

Update on Use of the Atrium Advanta V12LD Balloon Expandable Covered Stent for Treatment of Coarctation: from the OUS - Coarc trial

Elchanan Bruckheimer, MBBS.

**Director, Cardiac Catheterization, Section of Pediatric Cardiology,
Schneider Children's Medical Center - Israel, Petach Tikva, Israel.**

Potential conflicts of interest

Speaker's name: Elchanan Bruckheimer

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

- ☐ Research contracts
 - ✓ Consulting (Atrium Medical Corp)
 - ☐ Employment in industry
 - ☐ Stockholder of a healthcare company
 - ☐ Owner of a healthcare company
 - ☐ Other(s)
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Coarctation of the Aorta: Covered stent, bare stent or surgery?

- “There are known knowns; there are things we know that we know.

There are known unknowns; that is to say there are things that, we now know we don't know.

But there are also unknown unknowns – there are things we do not know we don't know.”

[Donald Rumsfeld, US Secretary of Defense on February 12, 2002]



- Limited knowledge
 - no **prospective** randomized controlled trials comparing surgery to stent [covered or bare] for treatment of native or recurrent coarctation.
-

What we do know...

- **Surgical repair is effective with low procedural mortality and morbidity**
 - **Stent implantation is effective with very low procedural mortality and low morbidity**
 - **Both methods are complicated long term by hypertension, reintervention for stenosis and aneurysm formation.**
-

Coarctation-Associated Aneurysms: A Localized Disease or Diffuse Aortopathy

Ourania Preventza, MD, James J. Livesay, MD, Denton A. Cooley, MD, Zvonimir Krajcer, MD, Benjamin Y. Cheong, MD, and Joseph S. Coselli, MD

Departments of Cardiovascular Surgery, Cardiology, and Radiology, The Texas Heart Institute at St. Luke's Episcopal Hospital/Baylor College of Medicine, Houston, Texas

Background. We evaluated the occurrence and treat- Eleven patients underwent endovascular repair (20.8%).

- 943 cases of coarctations repaired - aortic aneurysms were identified in 55 patients (5.8%) - forty-eight had undergone prior coarctation repair
- “....coarctation of the aorta is associated with subsequent aneurysm formation at the site of the previous coarctation repair and in contiguous and remote segments of the aorta and branch arteries.”

Adult Congenital Disease

Risk Factors for Aortic Complications in Adults With Coarctation of the Aorta

Jose Maria Oliver, MD,* Pastora Gallego, MD,‡ Ana Gonzalez, MD,* Angel Aroca, MD,*
Montserrat Bret, MD,† Jose Maria Mesa, MD*

Madrid and Sevilla, Spain

- In 235 patients [181 surgery, 28 transcatheter, 26 unrepaired – 44 aortic wall complications were found in 37 patients (16%)
- “...Severe aortic complications are prevalent in adults with repaired or non-repaired coarctation of the aorta. Intrinsic abnormalities of the aortic wall beyond that attributable to associated hemodynamic derangement or previous repair might be responsible for aortic complications...”

Original Studies

Procedural Results and Acute Complications in Stenting Native and Recurrent Coarctation of the Aorta in Patients Over 4 Years of Age: A Multi-Institutional Study

- 565 procedures of stent implantation performed in 555 patients with coarctation between 1989 and 2005 of which 553 (97.9%) were successful in reducing the gradient to less than 20 mm Hg
- 14.3% acute complications [0.3% mortality]
- 3.9% acute aortic wall complications included intimal tears, dissection, and aneurysm formation

PEDIATRIC AND CONGENITAL HEART DISEASE

Original Studies

Intermediate Follow-Up Following Intravascular Stenting for Treatment of Coarctation of the Aorta

- Thompson, ⁴ MD,
Shakeel, ⁹ MD,
Satin, ¹² MD,
Johnson, ¹ MD,
- 144/578 [24.9%] patients follow-up imaging [CT, MRI or aortography]
 - 18/144 [12.5%] patients had an aneurysm or developed a dissection /intimal tear. Most aneurysms were small and were managed conservatively although four patients required further intervention such as the implantation of a covered CP stent.

Balloon expandable stent implantation for native and recurrent coarctation of the aorta—prospective computed tomography assessment of stent integrity,

- 88 patients with coarctation
- 102 stent procedures
- four acute complications [3.7%] two [1.9%] aortic wall related.
- A follow up CT was performed on 95.9% of the patients of whom only one developed an aneurysm associated with redilation of a stent that had fractured. This was successfully treated with a covered stent.

Martin

Chakrabarti vs CCISC

- Similar percentages of native coarctations in their series
- Used the same definition for aneurysm formation.
- The differences in the rates of aneurysm formation between the groups
 - the small percentage of the CCISC cohort that underwent follow-up imaging
 - observation that can be made is that in the CCISC group 14/511 only [2.7%] stents implanted were covered as opposed to 26/94 [27.7%] of the stents used in Chakrabarti's series.

Large Diameter iCAST™/Advanta™ V12 Covered Stent Trial for Coarctation of the Aorta [CoArc]



CoArc: Objective

- **To evaluate the safety and efficacy of the Large Diameter Advanta™ V12 Covered Stent for treatment of native and recurrent coarctation of the aorta in selected children, adolescents, and adults.**
-

CoArc: Trial Design

| | |
|--------------------------------------|--|
| <i>Design:</i> | Prospective, Multicenter, Non-Randomized, Single Arm |
| <i>Population:</i> | Eligible patients, children and adults, with a diagnosis of native or recurrent coarctation of the aorta |
| <i>Sample Size:</i> | 70 subjects |
| <i>Investigational Sites:</i> | 9 sites in 7 Countries (Australia, Brazil, Canada, Germany, Israel, Italy, & UK) |
| <i>Enrollment:</i> | First patient enrolled: 30-Sep-09 Last patient enrolled: 23-Mar-12 |
| <i>Clinical F/U Visits:</i> | 30-day, 6, 12 (Primary Endpoint), 24, 36, 48, & 60 mo |

CoArc: Primary Endpoints

Primary Efficacy Endpoint:

- **A significant reduction in the gradient across the coarctation**
 - **Pre stent vs. immediately post stent & pre stent vs. 12 month follow-up**
 - **DV (diastolic velocity in cm/sec) and DV/SV (diastolic velocity /systolic velocity ratio) measured**

Primary Safety Endpoint:

- **The safety endpoint will include the evaluation of adverse events and complications occurring within 30 days of the procedure:**
 - **Major adverse vascular events (MAVE)**
 - **Major adverse events (MAE)**
-

CoArc: Secondary Endpoints

Secondary Endpoint:

- The secondary efficacy endpoint : An increase in the diameter of the (CoA) after stent placement such that the diameter of the coarctation will be $\geq 80\%$ of diameter of the transverse arch immediately distal to the left subclavian artery [isthmus] ($\text{CoA:DAo} \geq 0.8$) after the stenting procedure and maintain this increased diameter over a 12 month period.

Outcome Assessments:

- Device success, defined as the successful delivery and deployment of the study stent and intact retrieval of the delivery system
 - No post procedural (12 month) stent migration
 - MAE and MAVE at 12 months
-

CoArc: Site Information

| Site Ranking | | | | |
|--------------------------------|---------------------|------------------|---|-------------------|
| | <i>Investigator</i> | <i>Country</i> | <i>Institution</i> | <i>Enrollment</i> |
| 1 | <i>Pedra</i> | <i>Brazil</i> | <i>Instituto Dante Pazzanese de Cardiologia Paulo, Brazil</i> | 18 |
| 2 | <i>Butera</i> | <i>Italy</i> | <i>San Donato Hospital Milan, Italy</i> | 10 |
| 3 | <i>Birk</i> | <i>Israel</i> | <i>Schneider Children's Medical Centre Israel Petach Tikva, Israel</i> | 10 |
| 4 | <i>Benson</i> | <i>Canada</i> | <i>Hospital for Sick Children Toronto, Canada</i> | 9 |
| 5 | <i>Ewert</i> | <i>Germany</i> | <i>Dept. of Congenital Heart Diseases - Heart Institute Berlin, Germany</i> | 9 |
| 6 | <i>Martin</i> | <i>UK</i> | <i>Bristol Royal Hospital for Children Bristol, UK</i> | 6 |
| 7 | <i>Roberts</i> | <i>Australia</i> | <i>The Children's Hospital at Westmead Sydney, Australia</i> | 4 |
| 8 | <i>Schneider</i> | <i>Germany</i> | <i>Asklepios Klinik - Sankt Augustin Sankt Augustin, Germany</i> | 2 |
| 9 | <i>Sievert</i> | <i>Germany</i> | <i>CardioVascular Center Frankfurt, Germany</i> | 2 |
| Total Subjects Enrolled | | | | 70 |

CoArc Advanta V12LD Trial

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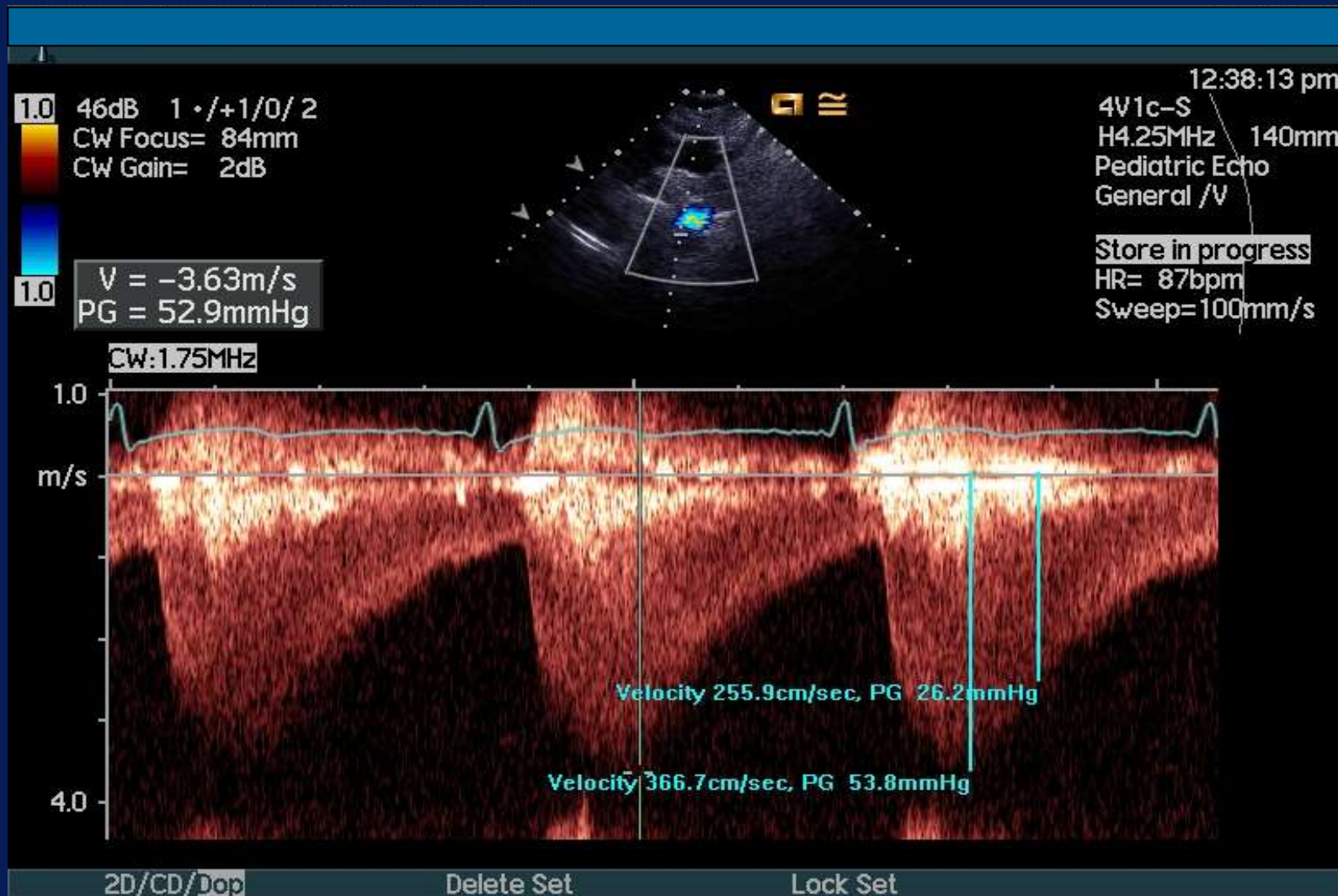
Cardiac Ultrasound

Doppler Echocardiographic Profile and Indexes in the Evaluation of Aortic Coarctation in Patients Before and After Stenting

Ju-Le Tan, MBBS, MRCP,*‡ Sonya V. Babu-Narayan, MBBS, MRCP,* Michael Y. Henein, MD, PhD,†
Michael Mullen, MD, MRCP,* Wei Li, MD, PhD*†

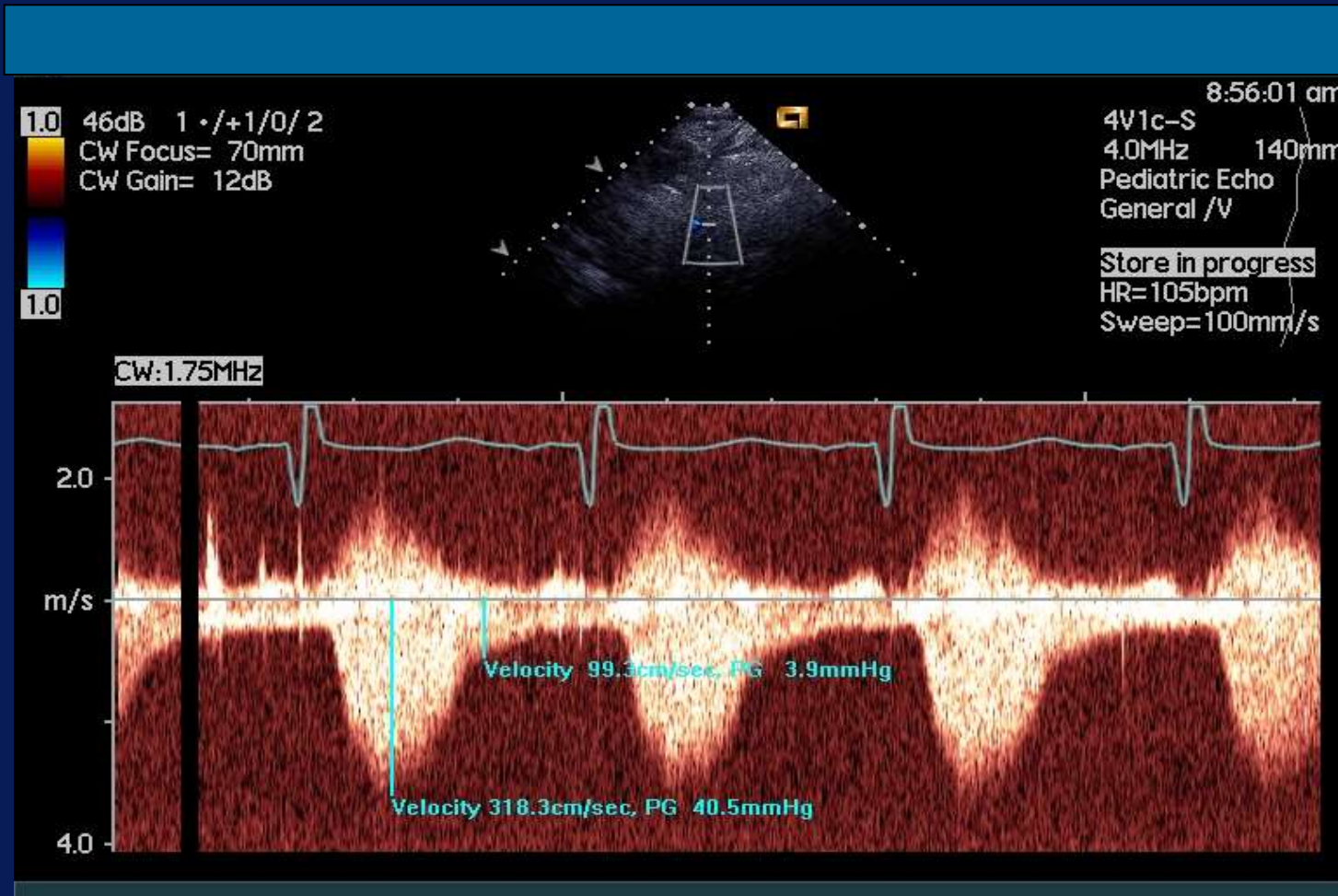
London, United Kingdom; and Singapore

10yr old male – severe native coarctation



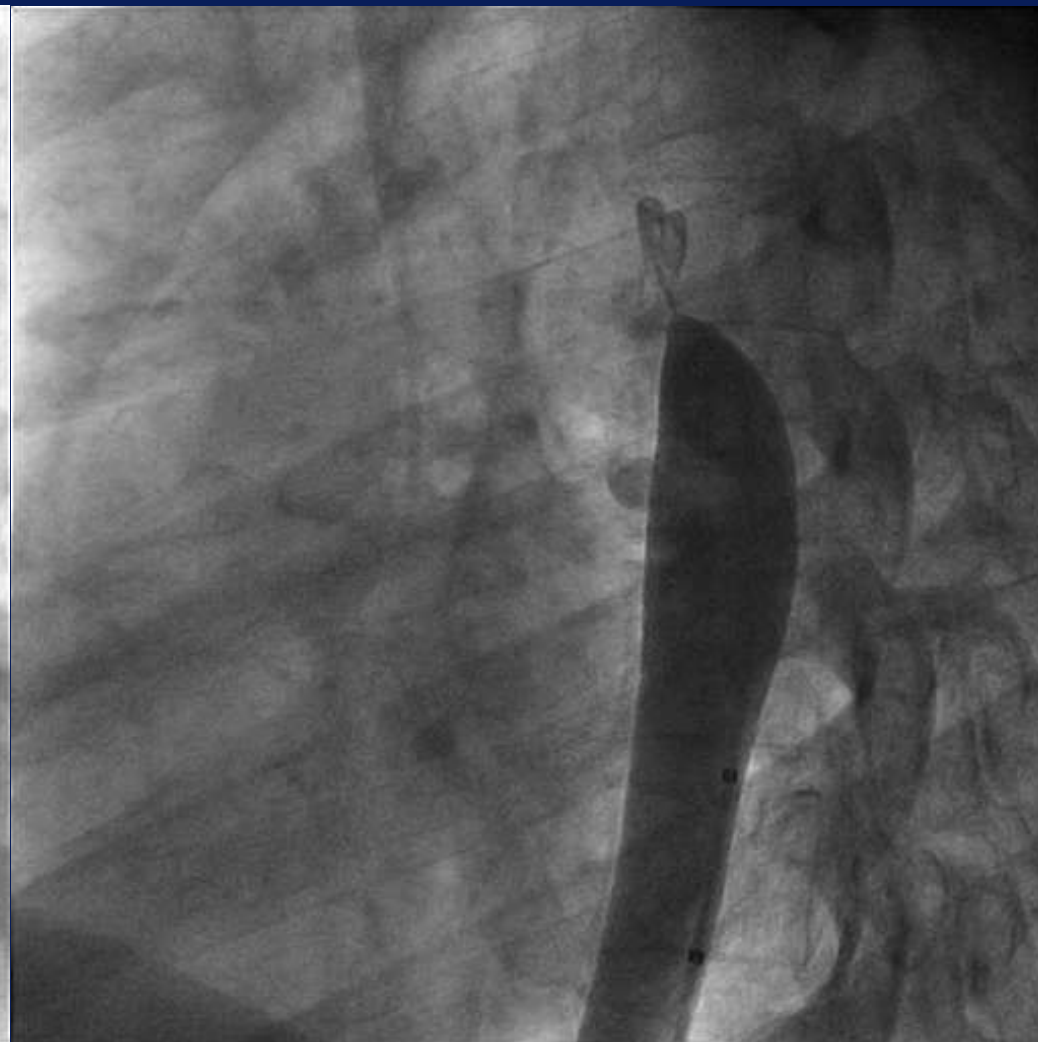
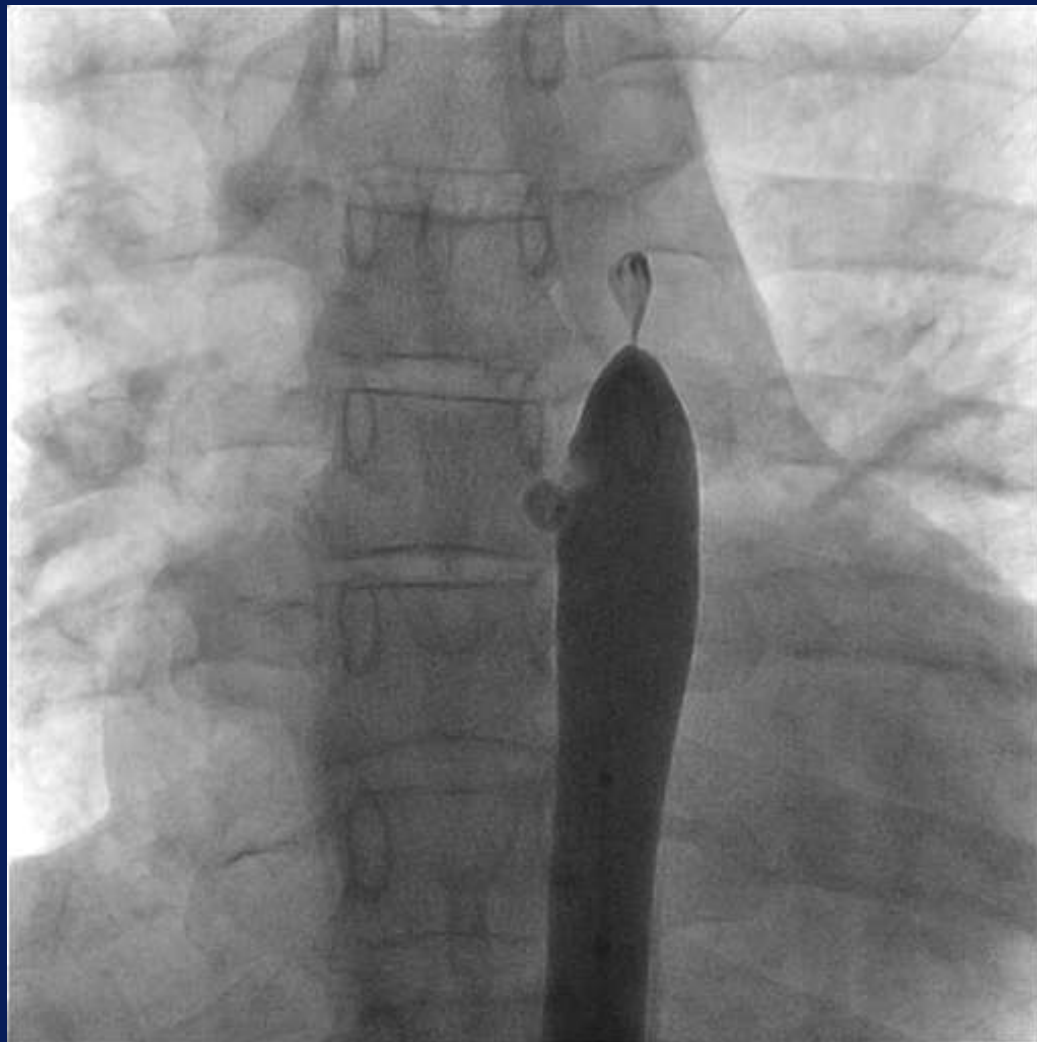
CW Doppler Thoracic aorta Diastolic tail DV/SV = 256/367 [0.70]

**10 yr old male – severe native coarctation
treated with Advanta V12LD dilated to 14mm**

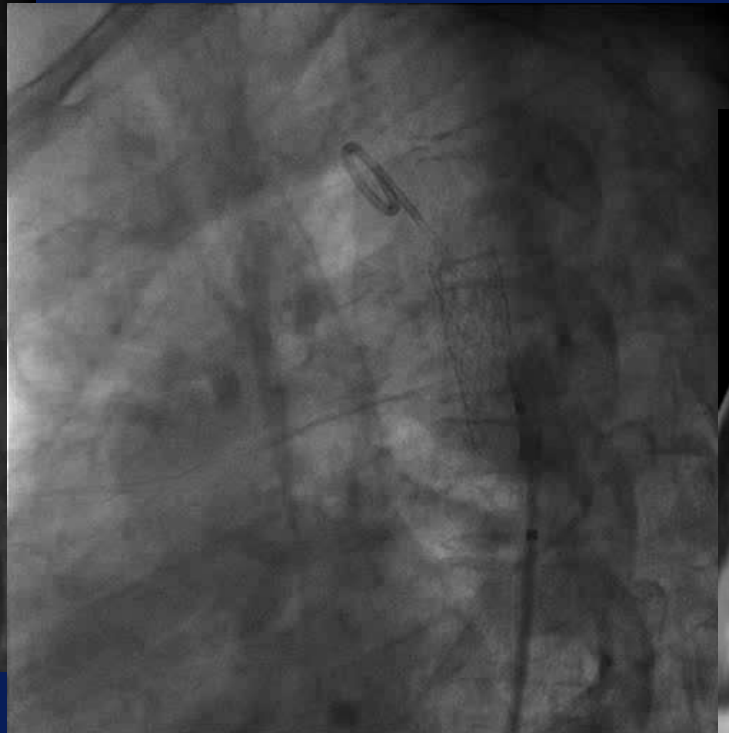
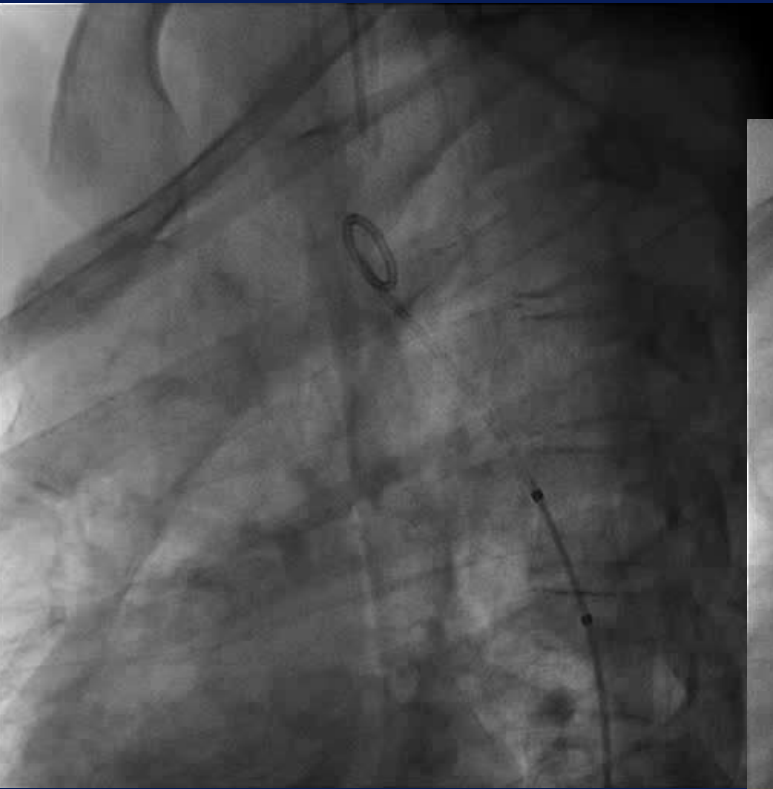


CW Doppler Thoracic aorta Minimal diastolic tail DV/SV = 99/318 [0.31]

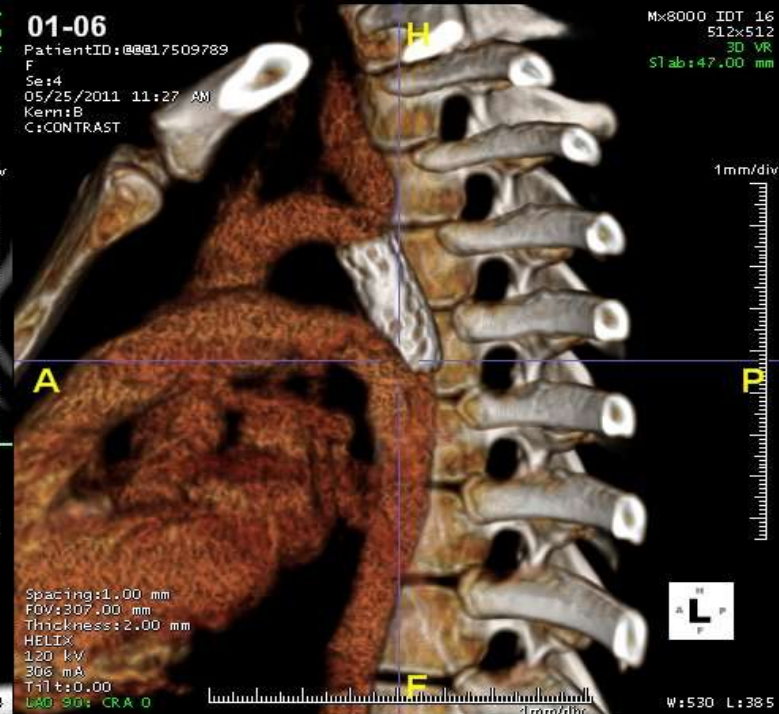
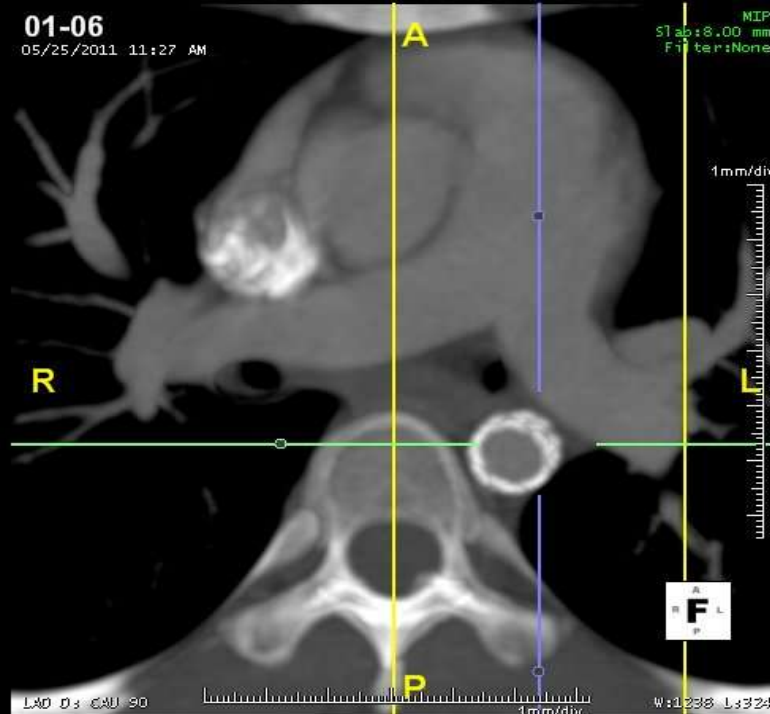
24 yr old male – severe native coarctation



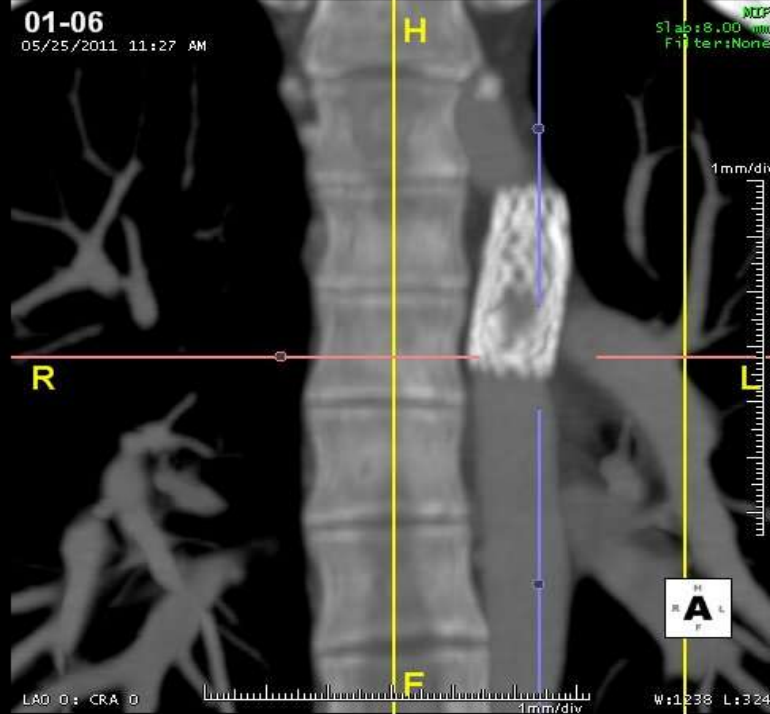
**Treated with Advanta V12LD dilated to 12mm
- post dilated to 16mm 3 months later**

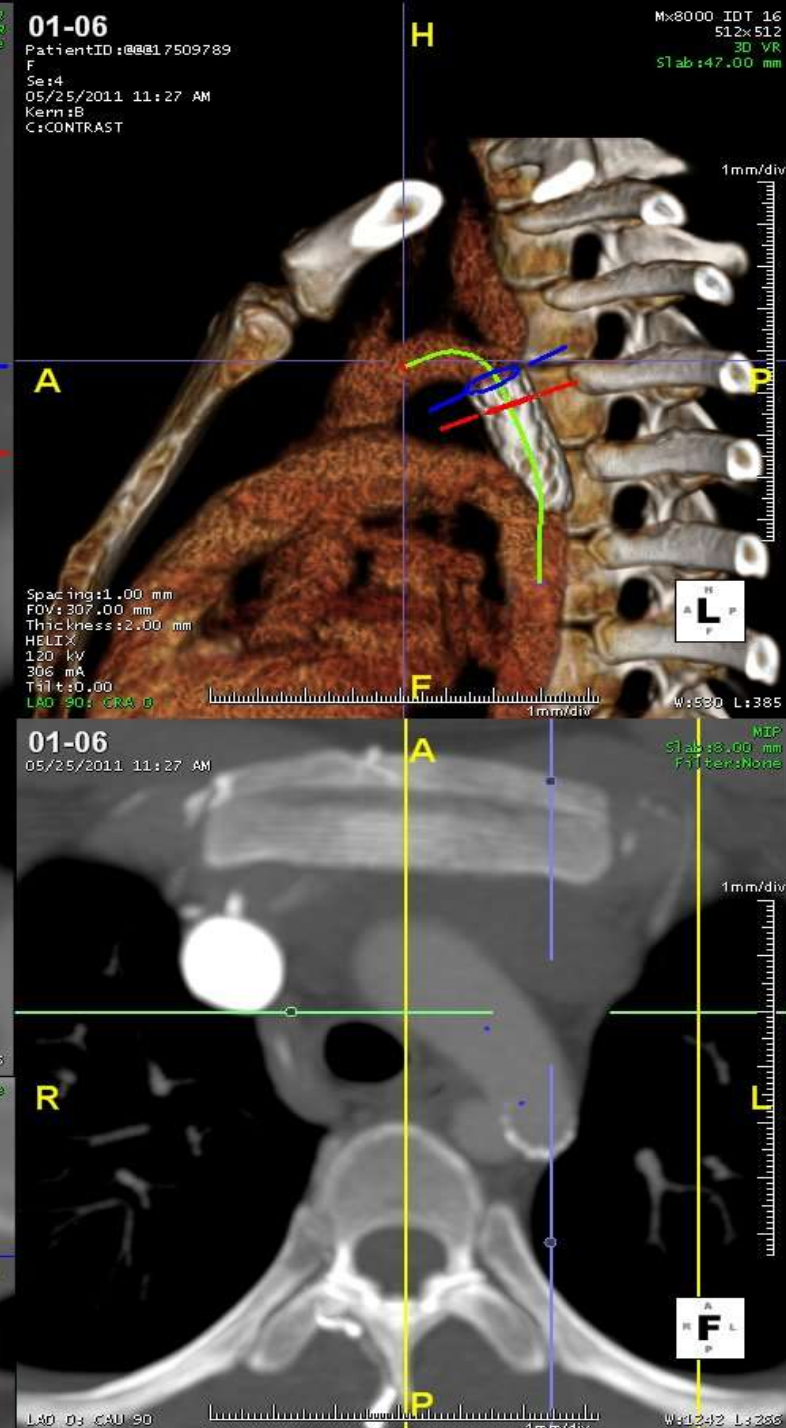
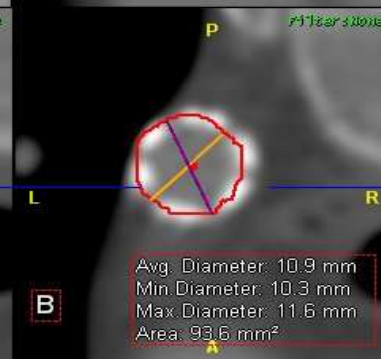
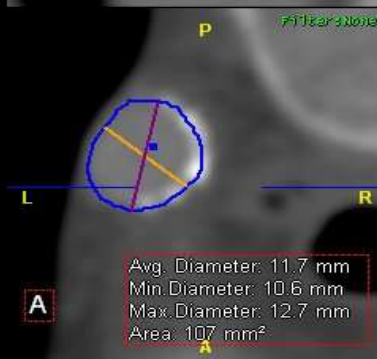
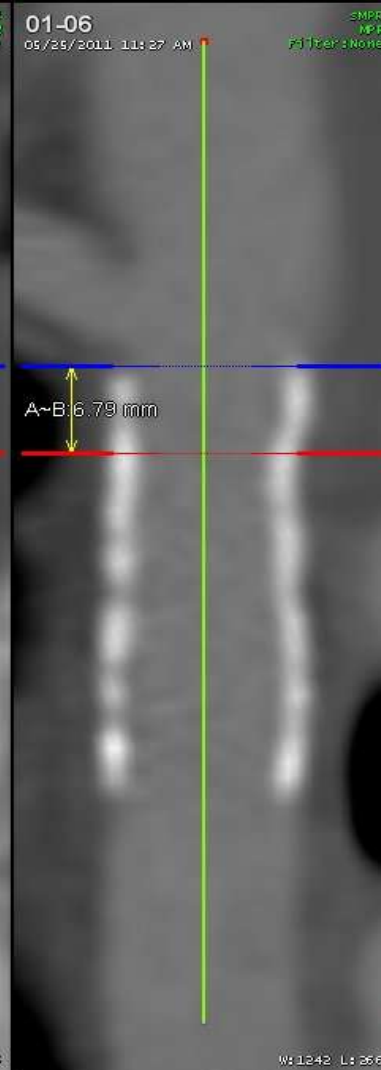
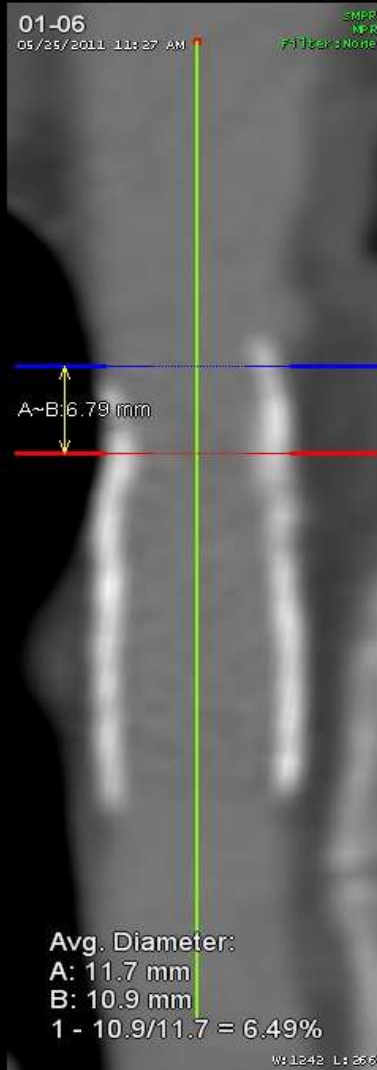


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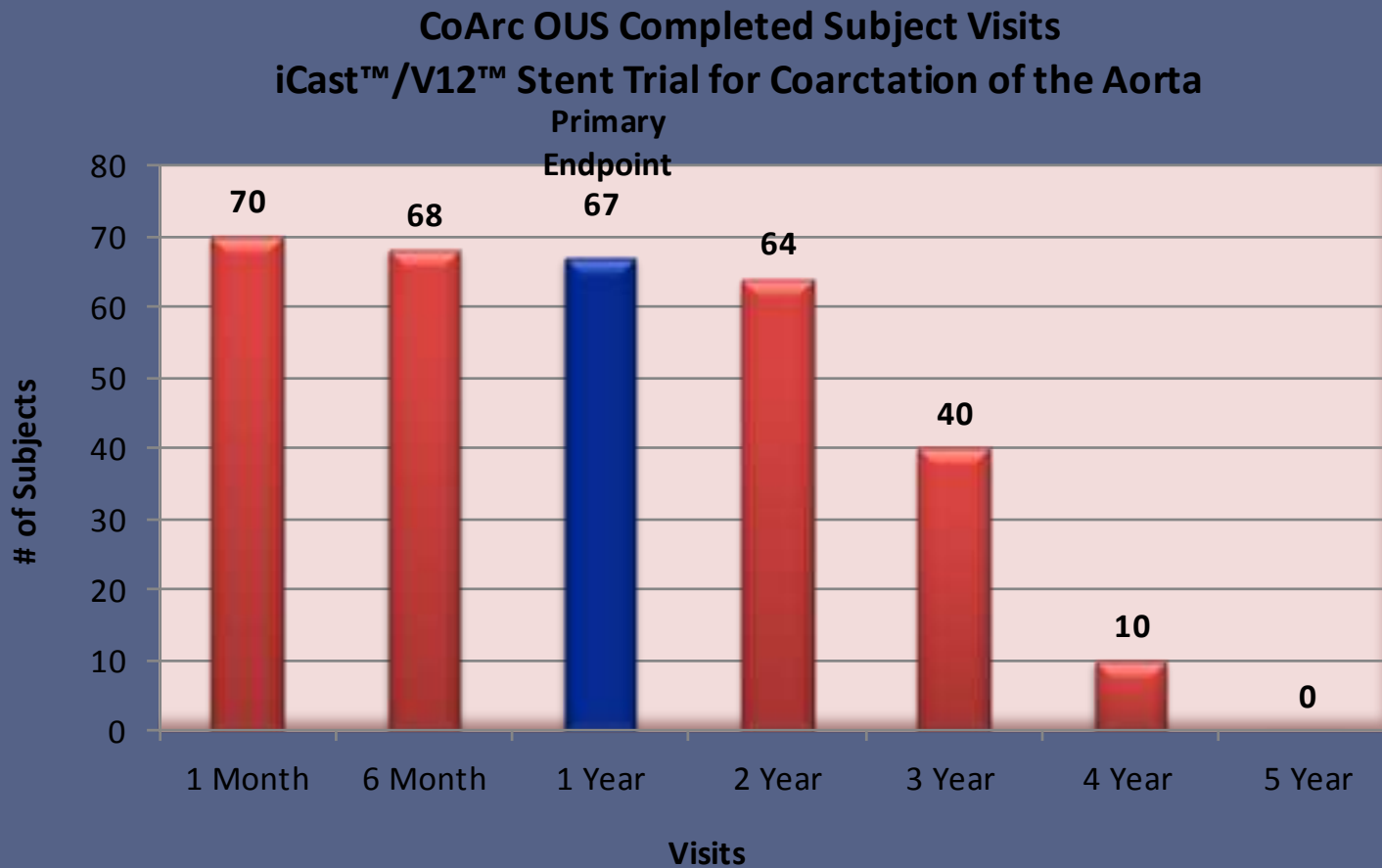


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CoArc: Subject Follow-up



70 Subjects Enrolled

3 Subjects Withdrew Consent & 2 Lost to Follow-up

Updated

24-04-14

CoArc: Subject Demographics

Demographics for the first 35 subjects to reach the primary endpoint:

| Characteristic | Parameter | Values for Patients (N=35) |
|--|----------------------------|----------------------------|
| Age | median [IQR] | 17.0 [13.0, 35.0] |
| | mean \pm SD | 23.9 \pm 16.3 (35) |
| | Min, Max | (7.0,75.0) |
| Sex | Male, n (%) | 65.7% (23/35) |
| | Female, n (%) | 34.3% (12/35) |
| Weight (kg) | median [IQR] | 57.8 [47.0, 73.0] |
| | mean \pm SD | 59.8 \pm 19.7 (35) |
| | Min, Max | (28.2,115.4) |
| Height (cm) | median [IQR] | 164.0 [151.0, 173.0] |
| | mean \pm SD | 160.9 \pm 14.1 (35) |
| | Min, Max | (127.0,180.0) |
| Time Since Coarctation Diagnosis (months) to Index Procedure | median [IQR] | 10.0 [3.0, 46.0] |
| | mean \pm SD | 53.9 \pm 110.6 (35) |
| | Min, Max | (0.0,486.0) |
| Previous Treatment to the Coarctation | Any, n (%) | 14.3% (5/35) |
| | Surgery, n (%) | 8.6% (3/35) |
| | Balloon Angioplasty, n (%) | 5.7% (2/35) |
| IQR = interquartile range; SD = standard deviation; Min = minimum; Max = maximum | | |

CoArc: Doppler Core Lab Measures

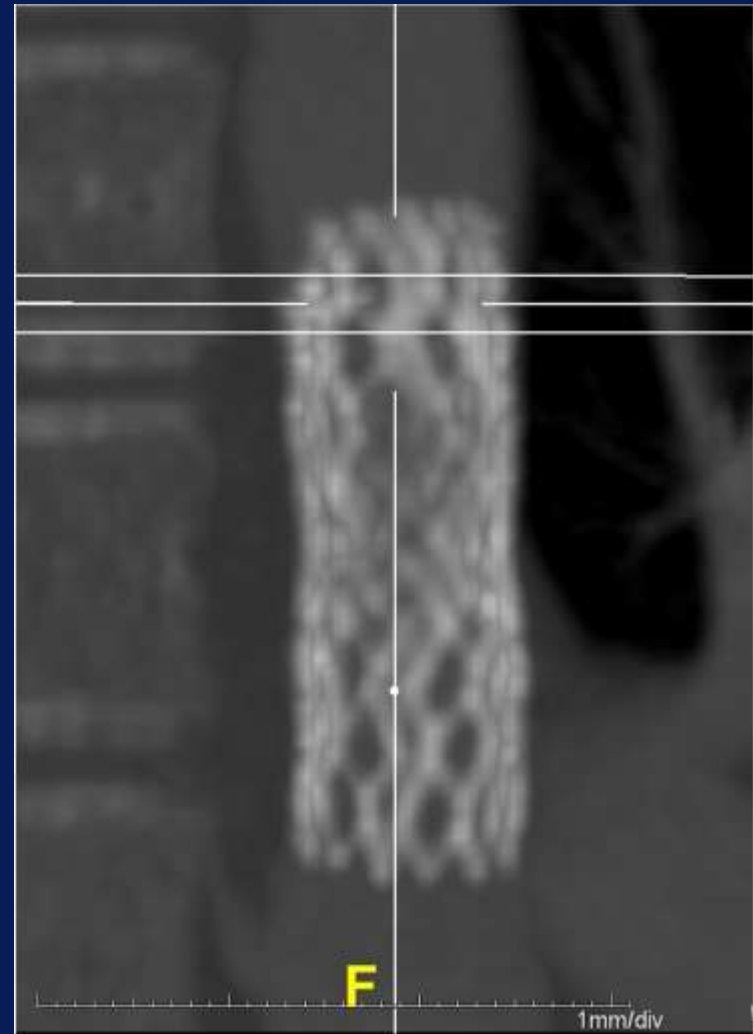
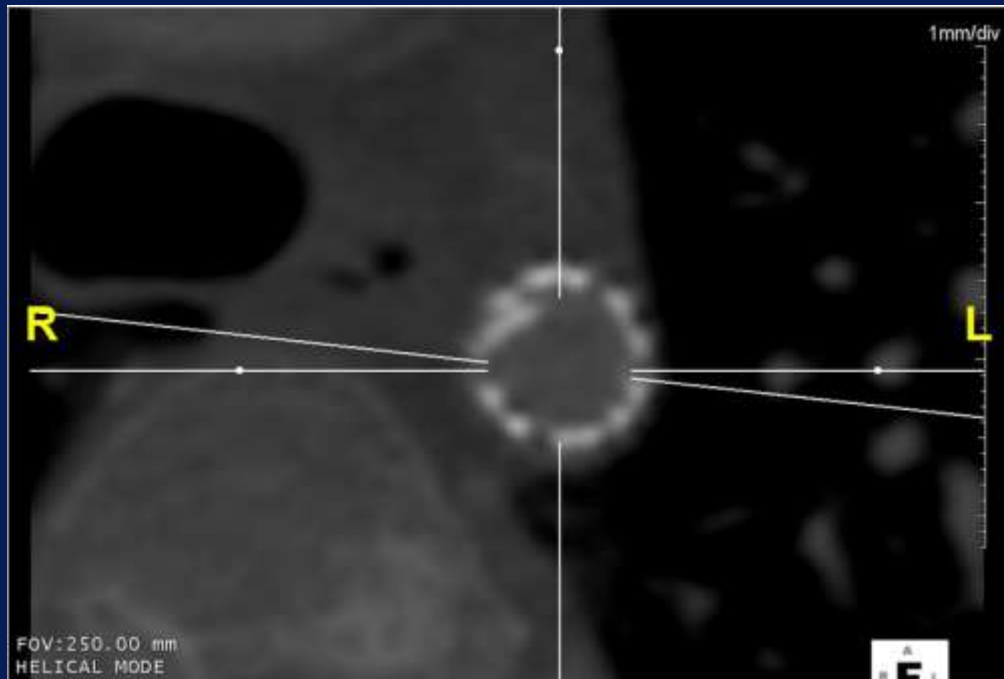
Summary of DV (cm/sec), SV (cm/sec) and DV/SV measured pre-stenting and post-stenting:

| DOPPLER | Statistic | Pre-Stenting Procedure | Post-Stenting Procedure (Discharge) |
|--|------------------|-------------------------|-------------------------------------|
| Peak Systolic Velocity (cm/sec) | N | 31 | 33 |
| | median [IQR] | 361.7 [320.7, 417.7] | 267.0 [214.9, 300.2] |
| | mean \pm SD | 359.2 \pm 75.7 (31) | 260.2 \pm 59.7 (33) |
| | Range (Min, Max) | (120.3, 458.4) | (138.7, 389.7) |
| Peak Diastolic Velocity (cm/sec) | N | 31 | 33 |
| | median [IQR] | 209.2 [165.7, 281.0] | 74.7 [46.0, 101.0] |
| | mean \pm SD | 207.7 \pm 89.8 (31) | 83.4 \pm 47.1 (33) |
| | Range (Min, Max) | (30.6, 360.4) | (3.1, 183.6) |
| DV/SV Ratio | N | 31 | 33 |
| | median [IQR] | 0.64 [0.43, 0.72] | 0.30 [0.21, 0.41] |
| | mean \pm SD | 0.57 \pm 0.22 (31) | 0.31 \pm 0.14 (33) |
| | Range (Min, Max) | (0.13, 0.92) | (0.01, 0.61) |
| IQR = interquartile range; SD = standard deviation; Min = minimum; Max = maximum | | | |

CoArc: Aortic wall damage

- 62 follow up CT scans [88% of patients] at 1 year
 - 1 patient had a small hematoma at implantation which spontaneously resolved
 - 1 patient had a small aneurysm at distal edge of the stent at implantation treated with a second stent 2 months later
 - 1 patient had an unrelated dissection treated endovascularly
-

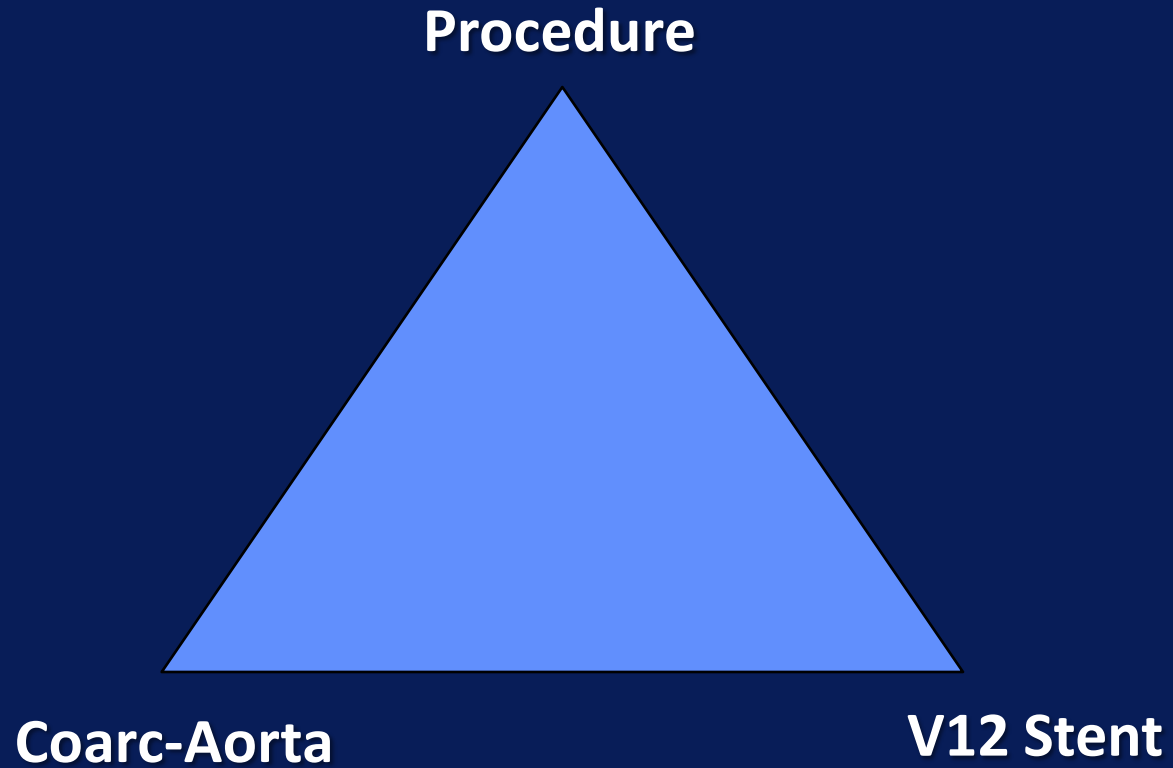
CoArc: Infolding



CoArc: Infolding



CoArc: Infolding



CoArc: Advantages, Limitations and Precautions

- **Advantages:**
 - stent: covered, premounted - low profile, open cell
 - study: prospective trial with hemodynamic and imaging follow up
 - **Limitations and Precautions:**
 - not randomized to surgery
 - nowadays impossible to perform
 - late complications – particularly aneurysm, hypertension, effect on aortic compliance
 - infolding of stent edge
-