Hyperacute stroke management:

New prehospital models for Switzerland

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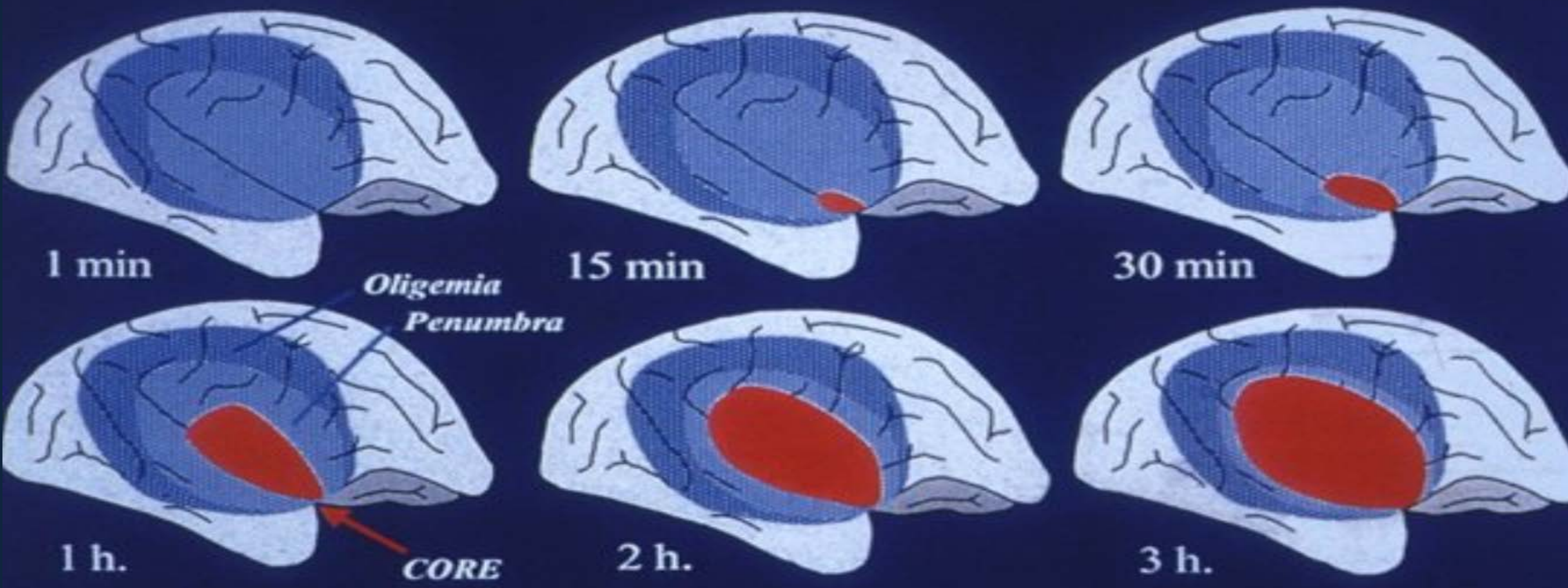
Inselspital Universitätsspital Bern
Universitäre Psychiatrische Dienste Bern
Neurochirurgie
Neurologie
Neuropädiatrie
Neuroradiologie
Psychiatrie

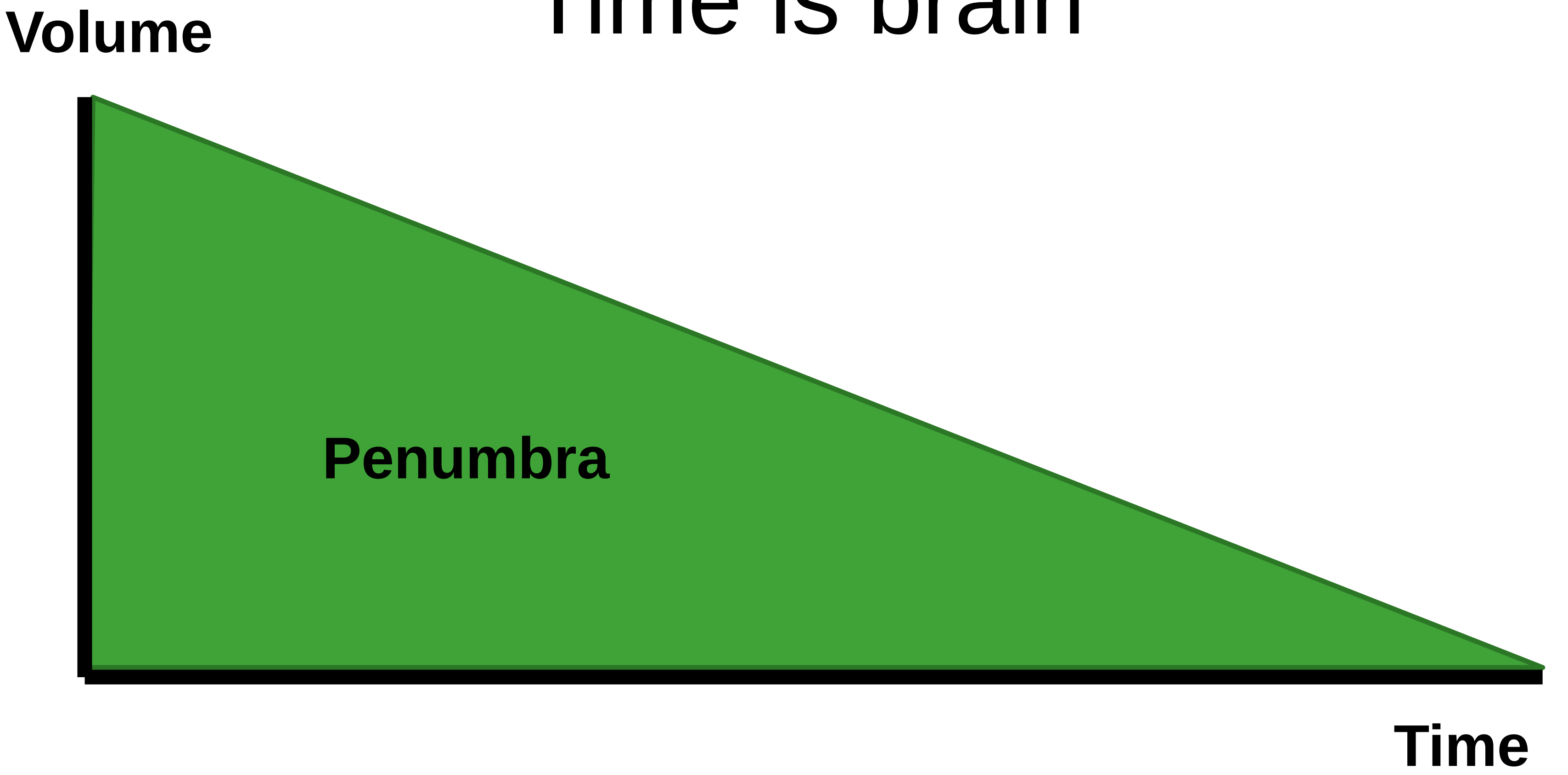
Disclosures

- Principal investigator ELAN trial
- Co-Principal investigator SWITCH trial
- Co-Principal investigator SWIFT DIRECT trial
- Consultant for Covidien/Medtronic and Stryker
- Research support: SNSF, SHF, Medtronic

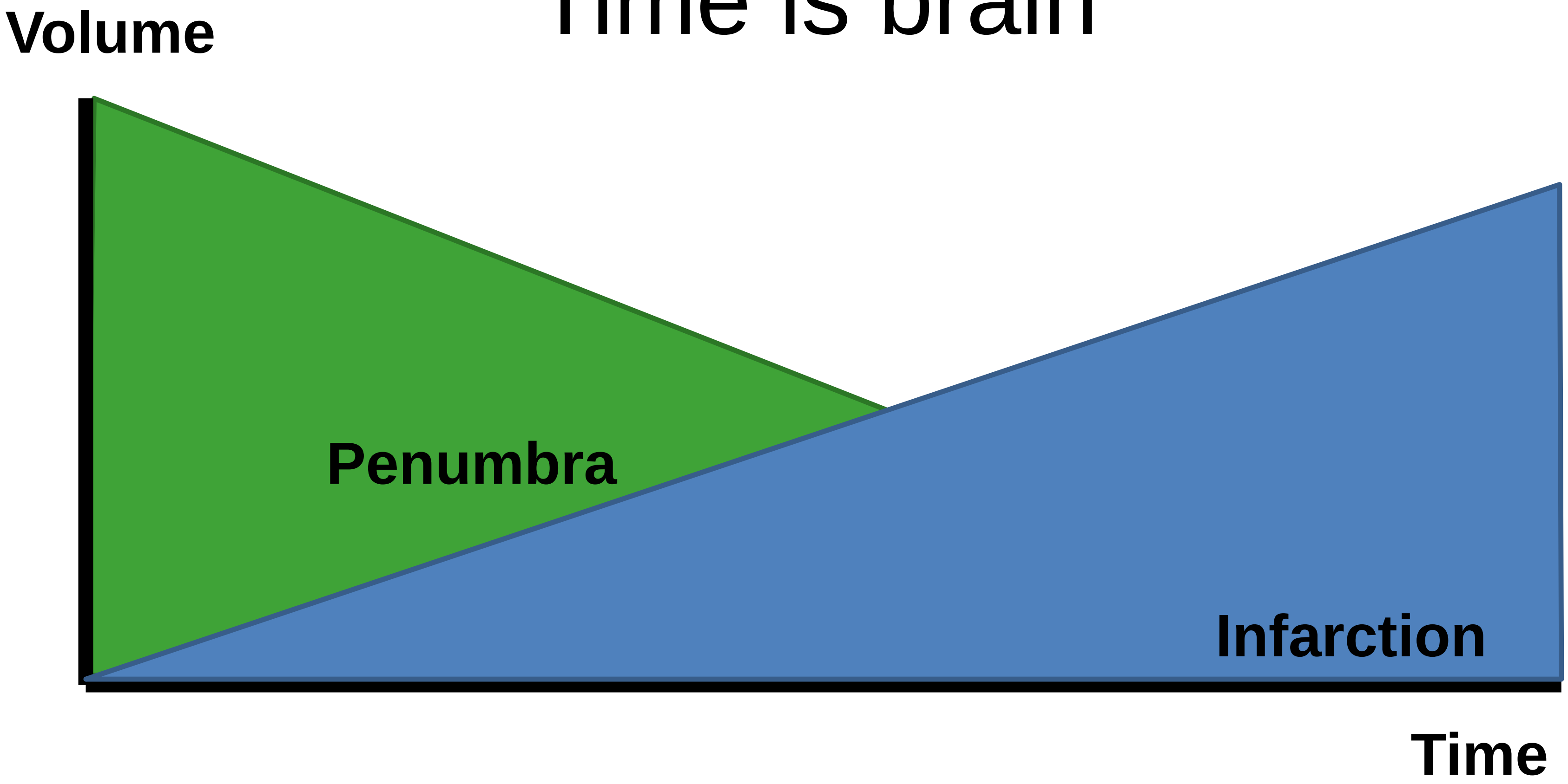


The Ischemic Penumbra : A Dynamic [time + space] concept

Time is brain

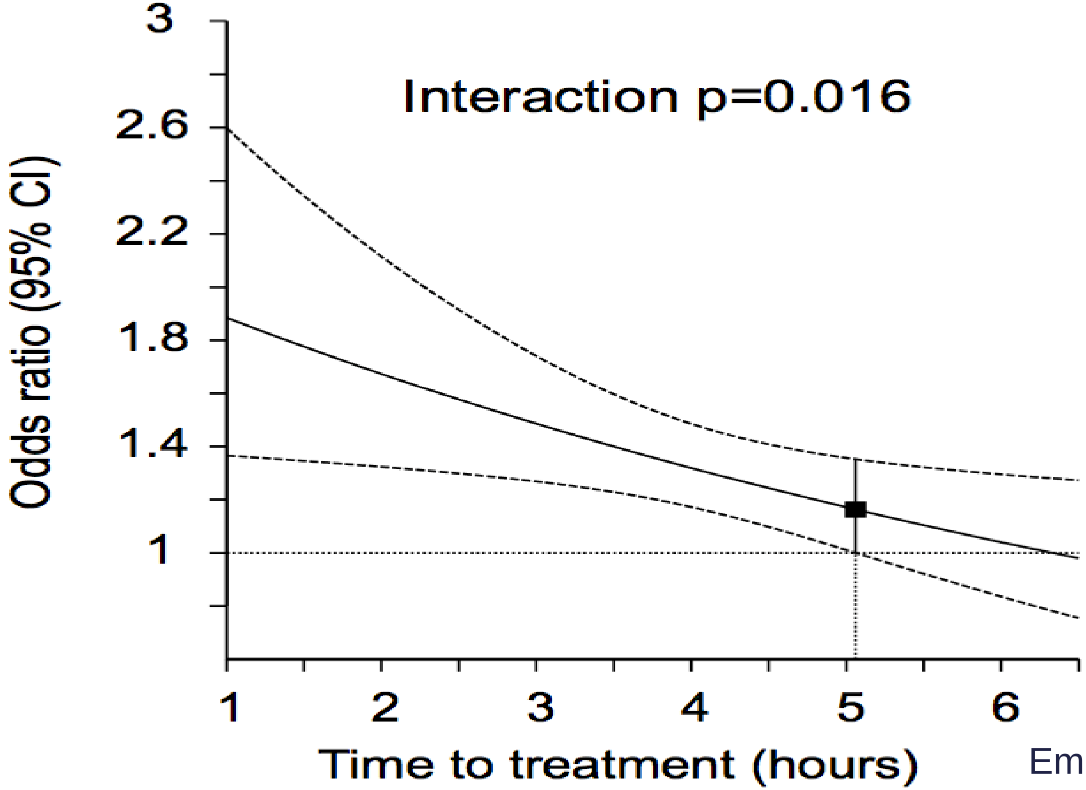


Time is brain



Effect on mRS 0-1 by treatment delay

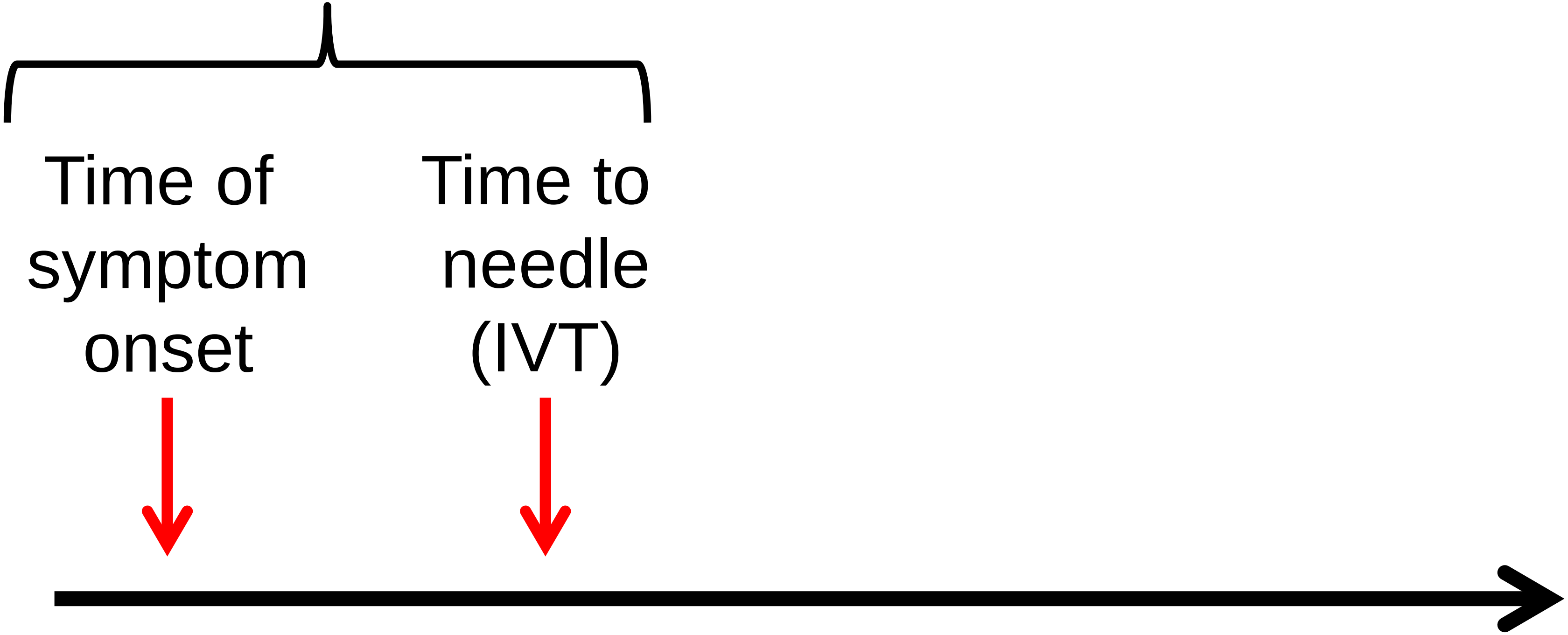
(ECASS, ATLANTIS, NINDS,EPITHET, IST-3)



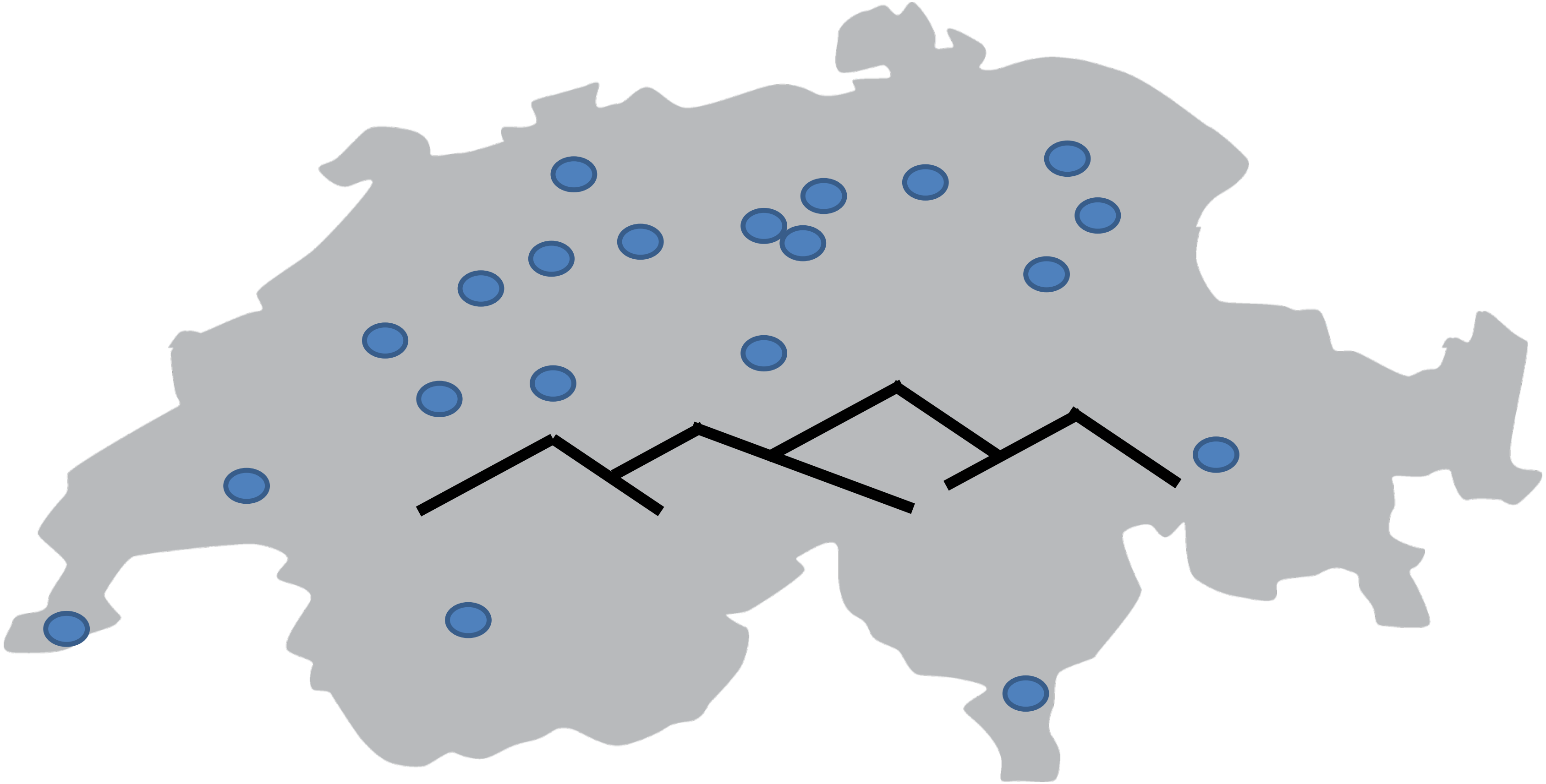
Emberson et al. Lancet 2014

Acute stroke treatment

Shorten time to needle!



Stroke Units in CH



Endovascular stroke treatment

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 1, 2015 VOL. 372 NO. 1

A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial

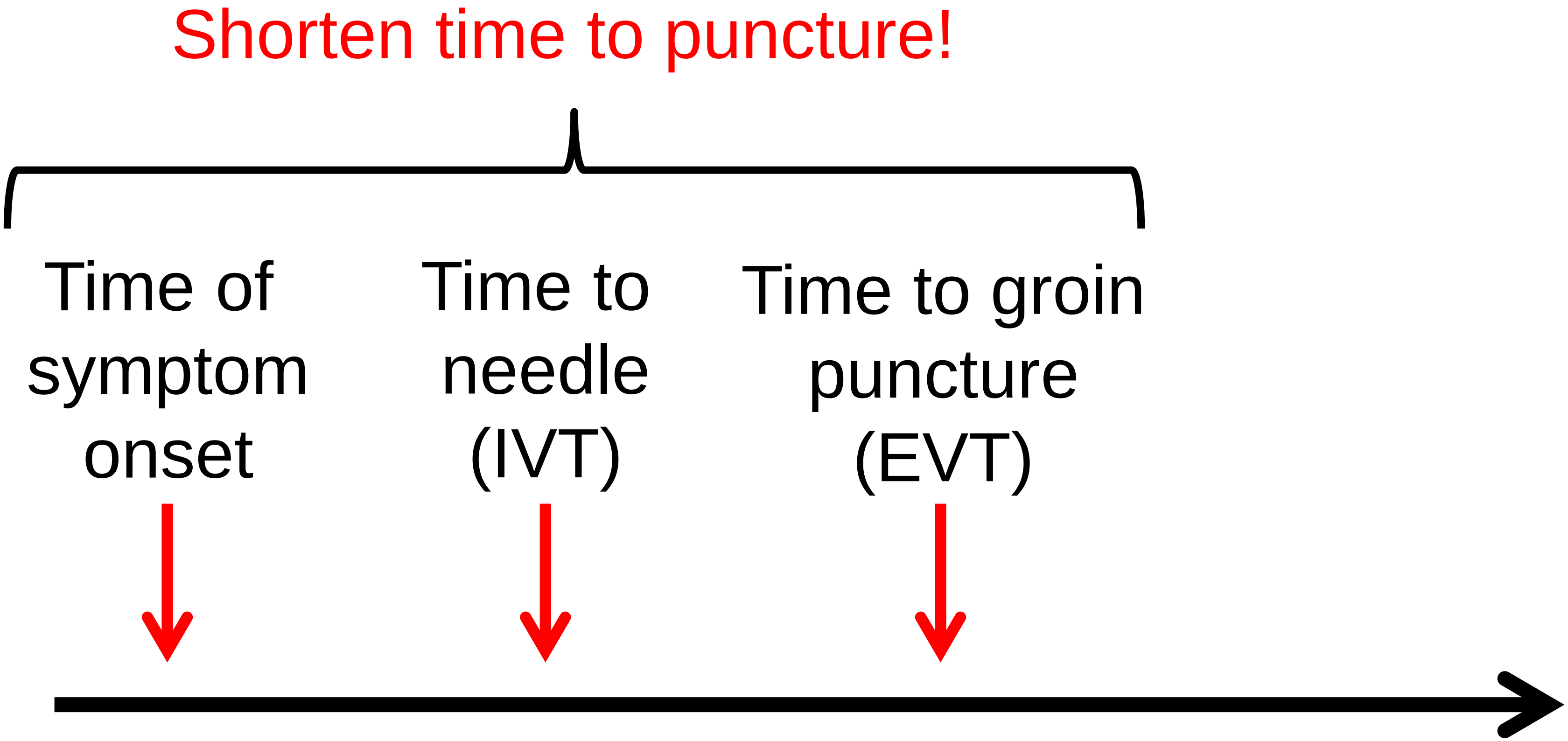
*Serge Bracard, Xavier Ducrocq, Jean Louis Mas, Marc Soudant, Catherine Oppenheim, Thierry Moulin, Francis Guillemin, on behalf of the THRACE investigators**

Aspiration Thrombectomy After Intravenous Alteplase Versus Intravenous Alteplase Alone

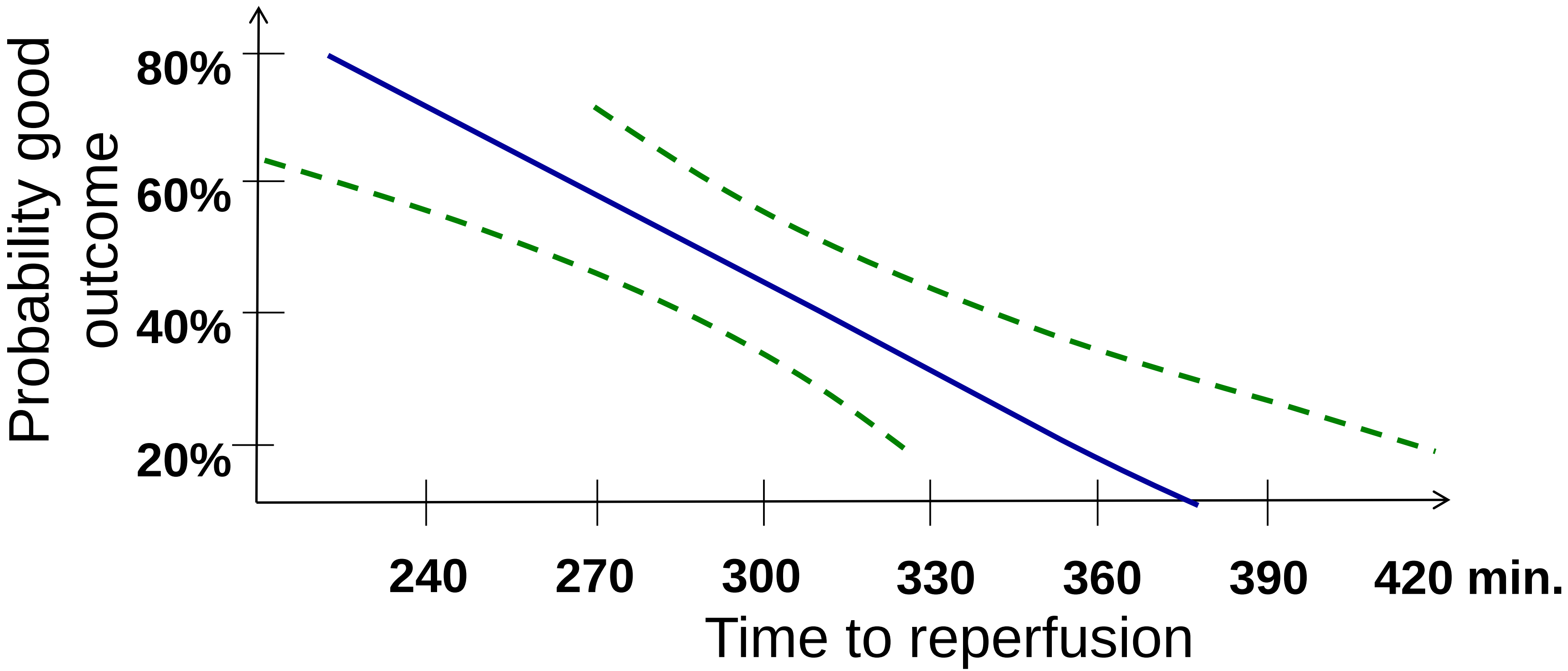
RESEARCH PAPER

Endovascular therapy for acute ischaemic stroke: the Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE) randomised, controlled trial

Acute stroke treatment



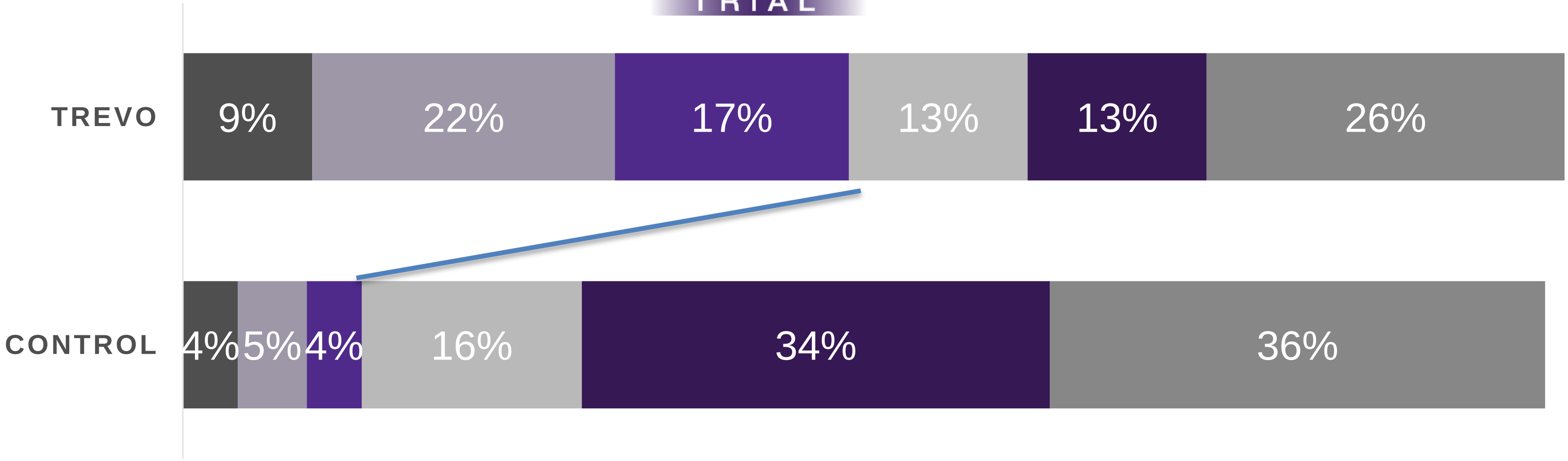
Benefit of endovascular reperfusion



Prabhakaran JAMA 2015; Khatri Lancet Neurology 2014; Mazhigi Circulation 2013

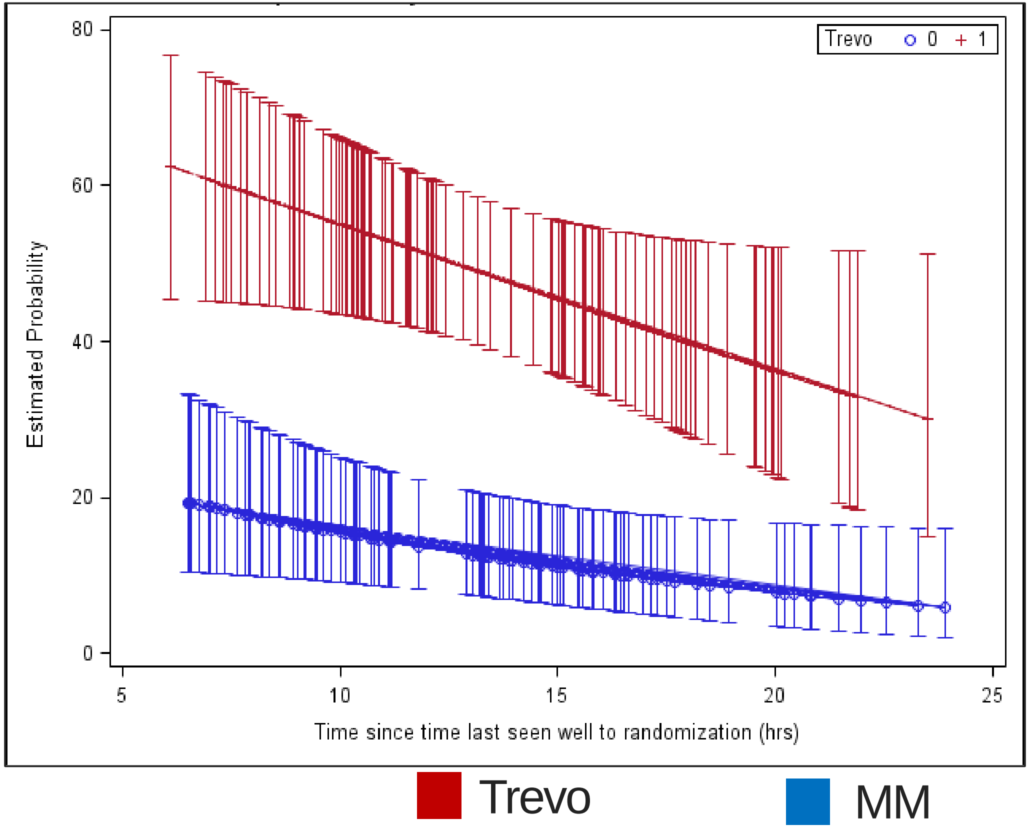
DAWN™

TRIAL

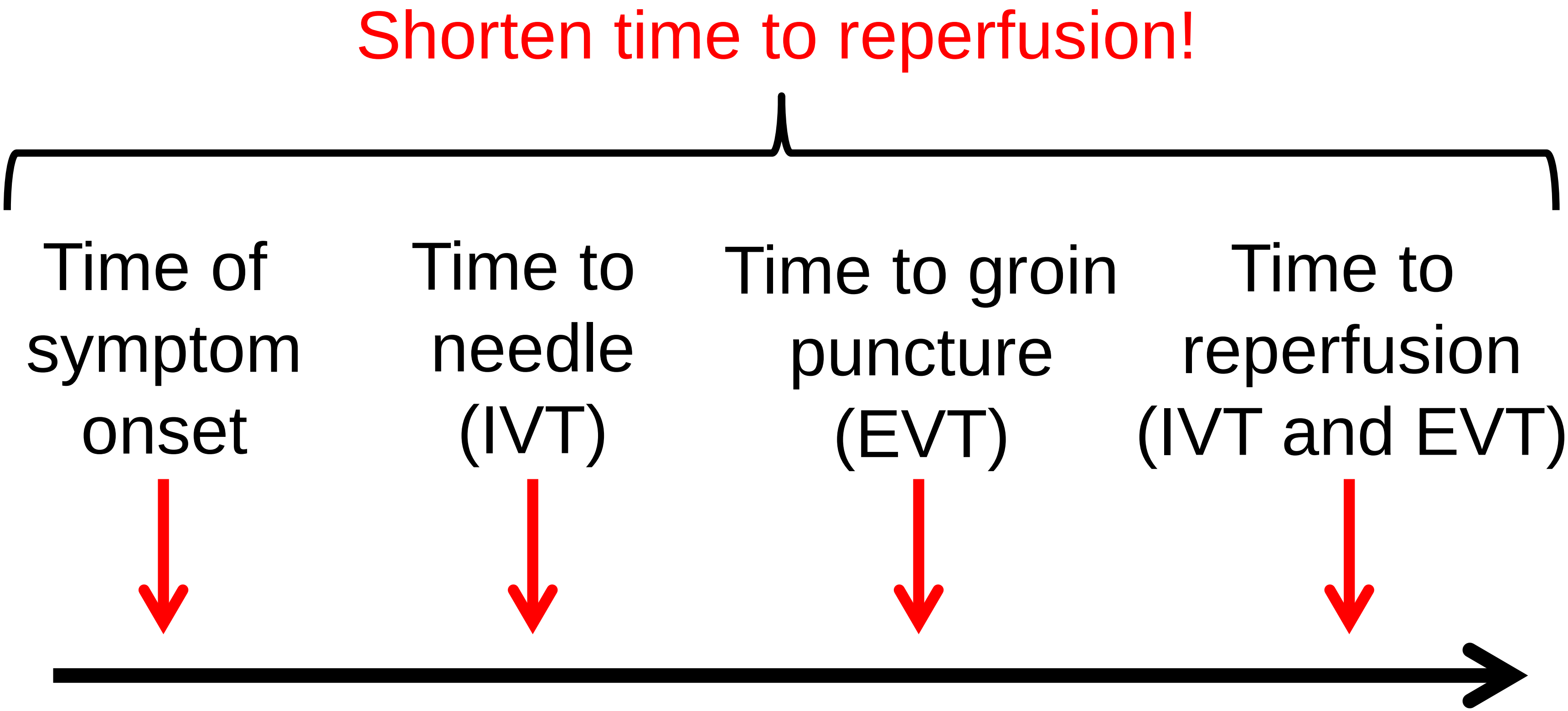


90 Day mRS 0-2 by TLSW to Randomization

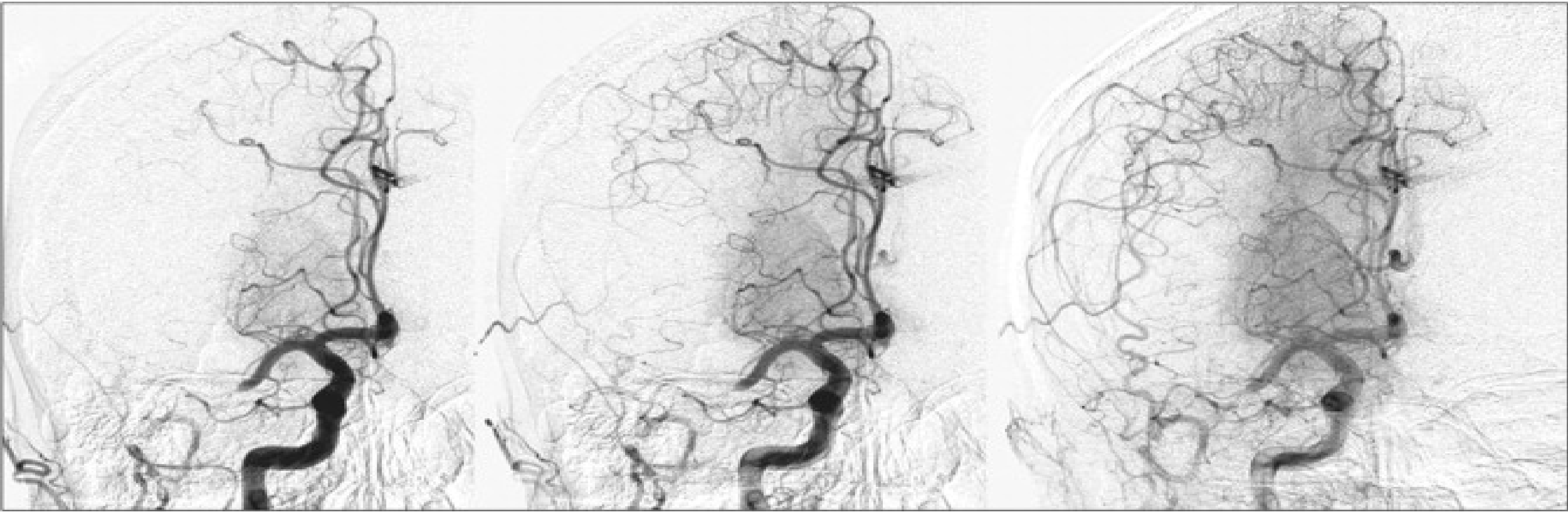
	Trevo	MM	P-value
6-12h	55.1%	20.0%	<0.001
12-24h	43.1%	7.4%	<0.001



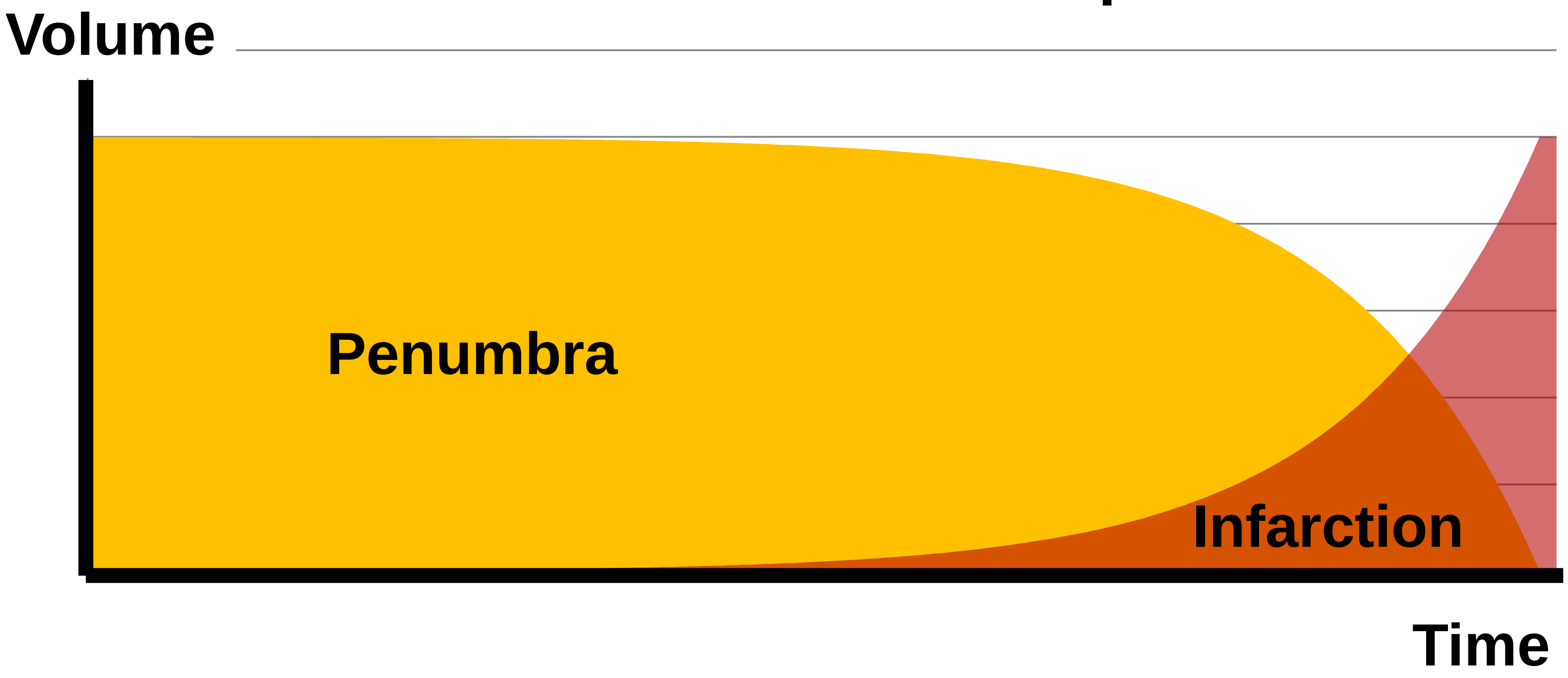
Acute stroke treatment



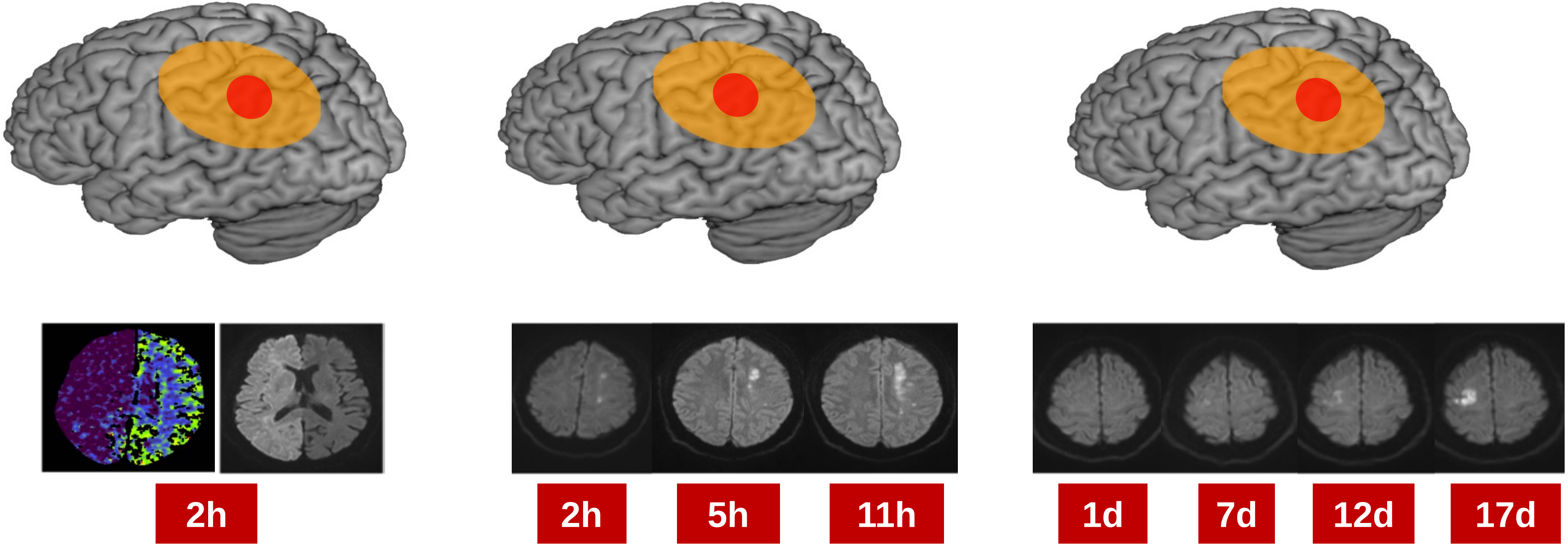
Impact of the collaterals



Time is brain, but collaterals set the pace!



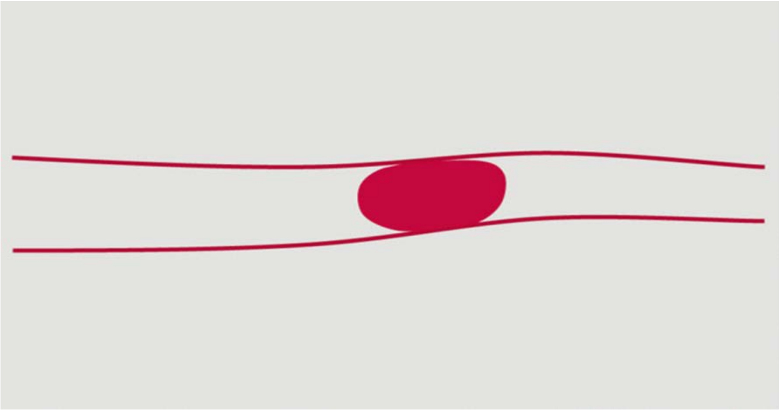
Variablity in infarct growth

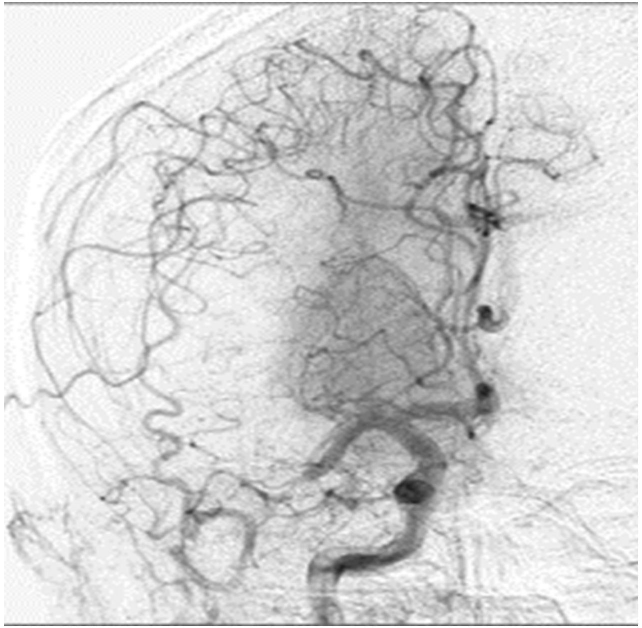


>460 billion neurons/min

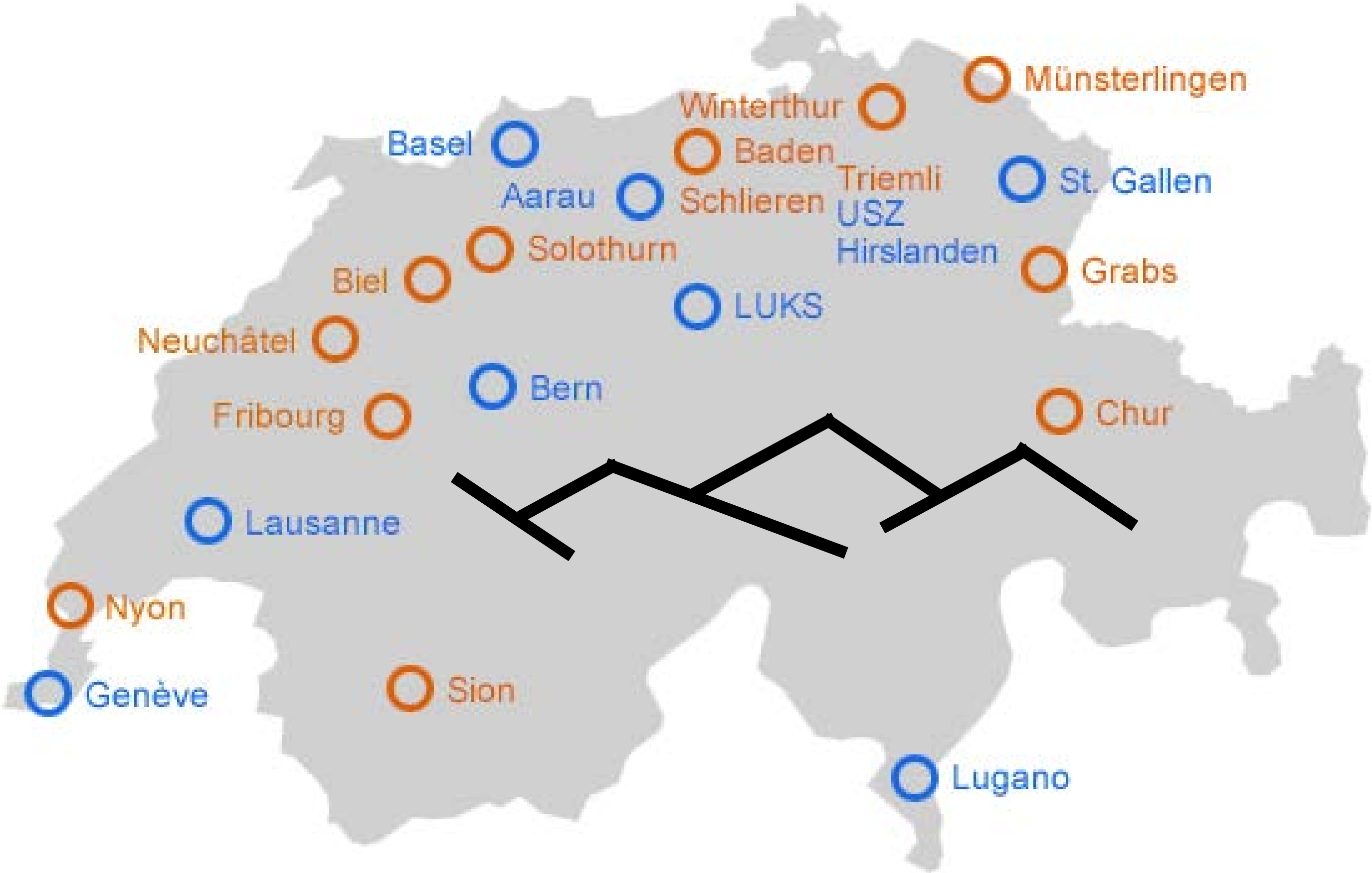
650.000 neurons/min

9000 neurons/min

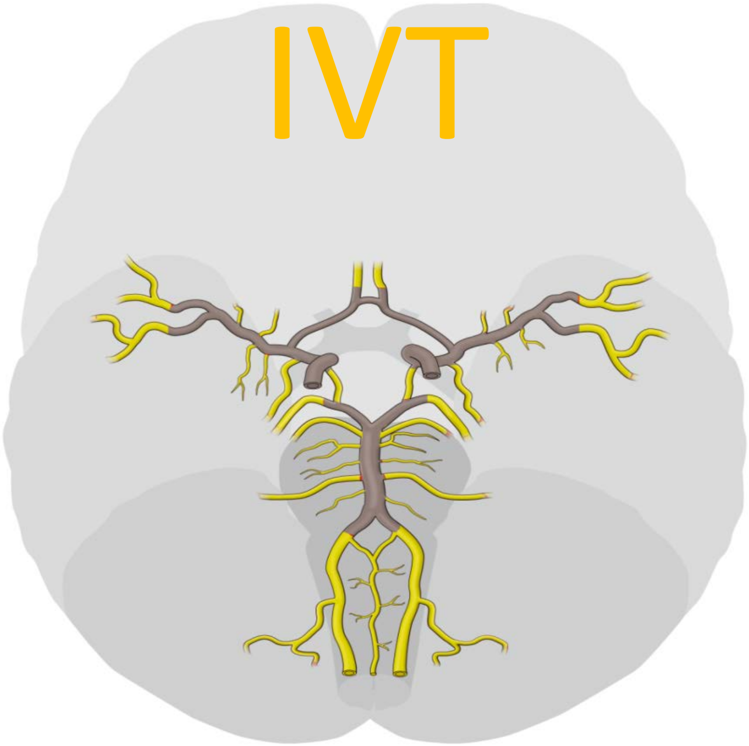


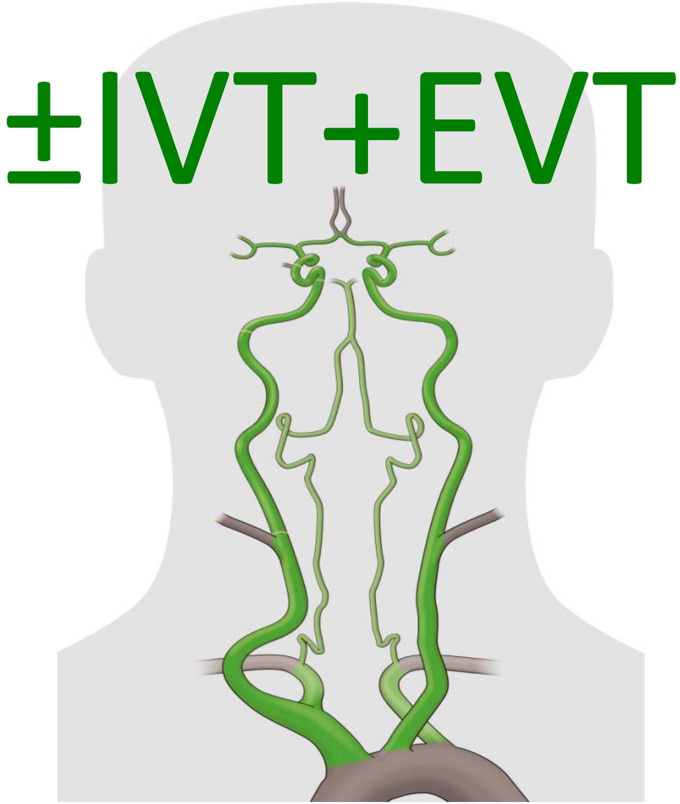


Stroke centers and units



Best candidates for…





Stroke treatment 2018

- To treat patients as soon and effective as possible
- Patients **with** LVO should be immediately transfered to an endovascular stroke center
- Patients **without** LVO should be transfered to the nearest thrombolysing stroke unit

Proportion of patients with LVO ?

Proportion of patients with LVO

24%

Clinical Selection Strategies to Identify Ischemic Stroke Patients With Large Anterior Vessel Occlusion

Results From SITS-ISTR (Safe Implementation of Thrombolysis in Stroke International Stroke Thrombolysis Registry)

Jan F. Scheitz, MD*; Azmil H. Abdul-Rahim, MBChB, Msc(StrokeMed)*;
Rachael L. MacIsaac, PhD; Charith Cooray, MD; Heidi Sucharew, PhD; Dawn Kleindorfer, MD;
Pooja Khatri, MD, MSc; Joseph P. Broderick, MD; Heinrich J. Audebert, MD;
Niaz Ahmed, MD, PhD; Nils Wahlgren, MD, PhD; Matthias Endres, MD;
Christian H. Nolte, MD*; Kennedy R. Lees, MD, FRCP*; on behalf of SITS Scientific Committee

Stroke 2016

CrossMark

31%

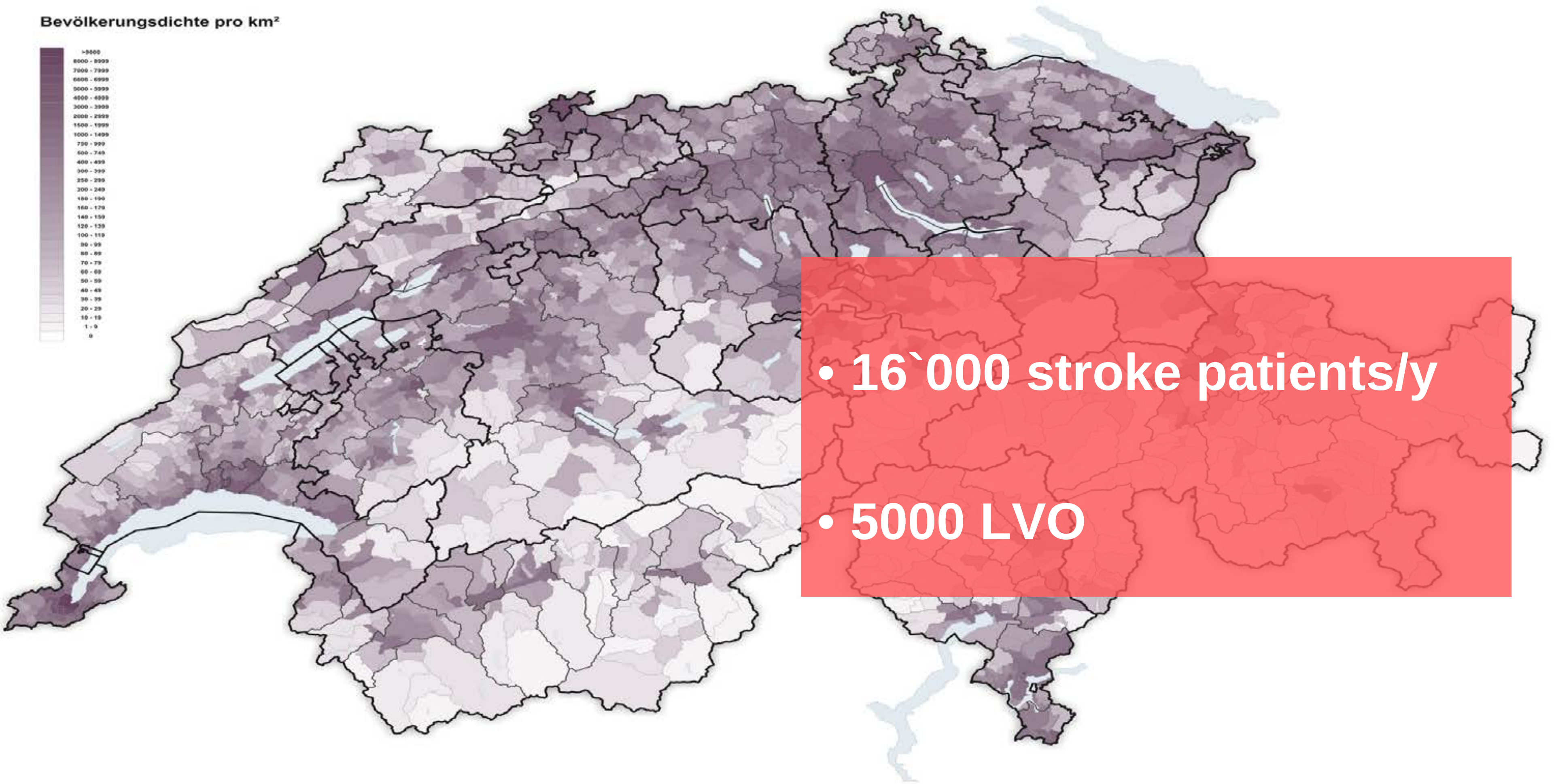
J NEUROL Science 2016

50%

Significance of Large Vessel Intracranial Occlusion Causing Acute Ischemic Stroke and TIA

Wade S. Smith, MD, PhD; Michael H. Lev, MD, FAHA; Joey D. English, MD, PhD;
Erica C. Camargo, MD, MMSc; Maggie Chou; S. Claiborne Johnston, MD, PhD;
Gilberto Gonzalez, MD, PhD; Pamela W. Schaefer, MD; William P. Dillon, MD;
Walter J. Koroshetz, MD; Karen L. Furie, MD, MPH

Stroke 2009



- 16`000 stroke patients/y
- 5000 LVO

Karte: wikipedia

Proportion of patients eligible for EVT ?

Eligibility and Predictors for Acute Revascularization Procedures in a Stroke Center

Peter Vanacker, MD, PhD; Dimitris Lambrou, PhD; Ashraf Eskandari, MD, RN;
Pascal J. Mosimann, MD; Ali Maghraoui, PhD; Patrik Michel, MD

Background and Purpose—Endovascular treatment (EVT) is a new standard of care for selected, large vessel occlusive strokes. We aimed to determine frequency of potentially eligible patients for intravenous thrombolysis (IVT) and EVT in comprehensive stroke centers. In addition, predictors of EVT eligibility were derived.

Methods—Patients from a stroke center–based registry (2003–2014), admitted within 24 hours of last proof of usual health, were selected if they had all data to determine IVT and EVT eligibility according to American Heart Association/American Stroke Association (AHA/ASA) guidelines (class I–IIa recommendations). Moreover, less restrictive criteria adapted from randomized controlled trials and clinical practice were tested. Maximum onset-to-door time windows for IVT eligibility were 3.5 hours (allowing door-to-needle delay of ≤60 minutes) and 4.5 hours for EVT eligibility (door-to-groin delay ≤90 minutes). Demographic and clinical information were used in logistic regression analysis to derive variables associated with EVT eligibility.

Results—A total of 2704 patients with acute ischemic stroke were included, of which 26.8% were transfers. Of all patients with stroke arriving at our comprehensive stroke center, a total proportion of 12.4% patients was eligible for IVT. Frequency of EVT eligibility differed between AHA/ASA guidelines and less restrictive approach: 2.9% versus 4.9%, respectively, of all patients with acute ischemic stroke and 10.5% versus 17.7%, respectively, of all patients arriving within <6 hours. Predictors for AHA–EVT eligibility were younger, shorter onset-to-admission delays, higher National Institutes of Health Stroke Scale (NIHSS), decreased vigilance, hemineglect, absent cerebellar signs, atrial fibrillation, smoking, and decreasing glucose levels (area under the curve=0.86).

Conclusions—Of patients arriving within 6 hours at a comprehensive stroke center, 10.5% are EVT eligible according to AHA/ASA criteria, 17.7% according to criteria resembling randomized controlled trials, and twice as many patients are IVT eligible (36.2%). **(*Stroke*. 2016;47:1844-1849. DOI: 10.1161/STROKEAHA.115.012577.)**

Key Words: cerebral revascularization ■ cerebrovascular occlusion ■ endovascular procedure ■ intravenous thrombolysis ■ stroke

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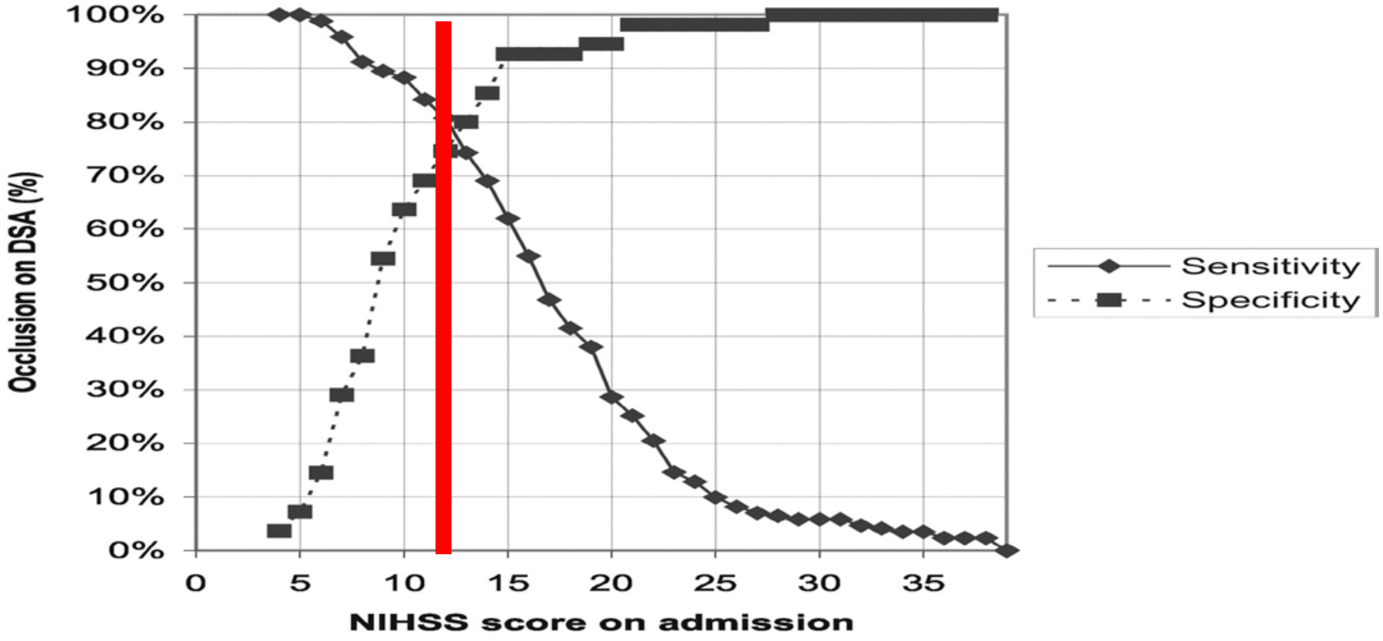
Key Words: cerebral revascularization ■ cerebrovascular occlusion ■ endovascular procedure ■ intravenous thrombolysis ■ stroke

17.7% according to criteria resembling RCTs

Clinical prediction of LVO ?

NIHSS and LVO on DSA



Sensitivity and specificity of NIHSS score on admission of all patients to find a central (ICA, M1, M2, or BA) occlusion on DSA (55 of 226 patients with peripheral occlusion).

Fischer U et al. Stroke 2005;36:2121-2125

NIHSS subitems

Table 3 Odds ratios of different NIHSS subitems predicting large vessel occlusion in acute anterior circulation stroke

	Odds ratio	Univariate 95 % CI	*p*
Best Gaze	9.60	6.765–13.632	<0.0001
Motor arms	7.60	5.589–10.204	<0.0001
Aphasia/neglect	7.13	5.352–9.492	<0.0001
Visual fields	7.00	3.981–12.370	<0.0001
Motor legs	5.78	4.436–7.560	<0.0001
LOC[a] altertness	5.64	3.732–8.522	<0.0001
Facial palsy	5.50	4.044–7.468	<0.0001
LOC[a] commands	4.50	3.287–6.157	<0.0001
LOC[a] questions	4.23	3.248–5.503	<0.0001
Dysarthria	3.20	2.480–4.119	<0.0001
Sensation	2.40	1.865–3.088	<0.0001
Limb ataxia	0.87	0.362–2.074	0.747

Heldner MR, …Fischer U. , J Neurol 2016

Clinical Selection Strategies to Identify Ischemic Stroke Patients With Large Anterior Vessel Occlusion

Results From SITS-ISTR (Safe Implementation of Thrombolysis in Stroke International Stroke Thrombolysis Registry)

Table 3. Sensitivity, Specificity, PPV, and NPV for Presence of LAVO at Certain Cutoffs of the NIHSS, Simplified NIHSS Scores, and NIHSS Symptom Profiles

	n/N (%)	Sensitivity	Specificity	PPV	NPV	Accuracy
Cutoffs of scores with >85% sensitivity and highest possible specificity						
NIHSS≥8	2183/3505 (63.2)	85.6	44.9	28.2	91.3	54.5
NIHSS≥6*	2677/3505 (76.4)	91.3	28.2	28.2	91.3	43.1
FAST≥2	3013/3505 (86.0)	96.6	17.3	26.5	94.3	36.0
FAST=3 or abnormal item best gaze	2410/3505 (68.8)	89.1	37.5	30.6	91.8	49.7
G-FAST≥3	2363/3505 (67.5)	88.7	39.1	31.0	91.8	50.8
C-STAT≥1	2414/3505 (68.9)	88.9	37.3	30.4	91.6	49.5
3I-SS≥1†	2702/3505 (77.1)	91.8	27.5	28.1	91.5	42.7
PASS≥1	3209/3505 (91.6)	97.2	10.2	25.1	92.2	30.7
RACE≥3	2137/3505 (61.0)	85.7	46.7	33.2	91.4	55.9
NIHSS profile A–E (at least PACS or worse) vs profile F	3155/3505 (90.0)	97.2	12.2	25.5	93.4	32.3
Cutoffs of scores with specificity >75% and highest possible sensitivity						
NIHSS≥14	1133/3505 (32.3)	63.1	77.2	46.1	87.1	73.9
G-FAST=4	1029/3505 (29.4)	56.7	79.0	45.5	85.5	73.7
C-STAT≥3	1051/3505 (30.0)	58.3	78.8	45.9	85.9	73.9
3I-SS=3†	383/3505 (10.9)	20.7	92.1	44.6	79.0	75.3
PASS=3	689/3505 (19.7)	38.5	86.2	46.2	81.9	74.9
RACE≥6	1154/3505 (32.9)	62.2	76.1	44.5	86.7	72.8
NIHSS profile A	793/3505 (22.6)	38.5	82.3	40.1	81.2	72.0
NIHSS profile B	775/3505 (22.1)	37.5	82.6	40.0	81.1	72.0

Stroke. 2017;48:290-297

Clinical Selection Strategies to Identify Ischemic Stroke Patients With Large Anterior Vessel Occlusion

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G-FAST≥3	2363/3505 (67.5)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
C-STAT≥1	2414/3505 (68.9)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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False positiv rate

False negativ rate

Stroke. 2017;48:290-297

Problem with scores

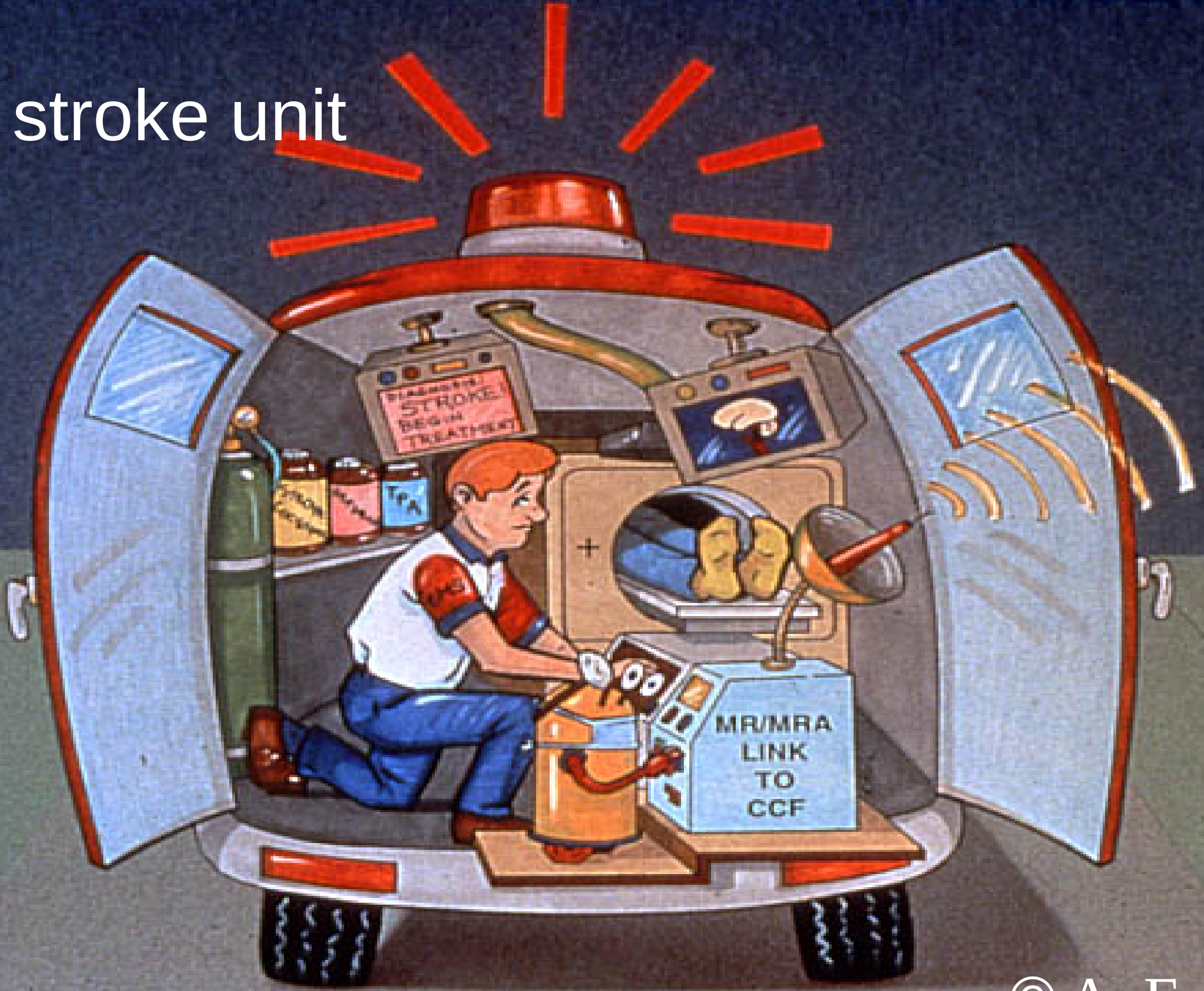
- Most scores not tested for **paramedics**
- Most scores <u>not</u> tested in the **prehospital setting** (only RACE has been validated)
- Most scores tested in patients with **ischaemic stroke only**
- If **specifity** is high **sensitivity** is low, and vice versa
- Stroke is <u>not</u> a stable disease! Clots are a moving target…

Models of prehospital stroke management

Models of prehospital patient management

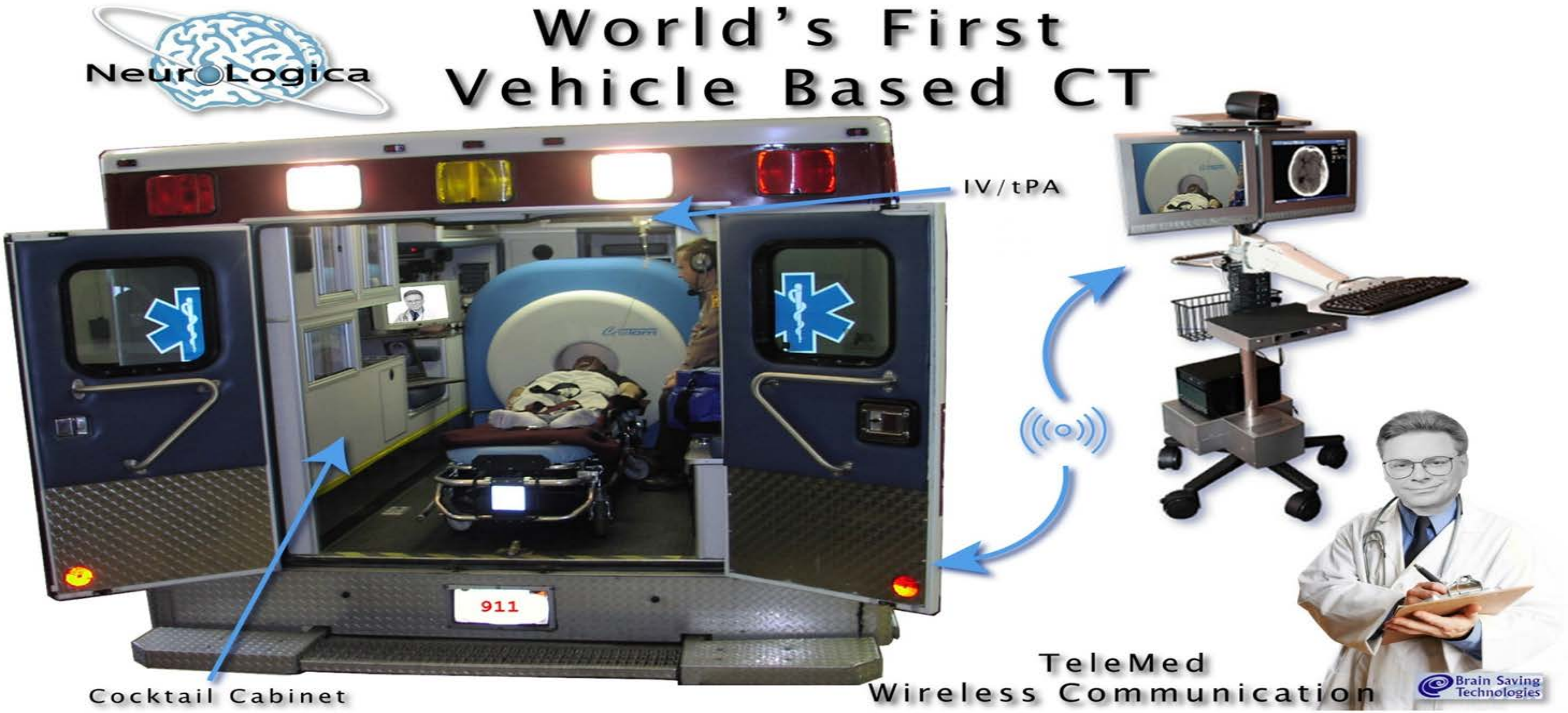
1. Drip and ship
2. Ship (Mothership)
3. Drip and drive
4. Mobile stroke unit

4. Mobile stroke unit



1986 CCF

World's First Vehicle Based CT



Mobile stroke units for prehospital thrombolysis, triage, and beyond: benefits and challenges

Klaus Fassbender, James C Grotta, Silke Walter, Iris Q Grunwald, Andreas Ragoschke-Schumm, Jeffrey L Saver

Lancet Neurol 2017; 16: 227–37

This online publication has

In acute stroke management, time is brain. Bringing swift treatment to the patient, instead of the conventional approach of awaiting the patient's arrival at the hospital for treatment, is a potential strategy to improve clinical

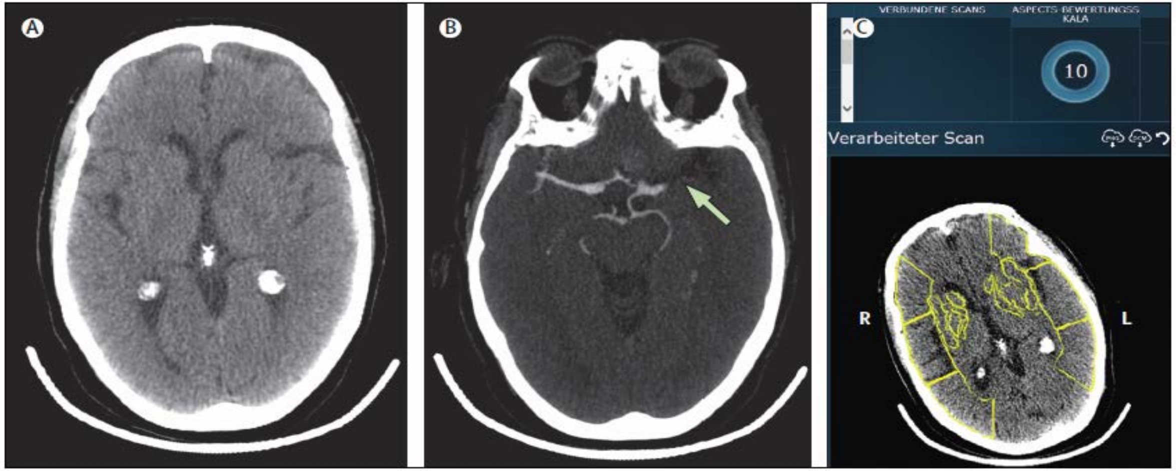
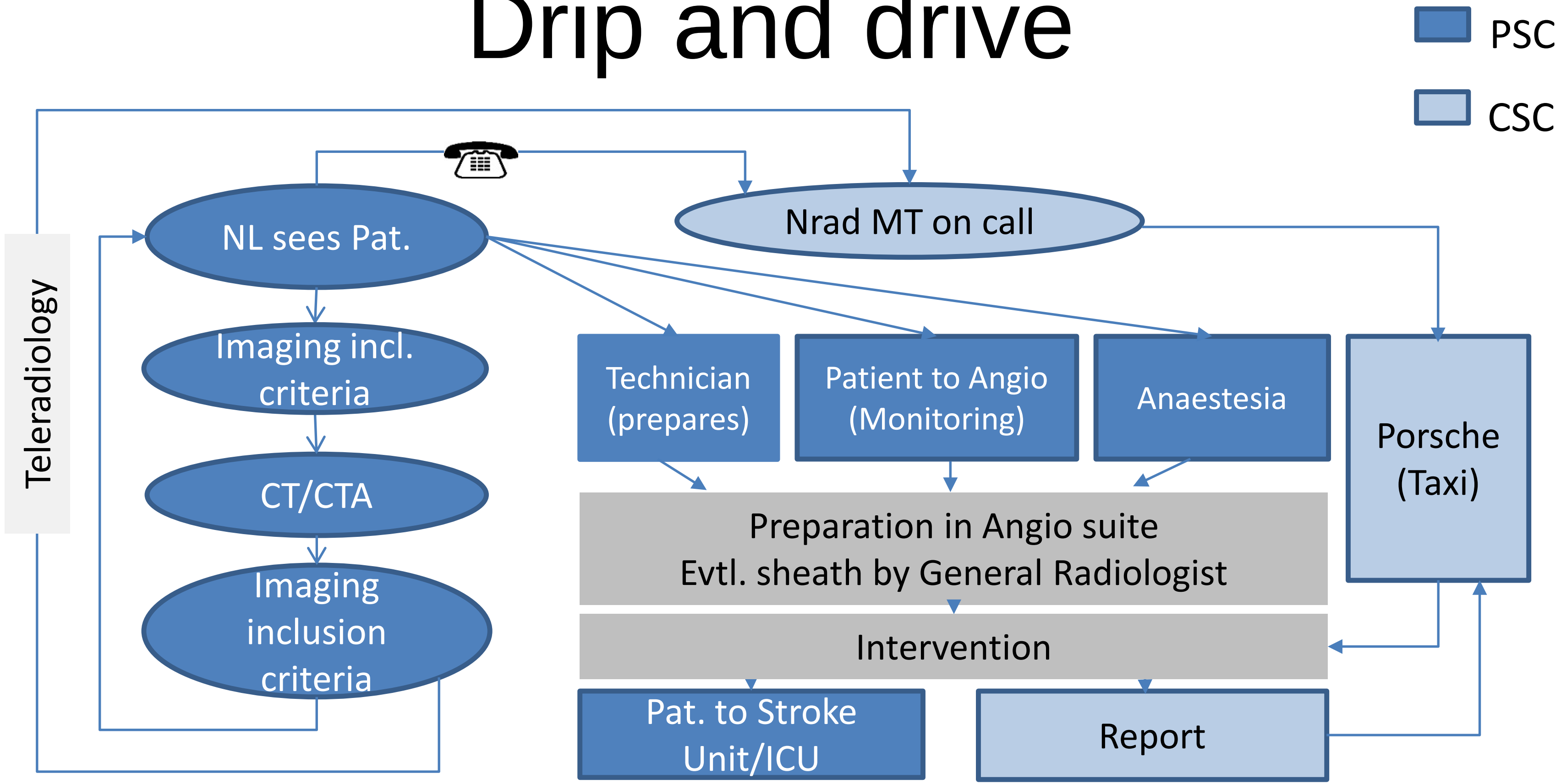


***Figure 2:* Multimodal imaging in a mobile stroke unit**
Non-contrast CT (A), CT angiography (B), and ASPECTS (C) done in a mobile stroke unit of a 73-year-old woman with acute right hemiparesis. Although the parenchyma shows no signs of infarction (ASPECTS 10), CT angiography allowed prehospital diagnosis of an occlusion of the left middle cerebral artery (B, arrow). Reproduced from Grunwald et al,[43] by permission of *Cerebrovascular Diseases* (Karger). ASPECTS=Alberta Stroke Program Early CT Score.

3. Drip and drive

Drip and drive



Brekenfeld et al., unpublished

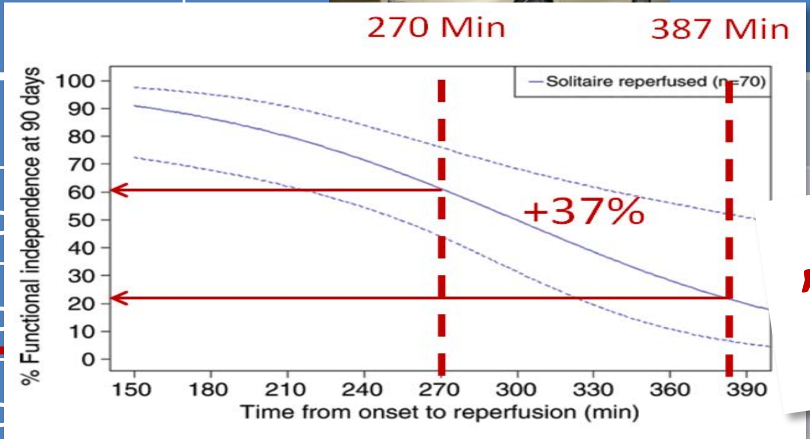
Hamburg: „Drip-and-Drive “ vs. „Drip-and-ship“

							P-Value
	N	Median (min.)	IQR (min.)	N	Median (min.)	IQR (min.)	
CT-ARR	40	**121**	108-134	32	**181**	157-219	<0.0001
O-DSA	31	88	59-124	23	84	67-100	NS
CT-DSA	41	**123**	93-147	23	**252**	228-275	<0.0001
CT-call	40	37	24-54	22	40	29-54	NS
O-R	22	**270**	249-319	11	**387**	368-416	<0.001

n=15

Brekenfeld, C et al. submitted, 2017

Hamburg: „Drip-and-Drive “ vs. „Drip-and-ship“



							P-Value
				N	Median (min.)	IQR (min.)	
C							
C							NS
C				23	**252**	228-275	<0.0001
CT-call	40	37	24-54	22	40	29-54	NS
O-R	22	**270**	249-319	11	**387**	368-416	<0.001

„Drip and drive“ saves 2h
(in Hamburg)

n=15

Brekenfeld, C et al. submitted, 2017

Models of prehospital patient management

1. Drip and ship
2. Ship (Mothership)
3. ~~Drip and drive~~
4. ~~Mobile stroke unit~~

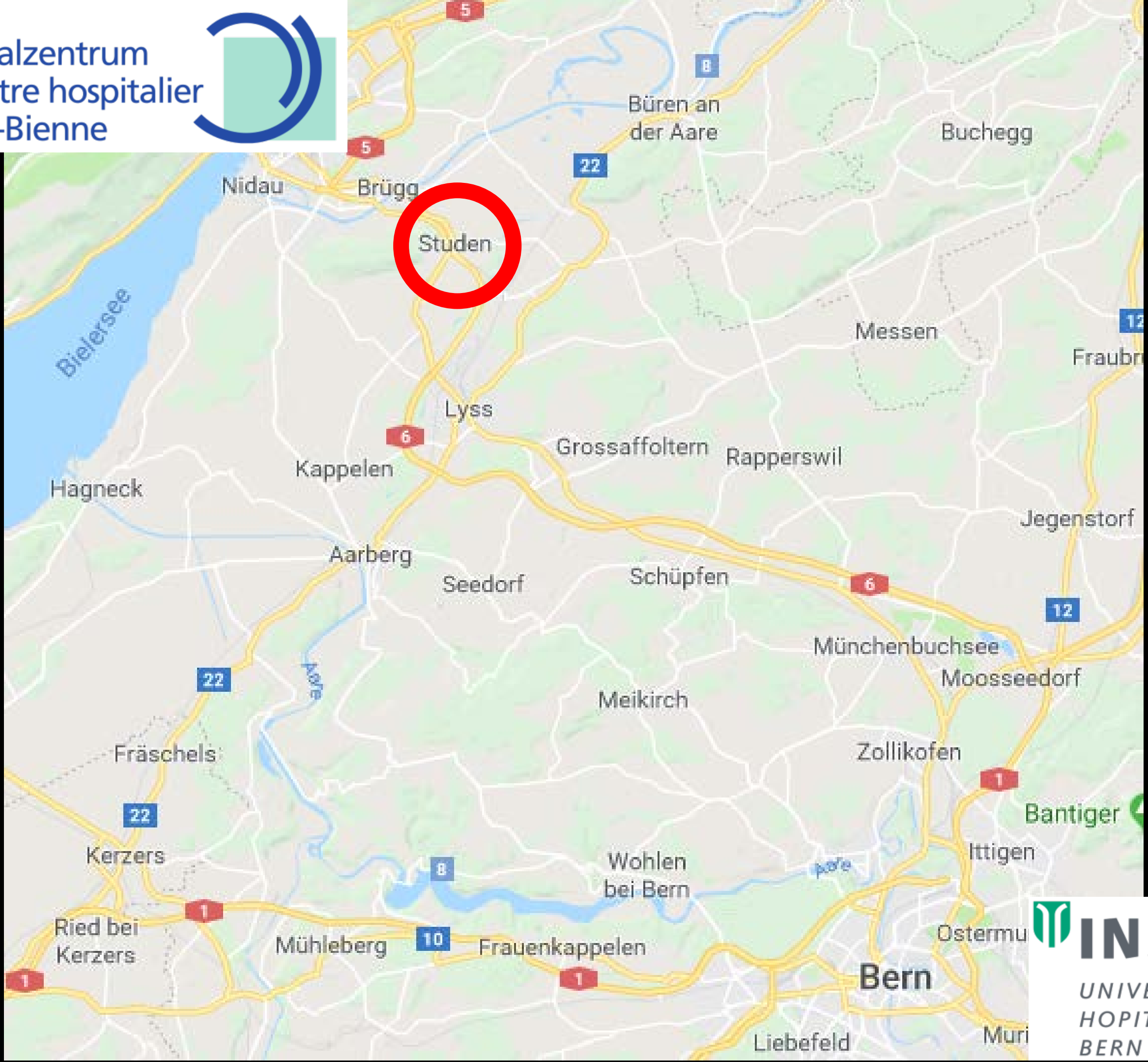
Spitalzentrum
Centre hospitalier
Biel-Bienne

Female

55 years

144 called
45 minutes
after symtom
onset

NIHSS 16



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Spitalzentrum
Centre hospitalier
Biel-Bienne

Female

55 years

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after symtom
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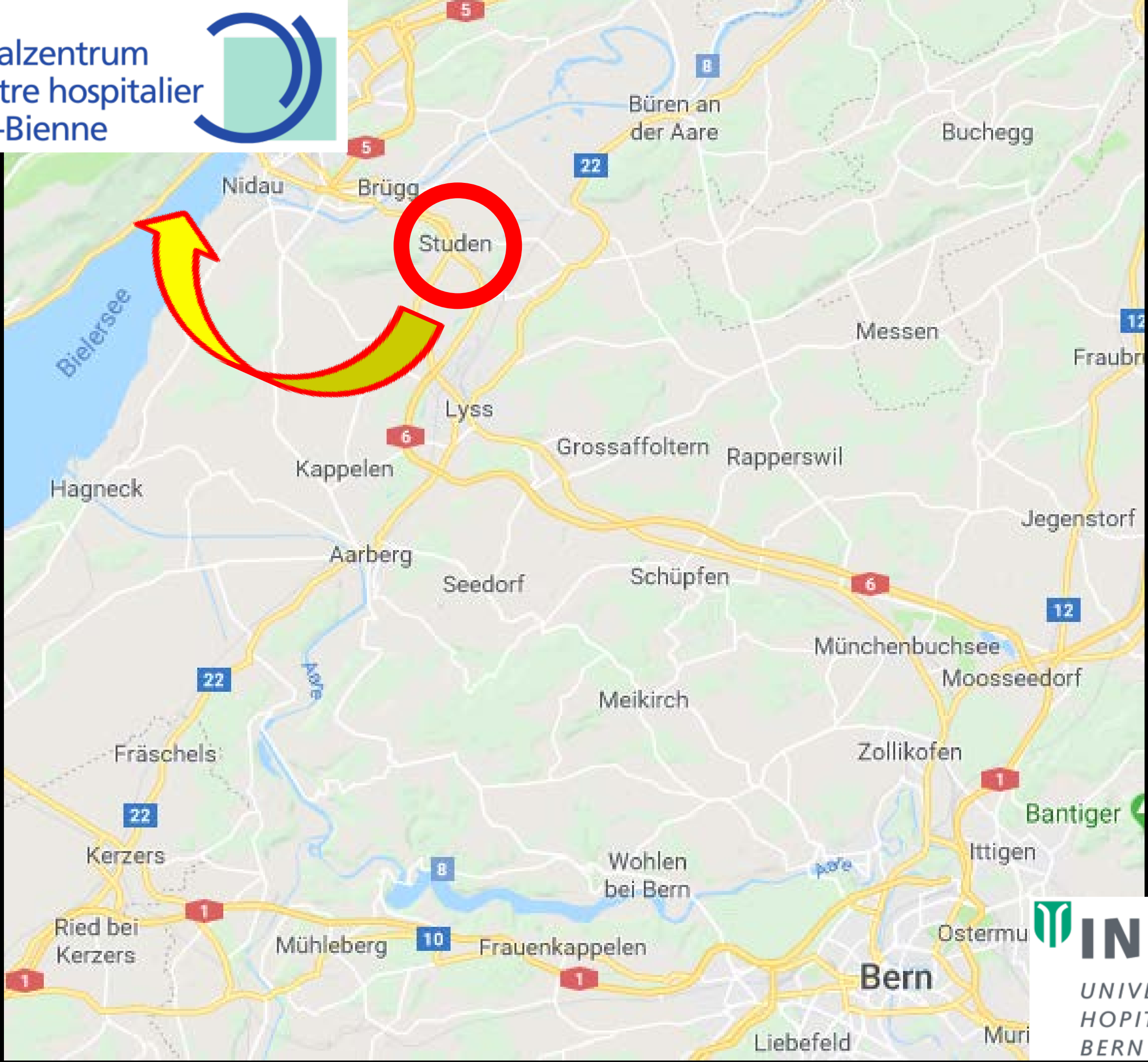

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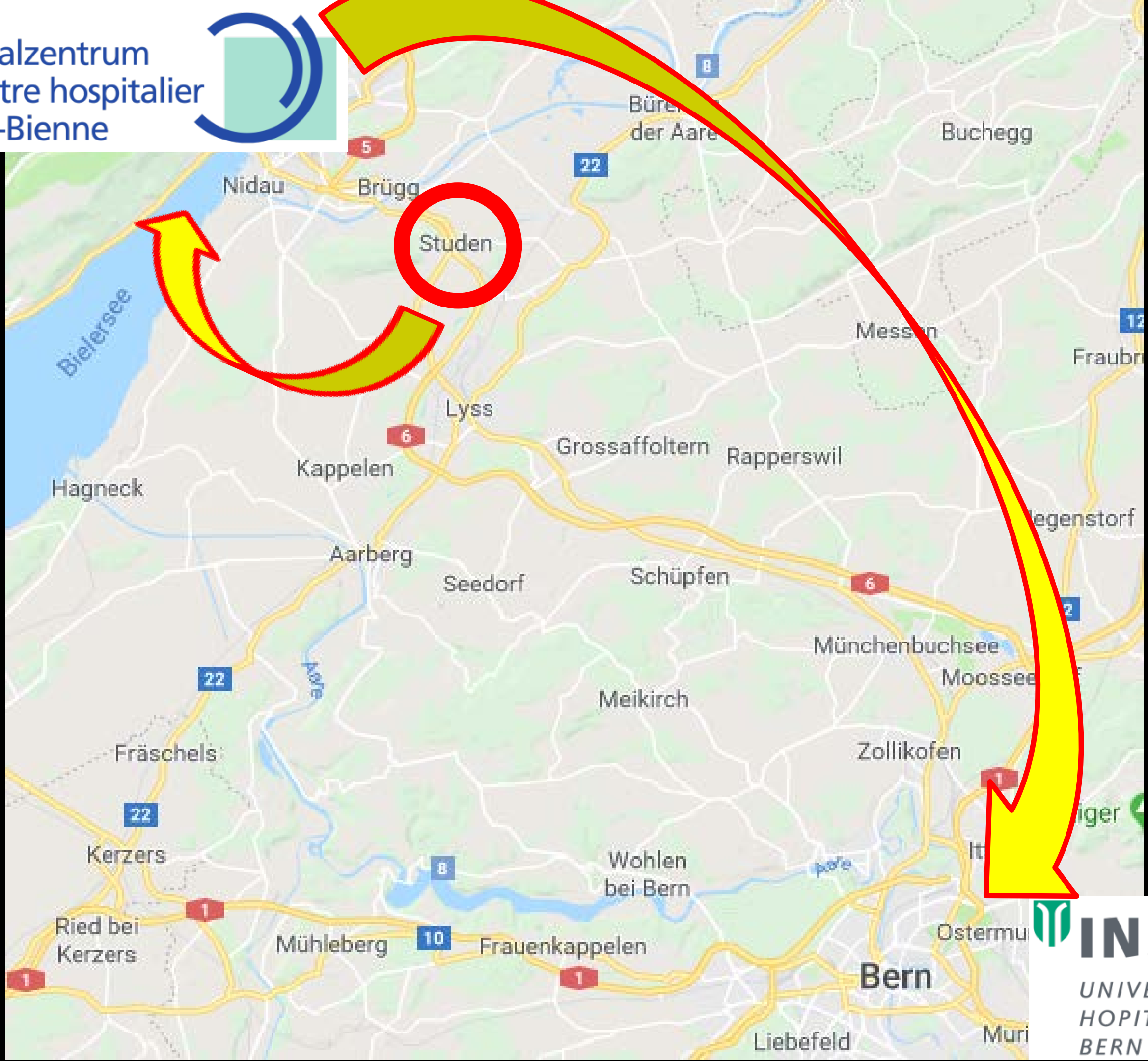

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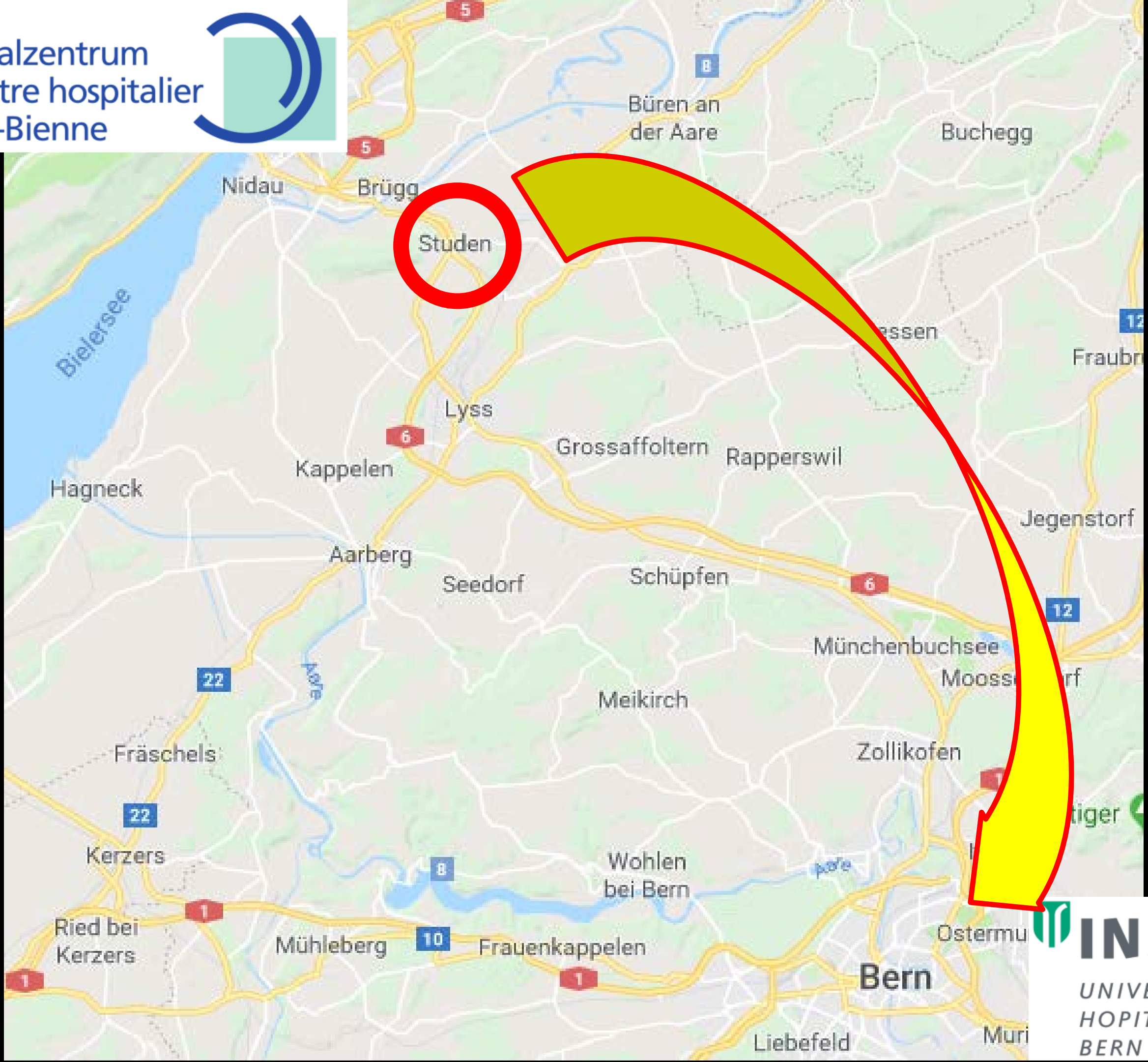

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Arguments

Drip and ship

Mothership

Advantages

- Earlier initiation of IVT
- Improved patient selection
- Higher proportion of IVT
- Preinterventional recanalisation

Disadvantages

- Delayed time to reperfusion
- Resources

Arguments

Drip and ship

Advantages

- Earlier initiation of IVT
- Improved patient selection
- Higher proportion of IVT
- Preinterventional recanalisation

Disadvantages

- Delayed time to reperfusion
- Resources

Mothership

Advantages

- Earlier initiation of EVT
- Shorter time to reperfusion
- Higher proportion of EVT

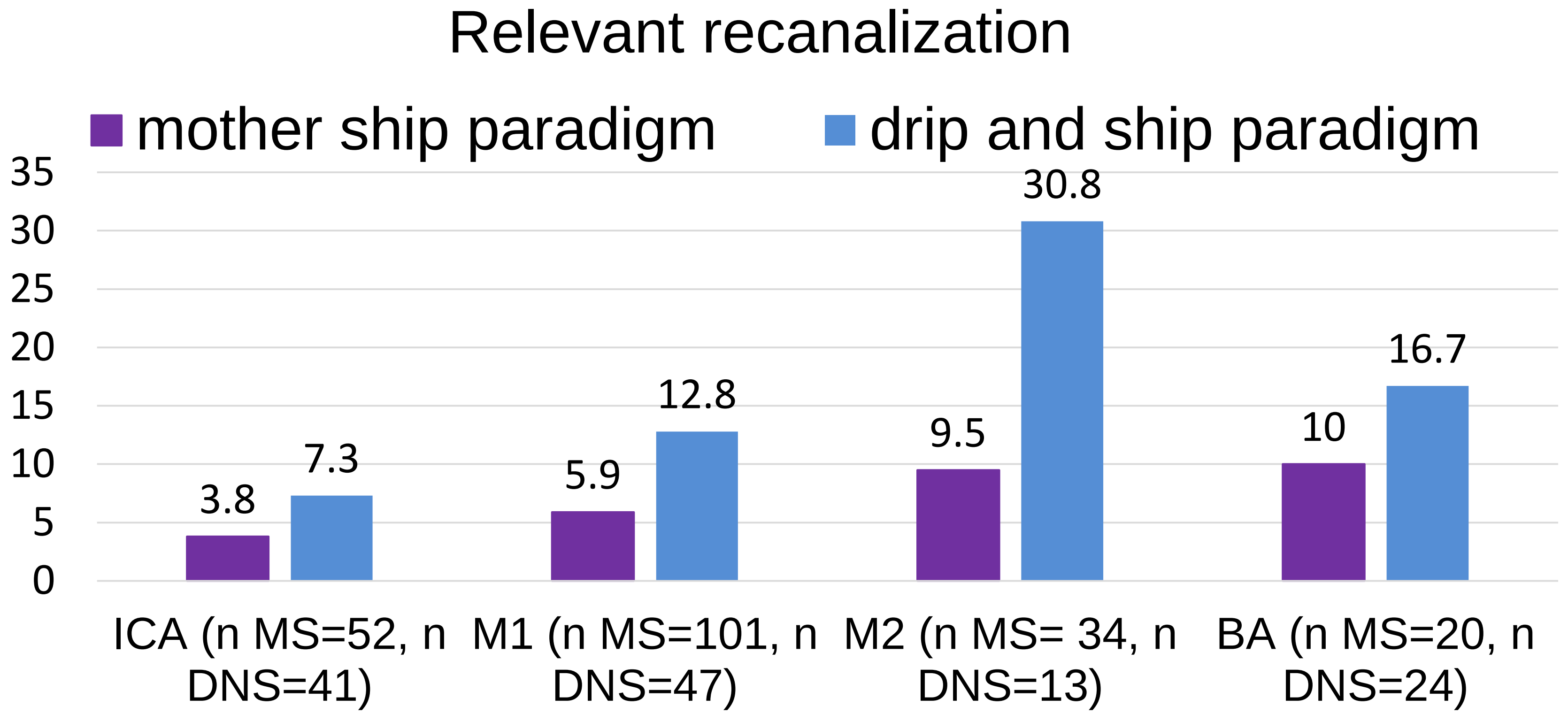
Disadvantages

- Delay (or even deny) of IVT
- Transfer of ineligible EVT patients (futile transports)
- Resources

Prioritize EVT?

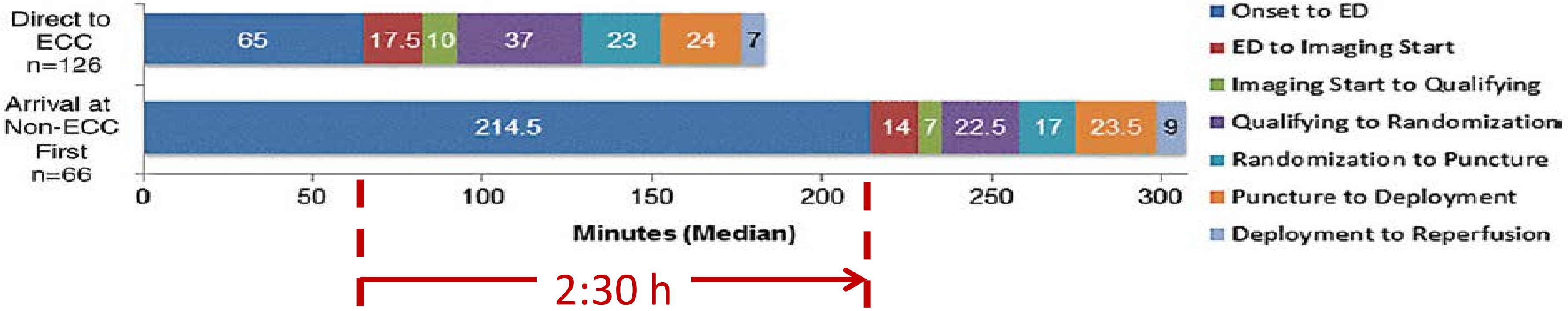
Prioritize IVT?

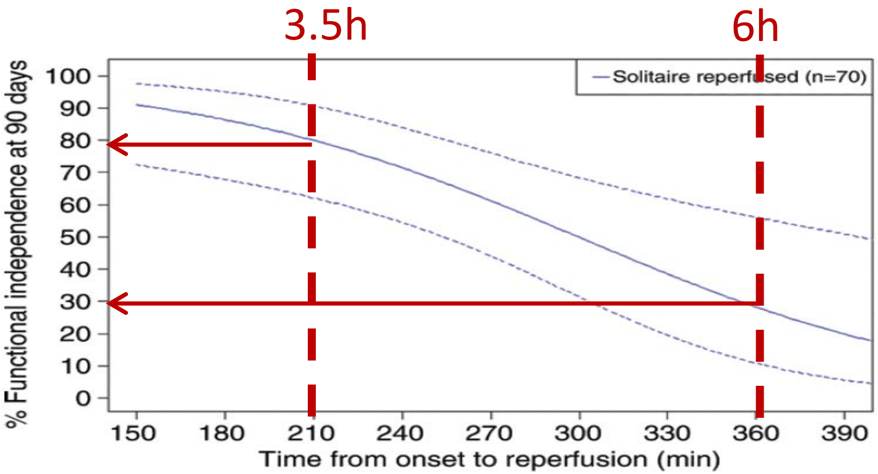
Intention to bridge (319 patients)



S. Jung et al. EJoN

Delay by Non-Endovascular-capable center?





Goyal, M et al. Radiology 2016 ePub

STRATIS: Systems of care study

- **Hypothesis:** Interhospital transfer from a community hospital to an endovascular-capable center may result in treatment delays and worse clinical outcomes compared to direct presentation.

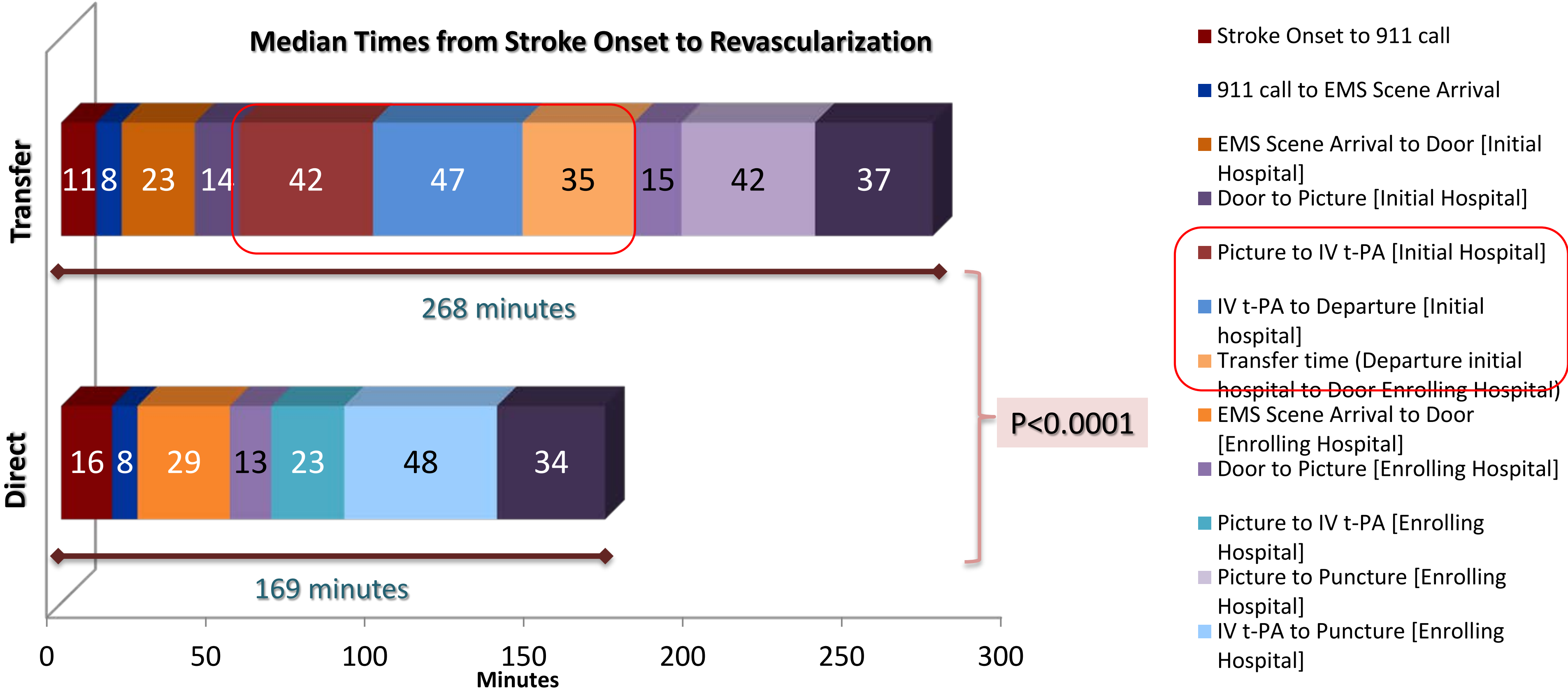
- **We assessed:**

1. real-world time metrics of stroke care delivery

2. outcome differences between direct and transfer patients undergoing mechanical thrombectomy based on 90d mRS

3. the potential impact of local hospital bypass

Time differences for tPA + MT

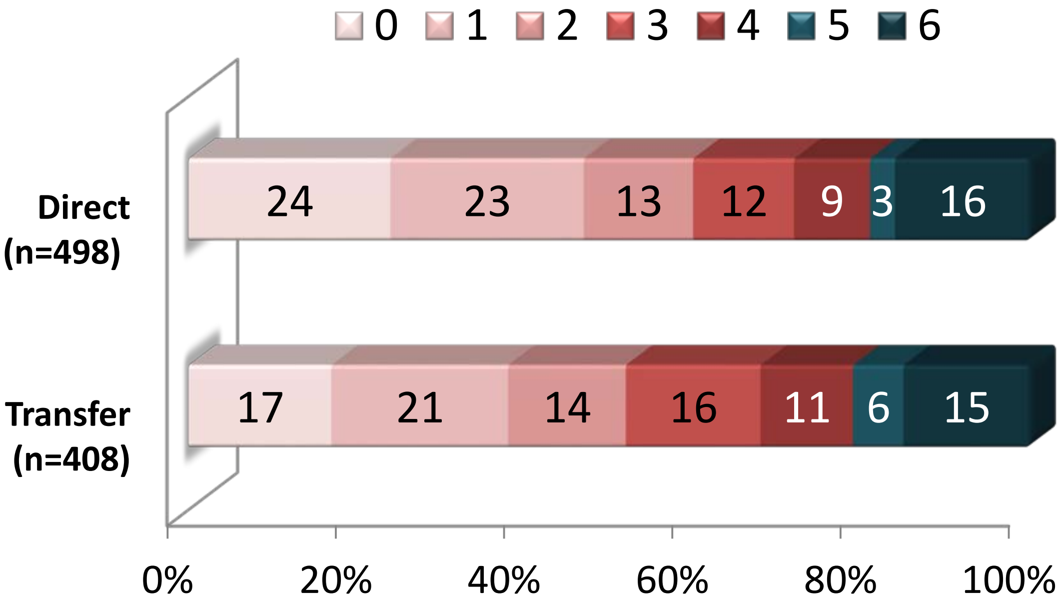


Outcome at 90 days

mRS 0-2:
- **60.0% direct**
- **52.2% transfer**
- OR 1.38 (1.06-1.79)

mRS 0-1:
- **47.4% direct**
- **38.0% transfer**
- OR 1.47 (1.13-1.92)

Mortality:
- **15.0% direct**
- **13.7% transfer**
- p=0.56



Shift analysis favored direct presentation (p=0.012 by Cochran-Mantel-Haenszel test).

STRATIS conclusions

- Interhospital transfer was associated with
  - significant **delays to treatment**, and
  - significantly **lower chance of good outcome**.

- Strategies to facilitate more rapid identification of LVO and direct routing to endovascular centers for some severe stroke patients may help to improve outcomes

Drip and ship

or

mothership ?

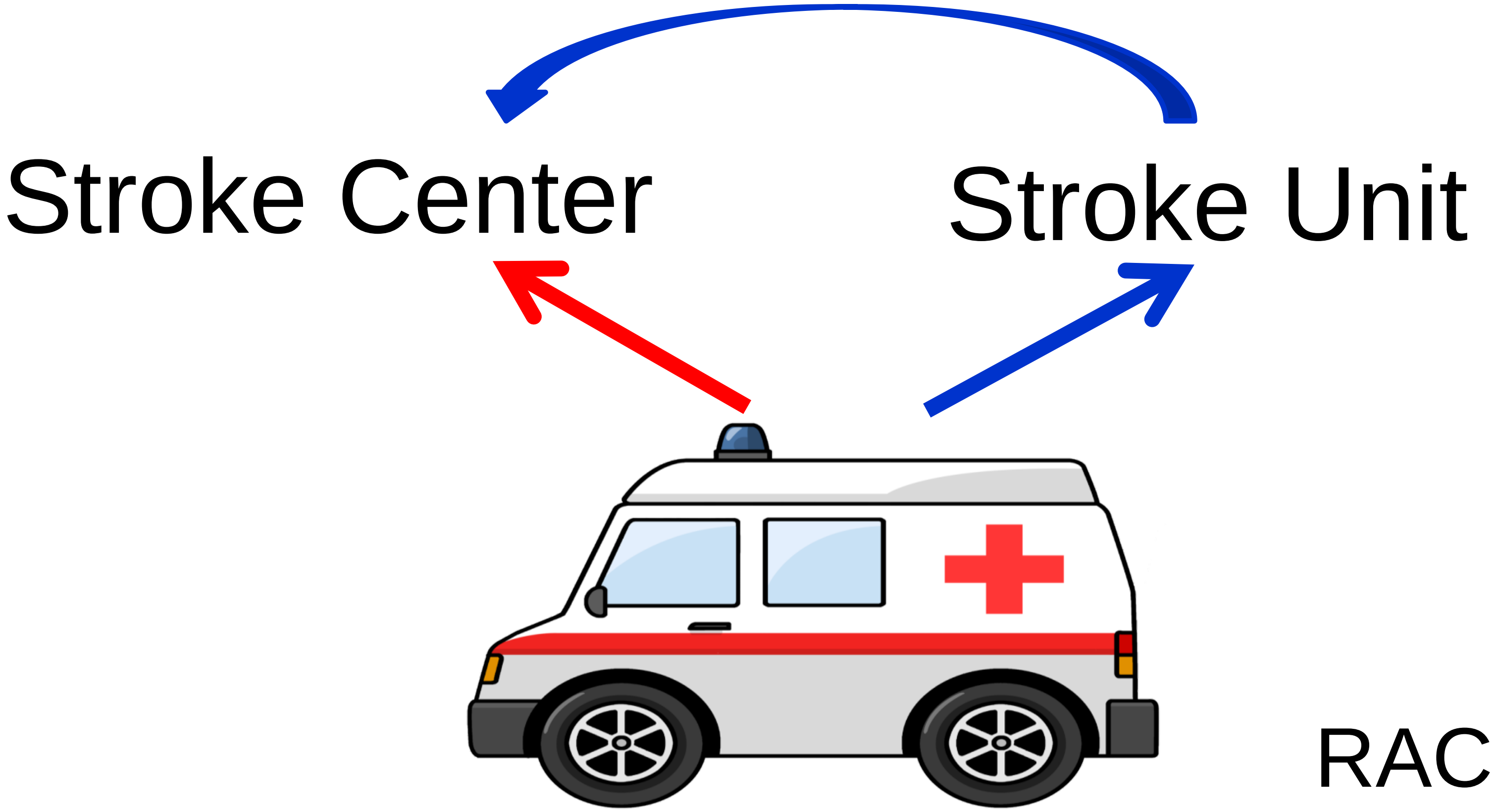
Randomized controlled trial!

Stroke Center

Stroke Unit

RACECAT

Randomized controlled trial!



RACECAT

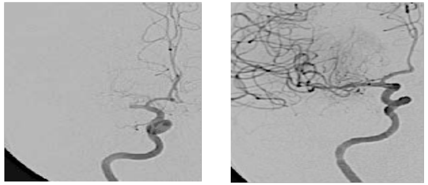
RACECAT (NCT02795962)

A Trial Comparing TRAnsfer to the Closest Local Stroke Center vs Direct Transfer to Endovascular Stroke Center of Acute Stroke Patients with Suspected Large Vessel Occlusion in the Catalan Territory.

- Prospective, multicenter, academic trial (unrestricted grant from Medtronic)
- Cluster randomized, controlled (pre-established temporal sequence)
- Acute stroke patients with suspected acute large vessel occlusion identified by EMS
- Two strategies will be compared:

A — Local Stroke Center (+/- iv tPA)

B — EVT Stroke Center (+/- iv tPA)



Perez de la Ossa N, Ribó M, Abilleira S. 2016

EUROPEAN STROKE JOURNAL

Guideline

European Stroke Journal
0(0) 1–8

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DOI: 10.1177/2396987317699144
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Recommendations from the ESO-Karolinska Stroke Update Conference, Stockholm 13–15 November 2016

Niaz Ahmed[1,2], Thorsten Steiner[3,4], Valeria Caso[5] and Nils Wahlgren[2]; for the ESO-KSU session participants*

A

B. Mechanical thrombectomy: 'Drip and ship' or 'load and go'?

For patients with a suspected LAO based on current clinical tools on field, there is uncertainty about the equipoise between drip and ship (that prioritizes early IVT and other standard of care therapies) and mother-ship (that prioritizes early endovascular thrombectomy) models. Data based on randomized controlled trials are needed to determine the most beneficial model for each particular patient (eligible or not for iv-tPA) in different geographical regions and to establish isochrones where a particular model may be beneficial (Grade C).

B

B. Mechanical thrombectomy: 'Drip and ship' or 'load and go'?

In the absence of evidence, for patients considered eligible to IVT in the field, if estimated transfer time to the nearest primary stroke centre is considerably shorter than time to a comprehensive stroke centre (approximately more than 30–45 min), the drip and ship model should be considered (Grade C).

B. Mechanical thrombectomy: 'Drip and ship' or 'load and go'?

C

In the absence of evidence, in a scenario where a primary stroke centre and comprehensive stroke centre are equidistant (approximately not more than 30–45 min apart) or when contraindications to IVT are known in the field, patients with suspected LAO in the field, should be considered for transfer directly to a comprehensive stroke centre, bypassing any closer primary stroke centres (Grade C).

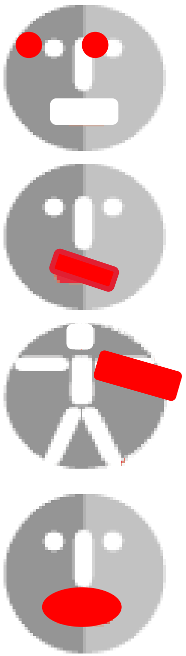
B. Mechanical thrombectomy: ‘Drip and ship’ or ‘load and go’?

D

In case of primary admission to a primary stroke centre, evaluation and treatment for patients with a possible LAO must be expeditious, to ensure a rapid secondary transfer to a comprehensive stroke centre, avoiding any sources of delay such as complex neuroimaging studies (i.e. perfusion studies) or waiting for effect of IVT. First picture to puncture time should be less than 90 min (Grade A).

What should
we do in
Switzerland ?

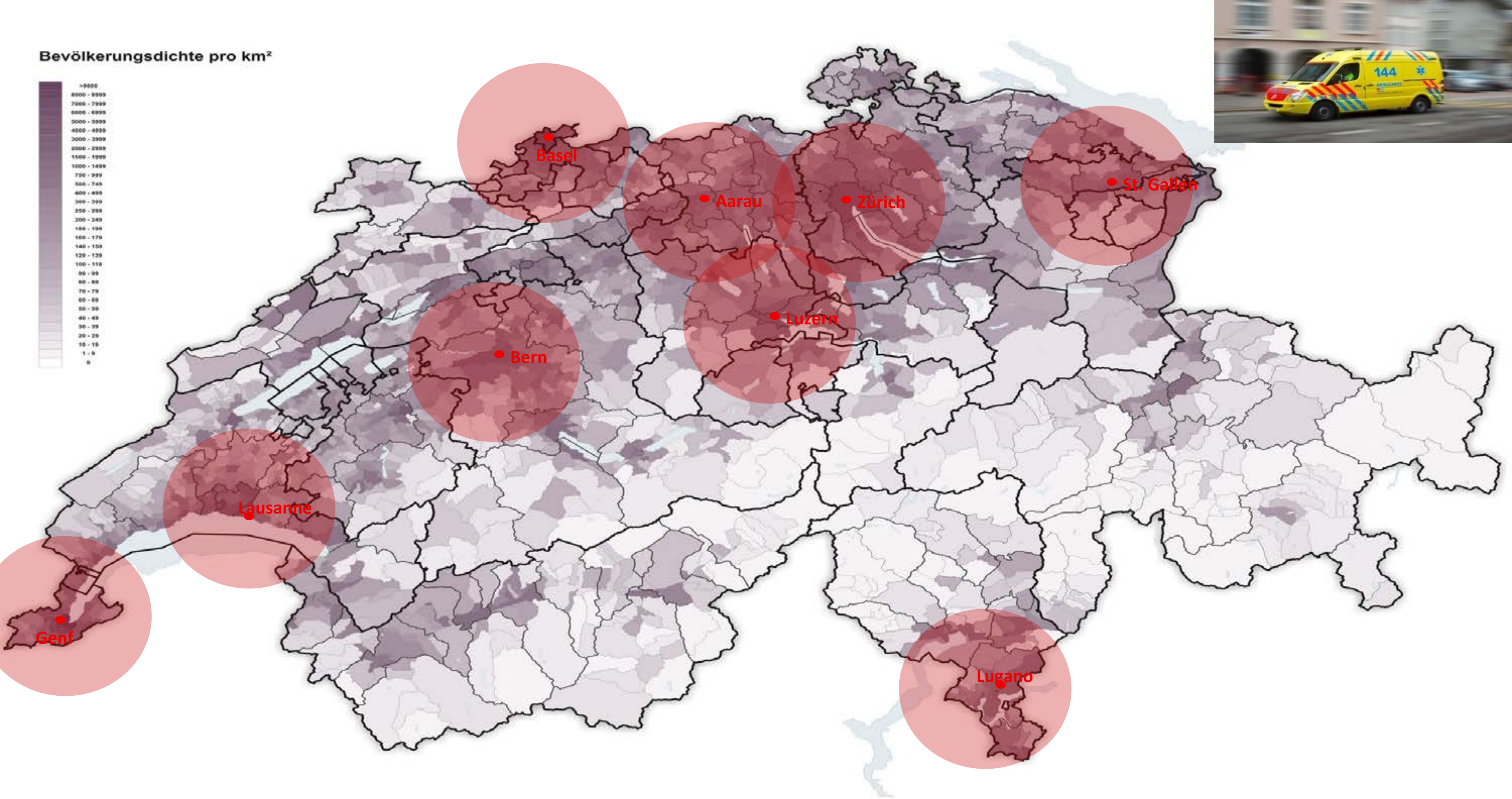
Score to identify LVO
Gaze-Face-Arm-Speech-Time



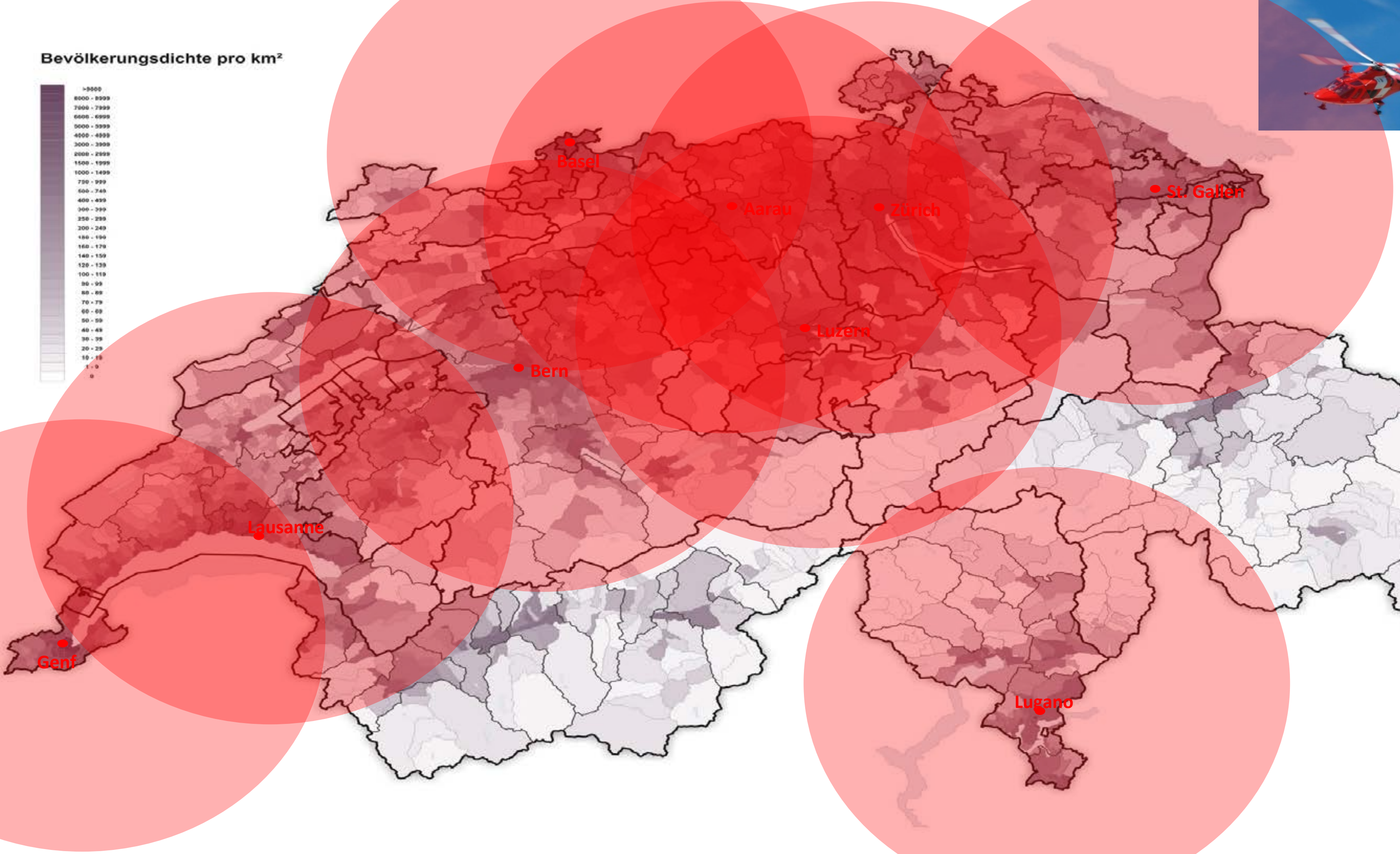
Gaze deviation	1
Face weakness	1
Arm weakness	1
Speech / language problem	1

Ideal candidates for direct transport

- High suspicion of LVO
- Time from symptom onset >4h and <24 hours
- Contraindications for IVT
  - Unknown time of symptom onset
  - Wake-up and siesta stroke
  - (N)OAC therapy
  - Prior surgery
  - Etc.



Karte: wikipedia



Karte: wikipedia

Conclusions

- No randomised evidence which prehospital model should be preferred
- Time is brain: shorten time to reperfusion
  - Stroke patients should be transferred as fast as possible (also after 4.5 hours!)
- Scores can help to identify patients with LVO
- Future:
  - Prehospital identification of LVO (ambulance)
  - Evidence needed for individualised treatment decisions

Thanks to

- Patrik Michel
- Simon Jung
- Marcel Arnold
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- Johannes Kaesmacher
- Mirjam Heldner
- Jan Gralla
- Jens Fiehler, Caspar Brekenfeld, Michael Froehler, Tudor Jovin, etc.

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