Acute Stroke Treatment
Collaterals in Acute Ischemic Stroke

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Consultant to Stryker and Covidien

NIH/NINDS P50NS044378, K24NS072272, R01NS077706, R13NS082049
Objectives

- role of collaterals in acute ischemic stroke
- collateral therapeutic strategies
invited speakers

David J Mikulis, MD (Toronto, ON, Canada)
Raul G Nogueira, MD (Atlanta, GA, USA)
Mark W Parsons, MD (Newcastle, Australia)
Rema Raman, PhD (San Diego, CA, USA)
Marc Ribo, MD, PhD (Barcelona, Spain)
Tatjana Rundek, MD, PhD (Miami, FL, USA)
Noriko Salamon, MD (Los Angeles, CA, USA)
Jeffrey L Saver, MD (Los Angeles, CA, USA)
Ashfaq Shuaib, MD (Edmonton, AB, Canada)
Cathy A Silva, MD (Cleveland, OH, USA)
Steven Warach, MD, PhD (Austin, TX, USA)
Max Winterton, MD (Charlottesville, VA, USA)
KS Lawrence Wong, MD (Hong Kong, China)
Albert J Yoo, MD (Boston, MA, USA)

participants
The broad array of leading experts on collateral circulation from around the globe is expected to draw interest from various disciplines related to neurovascular disorders, including basic, translational and clinical neuroscientists. The planned discussions on clinical trials will undoubtedly attract various academicians, industry representatives and possibly NIH staff. Networking opportunities and the dinner seminar on mentoring the next generation will entice junior investigators. Robust attendance of up to 200 participants at various levels of expertise may result from the central location of the conference on the UCLA campus, allowing multidisciplinary exchange of information, debate and innovation with regard to future steps in development of collateral therapeutic strategies from research to clinical practice. Every effort will be made to encourage participation by postgraduate students, to have parity in numbers of women, minorities and persons with disabilities.

registration
A dedicated website contains all meeting details, including online registration links with options to note handicap access, child or family care needs, and reduced registration rates for junior investigators. All participants will be required to register for the meeting, with a registration fee of $50 and a reduced rate of $25 for students, fellows and residents.

facilities and housing
The symposium welcome reception and interactive dinner seminar will convene at the W Hotel, immediately adjoining the UCLA campus. Symposium lectures will be held at UCLA Covel Commons, providing 5,925 square feet of space in an ideal networking venue for breaks and lunch. These comprehensive meeting facilities include child and family care, with access for individuals with disabilities. Housing is available at a wide range of hotels with convenient location.

funding support has been requested from industry, academic & governmental sources

further information at www.collateralperfusion.org or davidliebeskind@yahoo.com

www.collateralperfusion.org
co-chairs

David S Liebeskind, MD & Ashtaq Shuaib, MD

program description

The International Symposium on Collaterals to the Brain is a multidisciplinary scientific conference focused on collateral perfusion in acute and chronic neurovascular disorders. This conference will convene leading experts to cover key aspects of this burgeoning field, with a total of 200 participants for a 2-day conference in an academic setting. The confirmed program is structured into 5 sessions covering the history and translational research on collaterals, chronic role of collaterals, imaging features, acute stroke aspects, and considerations of clinical trial design for collateral theonomies. A seminar and panel discussion is devoted to mentoring the next generation of investigators in collateral perfusion. Publication plans include a detailed roadmap on research steps on collaterals for the next 5 years.

objectives

Collateral perfusion is a critical determinant of stroke risk, brain tissue fate of infarction or hemorrhage, stroke recovery and clinical outcome that impacts almost all acute and chronic ischemic disorders of the brain. Collateral circulation transcends the artificial distinction of acute stroke, recovery and prevention while serial imaging may depict this dynamic process over time. This conference is designed to allow cross-fertilization of new ideas, concepts, and methodologies to advance the field of stroke via collaterals. Measurable outcomes of this conference will be assessed, evaluating the impact of this symposium on the membership of new investigators, translational stroke research and the NINDS Stroke Progress Review Group priority for studies on collateral perfusion. Concrete objectives are:

- to define current status of collateral circulation in diagnosis, therapy and prevention of stroke
- to address existing gaps and demands for the next generation of multidisciplinary researchers on collateral perfusion in the brain
- to outline and publish a roadmap for next steps in translational research on collateral flow

rationale

Collaterals have recently become a mainstream focus of stroke research, yet a forum has never been established to dedicate attention to this in research priority. This conference forms the breakthroughs in the field where basic science and imaging advances have underscored the role of collaterals and the tools for trials of collateral theonomies have become available. Transformative research on collaterals via collaborations between academia, industry and funding agencies may greatly advance novel diagnostic strategies, drugs and devices for cerebral ischemia. The symposium is the basis for novel research collaborations, cultivation of new investigators and improved clinical practice in this aspect of our field.

agenda

November 6, 2012

Introduction & Welcome Reception

November 7, 2012

Collateral Circulation: From Old to New

- Historical perspective on collaterals: angiographic patterns and various correlates
- Of mice and men: translational research on collaterals
- Microvascular perfusion of collaterals: neuroprotection from thrombus to bedside
- Vascular homeostasis: atherosclerosis and artherosclerosis
- Central artherosclerosis: collateral theonomies from heart to brain
- Collateral advances in sync with cardiomyopathy

Collaterals into Chronic Phases

- Collaterals in axon from acute stroke to intracranial atherosclerosis
- Collaterals in intracranial atherosclerosis
- Endovascular therapy for intracranial atherosclerosis based on collateral status
- Hemodynamic and vascular reactivity of collateral perfusion in moyamoya
- Bypass for hemodynamic stroke
- Enhancing collaterals via ischemic preconditioning and synangiosis

Lunch

Imaging of Collaterals

- Ultrasound of collateral flow from acute to chronic cerebrovascular disorders
- ASPECTS for multimodal CT/MR as indirect marker of collateral perfusion
- CTA-S1 of collaterals for selection of acute endovascular therapies
- CT perfusion of collaterals in acute stroke
- MRI patterns of collaterals in acute stroke and clinical implications
- Serial imaging of collateral perfusion - acute on chronic

Dinner & Seminar: Mentoring the Next Generation on Collateral Perfusion

November 8, 2012

Collaterals in Acute Ischemic Stroke

- Optimizing thrombolytic reperfusion with collaterals
- Time to angiographic reperfusion and the role of collaterals
- Reperfusion via collaterals in acute stroke
- External counterpulsation for collateral augmentation
- Head positioning and hemodynamic interventions as collateral theonomies
- Stimulating collaterals?

Collateral Theonomies

- Malignant profiles of impaired collaterals: selection for collateral theonomies?
- Collateral theonomies: SENSITIS and other stroke trials
- Noninvasive imaging metrics for collateral theonomies: lessons from NOX
- Imaging biostatistics of collaterals in clinical trials
- Endpoints and outcome measures for trials of collateral theonomies
- Advancing collateral research in collaborative stroke imaging networks

Concluding Remarks & Next Steps
framework for flow
framework & basis for flow

stroke 2013

dynamic aspect of cerebral ischemia, artificial separation of phases in ischemic stroke

continuum of flow or homeostasis of brain perfusion

serial imaging may capture evolution of injury and impact of reperfusion

imaging core infrastructure now exists to measure angiographic and tissue biomarkers of ischemia
stroke 2013

- prevention
  - recognition of numerous vascular risk factors from hypertension to glucose intolerance to dyslipidemia
  - embolic source and microvascular disease
  - novel anticoagulants, devices, and other therapies

- optimal medical therapy

- paradoxical omission of hypoperfusion and ischemia
  - remainder of lecture on flow
  - bias regarding collaterals
time is not brain!

- across population of stroke cases studied from onset to chronic phase, not in a given patient during early phases
- time of symptom onset ≠ time of vascular occlusion
- collaterals prone to failure over time
Early DWI

- 307 stroke patients (mean age 69±17 years, 51% female) from 2004-2012 had DWI with TLKW < 4.5 hours (mean 147±62 min)
- DWI lesion volume (median 3.67cc) varied extensively (TLKW-DWI < 1 hour (n=8) 0.40cc (0-93cc), 1-2 hours (n=126) 3.02 (0-265), 2-3 hours (n=78) 2.18 (0-103), 3-4.5 hours (n=95) 6.96 (0-227))
- Negligible correlation (r=0.175, p=0.002) noted for DWI lesion volume and TLKW-DWI time duration
- DWI-negative findings < 4.5 hours occurred in 8.5%
- Malignant strokes (>70cc) were noted in 7.5%
- Older age was associated with DWI-negative strokes (mean 77 vs. 68 years, p=0.013)
- TLKW-DWI time duration was unrelated to DWI-negative strokes, yet malignant stroke was more common later (p=0.009)
- Majority of malignant strokes on DWI had TLKW during daytime
imaging perspective on time

- hyperacute?
- acute?
- subacute?
- chronic?
flow determines time

- If collaterals compensate for arterial occlusion or stenosis, symptoms may be negligible or absent.
- Pace of collateral recruitment may influence the timeline of symptom progression.
- Poor collaterals may predispose to impaired reperfusion:
  - No reflow
  - Reperfusion injury or hemorrhagic transformation
continuum and homeostasis of flow

balance of antegrade flow and collateral perfusion
cerebral arteriogenesis

- process of collateralization
- pressure drop
- reverse flow
- increased shear stress
- cytokine release
- hypertension
- vascular remodeling
imaging infrastructure

- serial imaging routinely used in clinical practice
- saga of imaging in stroke trials...
  - secondary to clinical outcomes
  - exploratory or ancillary
  - impact of funding source, cost, implications
  - systematic, prospective versus retrospective
  - imaging insurance on understanding pathophysiology
- ongoing, large-scale imaging core lab activities
prehospital neuroprotection
neuroprotection

- early ischemia in FAST-MAG
- neuroprotection via collaterals
- combined neuroprotection and revascularization
Los Angeles and Orange Counties
Ethnically diverse population 13.3 million
59 receiving hospitals
353 rescue ambulances
3300 paramedics
>400 emergency physicians
>100 neurologists, neurosurgeons
Chain Cell Forwarding System

Direct Call

First On-Call Investigator
Call Forwarding (30 Seconds)
Second On-Call Investigator
Call Forwarding (30 Seconds)
Third On-Call Investigator

Call Forward to First Investigator (30 Seconds)

Voice-Over-Internet Phone (VOIP) System

Direct Call to VOIP System to English Line (Blue) and Spanish Line (Red)

English-Line First On-Call Investigator
English-Line Second On-Call Investigator
English-Line Third On-Call Investigator

Spanish-Line First On-Call Investigator
Spanish-Line Second On-Call Investigator
Spanish-Line Third On-Call Investigator
FAST-MAG (n=1470)

- currently enrolled n=1584 (6/18/12)
- age 69 (range 39-95)
- female 42%

index event diagnosis
- cerebral ischemia 71.9%
- intracerebral hemorrhage 24.4%
- stroke mimic 3.7%

stroke severity
- LAMS (prehospital) 4.0 (range 1-5)
- NIHSS (hospital arrival, after Rx start) 11.4 (range 0-40)
FAST-MAG times (n=1470)

- Stroke onset to study drug (median) 46 mins
- Paramedic arrival on scene to drug (mean) 25 mins
- Paramedic arrival on scene to ED (mean) 35 mins
- Treated within 1 hour of onset 73%
- Treated 1-2 hr after onset 24%
FAST-MAG imaging

- Initial ASPECTS median 9 (IQR 8-10) to 7 (IQR 4-9) at 24 hrs
penumbral neuroprotection
thrombolysis
extend thrombolysis

- intravenous thrombolysis – early and late
- baseline imaging patterns predict response
- revascularization – recanalization and reperfusion
- serial imaging of thrombolysis
- hyperperfusion and hemorrhage
early and late – time matters?

Diagnosis and treatment of patients with stroke in a mobile stroke unit versus in hospital: a randomised controlled trial

Silke Walter, Panagiotis Kostopoulos, Anton Haass, Isabel Keller, Martin Lesmeister, Thomas Schlechtriemen, Christian Roth, Panagiotis Papanagiotou, Iris Grunwald, Helmut Schumacher, Stephan Helwig, Julio Viera, Heiko Körner, Maria Alexandrou, Umut Yilmaz, Karin Ziegler, Kathrin Schmidt, Rainer Dabew, Darius Kubulus, Yang Liu, Thomas Volk, Kai Kronfeld, Christian Ruckes, Thomas Bertsch, Wolfgang Reith, Klaus Fassbender

The NEW ENGLAND JOURNAL OF MEDICINE

Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke

Werner Hacke, M.D., Markku Kaste, M.D., Erich Bluhmki, Ph.D., Miroslav Brozman, M.D., Antoni Dávalos, M.D., Donata Guidetti, M.D., Vincent Larrue, M.D., Kennedy R. Lees, M.D., Zakaria Medeghri, M.D., Thomas Machnig, M.D., Dietmar Schneider, M.D., Rüdiger von Kummer, M.D., Nils Wahlgren, M.D., and Danilo Toni, M.D., for the ECASS Investigators®
Key Results of the DEFUSE Study

- **Target Mismatch** pattern (49%)
  - Benefit substantially from early reperfusion
- **Match** pattern (15%)
  - No benefit from early reperfusion
- **Small DWI / PWI lesions** (28%)
  - Associated with favorable outcomes
- **Malignant MRI** pattern (8%)
  - Predicts severe ICH following reperfusion
ASPECTS
Bayesian PWI – collateral perfusion
ASL & DSC MRI

ASL MRI in 3 example cases of acute MCA ischemic stroke, revealing DATE score of 0 (left), DATE 1 (middle), and DATE 2 (right).
Permeability – CTP and PWI

Figure 1: Illustrative example of a concentration versus time curve $\Delta R^2$ (orange), as well as its y-variant fit $\Delta R^2$ (blue). The peak $(\text{max}(\Delta R^2))$ corresponds to the maximum value on the fitted curve. $t_a$ and $t_h$ define the dynamic phase comprised between the onset of the equilibration phase measured at half width of the descending $\Delta R^2$ curve and the end of measurements. The PB area corresponds to the difference between the actual $\Delta R^2$ and the fitted curve $\Delta R^2$. From this area, it is possible to derive $rP$ (Eq. (2)) and $sR$ (Eq. (3)). In addition to these ratios, the contrast slope (CS) and the final contrast (FC) are also used as permeability features.

Figure 2: Illustration of the framework used to predict hemorrhagic transformation (HT) on ischemic stroke patients. A permeability feature map is first extracted from source perfusion weighted images (PWI). Intensity histograms are then computed from each hemisphere and used as input features to a classifier trained to discriminate between HT and control patients.
definitive reperfusion
defining definitive reperfusion

- reperfusion of downstream tissue
- angiographic measures of TICI and collaterals
- endovascular therapies
- serial imaging of reperfusion injury
- definitive reperfusion with good clinical outcome
recanalization & reperfusion
<table>
<thead>
<tr>
<th>Grade 0:</th>
<th>No Perfusion. No antegrade flow beyond the point of occlusion.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1:</td>
<td>Penetration With Minimal Perfusion. The contrast material passes beyond the area of obstruction but fails to opacify the entire cerebral bed distal to the obstruction for the duration of the angiographic run.</td>
</tr>
<tr>
<td>Grade 2:</td>
<td>Partial Perfusion. The contrast material passes beyond the obstruction and opacifies the arterial bed distal to the obstruction. However, the rate of entry of contrast into the vessel distal to the obstruction and/or its rate of clearance from the distal bed are perceptibly slower than its entry into and/or clearance from comparable areas not perfused by the previously occluded vessel, eg, the opposite cerebral artery or the arterial bed proximal to the obstruction.</td>
</tr>
<tr>
<td>Grade 2a:</td>
<td>Only partial filling (&lt;%) of the entire vascular territory is visualized.</td>
</tr>
<tr>
<td>Grade 2b:</td>
<td>Complete filling of all of the expected vascular territory is visualized, but the filling is slower than normal.</td>
</tr>
<tr>
<td>Grade 3:</td>
<td>Complete Perfusion. Antegrade flow into the bed distal to the obstruction occurs as promptly as into the obstruction and clearance of contrast material from the involved bed is as rapid as from an uninvolved other bed of the same vessel or the opposite cerebral artery.</td>
</tr>
</tbody>
</table>
Collateral Flow Grade Definitions

Grade 0: No collaterals visible to the ischemic site
Grade 1: Slow collaterals to the periphery of the ischemic site with persistence of some of the defect
Grade 2: Rapid collaterals to the periphery of ischemic site with persistence of some of the defect and to only a portion of the ischemic territory
Grade 3: Collaterals with slow but complete angiographic blood flow of the ischemic bed by the late venous phase
Grade 4: Complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by retrograde perfusion
N/A: not applicable based on territory or injections available
### DEFUSE-2 Definitions

<table>
<thead>
<tr>
<th>Variable</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target Mismatch</td>
<td>PWI(Tmax&gt;6s) / DWI $\geq$1.8 AND DWI $&lt;$70 ml AND PWI(Tmax&gt;10s) $&lt;$100 ml</td>
</tr>
<tr>
<td>Reperfusion (PWI criteria)*</td>
<td>$&gt;$50% reduction in PWI(Tmax&gt;6s) volume at early follow-up</td>
</tr>
<tr>
<td>Reperfusion (DSA criteria)**</td>
<td>TICI 2b or 3 at completion of procedure</td>
</tr>
<tr>
<td>Favorable Clinical Response</td>
<td>$\geq$8 point improvement in NIHSSS at day 30 or NIHSSS of $\leq$1 at day 30</td>
</tr>
</tbody>
</table>

*in patients with a baseline PWI(Tmax>6s) lesion that is $\geq$10 ml

**in patients with a major vessel occlusion (TICI 0 or 1) on baseline imaging
## TREVO 2 vs. SWIFT: Differences

<table>
<thead>
<tr>
<th></th>
<th>TREVO 2</th>
<th>SWIFT</th>
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</thead>
<tbody>
<tr>
<td>Number of Passes with Device</td>
<td>Up to 6 passes with study device. Study device ≥3 passes unless successful.</td>
<td>Up to 3 passes with study device.</td>
</tr>
<tr>
<td>Primary Efficacy Endpoint</td>
<td>Successful Recanalization with Study Device</td>
<td>Successful Recanalization with Study Device AND no sICH</td>
</tr>
<tr>
<td>Definition of Revascularization</td>
<td>TICI 2a, 2b or 3 (Core Lab 1)</td>
<td>TIMI 2/3 in all treatable vessels (Core Lab 2)</td>
</tr>
<tr>
<td>“Roll-In” Phase</td>
<td>None</td>
<td>2 roll-in patients prior to randomization</td>
</tr>
</tbody>
</table>
| Definition of Good Outcome | mRS ≤2                                                                | mRS ≤2, OR
↓NIHSS ≥ 10 points, OR return to baseline mRS                        |
| Baseline mRS Inclusion  | mRS 0-1 (Evaluator 1)                                                   | mRS 0-5 (Evaluator 2) [median 0; mean 0.5]                           |
| 90-day mRS Loss to F/U  | Trevo: 3%                                                               | Solitaire: 5%
Merci: 3%                                                             | Merci: 13%                                                           |
| sICH                    | (ECASS III) Any apparently extravascular blood in the brain/cranium associated with a ↑ of NIHSS ≥ 4, or death and was identified as the predominant cause of the neurological deterioration. (Core Lab 1) | Any parenchymal hematoma, subarachnoid hemorrhage, or intraventricular hemorrhage associated with a ↑ of NIHSS ≥ 4 within 24hr. (Core Lab 2) |
## TREVO 2 vs. SWIFT: Comparisons

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Trevo2 Trevo (n=88)</th>
<th>Trevo2 Merci (n=90)</th>
<th>Trevo2 p-value (n=178)</th>
<th>SWIFT Solitaire (n=58)</th>
<th>SWIFT Merci (n=55)</th>
<th>SWIFT p-value (n=113)</th>
<th>mTrevo2 vs. mSWIFT</th>
<th>tTrevo2 vs. mSWIFT</th>
<th>sSWIFT vs. mTrevo2</th>
<th>tTrevo2 vs. sSWIFT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Successful Recanalization</strong>*</td>
<td>86.4% (76/88)</td>
<td>60.0% (54/90)</td>
<td>&lt; 0.0001</td>
<td>68.5% (37/54)</td>
<td>30.2% (16/53)</td>
<td>&lt; 0.0001</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>TICI 2b-3 67.8%</td>
<td>TICI 2b-3 43.4%</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td><strong>mRS 0-2 at 90d</strong></td>
<td>40.0% (34/85)</td>
<td>21.8% (19/87)</td>
<td>0.013</td>
<td>36.4% (20/55)</td>
<td>29.2% (14/48)</td>
<td>0.530</td>
<td>0.404</td>
<td>0.261</td>
<td>0.082</td>
<td>0.724</td>
</tr>
<tr>
<td><strong>mRS ≤ 2, OR ↑NIHSS ≥10 points, OR return to baseline mRS at 90 days</strong></td>
<td>52.9% (45/85)</td>
<td>42.5% (37/87)</td>
<td>0.222</td>
<td>58.2% (32/55)</td>
<td>33.3% (16/48)</td>
<td>0.017</td>
<td>0.358</td>
<td>0.032</td>
<td>0.085</td>
<td>0.603</td>
</tr>
<tr>
<td><strong>Mortality at 90-days</strong></td>
<td>33.0% (29/88)</td>
<td>23.6% (21/89)</td>
<td>0.184</td>
<td>17.2% (10/58)</td>
<td>38.2% (21/55)</td>
<td>0.020</td>
<td>0.089</td>
<td>0.590</td>
<td>0.412</td>
<td>0.038</td>
</tr>
<tr>
<td><strong>Mortality at 30-days</strong></td>
<td>26.1% (23/88)</td>
<td>23.6% (21/90)</td>
<td>0.729</td>
<td>15.5% (9/58)</td>
<td>27.3% (15/55)</td>
<td>0.168</td>
<td>0.692</td>
<td>1.000</td>
<td>0.298</td>
<td>0.155</td>
</tr>
<tr>
<td><strong>mRS 0-3 at 90d</strong></td>
<td>49.4% (42/85)</td>
<td>37.9% (33/87)</td>
<td>0.166</td>
<td>56.4% (31/55)</td>
<td>37.4% (18/48)</td>
<td>0.075</td>
<td>1.000</td>
<td>0.208</td>
<td>0.038</td>
<td>0.489</td>
</tr>
<tr>
<td><strong>SICH</strong>*</td>
<td>6.8% (6/88)</td>
<td>8.9% (8/90)</td>
<td>0.782</td>
<td>1.7% (1/58)</td>
<td>10.9% (6/55)</td>
<td>0.057</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Source: [http://www.graphpad.com](http://www.graphpad.com). Fisher's exact test. Two-tailed P value

**Note:** >400 patients would be needed to demonstrate a difference in TICI 2-3 of 80% vs. 90% (80% power). >3000 patients for a 90-day mRS 0-2 40% vs. 45%!!!
118 eligible patients, mean age 65.5 yrs, mean time to enrollment 5.5 hrs, 58% “favorable penumbral pattern”.

“favorable penumbral pattern”

- improved outcomes, smaller infarct volumes, attenuated infarct growth, compared with nonpenumbral pattern, regardless of treatment assignment.
From 2006-2012, 331 cases prospectively evaluated

- baseline 276/331 (83%) with adequate collateral views
- target 278/331 (84%) with adequate collateral views

Prospective analysis feasible with standard angiography

Only history of hypertension in anterior circulation subgroup, associated with collateral grade
Collateral grade was strongly associated with:
- recanalization (AOL)
- reperfusion
- discharge location
- disability or good clinical outcome at Day 90

Collateral grade was unrelated to:
- hemorrhage within 30 hours of IV tPA initiation
- death within 90 days
ASPECTS of collaterals

Collaterals were strongly related to ASPECTS at baseline (p<0.001):
- 0-1 - median 8 (3-10)
- 2 - 9 (5-10)
- 3 - 9 (7-10)
- 4 - 9 (8-10)

Collaterals were strongly related to ASPECTS at 24 hrs (p<0.001):
- 0-1 - median 1 (0-5)
- 2 - 6 (0-10)
- 3 - 8 (0-10)
- 4 - 8 (4-8)
Collaterals, SICH and outcome

Partial or worse collaterals were associated with symptomatic hemorrhage \((p=0.075)\).

Better collaterals were linked with TICI 2b/3 reperfusion \((p=0.019)\), better median NIHSS at Day 7/discharge \((p<0.001)\) and better Day 90 mRS \((p<0.001)\).

Better collaterals were noted in patients with successful revascularization without symptomatic hemorrhage, mean 2.3 \((95\% \text{ CI } 2.1\text{-}2.5)\) vs. 1.9 \((95\% \text{ CI } 1.7\text{-}2.2)\), \(p=0.021\).
166/177 cases in TREVO 2 were anterior circulation occlusions
Baseline ASPECTS was ≤ 7 in 83/166 (50%) cases
Baseline ASPECTS score ≤ 7 was unrelated to age, gender, or any other clinical parameter other than NIHSS score (median 19 (17-23) vs. 17 (13-20) for ASPECTS > 7, p<0.001) and clot location (more ICA than M2 occlusions, p=0.044)
Univariate imaging predictors of good clinical outcome at day 90 included baseline ASPECTS (OR 1.82, p<0.001), baseline ASPECTS ≥ 8 (OR 2.64, p=0.006), collateral grade (OR 1.85, p=0.003), post-procedure TICI (OR 2.11, p<0.001), 24-hour ASPECTS (OR 1.67, p<0.001) and 24-hour ASPECTS ≥ 8 (OR 4.38, p<0.001)
Time to TICI 2a or greater was not predictive
Multivariate analyses showed that 24-hour ASPECTS (OR 1.70, p<0.001) and post-procedure TICI (OR 2.49, p=0.003) best predicted good outcome
Impact of Collaterals

- **Smaller Strokes**
  - Baseline DWI lesion volume ($b \ 0.025$, $p=0.001$)

- **More Reperfusion**
  - Higher TICI reperfusion rates ($\rho 0.191$, $p=0.043$)

- **Less Hemorrhage**
  - Lower hemorrhagic transformation rates ($\rho -0.229$, $p=0.015$)

- **Better Clinical Outcomes**
  - mRS at discharge inversely correlated with collateral grade ($\rho -0.317$, $p=0.001$)
TREVO 2 – perfusion angiography

PA CBF

TICI
flow from prehospital to reperfusion
Serial ASPECTS as a Novel Endpoint

ASPECTS change from 8 at baseline to 3 at 24 hrs
collaterals & hemorrhage in AIS
definitive reperfusion

qualified by clinical outcome at day 90, not arbitrarily defined as effective

- optimal degree of TICI reperfusion unestablished (2a or 2b?)
- SICH ignores other forms of hemorrhage
- reperfusion injury unexplored
- vessel-specific definitions (ICA, M1, M2)
conclusions & collaterals
conclusions

- framework for flow exists
- homeostasis of flow, balanced by collaterals
- hemodynamics as future of ischemic stroke