Leçons pratiques apprises des registres AVC

Thrombolysis, Thrombectomy

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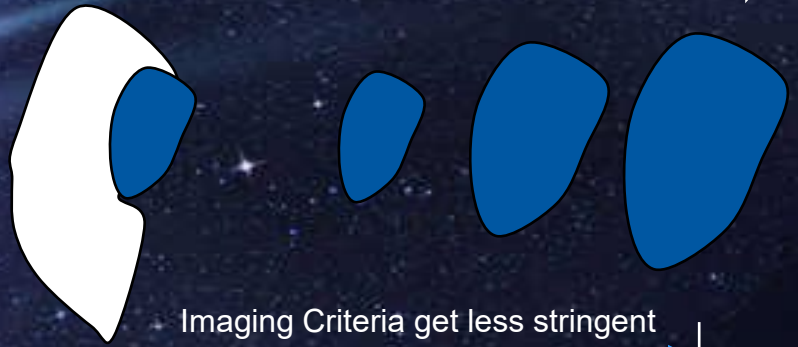
ASTRAL

The Acute STroke Registry and Analysis of Lausanne (ASTRAL): Design and Baseline Analysis of an Ischemic Stroke Registry Including Acute Multimodal Imaging
Patrik Michel, Céline Odier, Matthieu Rutgers, Marc Reichhart, Philippe Maeder, Reto Meuli, Max Wintermark, Ali Maghraoui, Mohamed Faouzi, Alexandre Croquelois and George Ntaios
Stroke 2010;41:2491-2498; originally published online Oct 7, 2010;

Day of birth: 2002 “A moment of joy, of thankfulness to patients/their next-of-kin/physicians/nurses/scientists/students and scientist for their tireless support, and of hope to continue to improve patient care and outcomes”
Full Name: The **A**cute **ST**roke **R**egistry and **A**nalysis of **L**ausanne

Ready to Treat All ?

Parents:
Papa (idea, promotor): Patrik Michel
Moral, data and scientific support : George Ntaios, Céline Odier, Matthieu Rutgers, Marc Reichhart
Radiologists : Philippe Maeder, Reto Meuli, Max Wintermark
Technical support: Ali Maghraoui, Alexandre Croquelois
Statistics: Mohamed Faouzi
Acronym «ASTRAL» invented by Matthieu Rutgers
(Belgian fellow, later president of Belgian Stroke Council)



Era of Darkness
IVT (3 hours) 2005
IVT (4.5 hours) 2008
infancy
Launch of SSR 2014
MT + IVT (6 hours) 2015
adolescence
Imaging Criteria get less stringent
Time window opens to 24h
2023
Adulthood. 2021: Recognition as CHUV registry

Current Recommendations of IVT/ MT in Stroke

Thrombolysis (IVT)

- Symptom onset < 4.5h: IVT
- Symptom onset 4.5 – 9h:
  - Core/ Perf. mismatch imaging
  - with target mismatch*: IVT
- Wake-up Stroke (> 4.5h):
  - DWI/FLAIR mismatch: IVT
  - Core/Perf. mismatch: IVT

(+)

Thrombectomy (MT)

- Symptom onset < 8h: MT
- Symptom onset < 24h
  - Core/ Perf. mismatch imaging
  - DAWN-based selection (clinical/radiological)

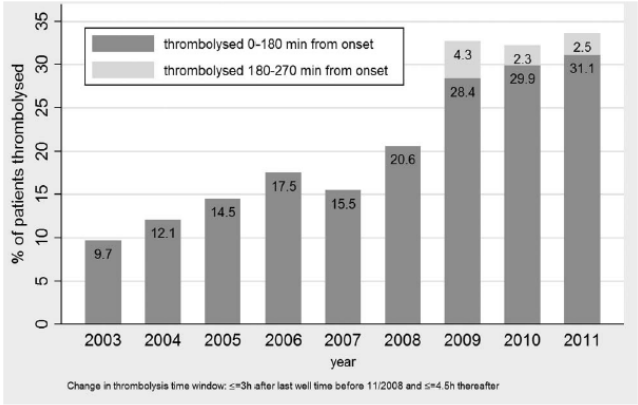
Infarct core** < 70ml
Mismatch Volume*** > 10ml
Mismatch Ratio*: > 1.2
** ADC < 620um2/s or rCBF < 30%
*** Tmax > 6s

Turc et al., ESO/ ESMINT Guidelines MT (ESO 2019)
Berge et al., ESO Guidelines IVT (ESO 2021)
Clinical Translational Neurosciences (CTN) June 2021 https://doi.org/10.1177/2514183X21999228

Whom do we NOT thrombolyse/ thrombectomize and WHY ?

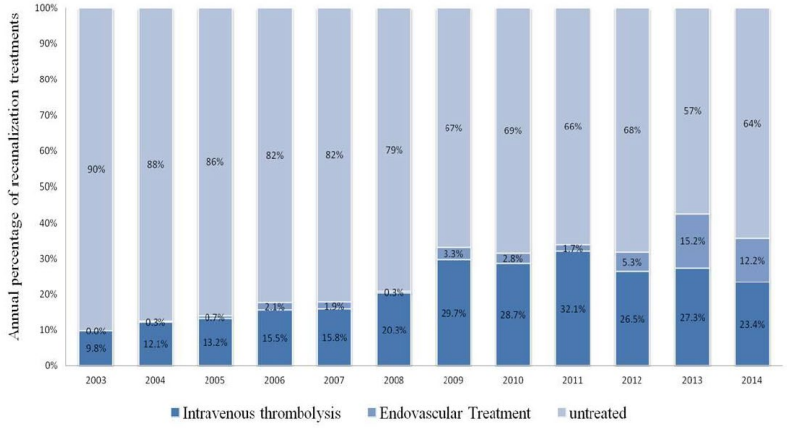
ASTRAL 2003 – 2011 (IVT):
2019 non-thrombolysed patients

- Admission delays
- **Stroke severity (mostly mild)**
- **Advanced Age**



ASTRAL 2003 – 2014 (MT):

- 17.7% eligibile within 6 hours
- **Younger age, shorter delays, higher stroke severity** were associated with EVT eligibilitiy



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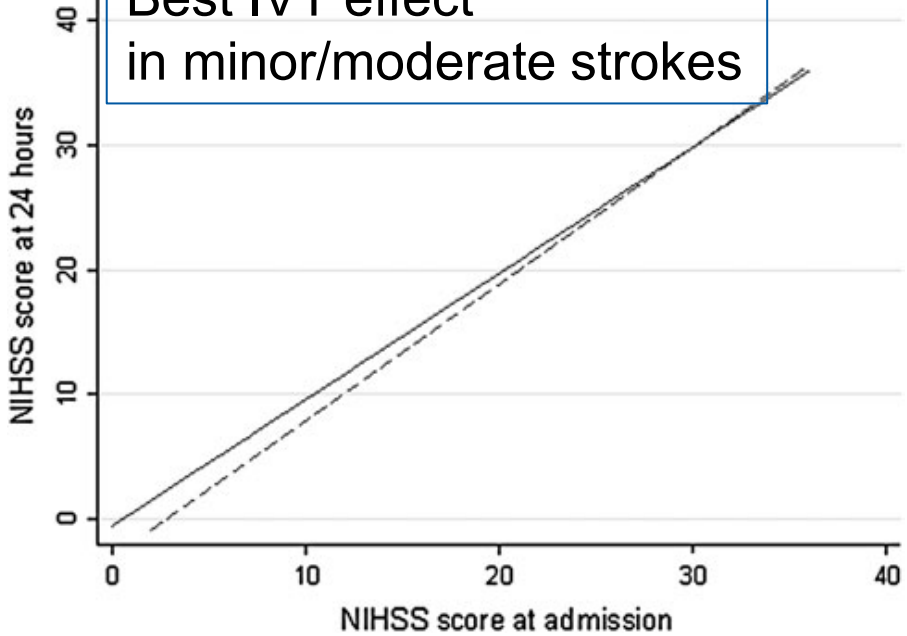
Reiff and Michel, Emerg Med J 2016

Vanacker et al., Stroke 2016

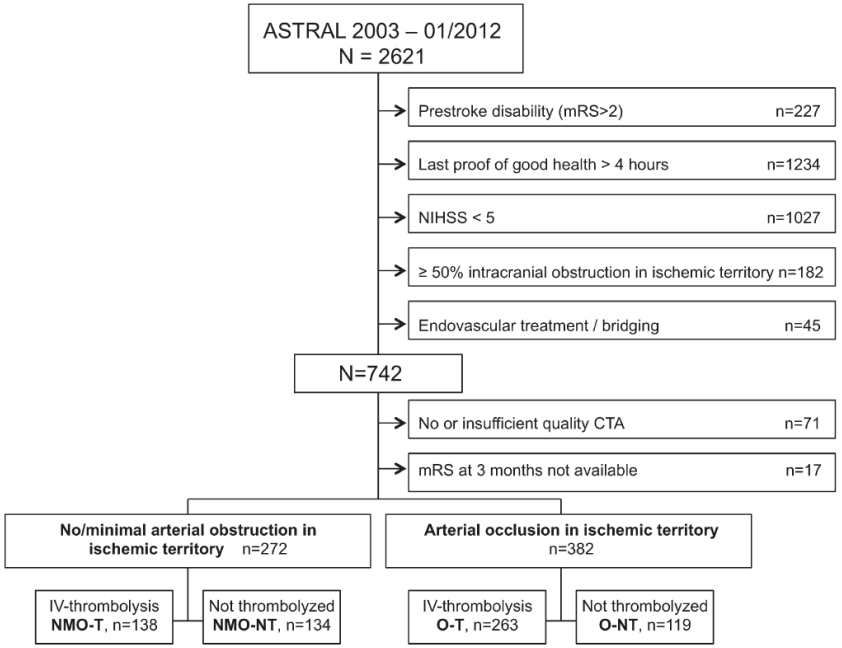
When is the effect of IVT best ?

ASTRAL (n=1730)
Best IVT effect
in minor/moderate strokes



Ntaios et al., J Neurol 2012

Best IVT effect in patients with arterial occlusions (CTA)



Medlin et al., Stroke 2015

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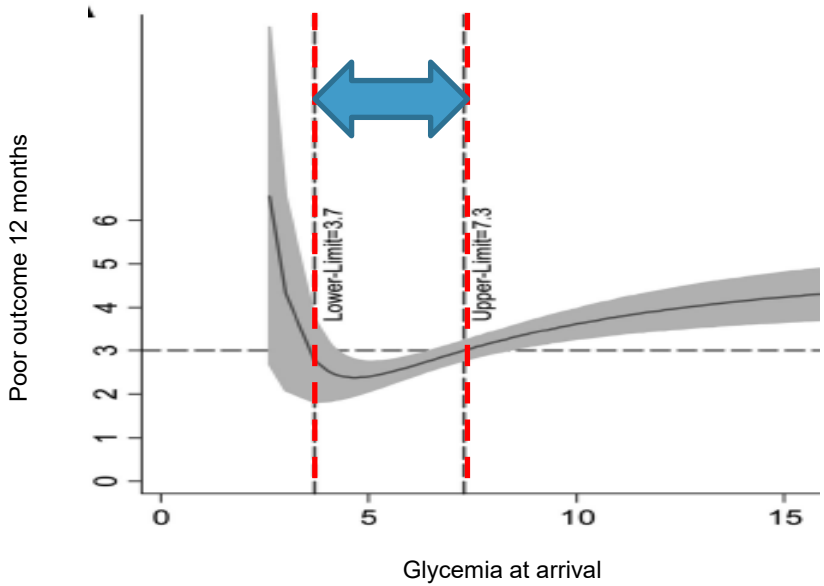
Acute stroke and admission glucose

Clinical outcome at 3 months (n = 1446)



Ntaios et al., Stroke 2010

Early vs. late EVT: more or less dangerous ?

ASTRAL retrospective analysis of complications

Type of complication	Early EVT	Late EVT	P (adjusted)
Procedural complications (Inguinal access, embolization in non-ischemic territory, dissection, arterial perforation/SAH)	16%	16%	0.90
Cerebrovascular complications (Parenchymal hemorrhage, ischemic mass effect, 24h reocclusion)	17%	20%	0.66
Incomplete recanalisation (TICI <2b)	8%	9%	0.36

→ Similar risks in early and late thrombectomy

Does Imaging selection help IVT/ MT decisions ?

Added value of CT-Perfusion (n = 1994)

ASTRAL: N = 273 NCCT | N = 411 NCCT + CTA | N = 1310 NCCT + CTA + CTP

More likely to receive MCTI if:
younger, lower baseline NIHSS, less risk factors, lower creatinine

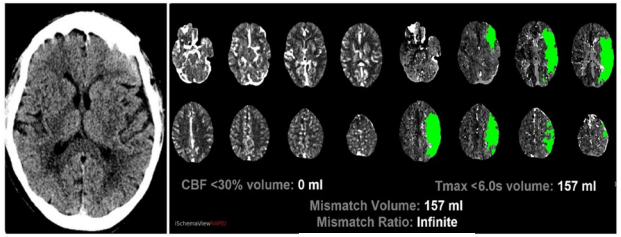
+ adjustment

Outcome with MCT:
Lower 12-month mortality, fewer unknown stroke mechanisms, no added renal risk.

Bill et al., EJN 2017

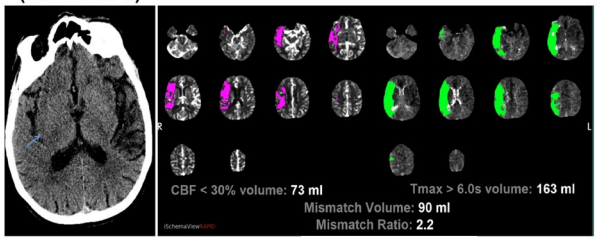
What else can we learn from acute stroke CT imaging ?

Correlation ASPECTS and CTP core (n= 1046) ?



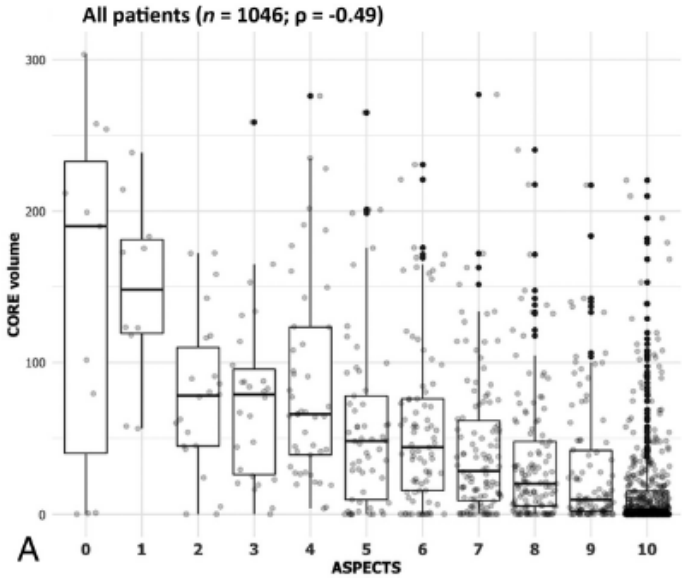
Favorable CT (ASPECTS=9)

Sarraj et al. 2020 SELECT trial



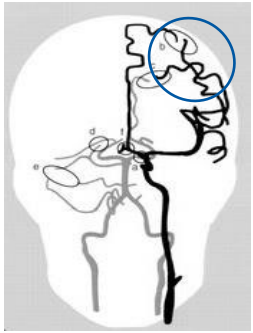
Favorable CT (ASPECTS=9)

Only moderate correlation.
better in late-arriving patients (6-24h)
and with LVO

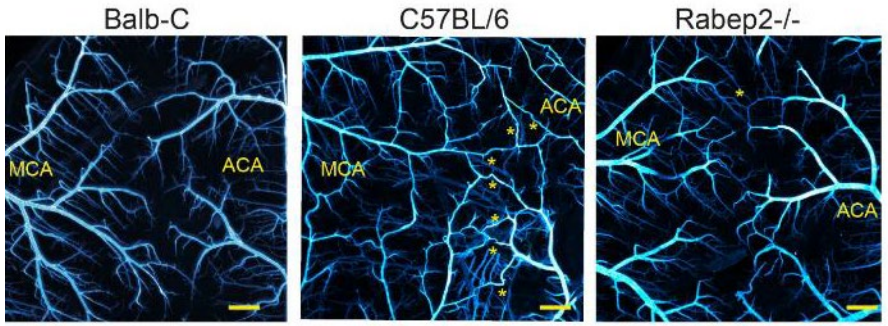


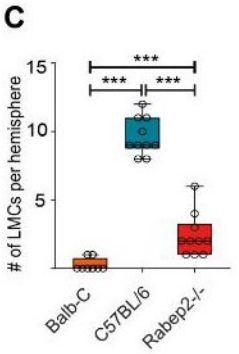
Nanoni et al., AJN 2021

Leptomeningeal Collaterals and Outcome

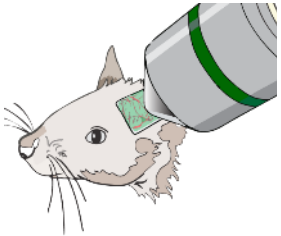


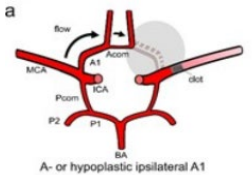
Liebeskind et al.,2013

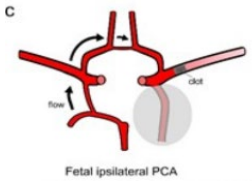




Binder et al. in revision 2023





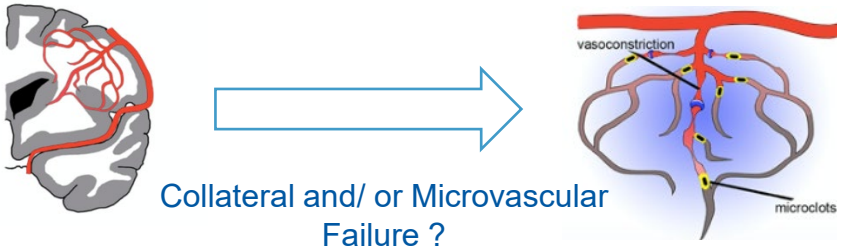


Westphal et al. 2021

ASTRAL (n=857): what factors determine better collaterals (LMCs)?

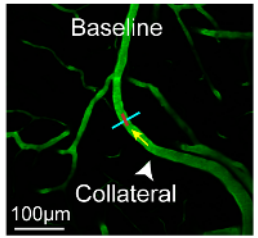
- Younger age, dyslipidemia, lower creatinine
- Shorter delay from symptom onset to imaging

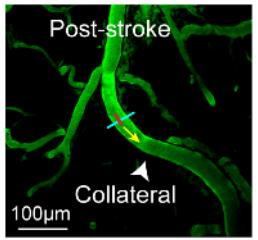
Nannoni et al., J Neurol 2019



Collateral and/ or Microvascular Failure ?

El Amki and Wegener 2017





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Predicting outcome: The ASTRAL Score

- ASTRAL, DRAGON, SEDAN outperformed physicians
- competition of 244 stroke experts against ASTRAL Score) to predict mRS > 2 at 3 months
- Experts were accurate in 56.8% while ASTRAL was in 86.5%)

Our stroke outcome predictions are often wrong !

Table 2 Integer-based prognostic ASTRAL score for the calculation of probability of unfavorable outcome in patients with acute ischemic stroke

Covariates	Score points
Age: for every 5 y[a]	1
Severity: for every NIHSS point[a]	1
Time delay from onset to admission >3 h[b]	2
Range of visual field defect[c]	2
Acute glucose >7.3 or <3.7 mmol/L[d]	1
Level of consciousness decreased[e]	3

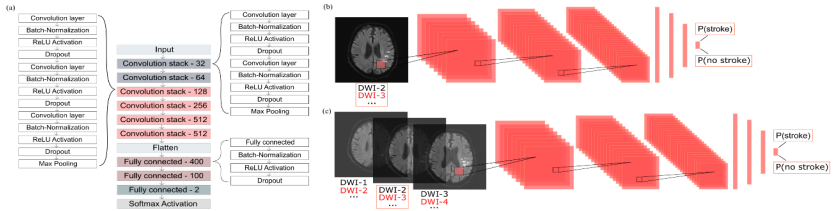
Do we get better when including imaging ?

Ntaios et al., Neurol 2012 Ntaios et al., Europ J Neurol 2016

We need to show that AI can reach good prediction performance

- 5 Stroke experts (4 Swiss, 1 non-Swiss, 2 different Stroke Centers)
- 60% female
- 45 years of experience with acute stroke patient treatment

Convolutional
Neural
Network



- 1 CNN model
- 3 years of experience with stroke data

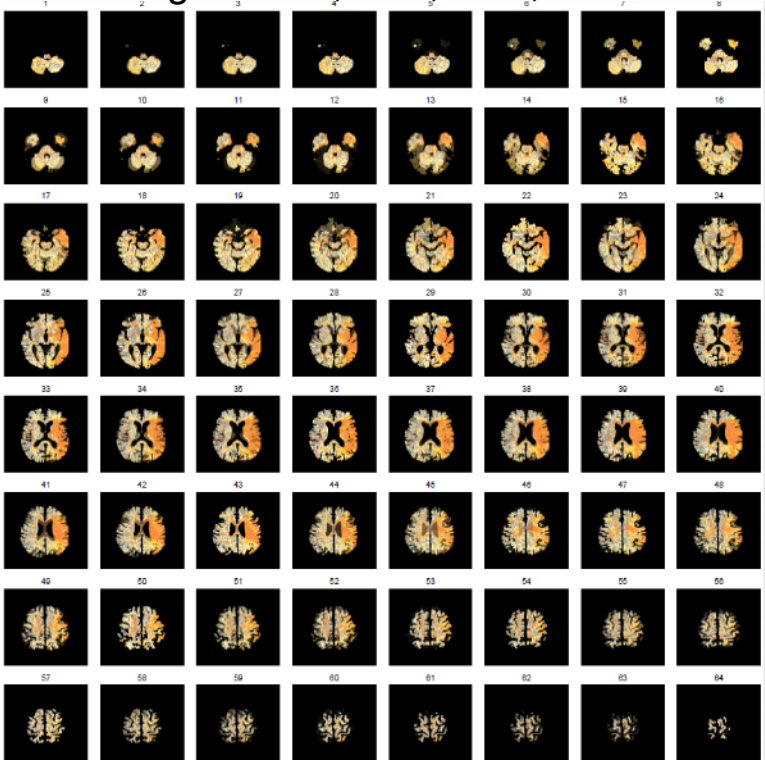
Outcome-Prediction Competition: the Task

- 50 Patients with MCA-M1 occlusion und MT
- Prediction: 3 months outcome (mRS)
- Data either: 1) clinical, 2) imaging or 3) combination of both

222 patients with M1-occlusion: 50% mRS >/= 3

	2
ID	516341.00
Age (y)	54.00
Sex (1: female)	0.00
Independent before stroke (1: yes)	1.00
NIHSS on admission	15.00
Oral anticoagulation (1: yes)	0.00
Statin therapy (1: yes)	0.00
Antihypertensive therapy (1: yes)	1.00
SBP (mmHg)	158.00
DBP (mmHg)	91.00
Glucose (mmol/L)	7.10
HbA1C (%)	6.10
LDL (mmol/L)	1.15
HDL (mmol/L)	1.68
TG (mmol/L)	0.89
CRP (mg/L)	3.00
INR	1.00
Atrial fibrillation (1: yes)	0.00
Diabetes (1: yes)	1.00
Hypertension (1: yes)	1.00
Hypercholesteraemia (1: yes)	1.00
Smoker (1: yes)	1.00
CHD (1: yes)	1.00
pAVK (1: yes)	0.00
Previous stroke or tia (yes)	1.00
Infarct side (1: left, 2: right)	2.00
Additional occlusions (yes)	0.00
Collateralization (0: good, 1: moderate, 2: poor)	1.00
Time onset to imaging (min)	171.00

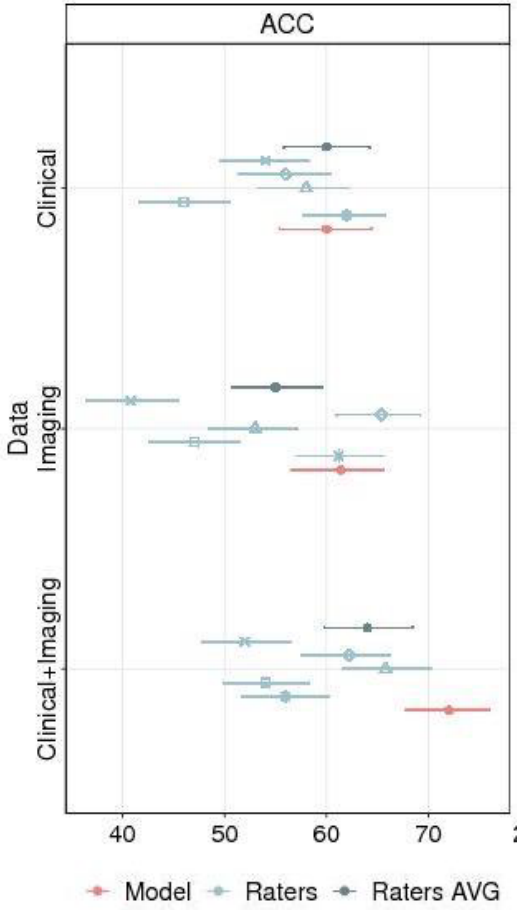
Images: DWI, CBF, CBV, Tmax> 6s



- Predict BINARY outcome (mRS good = 0-2 or bad 3-6)

Herzog et al., *Stroke 2023*

Who performed better?



- Large variability in the prediction of experts
- ACC around 0.6 for experts with clinical data
- ACC around 0.5 for experts with imaging data
- ACC around 0.65 for experts using both data types

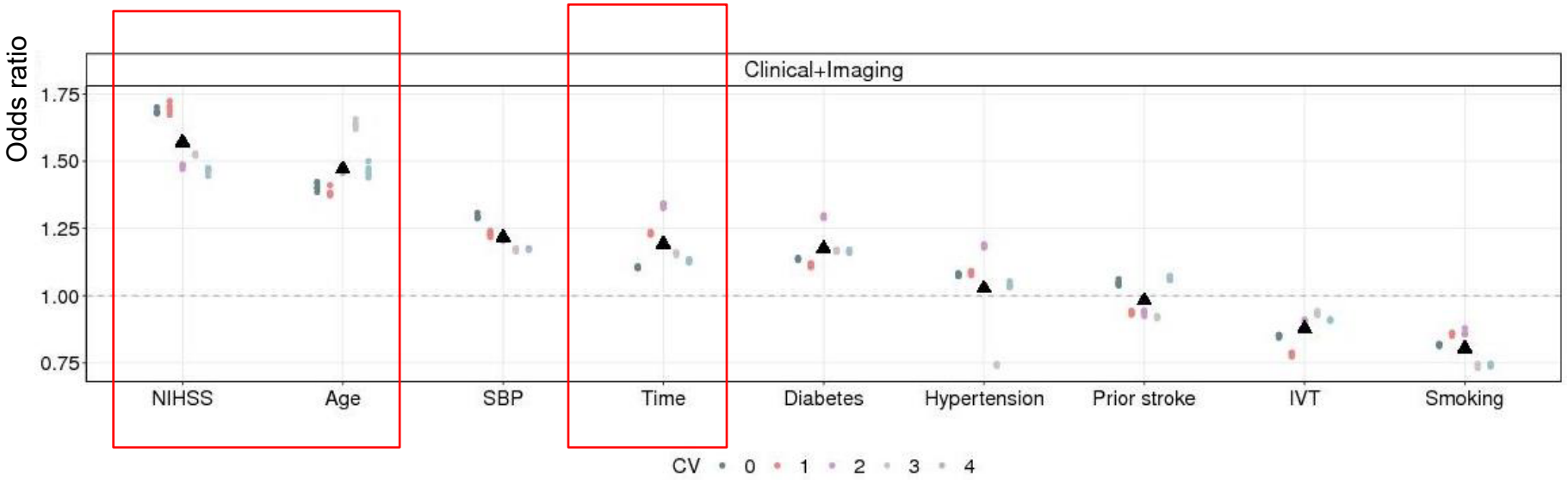
- Model outperforms experts when imaging is availble

There are more important features in the images.
Deep Learning may help to find them.

Hamann et al., *EJN* 2021

Herzog et al., *Stroke* 2023

Which variables were important for model and clinicians ?



ASTRAL: such different stroke outcomes:
Is there inequality in treatments ?

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Herzog et al., *Stroke* 2023

Inequalities in Thrombolysis and Thrombectomy

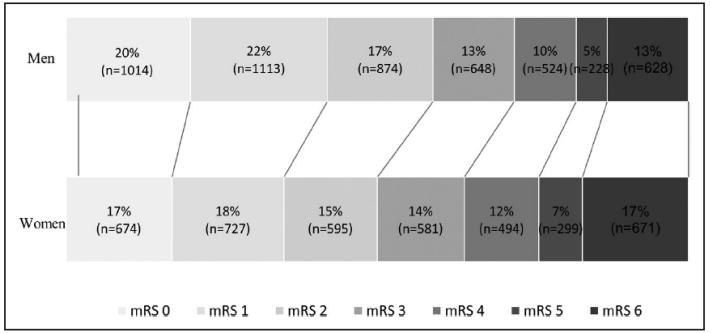
Stroke Severity and Outcome: Socioeconomic factors

- Of 1062 patients: 203 private (PI) and 850 basic insurance (BI)
- Mean NIHSS admission was higher for BI and outcome worse

Future Perspectives:
- Why do Swiss Stroke Centers treat 45% women vs. 55% men ?
- Sex-dependent socioeconomic factors

Stroke Severity and Outcome: Sex differences

- Women tend to have worse outcomes in stroke despite good IVT effect
- N = 3993 (ASTRAL) N = 9495 (TRISP)
- Women are older at the time of stroke
- After adjusting for age:
  women have higher risk of 3m disability



Rey et al., Eur J Neurol 2011
Medlin et al., Eur J Neurol 2020

Spaander et al., Stroke 2017 (TRISP)

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What about Chameleons and Mimics ?

Stroke-Chameleons:
Strokes that go un-noticed
- Do not receive appropriate treatment «undertreated»

ASTRAL: 47 out of 2200 AIS (2.1%)
- Younger age
- Less typical risk factor profile
- More cerebellar stroke

Stroke-Mimics
Non-Strokes that are falsely treated as stroke
- Do not receive appropriate treatment «overtreated»

TRISP: 100 out of 5581 AIS w. IVT (1.8%)
- Younger age, more females
- Less typical risk factor profile
- Low complication rate of IVT

Suspect a stroke, even if age and lack of risk factors dont let you think of it.
If you treat them unnecessarily: the risk of harm is very low.

ASTRAL teaches us about other special situations…

Chelsea Beck, The Atlantic March 9 2017

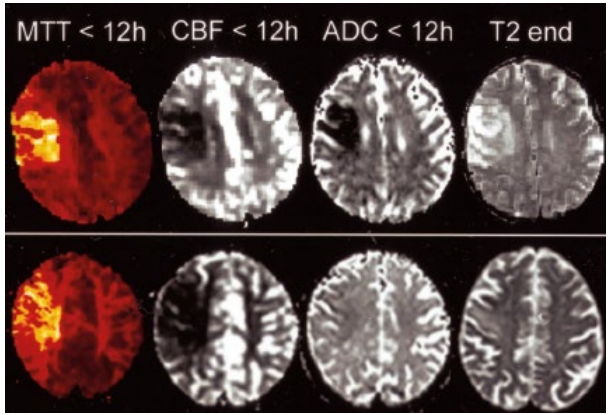
Strambo et al., J Stroke and Cerebrovasc Dis 2019

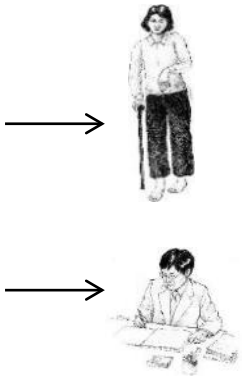
Correia et al., Int J Stroke 2016

- N = 10, 60% female HICE (Hairdresser-related cerebrov. events)
- No predilection for posterior circulation
- Only 2 dissections (ICA)
- Hypotension during hot air drying ?

- N = 17 SASs (51 controls)
- Median age 51 years
- 65% dissection (3 with minor falls while skiing)

Preconditioning by Preceding Ischemic Events (PIE) ?





Could preceding TIA or minor stroke be like «preconditioning»
What doesnt kill you makes you stronger ?

Wegener et al., *Stroke* 2004 (n=65)

ASTRAL: n= 3530; 1001 (28%) >/= 1 preceding cerebral ischemic event

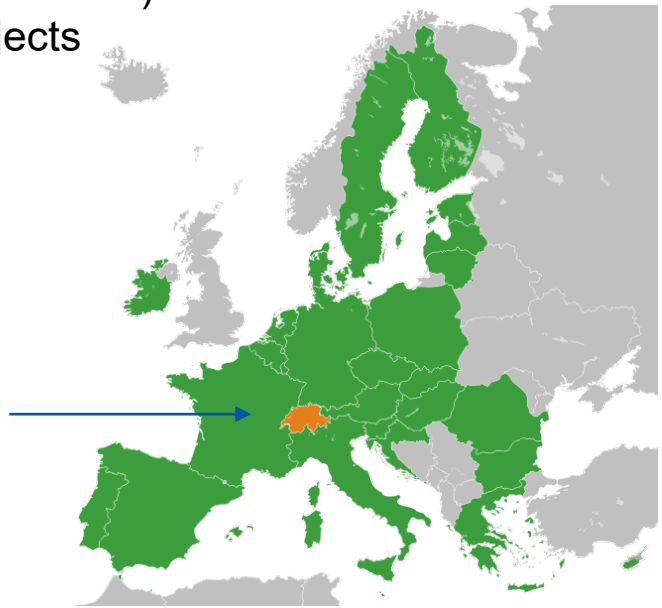
PIE independently associated with reduced severity of stroke;
but not with better long-term outcome.

Correia et al., *J Am Heart Assoc* 2021

Lessons Learned: We need more data from registries like ASTRAL to:

- Generate hypotheses and derive exploratory knowledge about stroke
- Be more representative (less inequalities)
- Collect Big data (Current Pooling Planned)
- Foster collaborations and joint projects
- Plan prospective clinical trials

ASTRAL	SSR	TRISP
Lausanne Registry	*Swiss Registry*	*European Registries*



ASTRAL- Family
The Future is bright!

Intelligent study design, knowledge of whats important, creativity „out-of-the-box“ projects, big power due to large patient numbers, excellent analysis methods, critical and smart interpretation of results, inclusive, collaborative work….

Thank you !

Many things not mentioned:

- Stroke in the posterior territory
- Intracranial dissections
- Many more imaging studies
- ….