TRAVERSE

Transseptal vs. Retrograde Aortic Ventricular Entry to Reduce Systemic Emboli

Gregory M. Marcus, MD, MAS, Roderick Tung, MD, Trisha F. Hue, PhD, MPH, Feng Lin, MS, J. Peter Weiss, MD, Wendy Tzou, MD, Henry Hsia, MD, Ashkan Ehdaie, MD, Daniel Cooper, MD, T. Jared Bunch, MD, Jeffrey Arkles, MD, Babak Nazer, MD, Adam Lee, MBBS, Alexios Hadjis, MD, Duy Nguyen, MD, Mihail Chelu, MD, PhD, Joshua Moss, MD, Jonathan Hsu, MD, Miguel Valderrábano, MD, Prashant Bhave, MD, Andrew Beaser, MD, Arvindh Kanagasundram, MD, Oussama Wazni, MD, Jason Bradfield, MD, Grace Wall, Kathleen Chang, Michelle Yang, Gabrielle Montenegro, Sabrina Jarrott, Joel Kramer, PsyD, Anthony Kim, MD, MS, Edward P. Gerstenfeld, MD, MS, William Dillon, MD

pcori

UCSF

University of California
San Francisco

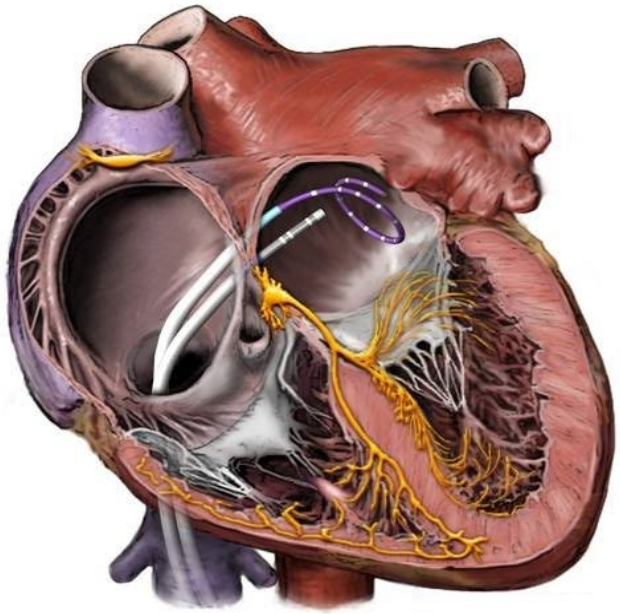
Catheter Ablation for Ventricular Arrhythmias

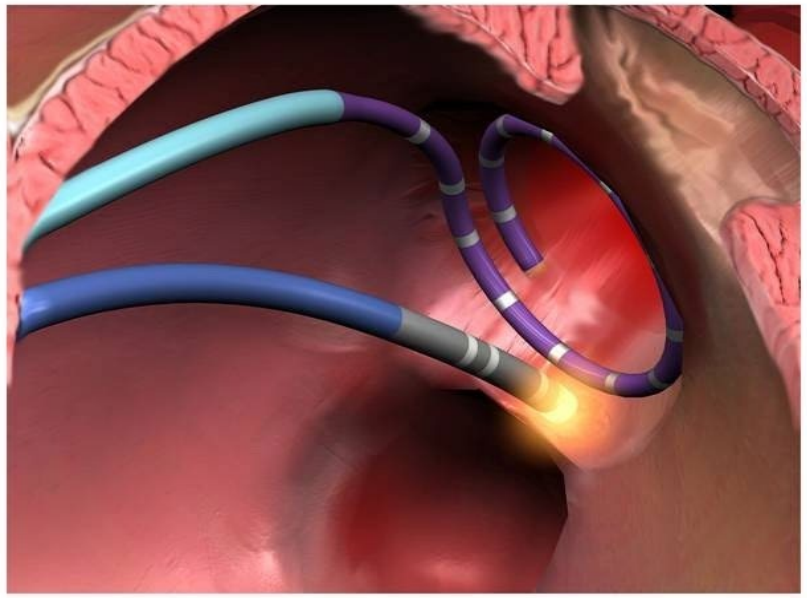
- Class 1 recommendation for recurrent VT and PVCs per AHA/ ACC/ HRS guidelines[1]
- Utilization of ablation for ventricular arrhythmias has increased 5-fold in recent years[2]

1. Al-Khatib et al. *Circulation* 2017
2. Palaniswamy et al. *Heart Rhythm* 2014

Catheter Ablation and the Brain?

- Multiple studies have demonstrated new brain emboli on MRI after ablation for atrial fibrillation in about 15%-25% of cases[1-4]





- WHY?
  - Cardioversions
  - Large number of burns
  - Long catheter dwell times
  - Low flow chamber
  - AF itself (clot in LAA)

1. Gaita et al. *Circulation* 2010
2. Schrikel *Europace* 2010
3. Herrara *J Am Coll Cardiol* 2011
4. Deneke *J Cardiovasc Electrophys* 2015

Cerebral Emboli after LV Ablation

ORIGINAL RESEARCH ARTICLE

Brain Emboli After Left Ventricular Endocardial Ablation

Circulation. 2017;135:867–877.

ORIGINAL RESEARCH ARTICLE

Editorial, see p 878

Isaac R. Whitman, MD
Rachel A. Gladstone, BA
Nitish Badhwar, MD
Henry H. Hsia, MD
Byron K. Lee, MD
S. Andrew Josephson, MD
Karl M. Meisel, MD
William P. Dillon, Jr., MD
Christopher P. Hess, MD, PhD
Edward P. Gerstenfeld, MD
Gregory M. Marcus, MD, MAS

BACKGROUND: Catheter ablation for ventricular tachycardia and premature ventricular complexes (PVCs) is common. Catheter ablation of atrial fibrillation is associated with a risk of cerebral emboli attributed to cardioversions and numerous ablation lesions in the low-flow left atrium, but cerebral embolic risk in ventricular ablation has not been evaluated.

METHODS: We enrolled 18 consecutive patients meeting study criteria scheduled for ventricular tachycardia or PVC ablation over a 9-month period. Patients undergoing left ventricular (LV) ablation were compared with a control group of those undergoing right ventricular ablation only. Patients were excluded if they had implantable cardioverter defibrillators or

Cerebral Emboli after LV Ablation

- None of those undergoing RV ablation experienced a cerebral embolism
- 7 (58% of all LV or 64% of all retrograde aortic cases) had a new brain embolism

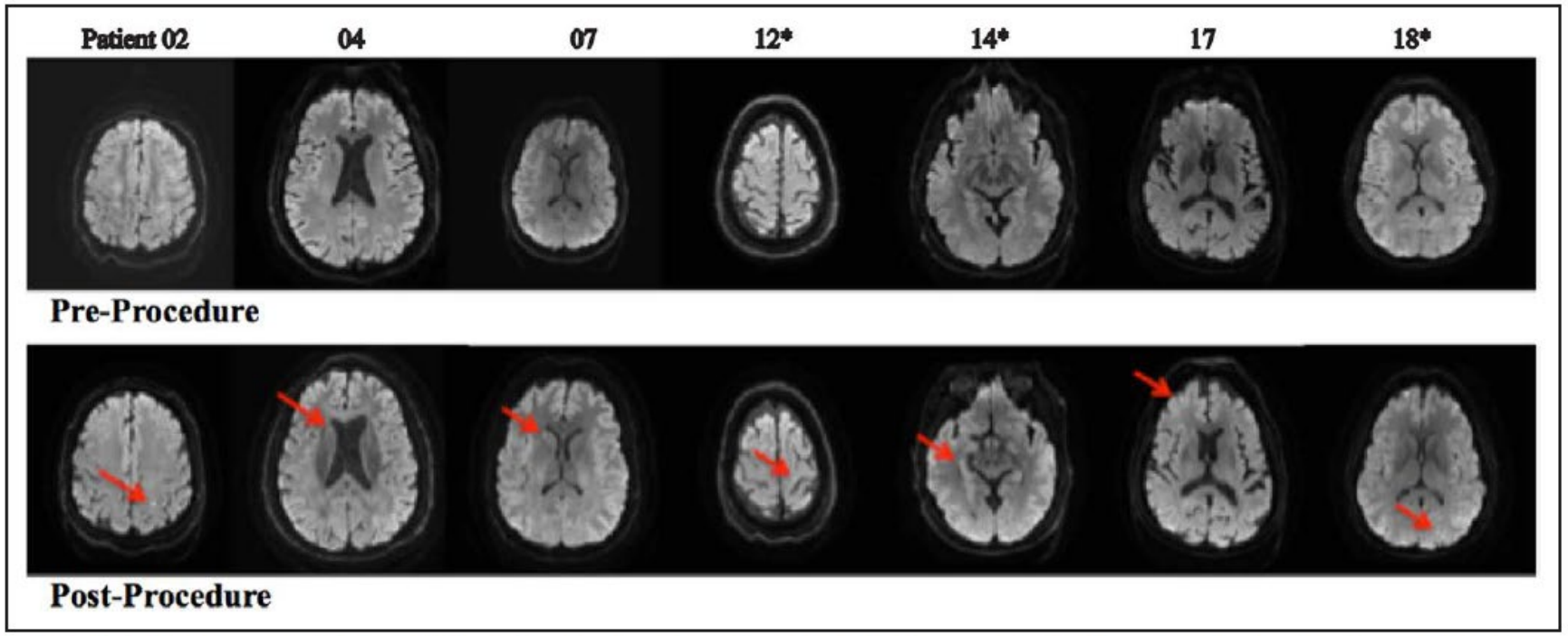


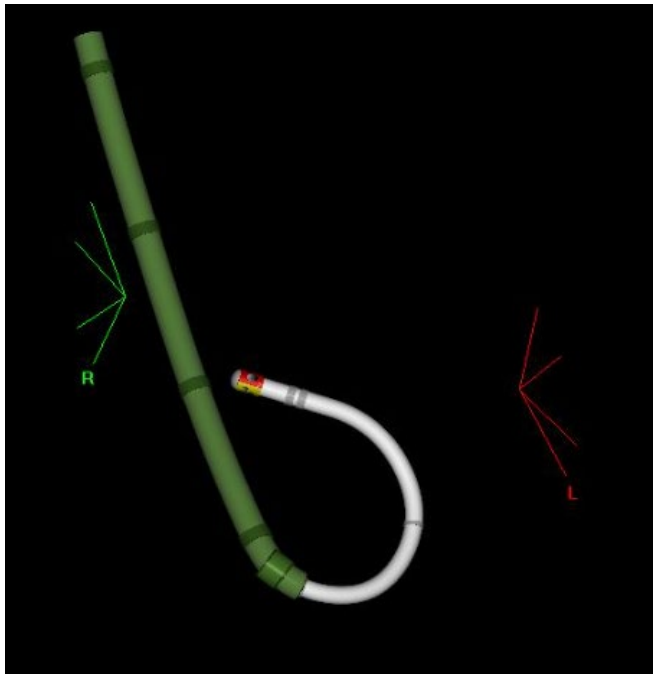
Figure 2. Diffusion-weighted MRI of the brain of each patient with representative cerebral emboli postablation. Images before left ventricular ablation (**Top**) and representative corresponding postprocedural images (**Bottom**) showing embolic lesions. *These patients were found to have multiple embolic lesions on postprocedure MRI: Patient 12 (3 lesions), patient 14 (4), and patient 18 (5).

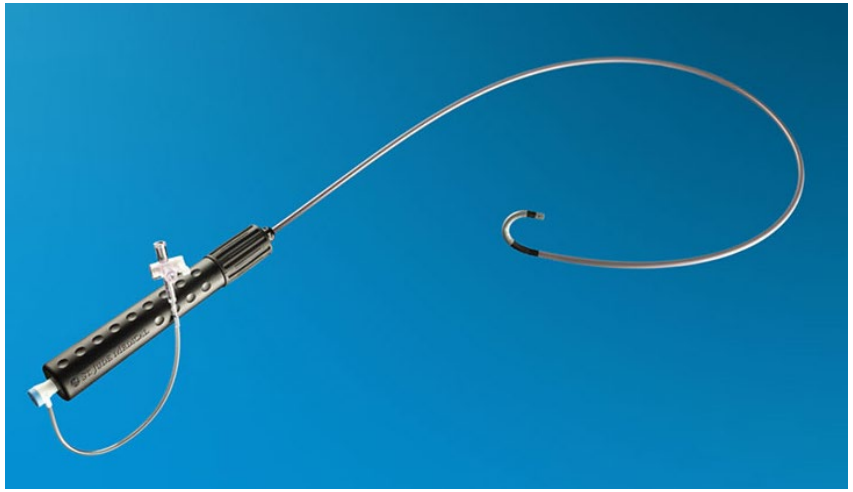
Cerebral Emboli and other LV Procedures

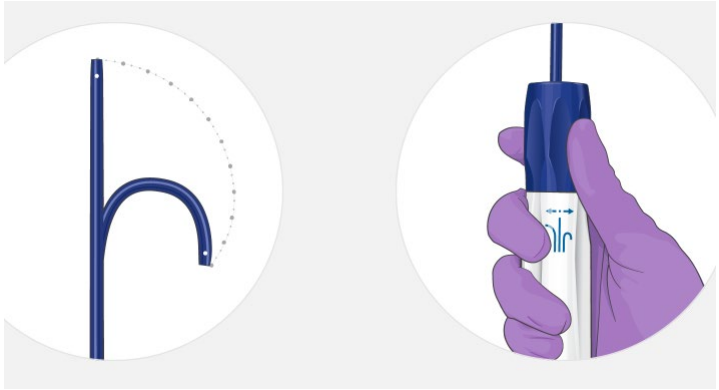
- Diagnostic aortic valve studies carry a ~20% risk of cerebral emboli[1]
- Diagnostic coronary angiography carries a ~20% risk of cerebral emboli[2]

1. Omran et al. *Lancet* 2003
2. Kim et al. *int J Cardiol* 2011

Transseptal Approach Common, Easier with Deflectable Sheaths







We Sought Funding from PCORI to Conduct A Randomized Trial

- **<u>Aim 1</u>: (PRIMARY OUTCOME) To test the hypothesis that a transseptal approach to left ventricular ablation results in a substantial reduction in cerebral emboli compared to a retrograde aortic approach.**

- **<u>Aim 2</u>: To test the hypothesis that a transseptal approach to left ventricular ablation mitigates neurocognitive decline compared to a retrograde aortic approach.**

Key Inclusion Criteria

- Age ≥ 18 years
- Planned/scheduled endocardial ventricular tachycardia (VT) or premature ventricular contraction (PVC) catheter ablation procedure
- Plan is to pursue an ablation target in the left ventricular endocardium that can be accessed by either a transseptal or retrograde aortic approach

Key Exclusion Criteria

- Any contraindication to MRI (as defined by the institution performing the MRI)
- Clinical contraindication to a retrograde aortic approach as determined by the treating physician, including:
  - Severe Aortic stenosis
  - Mechanical aortic valve
- Clinical contraindication to a transseptal puncture as determined by the treating physician , including:
  - Severe Mitral valve stenosis
  - Mechanical Mitral valve
  - ASD or PFO closure device that would preclude a transseptal puncture
  - Mitralclip or Alifieri mitral valve repair that would preclude a transseptal puncture
- Planned or known need to perform either a retrograde aortic approach or transseptal approach

Study Flow

Screening

- Initial inclusion/exclusion evaluation
- Informed consent

Initial Screening Measures

- Medical history, including utilization of clinically available ECG and ambulatory ECG monitoring
- Medication inventory

Final Screening/Enrollment Measures

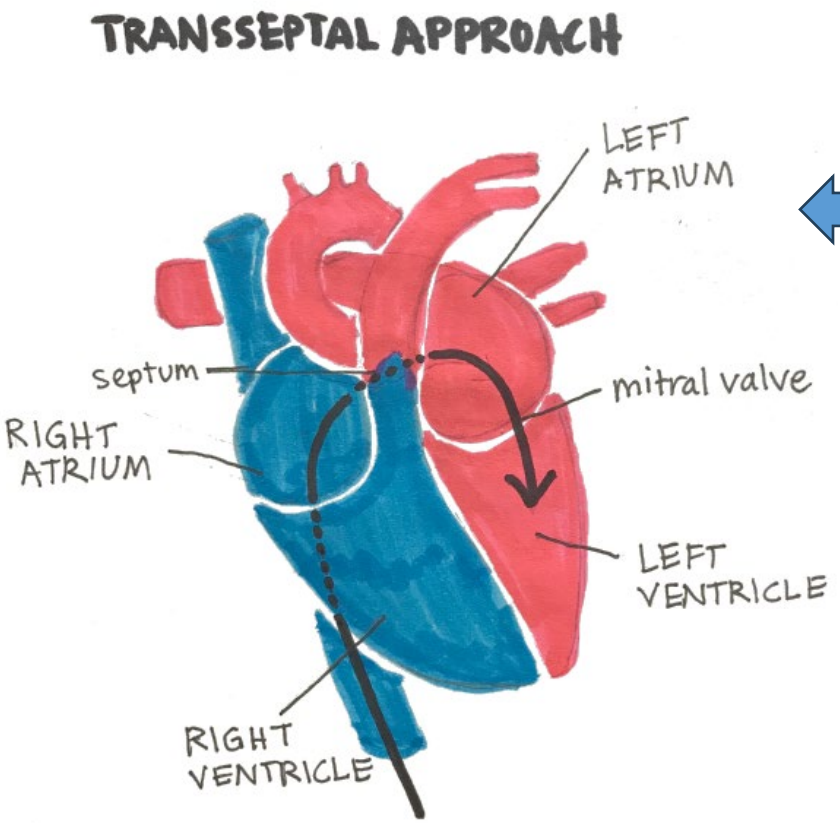
- Brain MRI [1]
- Neurocognitive function testing [1,2]
- NIH Stroke Scale evaluation [1]
- hrQOL/Physical Activity (PA) questionnaire [1]

1: must be performed within 30 days prior to study treatment
2: must be performed >24 hours free of sedating medications

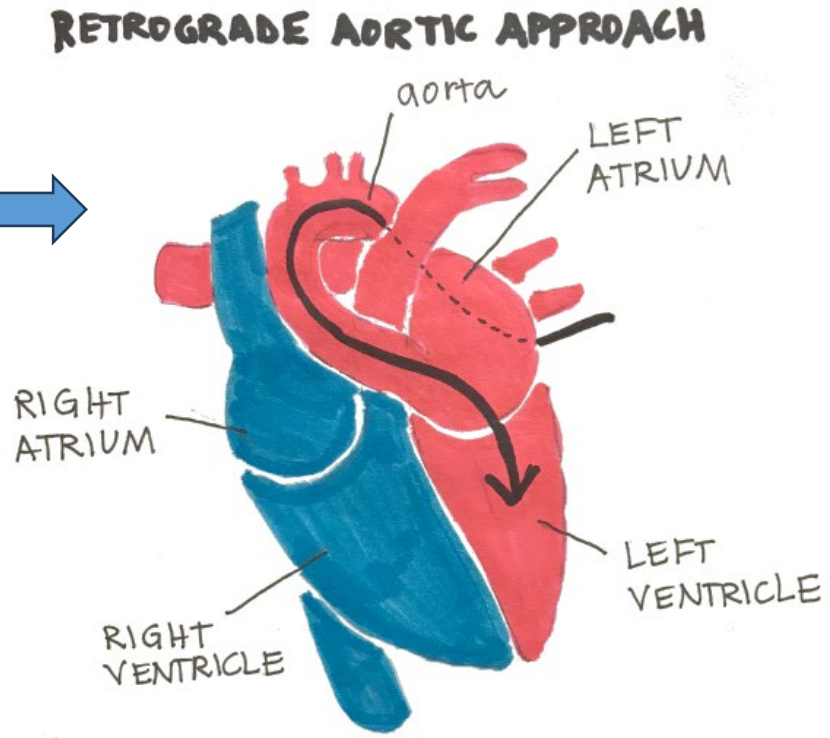
Baseline Visit (V1c)

- Anthropometry, Vital signs [3]
- Study Enrollment (Randomization)
- Study Ablation Treatment
- AE/SAE evaluation

3: may be performed within 30 days prior to study treatment



Randomized 1:1 in blocks by site



Study Flow

Day 1 Post-Ablation Visit (V2)

- Brain MRI
- NIH Stroke Scale evaluation
- Discharge summary/Medication inventory
- AE/SAE evaluation

Month 1 Visit (V3)

- Medical care utilization/Medication inventory
- Documentation of results of ECGs and any ambulatory ECG monitoring obtained for clinical purposes, if available
- hrQOL/PA questionnaire
- AE/SAE evaluation

Month 6 Visit (V4)

- Neurocognitive function testing
- Medical care utilization/Medication inventory
- Documentation of results of ECGs and any ambulatory ECG monitoring obtained for clinical purposes, if available
- hrQOL/PA questionnaire
- Vital signs, Weight
- AE/SAE evaluation

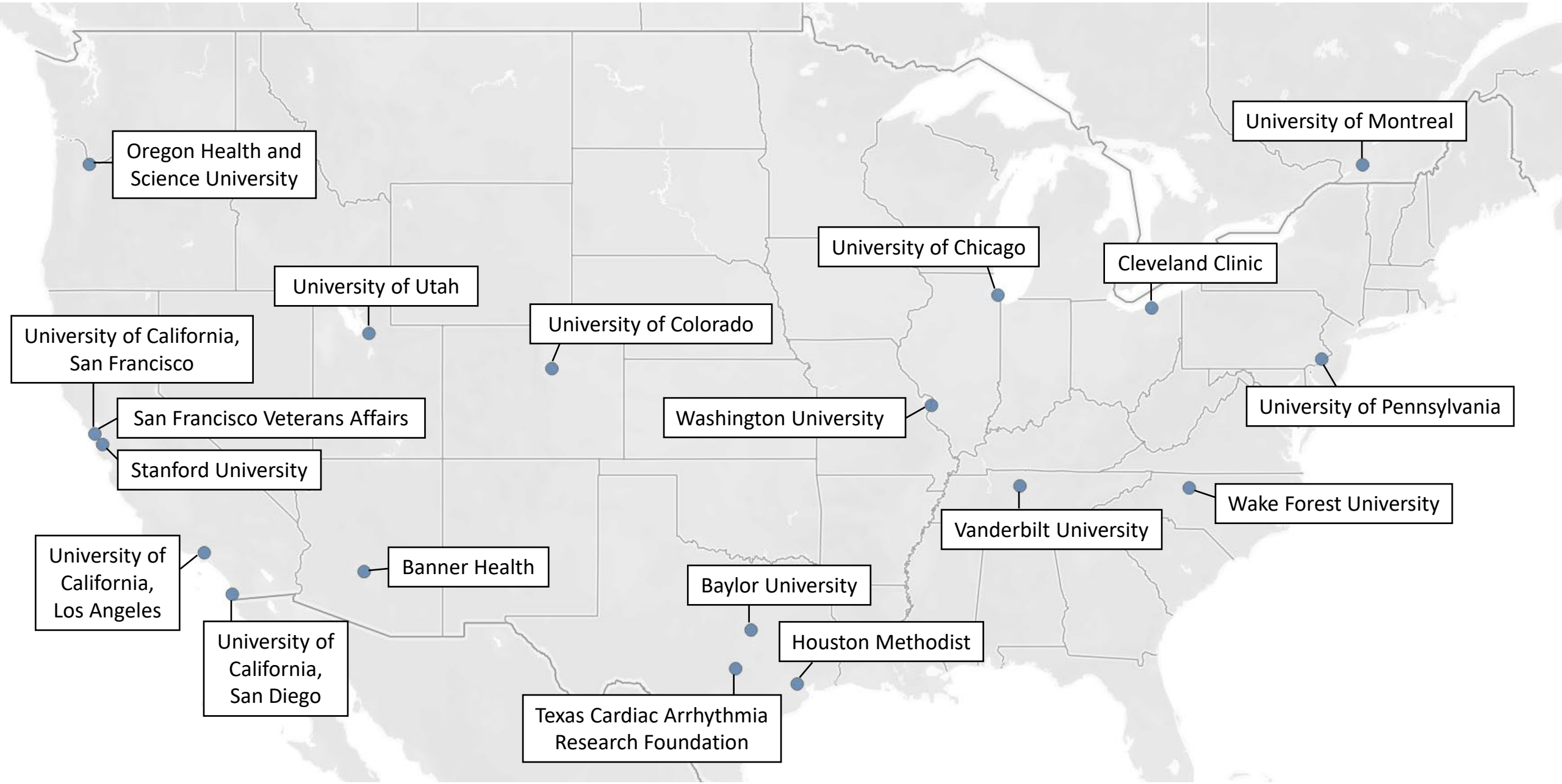
Response to COVID-19 Challenges

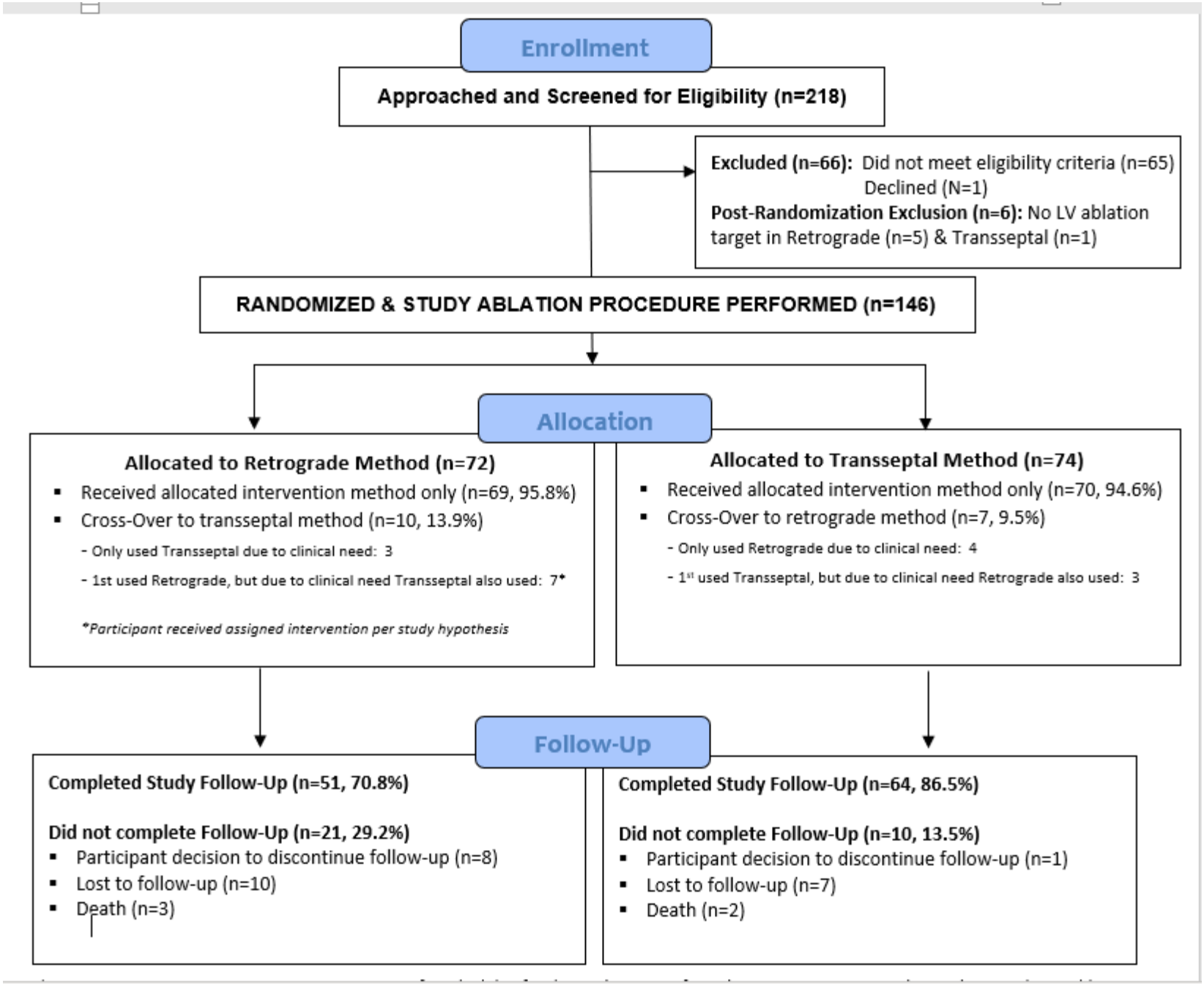
1. Abbreviated neurocognitive function exam that can be administered via Zoom
   - Includes 5/7 tests in the full exam (other 2 are dependent on reaction time)
   - Studies have shown that remote neuropsychological testing is a valid and reliable alternative to traditional face-to-face assessment (*Brearly et al., 2017; Collum et al., 2014; Wadsworth et al., 2018*)
2. Waiver for pre-ablation brain MRI so ppt will only be required to have the Day 1 post-ablation MRI
   - Post-ablation MRI will be performed using FLAIR imaging in the axial and coronal planes DWI-MRI
   - Dr. William Dillon (neuroradiologist) and Dr. Anthony Kim (neurologist) agree that DWI signal will identify the acute post-ablation lesions

Power Calculations

- Assumptions:
  - 60% incidence of cerebral emboli (we observed 64% in retrograde aortic approach) in the retrograde aortic approach
  - 20% incidence of cerebral emboli in the transseptal group (based on the AF ablation literature)
  - A 10% cross-over rate
  - A 25% loss to follow-up or post-randomization exclusion

- 150 participants will provide >95% power to detect a statistically significant difference


Oregon Health and Science University
University of Montreal
University of Chicago
Cleveland Clinic
University of Utah
University of Colorado
University of California, San Francisco
San Francisco Veterans Affairs
Washington University
University of Pennsylvania
Stanford University
Wake Forest University
Vanderbilt University
University of California, Los Angeles
Banner Health
Baylor University
University of California, San Diego
Houston Methodist
Texas Cardiac Arrhythmia Research Foundation


Enrollment
Approached and Screened for Eligibility (n=218)
Excluded (n=66): Did not meet eligibility criteria (n=65)
Declined (N=1)
Post-Randomization Exclusion (n=6): No LV ablation target in Retrograde (n=5) & Transseptal (n=1)
RANDOMIZED & STUDY ABLATION PROCEDURE PERFORMED (n=146)
Allocation
Allocated to Retrograde Method (n=72)
Received allocated intervention method only (n=69, 95.8%)
Cross-Over to transseptal method (n=10, 13.9%)
- Only used Transseptal due to clinical need: 3
- 1st used Retrograde, but due to clinical need Transseptal also used: 7*
*Participant received assigned intervention per study hypothesis
Allocated to Transseptal Method (n=74)
Received allocated intervention method only (n=70, 94.6%)
Cross-Over to retrograde method (n=7, 9.5%)
- Only used Retrograde due to clinical need: 4
- 1st used Transseptal, but due to clinical need Retrograde also used: 3
Follow-Up
Completed Study Follow-Up (n=51, 70.8%)
Did not complete Follow-Up (n=21, 29.2%)
Participant decision to discontinue follow-up (n=8)
Lost to follow-up (n=10)
Death (n=3)
Completed Study Follow-Up (n=64, 86.5%)
Did not complete Follow-Up (n=10, 13.5%)
Participant decision to discontinue follow-up (n=1)
Lost to follow-up (n=7)
Death (n=2)

Baseline Characteristics

	Retrograde Aortic (n=72)	Transseptal (n=74)
Age	63.2 ± 12.5	65.3 ±11.3
Female	12 (17%)	18 (24%)
White	60 (83%)	67 (91%)
Black	5 (7%)	2 (3%)
Asian/ Pacific Islander	5 (7%)	2 (2%)
Native American	1 (1%)	0
Other	1 (1%)	3 (4%)
Hispanic	4 (6%)	4 (5%)
BMI ($kg.m^2$)	31 ± 7	30 ± 8
Diabetes	13 (18%)	16 (22%)
Hypertension	26 (36%)	28 (38%)
Coronary Disease	40 (56%)	34 (46%)
Heart Failure	39 (54%)	32 (43%)
Stroke	2 (3%)	5 (7%)

Baseline Characteristics

	Retrograde Aortic (n=72)	Transseptal (n=74)
Aortic Vascular Disease	0	1 (1%)
Congenital Heart Disease	1 (1%)	5 (5%)
History of DVT	5 (6%)	6 (8%)
Hypercoagulable syndrome	1 (1%)	1 (%)
Pulmonary embolism	5 (7%)	5 (7%)
CABG	8 (11%)	9 (12%)
Median Pack years smoked (IQR)	0 (0-13.5)	0 (0-9.25)
Atrial Fibrillation	22 (31%)	30 (40%)
Sustained VT	31 (43%)	34 (46%)
Polymorphic VT	0 (0%)	3 (4%)
VF	1 (1%)	2 (3%)
PVCs	49 (68%)	46 (62%)
Creatinine	1.08 ± 0.32	1.12 ± 0.45

Procedural Characteristics

	Retrograde Aortic (n=72)	Transseptal (n=74)	P value
Underwent retrograde aortic approach only	62 (86%)	4 (5%)	
Transseptal only	3 (4%)	67 (91%)	
Both, started with retrograde aortic	7 (10%)	0 (0%)	
Both, started with transseptal	0 (0%)	3 (4%)	
Maximum BP	154 ± 32	160 ± 34	0.31
Minimum BP	83 ± 25	86 ± 29	0.43
Electrical cardioversion/ defibrillation	17 (24%)	19 (27%)	0.85
Mean ACT	296 ± 42	298 ± 64	0.86
Target location			0.42
Near mitral annulus	9 (15%)	5 (9%)	
Near conduction system	8 (13%)	5 (9%)	
Papillary muscles	12 (20%)	19 (35%)	
Other	20 (33%)	18 (33%)	

Procedural Characteristics

	Retrograde Aortic (n=72)	Transseptal (n=74)	P value
Median ablation time (minutes)	18 (7-32)	15 (7-32)	0.07
Average power (watts)	42 ± 16	42 ± 14	0.88
Maximum power (watts)	44 ± 7	44 ± 11	0.68
Left heart time (minutes)	154 ± 86	140 ± 79	0.29
Median fluoroscopy time (minutes)	6.6 (0.4-12.1)	9.5 (2.4-21.7)	0.014
Procedure time (minutes)	238 ± 116	237 ± 104	0.98
Total fluids in (ml)	1,406 ± 938	1,702 ± 1,545	0.17
Net fluids in versus out	881 ± 802	932 ± 783	0.71

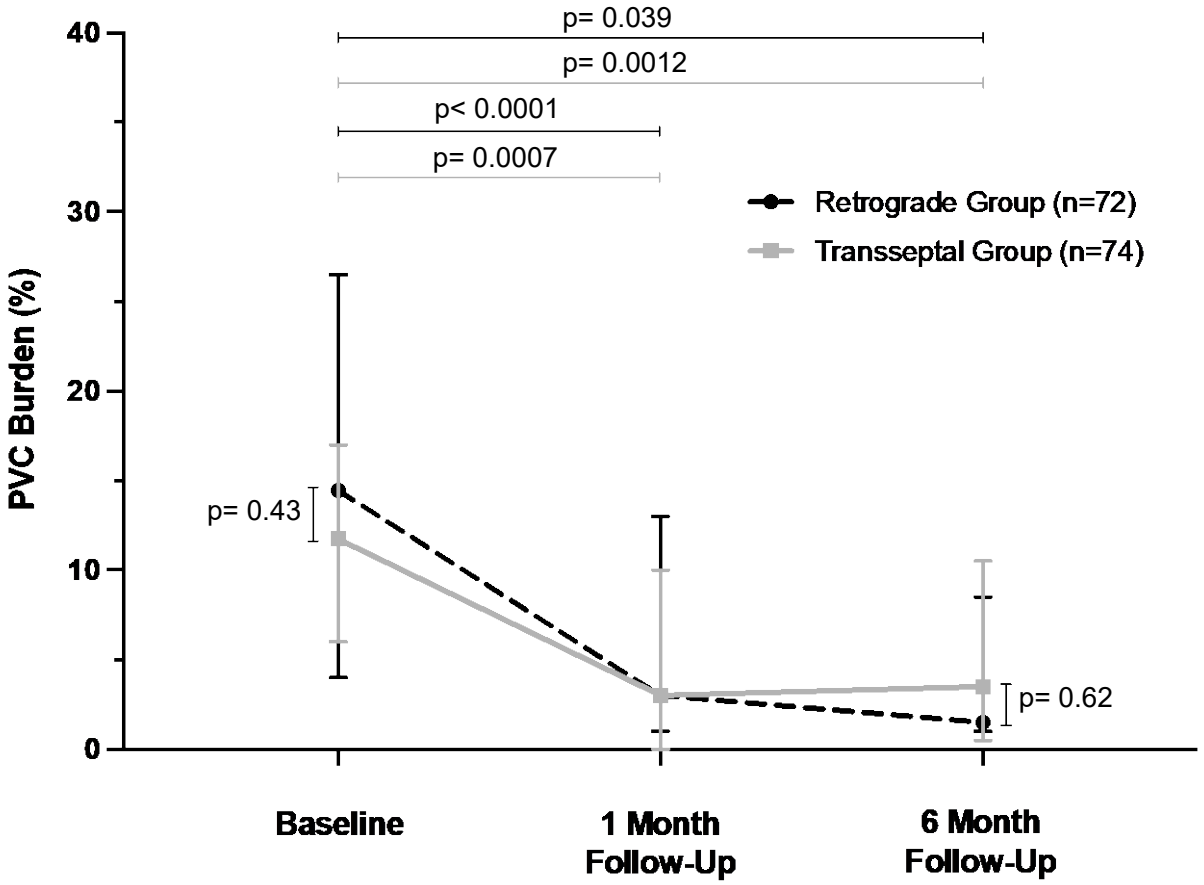
Complications within 30 days

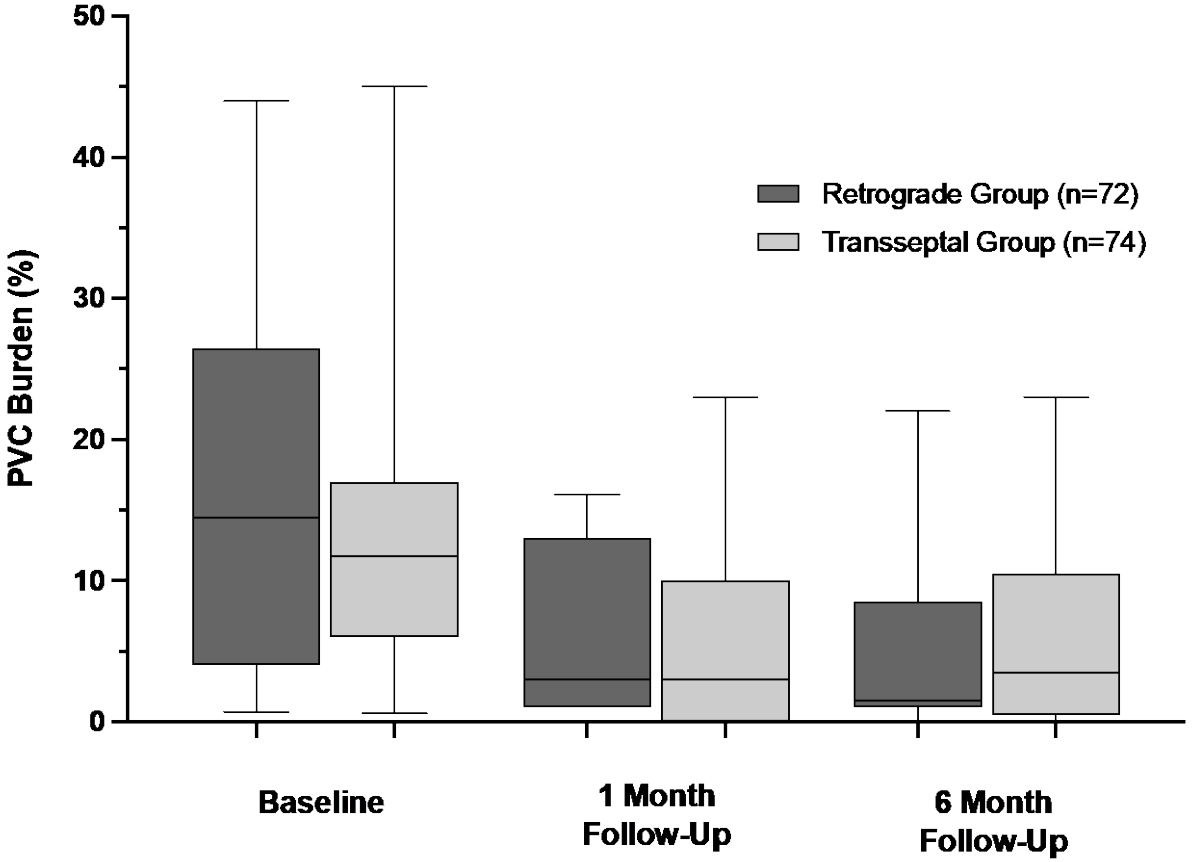
	Retrograde Aortic (n=72)	Transseptal (n=74)	P value
Total hospital days (median, IQR)	1 (1-2)	1 (1-3)	0.44
Total ICU days (median, IQR)	0 (0-0)	0 (0-0)	0.39
Pericardial effusion	0	4	0.12
Vascular injury (AV fistula, pseudoaneurysm)	2 (3%)	0	0.24
Myocardial infarction	0	0	
Stroke/ TIA			
Pneumothorax/ hemothorax	0	0	
Bleeding requiring surgical intervention or transfusion	0	4	0.12
Peripheral infarct	0	0	
Other cardiovascular disease-related complication	5 (7%)	3 (4%)	0.72
Death	0	0	

Efficacy

	Retrograde Aortic (n=72)	Transseptal (n=74)	P value
Intra-procedural success			0.66
Unable to ablate	3 (5%)	4 (6%)	
Reduced burden/ inducibility	17 (26%)	22 (33%)	
Complete success	46 (70%)	41 (61%)	
1 month visit (median 39 days)			
Eradication of target	35 (58%)	40 (64%)	0.29
Sustained VT observed	1 (2%)	2 (3%)	1.0
Appropriate ICD shocks	2 (3%)	1 (1%)	1.0
Improved symptoms	45 (63%)	53 (72%)	0.61
6 month visit (median 198 days)			
Eradication of target	31 (59%)	40 (64%)	0.94
Sustained VT observed	4 (7%)	2 (3%)	0.41
Appropriate ICD shocks	3 (4%)	1 (1%)	0.30
Improved symptoms	41 (55%)	55 (74%)	0.66

PVC Burden Pre and Post Ablation



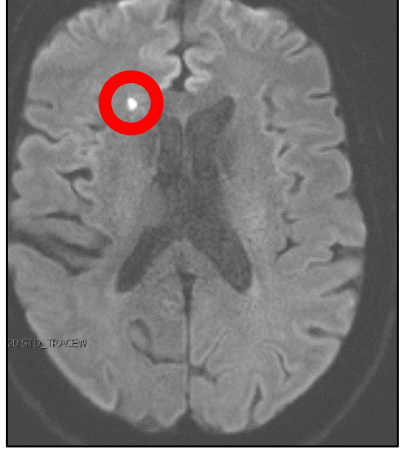


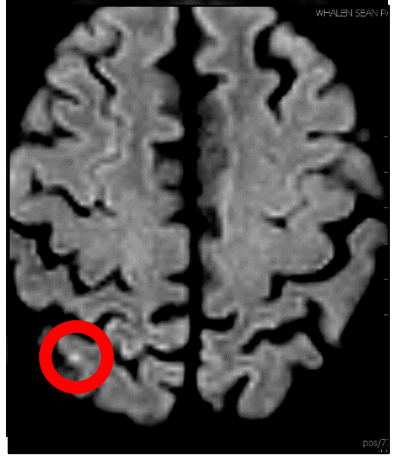
Pre-procedure MRIs

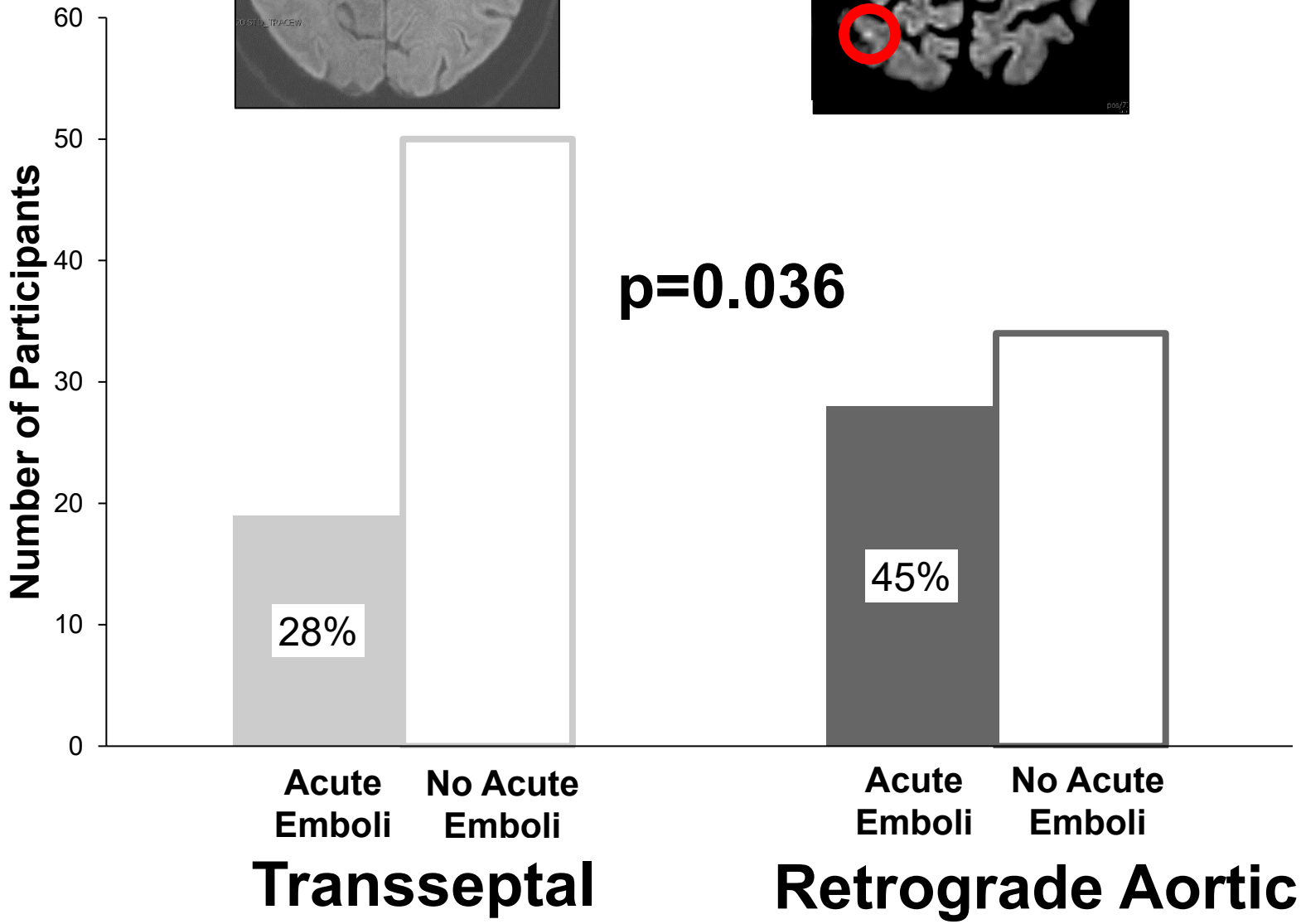
- Seventy participants (35 in each initial randomization group; among the modified intention to treat group, 34 in the transseptal group and 31 in the retrograde aortic group)
- None had an acute diffusion abnormality indicative of an acute brain embolism
- 131 (90%) of all participants had a post-operative day #1 MRI
  - 62 (86%) in the retrograde aortic group and 69 (92%) in the transseptal group

Primary Outcome

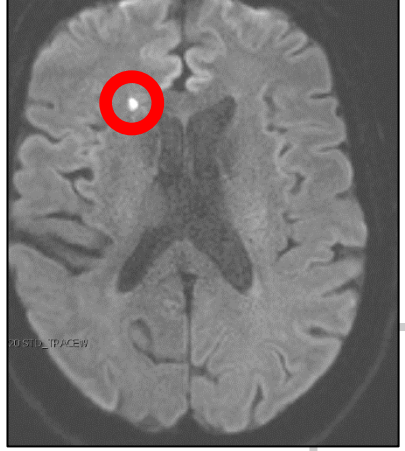
Intention-to-Treat



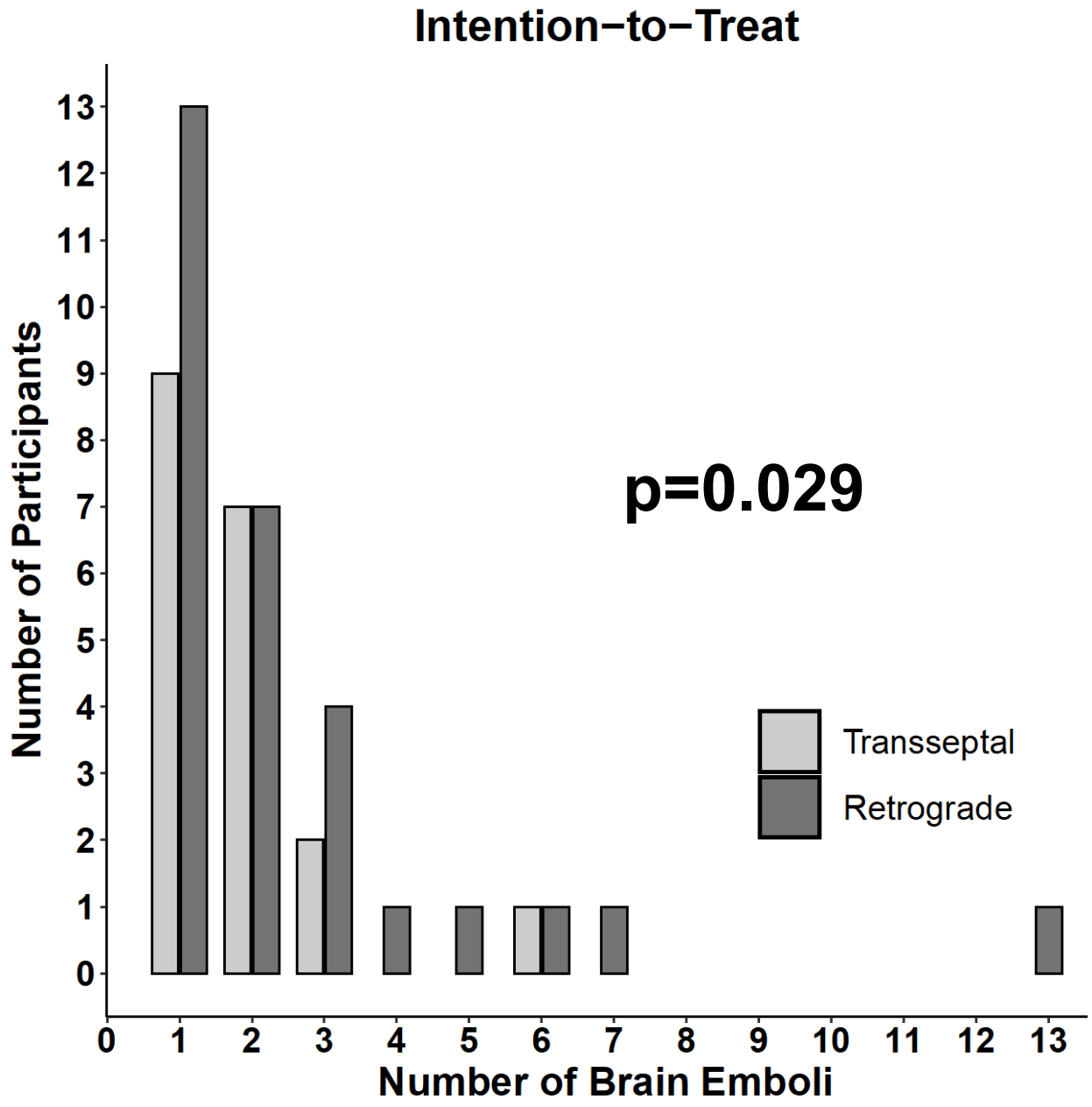


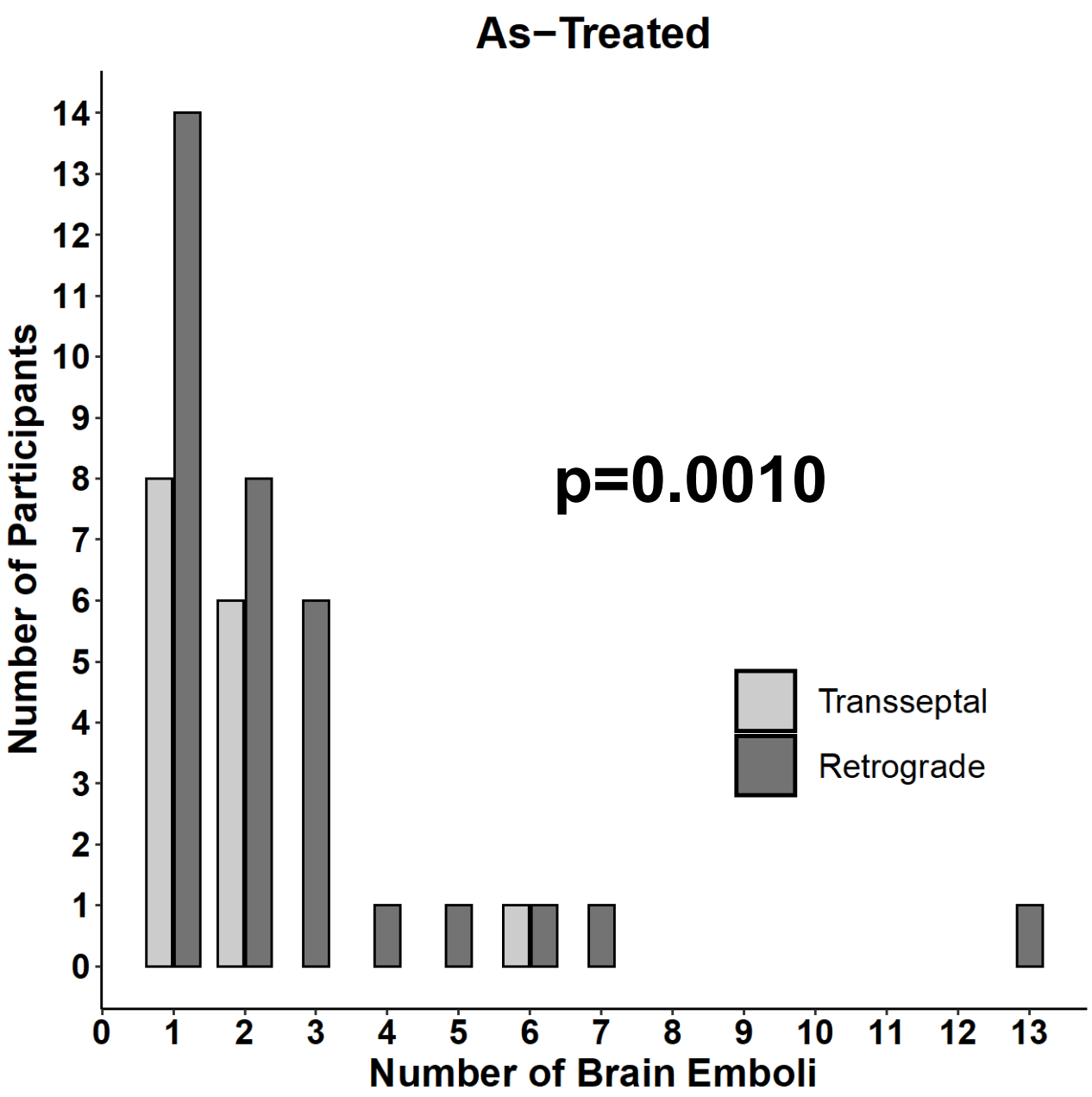


As-treated



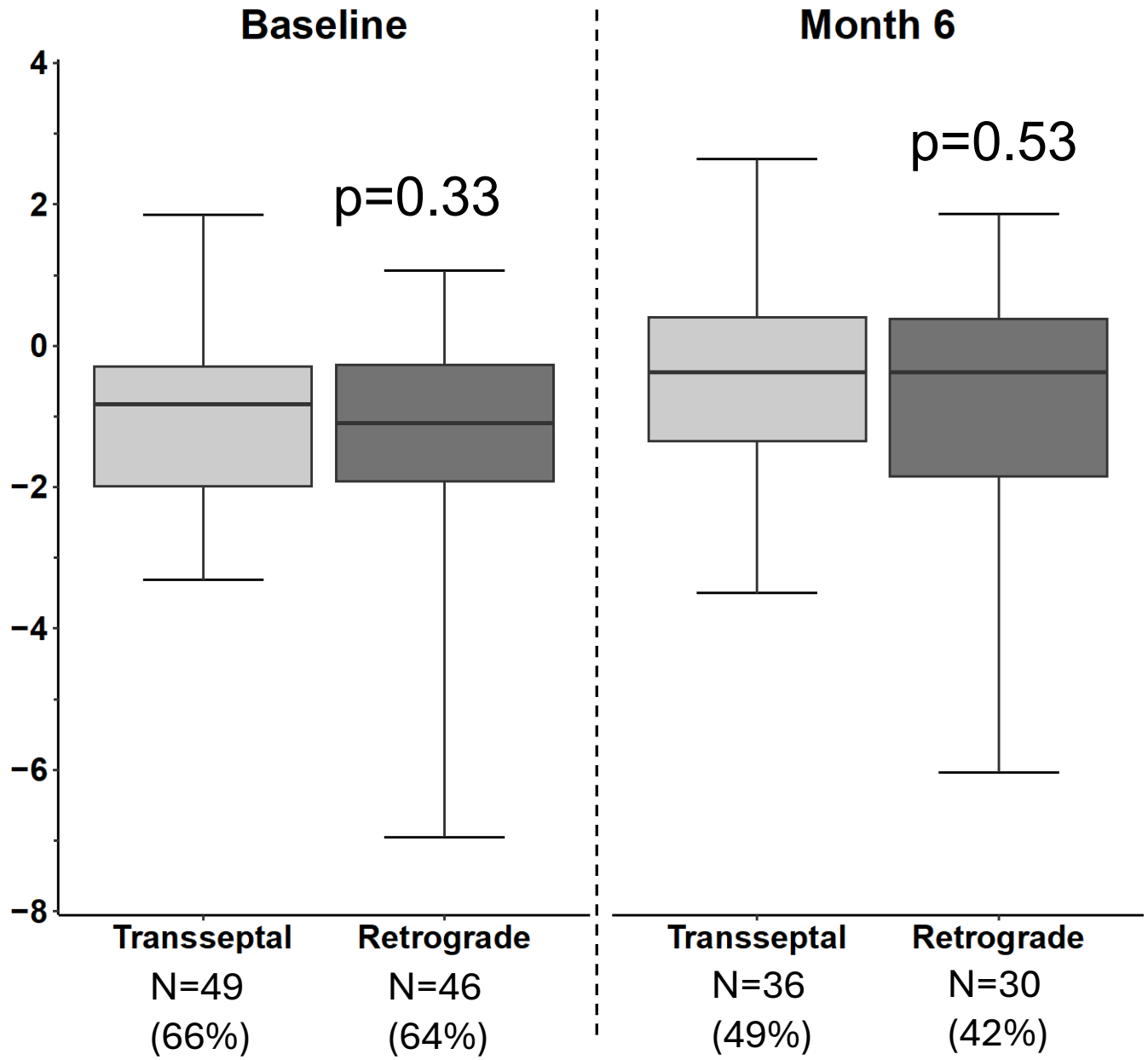
Number of Participants
60
50
40
30
20
10
0
23%
49%
p=0.0016
Acute Emboli
No Acute Emboli
Acute Emboli
No Acute Emboli
Only Transseptal
Any Retrograde Aortic


Intention−to−Treat
Number of Participants
Number of Brain Emboli
p=0.029
Transseptal
Retrograde


As−Treated
Number of Participants
Number of Brain Emboli
p=0.0010
Transseptal
Retrograde

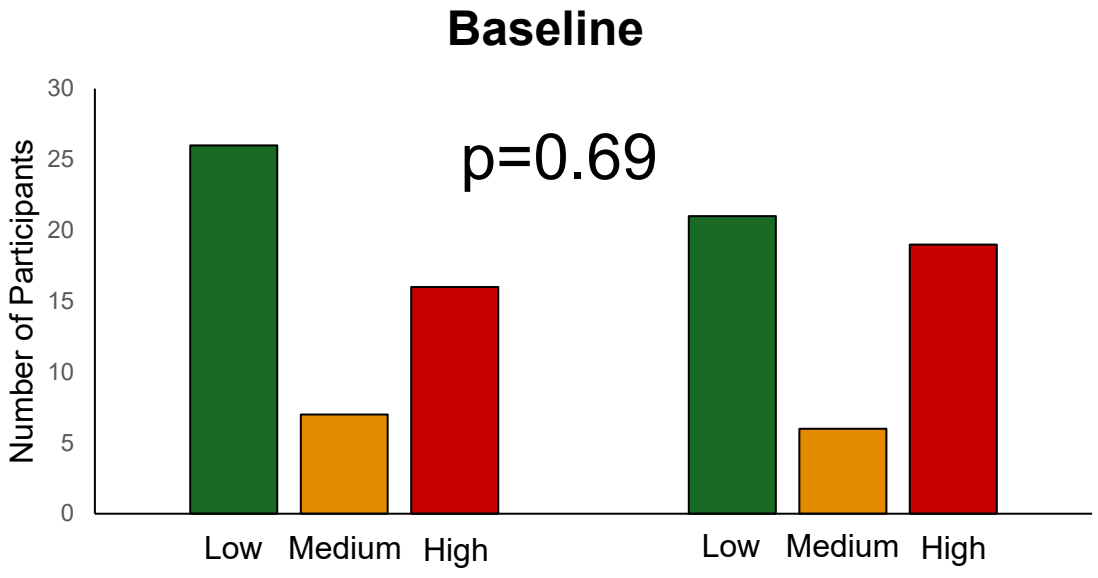
Cognitive Composite Score

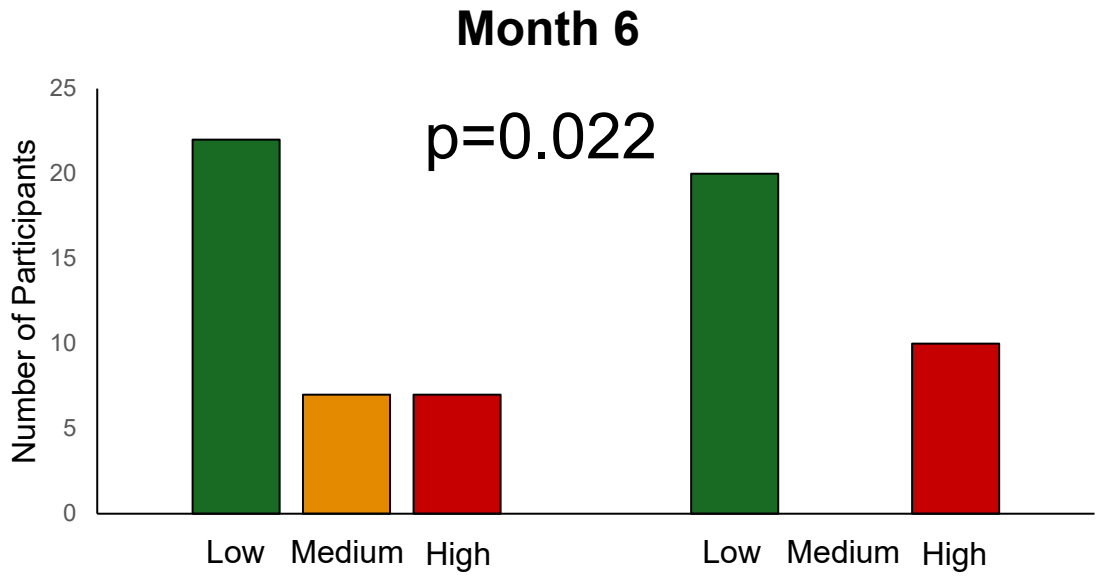
Intention-to-Treat Analysis



Likelihood of Cognitive Impairment

Intention-to-Treat Analysis





Limitations

- The study may have been insufficiently powered to detect differences in efficacy and complications
- There was substantial loss of follow-up for the 6 month neurocognitive assessment
- The brain emboli may be the “canary in the coalmine” that we can see
  - We did not assess potential impacts of emboli to other organs that may have occurred
- The presence of these infarcts does not necessarily detract from the overall benefit of the procedure, but rather may point to the optimal approach

Conclusions

- A transseptal approach to endocardial left ventricular catheter ablation results in significantly less frequent acute brain emboli compared to a retrograde aortic approach
- The transseptal approach may mitigate against neurocognitive decline after these procedures, although missing data at 6 months precludes confident conclusions
- These data suggest that a transseptal approach to other transcutaneous left ventricular (or perhaps aortic root) procedures may be beneficial
- These data may also suggest that emboli affecting other organs may more often occur with retrograde aortic access

Thank You