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UNIVERSITAT DE BARCELON

Facultat de Medicina

REVASCULARIZATION OPTIONS IN ISCHEMIC STROKE

J. Blasco, MD
NeuroInterventional Radiology Dpt
Hospital Clinic – Barcelona
Catalonia - Spain

SUMMARY

1. General overview
2. Mechanical Thrombectomy evolution in Europe
3. Our experience with Trevo
4. Latest update

GENERAL OVERVIEW

GENERAL OVERVIEW

Stroke is the leading combined cause of death and disability worldwide

More than 15 million people suffer a stroke each year.

85% are ischemic

Worst outcomes: Large IC vessel occlusion

High severity stroke

Age

Approved pharmacological treatments have limited efficacy in these populations

GENERAL OVERVIEW

- IV rt-PA has been shown to improve 3-month outcome if administered within 3 – 4.5 hour window

- IV rt-PA has limited efficacy in the setting of large artery occlusions

- Percentage of AIS treated with IV thrombolysis is less than 5% due to the narrow time window

- Effort is being done to determine which patients beyond this time window would benefit from reperfusion therapies

GENERAL OVERVIEW

Potential Advantages of Mechanical Thrombectomy Devices

Avoid high doses of fibrinolytic drugs (Less hemorrhagic events? Especially if we go beyond 3 hour window)

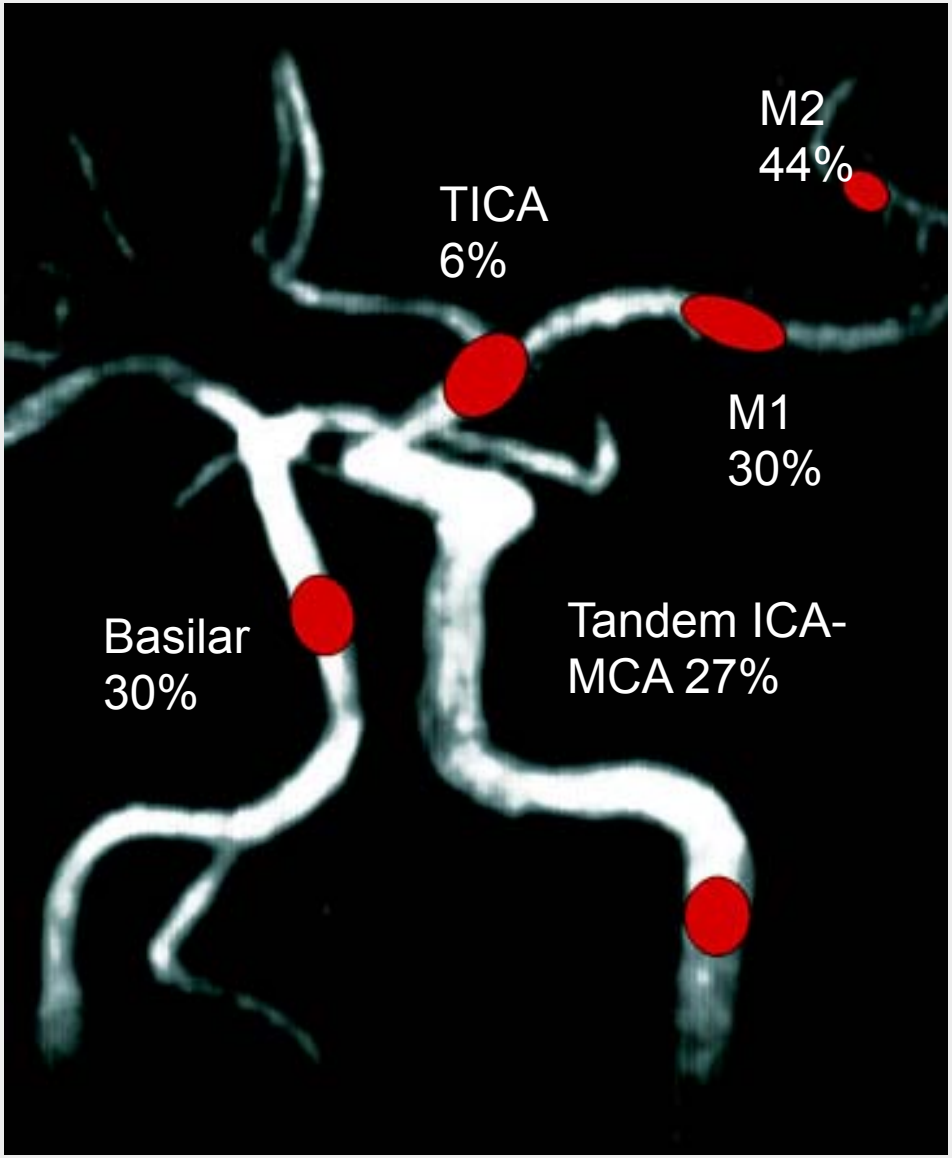
Longer time window

Faster recanalization

More effective in large vessel occlusions

Only a minor percentage of pts who receive rt-PA will achieve total recanalization

GENERAL OVERVIEW



Alexandrov AV. Current and future recanalization strategies for acute ischemic stroke. J Intern Med. 2010 Feb;267(2):209-19.

GENERAL OVERVIEW

Potential Drawbacks of Mechanical Thrombectomy Devices

Higher risk of vessel damage (?)

Clot fragmentation into unaffected territories

Limited availability

GENERAL OVERVIEW - CONCLUSIONS

Moving towards using mechanical thrombectomy as front-line therapy in selected cases associated with IV rt-PA

These devices are able to achieve higher recanalization rates

The on-going registries and trials should help us to clarify their role in AIS and to determine which patients would benefit more in terms of better functional outcome

MECHANICAL THROMBECTOMY EVOLUTION (IN EUROPE)

MECHANICAL THROMBECTOMY

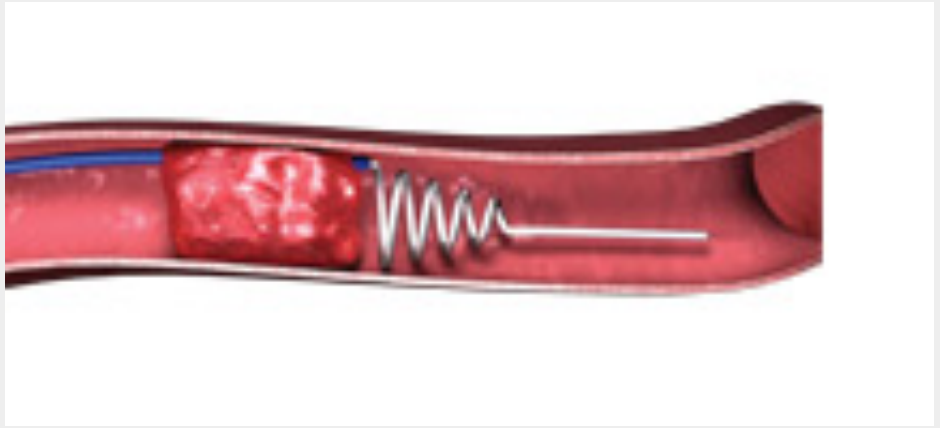
Microcatheter + Microguidewire fragmentation

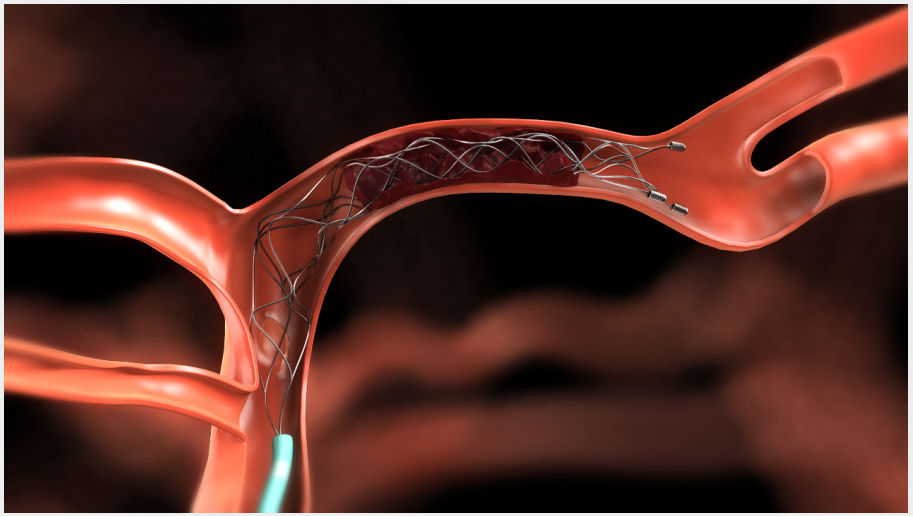
Angioplasty +/- Stenting

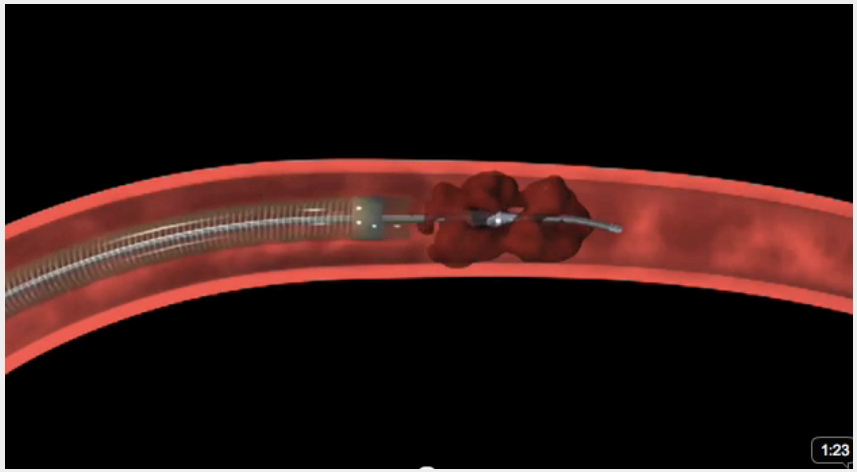
Mechanical Thrombectomy: Suction Devices

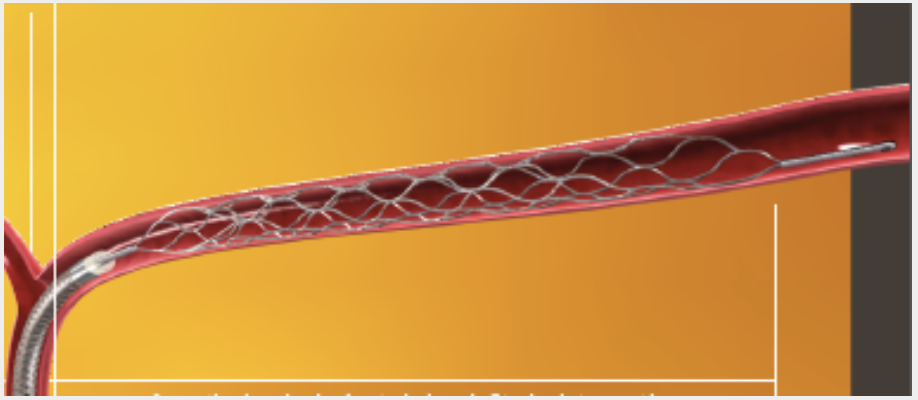
Mechanical Thrombectomy: Retrieval Devices

MECHANICAL THROMBECTOMY









MECHANICAL THROMBECTOMY

Suction Devices – Penumbra Stroke System

- **Main keypoints**

- Acts on the proximal part of the occluded artery
- Two mechanisms: aspiration + stent like device
- Both devices got CE approval but only the aspiration one received the FDA approval
- Penumbra Pivotal Stroke Trial (2009) showed good recanalization rates but very poor good clinical outcomes

MECHANICAL THROMBECTOMY

Suction Devices

Penumbra Pivotal Trial – 2009

Prospective multicenter , single arm trial

125 Patients

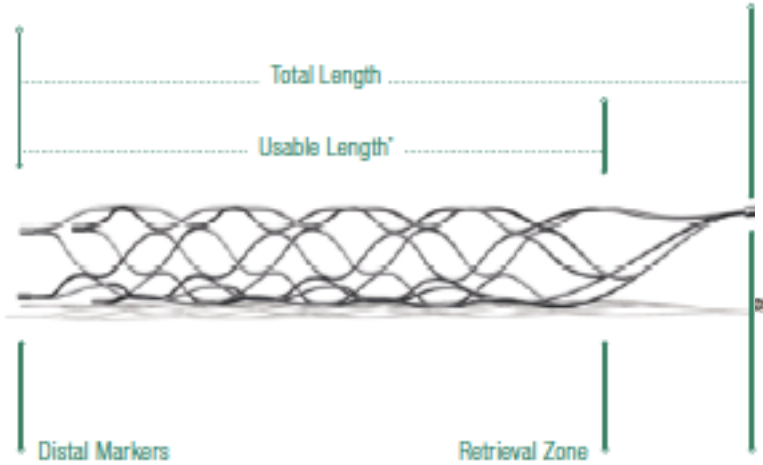
Baseline NIHSS	18
Revasc TICI 2-3	82 %
Sympt ICH	11 %
90 day mortality	33 %
90 day mRS<=2	**25 %**

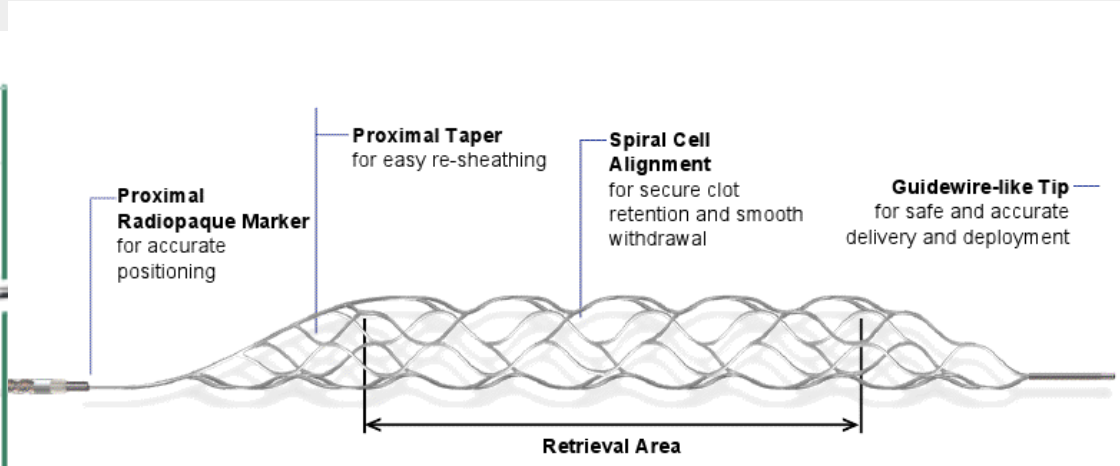
MECHANICAL THROMBECTOMY

Endovascular Retrieval Devices: Stentrievers

Solitaire™ FR
Revascularization
Device

TREVO™



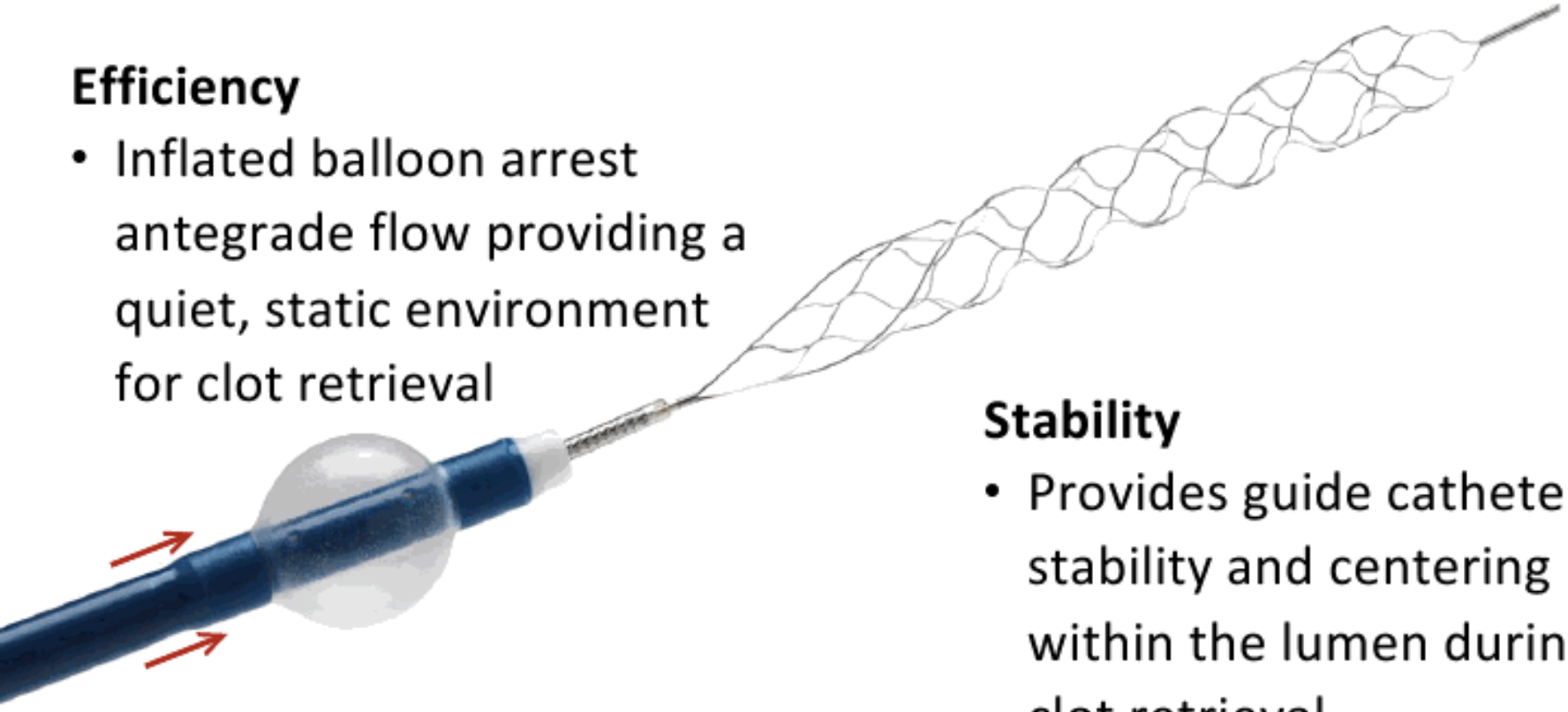


FLOW ARREST

The Use of Balloon Guide Catheters with Stentrievers

Efficiency

- Inflated balloon arrest antegrade flow providing a quiet, static environment for clot retrieval



Stability

- Provides guide catheter stability and centering within the lumen during clot retrieval

OUR EXPERIENCE WITH TREVO

PROTOCOL

Inclusion Criteria

AIS with angiographic confirmation of persistent large vessel occlusion	
Age	> 18
Time Window	8 h.
Bridging IV tPA	54%
No General Anesthesia performed unless severe instability	

PROTOCOL II

Exclusion Criteria

Basal CT or MR with evidence of hemorrhage or significant mass effect

For anterior circulation: Hypodensity on CT>1/3 of the MCA territory, significant ischemic volume on Perfusion CT or in MR diffusion sequences

For posterior circulation: significant ischemic volume on Perfusion CT or in MR diffusion sequences

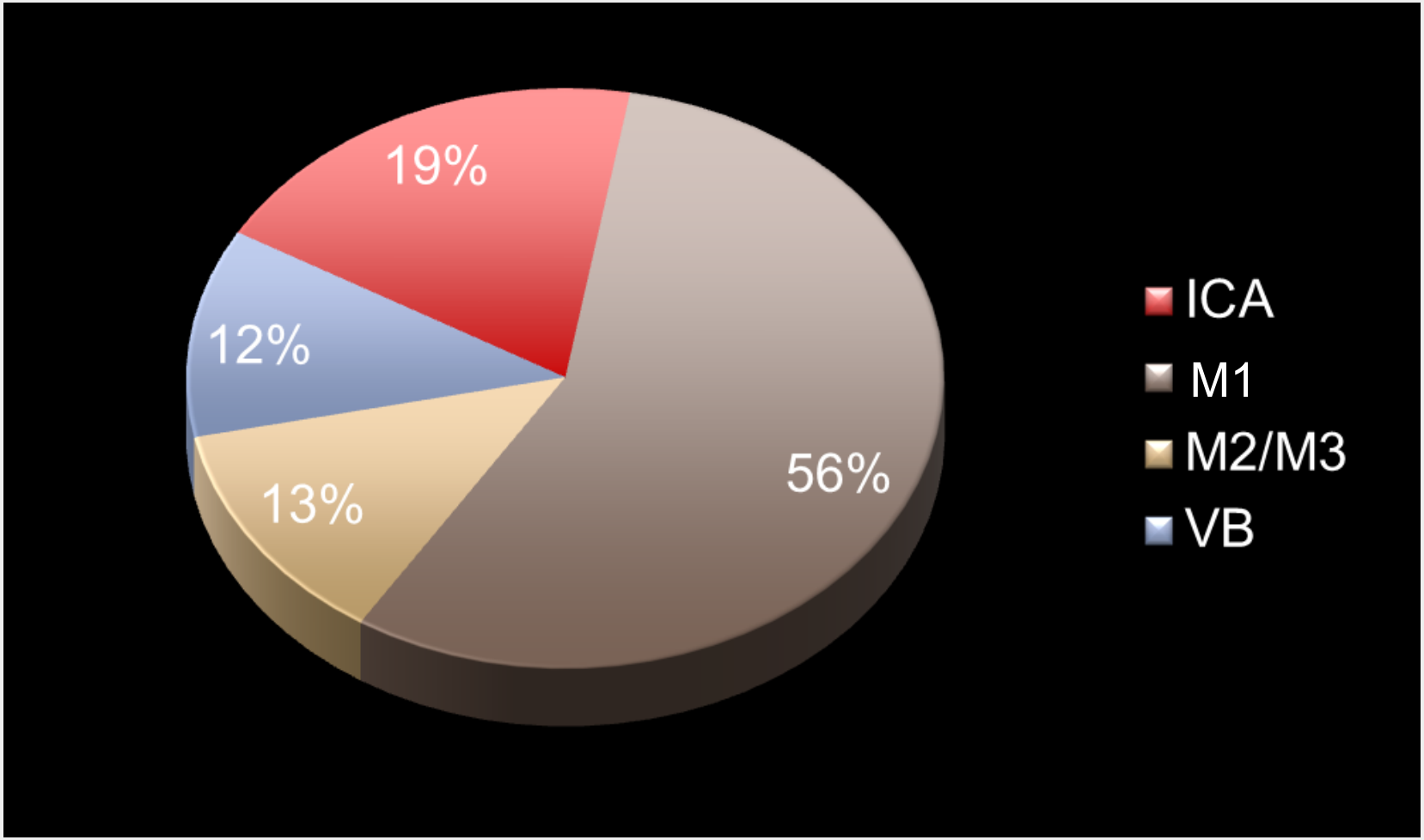
Others: Glucose<50 or >400, known coagulation disorders, INR>3, sustained SBP>185 or DBP>110, evidence of intracranial tumor or vasculitis

Main characteristics of the study population

Period of time	Oct 08 - Jan 2012
Age (mean)	68.5 (range 29-90)
Gender Male	57 (53.8%)
Number of patients	104 consecutive
Basal median NIHSS score	17.1 (range 2-42)
Ant.Circulation	88%
Post. Circulation	12 %
Median time from stroke onset to groin puncture	242 mins (70-870)
Mean Treatment duration in minutes	81.20 (20-369)

OUR EXPERIENCE WITH TREVO

Sample Details: Vessel Occlusion



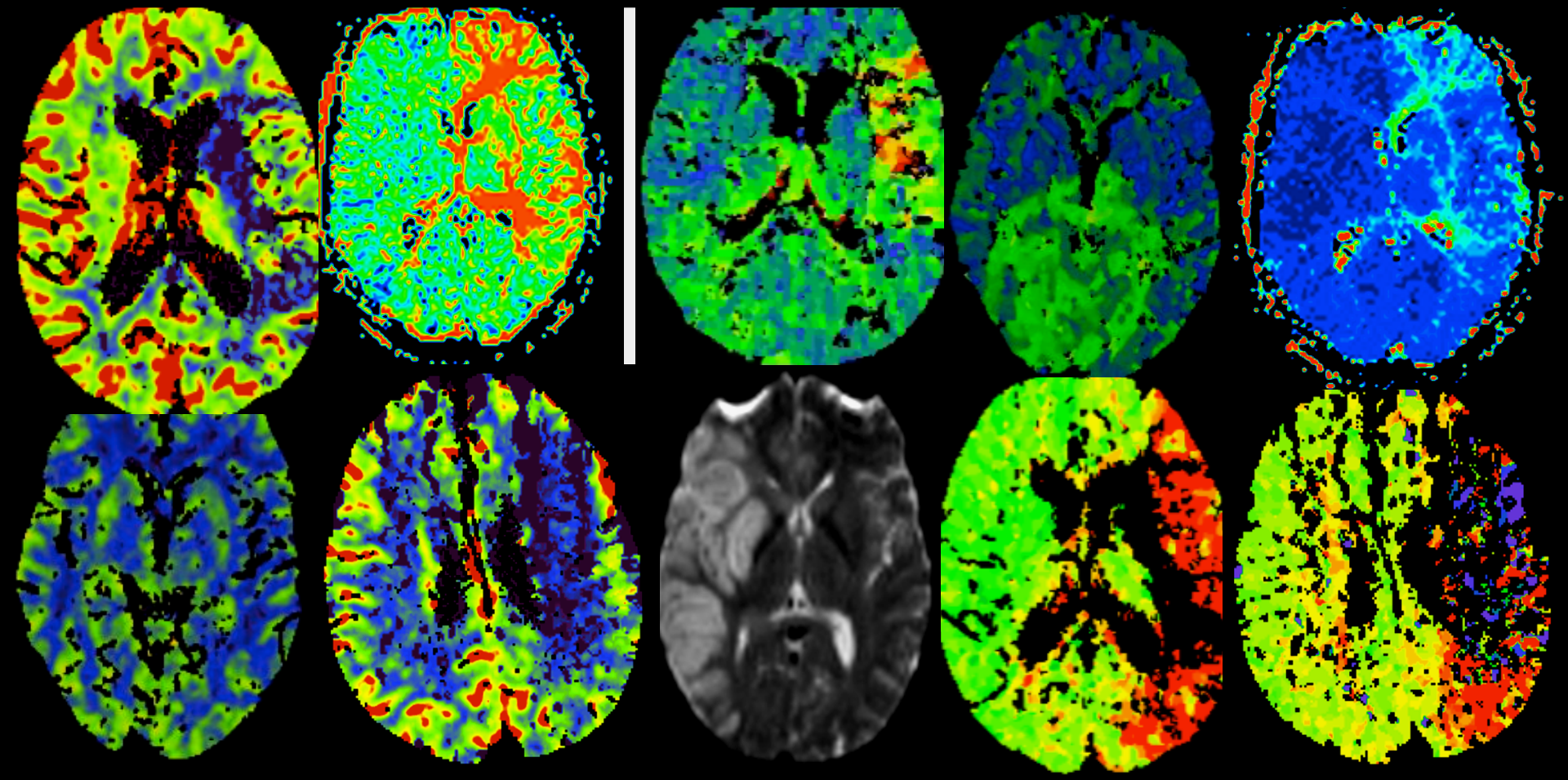
Main characteristics of the study population

n=104 Consecutive Cases

Site of intracranial occlusion		
Carotid	92	87.3%
Carotid T	20	18.9%
Proximal M1	37	34.9%
Distal M1	21	19.3%
M2	13	13.3%
Basilar artery	12	12.7 %
Carotid Stenting during procedure	26	24.5%

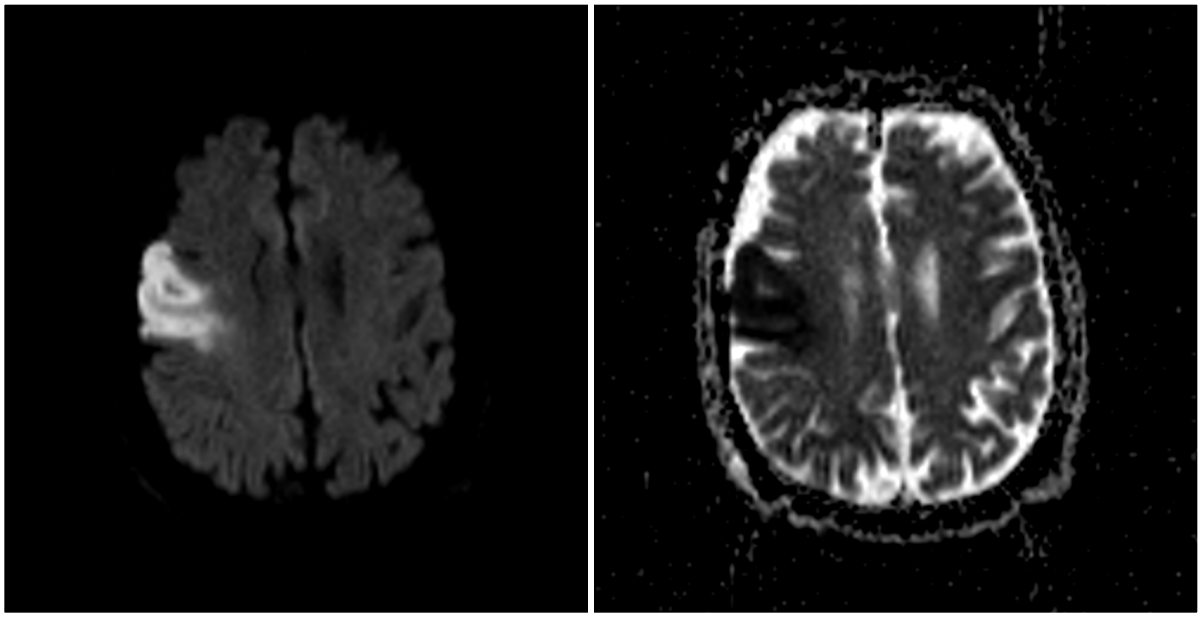
Selection of Patients

¿ MR vs. CT ?



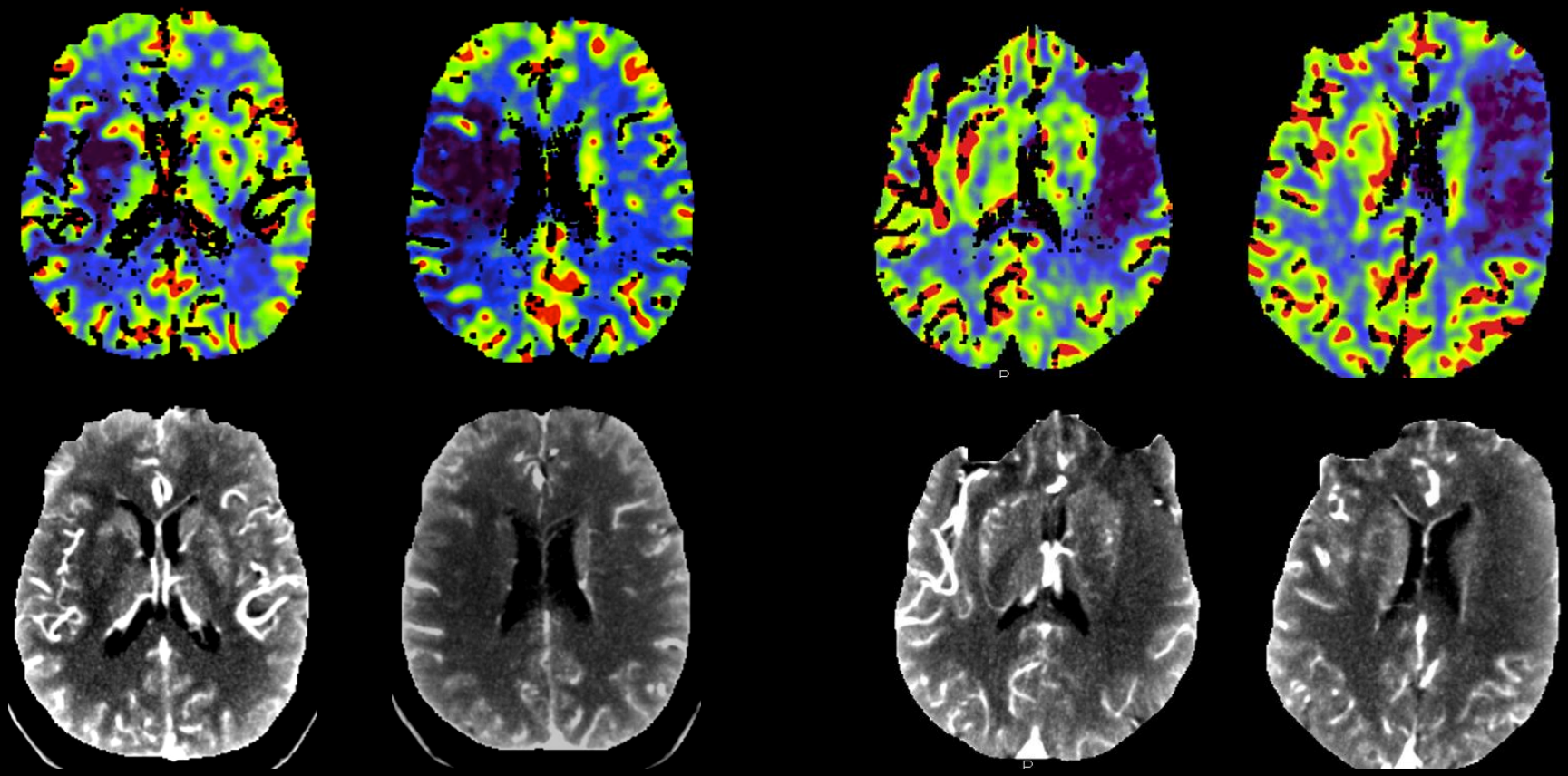
MR vs CT

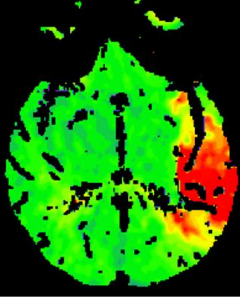
DW-MR are superior in the detection of acute ischemic changes, with high sensibility and specificity (LOE: A)



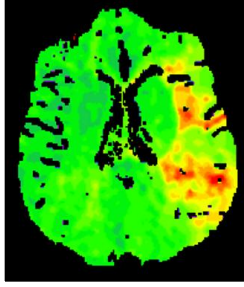
MR vs CT

CTA-SI is comparable to DWI in the detection of acute ischemic changes, with the exception of tiny lesions in the posterior fosa. (Class IIa, LOE: B)





CTA and Perfusion CT



PRO

. Availability

. High Resolution

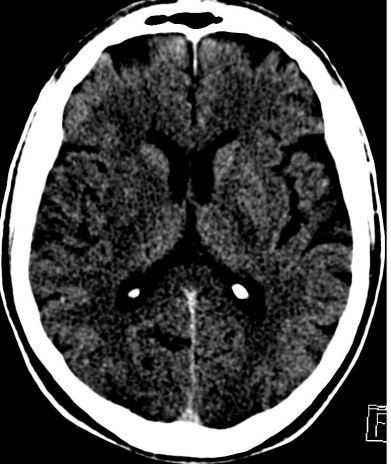
. Fast acquisition

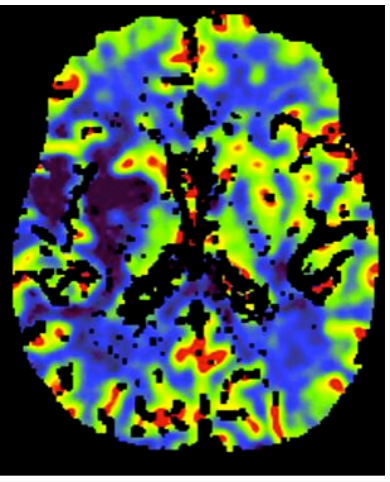
CON

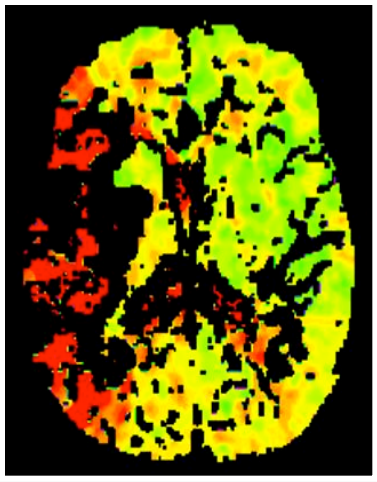
. Limited slices in some equipments

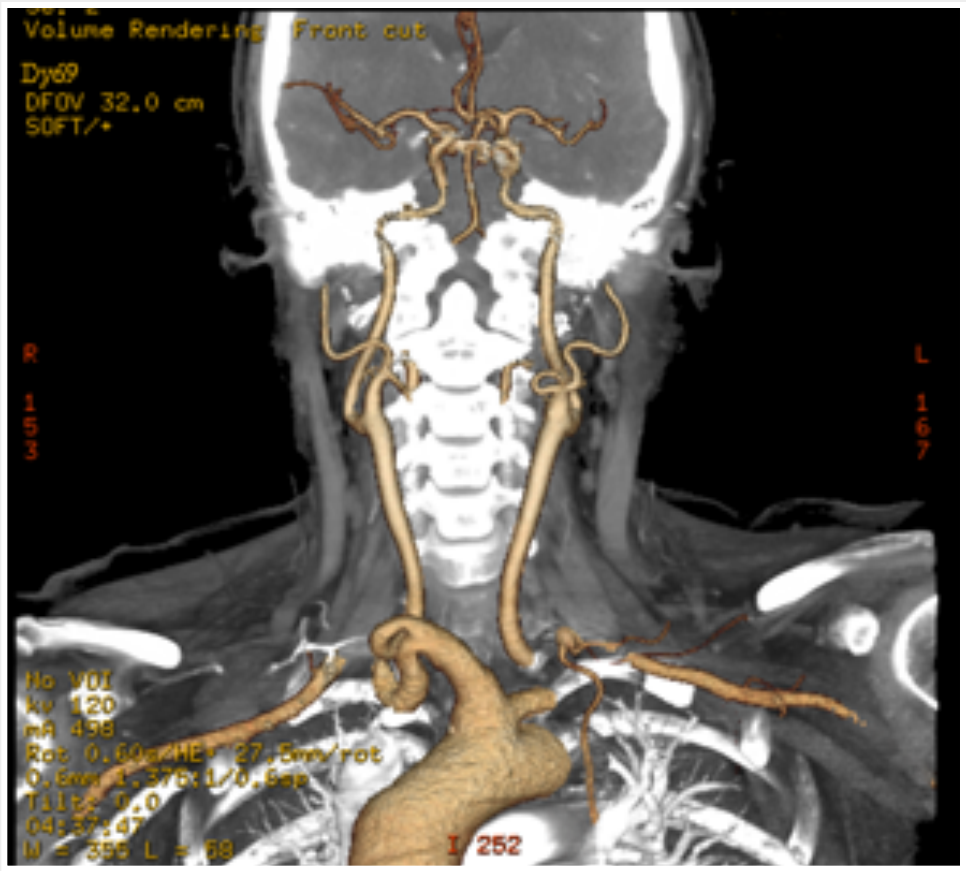
. Contrast

. Radiation

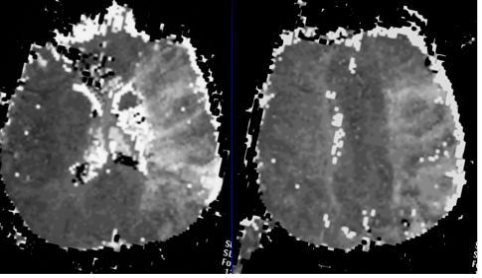








FDA: A comprehensive stroke CT protocol that includes an unenhanced and postcontrast head CT, PCT, and CTA of the cervical and intracranial arteries may deliver a mean effective dose up to 6 times that of a standard, unenhanced head CT



MRA and Perfusion MR

PRO

. No Radiation

. Whole Brain

. No Iodinated Contrast

CON

. Less availability

.Nephrotoxicity

. Longer acquisition

Quantitative Assessment of Core/Penumbra Mismatch in Acute Stroke

CT and MR Perfusion Imaging Are Strongly Correlated When Sufficient Brain Volume Is Imaged

Pamela W. Schaefer, MD; Elizabeth R. Barak, MD; Shahmir Kamalian, MD; Leila Rezai Gharai, MD; Lee Schwamm, MD; Ramon Gilberto Gonzalez, MD, PhD; Michael H. Lev, MD

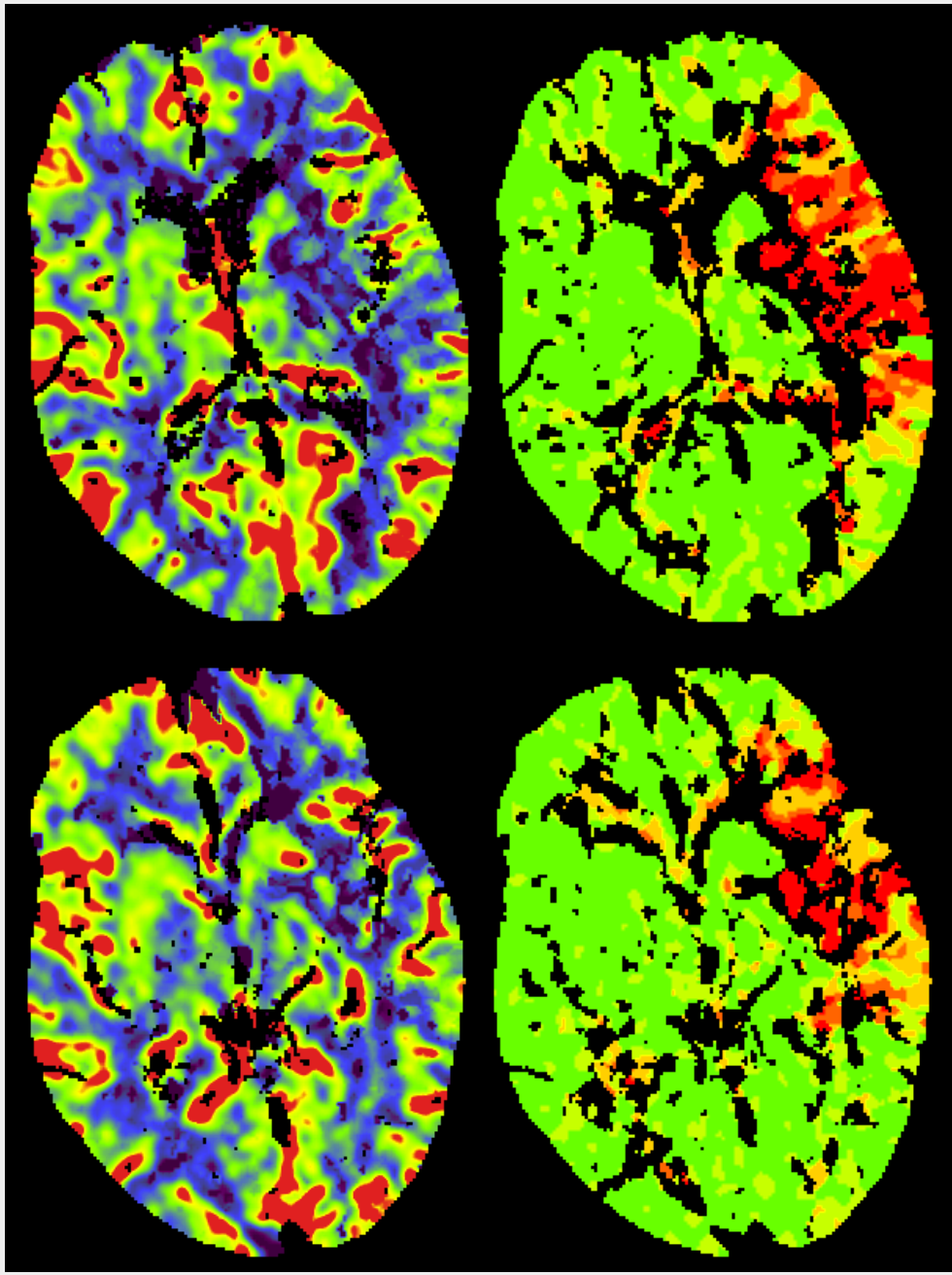
Background and Purpose—Our purpose was to determine (1) the correlation between quantitative CT and MR measurements of infarct core, penumbra, and mismatch; and (2) whether the difference between these measurements would alter patient selection for stroke clinical trials.

Methods—We studied 45 patients with acute middle cerebral artery stroke imaged a mean of 3.8 hours after onset (range, 0.48 to 8.35 hours) who underwent CT perfusion and MR diffusion (DWI)/perfusion imaging within 3 hours of each other. The DWI and MR-mean transit time (MTT) abnormalities were visually segmented using a semiautomated commercial analysis program. The CT-cerebral blood volume) and CT-MTT lesions were automatically segmented using a relative cerebral blood volume threshold of 0.56 and a relative MTT threshold of 1.50 on commercially available software. Percent mismatch was defined as [(MTT−DWI)/DWI volume]×100. Pearson correlation coefficients were calculated.

Results—There were significant correlations for DWI versus CT-cerebral blood volume lesion volumes (r^2=0.88, P<0.001), for MR-MTT versus CT-MTT lesion volumes(r^2=0.86, P<0.001), and for MR-MTT/DWI versus CT-MTT/CT-cerebral blood volume mismatch lesion volumes(r^2=0.81, P<0.001). MR perfusion and CT perfusion agreed for determining: (1) infarct core < versus ≥100 mL in 41 of 45 (91.1%); (2) MTT lesion size < versus >2 cm diameter in 42 of 45 (93.3%); (3) mismatch < versus >20% in 41 of 45 (91.1%); and (4) inclusion versus exclusion from trial enrollment in 38 of 45 (84.4%) patients. Six of 7 disagreements were due to inadequate CT coverage.

Conclusion—Advanced MR and CT perfusion imaging measurements of core/penumbra mismatch for patient selection in stroke trials are highly correlated when CT perfusion coverage is sufficient to include most of the ischemic region. Although MR is currently the preferred imaging method for determining core and penumbra, CT perfusion is comparable and potentially more available. (***Stroke*****. 2008;39:2986-2992.)**


A



APM0769/A/5224, 2012-04

Technique

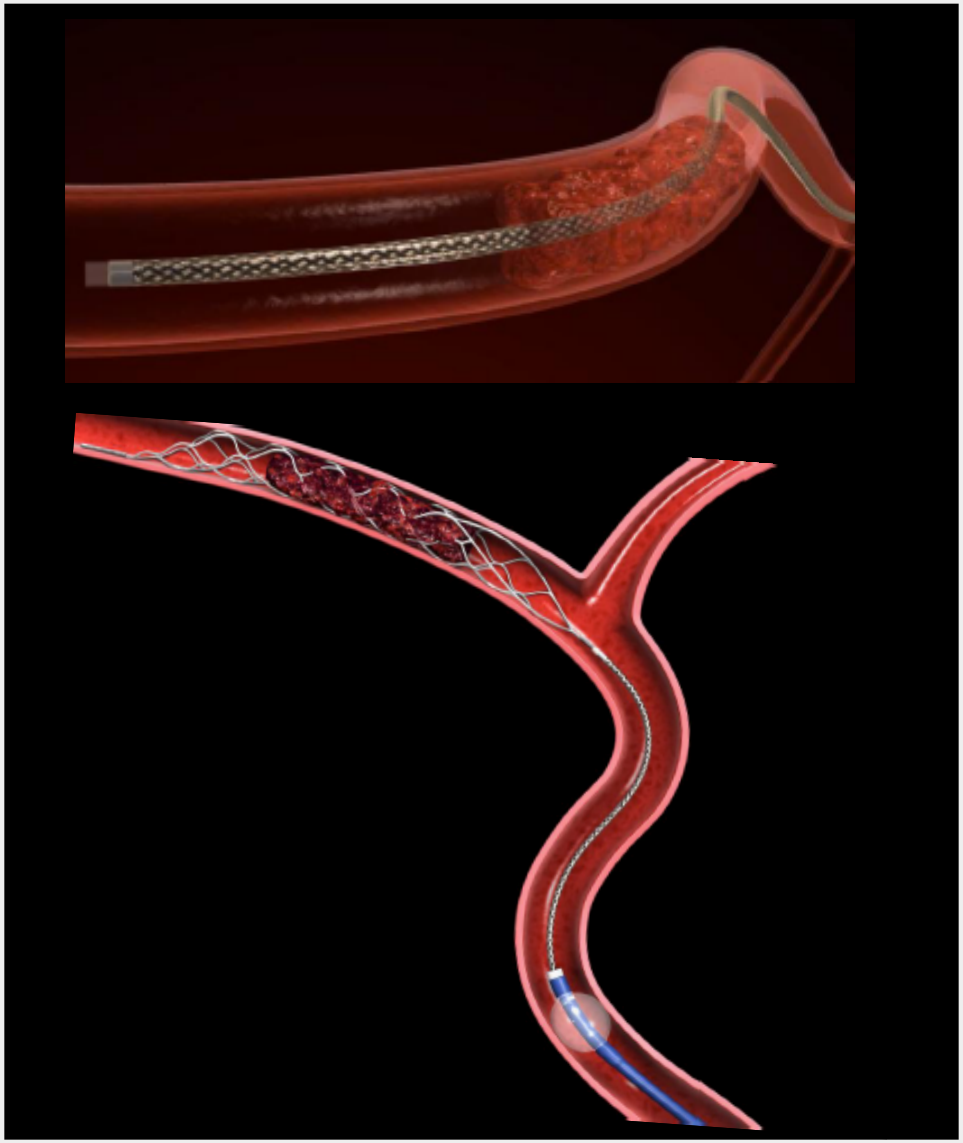
BGC 8F whenever possible, if not a standard 6F or 7F guiding catheter was used

DAC between 4.3 - 5.2 F was used in cases with severe tortuosity to achieve better stability

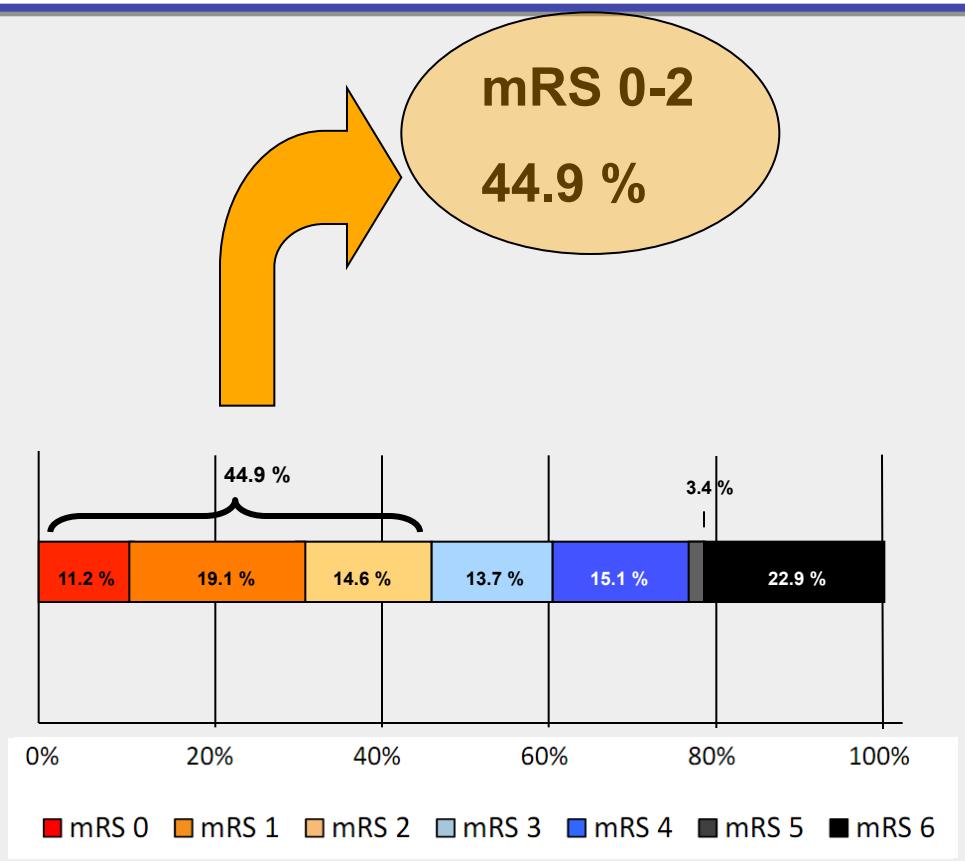
Trevo microcath with a 0.014 guidewire was used to go through the thrombus into a normal vessel

Trevo stentriever device was deployed at the level of the thrombus and left in place for 3 min.

Trevo retrieval was done with flow arrest and aspiration whenever a BGC was used



Efficacy - Clinical Impact - mRS 90 days



90 day

Trevo (n=104)

Efficacy - Recanalization Rate ONLY TICI 3-2

ONLY TREVO PROCEDURE (87)	**82.7 %**
TREVO + OTHER MECHANICAL DEVICE (17%) **(Solitaire, n= 7; Merci, n= 5 and Solitaire and Merci, n = 3)**	**91.8 %**

Safety Variables

Saf 1: % of pts with symptomatic IC hemorrhage in the first 36 hours defined as PH2 or remote PH with at least 4 NIHSS points worsening

Saf 2: Mortality at 90 days

Safety Variables

SAF1 **SYMPTOMATIC HEMORRHAGE**	**11.5%**
SAF2 **MORTALITY AT 90 DAYS**	**22.9%**

Comparison Table

	n	*NIHSS basal*	*TIMI 2-3*	*MAIN DEVICE ALONE RECANALIZATION RATE*	*mRS 0-2 (90d)*	*mRS 6 (90d)*	*sICH*
TREVO - SINGLE CENTER - H.CLINIC	**104**	**17**	**92%**	**83%**	**45%**	**23%**	**11%**
Multi MERCI (Smith et al 2008)	164	19	68%	55%	36%	34%	10%
PENUMBRA (PPST , 2009)	125	17	82 %*	82%	25%	26%	11%

Higher recanalization rates
Better outcomes

*Recanalization of the site of primary occlusion alone.

Comparison Table – Retrievable Stents

Author, year	*n*	*Mean Age*	*NIHSS basal*	*TIMI 2-3 %*	*mRS 0-2 (90d) %*	*mRS 6 (90d) %*	*sICH %*
San Roman et al. Stroke 2012	104	68.5	17	83	45	23	11.5
San Roman et al, Last 46 cases	**46**	**64.91**	**17**	**88**	**51.7**	**14**	**8.5**

Comparison Table – Retrievable Stents

Author, year	*n*	*NIHSS basal*	*TIMI 2-3*	*mRS 0-2 (90d)*	*mRS 6 (90d)*	*sICH*
Machie, 2011	56	15.8	89	46	NA	3.5
Costalat, 2011	50	14.7	84	54	12	2
Mourand, 2011	40	18	65	39	41	18
Mittef, 2011	26	NA	96.1	42.3	NA	7.6
Roth, 2010	22	19	90	50	18.1	9
Castaño, 2010	20	18	100	45	20	10
Stampfl, 2011	18	19	88	33.3	66	16.6
Rohde, 2011	10	19	100	63	30	20
San Roman et al , 2012	104	17	82	44.9	23	11

Single Centre Experience with Trevo stentriever device in AIS: Safety and Efficacy in 104 consecutive patients

Stroke

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Stroke Association℠

A Division of American Heart Association

Single-Center Experience of Cerebral Artery Thrombectomy Using the TREVO Device in 60 Patients With Acute Ischemic Stroke

Luis San Román, Victor Obach, Jordi Blasco, Juan Macho, Antonio Lopez, Xabier Urra, Alejandro Tomasello, Alvaro Cervera, Sergio Amaro, Joan Perandreu, Jordi Branera, Sebastián Capurro, Laura Oleaga and Angel Chamorro

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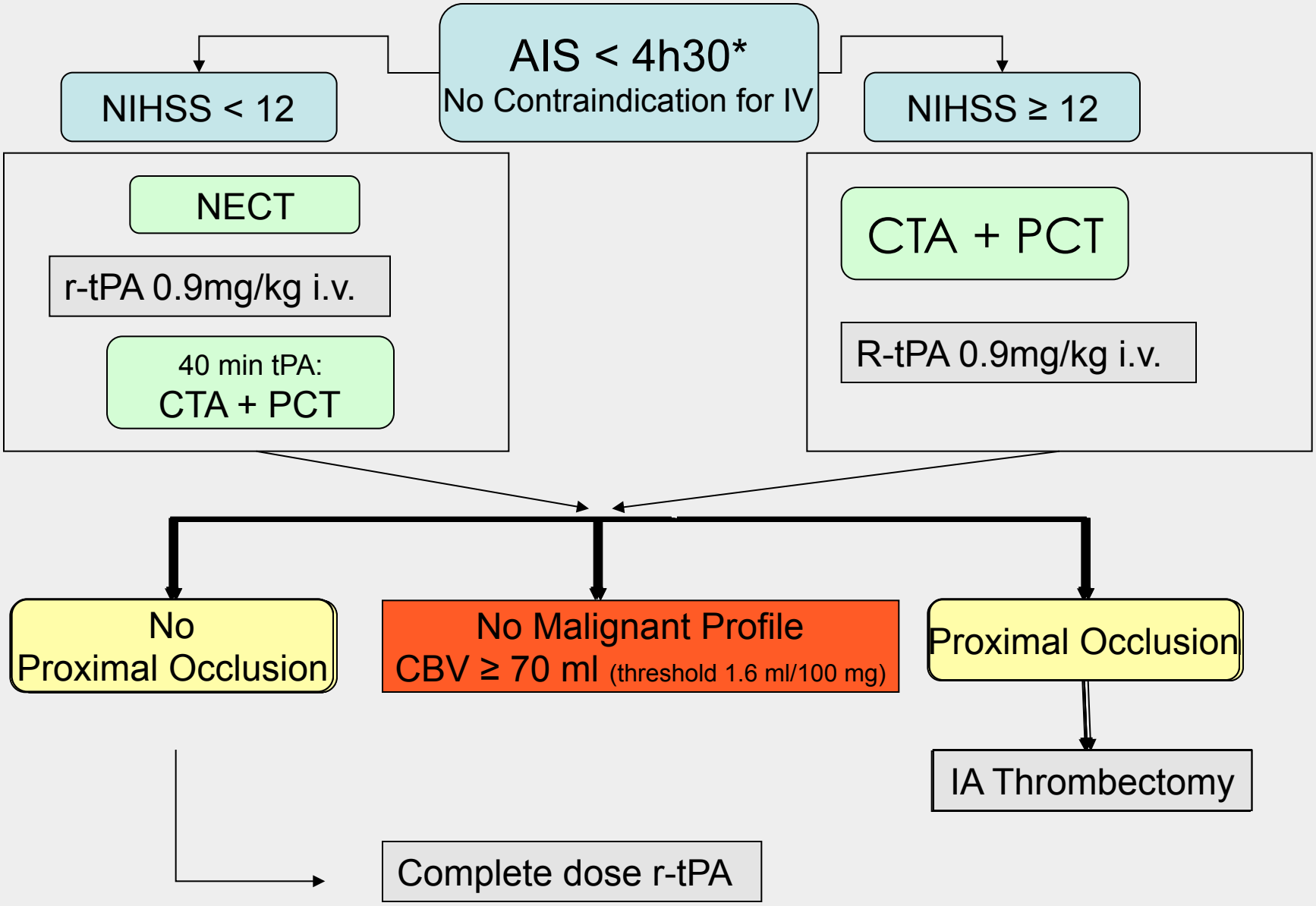
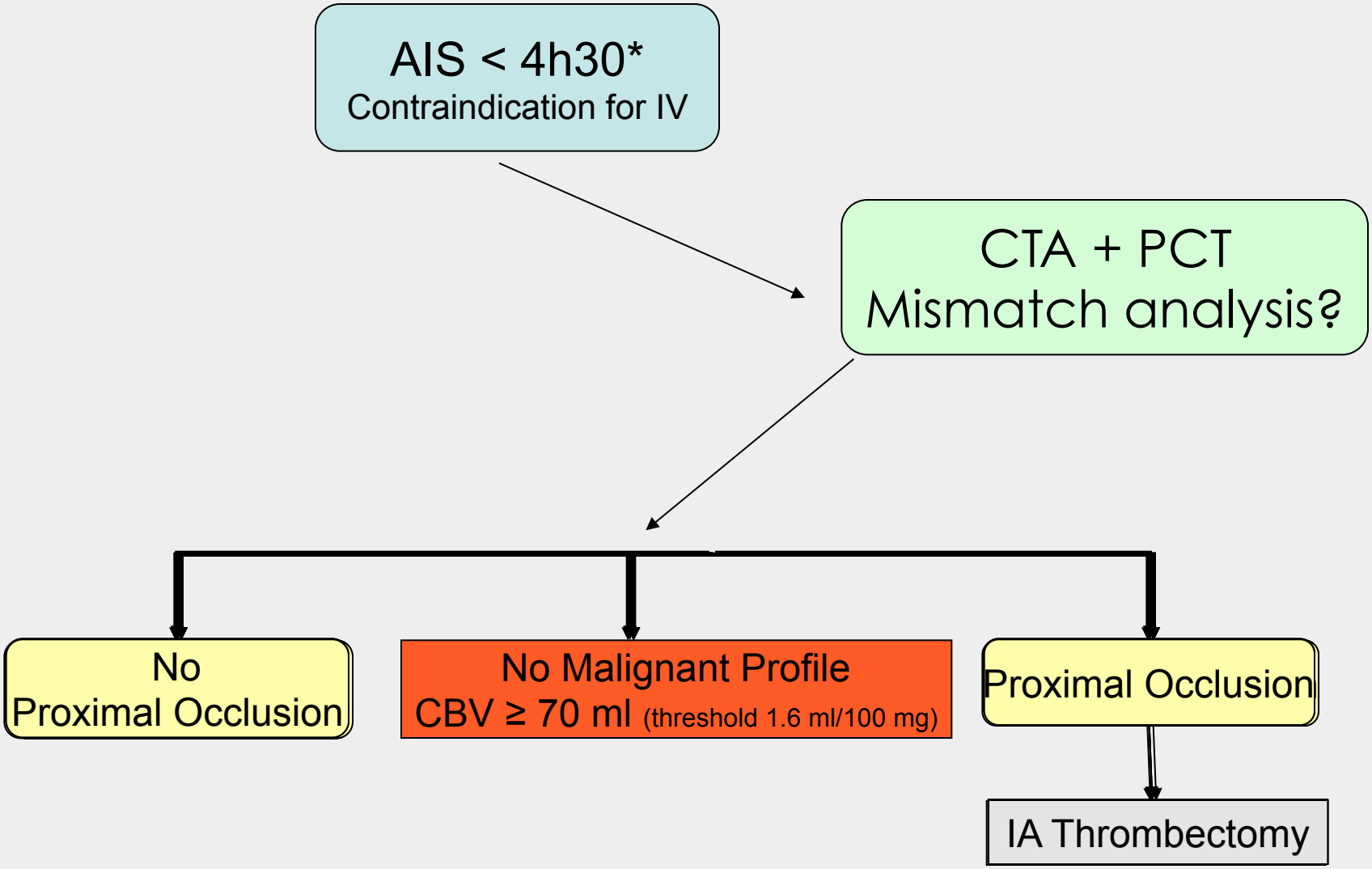
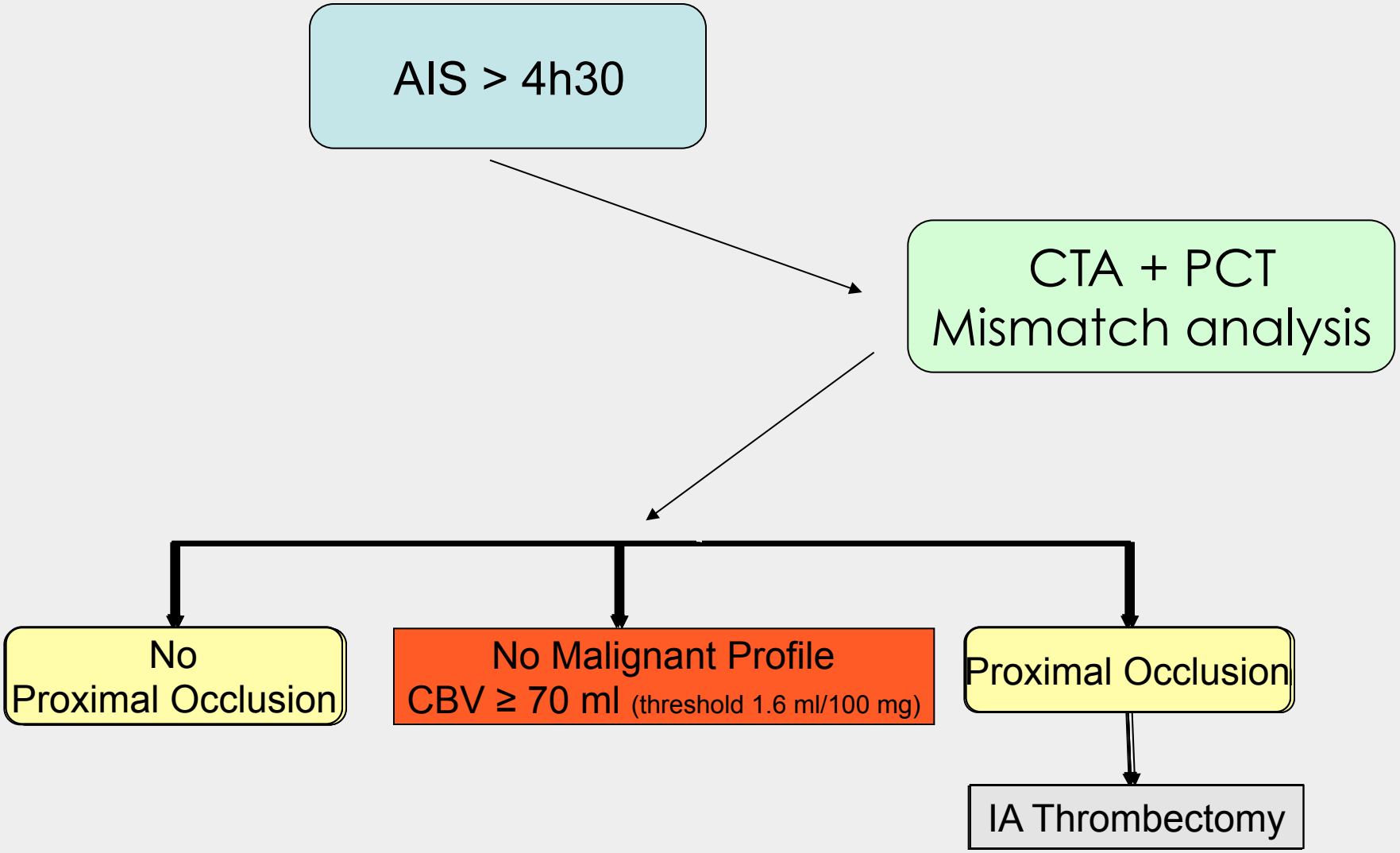

AIS < 4h30*
No Contraindication for IV
NIHSS < 12
NIHSS ≥ 12
NECT
r-tPA 0.9mg/kg i.v.
40 min tPA:
CTA + PCT
CTA + PCT
R-tPA 0.9mg/kg i.v.
No
Proximal Occlusion
No Malignant Profile
CBV ≥ 70 ml (threshold 1.6 ml/100 mg)
Proximal Occlusion
IA Thrombectomy
Complete dose r-tPA


AIS < 4h30*
Contraindication for IV
CTA + PCT
Mismatch analysis?
No
Proximal Occlusion
No Malignant Profile
CBV ≥ 70 ml (threshold 1.6 ml/100 mg)
Proximal Occlusion
IA Thrombectomy


AIS > 4h30
CTA + PCT
Mismatch analysis
No
Proximal Occlusion
No Malignant Profile
CBV ≥ 70 ml (threshold 1.6 ml/100 mg)
Proximal Occlusion
IA Thrombectomy

Our Experience with Trevo - Conclusions

PRO: Easy to use

No device-related complications

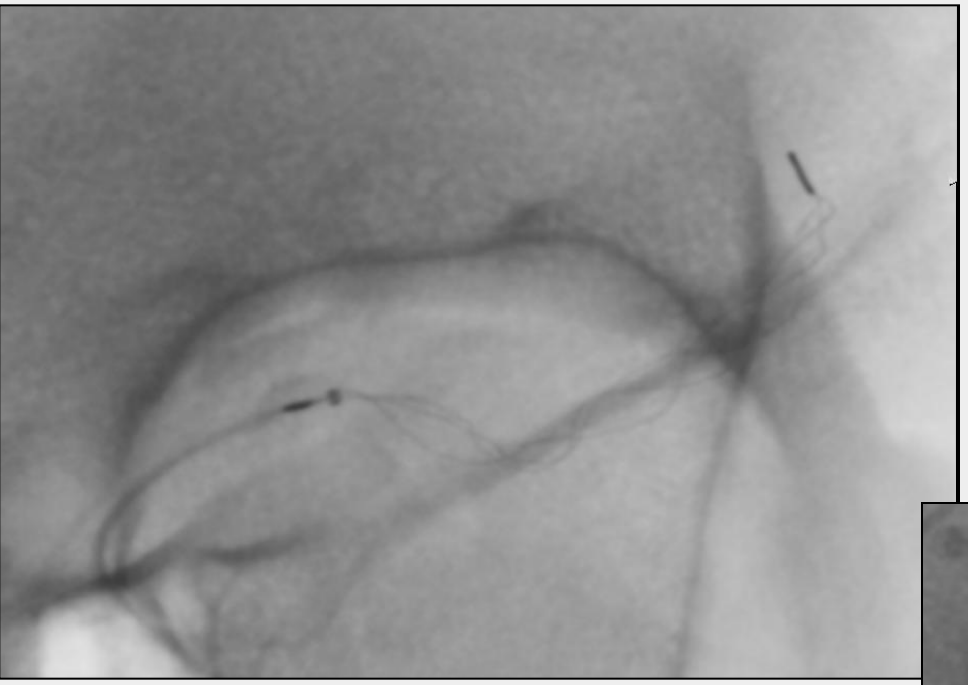
Excellent navigability and delivery

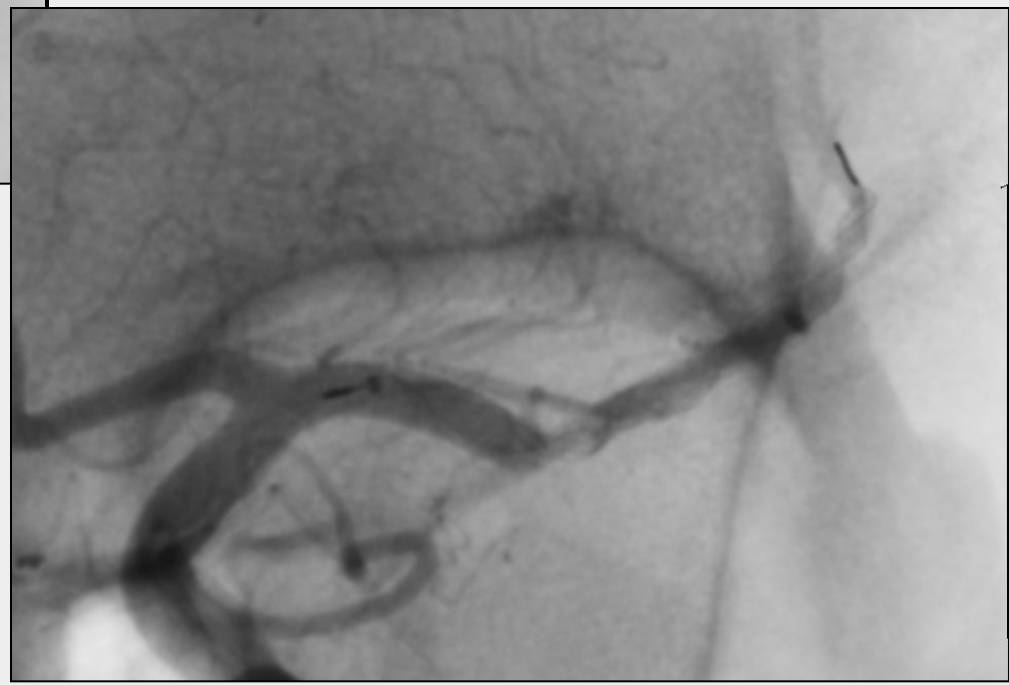
Atraumatic distal guidewire tip

Good visibility of markers

Our Experience with Trevo - Conclusions

Our Experience with Trevo - Conclusions





Our Experience with Trevo - Conclusions

PRO: Easy to use – No device-related complications

Excellent navigability and delivery

Atraumatic distal guidewire

Good visibility of markers

CON: Painful during delivery and retraction

Microcath navigability could be improved

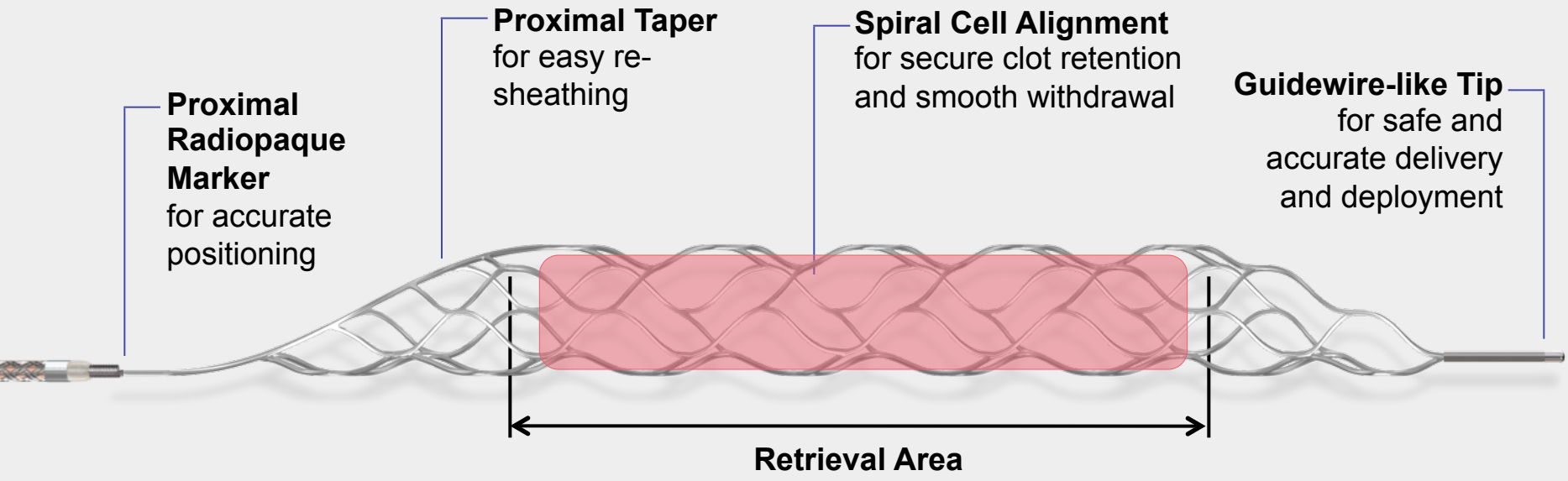
High Recanalization rates with mechanical thrombectomy devices are STILL not having enough impact on better clinical outcomes. Careful selection of patients is mandatory

Tips & Tricks

- Multimodal imaging should always be performed in order to determine the amount of salvageable tissue and to diminish the rate of futile recanalization

- Careful positioning of the device is crucial

Tips & Tricks



TREVO® PRO

Tips & Tricks

- The stentriever device should be left in place for at least 3-4 min. to improve efficacy

- We believe flow arrest and aspiration should be performed during device retrieval whenever possible (almost 90% of the cases a BGC was used)

OUR EXPERIENCE WITH TREVO - CONCLUSIONS

- Time to recanalization and recanalization rates are main key factors in achieving good clinical outcomes

- These very high recanalization rates should lead us to higher percentage of patients with good clinical outcomes

OUR EXPERIENCE WITH TREVO - CONCLUSIONS

- Other issues should be analysed such as collaterals, distal embolization, volume of infarcted tissue before treatment….

- Educational programs and rigorous organization are extremely necessary to get the patients as soon as possible to the stroke center to diminish the time to recanalization as much as possible

LATEST UPDATE

MOST RECENT PUBLICATIONS

SWIFT

RCT

MERCI Vs SOLITAIRE

TREVO2

RCT

MERCI Vs TREVO

Neuroradiology
DOI 10.1007/s00234-012-1075-z

INVITED REVIEW

Future trials of endovascular mechanical recanalisation therapy in acute ischemic stroke patients: a position paper endorsed by ESMINT and ESNR

Part I: Current situation and major research questions

Jens Fiehler · Michael Söderman · Francis Turjman · Philip M. White · Søren Jacob Bakke · Salvatore Mangiafico · Rüdiger von Kummer · Mario Muto · Christophe Cognard · Jan Gralla

Received: 2 July 2012 / Accepted: 13 July 2012

MOST RECENT PUBLICATIONS

TREVO 2
Randomized Controlled Trial Trevo (n=88) vs Merci (n=90)
Independent Clinical Events Committee and Independent Core Lab
26 centres in USA and 1 centre in Europe
Primary Efficacy Endpoint: Revasc TICI 2 or more
Primary Safety Endpoint: Procedure related Adverse Events 24 h

MOST RECENT PUBLICATIONS

SWIFT
Randomized Controlled Trial Solitaire (n=58) vs Merci (n=56)
Independent Clinical Events Committee and Independent Core Lab
17 centres in USA and 1 centre in Europe
Primary Efficacy Endpoint: Revasc TICI 2 or more without SICH
Primary Safety Endpoint: Procedure related Adverse Events 24 h

MOST RECENT PUBLICATIONS

ENDPOINTS	TREVO 2	SWIFT
Primary Revasc Endpoint	86 % vs 60%	61% vs 24%
Good Clinical Outcome	40 % vs 22%	58% vs 33%
Symptomatic ICH	4 % vs 2 %	2 % vs 11%
Death	33 % vs 24%	18 % vs 44%

MOST RECENT PUBLICATIONS

FACTS

BOTH RCT SHOWED BENEFIT FOR STENTRIEVERS OVER MERCI

BETTER REVASC RATES AND GOOD CLINICAL OUTCOMES

LESS DEVICE RELATED COMPLICATIONS

THIS DATA SUPPORT THE USE OF THESE DEVICES FOR RCT COMPARING THROMBECTOMY VS MEDICAL TREATMENT

CONCLUSIONS

- Stroke gives INR the opportunity to progress from an experience-based discipline into a specialty supported by clinical trial evidence
- MT is a highly dynamic field in INR and provides a great chance for succesful trials designed and conducted with all the neighbouring specialties
- Nowadays the key research questions are the comparisons between MT+IVT and IVT both in eligible and non-eligible AIS patients

REVASCAT

CATALUNYA (SPAIN)	
RANDOMISATION	SOLITAIRE VS BEST MEDICAL TREATMENT
NUMBER OF CENTERS	4 COMPREHENSIVE STROKE CENTERS
NUMBER OF PATIENTS	690
EXTERNAL CORE LAB	YES
INCLUSION CRITERIA	ICA OR M1 OCCLUSION < 8 h
PRIMARY ENDPOINT	mRs 0-2 AT 90d

THANK YOU

+100

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