Recanalization most important in outcome

Molina CA et al. Stroke 2004

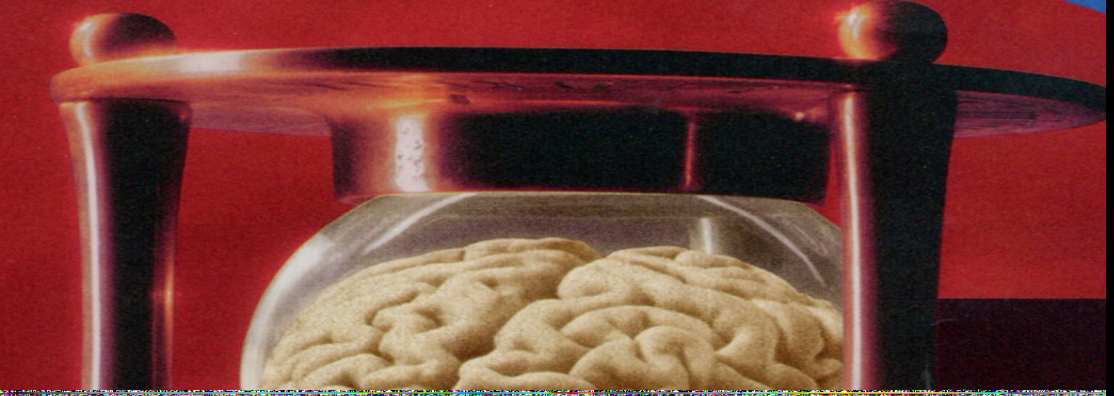
TABLE 2. Independent Predictors of Good Outcome on Logistic Regression Model

Factor	Coefficient (SE)	OR (95% CI)	*P*
Constant	0.467 (0.69)	. . .	
Recanalization	1.41 (0.26)	4.11 (2.42–6.95)	<0.001
NIHSS score	−1.03 (0.4)	0.35 (0.16–0.78)	0.0013
ASPECTS value	1.09 (0.49)	2.98 (1.13–7.85)	0.0253
SBP	−1.12 (0.43)	0.32 (0.13–0.76)	0.0116
Proximal occlusion	−1.37 (0.45)	0.25 (0.10–0.61)	<0.001


Req Nu
M 20
DOB: 14
27

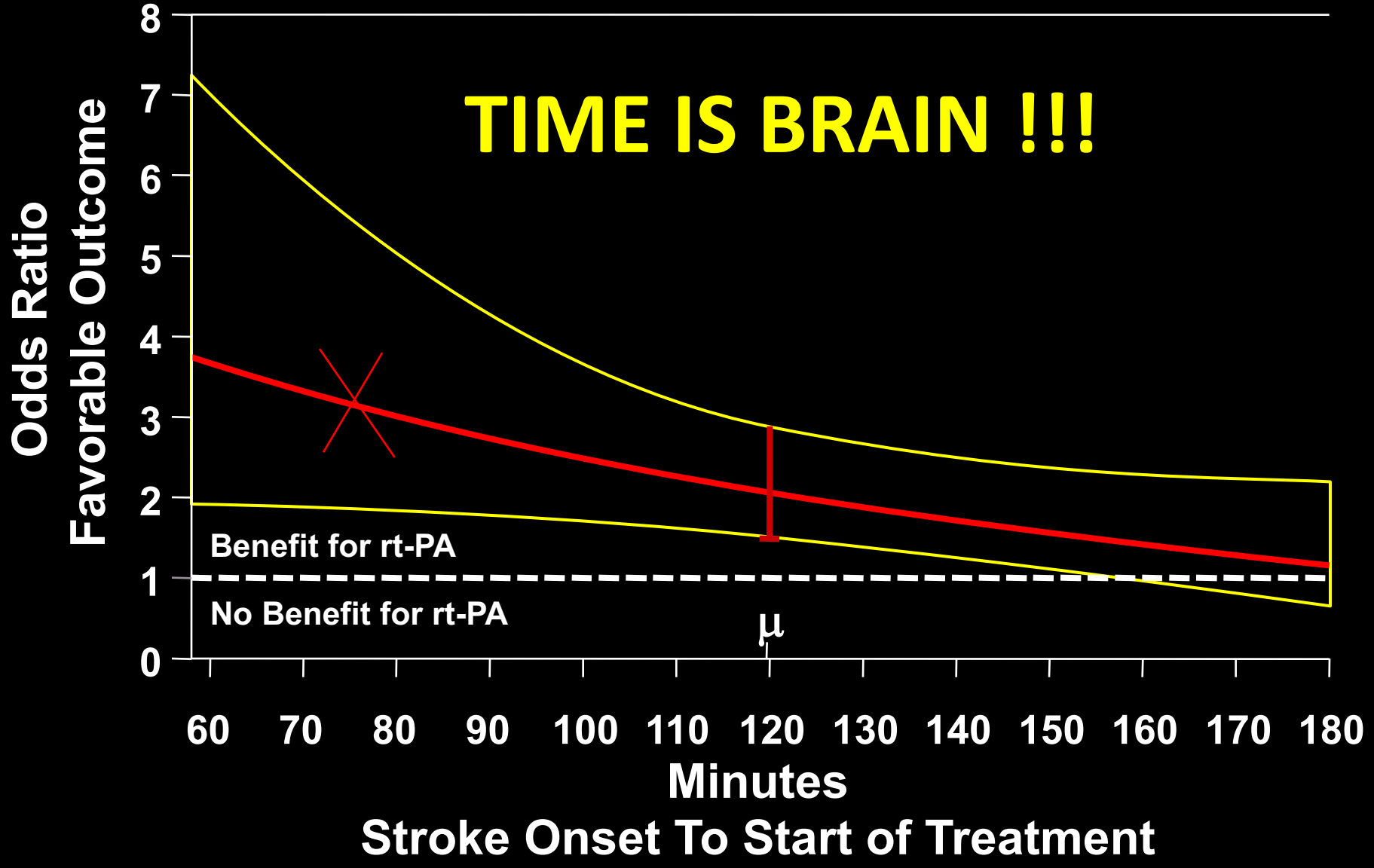

M
D


M 20
DOB: 14
28



Time is Brain

NINDS TPA Stroke Study:
Time to Treatment and Odds Ratio of Favorable Outcome



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Molina CA et al. Stroke 2004

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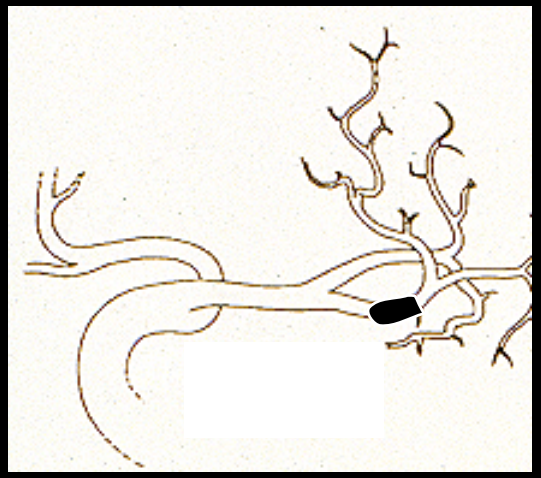
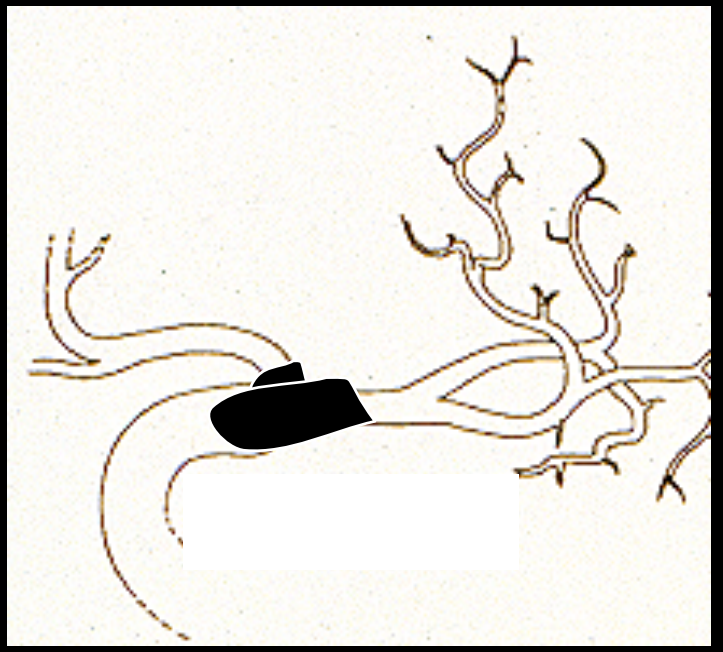
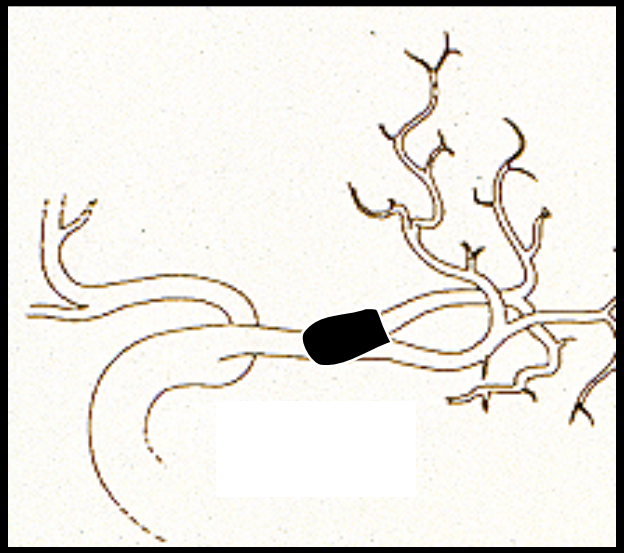
Recanalization Rates Suboptimal



44%
35-40%



11%
8%

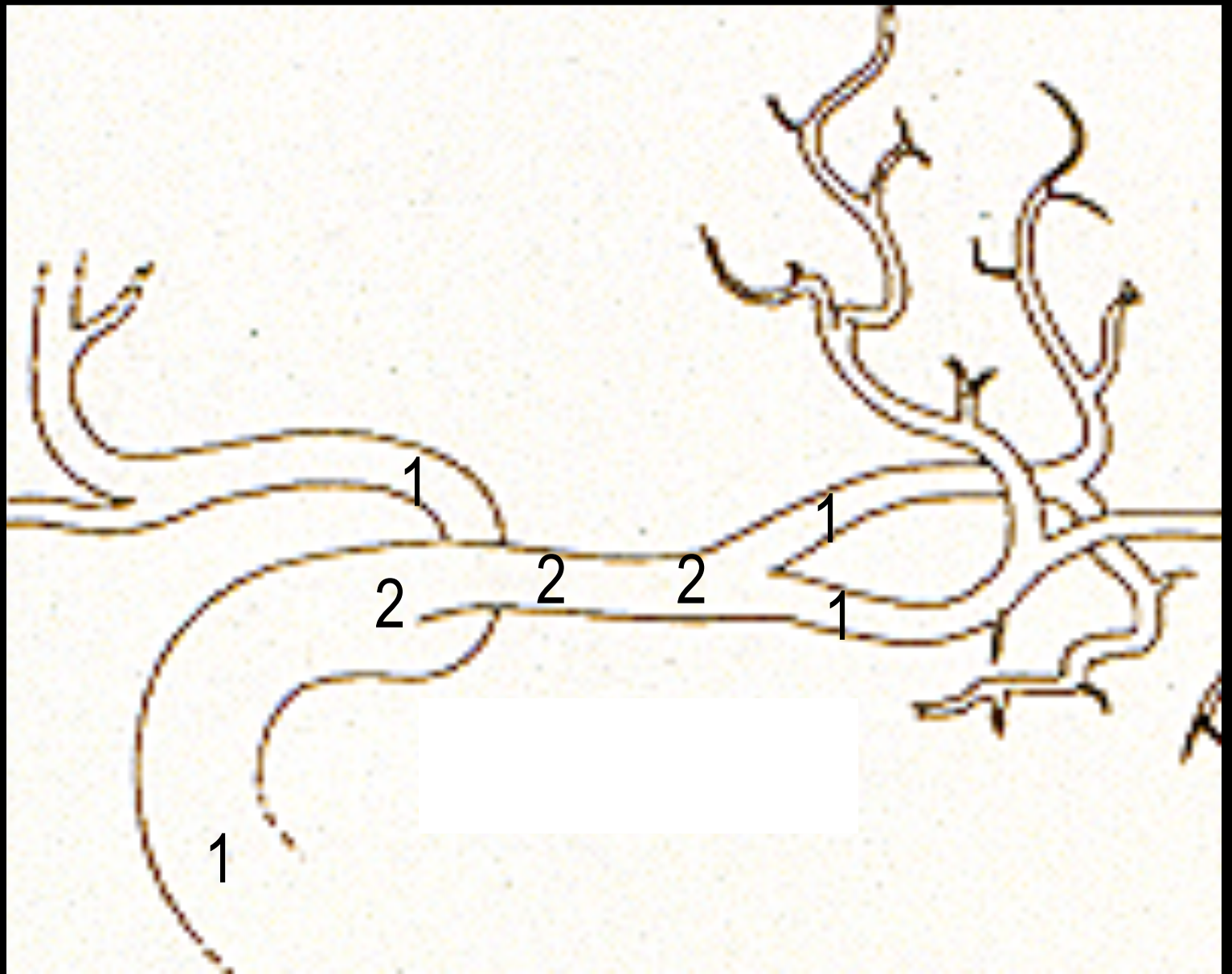


29%
26%

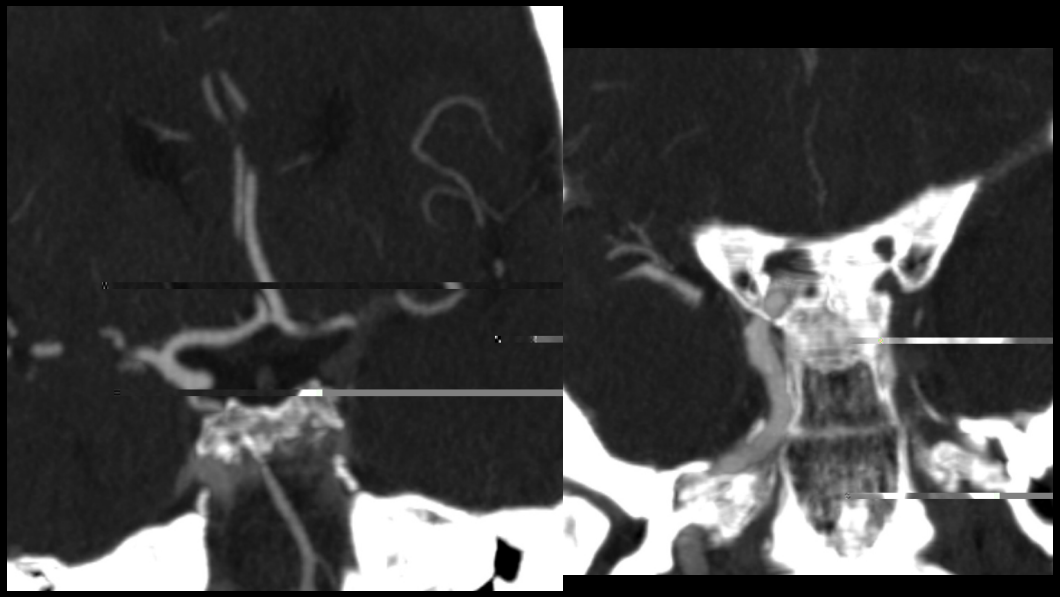
large clot burden
blind alley or dead end thrombus
platelet rich or older clot
plasminogen steal phenomenon
nonthrombotic occlusion

Stroke 2003 (abstract) del Zoppo GJ et al. Ann Neurol 1992 32:78-86

Clot Burden Scale V Peutz (abstract) ASA 2007



Example



infraclinoid ICA (1), supraclinoid ICA (2), proximal M1 (2)

CBS=10-1-2-2=5

Clot Burden Scale

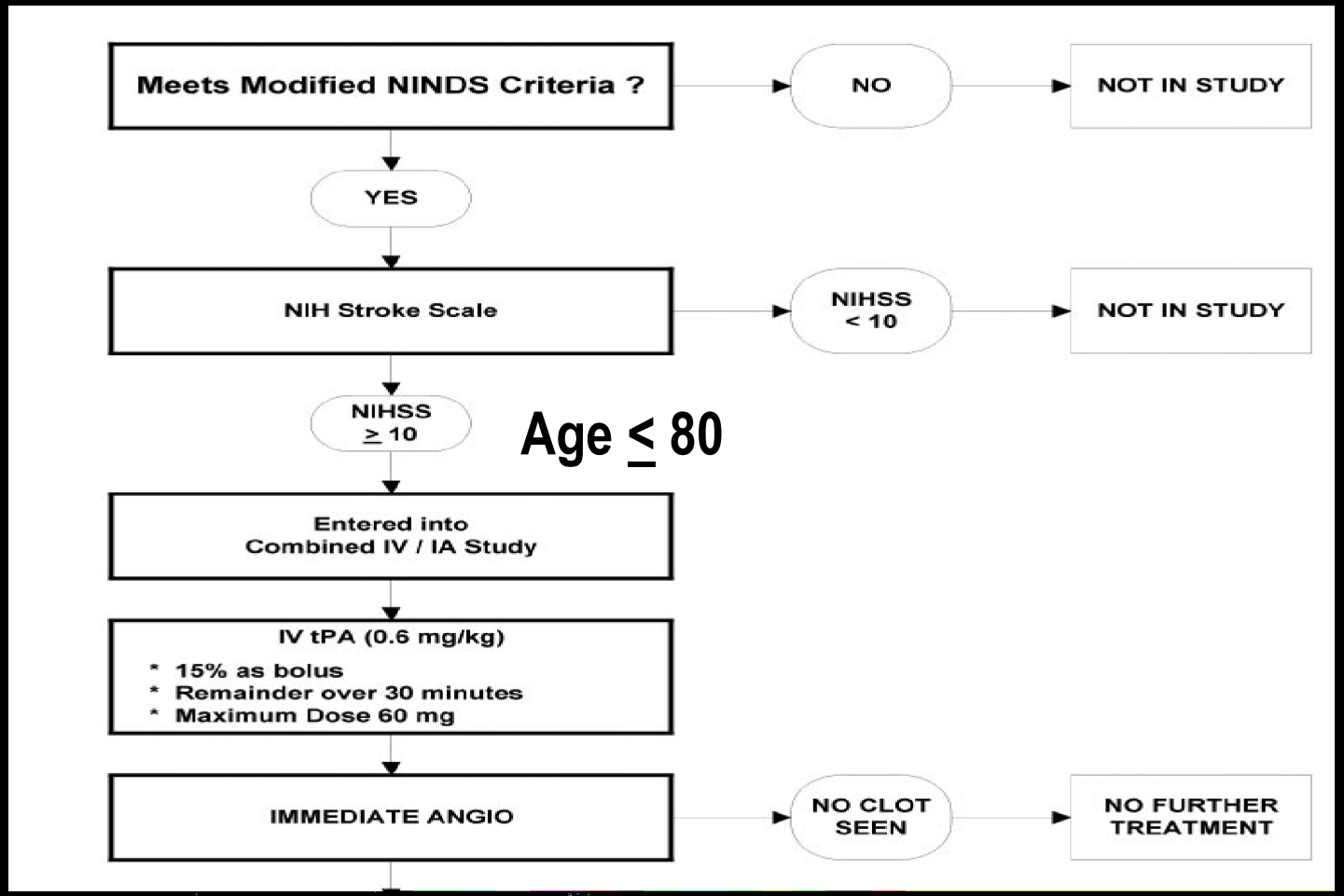
CBS	n	mRS 0-2 (%)	mRS 6 (%)	FU-ASPECTS (mean)	HT (%)	HI (%)	PH (%)
≤ 5	23	13	43	2.9	57	29	29
6-7	36	33	14	4.6	44	26	19
8-9	81	46	12	5.3	21	13	8
10	104	59	7	8.1	14	11	3

EMS Bridging Study

- IV vs. IV-IA tPA randomized trial (phase I)
- 0.6 mg/kg tPA dose IV followed by max 20mg IA tPA
- 35 patients
- no difference in outcomes between the 2 groups although trend to higher mortality in the IV-IA group
- 1 symptomatic ICH in the IA group

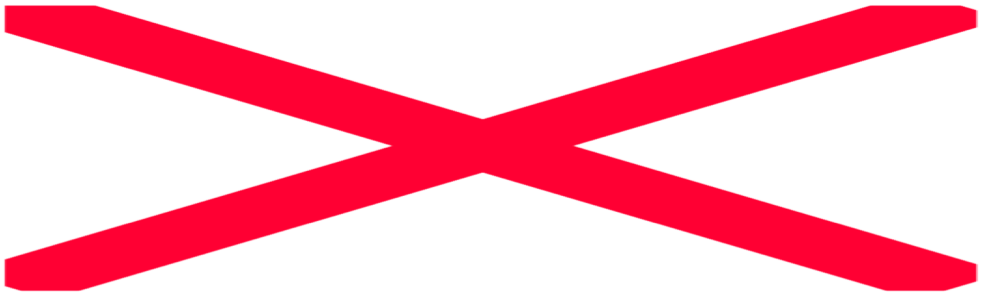
IMS Trial IV+IA Thrombolysis

Stroke 2004;35:904-912



Treatment Initiated a little slower than NINDS rt-PA study

Stroke 2004;35:904-912



IMS Safety

Stroke 2004;35:904-912

	IMS (N = 80)	NINDS Placebo (N = 211)	NINDS T-PA (N = 182)
Mortality (%) At 3 months	16%	24%	21%
Symptomatic ICH (%)	6%	1%	7%
Serious Bleeding Event (%)	3%	½ %	1%

Favorable Outcome at 3 months (%)*

Stroke 2004;35:904-912

	IMS (N = 80)	NINDS Placebo (N = 211)	Odds Ratio (95% CI)
Rankin 0 -1	**30%**	**18%**	**2.29 (1.9, 4.4)**
Rankin 0-2	**43%**	**28%**	**2.04 (1.2, 3.6)**
NIHSS ≤ 1	**25%**	**15%**	**2.24 (1.2,4.5)**

Adjusted for baseline NIHSS and time-to-treatment

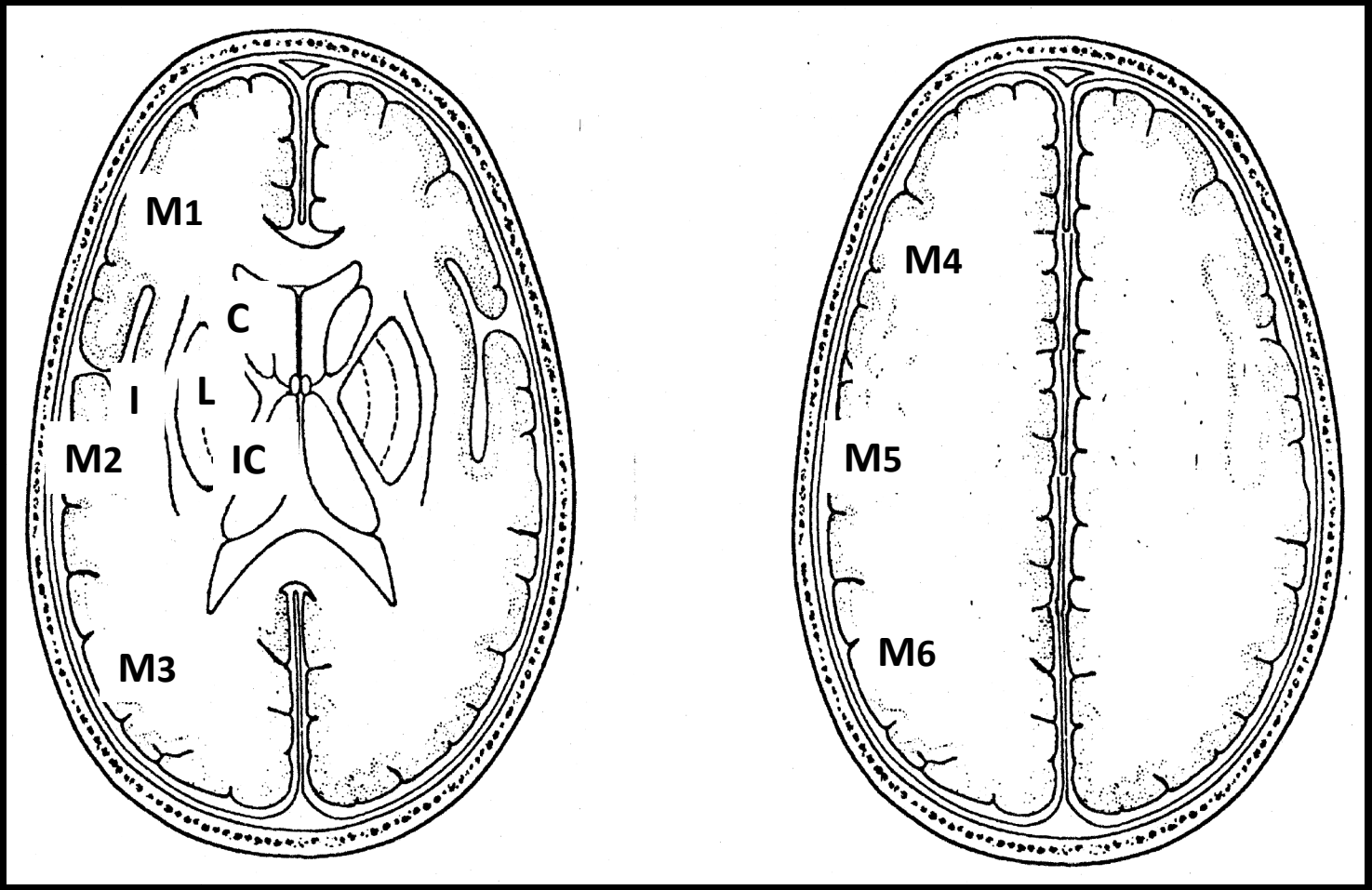
Favorable Outcome at 3 months (%)*

Stroke 2004;35:904-912

	IMS (N = 80)	NINDS tPA (N = 211)	P-value
Rankin 0-2 bNIHSS 10-19	**43%**	**47%**	**p=NS**
Rankin 0-2 bNIHSS ≥20	**42%**	**21%**	**p=0.0502**

ASPECTS

Lancet 2000;355:1670-1674

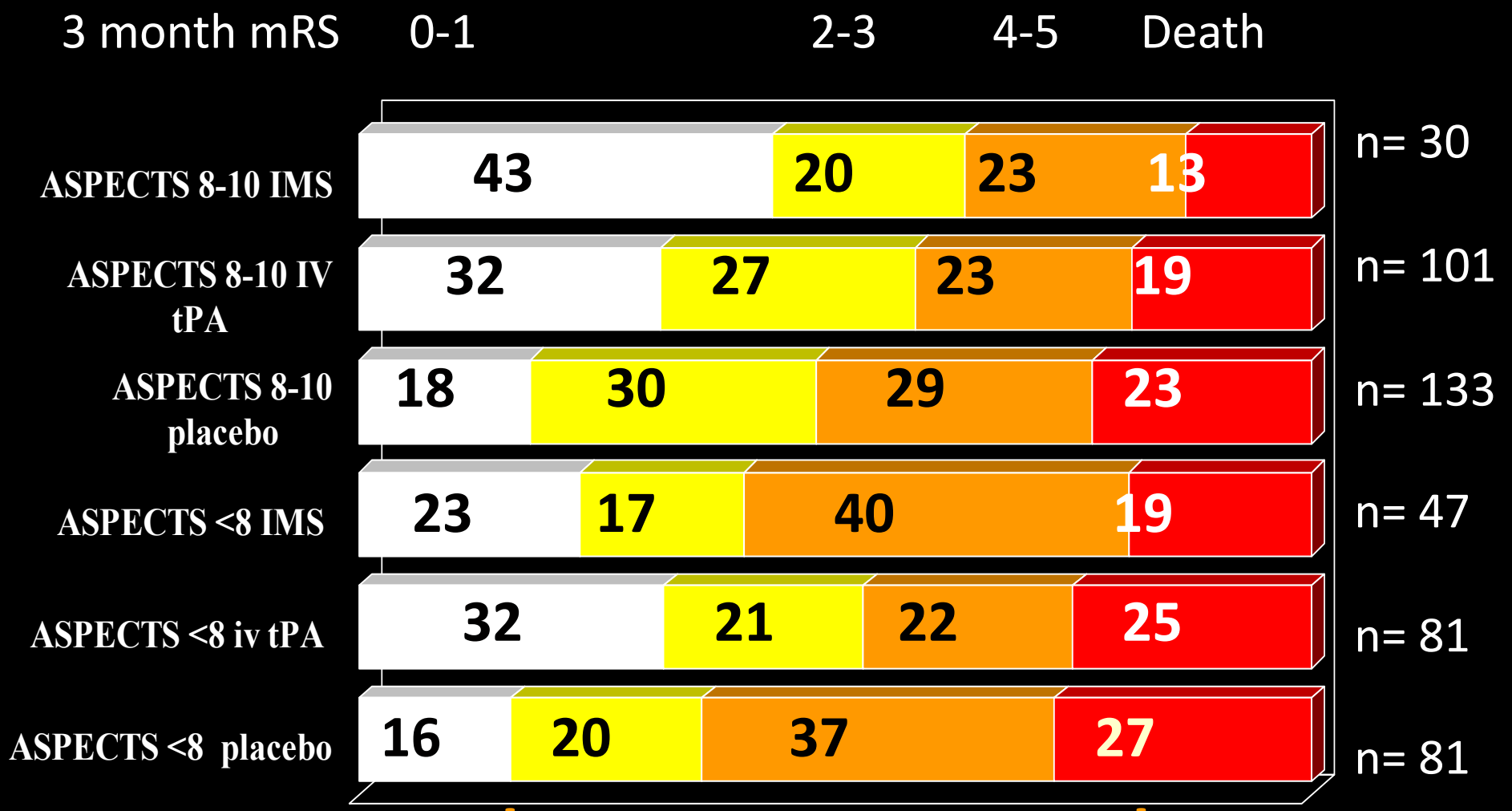


10 – normal

0 - total MCA infarct

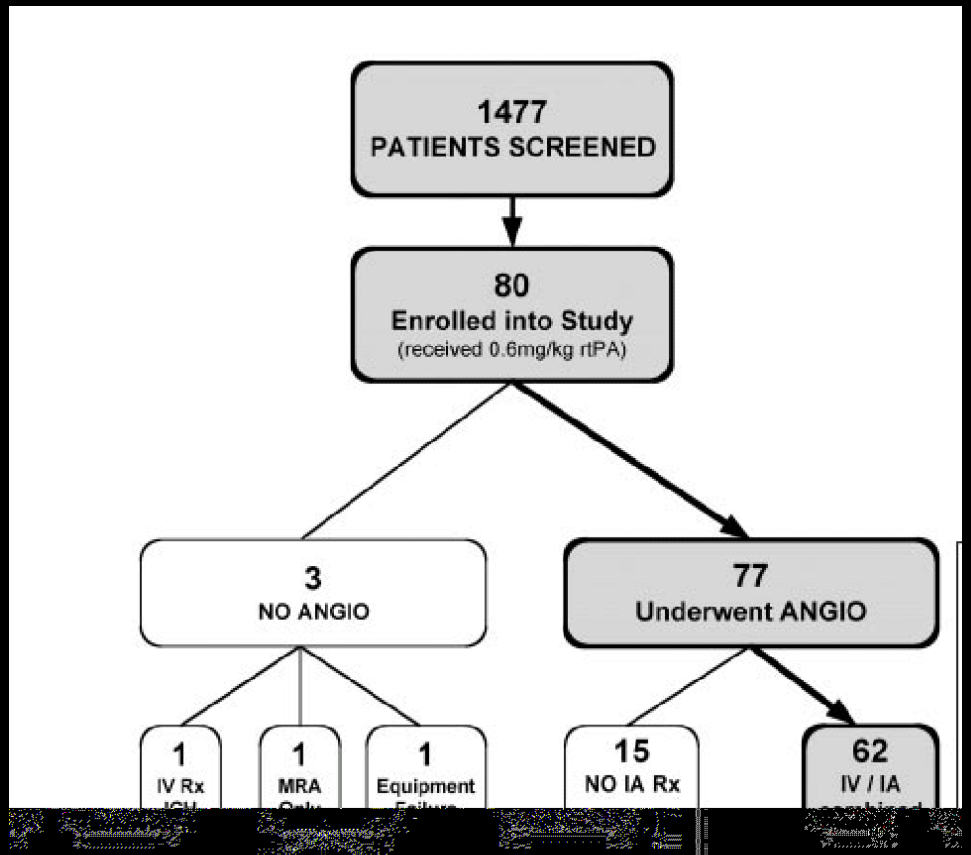
CT might predict iv/ia benefit <3 hrs

IMS and NINDS rtPA studies and ASPECTS



Preliminary Results

Angiogram Negative Cases



Derivation of Transcranial Doppler Criteria for Rescue Intra-arterial Thrombolysis

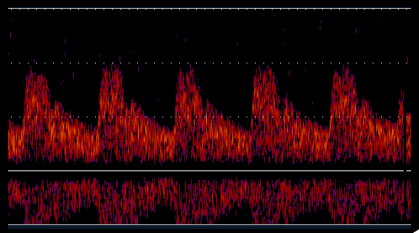
Multicenter Experience From the Interventional Management of Stroke Study

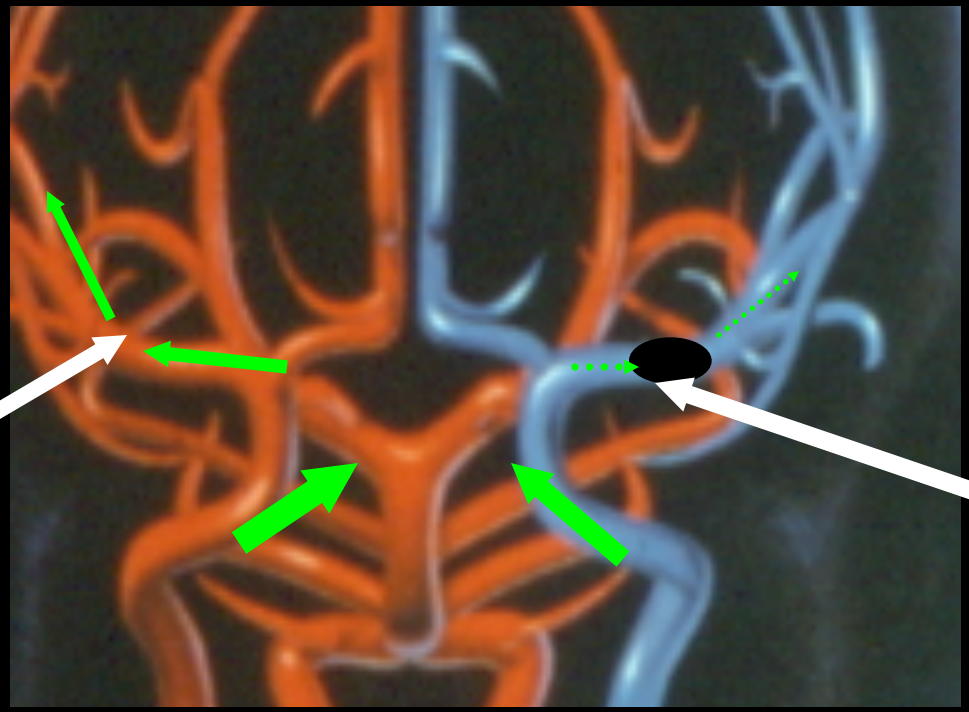
Maher Saqqur, MD; Ashfaq Shuaib, MD, FRCPC; Andrie V. Alexandrov, MD; Michael D. Hill, MD; Sergio Calleja, MD; Thomas Tomsick, MD; Joseph Broderick, MD; Andrew M. Demchuk, MD

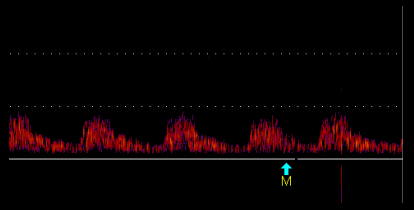
Stroke 2005;36:865-868

Affected MCAMFV/ Contralesional MCA MFV<0.6

100% PPV
84% NPV





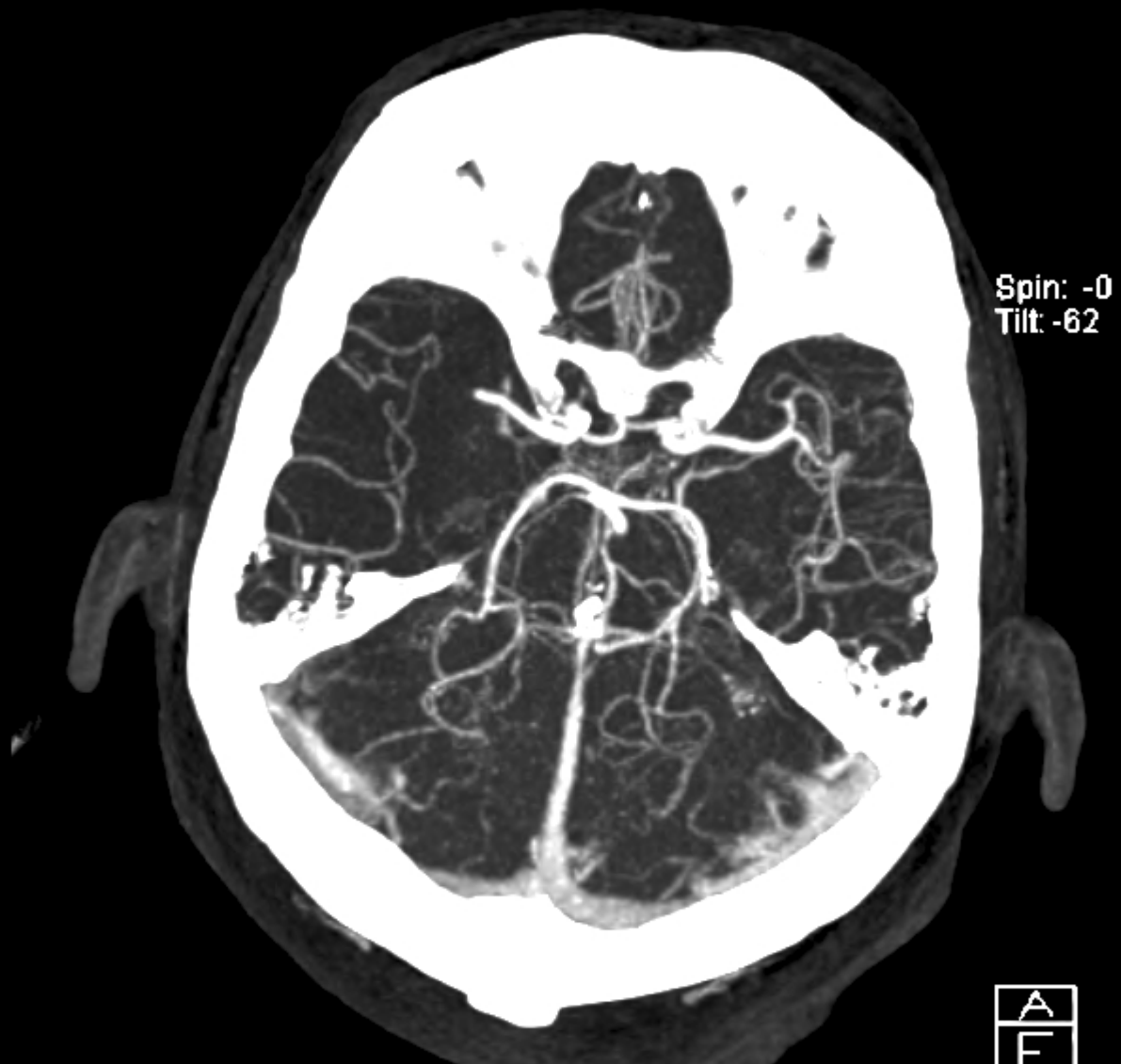


70 cm/s

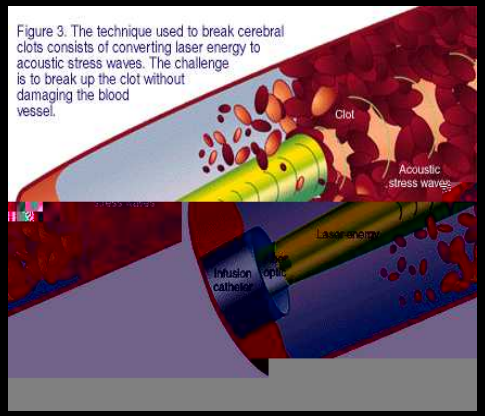
20 cm/s

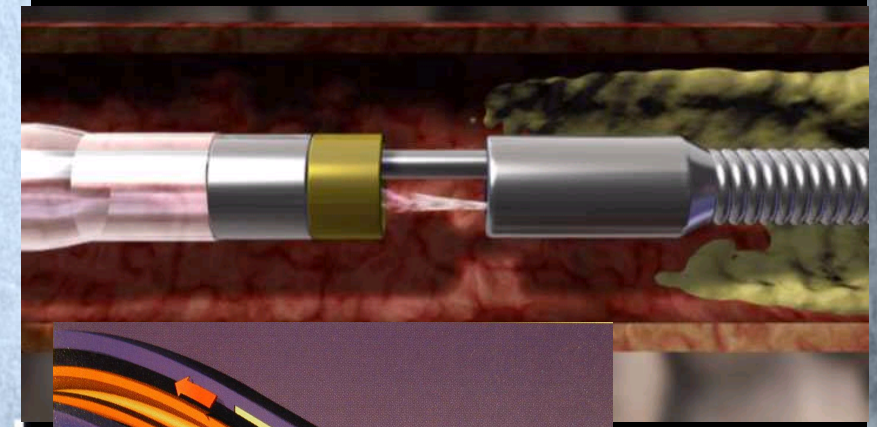
20/70=0.28

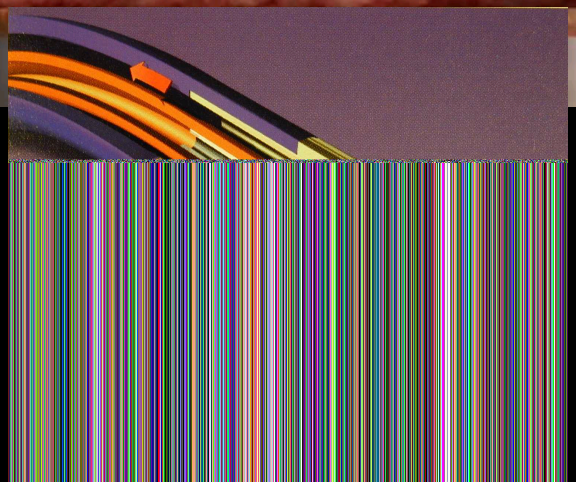
CT angiography

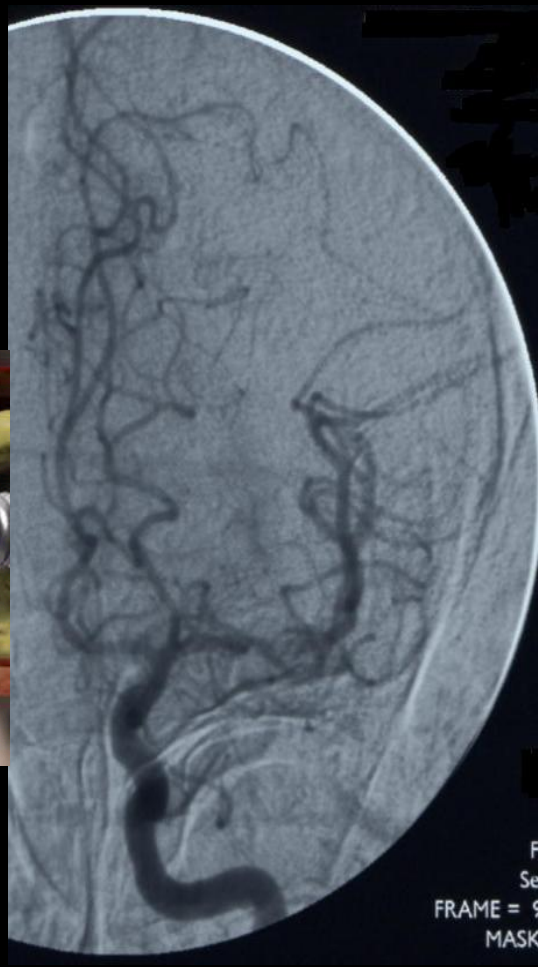


Clot Dissolution Devices



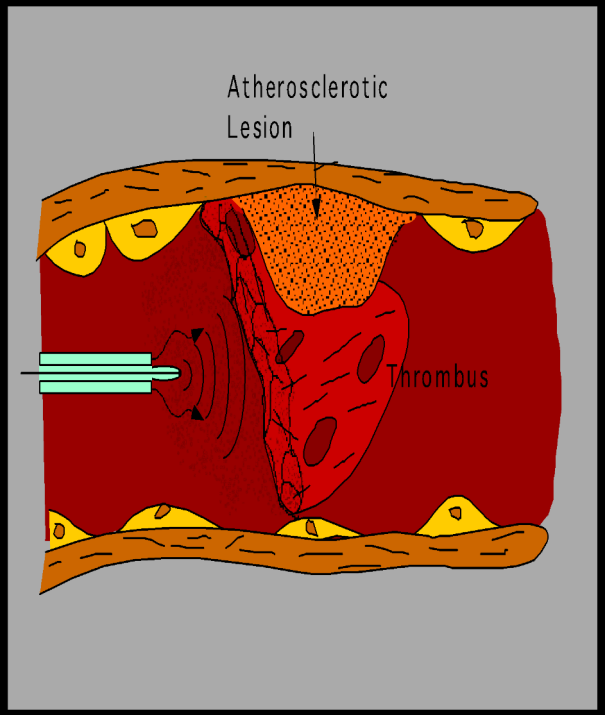






IMS-2

0.6 mg/kg iv + up to 22 mg ia tPA+
EKOS Sonolysis system



IMS II Efficacy

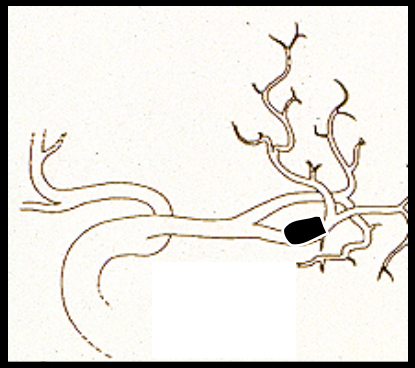
3-month outcome	IMS II N=81	NINDS Placebo N=211	Odd Ratio* (95% CI)	NINDS rt-PA N=182	Odds Ratio* (95% CI)
mRS 0-1	33%	18%	**2.78 (1.46, 5.31)**	32%	1.36 (0.72, 2.56)
mRS 0-2	46%	28%	**2.82 (1.54, 5.16)**	39%	1.74 (0.95, 3.19)
NIHSS </=1	27%	15%	**2.84 (1.40, 5.73)**	25%	1.85 (0.92, 3.70)
BI 95-100	53%	30%	**3.24 (1.80, 5.85)**	42%	**2.29 (1.24, 4.23)**
Global Test Statistic	NA	NA	**2.88 (1.66, 4.99)**	NA	**1.85 (1.06, 3.23)**
NIHSS 0-2 @24 hours	19%	3%	**7.07 (2.54, 19.63)**	14%	2.27 (0.996, 5.16)

***Adjusted for age, baseline NIHSSS, and time to treatment**

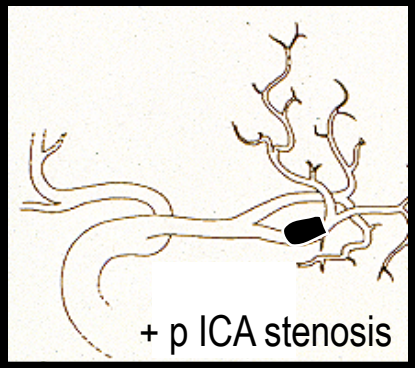
IMS I and II Safety Results

	IMS II N = 81	IMS I N = 80	NINDS rt-PA N = 182	NINDS Placebo N = 211
Mortality (at 3 Months)	**16%**	16%	21%	24%
Symptomatic ICH (≤36 hrs)	**9.9%**	6.3%	6.6%	1%
PH2s	**8.8%**	7.5%	3.6%	0.5%
Asymptomatic ICH (≤ 36 hrs)	**32.1%**	42.5%	6.0%	5.7%
Serious Bleeding (Non ICH)	**2.5%**	2.7%	1%	0.5%

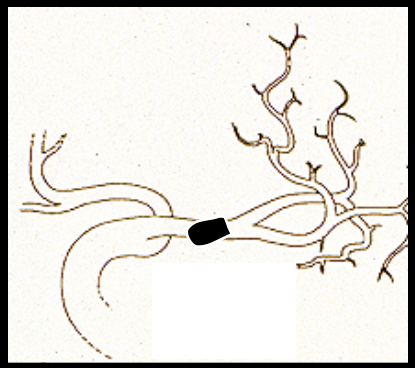
Recanalization Rates better especially for M2 occlusion



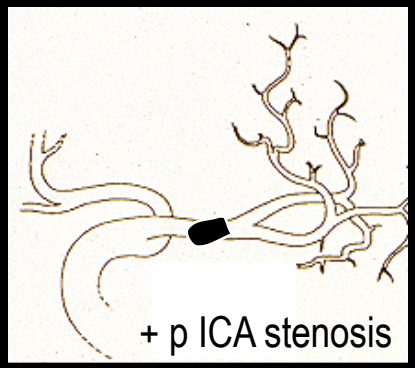
50% TIMI 2/3
75% good outcome

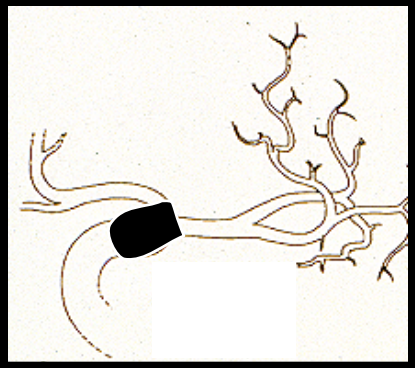


67% TIMI 2/3
20% good outcome

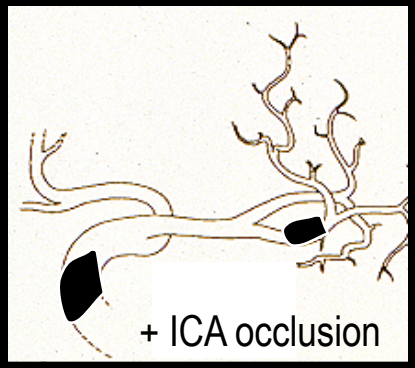


29% TIMI 2/3
37% good outcome





42% TIMI 2/3
14% good outcome



20% TIMI 2/3
20% good outcome

TABLE 1. AOL and TIMI Score Definitions

Score	AOL Recanalization	Score	TIMI Reperfusion
0	No recanalization of the primary occlusive lesion	0	No perfusion
I	Incomplete or partial recanalization of the primary occlusive lesion with no distal flow	1	Perfusion past the initial occlusion, but no distal branch filling
II	Incomplete or partial recanalization of the primary occlusive lesion with any distal flow	2	Perfusion with incomplete or slow distal branch filling
III	Complete recanalization of the primary occlusion with any distal flow	3	Full perfusion with filling of all distal branches, including M3, 4

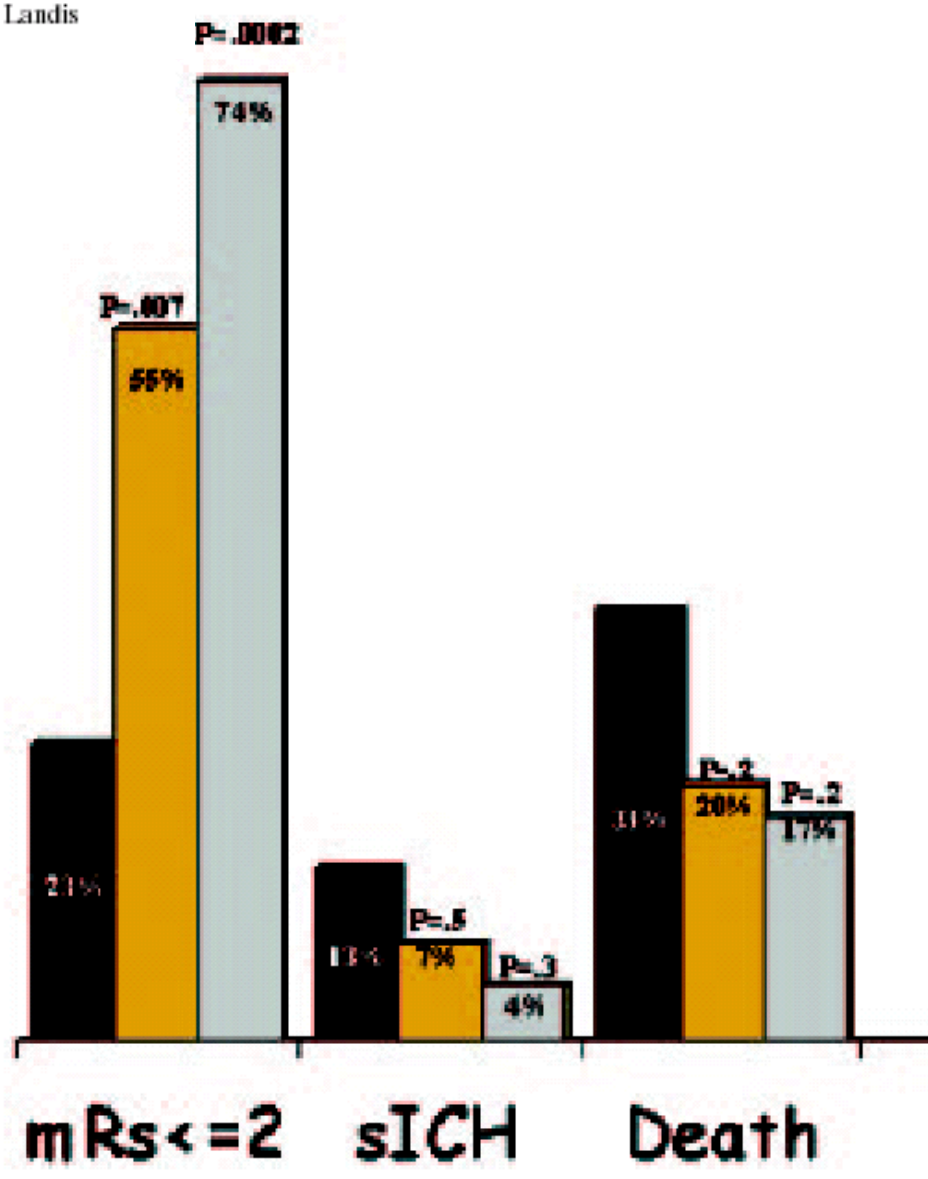
AOL and TIMI Scores	Good Clinical Outcon (mRS 0 to 2)
II–III and 2–3	18/33 (54.5%)
II–III and 0–1	3/10 (30.0%)
0–I and 0–1	4/18 (22.2%)
Total	25/61 (41.0%)

Thrombolytic Therapy of Acute Ischemic Stroke: Correlation of Angiographic Recanalization with Clinical Outcome

Osama O. Zaidat, Jose I. Suarez, Jeffrey L. Sunshine, Robert W. Tarr, Michael J. Alexander, Tony P. Smith, David S. Enterline, Warren R. Selman, and Dennis M. D. Landis

AJNR Am J Neuroradiol 26:880–884, April 2005

n=96 patients
41 IA
55 IV/IA

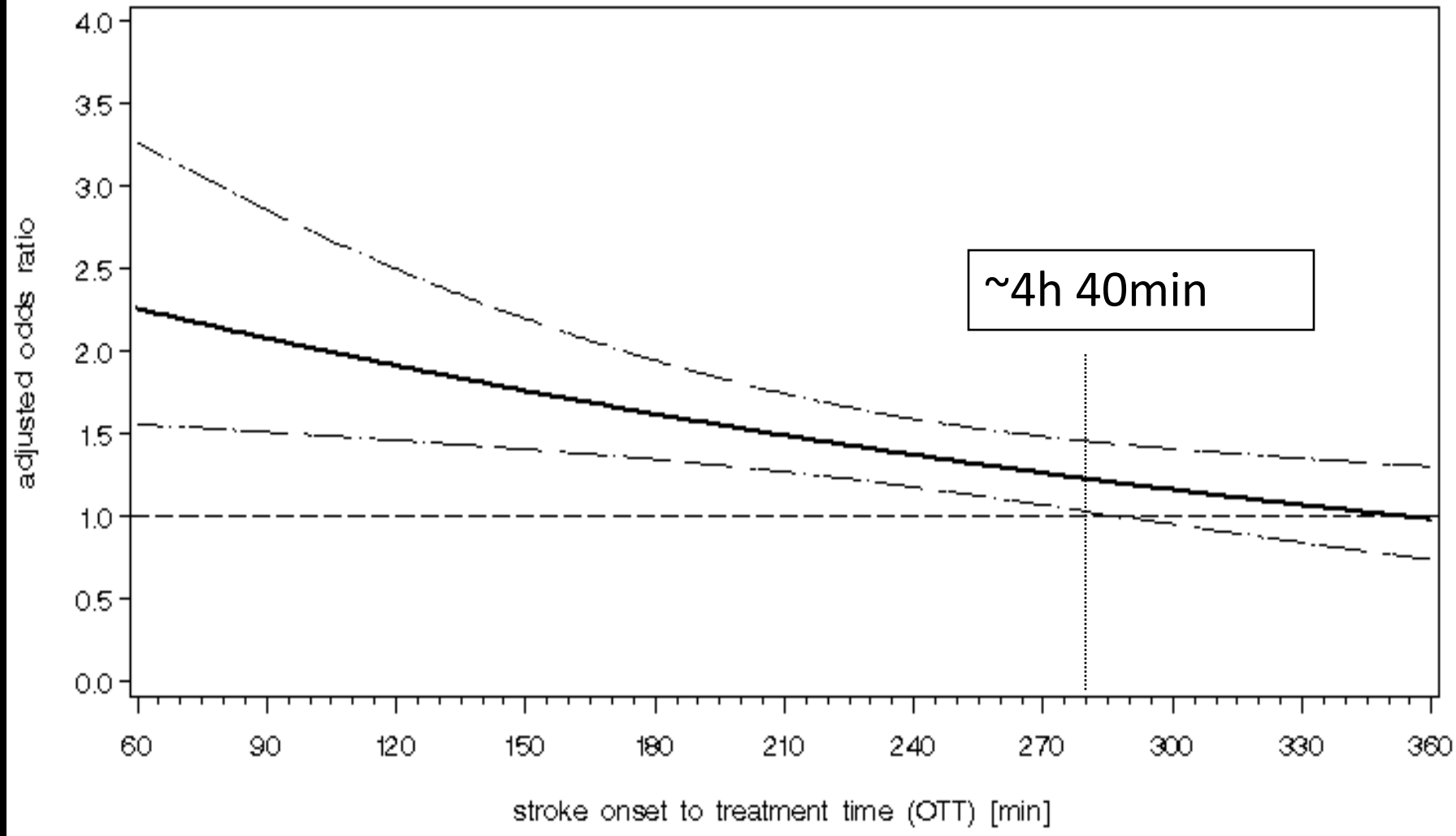


Diminishing Returns over Time

Favorable Outcome (mRS 0-1, BI 95-100, NIHH 0-1) at Day 90 Adjusted odds ratio with 95% confidence interval by stroke onset to treatment time (OTT) ITT population (N=2776)

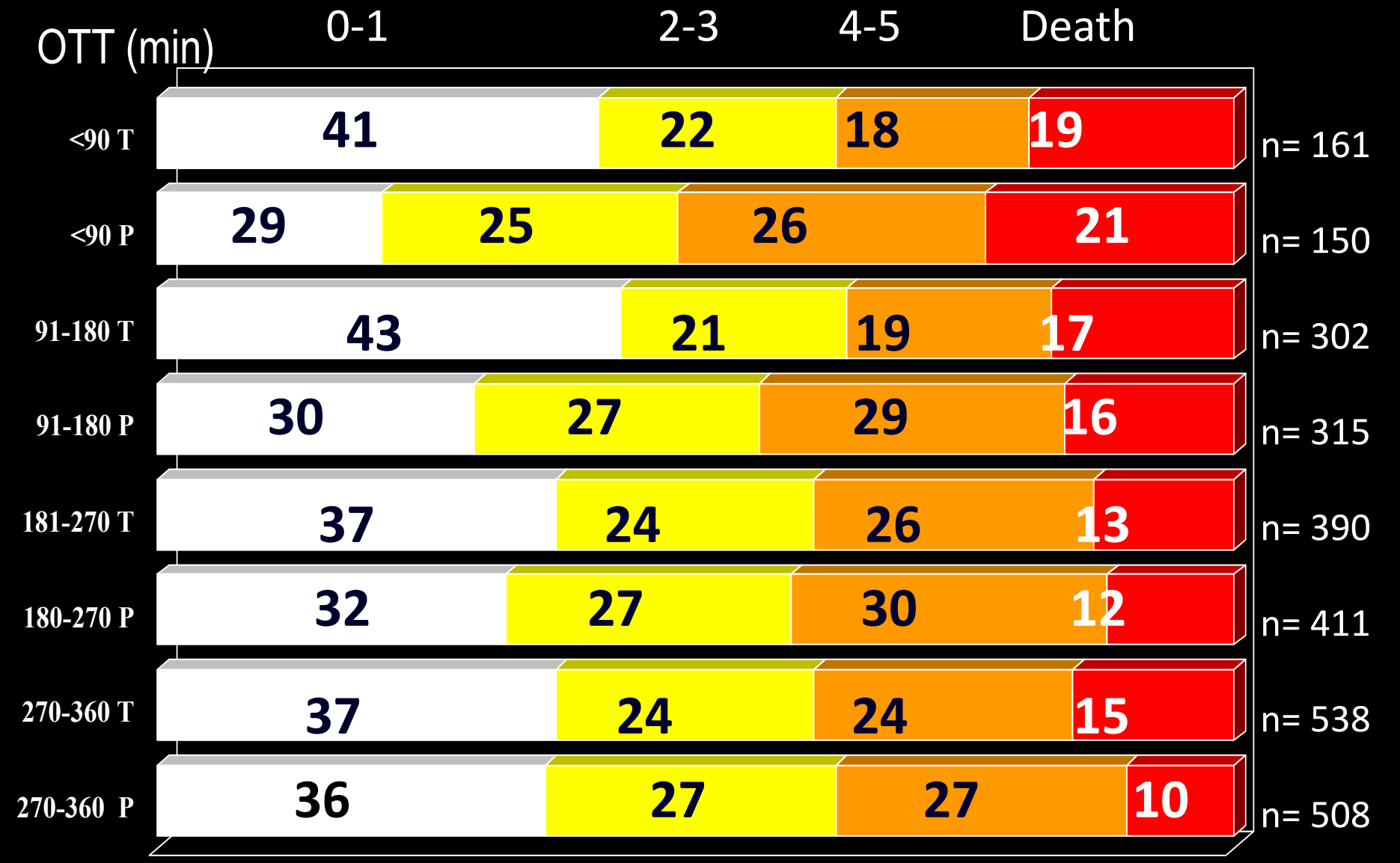
Lancet 2004;363:768-774.

Pooled Analysis NINDS tPA, ATLANTIS, ECASS-I, ECASS-II



TPA Benefit by Time
3 months mRS

Lancet 2004;363:768-774.



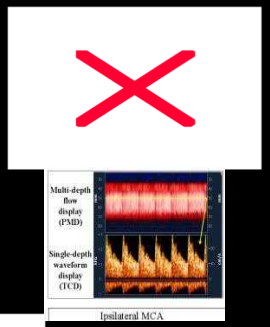
Benefit versus Time to Treatment

Global Statistical Approach: mRS 0-1, BI 95-100, NIHSS 0-1 at 90 days

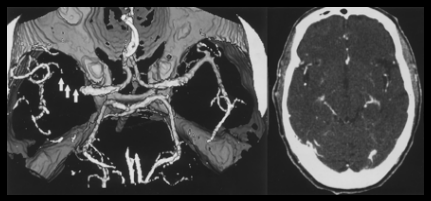
Lancet 2004;363:768-774.

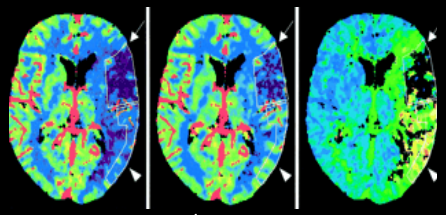
Interval (min)	n	Adjusted OR	Unadjusted OR
0-90	311	2.81 (1.75-4.50)	1.96 (1.30-2.95)
91-180	617	1.55 (1.12-2.15)	1.65 (1.23-2.22)
181-270	801	1.40 (1.05-1.85)	1.34 (1.04-1.72)
270-360	1046	1.15 (0.90-1.47)	1.04 (0.84-1.29)

TCD

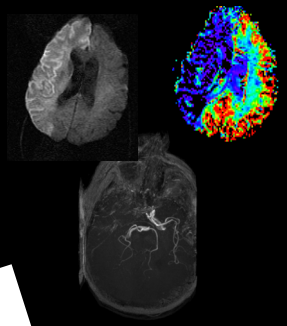


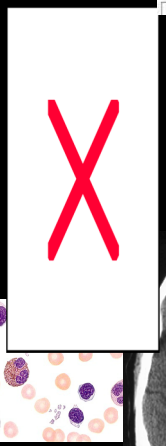
CT

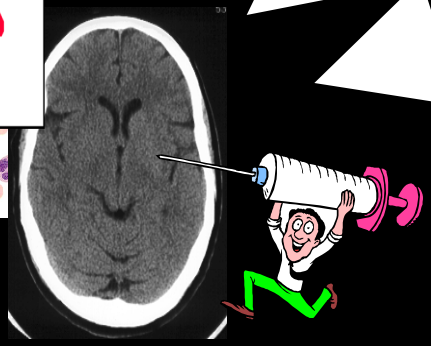




MRI







0 1 2 3 4 5 6 7 8 9 10 11 12

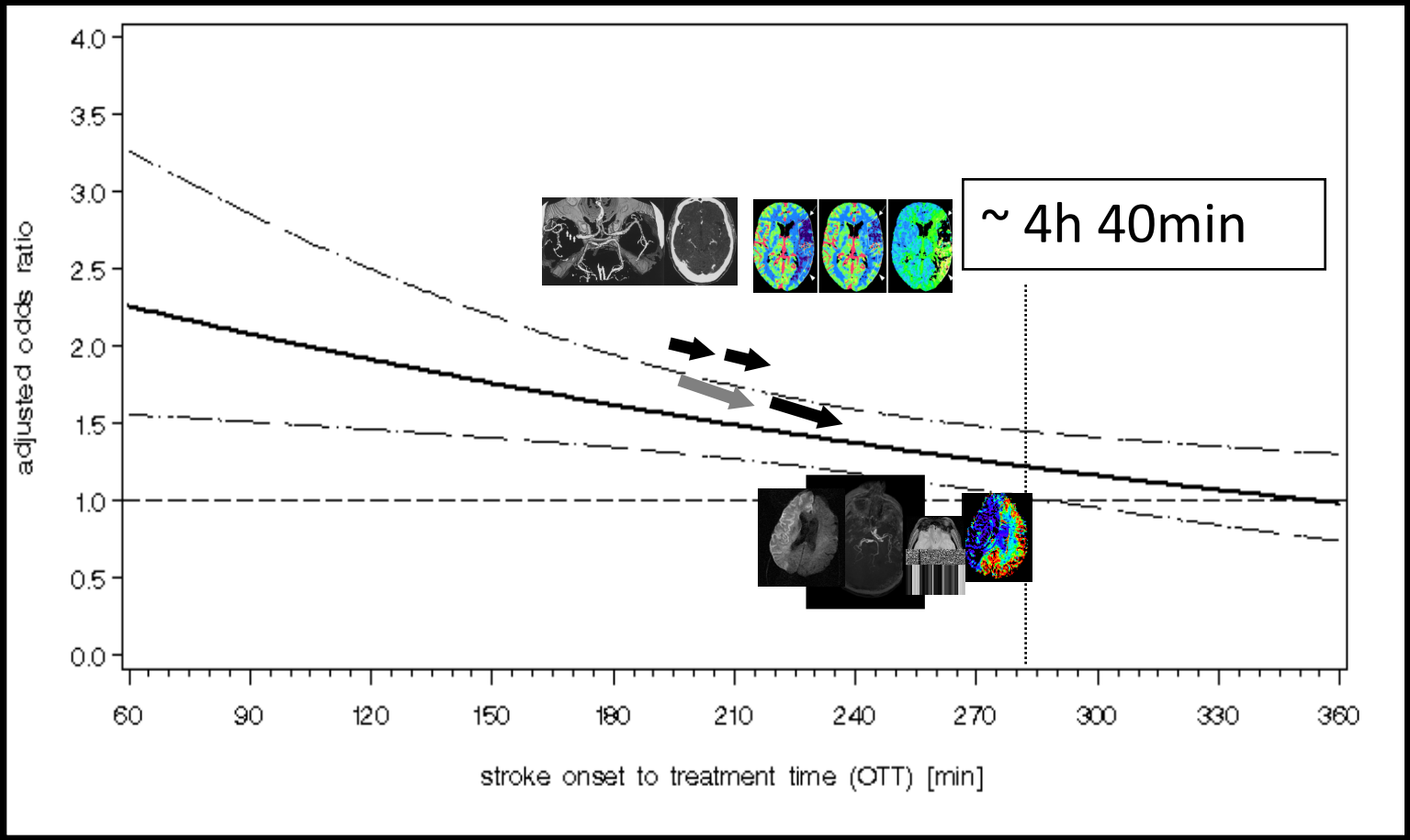
hours

Time is Brain

Favorable Outcome (mRS 0-1, BI 95-100, NIHH 0-1) at Day 90

Adjusted odds ratio with 95% confidence interval by stroke onset to treatment time (OTT) ITT population (N=2776)

Pooled Analysis NINDS tPA, ATLANTIS, ECASS-I, ECASS-II



Courtesy Brott T et al