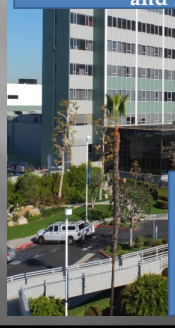
Challenges & Successes with Endografs in the Treatment of Ascending Aortic Dissections (TAADs), Penetrating Ulcers and Pseudoaneurysms



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Disclosures

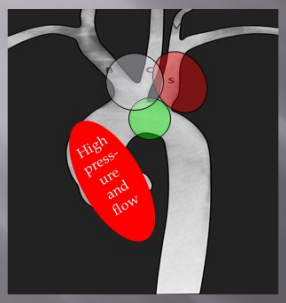
Speaker name: Rodney A. White, MD

☑ I have the following potential conflicts of interest to report:

- Advisory Boards
  Intact Vascular, AneuMed, Intressa

☑ Off-Label Use of devices discussed only in context of FDA approved IDE studies

Technical challenges for Endovascular Repair



- Anatomical
  - Short Distance between the LSCA and LCCA
  - Arch angulation
  - Ascending – descending aortic size discrepancy
- Technical
  - Device Delivery
  - Orientation, conformability
- Physiological
  - Coronary/cerebral perfusion
  - High hemodynamic forces
- Complications
  - Stroke, type A dissection, valve interactions

Physician-Sponsored IDE Application

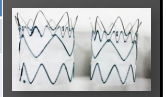
Study Title:	Proposed Single Center Investigational Device Exemption: Feasibility of Endovascular Repair of Ascending Aortic Pathologies
Investigational Device:	Valiant® Thoracic Stent Graft with the Captivia Delivery System*

*CAUTION-Investigational device. Limited by Federal (or United States) law to investigational use.

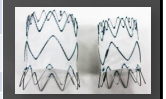
Valiant PS IDE device is a modified Valiant Thoracic Stent Graft with Captivia Delivery System.

Commercialized Valiant Captivia vs Valiant PS-IDE				
	Commercialized Valiant Captivia		Valiant PS-IDE*	
Proximal Configuration	FreeFlo	Closed Web	FreeFlo	Closed Web
Distal Configuration	Closed Web	Bare Spring	Closed Web	Bare Spring
Covered Lengths	100, 150, 200 mm	100, 150, 200 mm	40, 60, 80 mm	40, 60, 80 mm
Diameters	22-46 mm	22-46 mm	30-46 mm	30-40 mm
Delivery System	Captivia w/Tip Capture	Captivia Non Tip Capture	Captivia w/Tip Capture	Captivia Non Tip Capture

Freeflo



Closed Web



*CAUTION-Investigational device. Limited by Federal (or United States) law to investigational use.

Inclusion Criteria

- Patient must have a Type A thoracic aortic dissection, retrograde Type A thoracic aortic dissection, intramural hematoma, penetrating ulcer or pseudoaneurysm of the ascending thoracic aorta affecting the area between the Sinus of Valsalva and the innominate artery orifice (with no involvement of the aortic valve) and be considered candidates for endovascular repair;
  - Patient must also have at least one cm proximal and distal landing zones in the ascending aorta
  - Aorta between 28-44 mm in diameter;
- The patient must be deemed high-risk surgical candidate according to the following established criteria:
  - ASA class IV

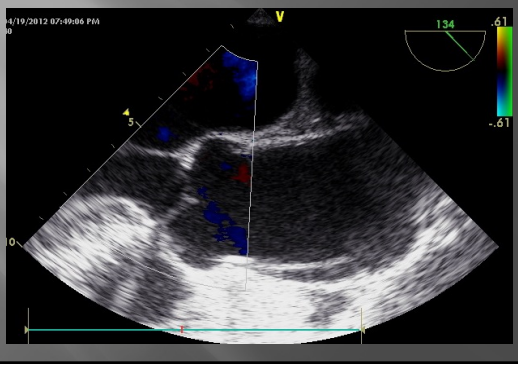
Ascending Aortic TEVAR PSIDE Feasibility Study

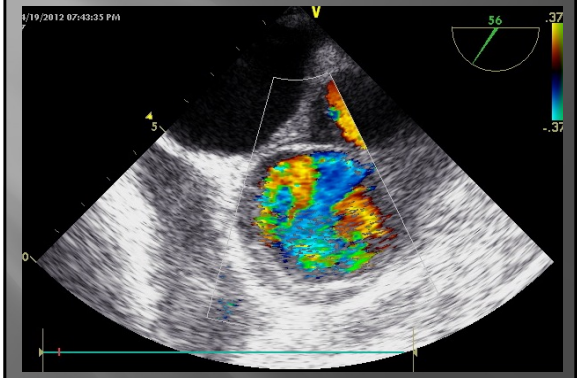
- Evaluate Valient thoracic endografts for treatment of ascending thoracic lesions with preserved "tubular" aortic anatomy (non-aneurysmal)
  - deployment accuracy
  - stability of device in ascending aorta
  - assess aortic remodeling

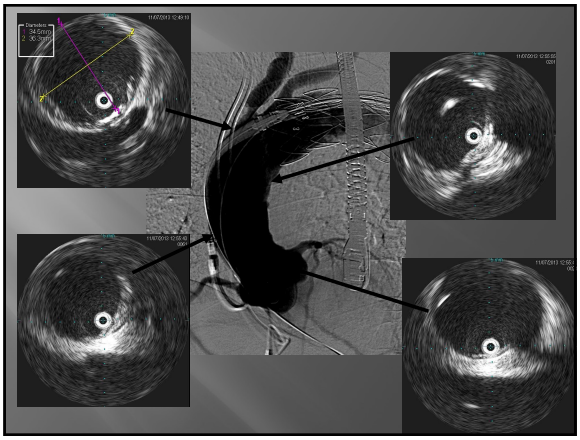
Case Reviews

- Since 2013, 15 patients have been treated
  - 6 pseudoaneurysms
  - 3 intramural hematoma
  - 5 Type A dissection
  - 1 Penetrating ulcer
- All ASA grade 4-5 deemed high risk for surgical repair
- 11patients treated 2013-16
  - 5 pts with IMH & Type A had 1 - 5 yr f/u
  - 5 pts with pseudoaneurysm had 1-7 yr f/u
- 2 patients treated with last 12 months

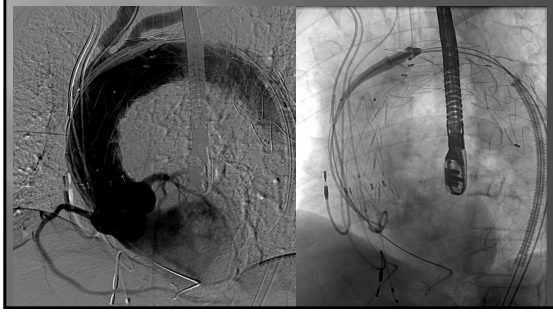
Intramural Hematoma



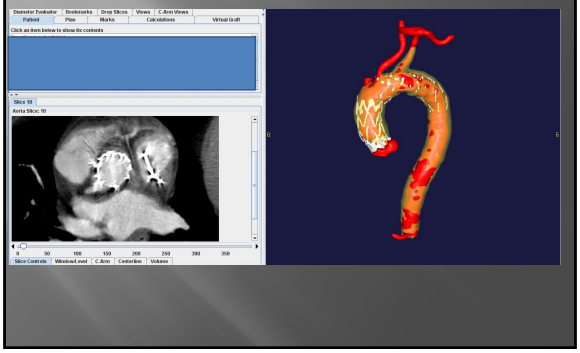




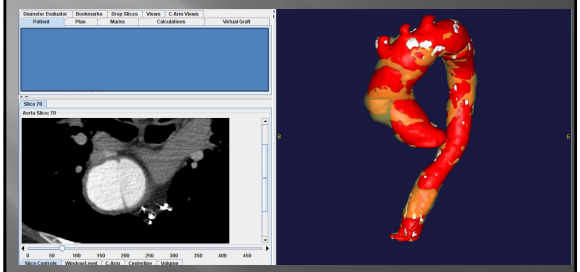
Procedural Details
Similar to TAVR procedures
Wire position, pacing, TEE & IVUS



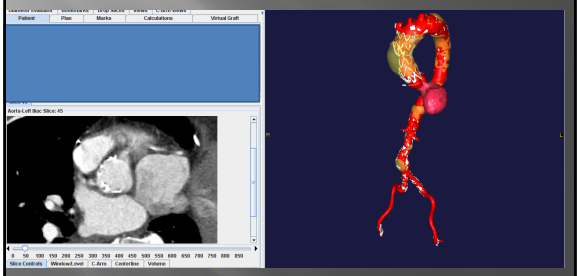
4 year Follow-up



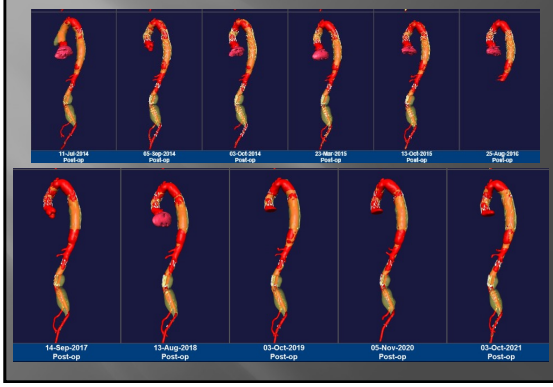
Post-surgical Pseudoaneurysm



4 yr post deployment

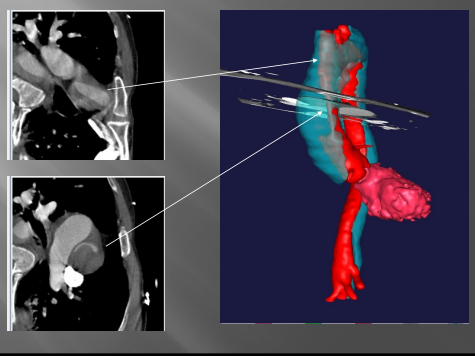


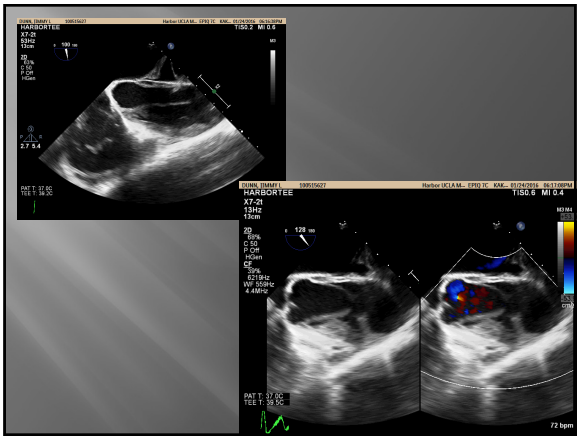
Pseudoaneurysm 7 yr Followup - Max diameter ascending aorta 44 to 40 mm



Endografts for Ascending Dissection

Ascending Dissection

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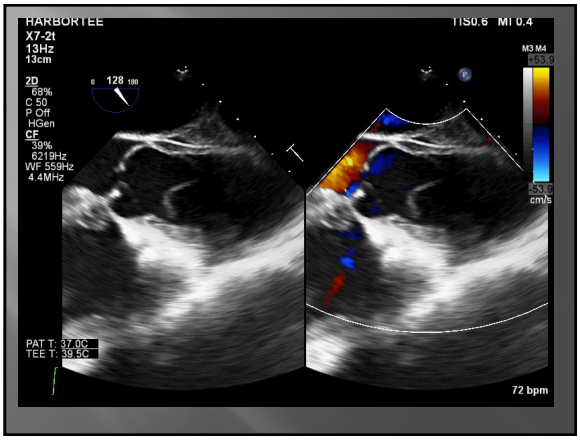
X7-2t
13Hz
13cm
TIS0.6 MI 0.4
2D
68%
C 50
P Off
HGen
CF
39%
6219Hz
WF 559Hz
4.4MHz
PAT T: 37.0C
TEE T: 39.5C
72 bpm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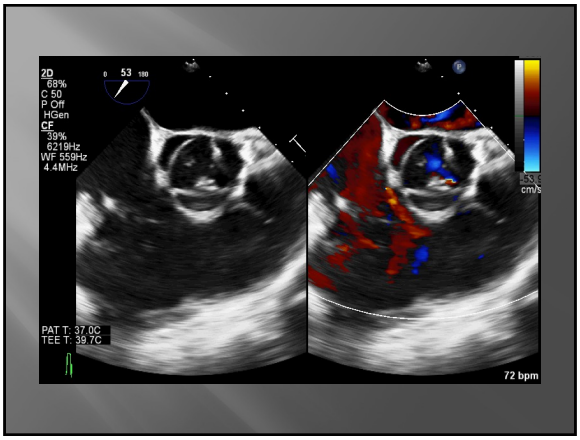
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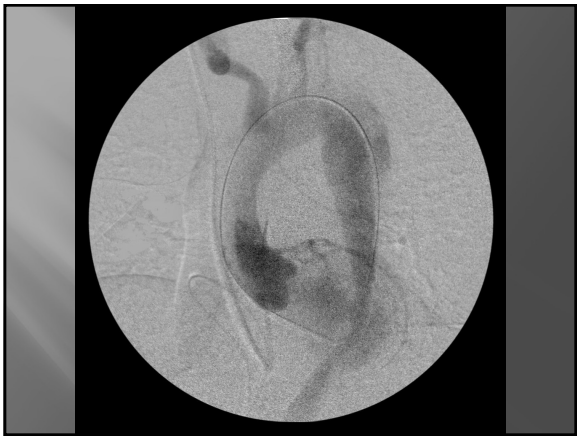

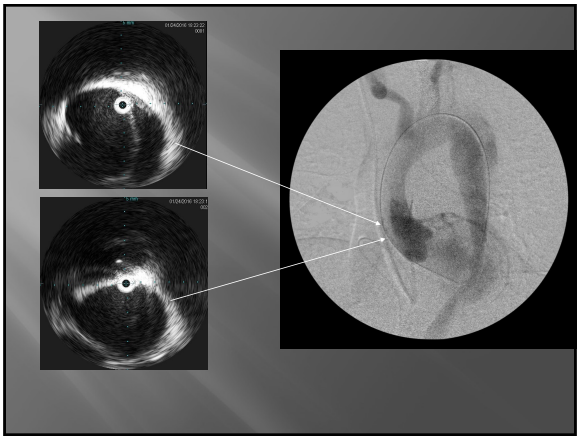

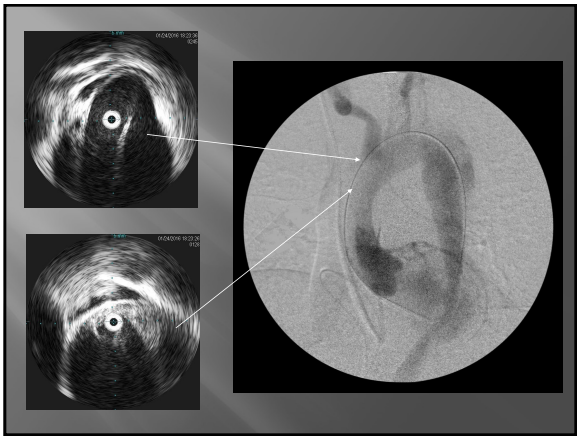

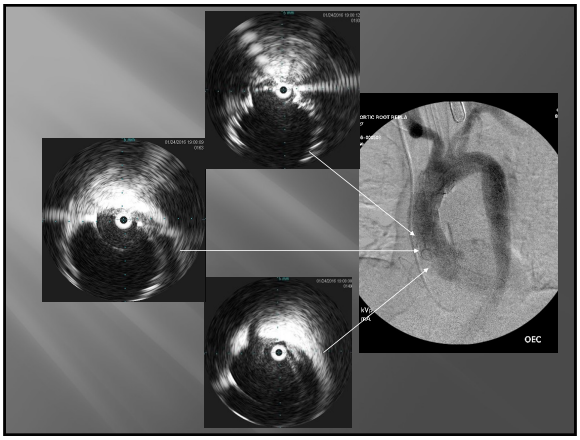
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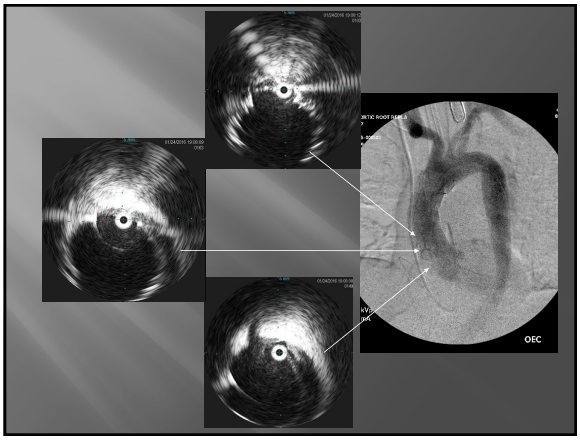
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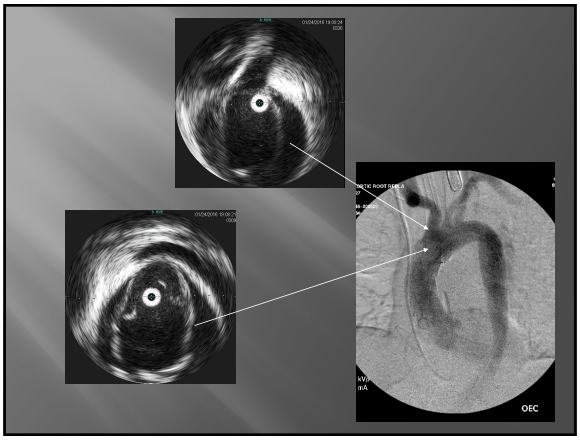
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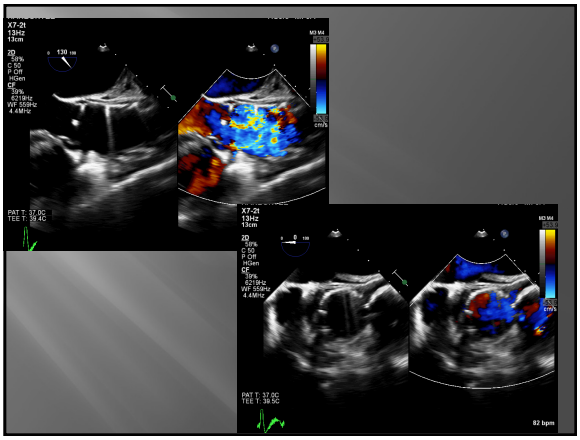
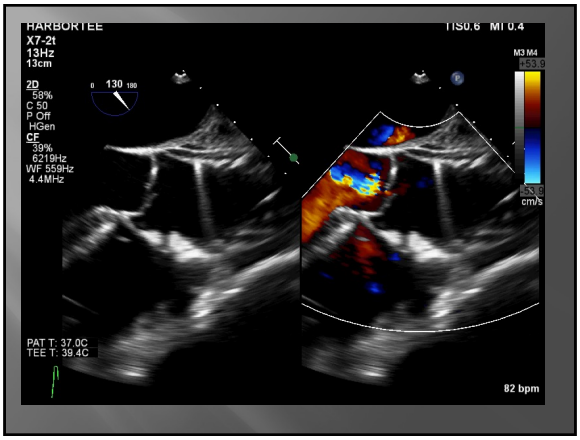

82 bpm


HARBORTEE
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6219Hz
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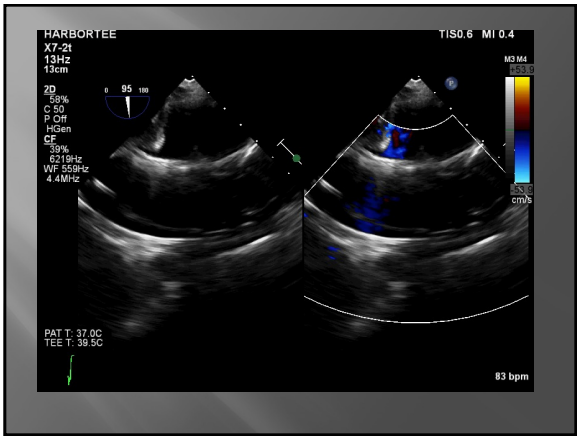
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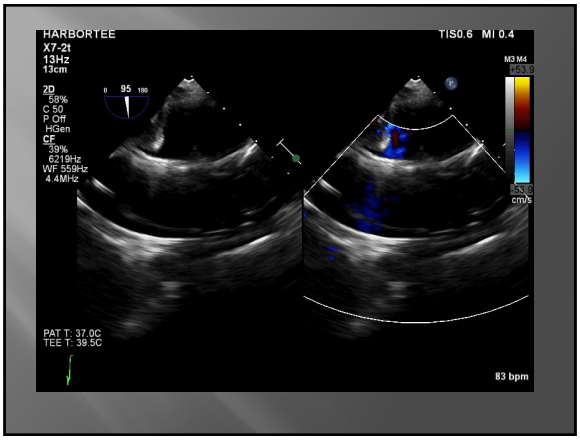
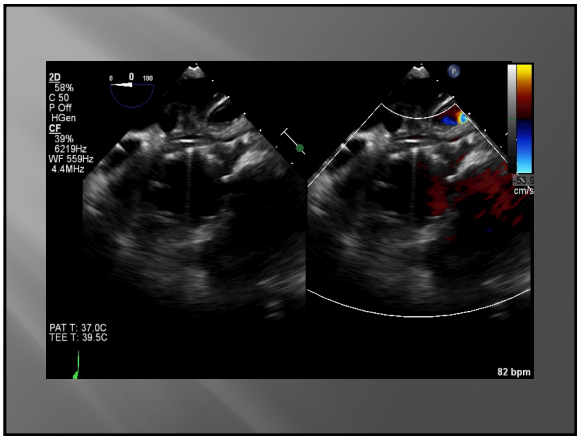
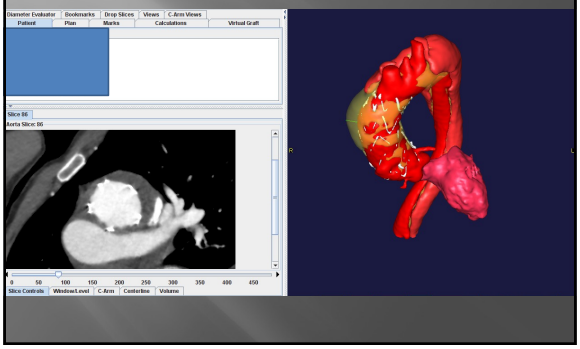
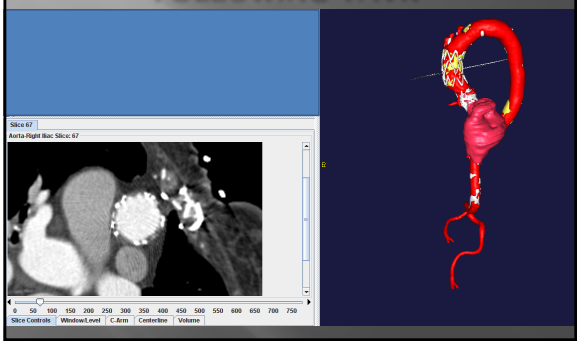


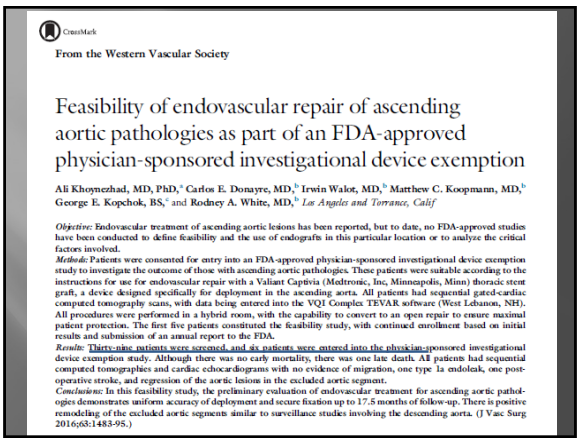


18 Month Follow-up



ASCENDING DISSECTION FOLLOWING TAVR





CrossMark

From the Western Vascular Society

Feasibility of endovascular repair of ascending aortic pathologies as part of an FDA-approved physician-sponsored investigational device exemption

Ali Khoynezhad, MD, PhD,[a] Carlos E. Donayre, MD,[b] Irwin Walot, MD,[b] Matthew C. Koopmann, MD,[b] George E. Kopchok, BS,[c] and Rodney A. White, MD,[b] *Los Angeles and Torrance, Calif*

Objective: Endovascular treatment of ascending aortic lesions has been reported, but to date, no FDA-approved studies have been conducted to define feasibility and the use of endografts in this particular location or to analyze the critical factors involved.

Methods: Patients were consented for entry into an FDA-approved physician-sponsored investigational device exemption study to investigate the outcome of those with ascending aortic pathologies. These patients were suitable according to the instructions for use for endovascular repair with a Valiant Captivia (Medtronic, Inc, Minneapolis, Minn) thoracic stent graft, a device designed specifically for deployment in the ascending aorta. All patients had sequential gated-cardiac computed tomography scans, with data being entered into the VQI Complex TEVAR software (West Lebanon, NH). All procedures were performed in a hybrid room, with the capability to convert to an open repair to ensure maximal patient protection. The first five patients constituted the feasibility study, with continued enrollment based on initial results and submission of an annual report to the FDA.

Results: Thirty-nine patients were screened, and six patients were entered into the physician-sponsored investigational device exemption study. Although there was no early mortality, there was one late death. All patients had sequential computed tomographies and cardiac echocardiograms with no evidence of migration, one type Ia endoleak, one postoperative stroke, and regression of the aortic lesions in the excluded aortic segment.

Conclusions: In this feasibility study, the preliminary evaluation of endovascular treatment for ascending aortic pathologies demonstrates uniform accuracy of deployment and secure fixation up to 17.5 months of follow-up. There is positive remodeling of the excluded aortic segments similar to surveillance studies involving the descending aorta. (J Vasc Surg 2016;63:1483-95.)

Current Status of Ascending IDES & Industry Made Grafts

- FDA is fully supportive and willing to consider Physician Sponsored Investigational Device Exemptions (PSIDE)
  - -Requires submission of a complete IDE containing all the components needed for a commercial IDE addressing specific scientific questions not intended to support commercialization of the devices
- Currently several approved PSIDEs
  - - many approvals (including commercial studies) with approval for ascending aortic dissections, some including pseudoaneurysms, penetrating ulcers or IMH

Physician Sponsored IDEs (PSIDE)

- Benefits
  - enables investigation of endografts for treatment of critical ascending aortic lesions and alows legal billing of CMS and many carriers for procedures and devices

Physician Sponsored IDEs (PSIDE)

- Challenges & Liabilities
  - Requires significant time & financial support to prepare IDE, submit for institutional IRB approval and collect data and submit annual reports. Reporting required for 5 years, and now for life of the patient with annual imaging (CTA preferred)

Recent Activity Attempt to continue patient entry

- Petitioned FDA, both IRBs and CMS to approve Valient Navion for use in PSIDE
  - 14 months to complete approvals
- Valient Navion recall required return to Valient Captivia device although only 10 cm length remained in production
- Applied to FDA to allow shortening of 10 cm Valient Captivia to provide shorter lengths for ascending aortic repairs

Attempt to Continue Patient Entry

- FDA required resubmission of revised protocol including complete testing to document fatigue and durability testing
- Final recommendation was for request for Compassionate Use Approval for potential patients and withdrawal of Amended submission
  - potential loss of reimbursement if this option is persued

IDEs For Industry Made Devices

- Very limited in US currently – WL Gore is the active Industry IDE with limited centers in Feasibility and Phase 2 ARISE Trial
  - Enrollment has been limited to chronic ascending dissections, penetrating ulcers and pseudoaneurysms

Clinical Investigation

JOURNAL OF ENDOVASCULAR THERAPY

Journal of Endovascular Therapy
[–i]
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DOI: 10.1177/15266028221095018
www.jevt.org
SAGE

ARISE: First-In-Human Evaluation of a Novel Stent Graft to Treat Ascending Aortic Dissection

Eric E. Roselli, MD[1], Marvin D. Atkins, MD[2], William Brinkman, MD[3], Joseph Coselli, MD[4], Nimesh Desai, MD[2], Anthony Estrera, MD[4], Douglas R. Johnston, MD[1], Himanshu Patel, MD[1], Ourania Preventza, MD[4], Patrick R. Vargo, MD[1], Fernando Fleischman, MD[5], Bradley S. Taylor, MD[3], and Michael J. Reardon, MD[2] On behalf of the ARISE Investigators

Abstract

Background: Operative mortality for type A aortic dissection is still 10–20% at centers of excellence. Additionally, 10–20% are not considered as viable candidates for open surgical repair and not offered life-saving emergency surgery. ARISE is a multicenter investigation evaluating the novel GORE® Ascending Stent Graft (ASG; Flagstaff, AZ). **Objective**: The purpose of this study is to assess early feasibility of using these investigational devices to treat ascending aortic dissection. **Methods**: This a prospective, multicenter, non-randomized, single-arm study that enrolls patients at high surgical risk with appropriate anatomical requirements based on computed tomography imaging at 7 of 9 US sites. Devices are delivered transfemorally under fluoroscopic guidance. Primary endpoint is all-cause mortality at 30 days. Secondary endpoints include major adverse cardiovascular and cerebrovascular events (MACCE) at 30 days, 6 months, and 12 months. **Results**: Nineteen patients were enrolled with a mean age of 75.7 years (range 47–91) and 11 (57.9%) were female. Ten (52.6%) had DeBakey type I disease, and the rest were type II. Sixteen (84.2%) of the patients were acute. Patients were treated with safe access, (7/19 (36.8%) percutaneous, 10/19 (52.6%) transfemoral, 2/19 (10.5%) iliac conduit), delivery, and deployment completed in all cases. Median procedure time was 154 mins (range 52–392) and median contrast used was 111 mL (range 75–200). MACCE at 30 days occurred in 5 patients including mortality 3/19 (15.8%), disabling stroke in 1/19 (5.3%), and myocardial infarction in 1/19 (5.3%). **Conclusion**: Results from the ARISE early feasibility study of a specific ascending stent graft device to treat ascending aortic dissection are promising.

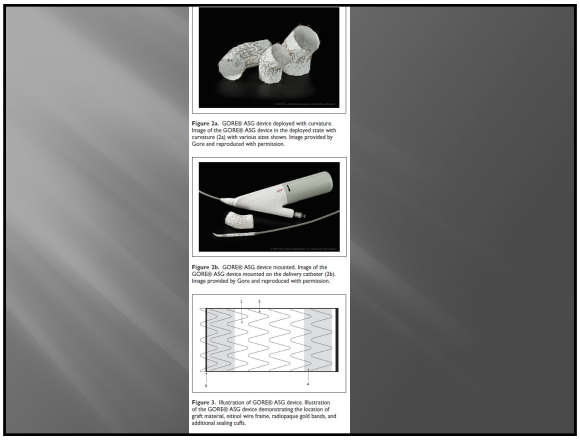


Figure 2a. GORE® ASG device deployed with curvature. Image of the GORE® ASG device in the deployed state with curvature (2a) with various sizes shown. Image provided by Gore and reproduced with permission.

Figure 2b. GORE® ASG device mounted. Image of the GORE® ASG device mounted on the delivery catheter (2b). Image provided by Gore and reproduced with permission.

Figure 3. Illustration of GORE® ASG device. Illustration of the GORE® ASG device demonstrating the location of graft material, nitinol wire frame, radiopaque gold bands, and additional sealing cuffs.

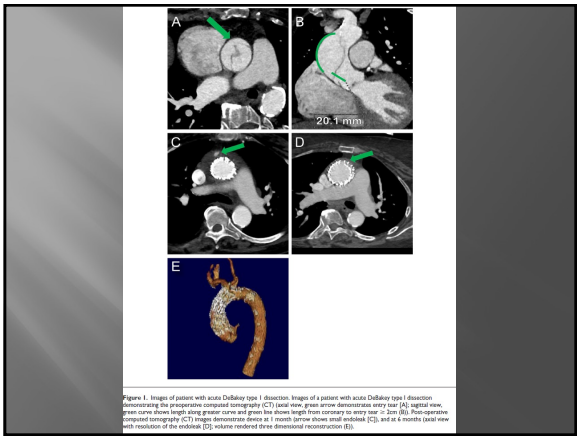
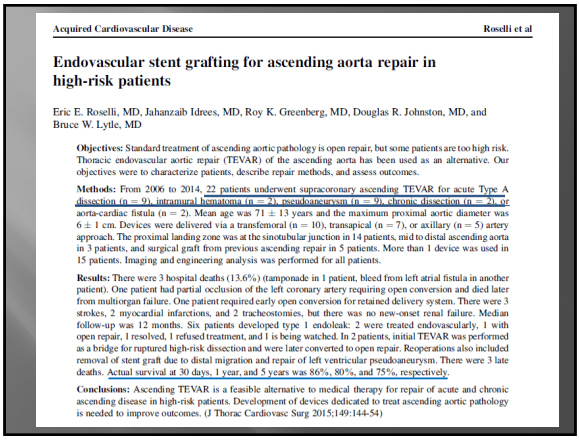


Figure 1. Images of patient with acute DeBakey type I dissection. Images of a patient with acute DeBakey type I dissection demonstrating the preoperative computed tomography (CT) (axial view, green arrow demonstrates entry tear [A]; sagittal view, green curve shows length along greater curve and green line shows length from coronary to entry tear = 2cm (B)). Post-operative computed tomography (CT) images demonstrate device at 1 month (arrow shows small endoleak [C]), and at 6 months (axial view with resolution of the endoleak [D]; volume rendered three dimensional reconstruction (E)).



Endovascular stent grafting for ascending aorta repair in high-risk patients

Eric E. Roselli, MD, Jahanzaib Idrees, MD, Roy K. Greenberg, MD, Douglas R. Johnston, MD, and Bruce W. Lytle, MD

Objectives: Standard treatment of ascending aortic pathology is open repair, but some patients are too high risk. Thoracic endovascular aortic repair (TEVAR) of the ascending aorta has been used as an alternative. Our objectives were to characterize patients, describe repair methods, and assess outcomes.

Methods: From 2006 to 2014, 22 patients underwent supracoronary ascending TEVAR for acute Type A dissection (n = 9), intramural hematoma (n = 2), pseudoaneurysm (n = 9), chronic dissection (n = 2), or aorta-cardiac fistula (n = 2). Mean age was 71 ± 13 years and the maximum proximal aortic diameter was 6 ± 1 cm. Devices were delivered via a transfemoral (n = 10), transapical (n = 7), or axillary (n = 5) artery approach. The proximal landing zone was at the sinotubular junction in 14 patients, mid to distal ascending aorta in 3 patients, and surgical graft from previous ascending repair in 5 patients. More than 1 device was used in 15 patients. Imaging and engineering analysis was performed for all patients.

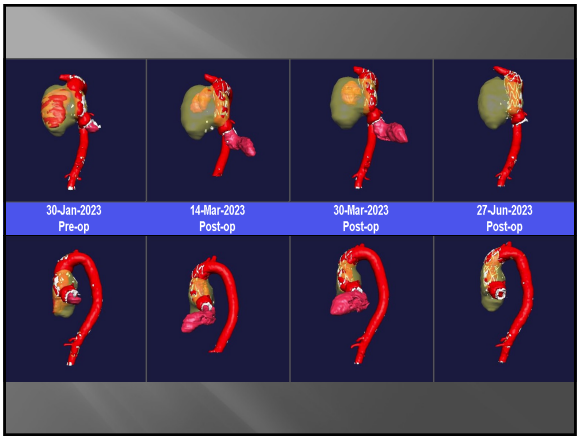
Results: There were 3 hospital deaths (13.6%) (tamponade in 1 patient, bleed from left atrial fistula in another patient). One patient had partial occlusion of the left coronary artery requiring open conversion and died later from multiorgan failure. One patient required early open conversion for retained delivery system. There were 3 strokes, 2 myocardial infarctions, and 2 tracheostomies, but there was no new-onset renal failure. Median follow-up was 12 months. Six patients developed type 1 endoleak: 2 were treated endovascularly, 1 with open repair, 1 resolved, 1 refused treatment, and 1 is being watched. In 2 patients, initial TEVAR was performed as a bridge for ruptured high-risk dissection and were later converted to open repair. Reoperations also included removal of stent graft due to distal migration and repair of left ventricular pseudoaneurysm. There were 3 late deaths. Actual survival at 30 days, 1 year, and 5 years was 86%, 80%, and 75%, respectively.

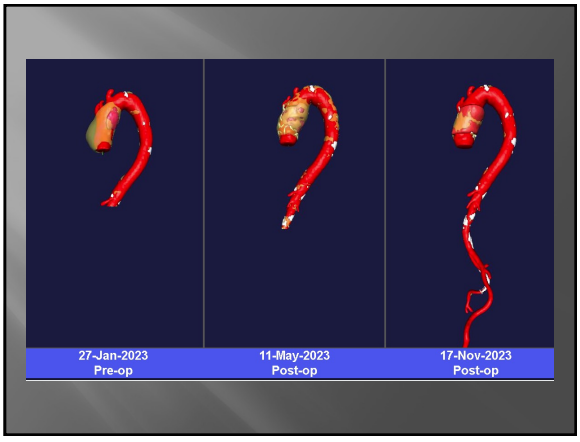
Conclusions: Ascending TEVAR is a feasible alternative to medical therapy for repair of acute and chronic ascending disease in high-risk patients. Development of devices dedicated to treat ascending aortic pathology is needed to improve outcomes. (J Thorac Cardiovasc Surg 2015;149:144-54)

Recent Cases

- 1 Ascending dissection
- 1 aortic pseudoaneurysm
- Procedures performed using either modified current Medtronic Thoracic device or 10 cm device without modification

Emphasizes Successes & Challenges of Ascending AorticEndografts



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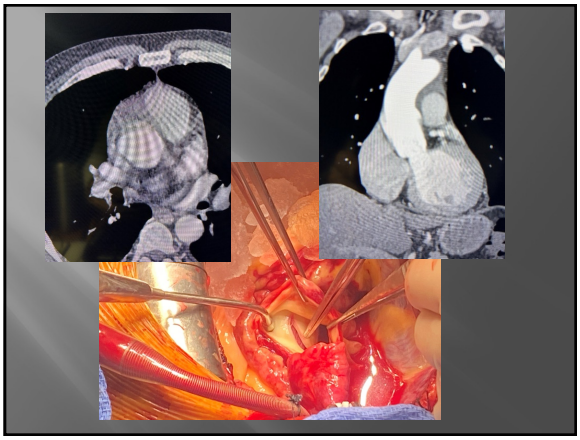

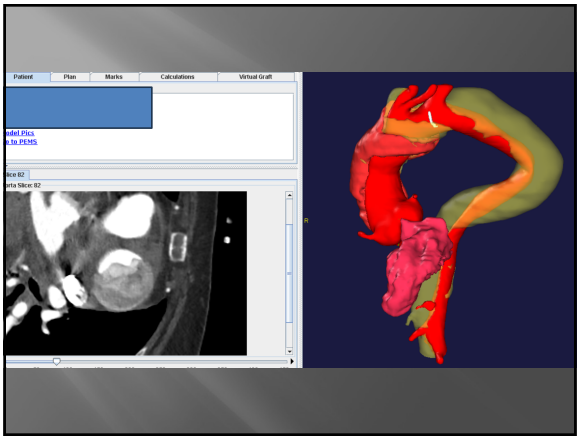
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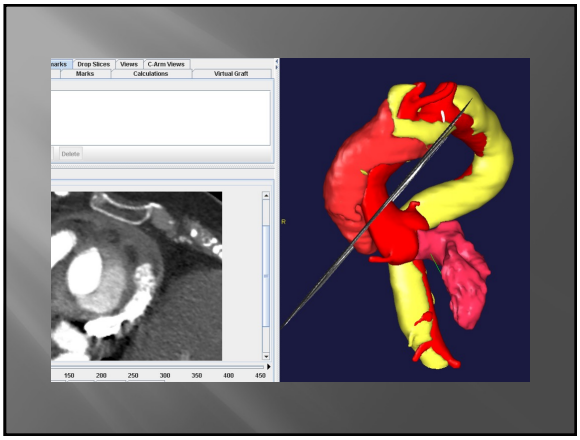
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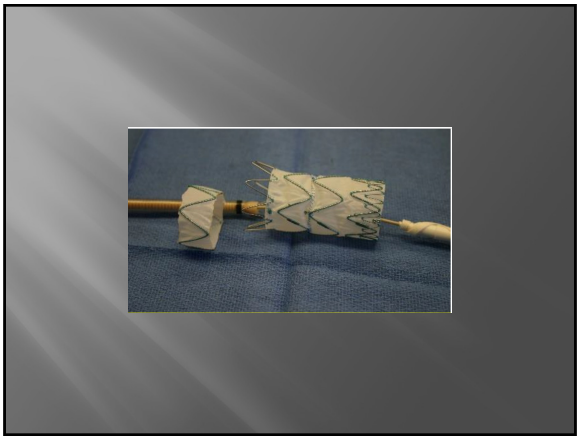

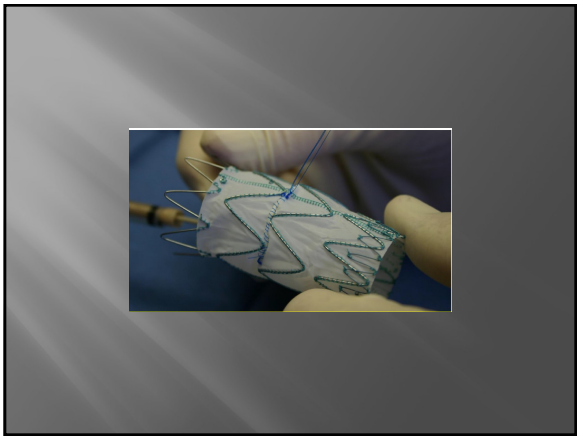

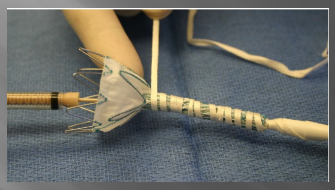

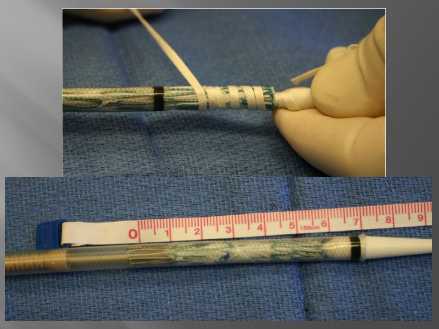

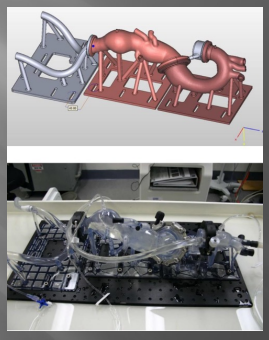

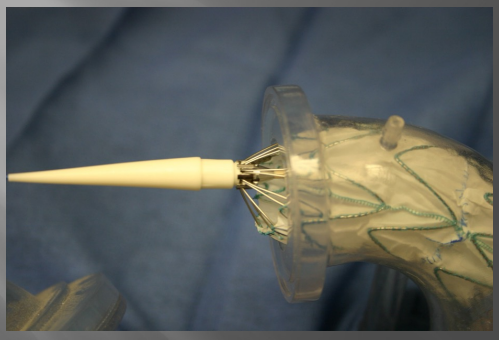

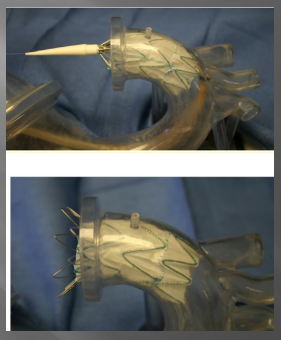

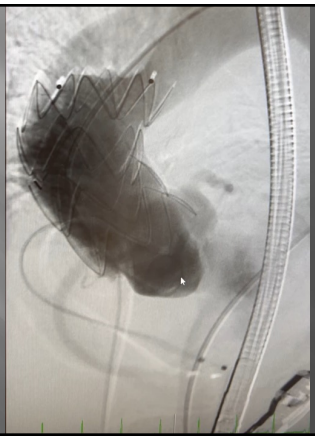

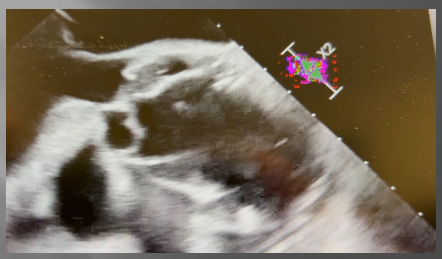

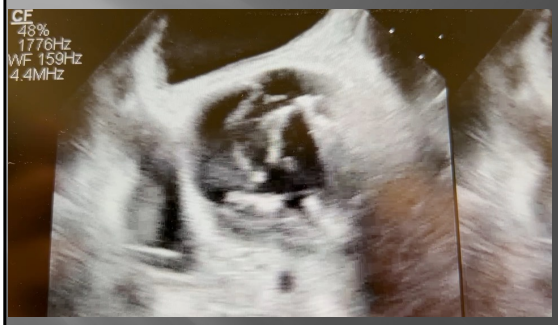

Next Steps

- Pause and assess cardiac status

- If stable, stop and see if trapped valve will release

- If aortic insufficiency not tolerated

  *reposition device with gentle balloon traction

  *evaluate for TAVR valve implant

*** Most important, pause and evaluate all possible options

Lessons Learned (for N th time)

- Stop when intended life-saving intervention completed unless additional interventions mandated to save the patient
- Live to fight a 2nd day – perfect result not required
- When something unintended occurs, stop and discuss alternatives – weigh risks of each and only proceed unless something else is required to save the patient

Conclusions

- Preliminary evaluation of modified Valient thoraicic endografts for "tubular" ascending aortic lesions including ascending dissections demonstrates:
  - accurate deployment
  - secure fixation
  - no migration
- Tortuous ascending aorta can lead to underestimation of length required for complete coverage of outer wall – transapical approach is an alternative for "horizontal heart" configurations

New Updates on Ascending Aortic Endografts

- 4-7 yr stability and healing for tubular ascending pathologies
  -pseudoaneurysms, penetrating ulcers, dissections, etc (aneurysms not evaluated)
- Several centers demonstrating feasibility for ascending aortic endografts repairs
- Slow commercial development with labor intensive PSIDEs being the only option