

## Late-Breaking Science Poster Abstracts

Wednesday, February 22, 2017, 6:15pm – 6:45pm

*LATE-BREAKING SCIENCE abstracts/studies presented at the INTERNATIONAL STROKE CONFERENCE 2017:*

*For late-breaking science being presented at ISC 2017, the embargo lifts when the first presentation begins in the scientific session in which the abstract is being presented: either 11:20 am CST on Wednesday, Feb. 22; 6:15 pm CST on Wednesday, Feb. 22; 11:00 am CST on Thursday, Feb. 23; 1:30 pm CST on Thursday, Feb. 23; or 11:53 am CST on Friday, Feb. 24. News media activities promoting late-breaking science are under embargo until the times noted above.*

**Presentation Number:** LBP1

**Publishing Title:** Association of Baseline ASPECTS and Collateral Score With Outcome Infarct Volume in Patients With Acute Ischemic Stroke due to Large Vessel Occlusions

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**Abstract Body:** Introduction: Radiological biomarkers can potentially play a key role in patient selection for intra-arterial therapy (IAT) in patients with acute ischemic stroke, as they are strongly associated with clinical outcome and benefit of IAT. The aim of this study was to assess the associations of baseline ASPECTS and collateral status with outcome infarct volume (OIV), and to determine whether these important radiological biomarkers modify the effect of IAT on OIV. Methods: Imaging data from the MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME and REVASCAT trials were pooled (HERMES). Primary outcome was OIV in mL on follow-up imaging,  $\log(x+1)$  transformed to account for zero values and for non-normality. ASPECTS was re-read on baseline NCCT by a core lab. Collateral status was graded on baseline CTA from 0 (absent) to 3 (excellent). The association between baseline ASPECTS and collateral status and OIV was examined with linear regression models controlling for prespecified baseline covariates and accounting for between-study variation. Results: Among 1088 patients included in the final analysis, baseline ASPECTS scores were median 8 (IQR 7-9). Outcome infarct volume was assessed

by MRI in 14% and CT in 86%, at median 26 hours (IQR 23-105) after randomization. ASPECTS was associated with OIV, with a relative ratio (RR) of 0.79 [95%CI 0.76-0.83]. Collateral status was associated with OIV, with worse grades corresponding to a larger OIV: grade 3 (n=416; median 25 ml [IQR 9-72]), reference; grade 2 (n=478; median 47 ml [IQR 13-109]), RR 1.32 [95%CI 1.12-1.55]; grade 1 (n=143; median 175 ml [IQR 72-284]), RR 2.48 [95%CI 1.93-3.18]; grade 0 (n=11; median 353 ml [IQR 94-444]), RR 4.26 [95%CI 2.02-9.01]). Other independent predictors of OIV included age, RR 0.94 [95%CI 0.88-0.99] per 10 years, baseline NIHSS, RR 1.21 [95%CI 1.12-1.30] per 5 points, presence of ICA-terminus occlusion, RR 1.61 [95%CI 1.21-2.13] versus M2 as a reference, and treatment with IAT, RR 0.73 [95%CI 0.62-0.87]. There was no evidence of interaction between ASPECTS (p=0.20) and collateral status (p=0.25) on IAT. Conclusion: In HERMES, baseline ASPECTS and collateral status were predictors of outcome infarct volume after acute ischemic stroke due to large vessel occlusion but did not modify the treatment effect.

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**Presentation Number:** LBP2

**Publishing Title:** Influence of Balloon, Conventional, or Distal Catheters on Angiographic and Clinical Outcomes in the STRATIS Registry

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**Abstract Body:** Background Higher rates of successful revascularization with the least number of passes correlate with improved clinical outcomes in acute stroke endovascular treatment. Different adjunctive technical approaches, such as proximal flow arrest using balloon guide catheter (BGC), large bore conventional guide catheter (CGC), or distal large bore catheter (DLBC) with lesional or regional aspiration, are aimed at improving revascularization rates. We present an analysis of the influence of thrombectomy techniques on angiographic and clinical outcomes from the STRATIS Registry. Methods STRATIS is a prospective, multicenter, observational single-arm registry of patients with large vessel occlusion treated with Solitaire/Mindframe  $\leq 8$  hours of symptoms onset. Technical approaches were grouped based on the first technique implemented: BGC; CGC; and DLBC. Posterior circulation target vessel occlusion and subjects with combined BGC and DLBC approach were excluded. A Core Lab blinded to clinical outcome extrapolated the techniques from the procedural reports. The main technical outcomes were: 1) First pass effect (FPE) defined as successful recanalization of  $\geq$ TICI2b after first device pass, 2) True FPE defined as TICI 3 or 2c after first pass; 3) Number of passes. Good clinical outcome was defined as mRS 0-2 at 90 days. Results 936 anterior circulation subjects were analyzed. The initial technical approach was 54% BGC, 32% DLBC, 8% CGC, and 6% mixed techniques. The groups were well balanced in reference to baseline factors. The rates of FPE were: 68%, 55%, and 43% ( $P < 0.001$ ), while the true FPE rates were: 48% vs. 34% vs. 26% ( $P < 0.001$ ) with BGC, DLBC, and CGC, respectively. The mean number of passes were:  $1.7 \pm 1.1$ ,  $2.0 \pm 1.3$ , and  $2.2 \pm 1.6$  ( $P < 0.001$ ), with BGC, DLBC, and CGC, respectively. The rates of successful recanalization of  $\geq$ TICI2b after all passes were 89% BGC, 88% DLBC, and 84% CGC ( $P = 0.51$ ). Rate of good clinical outcome was 62%, 50% and 45% with BGC, DLBC and CGC respectively ( $p = 0.001$ ). Conclusion Despite having similar final successful recanalization rates, BGC use as the first approach in STRATIS demonstrated a higher rate of good clinical outcome at 90 days compared to CGC and DLBC.

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Grant; Modest; Site PI for STRATIS, TREVO Registry, ARISE2 adn DAWN trials. Honoraria; Modest; Medtronic. Consultant/Advisory Board; Modest; Medtronic, Neuralanalytics, Inc.. Other; Modest; ESCAPE trial DSMB member. **T.L. Yao**: Consultant/Advisory Board; Modest; Medtronic (proctor). **D.S. Liebeskind**: Consultant/Advisory Board; Significant; Medtronic, Stryker. **N.H. Mueller-Kronast**: Consultant/Advisory Board; Modest; Medtronic.

**Presentation Number:** LBP3

**Publishing Title:** Primary Outcome Results of the Systematic Evaluation of Patients Treated With Neurothrombectomy Devices for Acute Ischemic Stroke (STRATIS) Registry

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**Abstract Body:** Background Since the publication of 5 seminal randomized trials in 2015 mechanical thrombectomy (MT) with stent retrievers has become standard of care for treatment of acute ischemic stroke patients due to large vessel occlusion, recommended by various guidelines across the world. Given the highly selected patient population in some of these randomized trials, questions remain whether process timelines, technical and functional outcomes can be achieved in a “real world” setting. Methods STRATIS is a prospective, multicenter, observational, single-arm registry designed to capture a “real world experience” without requirement of specialized imaging, age limits or technique exclusions at academic and non-academic centers in the USA. Patients with large vessel occlusion acute ischemic stroke were enrolled within 8 hours from symptom onset. Results A total of 984 patients at 55 sites were treated with Solitaire (n=953) or Mindframe Capture LP (n=31) as first device. The mean age was 67.7 years; 54.2% were male. The mean NIHSS was 17.3. IV-tPA was administered in 63.9%. The median time from onset to arrival in the enrolling hospital, door to groin, and groin to reperfusion were 138.5, 72, and 37 minutes, respectively. The Core lab adjudicated mTICI  $\geq 2b$  was achieved in 87.9%. Only 1.6% suffered a symptomatic intracranial hemorrhage. At 90 days, 56.6% achieved a mRS of 0-2 and the all-cause mortality was 14.4%. The benefit of treatment declined with age with 26.5% of patients  $\geq 90$  years of age achieving a mRS of 0-2 at 90 days. The overall median time from EMS scene arrival to puncture was 152 minutes. Each hour delay in this interval was associated with an 8.3% relative decline in the likelihood of achieving good outcome (mRS 0-2), or a number needed to harm of 18 per hour of delay. High enrolling centers ( $\geq 30$  patients) achieved significantly shorter median door to puncture times, 67 vs. 86 minutes ( $p < 0.001$ ). Conclusion This largest to date prospective Solitaire registry documents that MT can be safely performed in the community with similar process metrics and clinical outcomes to those observed in randomized trials. The decrease of clinical benefit over time warrants optimization of the pre-hospital and hospital system of care.

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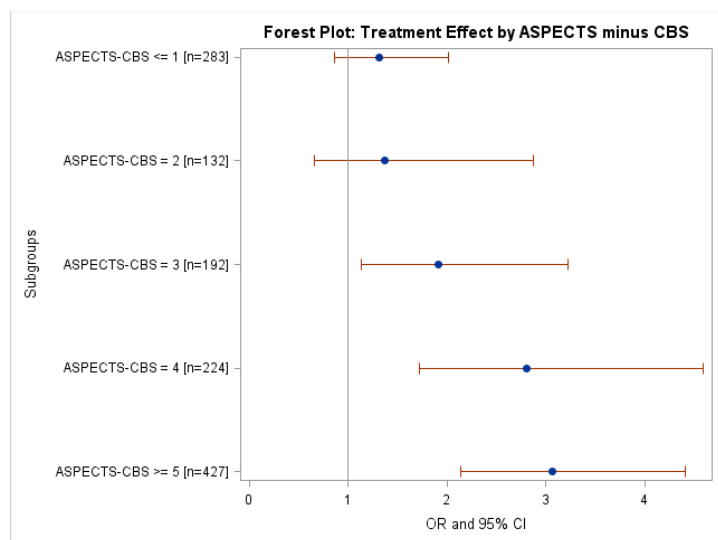
Neurovascular (J&J). **D.R. Yavagal**: Research Grant; Modest; Site PI for STRATIS, TREVO Registry, ARISE 2 and DAWN trials. Honoraria; Modest; Medtronic. Consultant/Advisory Board; Modest; Medtronic, Neuralanalytics, Inc.. Other; Modest; ESCAPE trial DSMB member. **T.L. Yao**: Consultant/Advisory Board; Modest; Medtronic (proctor). **D.S. Liebeskind**: Research Grant; Significant; NIH. Consultant/Advisory Board; Significant; Stryker, Medtronic. **D.C. Haussen**: None.

**Presentation Number:** LBP4

**Publishing Title:** Imaging Predictors of Clinical Outcome and Endovascular Treatment Response: Results From the Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials (HERMES)

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**Abstract Body:** Purpose: To investigate imaging alone or in combination for selection of acute ischemic stroke patients with anterior large vessel occlusion (LVO) likely to benefit from endovascular therapy (EVT). Methods: Pre-specified meta-analysis of individual patients' data from MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT and PISTE (1352 patients enrolled, thrombectomy, 667 [49.3%], control 685 [50.7%]). Treatment effect (ordinal mRS analysis) and risk of symptomatic intracranial hemorrhage by baseline imaging markers (ASPECTS score 8-10, 5-7, 0-4; involvement of MCA >1/3; hyperdense artery sign, occlusion site (ICA, M1, M2), clot burden score [CBS] 8-10, 5-7, 0-4; and collateral score 3, 2, 0-1) evaluated by a central imaging Core Lab. Results: Relative benefit for EVT on the 90-day mRS was consistent across all ASPECTS, collateral score and occlusion sites (pinteraction>0.05). Absolute benefit was highest with high ASPECTS, good collaterals and ICA occlusions. Lower CBS and presence of hyperdense sign was associated with increased benefit with EVT (pinteraction<0.05). Increased risk of sICH was noted for >1/3 MCA (adjusted OR, 5.6; 95%CI, 1.4-21.2) and ASPECTS 0-4 (adjusted OR, 5.7; 95%CI, 0.8-38.7). The Number Needed to cause sICH was 6.6 for MCA>1/3 and 4.7 for ASPECTS 0-4. A linear combination of ASPECTS and CBS scores modified the treatment effect. Larger ASPECTS minus CBS scores was associated with increasing odds of benefit with EVT (pinteraction = 0.007) (figure). Treatment effect by imaging factors on additional secondary outcomes (mRS 0-2, dramatic improvement at 24h, PH type 2 and mortality) will be presented. Conclusions: Baseline neuroimaging findings are either associated with a higher favorable response or higher risk of sICH in endovascular treated stroke patients. A simple linear combination of score categories, indicating less infarct extent (ASPECTS) and higher clot burden (CBS), may help to determine patients most likely to benefit from EVT.



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**Presentation Number:** LBP6

**Publishing Title:** Increased Blood Pressure Variability in the SPRINT Trial Is Associated With Incident Stroke

**Author Block:** Adam de Havenon, Univ of Utah, Salt Lake City, UT; David Tirschwell, Univ of Washington, Seattle, WA; Greg Stoddard, Jennifer J. Majersik, Adam Bress, Univ of Utah, Salt Lake City, UT

**Abstract Body:** Introduction: The Systolic Blood Pressure Intervention Trial (SPRINT) demonstrated a 25% reduction in cardiovascular events for systolic blood pressure (SBP) goal of <120 mmHg versus <140 mmHg. Stroke (combined hemorrhagic and ischemic) was an outcome. Increased blood pressure variability (BPV) has been associated with stroke. Our objective was to determine the association between BPV and incident stroke in SPRINT, a cohort with more aggressive blood pressure control than prior studies.

Methods: This is a secondary analysis of SPRINT data. The baseline blood pressure reading and readings after incident stroke were discarded. Patients with <4 total readings were excluded. BPV was analyzed per-patient, using all available readings to calculate: standard deviation (SD), coefficient of variation (CV), average real variability (ARV), and successive variation (SV). BPV differences between groups were tested with Student's t-test. Cox proportional hazards regression generated hazard ratios for incident stroke. Patients were censored at stroke or trial completion.

Results: Our analysis included 8,909 patients, 109 of whom developed stroke. Median follow-up was 3.3 years and number of readings per patient was 12 (IQR 10,13). All measures of BPV were higher in patients with incident stroke, Table 1. In the Cox model, the highest tertile of BPV was associated with incident stroke, Table 2, which was not affected by treatment arm assignment.

Conclusion: Higher BPV is associated with incident stroke in SPRINT, a cohort with unprecedented blood pressure control. Future studies may want to use blood pressure lowering medications that also reduce BPV, such as calcium-channel blockers.

**Table 1: Blood pressure mean and variability in patients with or without incident stroke in SPRINT.**

Measure of BPV (mean±SD)	Patients without stroke (n=8,800)	Patients with stroke (n=109)	p-value
SBP Mean	128.2±9.9	132.6±11.6	<0.001
DBP Mean	71.6±9.2	70.5±11.1	0.248
SBP SD	11.2±4.3	12.9±5.9	<0.001
DBP SD	6.8±2.3	7.6±2.9	<0.001
SBP CV	8.7±3.2	9.7±4.0	0.003
DBP CV	9.5±3.2	10.8±4.1	<0.001
SBP ARV	11.7±5.1	13.7±8.2	<0.001
DBP ARV	7.1±2.7	8.1±3.6	<0.001
SBP SV	14.7±6.1	16.6±8.9	0.001
DBP SV	8.8±3.2	9.7±4.0	0.003

SBP = systolic blood pressure  
DBP = diastolic blood pressure  
SD = standard deviation  
CV = coefficient of variation  
ARV = average real variability  
SV = successive variation

**Table 2: Cox proportional hazards models for SBP SD fitted to the outcome of incident stroke.**

Predictor of Stroke	Hazard ratio	95% confidence interval	p-value
SBP SD alone			
Lowest vs. Highest tertile	1.84	1.17–2.89	0.008
Interaction with treatment arm assignment	1.38	0.55–3.42	0.490
SBP SD, adjusted for SBP mean			
Lowest vs. Highest tertile	1.60	1.01–2.53	0.044
Interaction with treatment arm assignment	1.36	0.73–2.51	0.333
SBP SD, adjusted for multiple variables*			
Lowest vs. Highest tertile	1.62	1.01–2.58	0.045
Interaction with treatment arm assignment	1.29	0.52–3.22	0.588

\* Adjusted for patient age, gender, black race, aspirin use, statin use, number of blood pressure medications, smoking status, HDL and serum glucose level at trial enrollment.

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**Presentation Number:** LBP7

**Publishing Title:** Outcome Infarct Volume and Location as Prognostic Biomarkers for Effect of Intra-arterial Therapy on Functional Outcome After Acute Ischemic Stroke

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**Abstract Body:** Introduction: Infarct size is believed to be a key determinant of outcome. In addition, infarct location may also play an important role. Yet, it remains unclear to what extent improved functional outcome after IAT can be explained by tissue fate and infarct location.

Methods: We analyzed clinical and imaging data as part of the HERMES collaboration. Primary outcome was mRS at 90 days. OIVs and infarct locations were measured on follow-up CT or MR imaging. Location was defined as laterality and involvement in the 10 ASPECTS regions. Multivariate ordinal logistic regression including random effect for between-study variance was used to assess the association between OIV and location, and ordinal mRS. Model A included OIV, age, pre-stroke mRS and baseline NIHSS, whereas Model B additionally included location. Likelihood function tests (Akaike and Bayesian Information Criterion) were used to determine the optimal model. Mediation analysis was performed to investigate if a reduction in OIV is the underlying mechanism of an improved mRS after IAT.

Results: Among 1212 patients, 85% had follow-up CT imaging. Median OIV was 41 mL (IQR:13-115), and 36.6% (444/1212) achieved mRS 0-2. OIV was significantly associated with mRS score (OR 0.91, 95%CI 0.89-0.94) per 10 mL, as well as age, pre-stroke mRS, baseline NIHSS, IAT, and outcome ASPECTS involvement, but not laterality. Model B, including location, fitted the data better than Model A (AIC: 3541 vs 3484; BIC: 3545 vs 3491). This was due principally to the involvement of Internal Capsule (OR 0.35;  $p < 0.001$ ) and to a lesser extent Insula and M6 (resp. OR 0.69;  $p = 0.018$  and OR 0.71;  $p = 0.04$ ). The results showed only partial mediation of treatment effect by OIV, with an OR for IAT of 2.35 (95%CI 1.82-3.03) on mRS even after correcting for OIV.

Conclusion: In HERMES, OIV and outcome ASPECTS location were independent predictors of functional outcome. After correcting for OIV, patients in the IAT arm had significantly better clinical outcomes than

controls, suggesting that reduction in OIV, at least as measured in this dataset, may not entirely explain the clinical benefit observed with IAT.

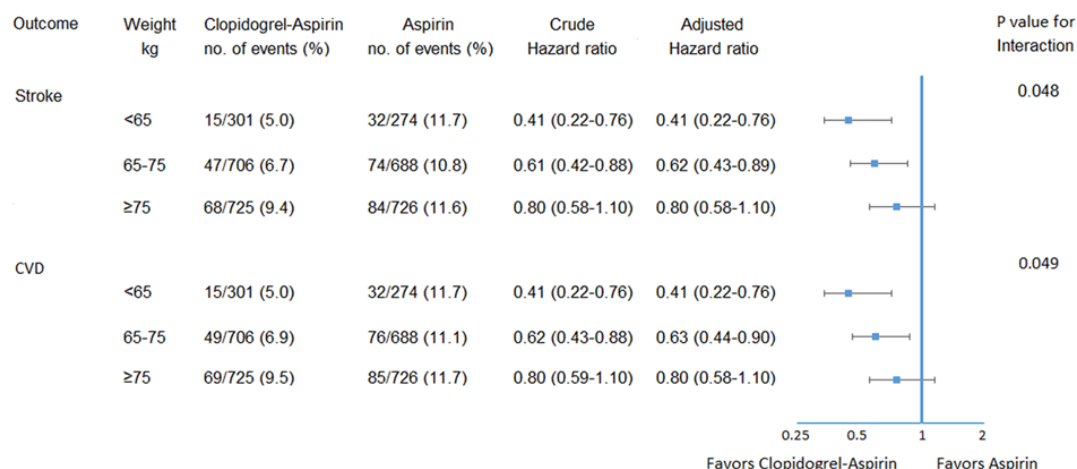
**Author Disclosure Block:** **A.M.M. Boers:** Ownership Interest; Modest; Nico-lab BV. **I.G.H. Jansen:** None. **H.A. Marquering:** Ownership Interest; Modest; Nico-lab BV. **B.K. Menon:** Honoraria; Modest; Penumbra. **L. San Román:** None. **M. Goyal:** Research Grant; Significant; Medtronic. Consultant/Advisory Board; Modest; Medtronic, Stryker, Microvention. **W.H. van Zwam:** Consultant/Advisory Board; Modest; Stryker, paid to institution. **Y.B.W. Roos:** None. **A.J. Yoo:** None. **L.F.M. Beenen:** None. **H.F. Lingsma:** None. **A. Demchuk:** Honoraria; Modest; Medtronic. **D.S. Liebeskind:** Consultant/Advisory Board; Significant; Stryker, Medtronic. **B.C. Campbell:** Research Grant; Significant; Significant; The ESCAPE, EXTEND-IA, REVASCAT and PISTE trials and HERMES collaboration received unrestricted grant support from Medtronic, the SWIFT PRIME trial was sponsored by Medtronic, the PISTE. **A. Dávalos:** Consultant/Advisory Board; Modest; Medtronic. **S. Brown:** Consultant/Advisory Board; Modest; Medtronic. **J.L. Saver:** Consultant/Advisory Board; Modest; Medtronic, Stryker, Neuravi, BrainsGate, Pfizer, Squibb, Boehringer Ingelheim (prevention only), ZZ Biotech, Cognition Medical, St. Jude Medical, Genentech (unpaid). **T.G. Jovin:** Consultant/Advisory Board; Modest; Codman, Neuravi, Medtronic (unpaid), Stryker (unpaid). Other; Modest; Silk Road (stock), Blockade (stock). **M.D. Hill:** Research Grant; Significant; Medtronic, Stryker, Bayer Canada, Boehringer Ingelheim. Other Research Support; Significant; Alberta Innovates Health Solutions. Honoraria; Modest; Boehringer Ingelheim, BMS-Pfizer, Bayer Canada. Ownership Interest; Modest; Calgary Scientific Inc.. Consultant/Advisory Board; Modest; Merck LLC. **P.J. Mitchell:** Research Grant; Significant; Codman Johnson and Johnson (to institution), Medtronic (to institution), Stryker (to institution). Consultant/Advisory Board; Modest; Codman Johnson & Johnson (unpaid). **D.W.J. Dippel:** Research Grant; Significant; AngioCare BV (to institution), Medtronic/Covidien/EV3 (to institution), MEDAC GmbH/LAMEPRO (to institution), Penumbra Inc. (to institution), Stryker (to institution), Top Medical/Concentric. **C.B.L. Majoie:** Research Grant; Significant; CVON/Dutch Heart Foundation grant (to institution), Stryker (to institution).

**Presentation Number:** LBP9

**Publishing Title:** No Superior Effect of Clopidogrel Added to Aspirin on Stroke Recurrence in Minor Stroke or TIA Patients With High Body Weight

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**Abstract Body:** Objective: To assess whether body weight would influence the efficacy and safety of dual antiplatelet therapy in minor stroke and TIA patients. Methods: The data of this post-hoc analysis came from the Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) trial. Male patients were enrolled in this study, who were divided into three groups based on body weight on admission (<65kg, 65-75kg and ≥75kg). The efficacy outcomes include stroke recurrence and combined vascular events (CVE); and the safety outcome includes any bleeding during 90 days of follow-up. The interaction of the treatment effects of the dual antiplatelet therapies among patients with different weight levels, was assessed by Cox proportional hazards models. Results: Dual antiplatelet therapy (DAT) is superior to mono antiplatelet therapy (MAT) for reducing the risk of stroke, among minor stroke/TIA patients with weight <65kg (n=575, 5.0% vs 11.7%; hazard ratio [HR], 0.41; 95% confidence interval [CI], 0.22-0.76) or 65-75kg (n=1394, 6.7% vs 10.8%, HR, 0.62; 95% CI, 0.43 to 0.89). However, there was no significant difference in stroke recurrence between DAT and MAT in patients with weight ≥75kg (n=1451, 9.4% vs 11.6%; HR, 0.80; 95% CI, 0.58 to 1.10). There was a significant interaction between weight and antiplatelet therapy on stroke recurrence (p<0.05). The similar result was found for CVE. We replicated our findings when using CVE as the outcome. A little more bleeding events were found in DAT group among patients with weight<65kg (3.7% vs 2.2%), but there was no significant difference. Interpretation: DAT does not show benefit in patients with higher weight, compared with MAT. No more bleeding events were found in DAT group than MAT group among patients with lower weight.



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**Presentation Number:** LBP10

**Publishing Title:** Combination of Fingolimod With Alteplase Between 4.5-6 Hours of Acute Ischemia Stroke: A Pilot Study

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**Abstract Body:** Background : Secondary inflammation, microvascular thrombosis, and disruption of the blood-brain barrier all contribute to limiting the narrow therapeutic window for alteplase to 4.5 hours in acute ischemic stroke. Fingolimod may attenuates the intravascular and parenchyma inflammation to increase blood flow during the reperfusion phase by inhibiting the homing of lymphocytes. We thereby aim to investigate the safety and efficacy of combination of fingolimod and alteplase within 4.5 to 6 hours in acute ischemic stroke. Methods: In this multi-center, nonrandomized, evaluator-blind study, patients with an intracranial anterior circulation occlusion, with infarct core volume < 80ml , meanwhile the perfusion lesion on transit-time maps that was >20% than the infarct-core lesion, with a volume of at least 15mL, were included. Patients were assigned into three groups: control group (treatment adhered to current AHA guidelines), standard dose alteplase group (0.9mg/kg), and fingolimod plus alteplase group (standard dose alteplase and three daily dose of oral fingolimod). All patients underwent pretreatment and 24-hour perfusion/angiographic imaging with CT, and no-contrast CT at 7days. Lymphocyte subsets were analyzed from all subjects. The co-primary end points were penumbra salvage and improvement in the NIHSS score between baseline and 24h. Results: 10 patients were assigned to the control group, 10 to alteplase group and 13 to fingolimod plus alteplase group. The fingolimod plus alteplase group exhibited greater penumbra salvage ( $66.8 \pm 42.5$  vs  $30.9 \pm 38.9$  mL,  $P=0.045$ ) and greater clinical improvement ( $3.4 \pm 2.5$  vs  $1.1 \pm 2.8$ ,  $P=0.04$ ) at 24 h, compared with the alteplase group. Longer-term clinical outcomes show a trend of fewer fingolimod plus alteplase group than alteplase alone, but with no statistical significance. Fingolimod did not increase the incidence of intracerebral bleeding and other serious adverse events over alteplase. Conclusions: In this pilot study, combination of fingolimod and alteplase within 4.5-6 h was associated with greater ischemia brain tissue salvage and better improved clinical outcomes in the early stage of acute ischemic stroke. Good recovery at 90 days did not differ between the three groups.

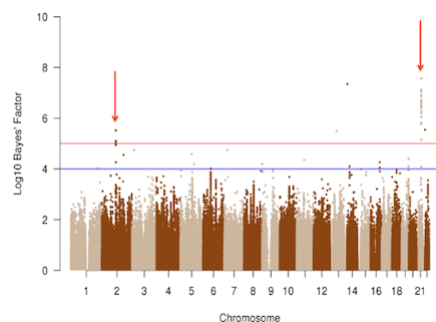
**Author Disclosure Block:** D. Tian: None. K. Shi: None. Z. Zhu: None. J. Yao: None. X. Yang: None. L. Su: None. S. Zhang: None. M. Zhang: None. Q. Liu: None. D. Huang: None. M. Lou: None. F. Shi: None.

**Presentation Number:** LBP12

**Publishing Title:** Meta-analysis of Transethnic Association (MANTRA) Reveals Loci Associated With Neurological Instability After Acute Ischemic Stroke

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**Abstract Body:** Introduction: Following acute ischemic stroke (AIS), neurological deficits can rapidly improve or deteriorate. Mechanisms such as reperfusion and hemorrhagic transformation contribute to early neurological instability, but little is known about genetic influences. Hypothesis: Common genetic variants influence early neurological outcomes after AIS. Methods: AIS patients were prospectively enrolled at four sites (St Louis, Barcelona, Helsinki and Krakow). Early neurological instability was quantified from NIHSS scores obtained within 6h and again at 24h after stroke onset:  $\Delta\text{NIHSS}_{24\text{h}} = \text{NIHSS}_{6\text{h}} - \text{NIHSS}_{24\text{h}}$ . Genotyping was generated for common variants, imputing up to 6 million SNPs. Heritability of  $\Delta\text{NIHSS}_{24\text{h}}$  was estimated by genome-wide complex trait analysis. The model used was:  $\Delta\text{NIHSS}_{24\text{h}} = \text{SNP} + \text{NIHSS}_{6\text{h}} + \text{age} + \text{gender} + \text{glucose} + \text{PCA1-4}$ . Samples were analyzed separately by site/ethnicity; joint analysis with a Bayesian approach correcting for population admixture (MANTRA) was performed. Results: Median NIHSS<sub>6h</sub> of 8 (IQR 4-16) and mean  $\Delta\text{NIHSS}_{24\text{h}}$  of 2 (IQR 0-5) were found in 2,614 patients. Estimated heritability of  $\Delta\text{NIHSS}_{24\text{h}}$  was 14.6%. Two novel loci influenced  $\Delta\text{NIHSS}_{24\text{h}}$  with genome-wide significance (Figure): rs35116504 (LBF=5.523) in an intron of FBLN7 (chromosome 2); and rs6517243 (LBF=7.568) in an intron of RCAN1 (chromosome 21). FBLN7 encodes fibulin-7, a matrix glycoprotein that is expressed by endothelial cells and regulates angiogenesis. RCAN1 encodes regulator of calcineurin 1 and has been implicated in Alzheimer's disease, Down's Syndrome, and atherosclerosis. Conclusion: Common genetic variants have a moderate influence on early neurological instability after ischemic stroke. We identified 2 novel genetic loci that implicate vascular mechanisms in early outcomes after AIS. Replication in an independent cohort is ongoing.



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**Presentation Number:** LBP13

**Publishing Title:** Child-Mediated Public Stroke Awareness among Minorities: Results of a Randomized Controlled Trial

**Author Block:** Olajide Williams, Ellyn Leighton-Herrmann Quinn, Alexandra Desorbo-Quinn, **Monique Hedmann**, Mindy Feldman Hecht, Columbia Univ Medical Ctr, New York, NY; Joseph P. Eimicke, Jian Kong, Jeanne Teresi, Res Div, Hebrew Home at Riverdale, Bronx, NY; William Gerin, The Pennsylvania State Univ, State College, PA; James Noble, Columbia Univ Medical Ctr, New York, NY

**Abstract Body:** School-based stroke education programs are effective in improving stroke knowledge of children, but it is uncertain whether stroke-literate children can inform their family members and respond appropriately during real life stroke events. Hip Hop Stroke (HHS) is a culturally tailored multimedia intervention designed to improve stroke literacy (knowledge of cardinal stroke symptoms, calling 911) of 4th-6th grade students (direct targets) and their parents (indirect targets). We evaluated the effectiveness of HHS on child to parent knowledge transfer in a cluster randomized controlled trial, randomized by school. Intervention children received HHS and attentional control children received nutrition education. Child-parent dyads completed stroke knowledge instruments at baseline, immediately post-program and 3-months later. 3081 children and 887 parents from 22 schools completed at least the baseline and immediate posttest instruments. The average cluster size within school was 140 children and 52 parents per school. Parents were mostly female (84.5%), 26-45 years old (77%), and African American (81.2%). Internal consistency (alpha) estimates for stroke recognition and action constructs of the instrument were >0.7 across each parental test sequence. At baseline, 17% (CI 13-21%) of parents in the control and 20% (CI 15-25%) in the intervention group demonstrated full stroke literacy (5 stroke symptoms, chest pain distractor, calling 911). This increased to 30% (CI 23-36%) immediately post-program in the intervention group, compared to 21% (CI 17-25%) in the control group. The intervention arm evidenced a significantly greater gain in knowledge relative to the control arm ( $p=0.0012$ ). Only 2% (CI 1-3%) of parents could identify all letters of the FAST (Face/Arm/Speech/Time) mnemonic at baseline. This increased to 20% at immediate posttest (CI 16-24%) and 17% at delayed posttest (CI 12-23%),  $p<0.0001$ . Three-year follow up of 315 parents revealed 27 (8.6%) self-reported stroke events affecting a family member (18 intervention, 9 control). Four children, all of whom were in the intervention group, were involved in calling 911. Implementation of Hip Hop Stroke leads to significant gains in stroke knowledge among parents of participating children.

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**Presentation Number:** LBP14

**Publishing Title:** Establishing the First Mobile Stroke Unit in New York City

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**Abstract Body:** Introduction Compared to standard care, specialized mobile stroke units (MSUs) are associated with faster thrombolysis times for acute ischemic stroke. We describe the implementation of the first MSU in New York and the East Coast of the U.S., in association with New York-Presbyterian Hospital (NYP) and the Fire Department of New York (FDNY). Methods The first steps to implement the NYP MSU were securing donor funds to build the unit and assembling a multi-disciplinary MSU team. The departments of neurology, emergency medicine, emergency medical services, radiology, laboratory services, information technology (IT), nursing, and pharmacy collaborated to operationalize the unit and develop training programs for clinical staff. Local stakeholders, including FDNY and the Regional Emergency Medical Services of New York City, were engaged to integrate the MSU into the New York City emergency dispatch system. Finally, clinical IT infrastructure was installed on the MSU and incorporated into NYP's existing information systems. The MSU is dual-dispatched to all suspected stroke calls with a basic life support unit and is staffed by two paramedics, one radiology technologist, and a vascular neurologist. The unit is operational on weekdays from 7 AM to 3 PM. Results The NYP MSU began operating on October 3rd, 2016 after 2 years of planning. Barriers to implementation included building an operational IT infrastructure, establishing a functional pre-notification system between the MSU and accepting hospitals, and integrating the MSU into institutional workflows for electronic documentation, order entry, and hospital registration. As of November 9th, 2016, the MSU responded to 30 calls. Of the 8 patients who were transported to the emergency department with suspected stroke, 5 were stroke mimics. Two patients were treated with IV thrombolysis within 90 minutes of symptom onset without complications. One patient received endovascular therapy. Conclusions The NYP MSU launched successfully in October 2016. Challenges to implementation included establishing a transfer-of-care process at receiving hospitals and integrating the unit into existing IT systems and clinical workflows.

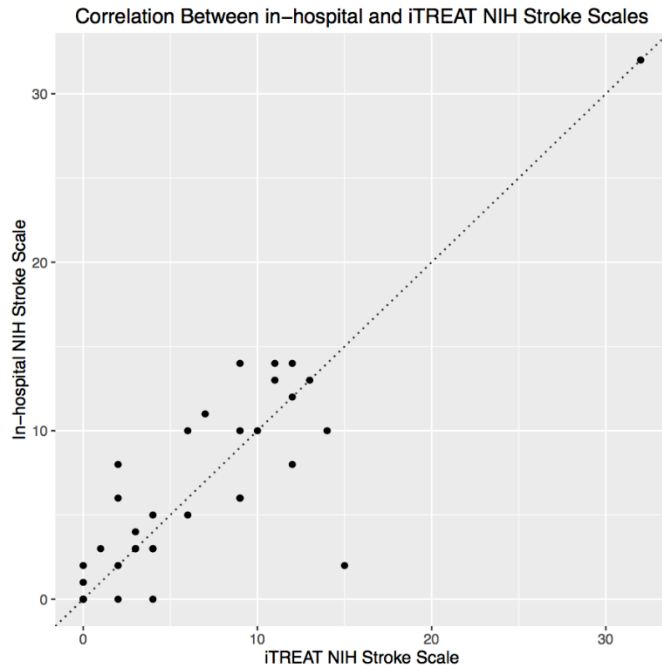
**Author Disclosure Block:** **B.R. Kummer:** None. **M.P. Lerario:** None. **A.C. Ganzman:** None. **B.B. Navi:** None. **D. Ribaud:** None. **S. Mir:** None. **S. Pishanidar:** None. **R. Mehendale:** None. **O. Williams:** None. **H. Kamel:** None. **R.S. Marshall:** None. **M.S.V. Elkind:** None. **M.E. Fink:** None.

**Presentation Number:** LBP15

**Publishing Title:** Feasibility of Ambulance-based Telestroke in a Rural EMS System: The iTREAT Study

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**Abstract Body:** Objectives: We previously used simulated scenarios to demonstrate that ambulance-based telestroke assessment is technically feasible and clinically reliable in a rural EMS setting. In the current analysis, we aimed to affirm feasibility with live acute stroke encounters. Methods: The iTREAT mobile telestroke platform is a low-cost, off-the-shelf system deployed with 7 rural ambulance agencies in central Virginia. EMS providers activate the system for any acute stroke or neurologic emergency. Upon activation, study investigators initiate a video call and assess the NIH Stroke Scale during ambulance transport. Mobile telestroke assessments are compared to a blinded hospital NIHSS obtained via standard acute stroke protocol. Statistical analysis includes agreement of the ambulance and hospital NIHSS using Spearman rank correlation ( $p < 0.05$ ) and Bland-Altman test comparing differences based on stroke severity. Results: Among 57 iTREAT activations, 39 were successful (68%), 14 unsuccessful (25%), and 4 interrupted prior to completion (7%). Successful activation varied by EMS agency, call volume, and iTREAT experience (range 38 - 84%). Of the unsuccessful activations, 12 resulted from logistical constraints (e.g. user error, call back delay) and 2 from actual issues with broadband connectivity. Ambulance and hospital NIHSS scores showed a positive rank-order correlation,  $\rho = 0.76$ ,  $P = 2.06 \times 10^{-7}$  (Figure). Bland-Altman analysis showed no significant difference in average scores:  $-0.06$  ( $-1.24$   $-1.13$ ). Median ambulance transport and mobile connectivity times were 25 and 10 minutes, respectively. Conclusion: Ambulance-based telemedicine facilitating acute stroke consultation is feasible in a rural EMS network. Further refinement is necessary to augment EMS proficiency and mobile broadband connectivity along ambulance routes. Next steps include a multicenter trial to explore efficacy and generalizability across varying emergency stroke systems.



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**Presentation Number:** LBP16

**Publishing Title:** A Novel Couples-Based Intervention for Stroke Survivors and Partner Caregivers Improves Mood and Quality of Life

**Author Block:** **Alexandra L Terrill**, Univ of Utah, Salt Lake City, UT; **Maija Reblin**, Moffitt Cancer Ctr, Tampa, FL; **Justin J MacKenzie**, Beth Cardell, Cynthia A Berg, Lorie G Richards, Jennifer J Majersik, Univ of Utah, Salt Lake City, UT

**Abstract Body:** **OBJECTIVE:** Depressive symptoms post-stroke occur in 30-50% of survivors and partner caregivers, which adversely affect function and quality of life. Further, emotional well-being is interdependent in couples: depression in one partner increases risk of depression in the other. Sustaining well-being in both partners is important for rehabilitation engagement and community re-integration, yet interventions to support couples after stroke are lacking. We aimed to pilot test a positive psychology-based intervention (PPI) in couples post-stroke. **HYPOTHESIS:** The PPI will improve mood and quality of life in stroke survivors and caregivers. **METHODS:** Participants were recruited through University-affiliated outpatient neurology and rehabilitation clinics. Couples consisted of one partner who had a stroke >6 months ago and a cohabiting partner caregiver. One or both partner(s) reported depressive symptoms. Participants engaged in an 8-week self-administered PPI, completing two activities alone and two together each week (e.g. expressing gratitude, practicing kindness). Activity booklets, tracking calendars, and weekly check-in calls were provided. Pre- and post-intervention measures included the PROMIS-Depression-SF, the Stroke Impact Scale (SIS 3.0) and Older Persons Quality of Life (OPQOL). Outcomes pre- vs post-PPI were analyzed via paired t-tests. **PARTICIPANTS:** Eleven community-dwelling couples were enrolled; 6 survivors and 5 partners were women. Mean age was 56 years (range: 27-84). Time since stroke ranged from 8 months to >5 years. **RESULTS:** Post-PPI, depressive symptoms significantly decreased ( $p=.04$ ), with half of stroke survivors and over 80% of caregivers reporting less depression. Survivors had improvement in the SIS meaningful activities domain ( $p=0.006$ ); survivors and partners improved in OPQOL overall life quality ( $p=0.05$ ). All other SIS and OPQOL subscales improved pre- vs post-PPI but did not reach significance in this small sample. **CONCLUSIONS:** Preliminary results suggest PPI may be effective for improving mood, engagement in meaningful activities, and quality of life in couples post-stroke. This represents a promising first step in a novel dyadic approach in this population.

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**Presentation Number:** LBP17

**Publishing Title:** Higher Systolic Blood Pressure Parameters Within 24 hours After Thrombectomy Independently Correlates With Worse Outcomes in Stroke Patients

**Author Block:** **Eva A Mistry**, Houston Methodist Hosp, Houston, TX; Akshitkumar M. Mistry, Vanderbilt Univ Medical Ctr, Nashville, TN; Mohammad O. Nakawah, Houston Methodist Hosp, Houston, TX; Michael T. Froehler, Rohan V. Chitale, Matthew R. Fusco, Vanderbilt Univ Medical Ctr, Nashville, TN; John J. Volpi, Houston Methodist Hosp, Houston, TX

**Abstract Body:**

Background:

Whether blood pressure control within 24 hours after thrombectomy (T24) for acute ischemic stroke affects patient outcome is unknown. We studied the association between several blood pressure parameters (BPPs) within T24 and patients' 90-day modified Rankin score (mRS).

Methods:

We retrospectively identified 116 patients at two institutions who underwent ICA, A1, M1, or M2 thrombectomy from April 2015 to July 2016. We excluded patients with a known pre-stroke mRS > 4, perioperative stroke with major cardiovascular surgeries, or terminal conditions. We correlated the highest, lowest, average, and range of systolic (SBP), diastolic, and mean arterial (MAP) pressures with 90-day mRS using ordered logistic regression. Other variables collected were: age, sex, NIH-stroke scale (NIHSS), history of hypertension (HTN), hyperlipidemia, diabetes, smoking, atrial fibrillation (Afib), time to groin puncture, post-thrombectomy thrombolysis in cerebral infarction (TICI) score, anticoagulant or antiplatelet medication use at baseline, tPA administration, hemorrhagic conversion (ICH), and antihypertensive (antiHTN) or pressor drip use within T24.

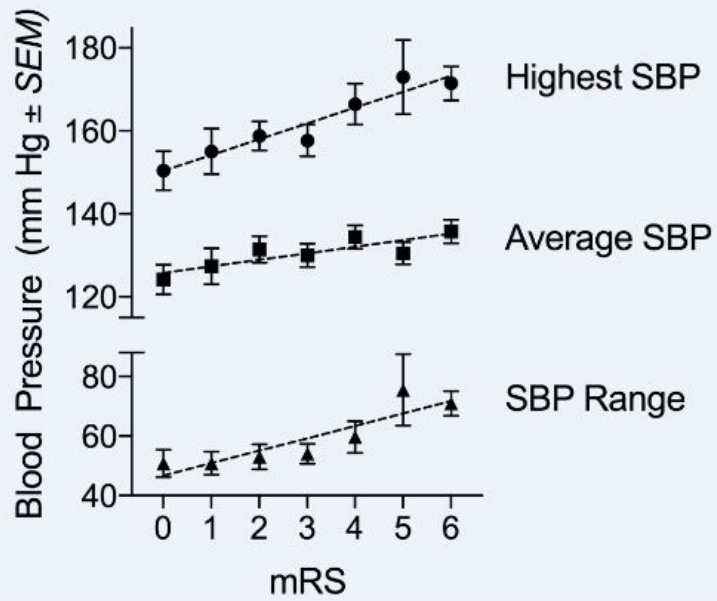
Results:

Average age was 64.5 years; 56% were females; and median NIHSS was 15. TICI 2b/3 was achieved in 86%. Symptomatic ICH was noted in 4 patients. In univariate analysis, highest, average, and range of SBP, range of MAP, age, HTN, Afib, NIHSS, antiHTN, and ICH significantly correlated with worse 90-day mRS. In multivariate analysis, highest (adjusted proportional odds ratio: 1.03 [1.01-1.05], p=0.007), average (1.03 [1.00-1.06], p=0.03), and range of SBP (1.02 [1.01-1.04], p=0.01) remained significant amongst the BPPs.

Conclusion:

High systolic pressures and large variations in them within T24 are associated with worse outcomes. Further prospective studies are warranted to confirm these findings and evaluate these variables as intervenable risk factors to improve outcomes after thrombectomy.

### Correlation of Systolic Blood Pressure Parameters with 90-Day mRS



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**Presentation Number:** LBP18

**Publishing Title:** Ischemic Injury Amplifies Hippocampal NLRP3 Inflammasome in Diabetes: Improvement of Spatial Memory and Cognition Deficits With NLRP3 Inhibition

**Author Block:** Rebecca Ward, John Paul Valenzuela, Augusta Univ, Augusta, GA; Sarah Cox, Medical Coll of Georgia, Augusta, GA; Adviye Ergul, Augusta Univ, Augusta, GA

**Abstract Body:** Diabetes increases risk and worsens progression of cognitive impairment via greater occurrence of small vessel disease and stroke but underlying mechanisms are not fully understood. Inflammation is a common finding in diabetes, stroke and cognitive impairment. We proposed that diabetes stimulates NLRP3 inflammasome and is associated with neurodegeneration in the hippocampus, a major domain for learning and memory. We further hypothesized that stroke amplifies NLRP3 activation and inhibition of NLRP3 will reduce cognitive deficits after stroke in diabetic rats. To address the first hypothesis, we measured NLRP3 expression and apoptosis in the hippocampus (DG) as well as spatial and recognition memory (Y-maze, novel placement and novel object recognition tests) in male control and type 2 diabetic rats (induced by high fat diet and low dose STZ injection). Next we measured NLRP3 and downstream targets caspase-1 and IL-1 in hippocampal neurons (HT22 cells) grown in high glucose + palmitate to mimic the in vivo model of diabetes. To address the second hypothesis, we determined hippocampal NLRP3 expression and neurological (sensorimotor and cognitive) deficits 14 days after stroke in control and diabetic rats. An additional group of diabetic rats was treated with MCC950 (3mg/kg), a small molecular inhibitor of NLRP3, at 1 and 3 h after reperfusion. NLRP3 activation was greater in diabetes both in vivo and in vitro. Cognitive function was impaired as early as 6 weeks after diabetes onset. NLRP3 activation was amplified and cognitive function was worsened by stroke in diabetes. NLRP3 inhibition by MCC950 improved sensorimotor and cognitive function. These results suggest that NLRP3 activation may contribute to hippocampal neurodegeneration leading to poor memory/cognitive deficits after stroke in diabetic animals.

SHAM	Control (n=5)	Diabetes (n=5)	
Blood Glucose (mg/dl)	84.0 ± 11.0	230.0 ± 56.0**	
Body Weight (kg)	432.7 ± 7.6	449.6 ± 9.4	
NLRP3 (% threshold area)	0.52 ± 0.09	2.84 ± 0.81*	
TUNEL positive cells	3.25 ± 0.63	12.25 ± 1.38	
Spatial Recognition Index	0.64 ± 0.02	0.56 ± 0.01*	
Object Recognition Index	0.80 ± 0.02	0.63 ± 0.02**	
Y-Maze (% time in novel arm)	63.3 ± 0.1	47.0 ± 0.1*	
STROKE	Control (n=7)	Diabetes (n=6)	Diabetes + MCC950 (3mg/kg) (n=3)
Blood Glucose (mg/dl)	76.3 ± 7.8	313.8 ± 43.5***	356.9 ± 12.6***
Body Weight (kg)	408.9 ± 33.0	341.7 ± 26.3**	327.7 ± 28.3**
Object Recognition Index			
BL	0.74 ± 0.05	0.64 ± 0.04**	0.64 ± 0.01
D14	0.75 ± 0.03	0.52 ± 0.07***, #	0.85 ± 0.01*
Y-Maze (% time in novel arm)			
BL	68.7 ± 2.1	47.0 ± 5.3***	44.7 ± 5.8
D14	46.0 ± 1.0#	38.5 ± 2.1*, #	57.0 ± 3.5*
Composite Score			
BL	14.00 ± 0.00	13.89 ± 0.17	13.89 ± 0.11
D14	12.16 ± 2.05	8.72 ± 4.09**	13.45 ± 0.40

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001 vs control; #p<0.05, ##p<0.01, ###p<0.001 vs BL; &p<0.05, ^p<0.01 vs diabetes

**Author Disclosure Block:** R. Ward: None. J. Valenzuela: None. S. Cox: None. A. Ergul: None.

**Presentation Number:** LBP20

**Publishing Title:** Heritability of Risk for Troponin Elevation After Acute Ischemic Stroke

**Author Block:** Derek Holder, Laura Ibanez, Laura Heitsch, Carlos Cruchaga, Jin-Moo Lee, Washington Univ Sch of Med, St. Louis, MO

**Abstract Body:** Introduction: Serum troponin levels are frequently elevated after acute ischemic stroke (AIS), and predict poor outcome. Although several demographic and risk factors have been associated with troponin elevation after AIS, little is known about genetic influences. Hypothesis: Troponin elevation after AIS is influenced by genomic factors. Methods: AIS patients were prospectively enrolled in the GENISIS (Genetics of Early Neurological Instability after Ischemic Stroke) study at Washington University in St Louis (N=634). Demographic and atherosclerotic risk factors were recorded, and patients were dichotomized by serum troponin-I elevation (defined by levels >99th percentile on two commonly used assays: platform 1  $\geq 0.07$  ng/mL, platform 2  $\geq 0.03$  ng/mL). Genome-wide genotyping was generated for common variants imputing up to 6 million SNPs. Heritability of risk for troponin elevation was estimated by genome-wide complex trait analysis (GCTA). A logistic regression was performed to identify independent covariates that influence troponin elevation in a model used for genetic analysis, including principal components (PC1-2) based on population substructure. Results: Age, blood pressure, baseline NIHSS, history of coronary artery disease, INR, sex, and serum creatinine at presentation were independently associated with AIS-induced troponin elevation, accounting for less than 15% of variance (see table). Adjusting for these independent covariates, GCTA revealed that common variants account for 38% of the variance in troponin elevation. In this relatively small cohort, no genome-wide associations were found, likely due to lack of power. Conclusion: Serum troponin elevation after AIS is strongly influenced by genomic factors—more so than demographic and atherosclerotic risk factors alone. Additional patients will be required in order to identify specific genetic variants associated with serum troponin elevation after AIS.

Variable	R <sup>2</sup>	P Value
Creatinine	0.033	$8.90 \times 10^{-7}$
Age	0.021	$7.68 \times 10^{-5}$
DBP	0.014	$2.88 \times 10^{-8}$
NIHSS	0.012	0.0267
SBP	0.009	0.044
CAD	0.007	0.0177
INR	0.006	0.0358
Sex	0.006	0.0311
Total R <sup>2</sup>	0.147	
Total R <sup>2</sup> (Adjusted)	0.129	$5.2 \times 10^{-16}$

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**Presentation Number:** LBP21

**Publishing Title:** Left Atrial Enlargement and Vascular Brain Injury: The Cardiovascular Health Study

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**Abstract Body:** Background and Purpose Recent evidence suggests that biomarkers of atrial dysfunction are associated with vascular brain injury in the absence of atrial fibrillation (AF). We hypothesized that left atrial diameter (LAD) is associated with vascular brain injury. Methods We analyzed data from the Cardiovascular Health Study (CHS), a prospective cohort of community-dwelling adults 65 years or older. LAD was obtained from baseline two-dimensional transthoracic echocardiogram. Among CHS participants who underwent brain MRI, we examined associations between LAD and each of brain infarcts and leukoaraiosis. Primary outcomes (n for analysis) were prevalent infarcts (3290), prevalent non-lacunar infarcts (3290), and degree of leukoaraiosis on initial MRI (3275). Secondary outcomes were incident infarcts (1272), incident non-lacunar infarcts (1630), and degree of leukoaraiosis on follow-up MRI adjusted for initial (1594). Relative risk and linear regression models were adjusted for vascular risk factors and potential confounders such as congestive heart failure, AF, and other atrial cardiopathy biomarkers: N-terminal pro B-type natriuretic peptide, p-wave dispersion on ECG, and E/A ratio on echocardiogram. RESULTS: Initial brain MRI was obtained on 3360 participants. Mean age was 72.3±5.0 years, 42.0% were men, and 30.8% participants had prevalent infarcts. In multivariable models adjusting for confounders, LAD was associated with prevalent infarcts (relative risk 1.12, 95%CI 1.03-1.22) and prevalent non-lacunar infarcts (RR 1.24, 95% CI 1.07-1.43), but not with leukoaraiosis. Follow up brain MRI was performed on 2116 participants and 19.5% had incident infarcts. LAD was not associated with incident infarcts (RR 1.05, 95% CI 0.86-1.29), non-lacunar infarcts (RR 1.13 95% CI 0.83-1.55) or leukoaraiosis. Analyses further adjusting for atrial cardiopathy biomarkers had similar results. CONCLUSIONS: LAD is independently associated with prevalent brain infarcts and non-lacunar infarcts but not leukoaraiosis, supporting a mechanistic relationship between LAD and vascular brain injury. Larger studies are needed to determine associations with incident infarcts and if the associated stroke risk could be reduced by anticoagulation therapy.

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**Presentation Number:** LBP22

**Publishing Title:** Severity of Intracranial Stenosis: Redefining Ischemic Impact With Computational Fluid Dynamics

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**Abstract Body:** Background: Traditional measures of intracranial stenosis (ICAS) have focused on luminal stenosis, yet moderate stenoses account for 40% of all recurrent strokes. Even within the “severe” category, only half of all cases exhibit hemodynamic insufficiency. We used computational fluid dynamics (CFD) to evaluate the impact of middle cerebral artery (MCA) stenosis with MRA in Chinese Intracranial Atherosclerosis (CICAS), delineating the effect of percent stenosis, plaque length and resultant hemodynamics. Methods: Three-dimensional CFD models were reconstructed based on time-of-flight magnetic resonance angiography (TOF-MRA) source images. The stenosis degree was graded into moderate (50-69%) and severe (70-99%) stenosis. The hemodynamic impact was evaluated using fractional pressure ratio (FPR), pressure drop (PD), pressure gradient (PG), and blood flow velocity. FPR was grouped into low FPR group and normal FPR group by 0.8. Results: 418 patients with 50-99% symptomatic MCA stenosis in CICAS were investigated. CFD were successfully reconstructed in 94 patients. 324 patients were excluded because of difficulties in reconstruction (e.g. multiple stenoses, lesion across branch points) (n=185), poor image quality (n=25), unavailability of MRA source image (n=61) and string signs (n=53). 13.83% were classified as severe stenoses, and 86.17% as moderate stenoses. The degree of stenosis was linearly related to PD 0.251 ( $p=0.015$ ),  $FPR < 0.8 -0.221$  ( $p=0.032$ ) and velocity 0.241 ( $p=0.019$ ). 38.46% of the severe stenoses and 16.05% of the moderate stenoses were in the low FPR group. In the moderate stenoses, the median (inter-quartile range) lesion length was significantly longer in low FPR group (10.35 (7.43, 14.38) mm) than in normal FPR group (7.06 (5.37, 9.32) mm)  $p=0.007$ . Conclusions: CFD definitions of hemodynamic impact reclassify and upgrade the severity in CICAS. Moderate stenoses may have significant hemodynamic impact, yet “severe” cases may reveal negligible hemodynamic risk. Lesion length and other factors likely impact the severity of ICAS far beyond degree of luminal stenosis. Key Words: Computational flow dynamics CFD; Middle cerebral artery MCA; Moderate Stenosis; Magnetic resonance angiography MRA

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**Presentation Number:** LBP23

**Publishing Title:** Improved Survival of Stroke Patients Contributed More Than Improvements in Stroke Prevention to the Recent Decline in Population-Based Mortality Rates From Stroke

**Author Block:** Olena Seminog, Peter Scarborough, Michael Goldacre, Univ of Oxford, Oxford, United Kingdom

**Abstract Body:** Introduction: Mortality rates from stroke have been falling in England. However, national estimates of the event rates (defined as hospital admissions for new stroke, plus sudden stroke deaths) and case fatality rates (CFRs) are not routinely available. Accordingly, it is unknown how much of the fall in stroke mortality is due to effective prevention, measured as decreasing event rates, or improved acute stroke care, measured as decreasing CFRs. Aim: To report trends in mortality, event rates and CFRs from acute stroke in England during 2001-2010, and explore the relative contribution of changes in stroke event rates and CFRs to the decline in mortality rates. Methods: Population-based study using person-linked routine hospital and mortality data from all England. Annual age-standardised and age-specific mortality rates, event rates and CFRs at 30 days were calculated. Trends in mortality and event rates were calculated as average annual percentage changes using logistic regression. The relative contribution of changes over time in event rates and CFRs to the decline in stroke mortality was calculated in age groups. Findings: There were 947497 acute strokes and 337085 stroke deaths. Age-standardised mortality rates nearly halved between 2001 and 2010: expressed as annualised rates, mortality rates declined by 7% (95%CI 6.9-7.2) per year in men and 6.6% (6.4-6.7) in women. Event rates declined by 2.1% (2.0-2.1) and 2.5% (2.4-2.5) in men and women, and CFRs by 5.1% (4.9-5.3) and 4.6% (4.4-4.7), respectively. However, there were variations in the average annual percentage change in rates between age groups. While mortality rates and CFRs declined in all age groups, event rates declined in older individuals, but increased in people aged under 55 by 2% per year. In men 80% and in women 70% of the decline in stroke mortality was attributed to declining CFRs, and the decline in event rates made smaller contributions of 20% and 30%. Conclusions: In conclusion between 2001-2010 overall mortality rates, event rates and CFRs from acute stroke declined in England. The major force behind the decline in stroke mortality was improved survival, while primary prevention contributed far less. The increase in stroke event rates in individuals aged under 55 years is worrying.

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**Presentation Number:** LBP24

**Publishing Title:** Less Experienced Telestroke Consultants are More Likely to Go On-Camera, but Less Likely to Administer tPA: Results from 600 Telestroke Consults at a Comprehensive Stroke Center

**Author Block:** Adam de Havenon, Jaleen Smith, Cory McCann, **Lee S. Chung**, Aleks Tkach, Peter M. Hannon, Jennifer J. Majersik, Univ of Utah, Salt Lake City, UT

**Abstract Body:** Introduction: Telemedicine increases geographical access to tPA and rates of tPA administration. However, the effective use of telemedicine requires training, which is not a standard component of ACGME-approved vascular neurology fellowships. As a result, many providers learn telestroke skills "on the job," which we hypothesized would result in inefficient telemedicine utilization.

Methods: We prospectively collected data on telestroke consults between July 2014 and September 2016 at a Comprehensive Stroke Center with over 10 years of telemedicine experience. Telestroke consultants are all fellowship-trained in vascular neurology or neurocritical care. Consults are initiated on the telephone and typically, but not always, followed by an on-camera consult. Decision to do a phone-only versus on-camera consult is at the discretion of the provider. Telestroke providers were dichotomized based on time from terminal medical training (<5 years versus ≥5 years). Intergroup comparisons were performed using the Mann Whitney U test.

Results: There were 4 telestroke providers with <5 years experience (median = 2 years) and 4 providers with ≥5 years experience (median = 12 years) who in sum performed 600 telestroke consultations, of which 471 were on-camera (78%). Providers with less experience were more likely to go on-camera than providers with more experience (83% vs. 72% of consults,  $p=0.021$ ), but were less likely to give tPA during on-camera consults (24% vs. 35%,  $p=0.020$ ). (see Table 1).

Conclusion: Our data present novel findings that are relevant to the ongoing discussion of incorporating telemedicine training into ACGME-approved vascular neurology fellowships. Telestroke consultants with less experience do not triage as many cases by phone and are less likely to administer tPA on camera, suggesting their use of telemedicine is not optimized, which supports formalized telemedicine training during vascular neurology fellowship.

Table 1: Telestroke characteristics between providers with less (<5 years) and more (≥5 years) experience.

Variable	Providers with <5 years experience (n=4)	Providers with ≥5 years experience (n=4)	p-value for difference
Total telestroke consults (phone-only and on-camera) (n)	347	253	0.310
Consults completed on-camera (n, %)	289, 83%	182, 72%	0.021
Any technical connection issue of those on-camera (n, %)	39, 10%	38, 15%	0.387
Technical issue that prevented completion of consult (n, %)	10, 26%	10, 26%	0.770
tPA administered via on-camera telestroke consult (n, %)	70, 24%	63, 35%	0.020

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**Presentation Number:** LBP26

**Publishing Title:** Neuroprotective Effect of Endurance Exercise Against Alcohol Induced Cognitive Dysfunctions

**Author Block:** Akash K George, Jyoti Bala, Kimberly Kelly, Neetu Tyagi, Univ of Louisville, Louisville, KY

**Abstract Body:** Previous data indicate that alcohol consumption induces mitochondrial dysfunction. Exercise has been recommended by clinicians as a secondary protective therapy; however, its effect on alleviating brain functions through mitochondrial involvements has not been fully explored. Therefore, we hypothesized that exercise mitigates alcohol-induced neurodegeneration and decline in cognitive function through mitochondrial remodeling. To test this hypothesis, we selected 10-12 weeks old male wild-type mice (C57BL/6, WT), grouped as follows: 1) WT, 2) WT+ Alcohol, 3) WT+ Exercise, 4) WT+ Alcohol+ Exercise. Mice were given an intraperitoneal injection of EtOH (1.5g/kg BW) or saline solution every day for 8 weeks. The mice were exercised for 8 weeks on a treadmill with a controlled speed of 7 meters/min for the first week, the speed of 10 meters/min for the second week and 11 meters/min in the following weeks and a total of 330 meters every day. After each 110 meters mice were given rest of 10 minutes. Cognitive and behavior alterations were assessed by novel object recognition, Passive avoidance, and Y-maze tests. Mitochondrial functions were evaluated by flow cytometry and confocal. Our results suggest significant improvement in cognitive functions in exercised alcohol administrated group, as compared to non-exercised alcohol administrated group. The involvement of mitochondrial remodeling in mice the following exercise was further confirmed and we found there was a significant increase in ATP production, membrane potential, oxygen consumption, copy- number as well as a decrease in reactive oxygen species when compared with non-exercised alcoholic mice. In addition, the effect of exercise on neuronal survival in the alcoholic brain was confirmed by fluoro-jade C reactivity. Taken together, our results indicate a myriad of beneficiary effects of exercise over mitochondrial pathology during alcoholism. Furthermore, our findings suggest exercise mitigates neurodegeneration and cognitive dysfunction and thereby improving total mitochondrial function.

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**Presentation Number:** LBP27

**Publishing Title:** Oral Carbon Monoxide as a Treatment for Stroke

**Author Block:** **Kyra J Becker**, Dannielle Zierath, Angela Shen, Univ of Washington Sch of Med, Seattle, WA; Howard Levy, Hillhurst Biopharmaceuticals, Montrose, CA; Leo Otterbein, Beth Israel Deaconess Medical Ctr, Boston, MA; Edward Gomperts, Brett Skolnick, Hillhurst Biopharmaceuticals, Montrose, CA

**Abstract Body:** Background: Carbon monoxide (CO) is a gasotransmitter produced endogenously by the breakdown of heme. While exposure to excessive CO may lead to toxic levels of carboxyhemoglobin (COHb), there is ample evidence that modest elevations in COHb may be neuroprotective. We developed an oral solution (HBI-002) that liberates CO into the circulation following ingestion anticipating that this substance could be used as a stroke therapeutic.

Methods: Male Lewis rats were subject to 2 hrs middle cerebral artery occlusion (MCAO), gavaged with varying doses of HBI-002 and COHb levels determined. Animals were sacrificed at 24 hours and infarct volume evaluated after staining with 2,3,5-triphenyl-2H-tetrazolium chloride. After the optimal dose was determined, animals were randomly assigned to gavage with HBI-002 or vehicle after MCAO and outcomes assessed by individuals masked to treatment status.

Results: Increasing doses of HBI-002 led to increasing levels of COHb ( $r=0.773$ ,  $P<0.001$ ). Infarct volume was inversely proportional to the dose of HBI-002 ( $r=-0.673$ ,  $P=0.006$ ). Dose volume was limited by gastric volume. The maximum tolerated dose volume was delivered at 1 hr and 2 hrs after MCAO. The highest COHb level achieved at this dose was  $5.2\pm 2.0\%$ . Neurological outcome at 24 hrs was better in HBI-002 treated animals ( $P=0.02$ ) and infarct volume significantly less ( $207.6 \text{ cc} \pm 103.4 \text{ cc}$  vs.  $95.1 \text{ cc} \pm 96.6 \text{ cc}$ ;  $P=0.005$ ,  $N=13$  and  $17$  respectively).

Conclusions: The oral formulation HBI-002 provides a unique method of administration of CO without the inherent safety issues associated with CO gas or Carbon Monoxide Releasing Molecules (CORMs). Modest elevations in COHb obtained with oral gavage following MCAO led to significant decreases in infarct volume and improvements in

neurological outcomes at 24 hours. Long-term outcome data will be available for presentation at ISC in 2017.

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**Presentation Number:** LBP28

**Publishing Title:** Drag Reducing Polymers Delivered Late After Stroke Onset Enhance Collateral Flow Reducing Ischemic Core Progression After Permanent Middle Cerebral Artery Occlusion in Rats

**Author Block:** Denis E Bragin, Olga A Bragina, Dept of Neurosurgery, Univ of New Mexico Sch of Med, Albuquerque, NM; Jun Wu, Dept of Neurosurgery, Xiangya Hosp, Central South Univ, Changsha, China; Hengzhou Lin, Dept of Neurosurgery, Shenzhen Second Hosp, Shenzhen Univ, Shenzhen, China; Devon A Lara, Dept of Neurosurgery, Univ of New Mexico Sch of Med, Albuquerque, NM; Yirong Yang, Dept Pharmaceutical Sciences, Univ of New Mexico Coll of Pharmacy, Albuquerque, NM; Marina V Kameneva, Univ of Pittsburgh, Pittsburgh, PA; Edwin M Nemoto, Dept of Neurosurgery, Univ of New Mexico Sch of Med, Albuquerque, NM

**Abstract Body:** Introduction: Thrombolytic therapy is used only 5-7% of eligible stroke patients due to a short therapeutic window and risk of hemorrhagic transformation. We previously showed that rheological modulation of cerebral blood flow (CBF) by nanomolar concentrations of drag-reducing polymers (DRP) applied 30 min to 3 hours after permanent middle cerebral artery occlusion (pMCAO) improved microvascular perfusion and neurologic outcome. We now test the hypothesis that the perfusion was improved due to enhancement of collateral flow.

Methods: DRP or saline (control) was i.v. injected 3 hours after pMCAO induction in rats (10 rats per group). Changes in cortical regional CBF were monitored through an optical skull window by Laser Speckle Contrast Imaging (LSCI) before and for 6 hours after pMCAO. Microvascular changes were simultaneously monitored by 2-photon laser scanning microscopy (2PLSM) and cerebral infarctions evaluated by MRI at the end of the study.

Results: LSCI revealed that pMCAO caused rapid progression of the ischemic area (flow < 25% of baseline) in the parietal cortex extending anterior and posterior from the peri-MCA territory ( $4.83 \pm 0.8$  mm<sup>2</sup> at the end of monitoring). DRP attenuated progression of the ischemic area to  $1.75 \pm 0.5$  mm<sup>2</sup>,  $P < 0.05$ . 2PLSM showed a significant increase of the number of anastomoses between MCA and ACA ( $\Delta 34 \pm 7\%$ ,  $P < 0.05$ ) and between the MCA and PCA ( $\Delta 28 \pm 6\%$ ,  $P < 0.05$ ). T2 MRI showed a decrease in infarction volume ( $\Delta = 23 \pm 8\%$ ) and increased in ipsilateral hemispheric CBF ( $\Delta 31 \pm 9\%$ ,  $P < 0.05$ ).

Conclusions: Enhancement of blood flow through leptomeningeal or pial collaterals between MCA and ACA or PCA watershed territories after permanent MCAO is one of the mechanisms of DRP effects leading to improvement of CBF, tissue oxygenation and neurological outcome. It is effective even without reperfusion and with delayed application after stroke onset suggesting an effective therapy targeting collateral flow after acute ischemic stroke.

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**Presentation Number:** LBP29

**Publishing Title:** The Fall Study of Gothenburg

**Author Block:** Carina U Persson, Inst of Neuroscience and Physiology, Rehabilitation Med, Sahlgrenska Acad, Univ of Gothenburg, Gothenburg, Sweden; Sigvar Kjellberg, Ellen Westerlind, Bodil Lernfelt, Per-Olof Hansson, Inst of Molecular and Clinical Med, Sahlgrenska Acad, Univ of Gothenburg, Gothenburg, Sweden

**Abstract Body:** Background and Purpose - Patients with acute stroke are at high risk of falling. Previous studies have mainly examined the risk of falling after discharge from hospital. The aim of this study was to analyze physiological, psychological, medical and cognitive factors as predictors of falls during hospitalization in patients with acute stroke.

Methods - A consecutive sample of 504 patients with a clinical diagnosis of stroke was included. Postural control, physical capacity and cognitive ability was examined using validated test methods. All falls during hospital stay were registered in the medical record and in a web-based application for deviations. Data regarding concomitant diseases and medication were collected from the medical records. The prediction of falls was analyzed using crude and multiple logistic regression analyzes.

Results - Sixty-five patients (13 %) fell one or more times during hospital stay. In the multiple analysis, the significant predictors for a fall during hospital stay were low score according to the modified version of the Postural Assessment Scale for Stroke Patients (odds ratio [OR] 2.84; 95% confidence intervals [CI]; 1.25-6.49,  $p<0.001$ ), high age (OR 1.04, 95% CI; 1.01-1.07,  $p=0.013$ ), male sex (OR 2.38, 95% CI; 1.29-4.39,  $p=0.006$ ), using walking aids (OR 2.94, 95% CI; 1.55-5.58,  $p<0.001$ ) and long length of stay (OR 1.05, 95% CI; 1.03-1.08,  $p<0.001$ ).

Conclusions - In conclusion, both stroke-specific impairment of postural control and personal demographic factors as age and sex are important predictors of falls acute after stroke.

Clinical Trial Registration - ULR: <https://clinicaltrials.gov/ct2/show/> Unique identifier: NCT02264470

Key Words: accidental falls, stroke, rehabilitation, risk factors

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**Presentation Number:** LBP30

**Publishing Title:** Variable Ischemic Stress in White Matter Hyperintensities of Stroke Patients With Large Vessel Occlusion

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**Abstract Body:** Background: In a study evaluating hemodynamic compromise by quantitative positron emission tomography (PET) measurements of oxygen extraction fraction (OEF) and cerebrovascular reserve (CVR) in stroke patients with large vessel occlusion, we report for the first time, that white matter and white matter hyperintensities (WMH) despite an apparent homogeneity vary in ischemic stress. WMH is increasingly recognized as an important factor in cerebrovascular ischemia and dementia ranging from mild cognitive impairment, vascular dementia and Alzheimer's disease and with cardiovascular risk factors (hypertension, diabetes, obesity and dyslipidemia, i.e. metabolic syndrome) that can increase the risk for stroke to 40%.

Methods: We studied seventeen patients who within the past six months, suffered large vessel occlusion (LVO) strokes and with occlusive vascular disease and sixteen controls by  $^{15}\text{O}$  positron emission tomography (PET) measurements of cerebral blood flow (CBF) with  $\text{H}_2^{15}\text{O}$  and cerebral metabolic rate for oxygen ( $\text{CMRO}_2$ ) with  $^{15}\text{O}$  gas and derived variables of OEF, OEF reactivity (OEFR) and CVR before and after acetazolamide vasodilatory challenge. Hemispheric WMH volumes were quantitated by manual segmentation of fluid-attenuated inversion recovery (FLAIR) magnetic resonance images (MRI).

Results: Hemispheric WMH volumes were significantly ( $P < 0.05$ ) higher in stroke patients compared to controls. In stroke patients with occlusive vascular disease, cerebrovascular Reactivity (CVR) was linearly and directly related to OEFR and CBF and  $\text{CMRO}_2$ .

Conclusions: WMH differ in degree of ischemic stress and are prevalent in patients with strokes and occlusive vascular disease exaggerating hemodynamic compromise of WMH.

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**Presentation Number:** LBP31

**Publishing Title:** 3K3A-APC Promotes Post-ischemic Neuronal Repair by Human Neural Progenitor Cells in Mice

**Author Block:** Yaoming Wang, **Zhen Zhao**, Sanket V Rege, Min Wang, Gabriel Si, Dept of Physiology and Biophysics and the Zilkha Neurogenetic Inst, Keck Sch of Med of the Univ of Southern California, Los Angeles, CA; Su Wang, Ctr for Translational Neuromedicine and the Dept of Neurology, Rochester, NY; John H. Griffin, Dept of Molecular and Experimental Med, The Scripps Res Inst, La Jolla, CA; Steven A. Goldman, Ctr for Translational Neuromedicine and the Dept of Neurology, Univ of Rochester Medical Ctr, Rochester, NY; Berislav V. Zlokovic, Dept of Physiology and Biophysics and the Zilkha Neurogenetic Inst, Keck Sch of Med of the Univ of Southern California, Los Angeles, CA

**Abstract Body:** Activated protein C (APC) is a blood protease with cell-signaling anti-apoptotic, anticoagulant and anti-inflammatory activities. Recombinant APC and/or its analogs, such as 3K3A-APC (Lys191-193Ala), have reduced (>90%) anticoagulant activity and are engineered to reduce APC-associated bleeding risk while retaining normal cell signaling activity, and have shown benefit in preclinical models of neurological disorders including ischemic stroke, multiple sclerosis, brain trauma, and amyotrophic lateral sclerosis. We tested the hypothesis that 3K3A-APC and neural stem cells (NSCs) might be developed as an effective combination therapy for neuronal repair after stroke. To test this hypothesis, we studied the effects of late post-ischemic 3K3A-APC treatment on in vivo production of neurons from transplanted NSCs, and the effects of this combination therapy on long-term neurological recovery and restoration of disrupted neural circuitry in post-ischemic murine brain. Specifically, C57BL/6 mice (8 weeks old) received distal middle cerebral artery occlusion (dMCAO). Human NSCs were cultured from fetal brain tissues and were stereotactically transplanted 7 days following dMCAO. 3K3A-APC was administered at 7, 9, 11, and 13 days post-stroke. In vivo imaging of transplanted cells, viral injection for anterograde labeling, voltage-sensitive dye imaging and behavioral tests were performed. In summary, our data show that APC agonist-based clinical therapeutics such as 3K3A-APC may strongly potentiate the in vivo integration and neurogenic activity of transplanted human NSCs. This observation may be of interest not only in the repair of stroke-damaged neural circuits, but also for clinical trials of NSCs for neurological disorders such as spinal cord injury and Parkinson's disease. Importantly, 3K3A-APC has advanced to Phase II clinical trial ("Safety Evaluation of 3K3A-APC in Ischemic Stroke (RHAPSODY)", NCT02222714, ZZ Biotech, LLC, see [www.zzbiotech.com/](http://www.zzbiotech.com/)) as a neuroprotectant for ischemic stroke and has enrolled 95 stroke patients to date. In conclusion, a future step is to combine 3K3A-APC treatment with the ongoing clinical trials with neural stem cell transplantation as a combination therapy for stroke.

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**Presentation Number:** LBP32

**Publishing Title:** Fried-breadstick Sign: A Novel Imaging Marker of Laminar Flow on Magnetic Resonance Angiography in Intracranial Atherosclerosis

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**Abstract Body:** Objective: We aim to report a novel imaging marker -- the Fried-Breadstick sign, and explore its clinical relevance.

Methods: We retrospectively reviewed our institutional, prospectively collected high-resolution magnetic resonance imaging database from January 2009 to August 2015. The Fried-Breadstick sign was identified as a continuous line of signal loss at the center of the internal carotid artery (ICA) from C6 to C7 on maximum intensity projection images (figure 1). Patients' middle cerebral arteries (MCAs) were classified as symptomatic, asymptomatic and control group based on the occurrence of ischemic stroke and presence of MCA plaque. The correlations among Fried-Breadstick sign, MCA stenosis degree, ICA bifurcation angle, and infarct patterns were investigated.

Results: Nine hundred and ninety-five MCAs out of 541 patients were analyzed, including 121 in symptomatic group, 415 in asymptomatic group, and 459 in control group. The Fried-Breadstick sign more likely occurred in control group (50%) than in symptomatic (29%) and asymptomatic (26%) groups ( $p < 0.001$ ). A significant decreasing of the Fried-Breadstick sign prevalence as the MCA stenosis degree increases was observed in both asymptomatic MCAs ( $p = 0.041$ ) and symptomatic MCAs ( $p = 0.011$ ). In symptomatic group, the Fried-Breadstick sign more likely occurred in the MCAs with non-embolic than with embolic infarct patterns ( $p = 0.009$ ). Logistic regression analysis suggested the stenosis degree (OR 0.373, 95%CI 0.174-0.802) and ICA bifurcation angle (OR 0.981, 95%CI 0.970-0.992) independently associated with the Fried-Breadstick sign.

Conclusions: We hypothesize the Fried-Breadstick sign represents well-formed laminar flow and relatively healthy intracranial hemodynamics. Further studies are required to investigate whether the absence of Fried-Breadstick sign is a marker of intracranial atherosclerosis vulnerability.

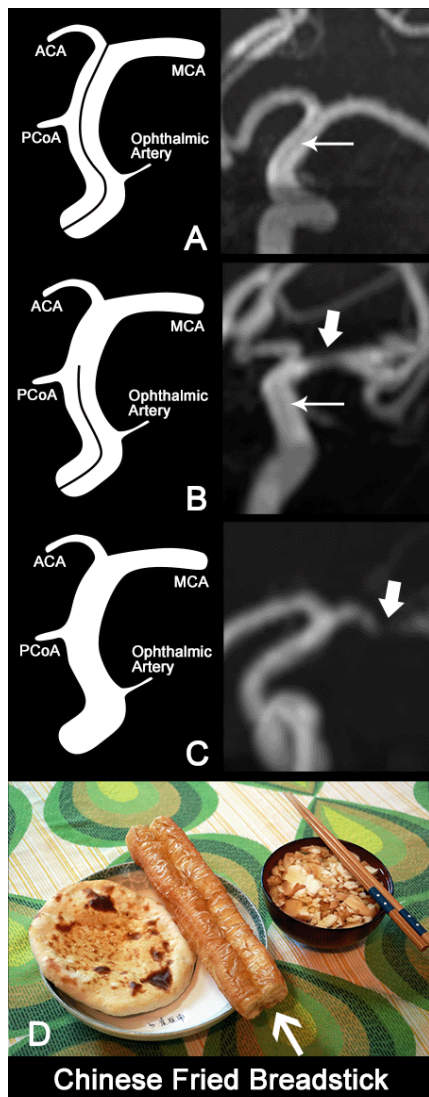


Figure 1. The example of Fried-Breadstick (FB) sign and real-life FB on maximum intensity projection (MIP) image. The black line depicted in the illustrations represents the signal loss seen on MIP images. The thin arrows point at the signal loss in internal carotid artery on MIP images. The thick arrows point out middle cerebral artery stenosis. A. Presence of FB sign; B. Abnormal FB sign. C Absence of FB sign. D. A traditional breakfast combo of real-life FB, soy bean curd and Shao Bing.

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**Presentation Number:** LBP33

**Publishing Title:** Do Patients at a Higher Risk for an Ischemic Stroke Have an Altered Peripheral Blood or Bone Marrow Cellular Composition?

**Author Block:** Rohan B Parikh, Anne-Cecile Huby, Lourdes Chacon, Ariadna Contreras, Micheline Resende, Texas Heart Institute, Houston, TX; Marjorie Carlson, University of Minnesota, Minneapolis, MN; Lem Moyé, Univ of Texas Sch of Public Health, Houston, TX; Jay H Traverse, Minneapolis Heart Institute Foundation at Abbott Northwestern Hospital, Minneapolis, MN; Timothy D Henry, Cedars-Sinai Heart Institute, Los Angeles, CA; Doris A Taylor, Texas Heart Institute, Houston, TX

**Abstract Body:** Stroke is a leading cause of death in the United States. Cardiovascular risk factors (CRFs) such as hypertension (HTN), diabetes, hyperlipidemia, vasculitis – all inflammatory states – are also major risk factors for stroke. Peripheral blood (PB) pro-inflammatory lymphocyte subpopulations increase following an ischemic stroke and are mediators of tissue damage. Cell therapy is a novel treatment for both acute myocardial infarction (AMI) and stroke. Given that tissue ischemia is common to both ischemic stroke and AMI and that patients with CRFs have an increased risk for stroke and a worse outcome, we compared the BM and PB composition of AMI cell therapy patients with and without CRFs to determine if differences in biomarkers or inflammatory cells were evident that might affect cell therapy.

Patients 14-21 days post AMI who consented for the CCTR LateTIME study biorepository (n=79) were classified according to the presence or absence of CRFs. PB and BM cell composition was determined at baseline via polychromatic flow cytometry; 43 cellular phenotypes were analyzed. Patients who did not complete the study or had incomplete cell composition data were excluded.

The frequency of PB CD3+ T-cells was higher in diabetics ( $82.36 \pm 6.85$ ) and patients with hypercholesterolemia ( $81.1 \pm 4.63$ ) versus non-diabetics ( $74.95 \pm 11.64$ , mean difference:  $7.411 \pm 2.583$ , CI =  $73.62-79.20$ ;  $p=0.007$ ) and patients with normal cholesterol ( $75.01 \pm 12.22$ , mean difference:  $6.086 \pm 2.170$ , CI =  $73.62-79.20$ ;  $p=0.006$ ). There was a significantly lower frequency of CD45+CD14+ monocytes in BM of diabetics ( $2.07 \pm 1.61$ ) versus non-diabetics ( $3.18 \pm 2.77$ ); mean difference:  $1.11 \pm 0.54$ , CI =  $2.31-3.51$ ;  $p=0.0484$ . The frequency of CD45+CD31bright cells was also lower in PB of diabetics ( $0.30 \pm 0.28$ ) versus non-diabetics ( $0.675 \pm 0.76$ ); mean difference:  $-0.37 \pm 0.13$ , CI =  $2.31-3.51$ ;  $p=0.0091$ .

We identified pro-inflammatory cell frequency increases and altered PB and BM composition in AMI patients with CRFs (compared to those with no CRFs). Given the pathophysiological similarity between AMI and ischemic stroke, we posit that similar compositional changes may occur in some stroke patients and play a role in how CRFs relate to worsened outcome after stroke.

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**Presentation Number:** LBP34

**Publishing Title:** Improving Rheo-Erythrocrine Functions: A Novel Therapeutic Approach for Efficient Cerebral Blood Flow (CBF) After Acute Ischemic Stroke (AIS)

**Author Block:** **Sumbul Fatima**, Chirayu D Pandya, Kumar Vaibhav, Molly Braun, Babak Baban, Krishnan M Dhandapani, Md Nasrul Hoda, Augusta Univ, Augusta, GA

**Abstract Body:** INTRODUCTION: Restoration of CBF is a primary goal after AIS; however, improved CBF may not reestablish optimum oxygen delivery due to RBCs poor deformability. Adequate rheology and erythrocrine (rheo-erythrocrine) functions are essential for the RBCs deformability and their passage through microvessels for oxygen delivery. Despite the absence of a nucleus, RBCs express functional nitric oxide synthase3 (eryNOS3) which modulate their deformability; however, the role of eryNOS3 is unexplored in AIS. HYPOTHESIS: We hypothesize that improved rheo-erythrocrine function is protective after AIS. METHODS: Aged C57/Bl6 male mice were subjected to embolic TE stroke. Laser ektacytometry was performed using 6- $\mu$ L of blood to determine the RBCs elongation index (EI), a rheological biomarker. eryNOS3 and nitric oxide (NO)-content in RBCs were quantified by flow cytometry as erythrocrine markers. RESULTS: Basal EI-value, eryNOS3-activity and NO-content in RBCs were significantly lower in NOS3-/- mice, or in mice deficient for the NOS3 regulators, S100A1 or AMPK $\alpha$ 1, as compared to WT. All 3 knock out (KO) showed reduced CBF recovery, poor behavioral outcomes and worse injury after stroke, as compared to WT. Remote Ischemic Conditioning (RIC) improved the EI-value with concurrent increase in eryNOS3-activity and NO-content in RBCs of WT but not in S100A1-/- or AMPK $\alpha$ 1-/- KO-mice. RIC was also ineffective in irradiation chimera mice deficient in circulating NOS3, primarily eryNOS3. RIC after stroke remained significantly protective via improved CBF in WT-mice, but not in any KO-mice. Moreover, administration of hydroxyurea, an FDA-approved therapy which increases NO in RBCs and improves their deformability, restored EI-values, increased CBF, and reduced stroke injury in all, WT and KO groups, as well as in diabetic mice without altering blood pressure. CONCLUSIONS: Assessment of rheo-erythrocrine function could provide a simple, rapid biomarker to monitor the effectiveness of RIC. As stroke-associated comorbidities (e.g. diabetes, hypertension) produce chronic erythrocytic rigidity, re-purposing hydroxyurea may provide an alternate therapeutic means to increase NO in RBCs and improve rheo-erythrocrine function after AIS.

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**Presentation Number:** LBP35

**Publishing Title:** Assessing Reperfusion in Recanalized Ischemic Stroke Patients Treated With Intra-Arterial Therapy Using CT Perfusion

**Author Block:** Eric Wright, Univ of Western Ontario, London, ON, Canada; Christopher d'Esterre, Univ of Calgary, Calgary, AB, Canada; Enrico Fainardi, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy; Ting-Yim Lee, Univ of Western Ontario, London, ON, Canada

**Abstract Body:** Results from the EXTEND-IA, ESCAPE and MRCLEAN trials revealed intra-arterial therapy (IAT) is superior to IV-tPA alone for patients with large vessel occlusions. Success of recanalization is judged using the modified thrombolysis in cerebral ischemia (TICI) scale on post-treatment digital subtraction angiography (DSA) images - with scores of 2b or 3 indicating successful recanalization. However, recanalizing blocked arteries does not always lead to reperfusion of the ischemic tissue or good functional outcomes (mRS  $\leq 2$ ). In three major IAT clinical trials, ~17% of IAT-treated patients had TICI scores of 2b or 3 but still suffered poor clinical outcomes. It is possible that post-procedural CT Perfusion (CTP) could help identify patients who may have poor functional outcomes due to incomplete tissue reperfusion after IAT. The objective of this study is to determine the association between reperfusion and outcome in a group of IAT-treated ischemic stroke patients with post-procedural TICI scores of 2b or 3. Ischemic stroke patients treated with IAT received admission and 24hr follow-up CTP, post-procedural DSA, and 3-month mRS evaluation. Ischemic tissue volume was quantified on admission and 24hr CTP images using time-to-max (Tmax) thresholds from our group's prior research. The difference in ischemic tissue volume from admission to 24hr post relative to the admission volume was used to quantify reperfusion scores. The association between good functional outcome and reperfusion score was evaluated using logistic regression and ROC analysis. Approximately 30.5% of the patients in our database had poor functional outcomes despite having post-procedural TICI scores of 2b or 3. The mean reperfusion scores for patients with good (n = 8) and poor (n = 10) functional outcomes were  $0.94 \pm 0.02$  and  $0.69 \pm 0.11$  respectively. ROC analysis was performed to find a threshold reperfusion score for separating patients with good or poor functional outcomes. The reperfusion score threshold that corresponded to the optimal operating point of the ROC curve was 0.85, the sensitivity and specificity of this threshold were 0.70 and 0.75 respectively. CTP may help identify patients who in future will report poor functional outcomes due to impaired tissue reperfusion after IAT.

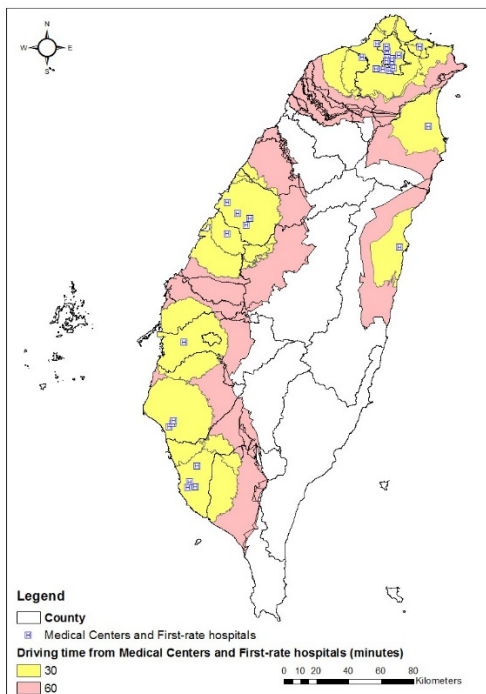
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**Presentation Number:** LBP37

**Publishing Title:** Geographic Analysis of Stroke Center Availability in Taiwan: Possible Impact on Stroke Patients Outcomes of Distance to Stroke Centers

**Author Block:** Dorji Harnod, Ta Chien Chen, Chu Hui Chang, Taipei Medical Univ Hosp, Taipei, Taiwan

**Abstract Body:** Purpose: Stroke is an important public health problem in Taiwan. Our research examines geographic variations in the mortality and morbidity of the stroke patients and the availability of the stroke centers. Geographic Information Systems (GIS) tools enable analysis to make the data-driven recommendations to government for providing the best and most timely healthcare to those stroke patients in the near future. Method: By using the National Insurance Data Bank from 2005 to 2009, all the stroke patients who sent to the hospitals were included in our research. Some hospitals could be the stroke centers after the accreditation from the Department of Health. All the stroke patients were recognized by using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) stroke codes (431-437). There were 29 stroke centers during these years. The Geographic Information System analyses included calculating the <60, and >60-minute ground transportation travel bands from the stroke patients' residence ZIP codes to the different acute stroke centers. Our research is interested in those patients who were more than a 60 minute travel time to the stroke centers. All GIS analyses were conducted using the ArcGIS software version 10.1. And, by the information from the Ministry of the Interior, we also recognize the counties with more population (more than 0.5 million). Results: We found there are four counties with more population (more than 0.5 million) have no stroke center, and one county with less population (less than 0.5 million) have no stroke center. Compare with the counties with stroke centers, the mortality rates in the stroke patients in the counties without stroke centers are higher(4.6% v.s 2.6%,  $p=0.04$ ). Conclusions: Strategies are needed to reduce the disparities in acute stroke care cross the Taiwan island and improve the outcomes.





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