

## Supplementary Online Content

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- eAppendix 1.** Devices and their Deployment
- eAppendix 2.** Outcomes and Ascertainment
- eAppendix 3.** Statistical Information
- eFigure.** Relative Risk of "Large Volume" Infarcts for Each Treatment Device Compared to Control
- eTable 1.** Baseline and Operative Characteristics
- eTable 2.** Incidence of Clinical or Radiographic CNS Infarction at 7 Days Post procedure Assuming Various Missing Data Mechanisms
- eTable 3.** Unadjusted and Adjusted Odds Ratios of Clinical or Radiographic CNS Infarction at 7 Days Post procedure
- eTable 4.** Neurocognitive Decline at 90 Days by Domain
- eReferences**

This supplementary material has been provided by the authors to give readers additional information about their work.

## **eAppendix 1. Devices and their Deployment**

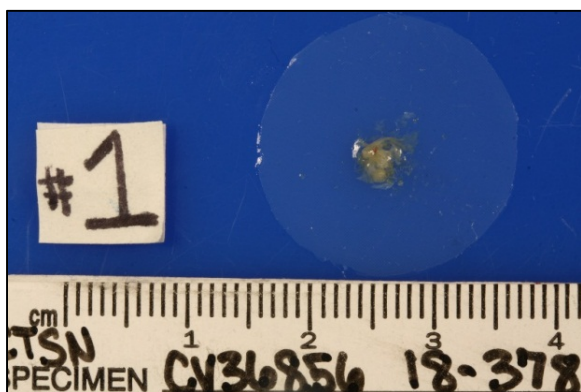
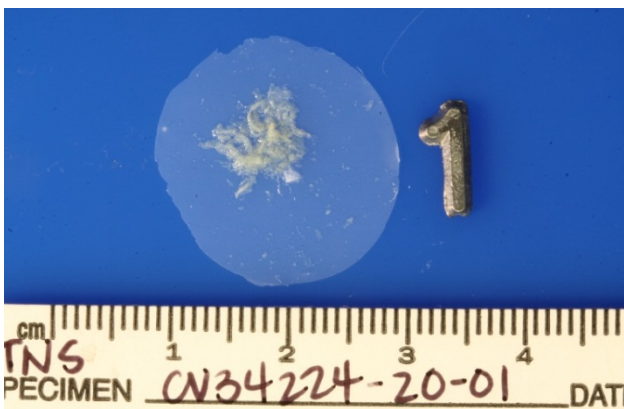
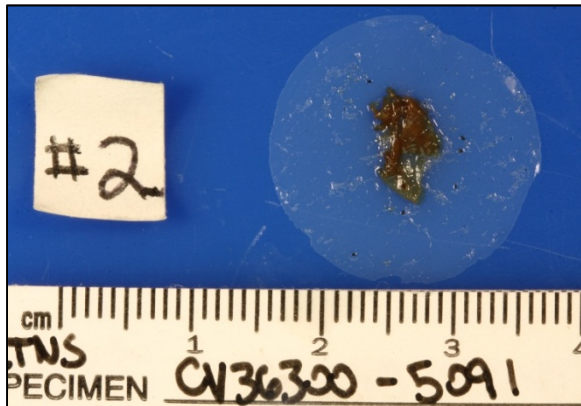
For patients assigned to the intra-aortic filtration device, the surgeon could use either the EMBOL-X® Access Device/Aortic Cannula or a standard cannula with the EMBOL-X® filter deployed through a separate introducer sheath. The EMBOL-X® filter consists of a heparin-coated polyester mesh with pore size designed to capture particulate emboli with diameters of more than 120 µm. The flexible wire filter frame allows the filter to conform to the interior diameter of the ascending aorta. The size of the distal ascending aorta is determined either by CT scan or intraoperative direct aortic measurement (TEE or epi-aortic ultrasound). The filter size is then selected based on the measured aortic size. The available filter sizes range from 26 mm to 37 mm. The filter is prepared and kept in saline until it is ready to load the filter into the filter introducer sheath to minimize potential air bubbles in the filter. The filter is deployed in the ascending aorta before the aortic cross clamp is placed and subsequently removed. A new filter should be deployed prior to removal of the aortic cross clamp and remains in place until the patient is weaned from cardiopulmonary bypass. It is recommended that the filter be exchanged after 60 minutes of deployment to avoid platelet aggregation on the filter.

For patients assigned to the suction-based extraction device, the surgeon used the CardioGard embolic protection device which is a curved tip 24-French aortic perfusion cannula, comprised of 2 hollow tubes. The first tube is the standard main forward-flow tube. The second tube attached to an existing bypass vent port, is a novel element located posteriorly to the main tube; its function is to facilitate blood and particle suction by directing the blood back to the reservoir of the coronary bypass machine, while the retrieved embolic material is eliminated through the filter of the venous reservoir. The

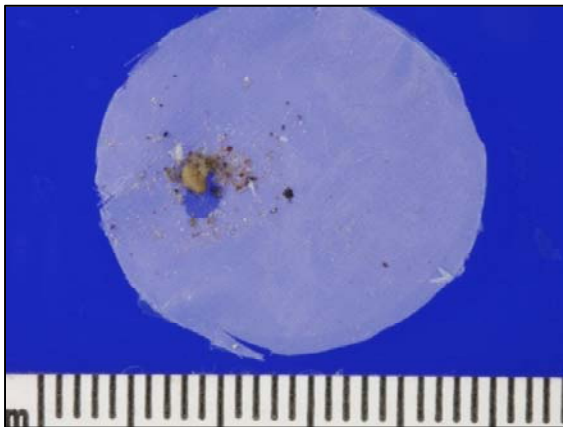
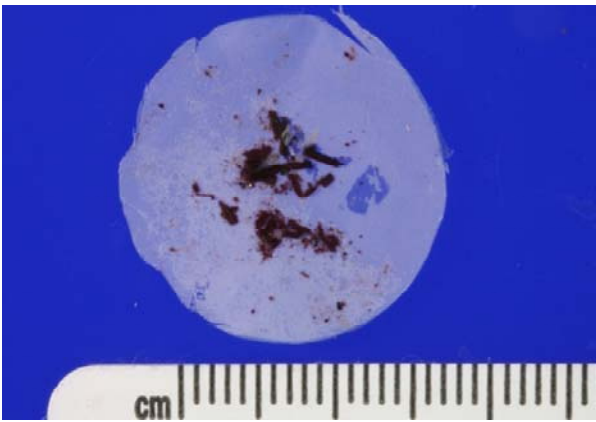
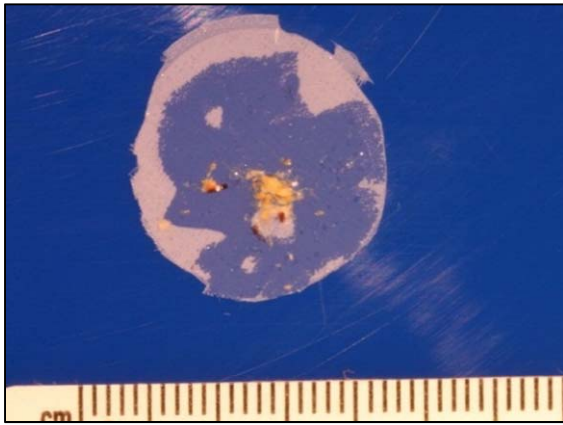
surgeon could use standard cannulation techniques to insert the aortic perfusion cannula.

Examples of debris captured for both devices are given below.

Debris captured using the EMBOL-X intra-aortic filtration device



Debris captured using the CardioGard suction-based extraction device



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## **eAppendix 2. Outcomes and Ascertainment**

### **Primary Outcome**

The primary purpose of cerebral embolic protection devices is to reduce cerebral emboli. The primary endpoint was freedom from clinical or radiographic CNS infarction at 7 ( $\pm$  3) days post procedure. The trial was designed so that all patients would undergo a 1.5 or 3.0 T diffusion-weighted MRI post-operatively to indicate whether they had radiographic evidence of brain infarction, which is the definition of stroke set out by the consensus panel of the AHA/ASA. To determine the clinical relevance of radiographic infarcts we required serial NIHSS assessments (days 1, 3, 7) in all patients to distinguish between clinically silent strokes and strokes with clinical symptoms. Moreover, recognizing that neuroimaging data either may not provide evidence of infarction or could be missing, which we estimated would be the case for 10% of patients, we included serial clinical NIHSS assessments, and neurological events identified in the course of providing treatment, to ensure that we didn't underestimate cerebral infarction events.

All MRIs were read by a core lab, blinded to treatment assignment (see below), and stroke events with clinical findings (NIHSS $\geq$ 2) were adjudicated by an EAC sub-committee, consisting of vascular neurologists blinded to treatment assignment. All protocol-defined neurological adverse events reported by the clinical sites were adjudicated by the overall EAC, which consists of stroke neurologists, cardiac surgeons, cardiologists and infectious disease specialists. There was no overlap in membership between the EAC and its sub-committee.

*Assessment of Radiographic Infarcts by the MRI Core Lab at the University of Pennsylvania*

The MRI processing and analysis in CTSN targets detection, segmentation and quantification of “DWI lesions” (acute strokes detectable on DWI scans) from the MRI data of each subject. The final result sheet reported the count and volume of DWI lesions in the whole brain, as primary MRI variables. As secondary variables, we additionally reported volumes of a set of cortical and sub-cortical anatomical regions of interest (ROIs), DWI lesion count and volume within these ROIs, and white matter hyperintensity (WMH) volumes within these ROIs.

The analysis was performed using the following MRI image modalities:

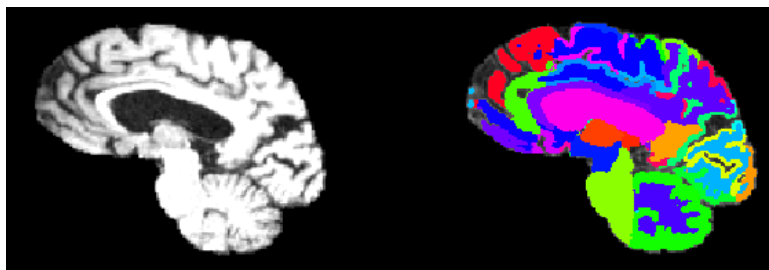
- T1-weighted
- FLAIR
- DWI (b1000)
- ADC

*Processing Pipeline Description:*

The processing pipeline includes a set of automatic and semi-automatic programs used for image pre-processing, ROI segmentation, DWI lesion segmentation and segmentation of WMHs. These processing modules are briefly described below.

*Image pre-processing:* T1-weighted, FLAIR and DWI scans of each subject were preprocessed for correction of intensity inhomogeneities. A multi-atlas label fusion-based segmentation method was applied for automatic removal of extra cerebral tissue in the T1 image.

*ROI Segmentation:* A new multi-atlas registration based label fusion method was applied for ROI segmentation. Multi-atlas segmentation has gained increasing interest in recent years and has shown significant improvement in accuracy over single-atlas-based segmentation. In this framework, multiple atlases with semi-automatically extracted ground-truth ROI labels are first warped individually to the target image using a non-linear registration method. A spatially adaptive weighted voting strategy is then applied to fuse the ensemble into a final segmentation. The method partitions the T1 scan of each subject into a set of 154 anatomical ROIs, which are also organized within a hierarchical structure to allow derivation of volumetric measurements in various resolution levels (103 additional derived ROIs including lobe and sub-lobe level).



*Segmentation into anatomical ROIs.*

*DWI Lesion Segmentation:* A semi-automated software tool was used for segmenting DWI lesions. The first component of this tool is a multi-modal image viewer that was used for viewing DWI, T1, FLAIR and ADC images aligned to the DWI image space. The tool allowed the user to manually label “seed points” for each visually detected lesion. The manual labeling of seed points was performed by an expert radiologist. An automated segmentation method was then applied on the detected seed points for the segmentation of DWI lesions. The automated method used the T1 and DWI scans of the subject, as well as the detected seed point information, to estimate expected normal DWI

intensity within brain, and to delineate the boundaries of the lesion on the DWI image using a technique known as “region-growing”.

**WMH Segmentation:** White matter lesions, which are typically characterized by hyperintense FLAIR signal, were segmented by applying a supervised-learning-based multimodal segmentation method on the FLAIR and T1-weighted images of each subject.

*Extraction of MRI Variables:* Total DWI lesion volume and count were calculated for each subject and reported as primary MRI outcomes. We also calculated and reported volumetric data (healthy volume and lesion volume and count) within each ROI.

*MRI Processing Quality Control (QC) Procedures:*

All initial, intermediate and final image files, and derived numerical values were verified and validated using a standardized QC protocol that included manual and automatic verification steps. Specifically, the visual QC was performed for each subject to verify a) initial scans, b) brain mask, c) ROI segmentation, d) DWI lesion segmentation, and e) WMH segmentation, using visualization tools that allow 3D image overlay. The automated QC involved application of existing tools that perform basic statistical tests for detection of data outliers. The final result sheet includes a set of QC flags to report eventual QC issues detected.

**Composite Clinical Endpoint**

The composite clinical endpoint is defined as follows: “the proportion of patients who have had a clinical ischemic stroke, acute kidney injury (AKI), or death within 30 days of surgery will be compared by group.” Clinical stroke and AKI are defined below.

*Clinical Stroke*



A new, temporary or permanent, focal or global neurological deficit ascertained by a standard neurological examination (administered by a neurologist or other qualified physician and documented with appropriate diagnostic tests and consultation note) that lasts longer than 24 hours (or less than 24 hours if there is evidence of infarction on neuroimaging). This definition focuses on ischemic stroke, including hemorrhagic conversion of an ischemic stroke. The NIH Stroke Scale (NIHSS) must be administered within 24 hours following the event if the event is not captured at a protocol-defined assessment time point to document the presence and severity of neurological deficits.

***Acute Kidney Injury (AKI)***

AKI is defined according to the Acute Kidney Injury Network (AKIN) criteria (Mehta, Kellum et al. 2007): An abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl ( $\geq 26.4 \mu\text{mol/l}$ ), a percentage increase in serum creatinine of more than or equal to 50% (1.5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours). AKI is further classified according to below.

**AKI Staging Criteria**

Stage	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine of more than or equal to 0.3 mg/dl ( $\geq 26.4 \mu\text{mol/l}$ ) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg per hour for more than 6 hours
2	Increase in serum creatinine to more than 200% to 300% (> 2- to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours

3 <sup>1</sup>	Increase in serum creatinine to more than 300% (> 3-fold) from baseline (or serum creatinine of more than or equal to 4.0 mg/dl [ $\geq 354 \mu\text{mol/l}$ ] with an acute increase of at least 0.5 mg/dl [ $44 \mu\text{mol/l}$ ])	Less than 0.3 ml/kg per hour for 24 hours or anuria for 12 hours
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## Delirium

Incidence of delirium was compared between groups using clinical assessment data derived from Confusion Assessment Method (CAM)-based delirium detection measures. The CAM-based determination of delirium required: 1.) the presence of acute change in mental status from pre-operative baseline or fluctuating post-operative mental status; 2.) objective evidence of attentional changes relative to pre-surgical baseline; and 3.) either evidence of disorganized thinking or altered level of consciousness. For patients who were extubated, the 3-minute Diagnostic Interview for CAM-defined Delirium (3D-CAM) was administered, while intubated patients were assessed for delirium via the Confusion Assessment Method for the ICU (CAM-ICU). The 3D-CAM has demonstrated high sensitivity and specificity (95% and 94%, respectively) in the detection of delirium in general, non-intensive care medical setting<sup>2</sup>. Among intubated patients, the CAM-ICU has demonstrated similar high levels of delirium detection sensitivity and specificity.

The 3D-CAM was administered prior to surgery to establish patient baseline attention and cognitive capacities, from which the determination of post-operative change in attention function from pre-surgical baseline was established. The 3D-CAM and/or

<sup>1</sup> Given wide variation in indications and timing of initiation of renal replacement therapy (RRT), individuals who receive RRT are considered to have met the criteria for stage 3 irrespective of the stage they are in at the time of RRT.

<sup>2</sup> Marcantonio ER, Ngo LH, O'Connor M, et al. 3D-CAM: Derivation and Validation of a 3-Minute Diagnostic Interview for CAM-defined Delirium. *Ann Intern Med.* 2014; 161(8): 554–561.

CAM-ICU measures were administered post-procedure on days 1, 3, and 7 ( $\pm$  3) days by neurology trainees or study coordinators who were certified to administer the 3D-CAM and CAM-ICU following successful completion of in-person delirium and neurocognitive assessment training by CTSN Neurocognition Core faculty.

## **eAppendix 3. Statistical information**

### **Interim Monitoring/Early Stopping**

We planned a single interim analysis with respect to the primary endpoint to give the option of early stopping should results strongly favor one arm or the other. In addition to the ethical concern of continuing a trial that shows a clear benefit in favor of one treatment, there is also a corresponding ethical concern of continuing a trial that has little chance of ever showing a benefit of one treatment compared to the other. As such, we also pre-specified that for each comparison of device therapy to control, conditional power under the original alternative hypothesis be computed at the interim look and that the DSMB use this to determine whether randomization be halted for futility. We proposed that consideration be given to halting the trial for futility if, given the data up to the point of the interim analysis, the probability of detecting a relative 35% reduction (from 50% to 32.5%) in the incidence of clinical or radiographic CNS infarction in patients randomized to an embolic protection device, compared to those randomized to no protection device, is less than 20%.

The interim analysis was performed at approximately 0.5 on the information scale. At the interim analysis, we computed conditional power both under the “current trend” and under the design alternative hypothesis as described by Cook and DeMets<sup>1</sup>. Under both scenarios conditional power was <10% for Suction-based Extraction vs. control and Intra-aortic Filtration vs. control. Because of the low conditional power, the DSMB recommended halting additional enrollment.

### **Missing Data Imputation Procedure**

The primary endpoint was freedom from clinical or radiographic CNS infarction at 7 ( $\pm$  3) days post procedure. Death within 7 days was considered as a treatment failure. Living patients without an observed stroke missing the MRI assessment had their total lesion volume imputed using a hot-deck multiple imputation procedure with distance-based donor selection as described in Siddique and Belin<sup>2</sup>. An advantage of this approach is that it does not require assuming ignorable missing data. In each randomization group, predictive mean matching was used to estimate missing data by

regressing observed outcomes on a set of observed covariates including age, sex, NIHSS and CAM measures; all selected prior to unmasking outcome data. Missing data was imputed based on "similar" cases; where similarity was defined as a monotonic distance function of the difference in predictive means between patients. Donors were chosen with probability inversely proportional to their distance from the donee. Missing values (donees) were replaced with observed values from donors in the same data set to provide realistic imputed values. An Approximate Bayesian Bootstrap (ABB) procedure<sup>3,4</sup> was used to incorporate parameter uncertainty into the hot-deck procedure and to account for non-ignorable missing data. Non-ignorability was incorporated by weighting each observed subject's probability of selection into the bootstrap sample either proportionally to size or proportionally to absolute distance from the mean, depending on the assumed missing data mechanism. For each assumed missing data mechanism, five imputations were performed and each data set analyzed separately with inferences combined using rules defined by Rubin<sup>5</sup>.

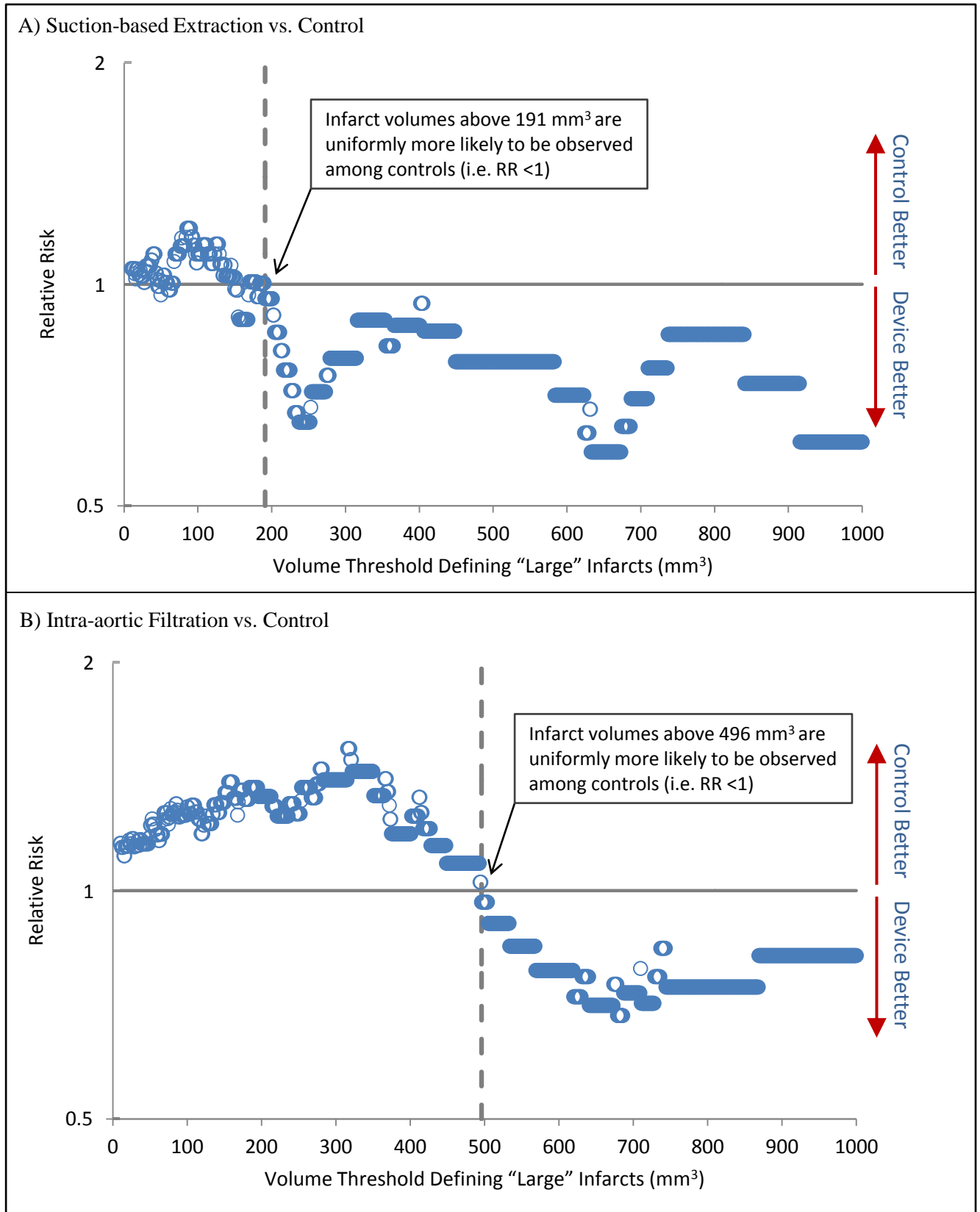
The primary analysis, assumed a non-ignorable missing data mechanism with volumes furthest away from the observed more likely to be selected with the probability of selection proportional to distance squared.

Sensitivity analyses assuming alternative non-ignorable missing data mechanisms as well as ignorable missing data were conducted to evaluate the robustness of the primary outcome result. These analyses and a description of the assumed missing data mechanism are given in eTable 2.

### **Stratified Analyses of the Primary Endpoint**

Randomization was stratified by procedure (isolated versus combined) and by clinical center. In both clinical center-adjusted and procedure-adjusted analyses of the primary endpoint, the Breslow-day test indicated no interaction between clinical center and treatment or between procedure and treatment for either Suction-based Extraction vs Control or Intra-aortic Filtration vs Control. Mantel-Haenszel odds ratios stratified by clinical center and by procedure are similar to unadjusted odds ratios (see eTable 3).

**eFigure.** Relative Risk of “Large Volume” Infarcts for Each Treatment Device Compared to Control



The plotted points in panels A and B depict the relative risk of “large” volume infarcts for each of the treatment devices compared to their controls as the cut-off value defining “large” varies from 10 to 1000 or above on the x-axis. Values  $< 1$  (below the solid line) favor the embolic protection device, and values  $> 1$  (above the solid line) favor the control.

**eTable 1.** Baseline and Operative Characteristics

	<b>Suction-based Extraction (N=118)</b>	<b>Control<sup>a</sup> (N=120)</b>	<b>Intra-aortic Filtration (N=133)</b>	<b>Control<sup>a</sup> (N=132)</b>
<b>Baseline Characteristics<sup>b</sup></b>				
Male sex	69 (58.5)	77 (64.2)	81 (60.9)	86 (65.2)
White	108 (91.5)	107 (89.2)	126 (94.7)	118 (89.4)
Age – yrs	74.6 (6.8)	73.4 (6.7)	73.6 (6.6)	73.6 (6.7)
<b>Medical and surgical history</b>				
Diabetes	48 (40.7)	36 (30.0)	36 (27.1)	37 (28.0)
Renal insufficiency	15 (12.7)	13 (10.8)	18 (13.5)	14 (10.6)
Myocardial infarction	16 (13.6)	8 (6.7)	15 (11.3)	10 (7.6)
Atrial fibrillation	14 (11.9)	16 (13.3)	13 (9.8)	16 (12.1)
Stroke or TIA	16 (13.6)	8 (6.7)	11 (8.3)	8 (6.1)
<b>SF-12<sup>c</sup></b>				
Physical Health Composite Score	41.4 (10.6)	40.5 (11.2)	40.1 (11.0)	40.2 (11.2)
Mental Health Composite Score	53.2 (9.3)	52.9 (9.3)	52.9 (9.6)	52.9 (9.4)
<b>Severe Cognitive Impairment<sup>d</sup></b>				
Verbal Memory	16/114 (14.0)	14/116 (12.1)	19/127 (15.0)	16/128 (12.5)
Executive Function	18/98 (18.4)	15/106 (14.2)	21/119 (17.6)	18/117 (15.4)
Auditory-Verbal Simple Attention	5/115 (4.3)	6/116 (5.2)	4/127 (3.1)	6/128 (4.7)
Visuomotor /Information Processing Speed	9/109 (8.3)	9/113 (8.0)	11/123 (8.9)	9/125 (7.2)
At least one deficit	37/102 (36.3)	28/109 (25.7)	36/121 (29.8)	31/120 (25.8)
White Matter Lesion Volume (mm <sup>3</sup> )	4592 (2433, 8377)	4719 (2201, 9776)	6303 (2686, 10027)	4704 (2265, 9776)
Presence of Large Cortical Lesions <sup>e</sup>	1/96 (1.0)	2/107 (1.9)	2/109 (1.8)	2/114 (1.8)
Maximum Atheroma Grade <sup>f</sup>	2.5 (0.7)	2.4 (0.6)	2.3 (0.7)	2.3 (0.6)
<b>Operative Characteristics<sup>b</sup></b>				
<b>Surgical Procedure</b>				
Isolated AVR	67 (56.8)	73 (60.8)	77 (57.9)	80 (60.6)
AVR & CABG	50 (42.4)	47 (39.2)	51 (38.3)	52 (39.4)
AVR & MV Repair ± CABG	1 (0.8)	0	5 (3.8)	0
Concomitant procedures <sup>g</sup>	17 (14.4)	19 (15.8)	23 (17.3)	20 (15.2)
Duration of cardiopulmonary bypass – min	104.9 (39.6)	102.2 (40.2)	109.1 (42.4)	101.7 (39.8)
Debris Captured in Filter(s)	79/106 (74.5)	-	115/116 (99.1)	-
<b>Type of Debris Captured</b>				
Calcification	30/106 (28.3)	-	23/116 (19.8)	-
Valve Tissue and/or Arterial Wall	53/106 (50.0)	-	113/116 (97.4)	-
Platelet-Rich Thrombus	55/106 (51.9)	-	39/116 (33.6)	-
Other	8/106 (7.5)	-	13/116 (11.2)	-

a As the trial began with randomization to Intra-aortic Filtration or control, the first 12 control patients served as controls for Intra-aortic Filtration only and 120 patients were common to both control groups.

b Categorical measures are presented as the number of patients and (%). If the denominator is not equal to the group sample size, data is presented as the number of patients/the number observed (%). White matter lesion volume is presented as median (IQR) and all other continuous measures are presented as mean (standard deviation).



c The SF-12 composite scores are normed as T-scores (mean=50, SD=10); a higher score indicates a better health state

d Severe cognitive impairment is defined as falling below 2 SD from the mean of an age-standardized population. Cognition was measured using a battery of tests including Hopkins Verbal Learning Test – Revised (HVLN-R), Controlled Oral Word Association Test (COWA), Trail Making Test – Parts A & B, Medical College of Georgia Complex Figures, and Wechsler Adult Intelligence Scale – 3<sup>rd</sup> Revision (WAIS-III, Digit Symbol Coding Subtest and Digits Span Subtest)

e A large cortical lesion is defined as having a chronic infarct involving cortical gray matter of maximum diameter greater than or equal to 4.0 cm

f Atheroma was examined in the ascending aorta and the aortic arch and graded according to Katz. The maximum grade is reported. Katz's grade ranges from 1 to 5 with 1 representing normal to mild intimal thickening and 5 indicating any thickness with mobile component.<sup>31</sup>

g The most common concomitant procedures were annular enlargement for valve placement, ascending aorta repair or replacement, and left atrial appendage ligation

**eTable 2.** Incidence of Clinical or Radiographic CNS Infarction at 7 Days Post-procedure Assuming Various Missing Data Mechanisms

Data	Missing Data	ABB Selection	PPS Factor (c) *	Non-ignorable missing data assumption	Suction-based Extraction vs. Control				Intra-aortic Filtration vs. Control			
					Device	Control	Absolute Difference (95% CI)	P-value	Device	Control	Absolute Difference (95% CI)	P-value
					Percent (SE)	Percent (SE)			Percent (SE)	Percent (SE)		
Observed	-	-	-	-	67.3 (4.7)	65.2 (4.5)	2.1 (-10.6, 14.9)	0.74	72.9 (4.1)	65.6 (4.4)	7.3 (-4.4, 19.1)	0.22
Imputed	Ignorable	Equal Probability	0	None; observations selected with equal probability	67.3 (4.8)	65.8 (4.4)	1.5 (-10.9, 13.8)	0.81	73.4 (4.1)	65.6 (4.3)	7.8 (-3.8, 19.3)	0.19
	Non-Ignorable	Probability Proportional to Size	1	Observations with highest volumes more likely to be selected with probability proportional to size	70.7 (4.4)	67.5 (4.3)	3.2 (-8.8, 15.2)	0.60	75.8 (3.7)	68.9 (4.0)	6.9 (-3.9, 17.6)	0.21
			-1	Observations with lowest volumes more likely to be selected with probability inverse to size	62.2 (5.4)	64.2 (4.6)	-2.0 (-16.4, 12.5)	0.79	69.5 (4.1)	63.3 (4.8)	6.1 (-6.6, 18.9)	0.34
			1	Observations with volumes furthest away from the mean most likely to be selected with probability proportional to distance	68.0 (4.9)	65.2 (4.5)	2.8 (-10, 15.6)	0.66	72.6 (4.1)	66.1 (4.5)	6.6 (-4.6, 17.7)	0.25
	2	Observations with volumes furthest away from the mean most likely to be selected with probability proportional to distance squared	68.0 (4.5)	66.7 (4.4)	1.3 (-11.2, 13.8)	0.84	74.4 (4.1)	67.6 (4.5)	6.9 (-4.2, 17.9)	0.22		

\*PPS Factor is proportionality at which observed cases with volume  $Y_{obs}$  are drawn into the bootstrap samples with probability proportional to  $Y_{obs}^c$  if probability proportional to size is indicated or probability proportional to  $|Y_{obs} - \bar{Y}|^c$  if absolute distance from mean is indicated.

Abbreviations: ABB is Approximate Bayesian Bootstrap; SE is standard error; CI are confidence intervals

**eTable 3.** Unadjusted and Adjusted Odds Ratios of Clinical or Radiographic CNS Infarction at 7 Days Post procedure

	Suction-based Extraction vs Control	Intra-aortic Filtration vs Control
Unadjusted OR	1.10 (0.62, 1.95)	1.41 (0.81, 2.46)
Mantel-Haenszel OR – Stratified by Clinical Center	1.05 (0.60, 1.85)	1.45 (0.83, 2.56)
Mantel-Haenszel OR - Stratified by Procedure	1.10 (0.62, 1.94)	1.42 (0.81, 2.46)

**eTable 4.** Neurocognitive Decline at 90 Days by Domain

	Suction-based Extraction			Control			P-value <sup>b</sup>	Intra-aortic Filtration			Control			P-value <sup>b</sup>
	No. Patients	No. w/ Decline <sup>a</sup>	%	No. Patients	No. w/ Decline <sup>a</sup>	%		No. Patients	No. w/ Decline <sup>a</sup>	%	No. Patients	No. w/ Decline <sup>a</sup>	%	
<b>Cognitive Domain<sup>c</sup></b>														
Verbal Memory	94	38	40.4	100	31	31.0	0.14	117	31	26.5	111	35	31.5	0.40
Visual Memory	95	25	26.3	101	27	26.7	0.93	116	36	31.0	112	32	28.6	0.75
Executive Function	83	25	30.1	89	28	31.5	0.65	103	19	18.4	99	31	31.3	0.053
Visuospatial/Constructional Praxis	98	28	28.6	102	38	37.3	0.22	117	31	26.5	113	41	36.3	0.08
Auditory-Verbal Simple Attention	96	28	29.2	101	34	33.7	0.96	117	36	30.8	112	37	33.0	0.75
Visuomotor/Information Processing Speed	93	30	32.3	97	26	26.8	0.17	110	43	39.1	108	33	30.6	0.19

a - Number with decline is defined as number of patients whose Z-score at day 90 decreased by 0.5 standard deviation relative to their baseline score. Z-scores were computed relative to the study population at baseline adjusting for age, education and gender.

b - P-value computed from a logistic regression model of decline adjusted for baseline score.

c - Cognition was measured using a battery of tests including Hopkins Verbal Learning Test – Revised (HVLN-R), Controlled Oral Word Association Test (COWA), Trail Making Test – Parts A & B, Medical College of Georgia Complex Figures, and Wechsler Adult Intelligence Scale – 3<sup>rd</sup> Revision (WAIS-III, Digit Symbol Coding Subtest and Digits Span Subtest)

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