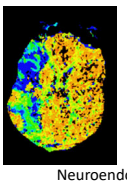
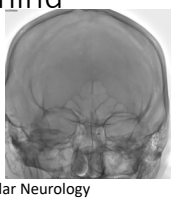
Mechanical Thrombectomy for Large Core Acute Ischemic Stroke: no LVO left behind





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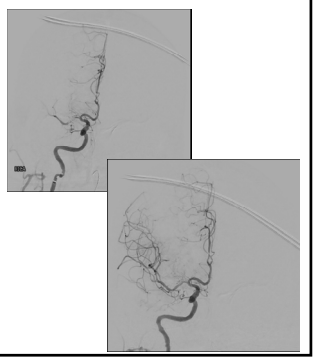
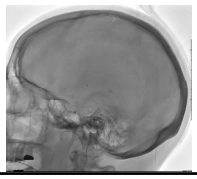
Time Is Brain

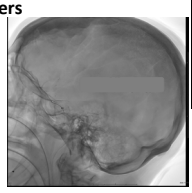
- "The typical patient loses 1.9 million neurons each minute in which stroke is untreated."[1]
- Establish Last Known Well
- Alteplase 1995 0-3 hours
- Alteplase 3-4.5 hours in 2008[2]
- TNK ongoing adoption



Endovascular Mechanical Thrombectomy (EVT)

- Merci Device PROACT 2 trial
- **Stent Retrievers**
- **Aspiration Catheters**





Mechanical Thrombectomy 0-8 hours

- Winter 2015 0-8 hours; 5 massively positive trials
  - mRS 0-2 NNT 4
  - **January 2015 MR CLEAN**
  - **ESCAPE***
  - **EXTEND IA***
  - **REVASCAT***
  - **SWIFT Prime***
- CT head; CT angiogram
- CTP perfusion
- HERMES meta-analysis – NNT 2.6 patients to improve 1 point on mRS scale

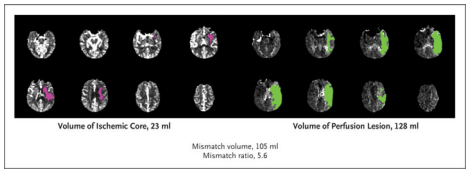
MODIFIED RANKING SCORE

SCORE	DESCRIPTION
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

* Stopped early for equipoise; achieved significant results at interim analysis

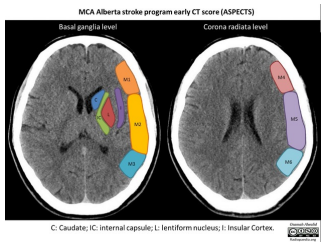
Extending the Window

- 6-24 hours – clinical vs imaging mismatch (MRI or CTP)
- 6-16 hours – DEFUSE 3* with perfusion imaging; mismatch ratio 1.5
- NNT 3 & 2 for mRS 2



* Stopped early for equipoise; achieved significant results at interim analysis

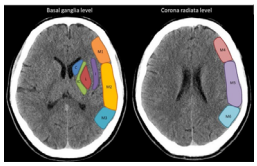
Large Core Windfall

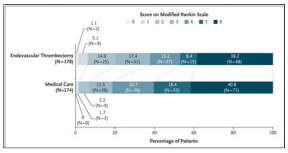


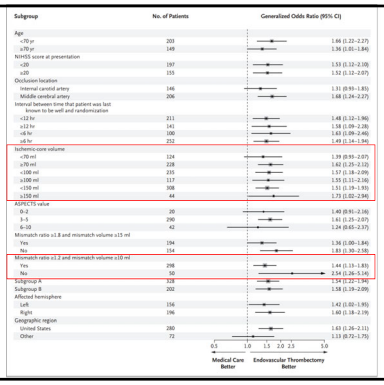
- Estimated 1 out of 5 LVOs present with a large core infarct (ASPECT score 3-5).
- ASPECTS Score –
  - score <7 predicts a worse functional outcome at 3 months as well as increases risk of symptomatic hemorrhage.
- ASPECTS score less than 8 treated with thrombolysis did not have a good clinical outcome in NINDS subgroup analysis.
- Poor inter-rater variability for ASPECTS

SELECT 2

- Lage core ASPECTS 3-5 within 24-hour onset comparing EVT to medical management for LVO's[3]
- mRS 2 or less: 20% intervention vs 7% medical
- mRS 3 or less: 37.9% intervention vs 18.7% medical

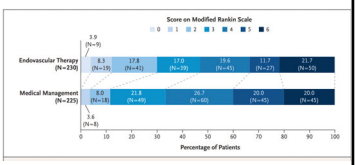






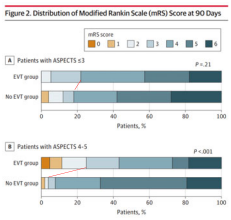
ANGEL - ASPECT

- Chinese study enrolled 456 patients for endovascular therapy vs medical management with ASPECTS 3-5
  - Also enrolled ASPECTS 0-2 if CTP core infarct 70-100ml
- 30% functional independence (mRS 2) at 3-months after thrombectomy compared to 11% medical arm[4]



RESCUE-JAPAN LIMIT

- 202 patients in Japan were enrolled with ICA/M1 occlusions with ASPECTS scores of 3-5 to EVT vs medical management. Primary outcome was to assess mRS 0-3 at 90 days
- NNT to achieve mRS 0-3: 3 patients
- NNT to achieve mRS 0-2: 5 patients[5]



Safety Outcomes of all studies

SELECT 2

Table 1. Safety Outcomes and Procedural Complications (Intention-to-Treat Population).*

Outcome	Endovascular Therapy (N=178)	Medical Care (N=174)	Relative Risk (95% CI)
Symptomatic intracranial hemorrhage within 24 hr — no. (%)†	1 (0.6)	2 (1.1)	0.49 (0.04 to 5.56)
Early neurologic worsening — no. (%)‡	44 (24.7)	27 (15.5)	1.59 (1.03 to 2.45)
Death from any cause within 90 days — no./total no. (%)	68/177 (38.4)	71/171 (41.5)	0.91 (0.71 to 1.18)
Arterial access-site complications — no. (%)			
Occlusion	3 (1.7)	—	
Hematoma	1 (0.6)	—	
Infection	1 (0.6)	—	
Vascular injury — no. (%)			
Dissection	10 (5.6)	—	
Perforation	7 (3.9)	—	
Vasospasm	11 (6.2)	—	
Other	2 (1.1)	—	

Table 2. Efficacy and Safety Outcomes.

Outcome	Endovascular Therapy (N = 230)	Medical Management (N = 225)	Treatment Effect (95% CI)*	P Value
Safety outcomes				
Symptomatic intracranial hemorrhage within 48 hr — no. (%)†	14 (6.1)	6 (2.7)	2.07 (0.79 to 5.41)	0.12
Any intracranial hemorrhage within 48 hr — no. (%)	113 (49.1)	39 (17.3)	2.71 (1.91 to 3.84)	<0.001
Death within 90 days — no. (%)	50 (21.7)	45 (20.0)	1.00 (0.65 to 1.54)	0.99
Decompressive hemicraniectomy during hospitalization — no. (%)	17 (7.4)	8 (3.6)	1.92 (0.78 to 4.73)	0.15

RESCUE-Japan LIMIT

Table 2. Outcomes

Outcome	No. (%) EVT group	No. (%) No-EVT group	OR (95% CI)	P value	P value for interaction
Safety outcomes					
Symptomatic intracranial hemorrhage within 48 h	3 (6.8)	2 (3.8)	1.83 (0.26-11.5)	.52	NA
Any intracranial hemorrhage within 48 h	21 (47.7)	16 (30.8)	2.05 (0.89-4.73)	.09	NA
Death within 90 d	8 (18.2)	10 (19.2)	0.93 (0.33-2.62)	.90	NA
Recurrence of cerebral infarction within 90 d	1 (2.3)	6 (11.5)	0.18 (0.03-1.54)	.12	NA
Decompressive craniectomy within 7 d	3 (6.8)	7 (13.5)	0.47 (0.11-1.94)	.30	NA

ANGEL-ASPECT

Intra-arterial tPA after EVT

- 24h from LKW after TICI 2b EVT
- mRS 0-1 favored EVT: NNT 6.
- Despite more hemorrhages, still large clinical benefit
- Not true RCT and cut short due to COVID 19
- Dose .225mg/kg up to 22.5mg max

JAMA | Preliminary Communication

Effect of Intra-arterial Alteplase vs Placebo Following Successful Thrombectomy on Functional Outcomes in Patients With Large Vessel Occlusion Acute Ischemic Stroke
The CHOICE Randomized Clinical Trial

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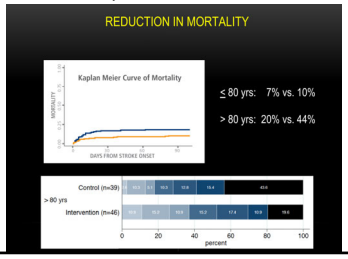
Age is just a number

- Age cutoffs are often arbitrary and mis-informed as shown by ESCAPE- IA [7]



Save the Neurons

- Multiple studies released over the last 18 months demonstrating aggressive tactics for reperfusion. While risks of complications are higher, improved patient outcomes are overwhelming in patients undergoing mechanical thrombectomy

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