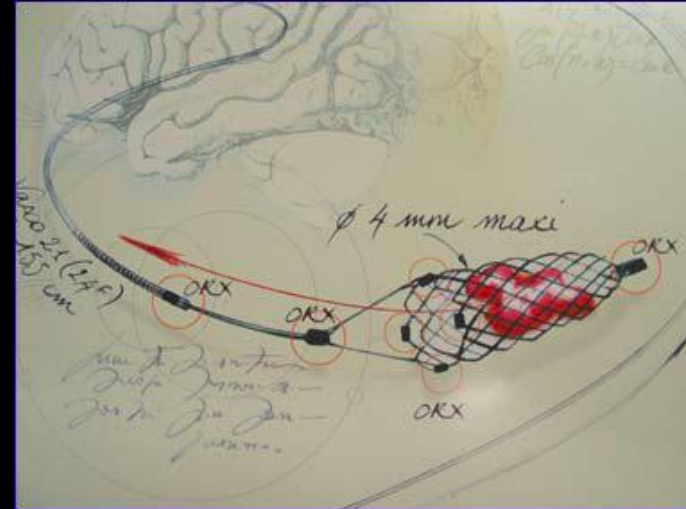
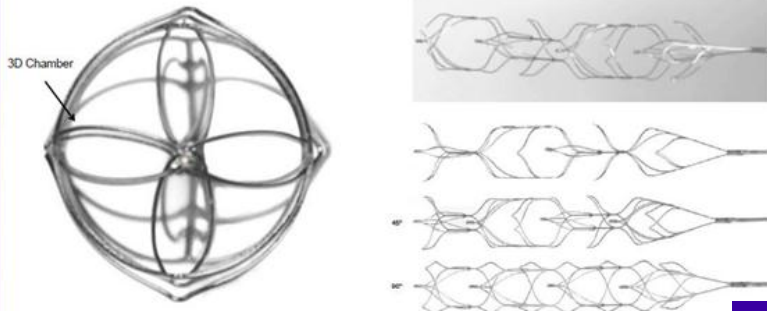
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TREVO 2 Results

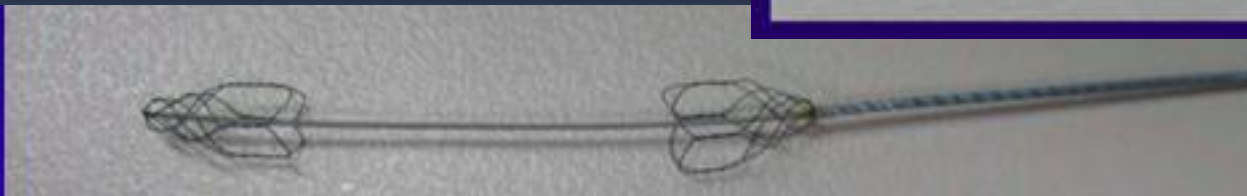
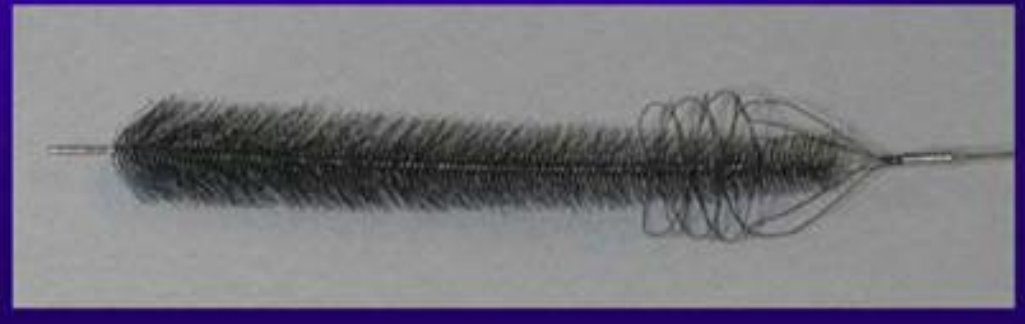
	Trevo™	Merci™
■ Recan.	86%	60% (OR 4.22, p<0.0001)
■ sICH	6.8%	8.9% (OR 0.75, p=0.78)
■ Mortality	33%	24% (OR 1.61, p=0.18)
■ go d mRS≤2	40%	22% (OR 2.39, p=0.013)

New Devices Being Tested

New Separator 3D



Phenox cage clot remover (CCR)



71 yo WM awoke with stroke NIHSS=14

Cerebral Angiogram 10:32AM

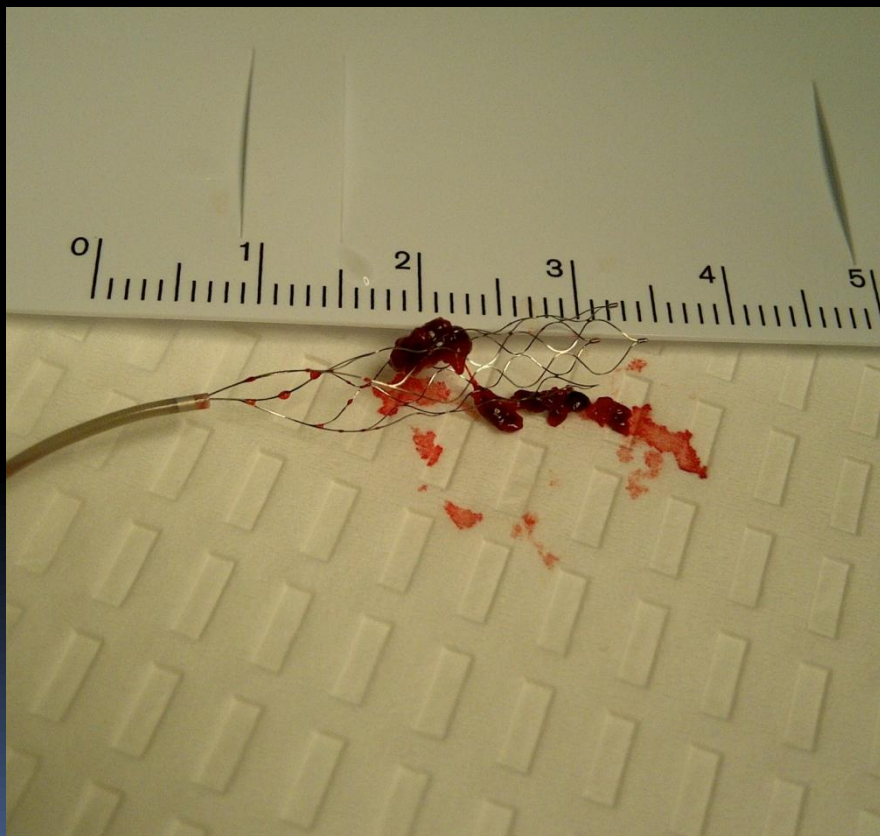


Solitaire FR Deployed 10:52AM



Result

Solitaire Withdrawn 11:02AM




Recanalization Confirmed 11:07AM


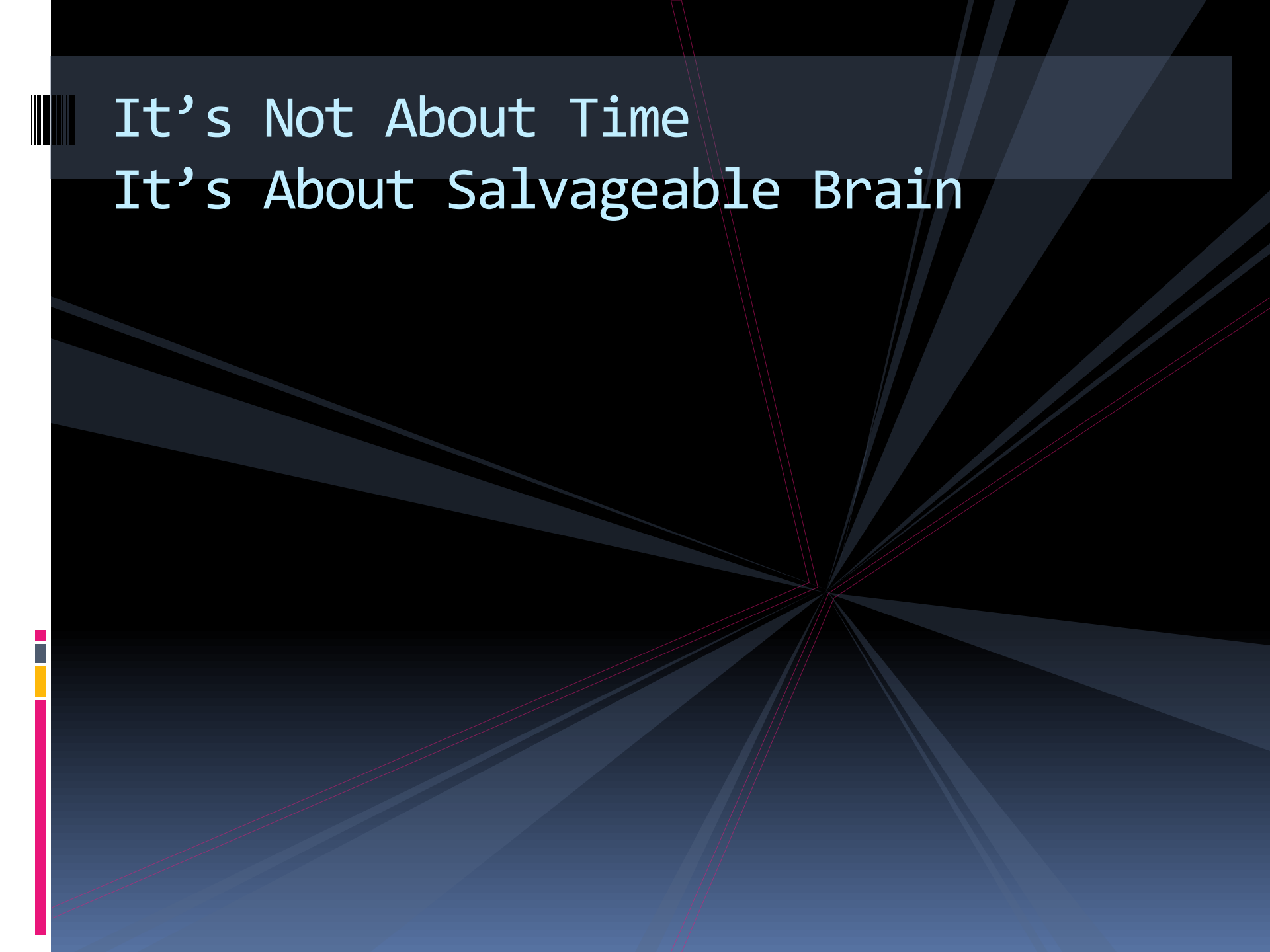


IMS 3 Trial

- NIH sponsored, Phase 3, randomized trial of IV tPA alone vs. IV tPA + IAT for AIS < 3hrs
- IAT arm initially reduced dose tPA + one of:
 - IA tPA
 - Ekos catheter
 - Merci
 - Penumbra
- 900pts planned
- Stopped after ~600pts due to futility



It's Not About Time
It's About Salvageable Brain



Endovascular Treatment of Acute Ischemic Stroke May Be Safely Performed With No Time Window Limit in Appropriately Selected Patients

Alex Abou-Chebl, MD

- N=55
- All patients Tx awake
- Treatment adjusted for pathology and risk of ICH
- Average Time-to-Tx 9.2±12.3hrs (1-68hrs)
 - Early N=34 3.4±1.6hrs
 - Late N=21 18.6±16hrs p<0.000001
- Mean NIHSS 19.7±5.7 (7-28)
 - Early 20.9±5.5
 - Late 17.8±5.5 p=0.048

Abou-Chebl A. Stroke 2010;41:1996-2000

Results

▪ TIMI 2/3	84%		
▪ Early		82.8%	
▪ Late		85.7%	p=1
▪ Symptomatic ICH	5(9.1%)		
▪ Early		3(8.8%)	
▪ Late		2(9.5%)	p=1
▪ Death @30 days	15(27.3%)		
▪ Early		10(29.4%)	
▪ Late		5(23.8%)	p=0.65
▪ 3 Month mRS≤2	41.8%		
▪ Early		41.2%	
▪ Late		42.9%	

Imaging-Based Patient Selection for Endovascular Tx

- 237 Anterior Circulation Strokes, retrospective
- Selected with CTP or DWI/PWI per institution
- Mean age 63.8 ± 16
- Mean NIHSS 15 ± 5.5
- Mean Time to Tx 15 ± 11.2
- sICH 8.86%
- 90 d Mortality 21.5%
- 90 d mRS ≤ 2 45%

Penumbral Imaging

- CT & MRI can measure ischemic core
 - CBV and DWI
- CTP and DWI/PWI can define
 - Hypoperfused tissue
- Combination defines Penumbra
- Ideally
 - Small to no ischemic core
 - Large perfusion defect

DEFUSE 2

- MRI Based Penumbra Imaging for IAT
- N=99
- 78 had Target Mismatch Pattern
 - 36 <6hrs & 42 >6hrs
- Favorable Outcomes- ≥ 8 pt NIHSS improvement or final score 0-1 @ 30d
- OR 2.9 with recanalization <6hrs
- OR 8.5 with recanalization >6hrs
- No reperfusion= lesion growth

Lansberg M et al. Lancet Neurol 2012;11:860-867

Conclusions

- Appropriately selected patients with salvageable brain tissue may be treated safely regardless of time window
 - Thorough Evaluation of
 - Pathophysiology
 - Arterial Anatomy
 - Brain Substrate
- Stroke Tx is best when it can be individualized
- Mechanical embolectomy may be safest and fastest approach