Time is brain e modelli organizzativi

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OUTLINE

- Il concetto di Time is Brain
- Il fattore tempo nel trattamento endovascolare dello stroke ischemico in fase acuta in base ai risultati degli ultimi trials
- Time is brain e non solo ….Impatto del Neuroimaging avanzato sulla strategia terapeutica
- Modelli organizzativi e prospettive future

TIME IS BRAIN

- Pooled analyses of major randomized controlled trials of intravenous thrombolysis (IVT) in acute ischemic stroke
- Longer times from stroke symptom onset to the initiation of IVT are associated with a lower likelihood of good clinical outcomes at 3 months

1. *Marler JR et al. Early stroke treatment associated with better outcome: the NINDS rt-PA stroke study. Neurology. 2000;55:1649–1655*
2. *Hacke W et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet. 2004;363:768–774*
3. *Lees KR et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. Lancet. 2010;375:1695–1703.*

Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials

Jonathan Emberson, Kennedy R Lees*, Patrick Lyden*, Lisa Blackwell, Gregory Albers, Erich Bluhmki, Thomas Brott, Geoff Cohen, Stephen Davis, Geoffrey Donnan, James Grotta, George Howard, Markku Kaste, Masatoshi Koga, Ruediger von Kummer, Maarten Lansberg, Richard I Lindley, Gordon Murray, Jean Marc Olivot, Mark Parsons, Barbara Tilley, Danilo Toni, Kazunori Toyoda, Nils Wahlgren, Joanna Wardlaw, William Whiteley, Gregory J del Zoppo, Colin Baigent†, Peter Sandercock†, Werner Hacke†; for the Stroke Thrombolysis Trialists' Collaborative Group*

Lancet 2014; 384: 1929–35
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http://dx.doi.org/10.1016/S0140-6736(14)60584-5

- Earlier treatment associated with bigger proportional benefits
- Benefit declining with time
  - Progressive disappearance of the ischaemic penumbra with time
- The effect of alteplase on a good outcome is driven by treatment delay

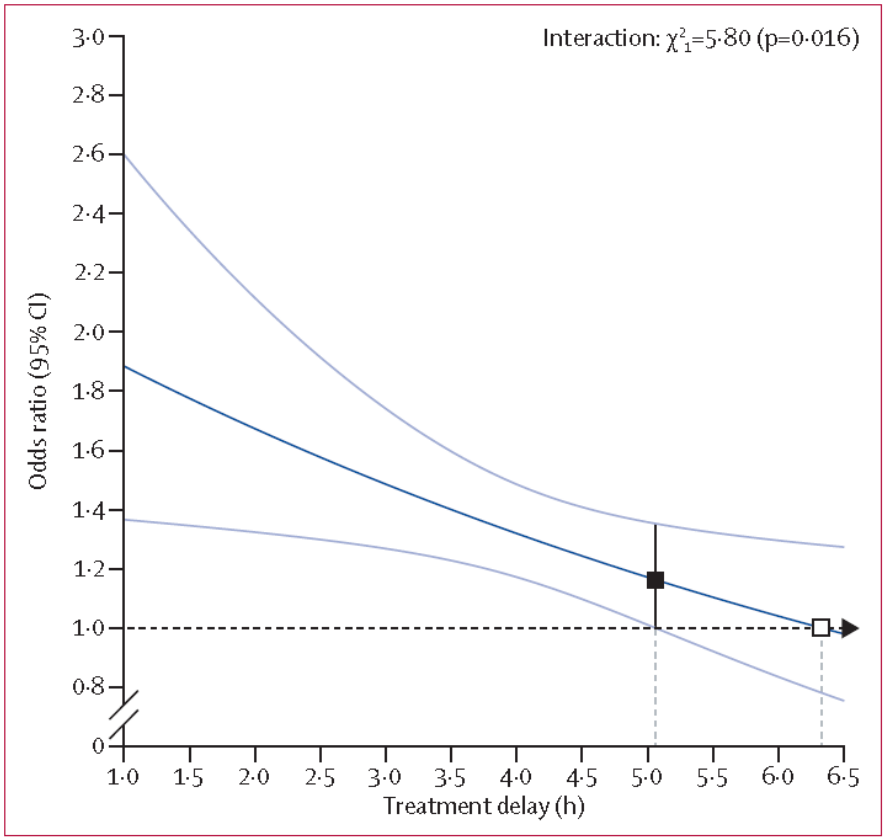

Figure 1: **Effect of timing of alteplase treatment on good stroke outcome (mRS 0–1)**

Time to Treatment With Intravenous Tissue Plasminogen Activator and Outcome From Acute Ischemic Stroke

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Gregg C. Fonarow, MD
Eric E. Smith, MD, MPH
Mathew J. Reeves, PhD
Maria V. Grau-Sepulveda, MD, MPH
Wenqin Pan, PhD
DaiWai M. Olson, PhD
Adrian F. Hernandez, MD, MHS
Eric D. Peterson, MD, MPH
Lee H. Schwamm, MD

Design, Setting, and Patients Data were analyzed from 58 353 patients with acute ischemic stroke treated with tPA within 4.5 hours of symptom onset in 1395 hospitals participating in the Get With The Guidelines-Stroke Program, April 2003 to March 2012.

Main Outcomes and Measures Relationship between OTT time and in-hospital mortality, symptomatic intracranial hemorrhage, ambulatory status at discharge, and discharge destination.

Conclusions and Relevance In a registry representing US clinical practice, earlier thrombolytic treatment was associated with reduced mortality and symptomatic intracranial hemorrhage, and higher rates of independent ambulation at discharge and discharge to home following acute ischemic stroke. These findings support intensive efforts to accelerate hospital presentation and thrombolytic treatment in patients with stroke.

JAMA. 2013;309(23):2480-2488 www.jama.com

Impact of Time to Treatment on Tissue-Type Plasminogen Activator–Induced Recanalization in Acute Ischemic Stroke

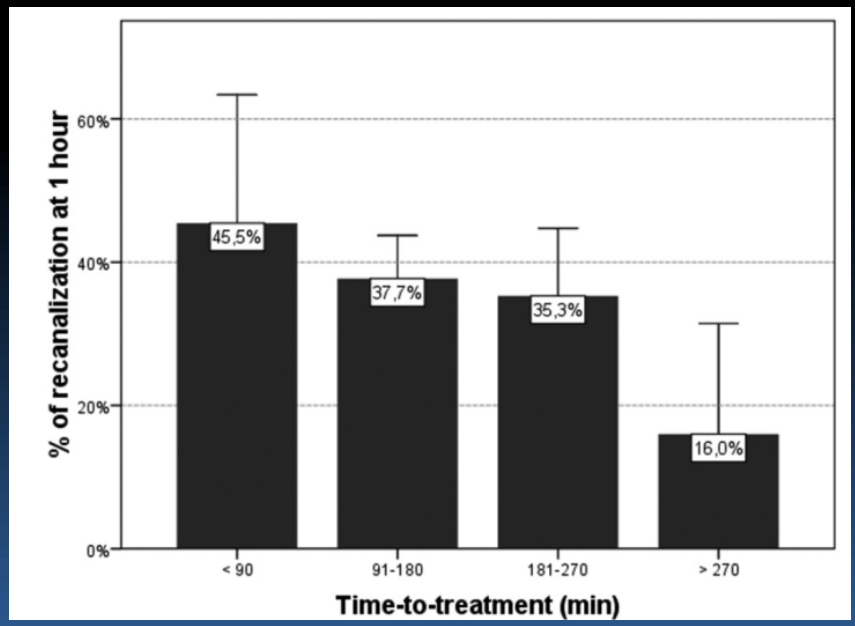
Marian Muchada, MD; David Rodriguez-Luna, MD, PhD; Jorge Pagola, MD, PhD; Alan Flores, MD; Estela Sanjuan, RN; Pilar Meler, RN; Sandra Boned, MD; Jose Alvarez-Sabin, MD, PhD; Marc Ribo, MD, PhD; Carlos A. Molina, MD, PhD; Marta Rubiera, MD, PhD

(*Stroke*. 2014;45:2734-2738.)

- IV tPA in 508 consecutive patients
- TCD at 1 hour after IV tPA
- No linear association between time to treatment and time to recanalization
- Trend toward lower recanalization rates in proximal intracranial occlusions treated after 90 minutes
- Late treated patients may have more old, complex, and organized thrombus
- Endovascular reperfusion therapies

Table 2. Variables Independently Related to Recanalization by Multiple Logistic Regression Analyses in All, Proximal, and Distal Occlusion Patients

	All Patients			Proximal Occlusion			Distal Occlusion		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age, y	0.98	0.966–1.002	0.084	0.975	0.952–0.999	0.039*	0.416	0.195–0.887	0.023*
Sex (male)	1.308	0.839–2.037	0.236	1.020	0.566–1.836	0.945	2.55	1.178–5.526	0.018*
Hyperglycemia	1.025	0.984–1.069	0.235	0.994	0.988–1.001	0.076	0.997	0.989–1.004	0.377
Baseline NIHSS score	0.305	0.1–0.933	0.037*	0.921	0.855–0.993	0.033*	1.065	0.992–1.143	0.083
Onset treatment ≤270	0.995	0.99–0.999	0.030*	0.605	0.154–2.375	0.471	NA	NA	NA



Published in final edited form as:
Lancet Neurol. 2014 June ; 13(6): 567–574. doi:10.1016/S1474-4422(14)70066-3.

Time to Angiographic Reperfusion and Clinical Outcome after Acute Ischemic Stroke in the Interventional Management of Stroke Phase III (IMS III) Trial: A Validation Study

Pooja Khatri, MD[1], Sharon D. Yeatts, PhD[2], Mikael Mazighi, MD[3], Joseph P. Broderick, MD[1], David S. Liebeskind, MD[4], Andrew M. Demchuk, MD[5], Pierre Amarenco, MD[3], Janice Carrozzella, MSN[1], Judith Spilker, BSN[1], Lydia D. Foster, PhD[2], Mayank Goyal, MD[5], Michael D. Hill, MD[5], Yuko Y. Palesch, PhD[2], Edward C. Jauch, MD[2], E. Clarke Haley, MD[6], Achala Vagal, MD[1], and Thomas A. Tomsick, MD[1] for the IMS III Trialists

- Longer time for reperfusion was associated with a decreased likelihood of good clinical outcome for every 30 minute delay
- Delay in time to angiographic reperfusion leads to a decreased likelihood of good clinical outcome
- Complexity of the intervention rather than the time itself

Synthesis Expansion trial

Post-hoc analysis of the effect of time on outcome in the two groups (ET and IVT)

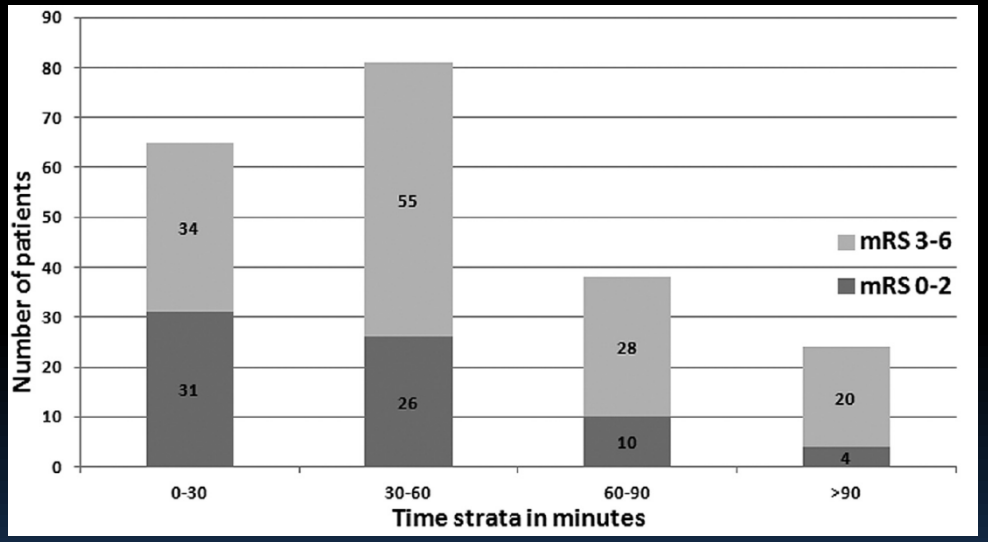
- EVT median time stroke onset- end of treatment 4h:46min
- IVT 3h:50min
- The proportion of ET patients with mRS 0-1 at 3 months was related to the duration of treatment (p=0.04) more than the delay in the beginning of the procedure (p=0.38);
- The duration and the complexity of the EVT worsens the prognosis more than the time itself

Microcatheter to Recanalization (Procedure Time) Predicts Outcomes in Endovascular Treatment in Patients with Acute Ischemic Stroke: When Do We Stop?

A.E. Hassan, S.A. Chaudhry, J.T. Miley, R. Khatri, S.A. Hassan, M.F.K. Suri, and A.I. Qureshi

AJNR Am J Neuroradiol 34:354–59 Feb 2013 www.ajnr.org

- Consecutive series single center 209 patients (2007-2010)
- Wide variability in the "procedure time"
- "Futile recanalization" after endovascular treatment



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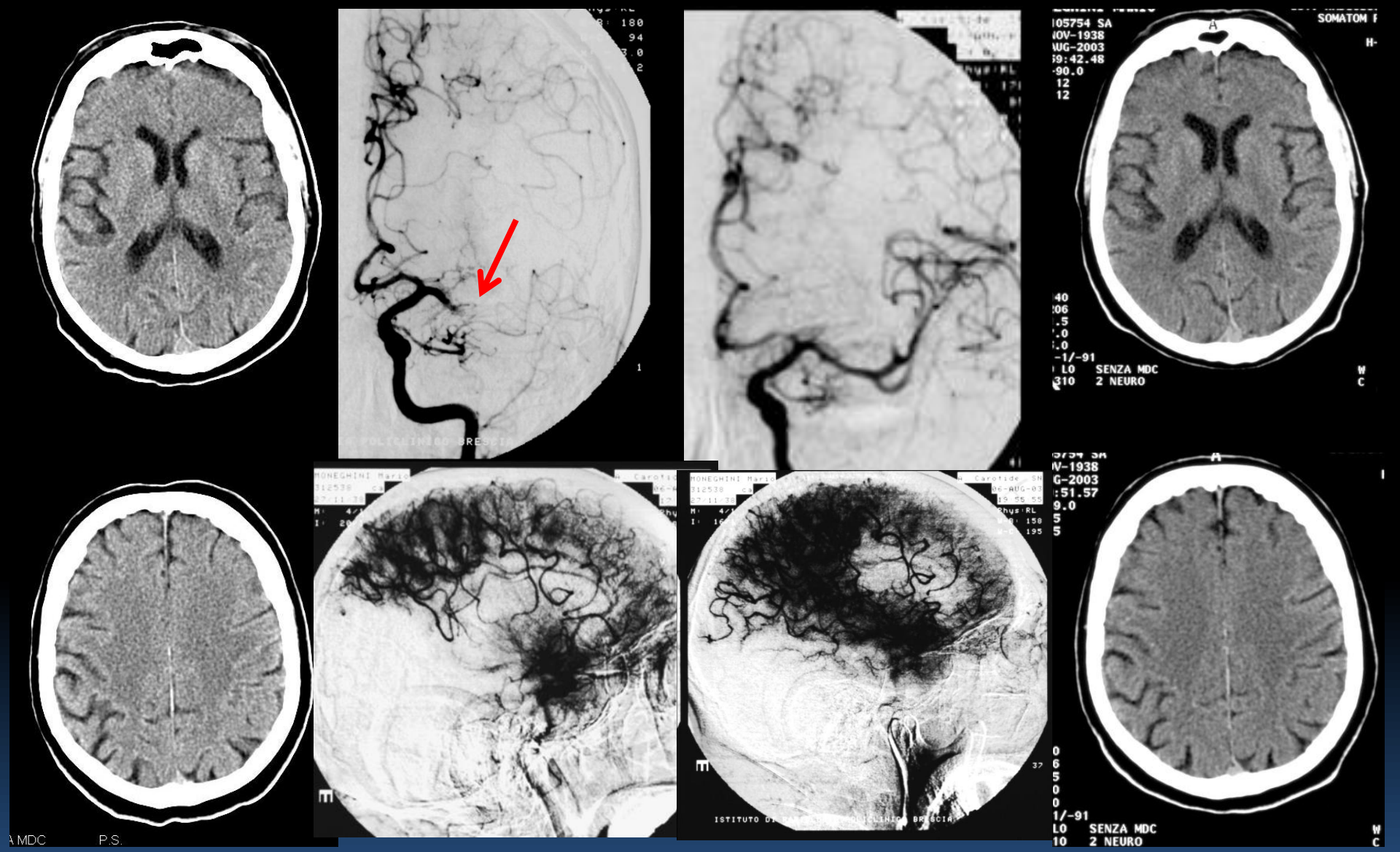
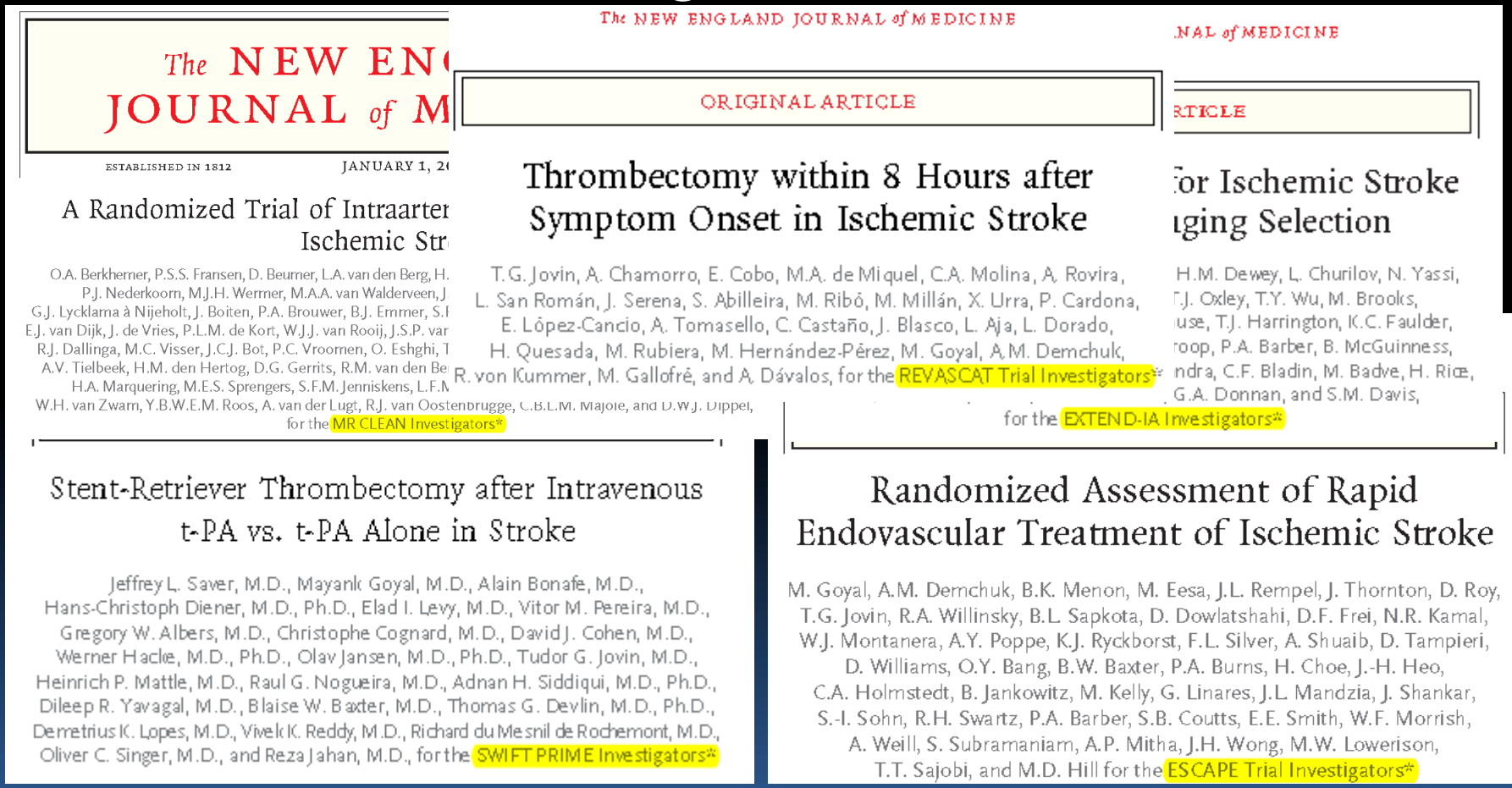


800.000 U Urokinasi Ricanalizzazione completa M1, incompleta M2

Le nuove evidenze scientifiche

Efficacia della trombectomia meccanica nei pazienti con stroke ischemico da occlusione di grandi vasi entro 6-8 ore dall'insorgenza dei sintomi



The NEW ENG
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A Randomized Trial of Intraarter
Ischemic Str

O.A. Berkhemer, P.S.S. Fransen, D. Beumer, L.A. van den Berg, H.
P.J. Nederkoorn, M.J.H. Wermer, M.A.A. van Walderveen, J
G.J. Lycklama à Nijeholt, J. Boiten, P.A. Brouwer, B.J. Emmer, S.F
E.J. van Dijk, J. de Vries, P.L.M. de Kort, W.J.J. van Rooij, J.S.P. var
R.J. Dallinga, M.C. Visser, J.C.J. Bot, P.C. Vroomen, O. Eshghi, T
A.V. Tielbeek, H.M. den Hertog, D.G. Gerrits, R.M. van den Be
H.A. Marquering, M.E.S. Sprengers, S.F.M. Jenniskens, L.F.M
W.H. van Zwam, Y.B.W.E.M. Roos, A. van der Lugt, R.J. van Oostenbrugge, C.B.L.M. Majoie, and D.W.J. Dippel,
for the MR CLEAN Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

T.G. Jovin, A. Chamorro, E. Cobo, M.A. de Miquel, C.A. Molina, A. Rovira,
L. San Román, J. Serena, S. Abilleira, M. Ribó, M. Millán, X. Urra, P. Cardona,
E. López-Cancio, A. Tomasello, C. Castaño, J. Blasco, L. Aja, L. Dorado,
H. Quesada, M. Rubiera, M. Hernández-Pérez, M. Goyal, A.M. Demchuk,
R. von Kummer, M. Gallofré, and A. Dávalos, for the REVASCAT Trial Investigators*

NAL of MEDICINE

RTICLE

for Ischemic Stroke
ging Selection

H.M. Dewey, L. Churilov, N. Yassi,
T.J. Oxley, T.Y. Wu, M. Brooks,
use, T.J. Harrington, K.C. Faulder,
roop, P.A. Barber, B. McGuinness,
ndra, C.F. Bladin, M. Badve, H. Rice,
G.A. Donnan, and S.M. Davis,
for the EXTEND-IA Investigators*

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

Jeffrey L. Saver, M.D., Mayank Goyal, M.D., Alain Bonafe, M.D.,
Hans-Christoph Diener, M.D., Ph.D., Elad I. Levy, M.D., Vitor M. Pereira, M.D.,
Gregory W. Albers, M.D., Christophe Cognard, M.D., David J. Cohen, M.D.,
Werner Hacke, M.D., Ph.D., Olav Jansen, M.D., Ph.D., Tudor G. Jovin, M.D.,
Heinrich P. Mattle, M.D., Raul G. Nogueira, M.D., Adnan H. Siddiqui, M.D., Ph.D.,
Dileep R. Yavagal, M.D., Blaise W. Baxter, M.D., Thomas G. Devlin, M.D., Ph.D.,
Demetrius K. Lopes, M.D., Vivek K. Reddy, M.D., Richard du Mesnil de Rochemont, M.D.,
Oliver C. Singer, M.D., and Reza Jahan, M.D., for the SWIFT PRIME Investigators*

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

M. Goyal, A.M. Demchuk, B.K. Menon, M. Eesa, J.L. Rempel, J. Thornton, D. Roy,
T.G. Jovin, R.A. Willinsky, B.L. Sapkota, D. Dowlatshahi, D.F. Frei, N.R. Kamal,
W.J. Montanera, A.Y. Poppe, K.J. Ryckborst, F.L. Silver, A. Shuaib, D. Tampieri,
D. Williams, O.Y. Bang, B.W. Baxter, P.A. Burns, H. Choe, J.-H. Heo,
C.A. Holmstedt, B. Jankowitz, M. Kelly, G. Linares, J.L. Mandzia, J. Shankar,
S.-I. Sohn, R.H. Swartz, P.A. Barber, S.B. Coutts, E.E. Smith, W.F. Morrish,
A. Weill, S. Subramaniam, A.P. Mitha, J.H. Wong, M.W. Lowerison,
T.T. Sajobi, and M.D. Hill for the ESCAPE Trial Investigators*

	MR CLEAN	ESCAPE	EXTEND-IA	SWIFT PRIME	REVASCAT
N	500 patients - 233 IAT - 267 control	316 - 165 IAT - 150 control	196	316 - 98 IAT - 98 control	- 206 - 103 IAT - 103 control
Device usage	**Open label** **Mostly stentrievers**	**Open label** **80% stentrievers**	**Only Solitaire**	**Only Solitaire**	**Only Solitaire**
Key selection criteria	CTA confrmation LVO	- CTA confirmation LVO - ASPECTS ≥6 - CTA Moderate/Good Collaterals	- CTA confirmation LVO - CTP Mismatch with ischemic core <70 ml	- CTA confirmation LVO - ASPECTS ≥6 - CTP Mismatch with ischemic core <50 ml	- CTA confirmation LVO - ASPECTS>7 - ASPECTS>7 CBV CTP maps
Baseline NIHSS	-17 IAT - 18 Control	- 16 IAT - 13 Control	- 17 IAT - 13 Control	- 17 IAT - 17 Control	- 17 IAT - 17 Control
Median ASPECTS	9 both IAT and Control	9 both IAT and Control	Not applicable	9 both IAT and Control	- 7 IAT - 8 control
mRS ≤2 @ 90 Days	IAT: 32.6% Control: 19.1%	IAT: 53% Control: 29.3%	IAT: 72% Control: 40%	IAT: 60.2% Control: 35.5%	IAT: 43.7% Control: 28.2%
Revas Rate IAT	58.7% TICI 2b/3	72.4% TICI 2b/3	86% TICI 2b/3	88% TICI 2b/3	65.7% TICI 2b/3
Mortality @ 90 Days	IAT 21% Control 22%	IAT 10% Control 19%	IAT 9% Control 20%	IAT 12.2% Control 25.6%	IAT 18.4% Control 15.5%
SICH	IAT 7.7%	IAT 3.6%	IAT 0%	IAT 1%	
Median Onset/groin puncture	260	241*	210	224	269

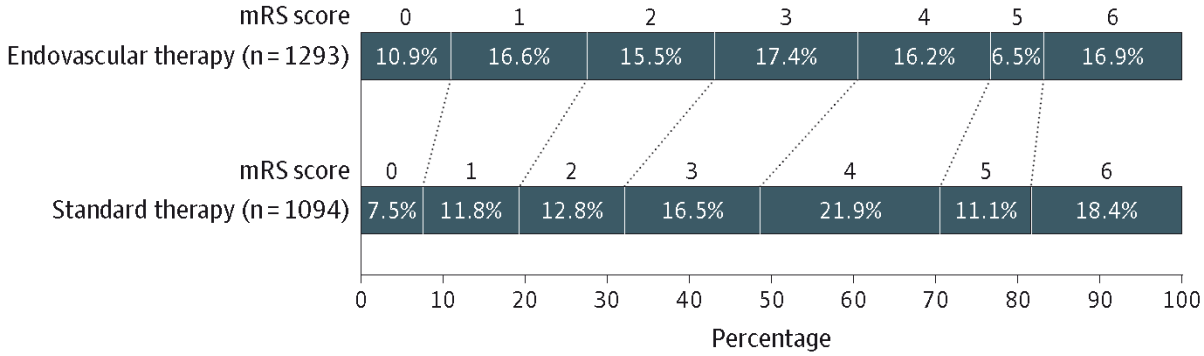
Original Investigation

Endovascular Thrombectomy for Acute Ischemic Stroke
A Meta-analysis

Jetan H. Badhiwala, MD; Farshad Nassiri, MD; Waleed Alhazzani, MD; Magdy H. Selim, MD; Forough Farrokhyar, PhD; Julian Spears, MD; Abhaya V. Kulkarni, MD; Sheila Singh, MD; Abdulrahman Alqahtani, MD; Bram Rochwerg, MD; Mohammad Alshahrani, MD; Naresh K. Murty, MD; Adel Alhazzani, MD; Blake Yarascavitch, MD; Kesava Reddy, MD; Osama O. Zaidat, MD; Saleh A. Almenawer, MD

Figure 2. Functional Outcomes of Endovascular Therapy vs Standard Therapy

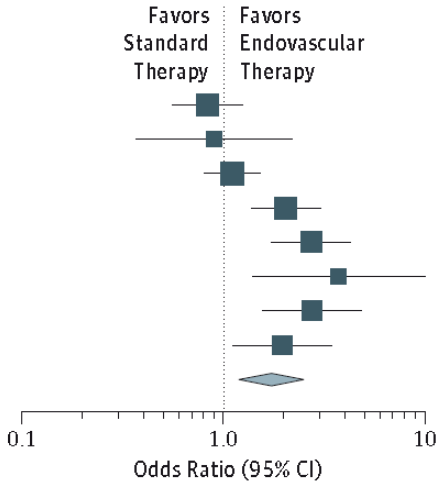
A Degree of disability at 90 d (modified Rankin Scale [mRS])



A Functional independence (modified Rankin Scale score 0-2) at 90 d

Source	Endovascular Therapy Events/No.	Standard Therapy Events/No.	Odds Ratio (95% CI)	P Value	Weight, %
SYNTHESIS,[26] 2013	76/181	84/181	0.84 (0.55-1.27)	.40	14.6
MR RESCUE,[27] 2013	12/64	11/54	0.90 (0.36-2.25)	.82	8.6
IMS III,[28] 2013	177/415	86/214	1.11 (0.79-1.55)	.55	15.6
MR CLEAN,[29] 2015	76/233	51/267	2.05 (1.36-3.09)	.001	14.7
ESCAPE,[30] 2015	87/164	43/147	2.73 (1.71-4.37)	<.001	13.9
EXTEND-IA,[31] 2015	25/35	14/35	3.75 (1.38-10.17)	.009	7.8
SWIFT-PRIME,[32] 2015	59/98	33/93	2.75 (1.53-4.94)	.001	12.4
REVASCAT,[33] 2015	45/103	29/103	1.98 (1.11-3.53)	.02	12.5
Overall	557/1293	351/1094	1.71 (1.18-2.49)	.005	100.0

$I^2 = 75.4\%$, $P < .01$



Original Investigation

Endovascular Thrombectomy for Acute Ischemic Stroke
A Meta-analysis

Jetan H. Badhiwala, MD; Farshad Nassiri, MD; Waleed Alhazzani, MD; Magdy H. Selim, MD; Forough Farrokhyar, PhD; Julian Spears, MD; Abhaya V. Kulkarni, MD; Sheila Singh, MD; Abdulrahman Alqahtani, MD; Bram Rochwerg, MD; Mohammad Alshahrani, MD; Naresh K. Murty, MD; Adel Alhazzani, MD; Blake Yarascavitch, MD; Kesava Reddy, MD; Osama O. Zaidat, MD; Saleh A. Almenawer, MD

- REVASCAT
  - included a 6-to-8-hour group
- ESCAPE
  - enrolled 49 patients at 6 to12 hours
- Definitive positive treatment effect has not been demonstrated in these subgroups

PLOS ONE

RESEARCH ARTICLE

Endovascular Treatment with Stent-Retriever Devices for Acute Ischemic Stroke: A Meta-Analysis of Randomized Controlled Trials

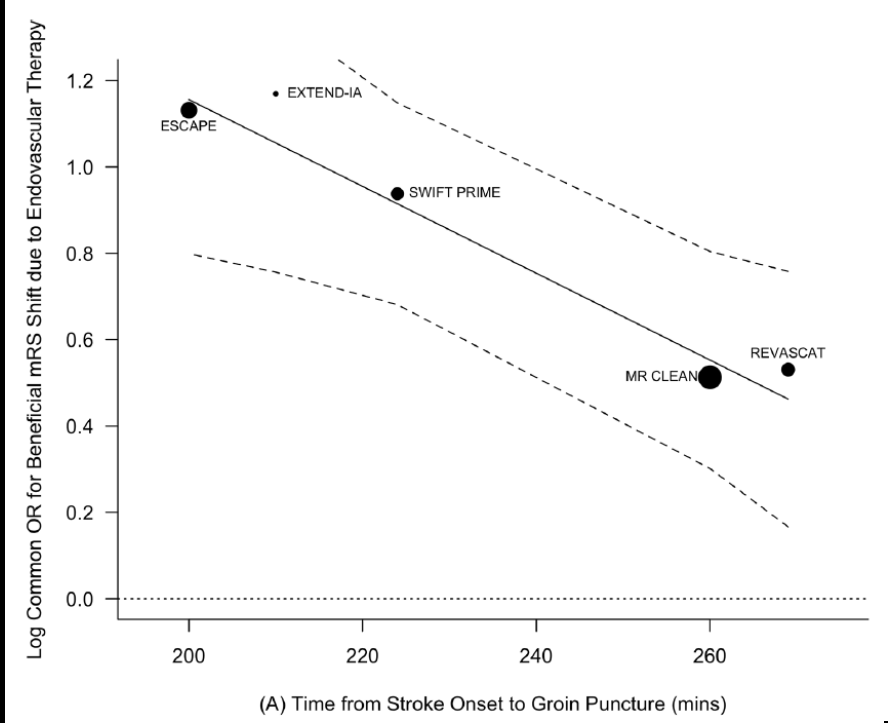
Chad K. Bush[1,2,3]*, Dayaamayi Kurimella[1], Lee J. S. Cross[1], Katherine R. Conner[1], Sheryl Martin-Schild[2,3], Jiang He[1,2], Changwei Li[1], Jing Chen[1,2], Tanika Kelly[1]*

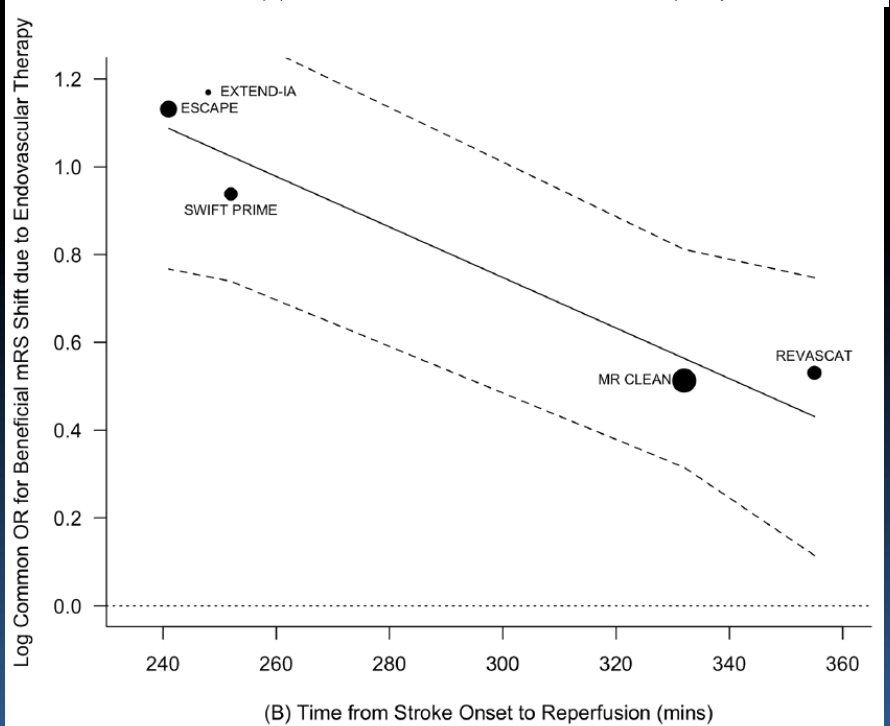
1 Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, Louisiana, United States of America, **2** Department of Medicine, Tulane University School of Medicine, New Orleans, Louisiana, United States of America, **3** Department of Neurology, Tulane University School of Medicine, New Orleans, Louisiana, United States of America

Table 1. Characteristics of Randomized Trials Included in the Meta-Analysis.

		Medical Management Arm			Endovascular Arm						
Trial, Publication Year	No. of Patients	Primary Treatment Modalities	Patients, N (%)	IV t-PA, N (%)	Primary Treatment Modalities	Patients, N (%)	IV t-PA, N (%)	Stent-Retriever Deployed, N (%)	mTICI 2b or 3 (Good Reperfusion), N (%)	Onset-to-Groin-Puncture Time, min (IQR)	Onset-to-Reperfusion Time, min (IQR)
MR CLEAN, 2014 [13]	500	IV t-PA if candidates[a]	267 (53.4%)	242 (90.6%)	IA thrombolysis[b] and/or mechanical thrombectomy[c] + IV t-PA if candidates[a]	233 (46.6%)	203 (87.1%)	190 (81.5%)	115 (58.7%)	260 (210–313)	332 (279–394) [30]
ESCAPE, 2015 [14]	315	IV t-PA if candidates[a]	150 (47.6%)	118 (78.7%)	Mechanical thrombectomy + IV t-PA if candidates[a]	165 (52.4%)	120 (72.7%)	130 (78.8%)	113 (72.4%)[d, e]	200 (116–315) [31]	241(176–359)[f]
EXTEND-IA, 2015 [15]	70	IV t-PA alone	35 (50%)	35 (100%)	Mechanical thrombectomy + IV t-PA	35 (50%)	35 (100%)	31 (88.6%)	25 (86.2%)[d]	210 (83–159)	248 (204–277)[g]
SWIFT PRIME, 2015 [16]	196	IV t-PA alone	98 (50%)	98 (100%)	Mechanical thrombectomy + IV t-PA	98 (50%)	98 (100%)	87 (88.8%)	53 (83.0%)	224 (165–275)	252 (190–300)[h]
REVASCAT, 2015 [17]	206	IV t-PA if candidates[a]	103 (50%)	80 (77.7%)	Mechanical thrombectomy + IV t-PA if candidates[a]	103 (50%)	70 (68%)	98 (95.1%)	67 (65.7%)	269 (201–340)	355 (269–430)[e]
OVERALL	1,287		653 (50.7%)	573 (87.7%)		634 (49.3%)	526 (83.0%)	536 (84.5%)	373 (80.4%)	200 to 269 min	241 to 355 min

- Time to groin puncture range 200-269 minutes
- Time to reperfusion range 241 to 355 minutes
- Shorter times
  - stroke onset to groin puncture *(P = 0.0077)*
  - stroke onset to reperfusion *(P = 0.0089)*
- Improved workflow efficiencies significantly influence the beneficial effects of endovascular treatment





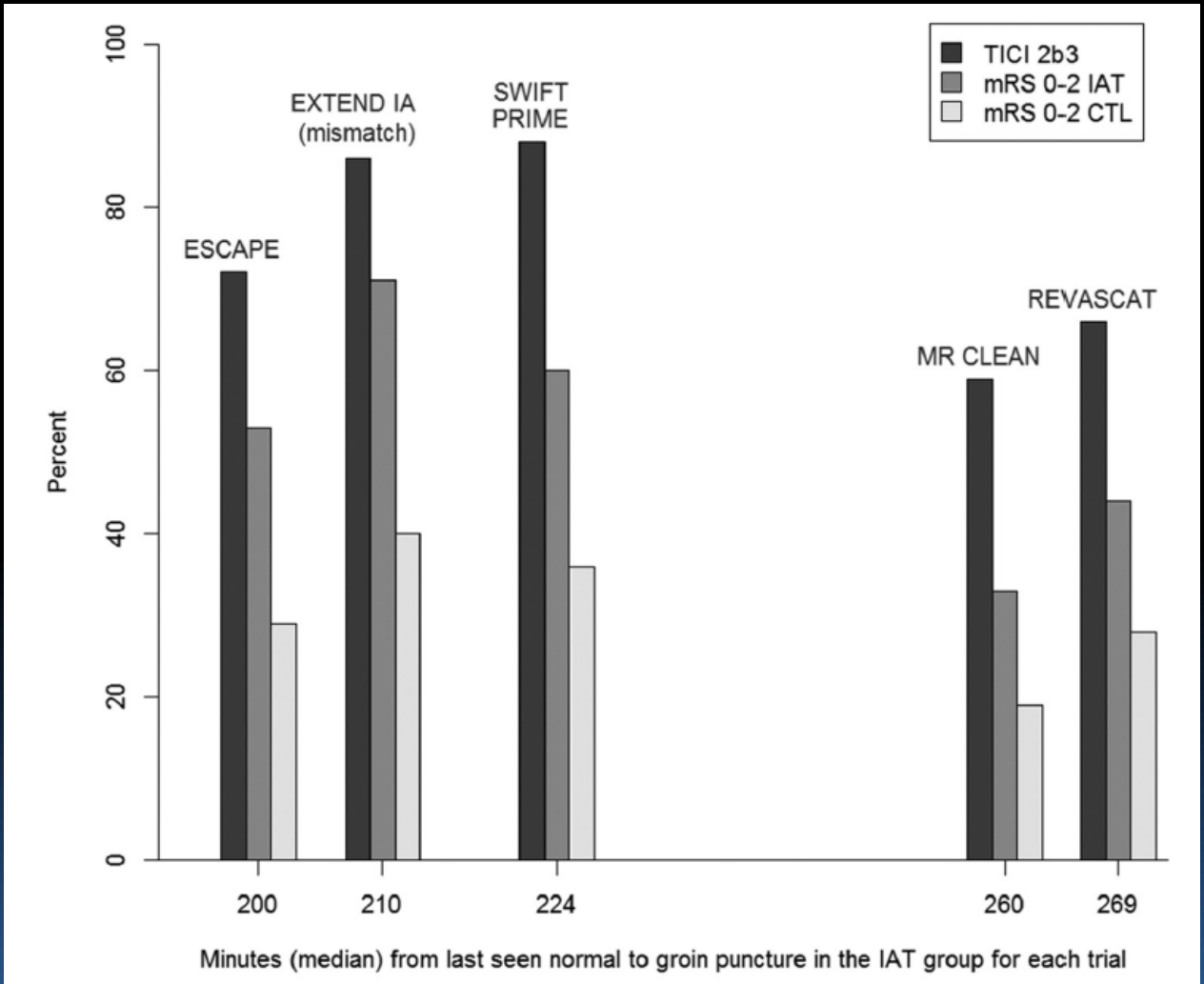
Endovascular intervention retained its positive association with better functional outcome for patients who did not receive IV t-PA as
well as for patients who did receive IV t-PA

	Ordinal Analysis of mRS Scores at 90 Days			
	Number of Studies	**Pooled OR [95% CI]**	**Effect P**	**Subgroup P[a]**
Overall Analysis	5	2.22 [1.66, 2.98]	<0.0001	
Gender				
Male	2 [14, 16]	2.60 [1.65, 4.10]	<0.0001	0.9255
Female	2 [14, 16]	2.53 [1.63, 3.90]	<0.0001	
Age				
< 70 years	2 [16–17]	2.41 [1.51, 3.84]	0.0002	0.8783
≥ 70 years	4 [13–14, 16–17]	2.26 [1.20, 4.26]	0.0113	
NIHSS Score				
< 17	3 [13, 16–17]	1.77 [1.22, 2.58]	0.0028	0.3761
≥ 17	4 [13–14, 16–17]	2.23 [1.58, 3.15]	<0.0001	
ASPECTS Score				
Low (< 8)	4 [13–14, 16–17]	1.82 [1.19, 2.79]	0.0061	0.5274
High (≥ 8)	4 [13–14, 16–17]	2.19 [1.61, 2.98]	<0.0001	
IV Alteplase				
Given	3 [13–14, 17]	1.85 [1.39, 2.46]	<0.0001	0.1884
Not Given	5 [13–17]	2.41 [1.76, 3.31]	<0.0001	

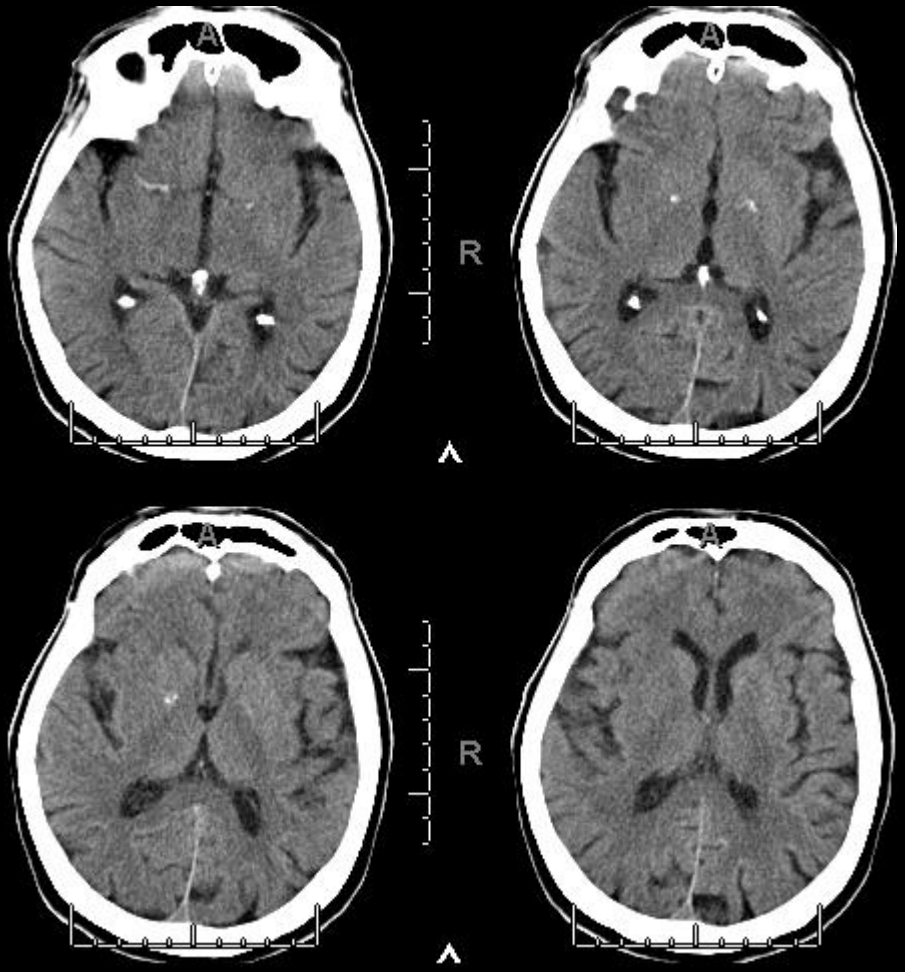
Stroke Neurologist's Perspective on the New Endovascular Trials

James C. Grotta, MD; Werner Hacke, MD

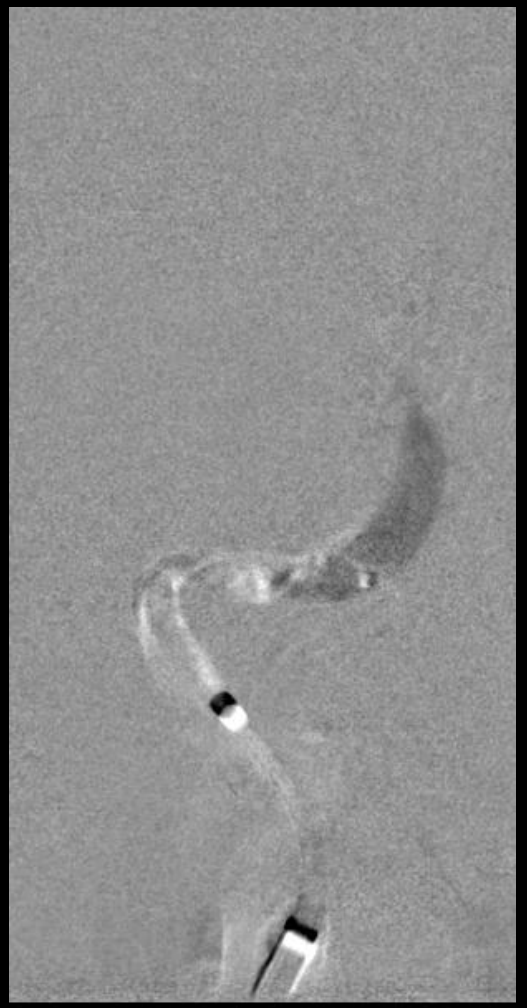
Stroke. 2015;46:1447-1452



79-yo Female, NIHSS 20, stroke onset 16:45



CT 18:18



Groin puncture 18:45

65-yo Female, NIHSS 20, stroke onset 16:45

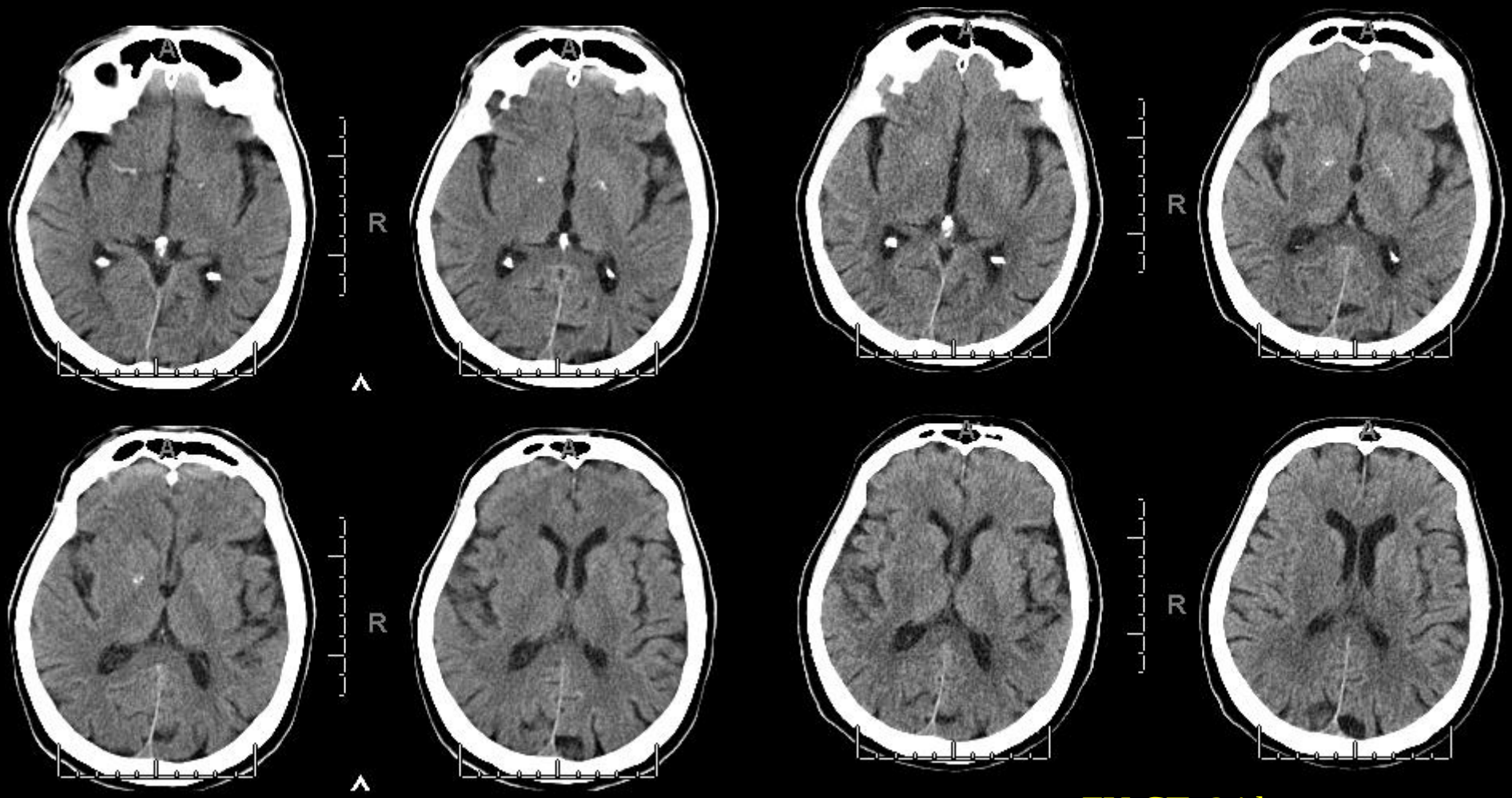
Thromboaspiration
(Penumbra system ACE 64)

TICI 3

End of procedure 19:20

65-yo Female, NIHSS 20, stroke onset 16:45

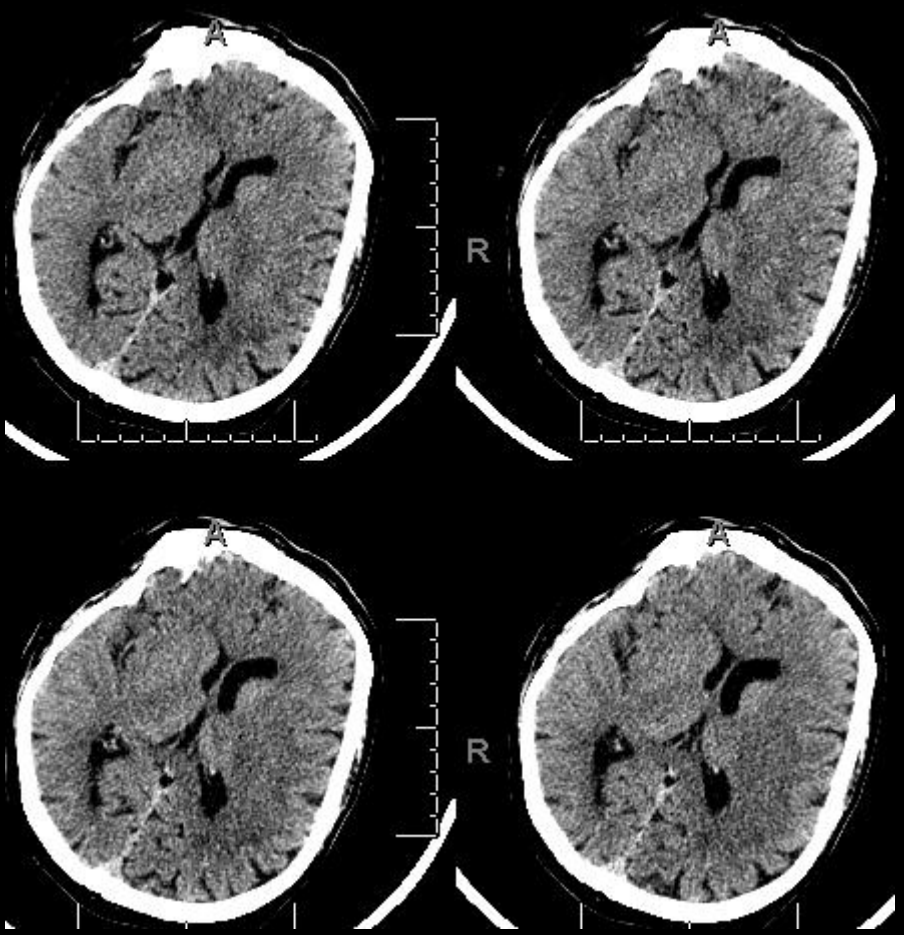
mRS 0@ 3 months



CT 18:18

FU CT 24 hrs

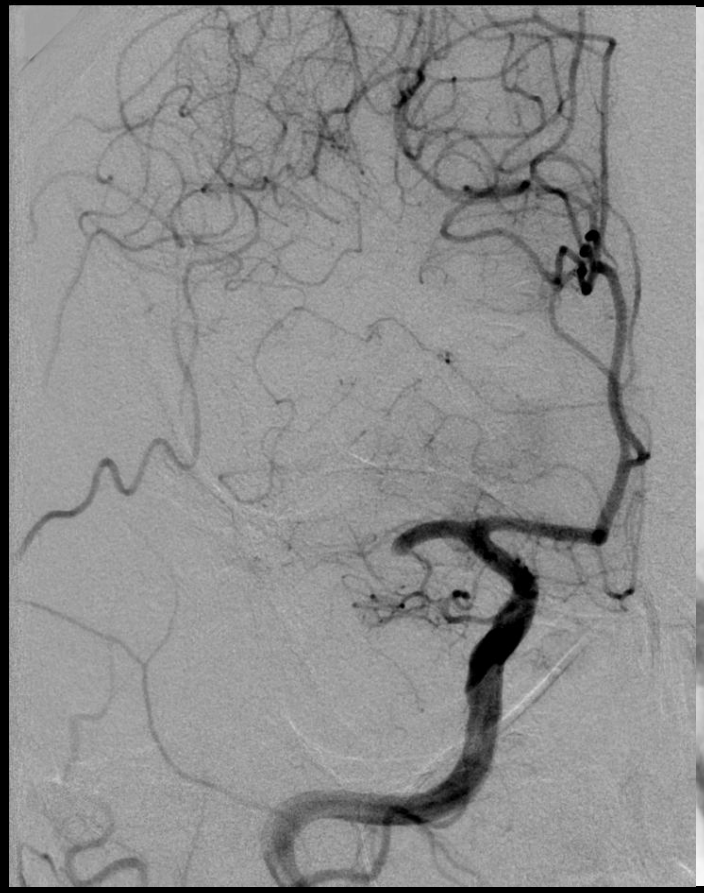
67-yo Male, NIHSS 15, stroke onset 18:50

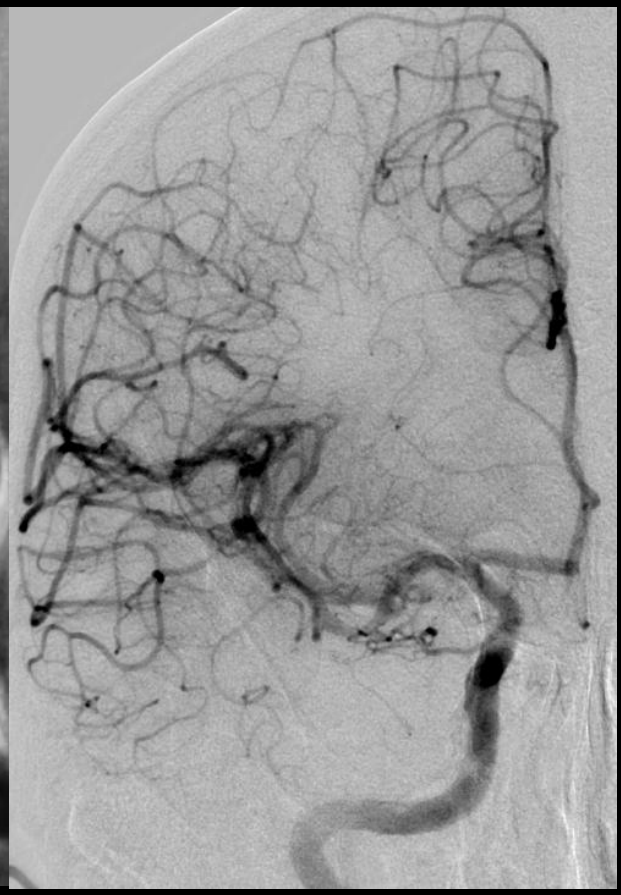


CT 20:05, peripheral hospital, telemedicine

Angio Suite: 22:15 Groin puncture 22:30

67-yo Male, NIHSS 15, stroke onset 18:50





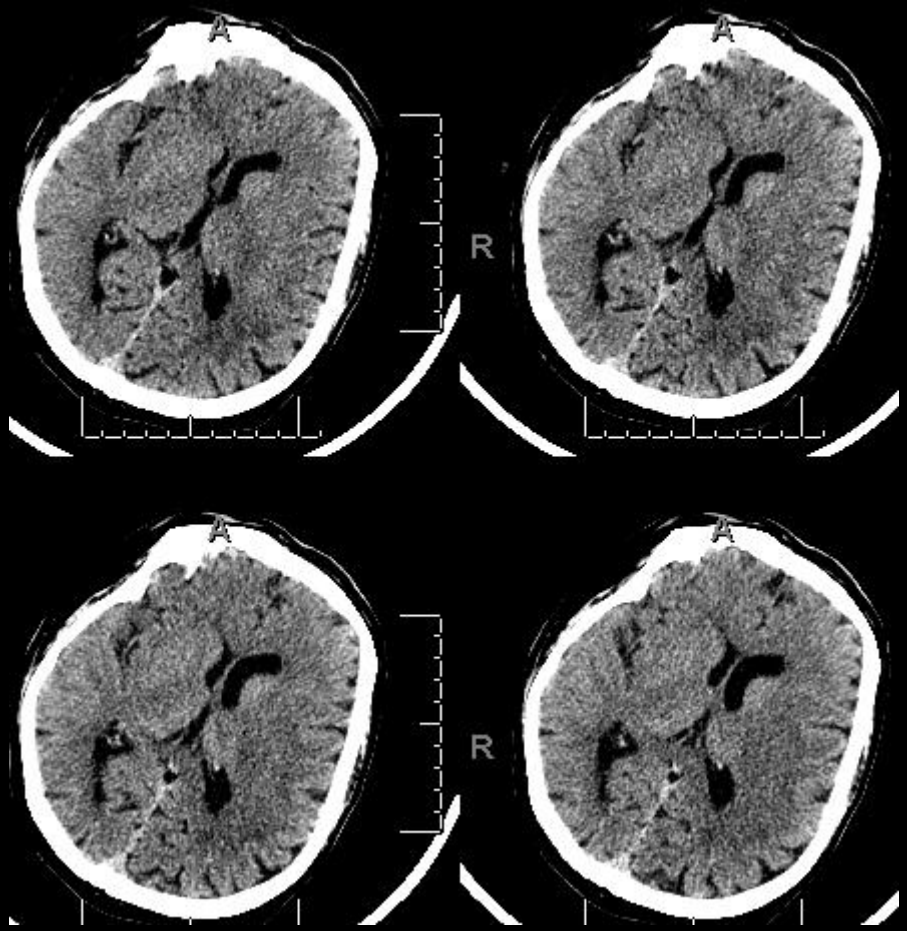
Thromboaspiration
(Penumbra system ACE 64)

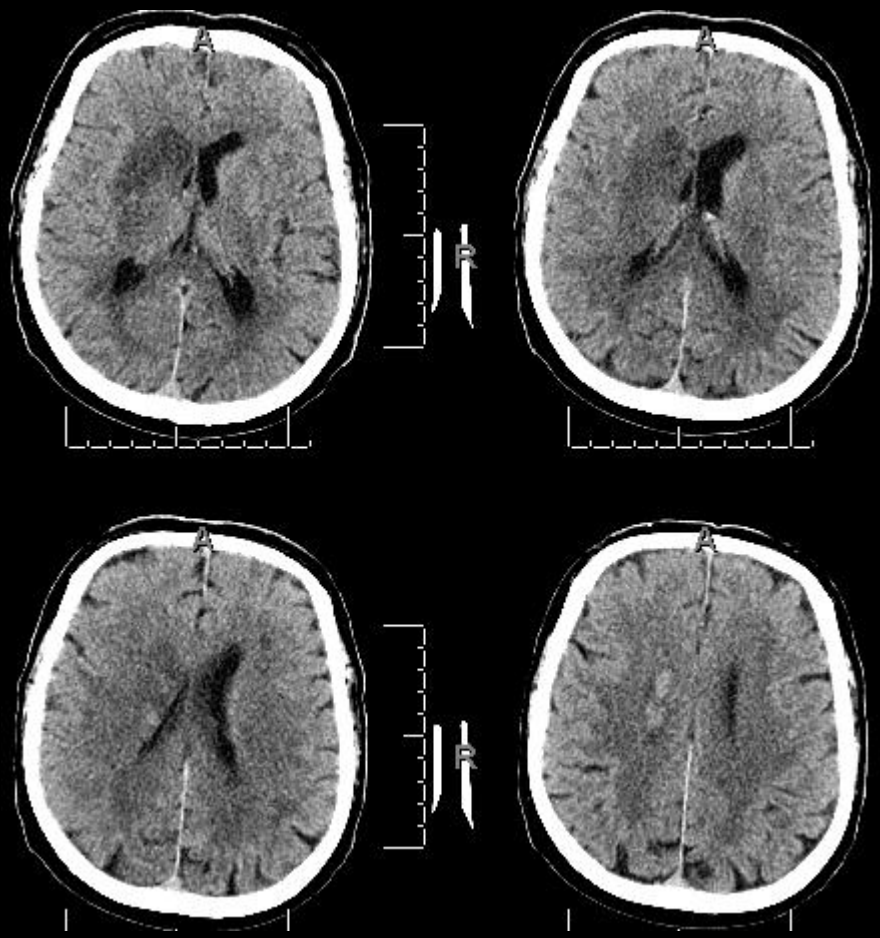
TICI 3

End of procedure 23:10

67-yo Male, NIHSS 15, stroke onset 18:50

mRS 2@ 3 months



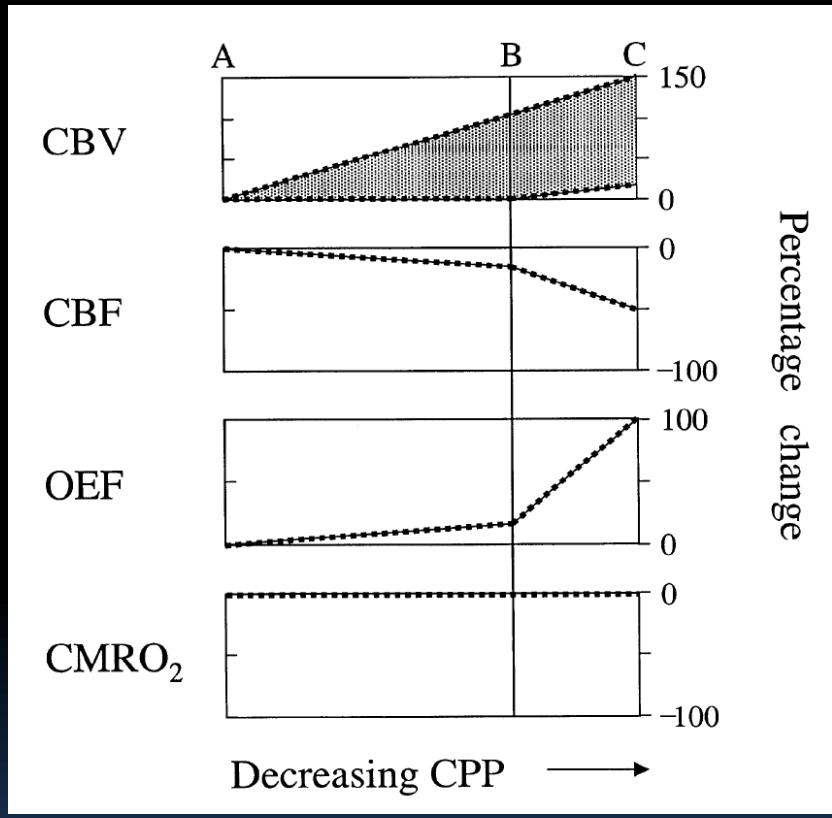


CT 20:05, peripheral hospital, telemedicine

FU CT 24 hrs

«Time is Brain»

- It’s actually not that simple
- Every patient is different
- Collateral flow is variable
- Time is relative
- Imaging is important

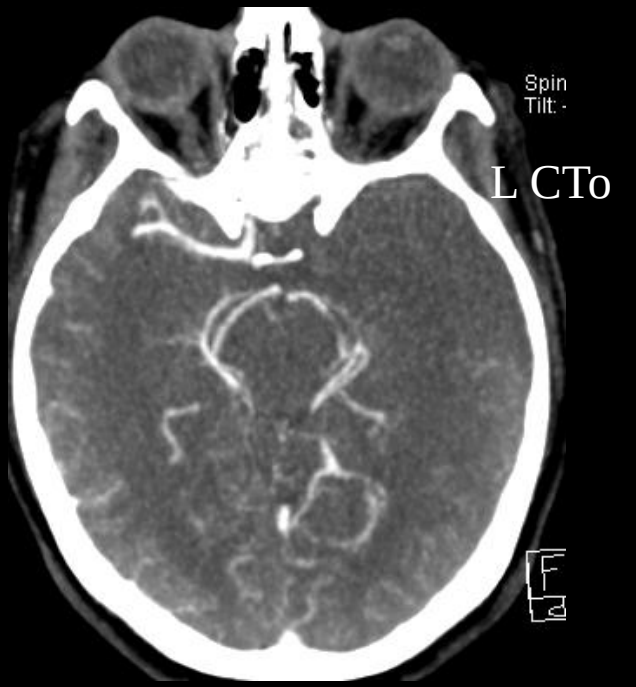


Derdeyn et al. Brain 2002

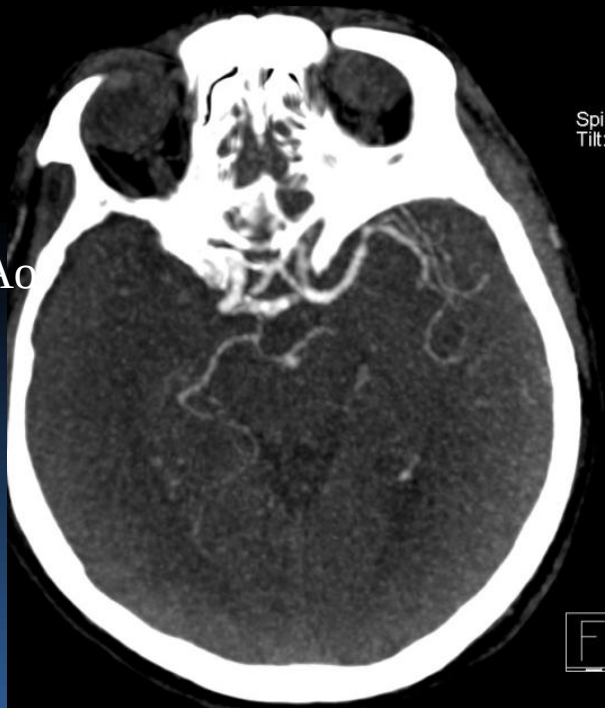
	MR CLEAN	ESCAPE	EXTEND-IA	SWIFT PRIME	REVASCAT
N	500 patients - 233 IAT - 267 control	316 - 165 IAT - 150 control	196	196 - 98 IAT - 98 control	- 206 - 103 IAT - 103 control
Device usage	**Open label** **Mostly stentrievers**	**Open label** **80% stentrievers**	**Only Solitaire**	**Only Solitaire**	**Only Solitaire**
Key selection criteria	-CTA confirmation LVO	- CTA confirmation LVO - ASPECTS ≥6 - CTA Moderate/Good Collaterals	- CTA confirmation LVO - CTP Mismatch ischemic core <70 ml	- CTA confirmation LVO - ASPECTS ≥6 - CTP Mismatch with ischemic core <50 ml	- CTA confirmation LVO - ASPECTS>7 - ASPECTS>7 CBV CTP maps
Baseline NIHSS	-17 IAT - 18 Control	- 16 IAT - 13 Control	- 17 IAT - 13 Control	- 17 IAT - 17 Control	- 17 IAT - 17 Control
Median ASPECTS	9 both IAT and Control	9 both IAT and Control	Not applicable	9 both IAT and Control	- 7 IAT - 8 control
mRS ≤2 @ 90 Days	IAT: 32.6% Control: 19.1%	IAT: 53% Control: 29.3%	IAT: 72% Control: 40%	IAT: 60.2% Control: 35.5%	IAT: 43.7% Control: 28.2%
Revas Rate IAT	58.7% TICI 2b/3	72.4% TICI 2b/3	86% TICI 2b/3	88% TICI 2b/3	65.7% TICI 2b/3
Mortality @ 90 Days	IAT 21% Control 22%	IAT 10% Control 19%	IAT 9% Control 20%	IAT 12.2% Control 25.6%	IAT 18.4% Control 15.5%
SICH	IAT 7.7%	IAT 3.6%	IAT 0%	IAT 1%	

ANGIO-TC

- Documentazione occlusione prima della randomizzazione
- Capacità di riconoscere le differenze tra i due gruppi IAT e IVT
- Garanzia di includere nel gruppo IAT tutti i pazienti “target” della terapia
- Gruppo di controllo con elevata probabilità di outcome non favorevole in assenza di IAT



L CTo



R MCAo

ANGIOTC
CIRCOLI COLLATERALI

The NEW ENGLAND JOURNAL of MEDICINE

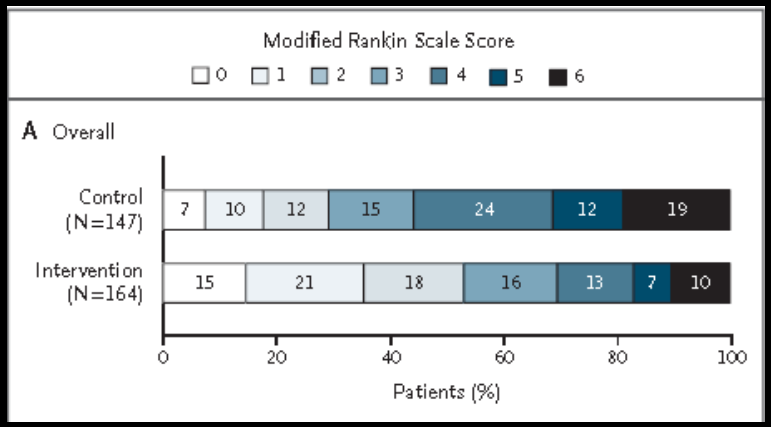
ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

T.T. Sajobi, and M.D. Hill for the ESCAPE Trial Investigators*

Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE)

- 316 patients (165 IAT, 150 control)
- CTA up to 12 hours from symptoms onset
- 84 min median time CT-Reperfusion
- Exclusion criteria
  - CT ASPECTS <6 (small core 6-10)
  - CTA poor collateral circulation
    - ✓ Moderate-to-good > filling of 50% or more of the MCA pial arterial circulation on CTA (multiphase CTA)



Multiphase CT Angiography: A New Tool for the Imaging Triage of Patients with Acute Ischemic Stroke[1]

Radiology
Bijoy K. Menon, MD
Christopher D. d'Esterre, PhD
Emmad M. Qazi, BSc
Mohammed Almekhlafi, MD[2]
Leszek Hahn, PhD
Andrew M. Demchuk, MD
Mayank Goyal, MD

Radiology: Volume 275: Number 2—May 2015

- 147 patients
- Single-phase CTA, multiphase CTA, and perfusion CT
- Interrater reliability (k = 0.81, *P* .001).
- Ability to predict clinical outcome modest (*C* statistic = 0.56, 0.63 for > 50% decrease in NIHSS over 24 hours)
- Better than models using single-phase CT angiography and perfusion CT

Good collaterals

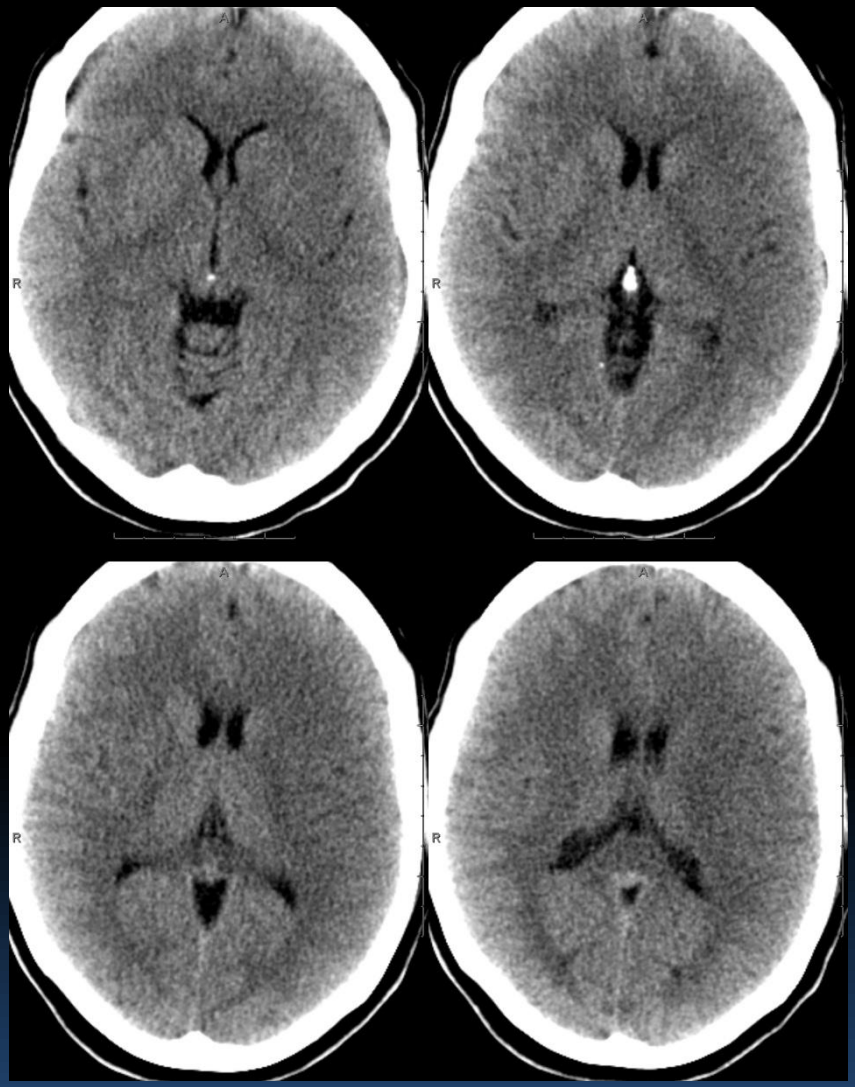
Intermediate collaterals

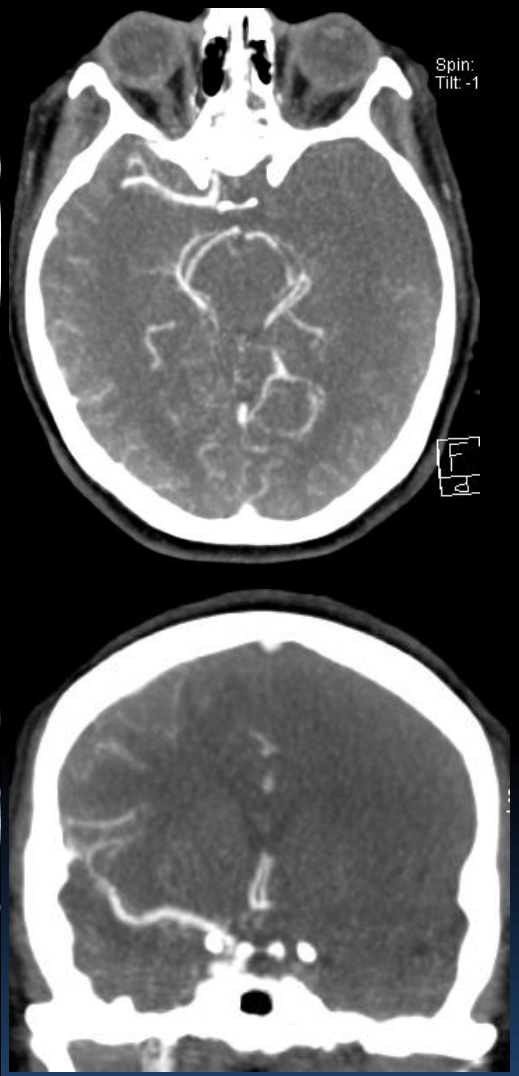
Poor collaterals

Category	Score	Description
Good	5	Compared to asymptomatic contralateral hemisphere, there is no delay and normal or increased prominence of peripheral vessels/ normal extent within the occluded arteries territory within the symptomatic hemisphere.
	4	Compared to asymptomatic contralateral hemisphere there is a delay of one phase in filling in of peripheral vessels but prominence and extent is the same.
Intermediate	3	Compared to asymptomatic contralateral hemisphere there is a delay of two phases in filling in of peripheral vessels but prominence and extent is the same or there is a one phase delay and decreased prominence (thinner vessels) / reduced number of vessels in some part of the territory occluded.
	2	Compared to asymptomatic contralateral hemisphere there is a delay of two phases in filling in of peripheral vessels and decreased prominence and extent or a one-phase delay and some regions with no vessels in some part of the territory occluded.
Poor	1	Compared to asymptomatic contralateral hemisphere there are just a few vessels visible in any phase within the occluded vascular territory.
	0	Compared to asymptomatic contralateral hemisphere there are no vessels visible in any phase within the occluded vascular territory.

F, 56 aa, occlusione T carotide, NIHSS 18

Circoli collaterali scarsi





Grado 0

PERFUSION CT

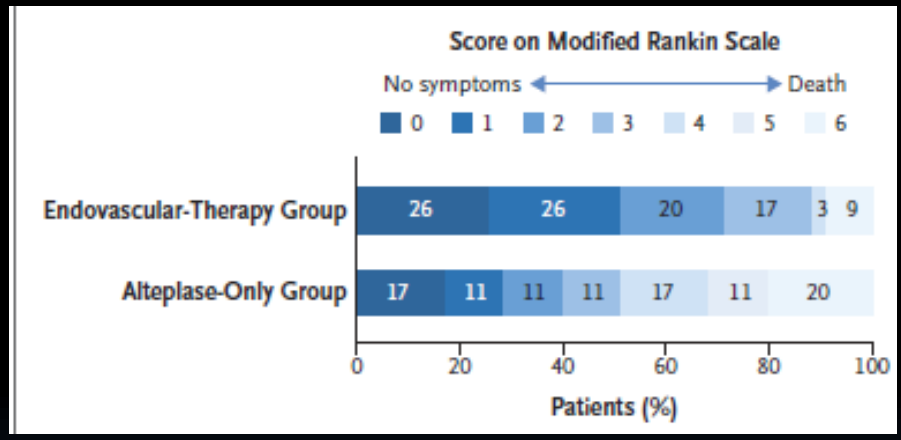
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

for the EXTEND-IA Investigators*

- Extending the Time for Thrombolysis in Emergency Neurological Deficits-Intra-Arterial (EXTEND-IA)
- 316 patients (165 IAT, 150 control)
- CT&CTP within 4.5 hrs
- Inclusion criteria
  - Target mismatch penumbral profile
    - fully automated, standardized volumetric processing (RAPID)
- Exclusion criteria
  - large ischemic cores on PCT
    > 70 ml (CBF<30%)



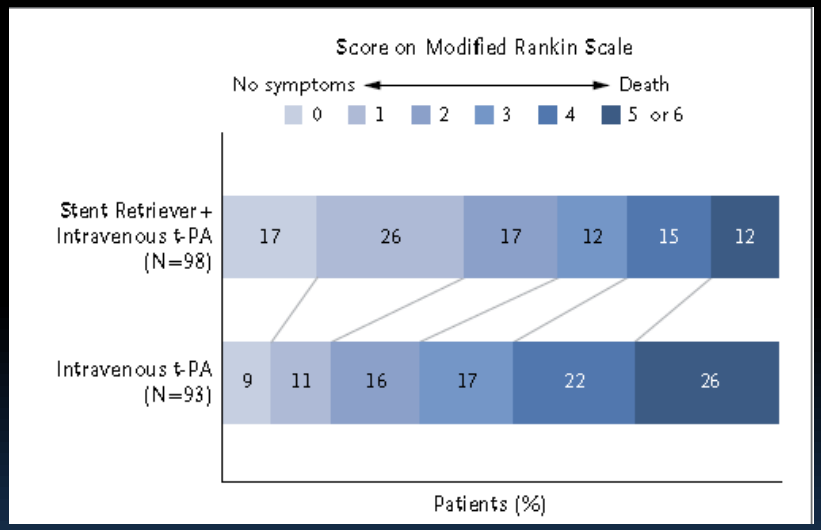
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

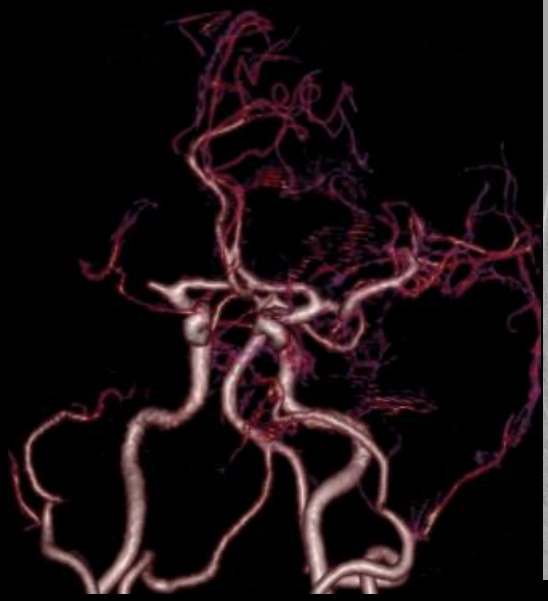
Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke

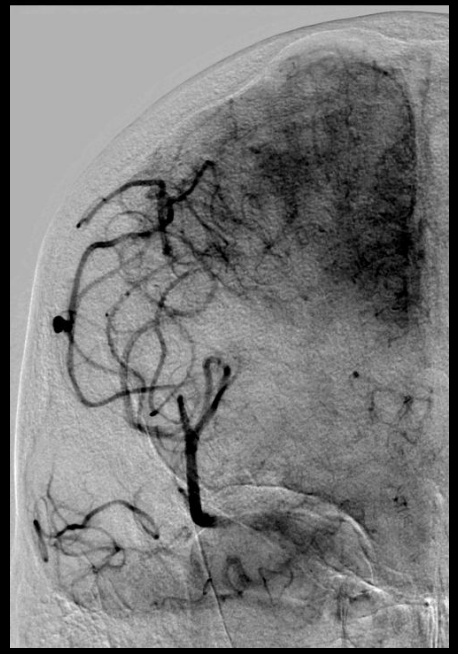
Oliver C. Singer, M.D., and Reza Jahan, M.D., for the SWIFT PRIME Investigators*

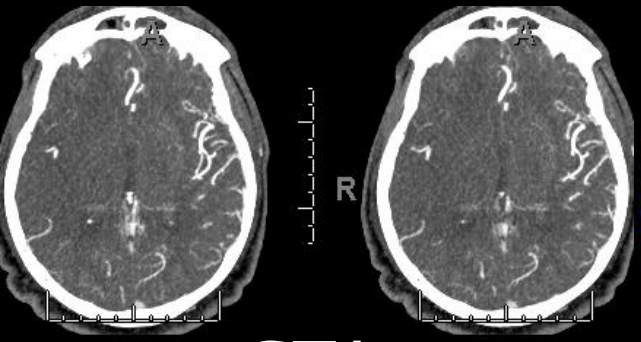
- Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME)
- Qualifying imaging at a study hospital;
- 196 patients (98, 98 control)
- Thrombectomy within 6 hours
- Inclusion criteria
  - Target mismatch penumbral profile
    - Operator independent image processing (RAPID)
- Exclusion of patients with large infarcts
  - large ischemic cores on PCT
    > 50 ml (CBF<30%)

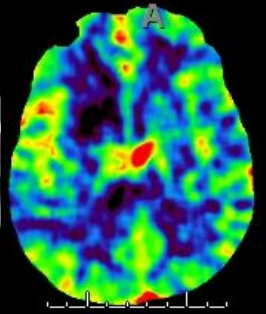


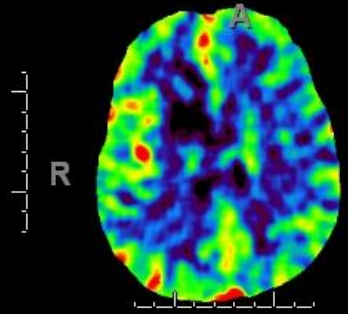
M, 70 aa, occlusione M1 dx, NIHSS 15

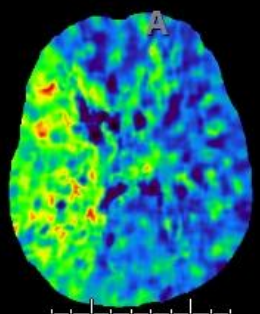


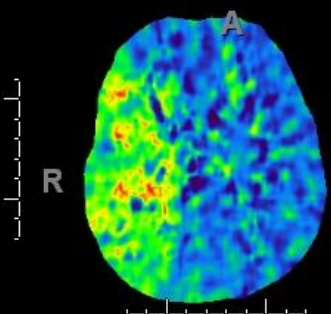








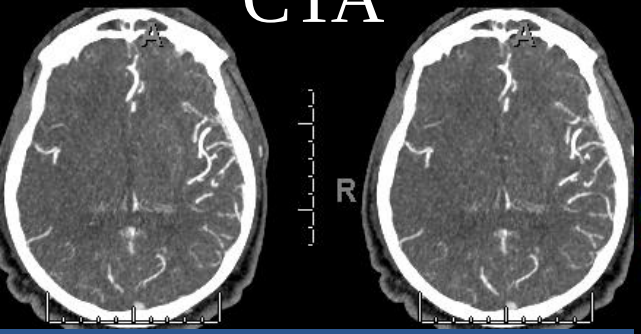


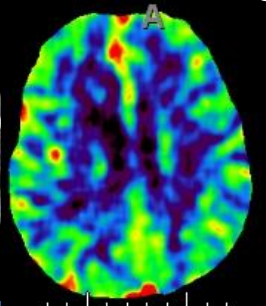


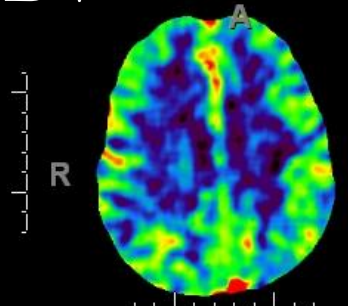
CTA

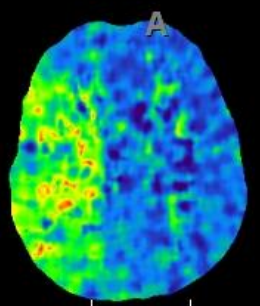
CBV

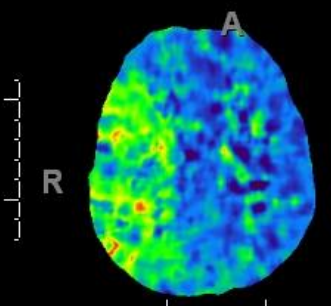
MTT







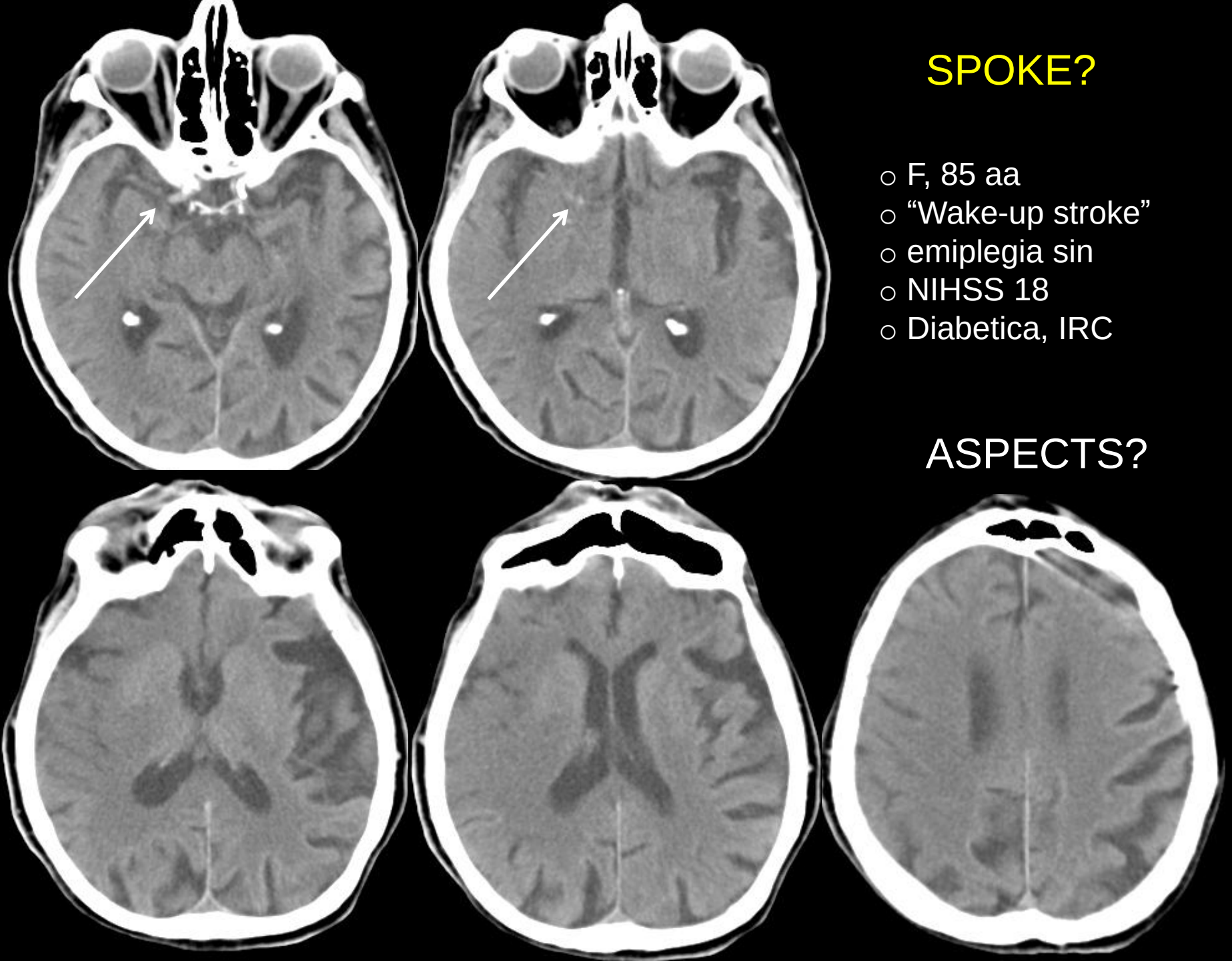




NEUROIMAGING
QUALE PROTOCOLLO?
…….senza ritardare l'inizio del trattamento….

NEUROIMAGING STROKE ISCHEMICO

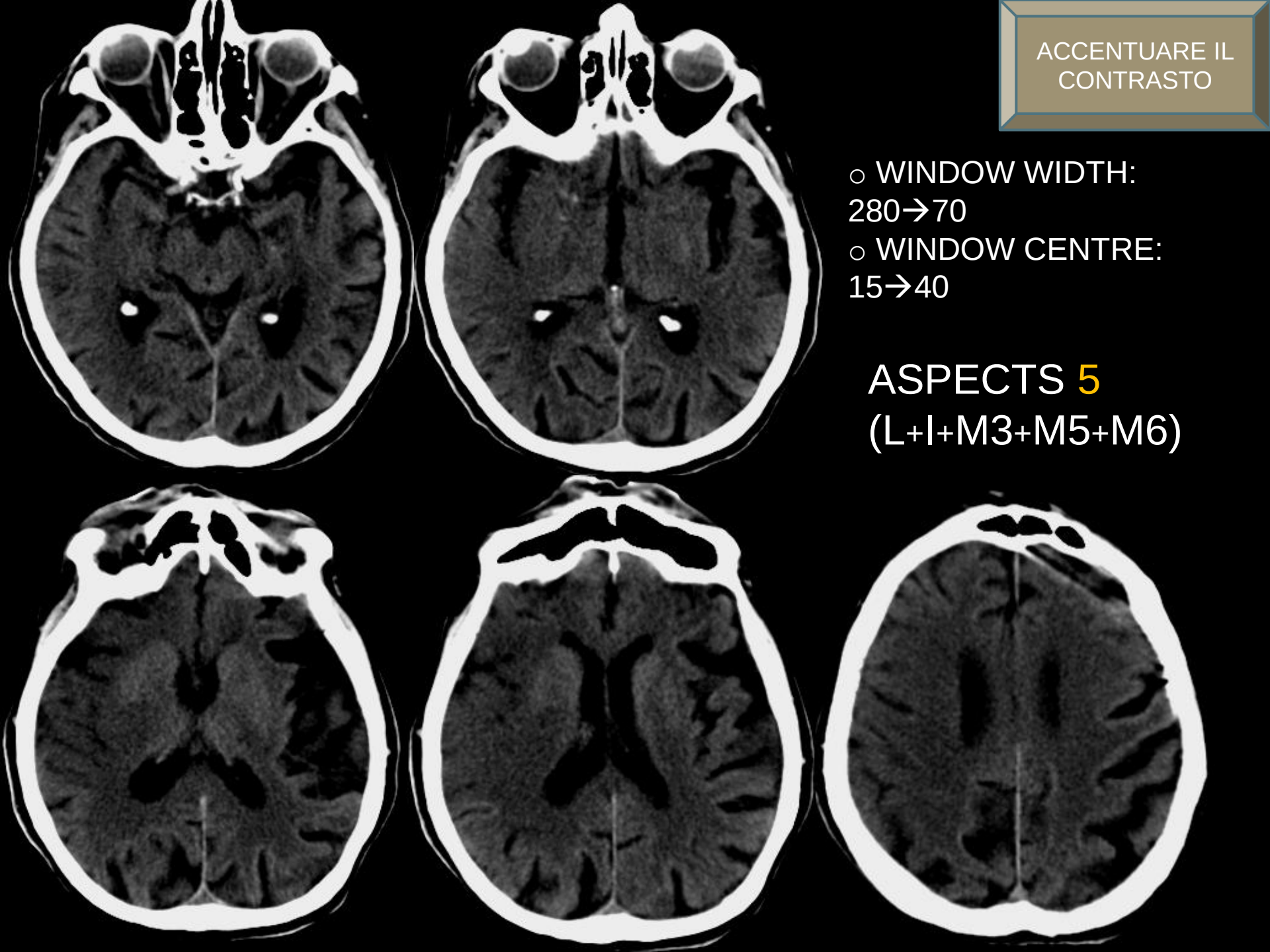
- “Baseline CT + NIHSS” non è più uno standard accettabile nei trials clinici
- La tecnologia attuale consente una rapida esecuzione di angio-TC (CTA) e TC-perfusione (CTP) con bassi livelli di irradiazione e quantità di mdc somministrata
- Trasferimento dei risultati dei trials alla pratica clinica



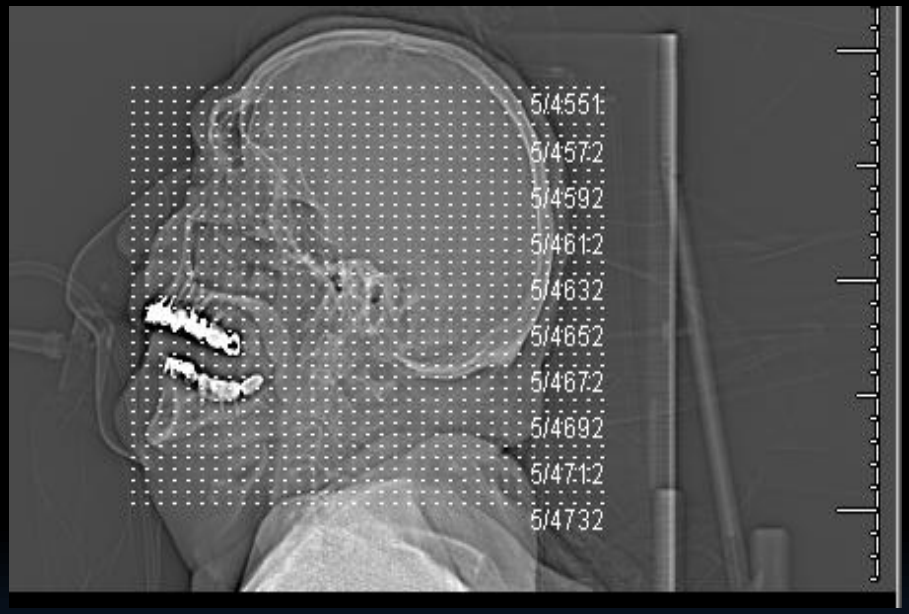
SPOKE?

- F, 85 aa
- “Wake-up stroke”
- emiplegia sin
- NIHSS 18
- Diabetica, IRC

ASPECTS?


ACCENTUARE IL CONTRASTO
WINDOW WIDTH: 280→70
WINDOW CENTRE: 15→40
ASPECTS 5
(L+I+M3+M5+M6)

INTEGRAZIONE ANGIOTC TSA - INTRACRANICA MULTIFASE - PERFUSIONE



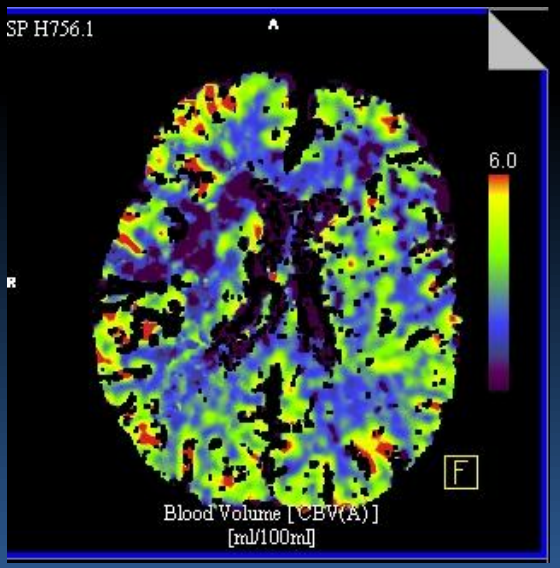
SOMMINISTRAZIONE DI UN UNICO BOLO DI MDC (50 ML)

- TC 128 strati
- protocollo angio-TC/perfusione con ampio range
- movimento continuo e bidirezionale del lettino durante l'acquisizione dei dati

Morhard et al. Advantages of extended brain perfusion computed tomography: 9.6 cm coverage with time resolved computed tomography-angiography in comparison to standard stroke-computed tomography. Invest Radiol 2010

ANGIOTC 4D

- TC encefalo senza mdc
- VOLUME 3D con mdc
- TC-perfusione
  - Risoluzione temporale ~ 1.8 s
- Angio-TC 4D "Time Resolved"
  - Campionamento sequenziale automatico dal volume dinamico di perfusione



SELEZIONE PAZIENTI

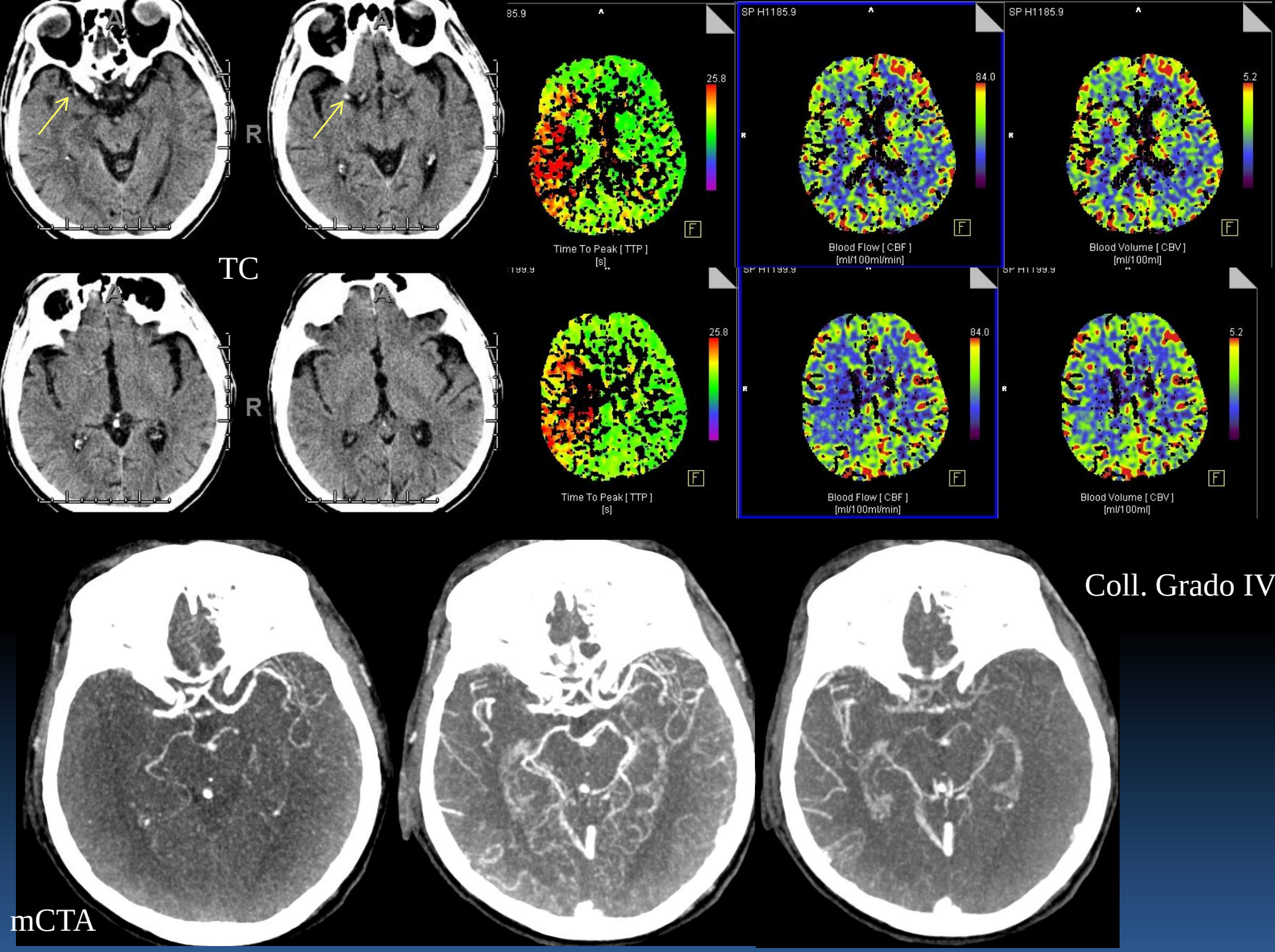
TROMBECTOMIA

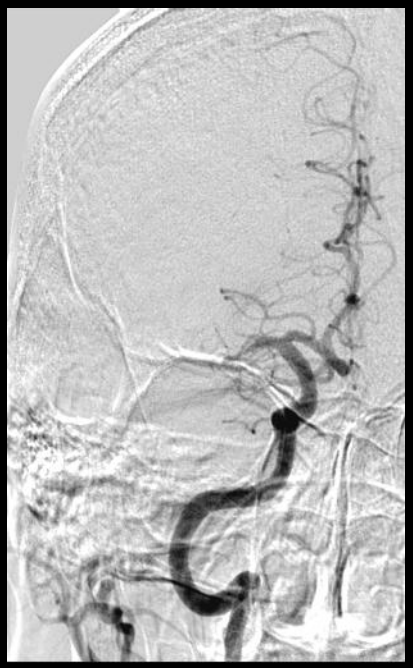
(HUB)

OCCLUSIONE PROSSIMALE (CTA)

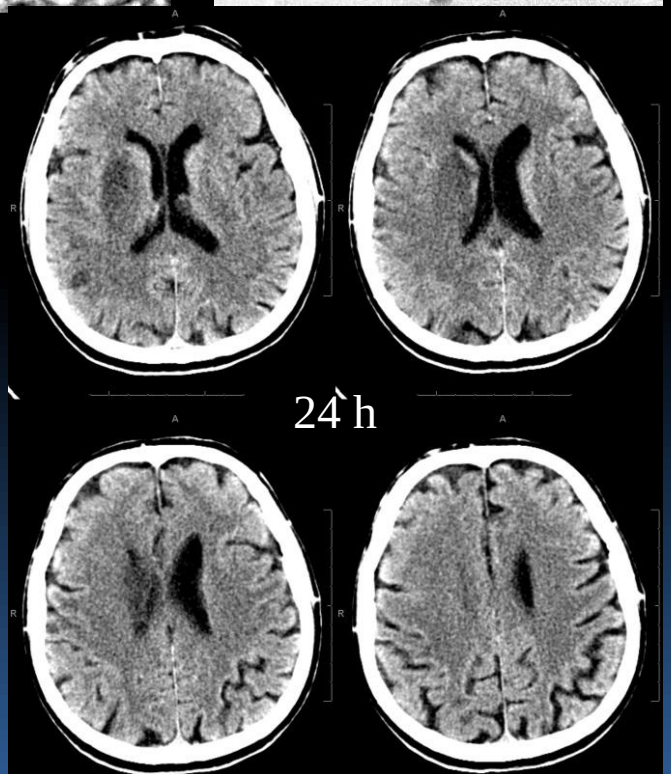
CIRCOLI COLLATERALI EFFICACI (mCTA)

PATTERN PENOMBRA FAVOREVOLE (PCT)


TC
Time To Peak [TTP]
[s]
Blood Flow [CBF]
[ml/100ml/min]
Blood Volume [CBV]
[ml/100ml]
25.8
84.0
5.2
Coll. Grado IV
mCTA





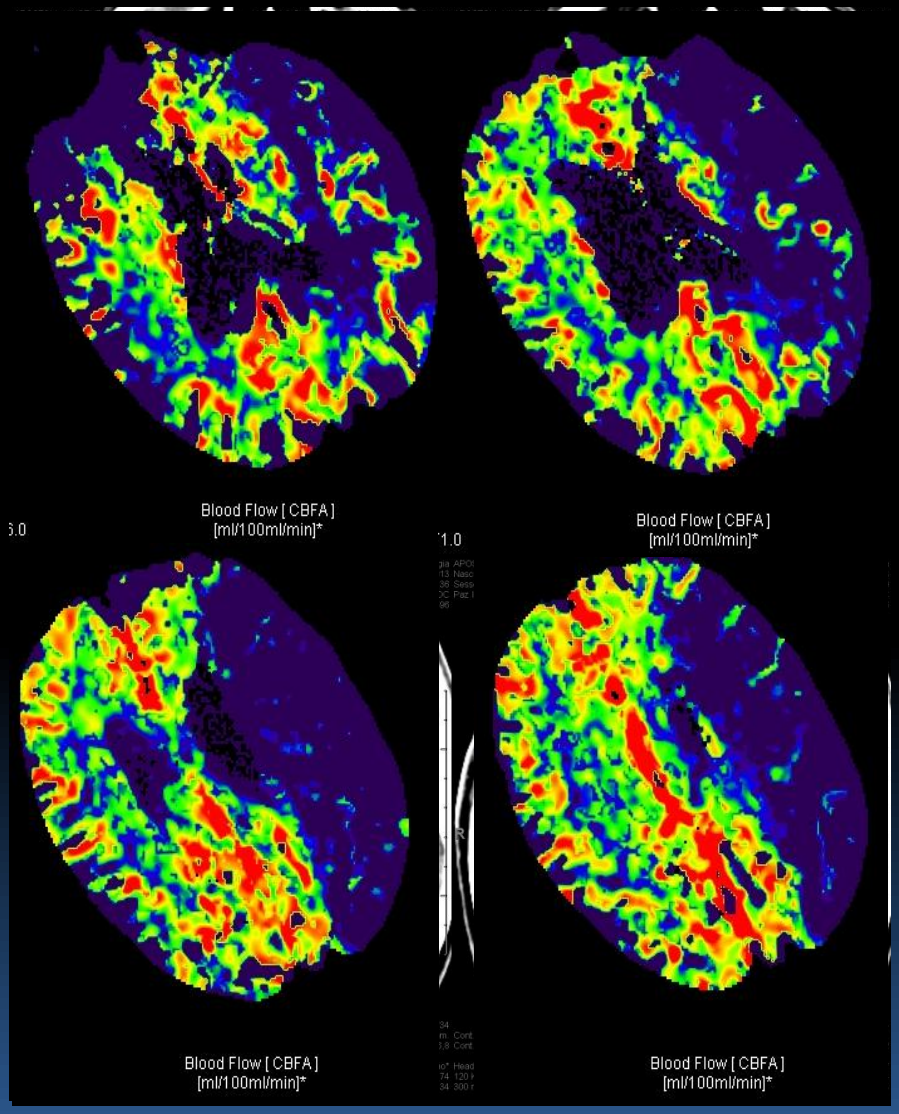

24 h

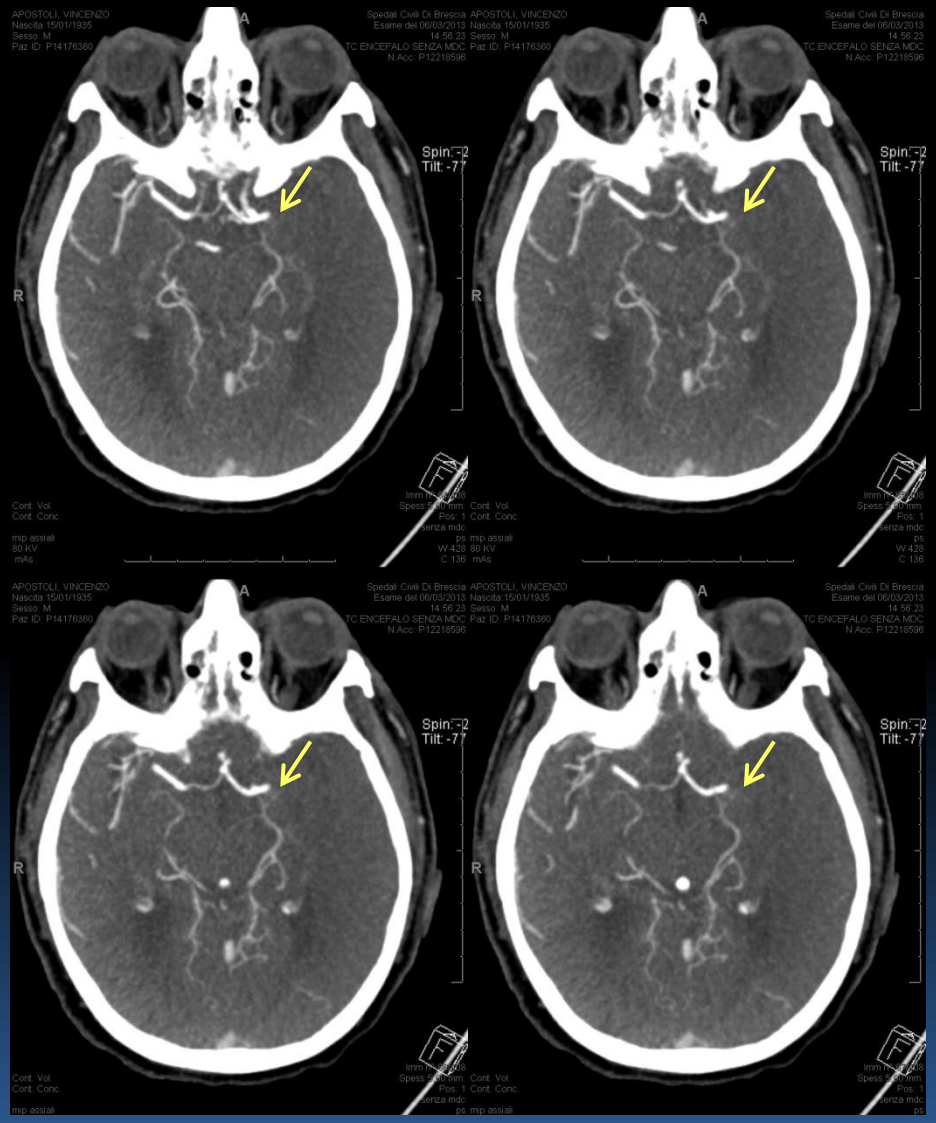
ESCLUSIONE PAZIENTI con

CORE ISCHEMICO AMPIO

CIRCOLI COLLATERALI SCARSI

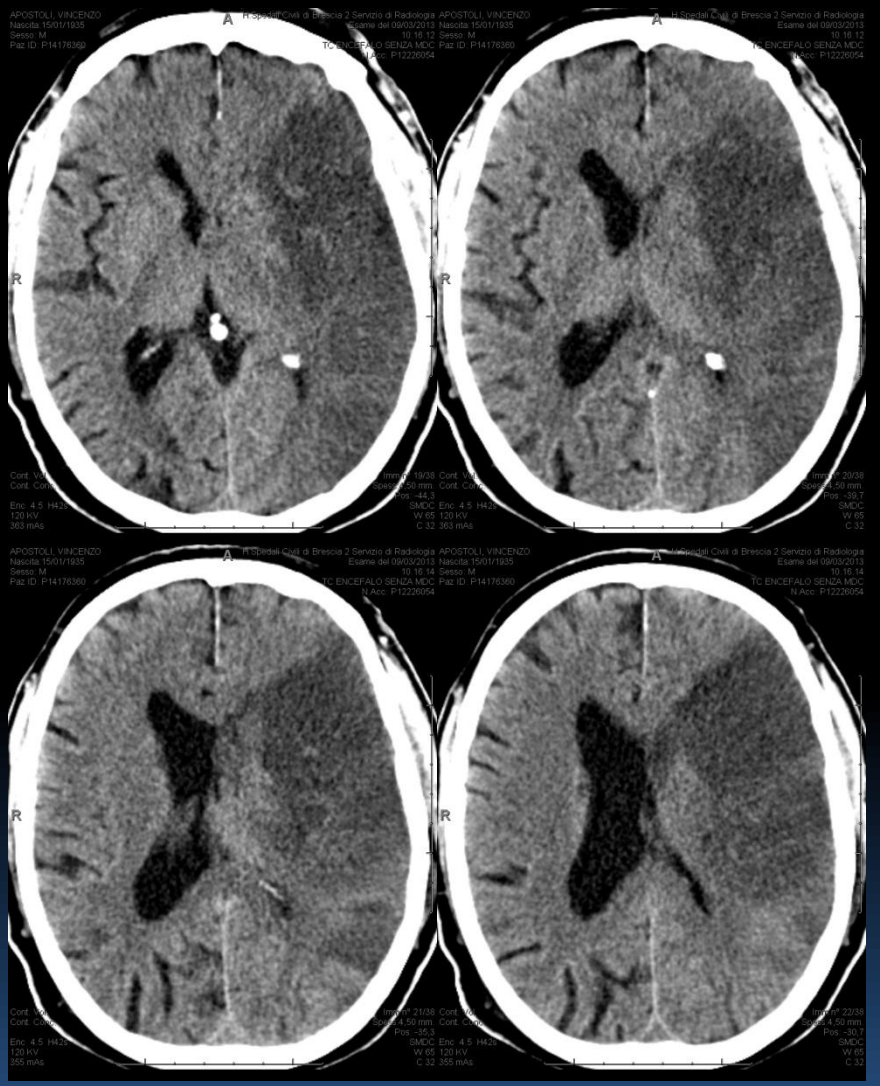
M, 77aa, emiplegia dx ed afasia, NIHSS 20
TC eseguita a 2h.30 dall'insorgenza dei sintomi





Trombolisi sistemica rt-PA iv > inizio angiografia dopo 45 min

Stent Solitaire in ACM sx



TAC a 72 h

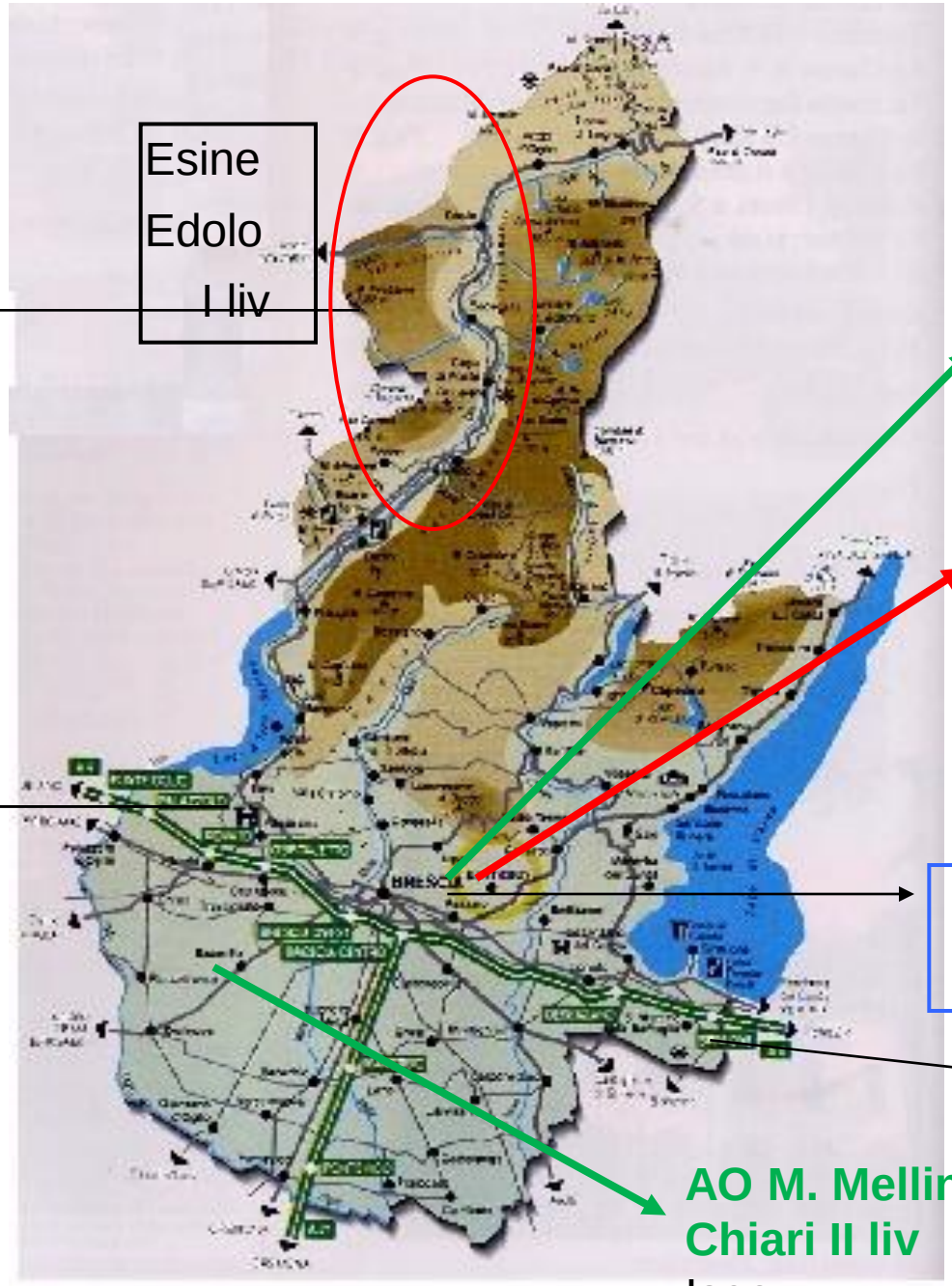
Modelli organizzativi

- Workflow efficiente
- Coordinamento
  - *Azienda Regionale Emergenza Urgenza*
  - *PS*
  - *Stroke Units*
  - *Neuroradiologia Interventistica*
- Imaging
  - Rapida identificazione occlusione acuta grossi vasi (LVO) e core ischemico ampio
- Inizio IV tPA e trasporto dei pazienti selezionati in sala angiografica per la trombectomia meccanica

Onset to arrival (Hub + Spoke)

- Educazione cittadini
- AREU
- Geografia
- Telemedicina

Golden Hour trombolisi venosa 60 min



Esine
Edolo
I liv

ASL Valle camonica

S.Anna II liv
Città di BS
Ome

AO Spedali Civili III liv

Neuroradiologia Interventistica H24/365 3 Interventisti

ASL Brescia

Poliambulanza III liv ?

AO Desenzano I liv

Popolazione residente 1.265.000

AO M. Mellini Chiari II liv
Iseo

Geographic Access to Acute Stroke Care in the United States

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Background and Purpose—Only 3% to 5% of patients with acute ischemic stroke receive intravenous recombinant tissue-type plasminogen activator (r-tPA) and <1% receive endovascular therapy. We describe access of the US population to all facilities that actually provide intravenous r-tPA or endovascular therapy for acute ischemic stroke.

Methods—We used US demographic data and intravenous r-tPA and endovascular therapy rates in the 2011 US Medicare Provider and Analysis Review data set. *International Classification of Diseases-Ninth Revision* codes 433.xx, 434.xx and 436 identified acute ischemic stroke cases. *International Classification of Diseases-Ninth Revision* code 99.10 defined intravenous r-tPA treatment and *International Classification of Diseases-Ninth Revision* code 39.74 defined endovascular therapy. We estimated ambulance response times using arc-Geographic Information System's network analyst and helicopter transport times using validated models. Population access to care was determined by summing the population contained within travel sheds that could reach capable hospitals within 60 and 120 minutes.

Results—Of 370351 acute ischemic stroke primary diagnosis discharges, 14926 (4%) received intravenous r-tPA and 1889 (0.5%) had endovascular therapy. By ground, 81% of the US population had access to intravenous-capable hospitals within 60 minutes and 56% had access to endovascular-capable hospitals. By air, 97% had access to intravenous-capable hospitals within 60 minutes and 85% had access to endovascular hospitals. Within 120 minutes, 99% of the population had access to both intravenous and endovascular hospitals.

Conclusions—More than half of the US population has geographic access to hospitals that actually deliver acute stroke care but treatment rates remain low. These data provide a national perspective on acute stroke care and should inform the planning and optimization of stroke systems in the United States. (***Stroke*. 2014;45:3019-3024.**)

TELESTROKE-BRESCIA : IL PROGETTO

Progetto presentato dalla ASL di Brescia ed autorizzato dalla Direzione Generale sanità della Regione Lombardia (Decreto Regionale n.° 9941 del 5/10/09.

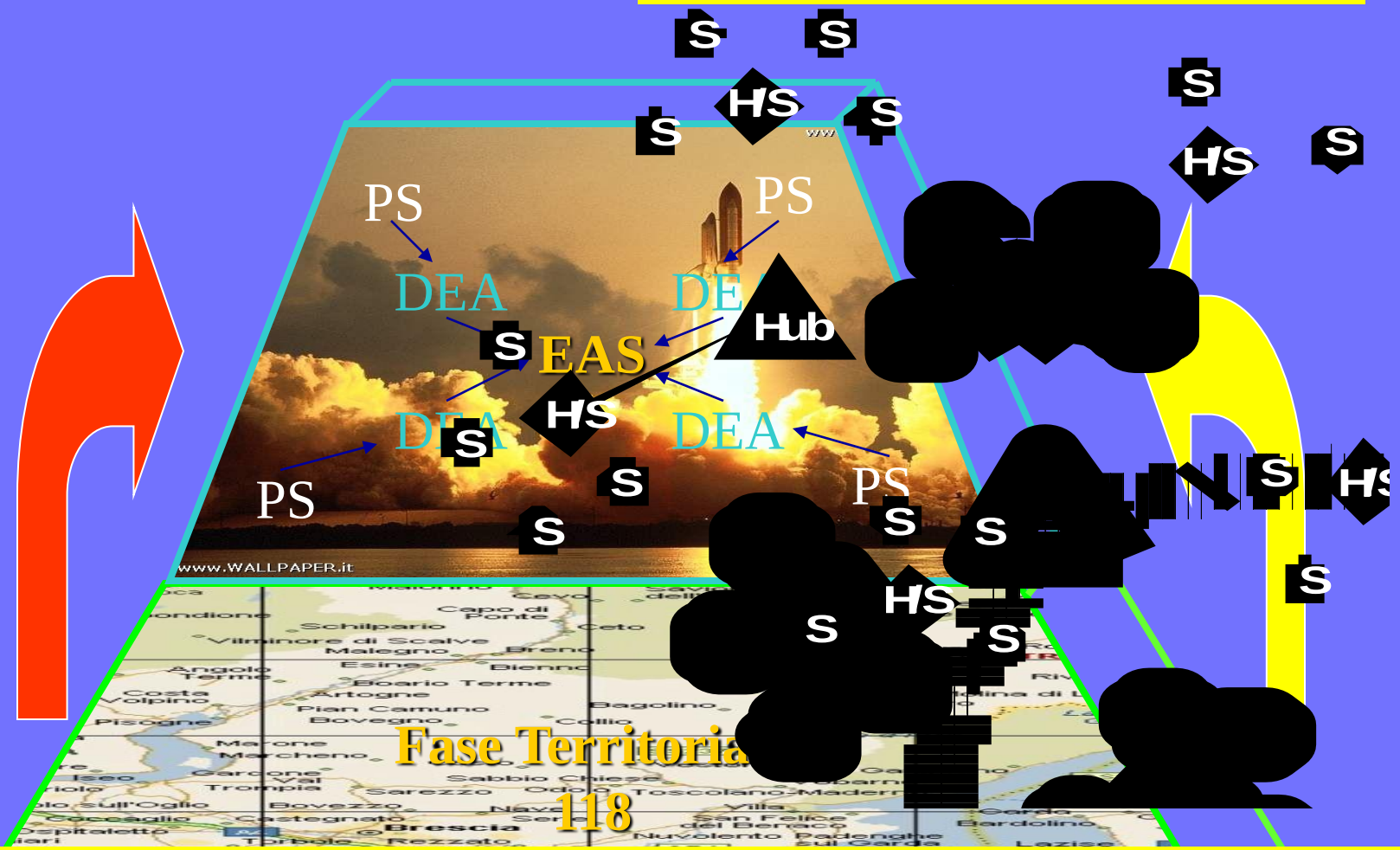
SPEDALI CIVILI BRESCIA
AZIENDA OSPEDALIERA
A.A.T. Brescia

AREU AZIENDA REGIONALE EMERGENZA URGENZA 118 RegioneLombardia

Regione Lombardia
ASL Brescia

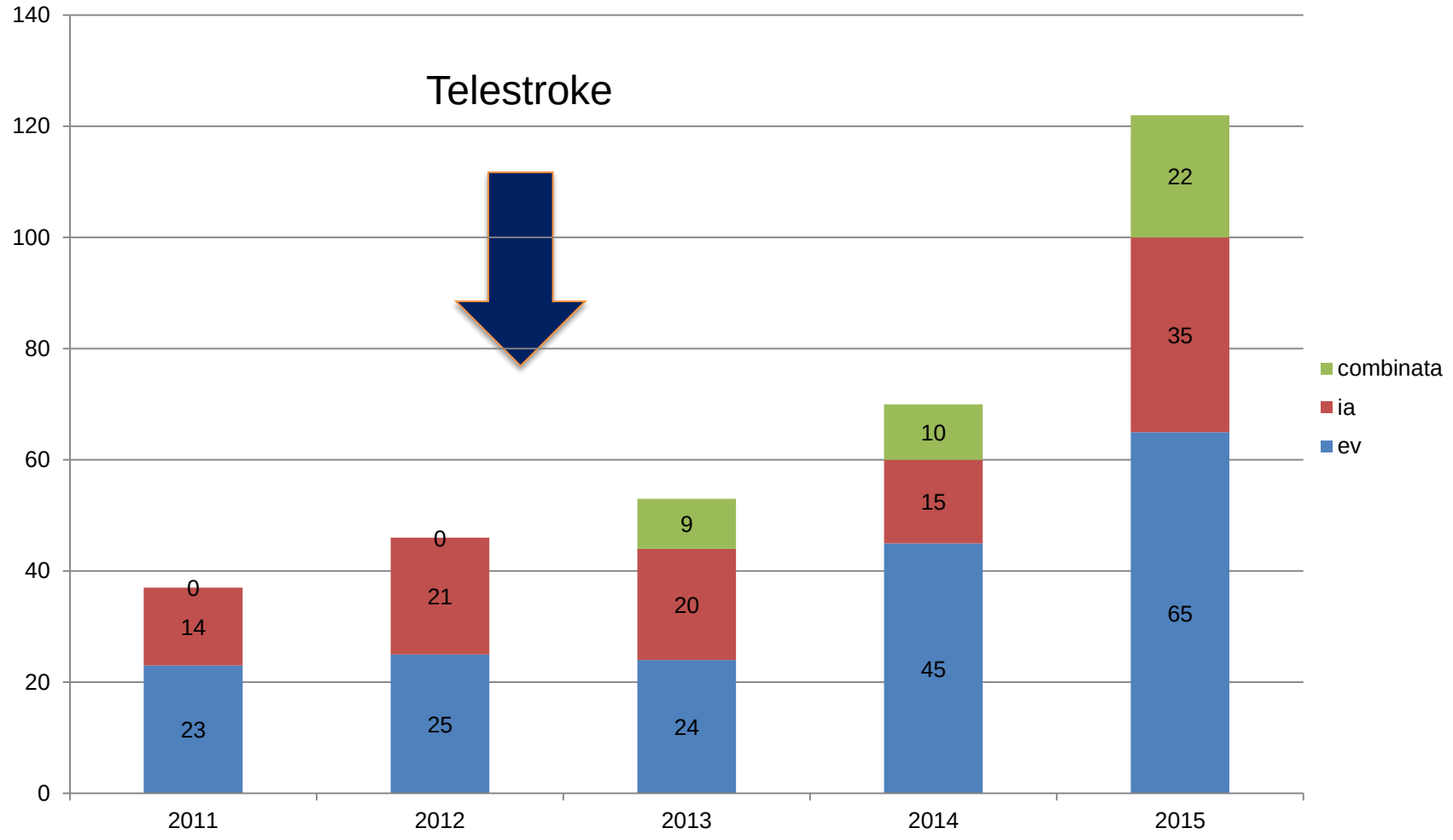
MODELLO

HUB & SPOKE



Il modello scelto è l' "hub and spoke“ che prevede l'esistenza di centri principali (hub) e centri periferici (spoke) che, attraverso reti organizzative, garantiscono a tutti i cittadini l'assistenza necessaria, indipendentemente dalla zona di residenza.

Trattamenti trombolitici dal 2011 Spedali Civili



Progetto telestroke

Dati di utilizzo da Novembre 2012 a Novembre 2014

Numero di consulenze neurologiche: 320 (200 ictus ischemici)

Pazienti con ictus ischemico centralizzati: 70 (35%)

Numero trombolisi effettuate: 12 (6%)

Numero potenziali trombolisi: 37 (18.5%)

Tempo medio di esecuzione consulenza: 17 min

TELESTROKE - BRESCIA
limiti

- Trombolisi IV non eseguita nei centri "spoke"
  - USA 1/6 trombolisi IV "drip&ship"
    Tekle WG et al. Stroke 2012
- Bassa percentuale di trasferimenti
- Bassa percentuale di trombolisi
  - Tempi di presentazione
  - Organizzazione percorso stroke nei centri "spoke"

Emergency transfer of acute stroke patients within the East Saxony telemedicine stroke network: a descriptive analysis

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Jessica Kepplinger[1]*, Imanuel Dzialowski[1], Kristian Barlinn[1], Volker Puetz[1], Claudia Wojciechowski[1], Hauke Schneider[1], Georg Gahn[2], Tobias Back[3], Gabriele Schackert[4], Heinz Reichmann[1], Ruediger von Kummer[5], and Ulf Bodechtel[1]

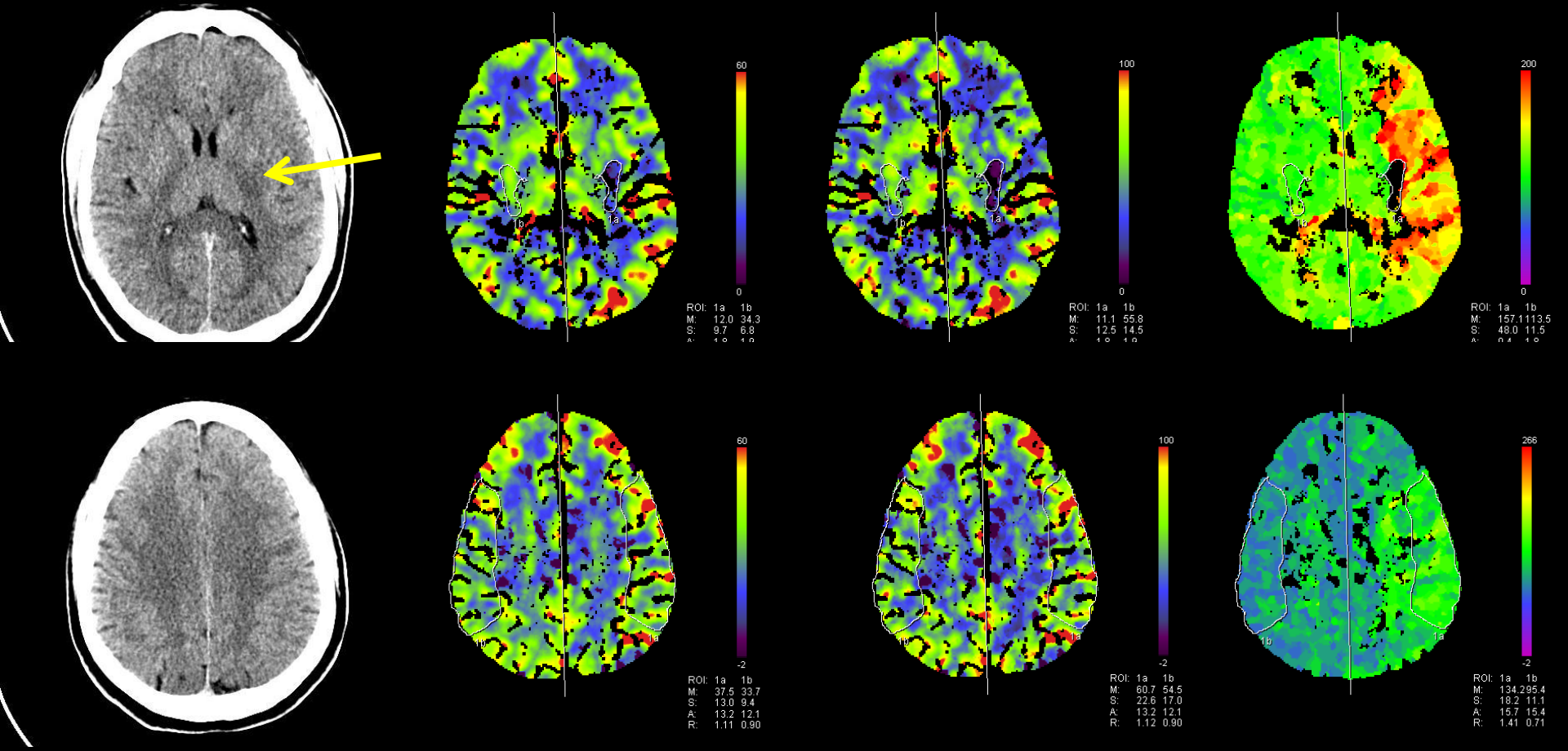
Table 1 Clinical characteristics and final diagnoses of all patients who were emergently transferred to the hub sites within the SOS-NET

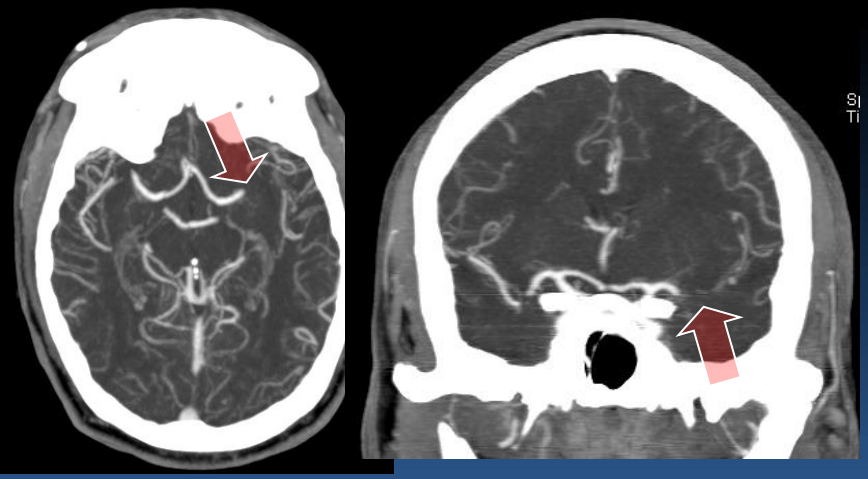
	Total	2009	2010	*P*
Spoke sites, *n*	–	9	13	
Teleconsultations, *n*	1413	550	863	
Emergent transfers, *n* (%)	339 (24)	139 (25)	200 (23)	ns
Clinical characteristics				
Age, years, mean ± SD	64 ± 14	63·8 ± 14·4	64 ± 14	ns
Gender, male, *n* (%)	182 (54)	76 (55)	106 (53)	ns
NIHSS score, median (range)	5 (0–40)	6 (0–32)	5 (0–40)	ns
NIHSS score, median (range)*	6 (0–40)	6·5 (0–32)	5 (0–40)	ns
Stroke diagnosis, *n* (%)	271 (80)	110 (79)	161 (81)	ns
Ischemic stroke	114 (34)	47 (34)	67 (34)	
TIA	8 (2)	5 (4)	3 (2)	
Intracranial haemorrhage	149 (44)	58 (42)	91 (46)	
Intracerebral	90 (27)	37 (27)	53 (27)	
Sub-arachnoidal	31 (9)	9 (6)	22 (11)	
Sub-dural	27 (8)	12 (9)	15 (8)	
Epidural spinal	1 (0·3)		1 (0·5)	
Drip and ship, *n* (%)	40 (35)	12 (26)	28 (42)	0·07
Nonstroke diagnosis, *n* (%)	68 (20)	29 (21)	39 (20)	ns
Brain tumour	15 (4)	9 (7)	6 (3)	
Seizure	17 (5)	5 (4)	12 (6)	
Other	36 (11)	15 (11)	21 (11)	

*NIHSS of confirmed strokes. NIHSS, National Institutes of Health Stroke Scale; ns, nonsignificant; SD, standard deviation; SOS-NET, Stroke East Saxony Network; TIA, transient ischemic attack.

Cosa potrebbe cambiare a breve…….

- Ospedali satellite
- Telemedicina
- TAC
- Angio-TAC
  - Standardizzazione-ottimizzazione
  - Attività formativa
- Interpretazione TAC + Angio-TAC centro HUB





M, 44 aa

08.30: insorgenza acuta emiparesi dx e disartria

10.30: TC ospedale provincia

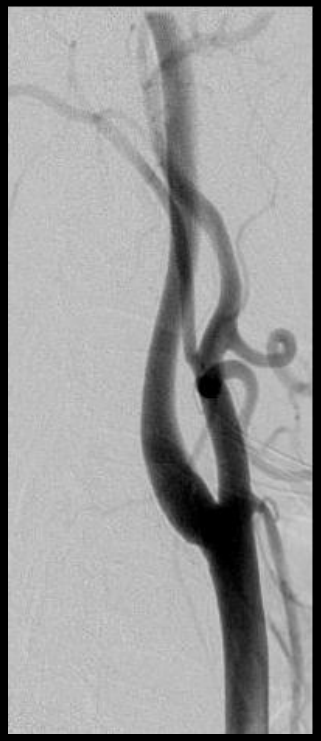
11.00 Teleradiologia

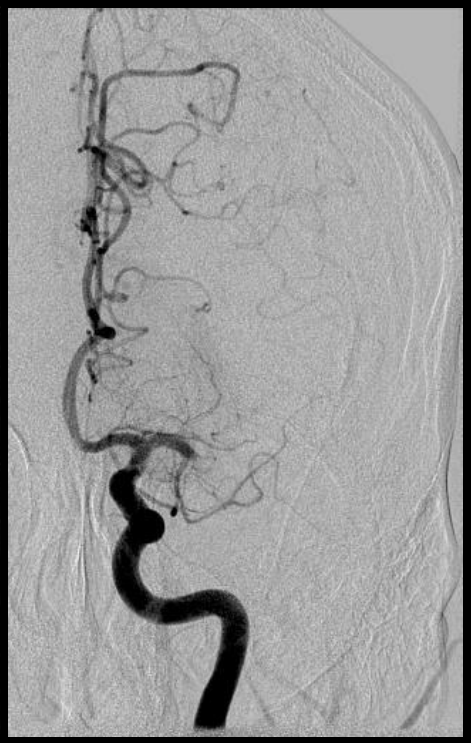
Ore 12.00: Stroke Unit Spedali Civili

NIHSS 10

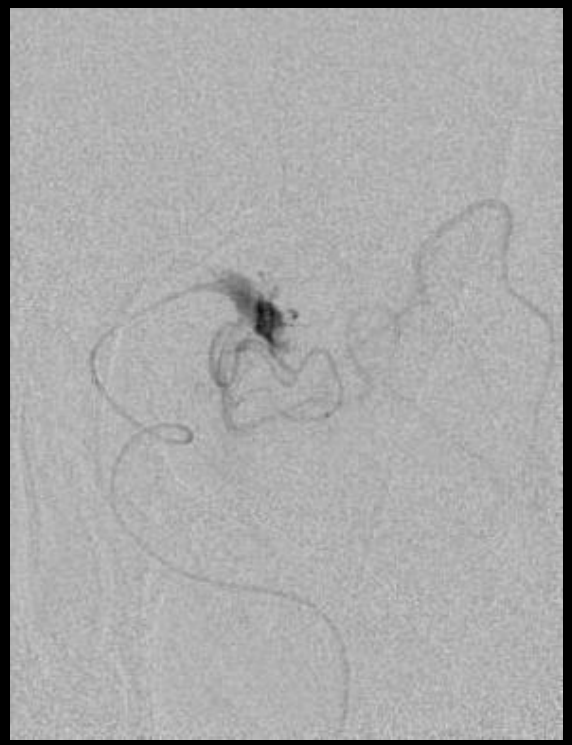
Ore 12:30: IV rtPA + Angio-TC + Perfusione

ANGIOGRAFIA





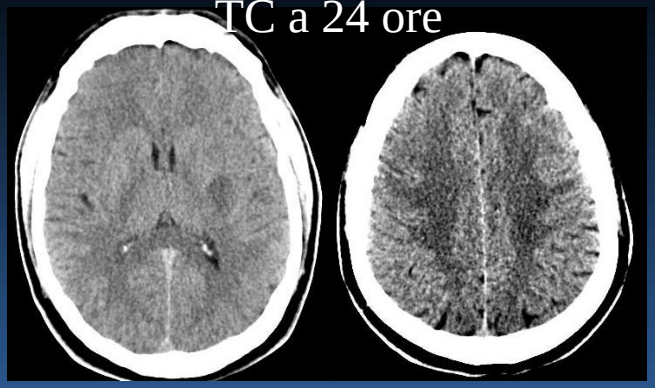
12.50



Tromboaspirazione

14.00

TC a 24 ore



- Dimissione domicilio dopo 9 gg (NIHSS 2)
- mRS 1 a 3 mesi

Mobile Stroke Treatment Units

- We cannot expect the patients disease biology to match our systems. Because the time window to treatment with stroke is so short, we must match our systems to biology *(Klaus Fassbender. MD, MSU pioneer)*

Original Investigation

Effects of Golden Hour Thrombolysis

A Prehospital Acute Neurological Treatment and Optimization of Medical Care in Stroke (PHANTOM-S) Substudy

Martin Ebinger, MD; Alexander Kunz, MD; Matthias Wendt, MD; Michal Rozanski, MD; Benjamin Winter, MD; Carolin Waldschmidt, MD; Joachim Weber, MD; Kersten Villringer, MD; Jochen B. Fiebach, MD; Heinrich J. Audebert, MD

JAMA Neurol. 2015;72(1):25-30.

- Stroke emergency mobile unit (STEMO)
- 6182 consecutive patients with a stroke dispatch
- 32.6% thrombolysis rates STEMO
- 22.0% thrombolysis rates conventional care ($P < .001$)
- The proportion of golden hour thrombolysis was 6-fold higher after STEMO deployment
- Patients who received golden hour thrombolysis had no higher risks for 7- or 90-day mortality and were more likely to be discharged home (adjusted odds ratio, 1.93 [95%CI, 1.09-3.41]; $P = .02$).

Door to Needle (HUB)

- Codice Stroke
- Comunicazione intraospedaliera
- Rapida esecuzione ed interpretazione TC
  - Stroke mimics
- r-tPA in sala TAC

Picture to Puncture (HUB)

- Passaggio cruciale
- Angio-TAC TSA-intracranica
- Sala angio in stand-by
- Elevati volumi di attività

TRIAL	Protocol	Onset to groin	Imaging to groin
MR CLEAN	6 hrs	260 min	?
ESCAPE	12 hrs	185 min	51
EXTEND IA	6 hrs	210 min	93
SWIFT PRIME	6 hrs	184 min	58

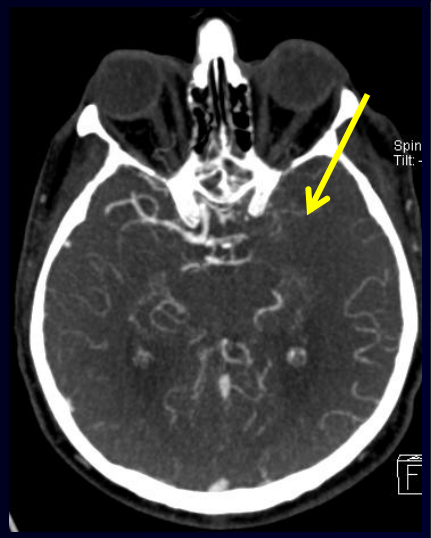
Puncture to Recan (HUB)

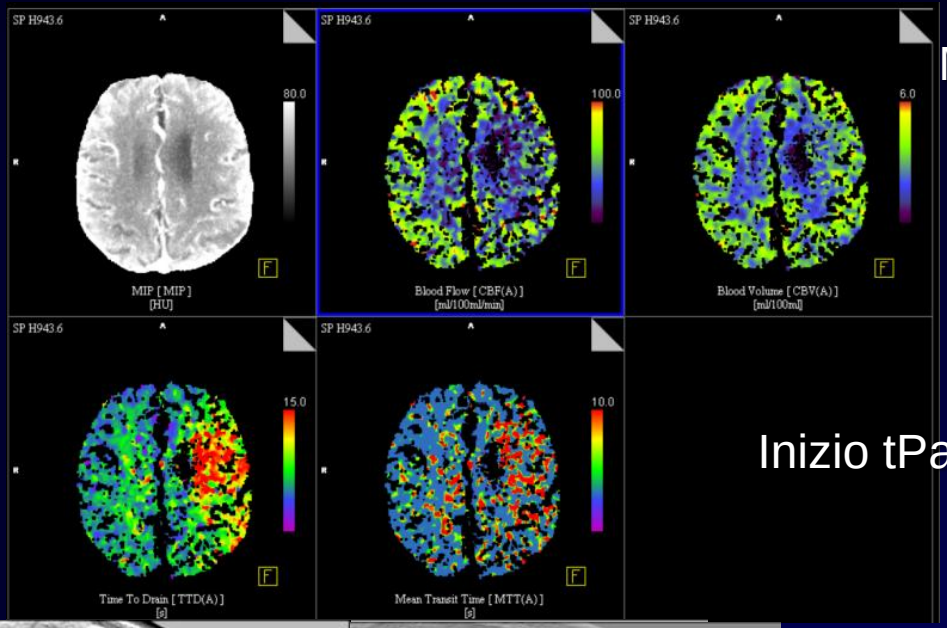
- Volume di attività = Esperienza
- Esperienza=Capacità di scelta
- Capacità di scelta=Outcome

TRIAL	Protocol	Onset to groin	Groin to Recan
MR CLEAN	6 hrs	260 min	?
ESCAPE	12 hrs	185 min	?
EXTEND IA	6 hrs	210 min	43 min
SWIFT PRIME	6 hrs	184 min	28 min (stent depl)

HUB (Brescia)

- Serie consecutiva 41 pazienti
- Trombolisi IV + trombectomia (trombo-aspirazione)
- Trombolisi IV eseguita direttamente alla TAC
  - Trasferimento in sala angiografica se grosso vaso occluso
- No anestesia generale (quando possibile)

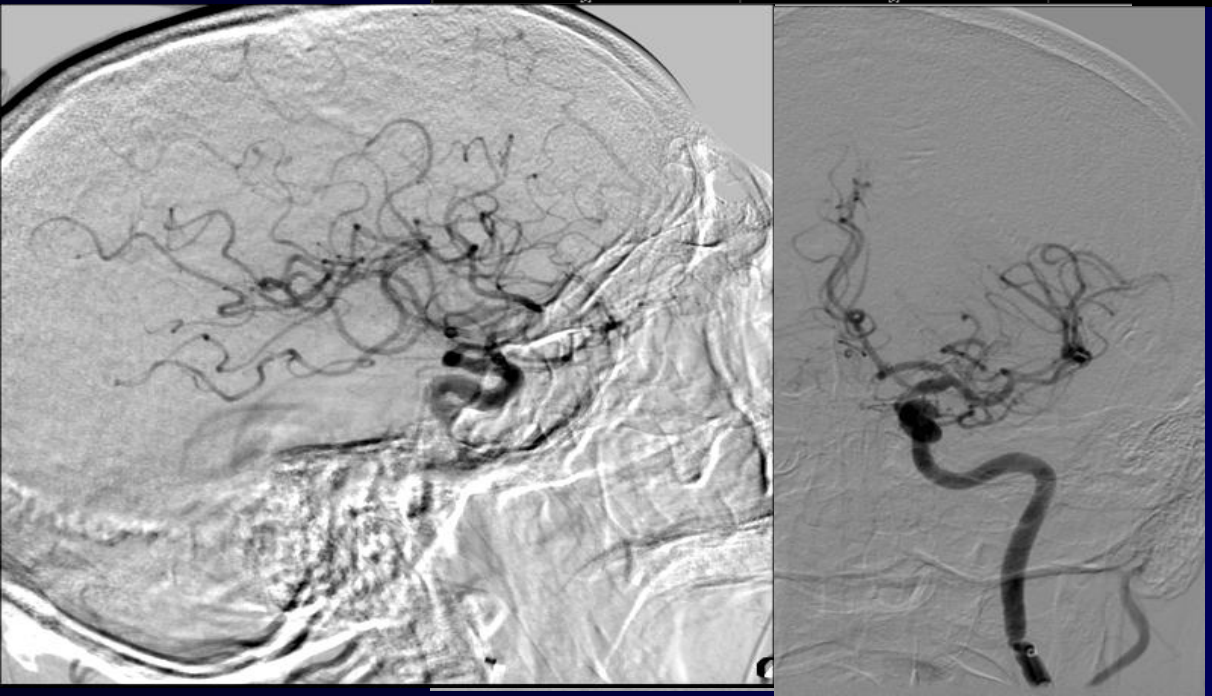




M,62 2:30 h, NIHSS 23

Tot 12 min

Inizio tPa IV e trasporto in sala angiografica



No anestesia generale
Catetere guida con pallone per blocco di flusso
Stentriever 1 passaggio

Puntura a. femorale >
Ricanalizzazione 28 min

NIHSS 8 a 24h

HUB (Brescia)

Stroke onset-Ricanalizzazione: 232.8 ± 52.2 min

Puntura Femorale-Ricanalizzazione: 47min

TICI≥ 2B = 29/35 (82.8%)

- NIHSS=18.6 ± 4.1
- MRS 3 mesi (≤2): 26/35 (74.2%)

Futuro del progetto telestroke - Brescia

Inizio trombolisi in periferia (previo consenso)

Implementazione Angio-TC nei presidi collegati

Trasferimento pazienti candidati a terapia endovascolare

Riduzione tempi trasporti secondari

Formazione continua del personale

Potenziamento rete telestroke