New TAVI Devices: More of the Same or Meaningful Differences?

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Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Physician Name</th>
<th>Company/Relationship</th>
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<tbody>
<tr>
<td>Eberhard Grube, MD</td>
<td>Medtronic, CoreValve: C, SB, AB, OF</td>
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<td></td>
<td>Sadra Medical: E, C, SB, AB</td>
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<td>Direct Flow: C, SB, AB</td>
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<td>Mitralign: AB, SB, E</td>
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<td>Boston Scientific: C, SB, AB</td>
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<td>Biosensors: E, SB, C, AB</td>
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<td>Cordis: AB</td>
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<td>Abbott Vascular: AB</td>
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<td>Capella: SB, C, AB</td>
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<td>Devax: SB, AB</td>
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Key
G – Grant and or Research Support  E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria     R – Royalty Income I – Intellectual Property Rights
SB – Speaker’s Bureau             O – Ownership OF – Other Financial Benefits'
Transcatheter AVR

Current Generation Devices

Edwards
~5,500 patients

CoreValve
~5,500 patients
Success, but Opportunity for Improvement

- Percutaneous Aortic Valve Replacement (PAVR) has established itself as a viable therapy
  - Solid clinical results
  - Expanding number of MD’s performing PAVR

- Challenges remain with current devices
  - Steep, unforgiving learning curves
  - Difficult to place with precision
  - Cannot be easily repositioned for optimization
  - Cannot be atraumatically removed if needed
  - Perivalvular Leaks
  - Permanent Pacemaker Implant
  - Stroke
Positioning is Critical

Anterior Mitral Leaflet
MDT Corevalve Positioning Challenges

- Challenging deployment in horizontal aorta
Edwards – Positioning Challenges

Migration of valve during deployment due to escape beats
AV-Block III° Following COREVALVE Implantation
Annulus and LVOT Calcification Grades Correlate With AR - 'Siegburg Score'

Mild = I
Moderate = II
Severe = III
Severe + extension = IV
Para-Valvular Regurgitation
POOLED* Monitored Edwards TAVI Echo AR Results

* REVIVE, REVIVAL, TRAVERCE and PARTNER EU
CoreValve Siegburg Experience

Aortic Regurgitation

Future Aortic Valve Concepts

- Direct Flow
- Sadra
- AorTx
- Jena Valve
- HLT
- ABPS PercValve
- EndoTech
- Ventor Embracer
Transcatheter Valve Therapy
Next Generation Devices

Sadra

DirectFlow

Low profile, repositionable,
(?) less peri-valvular AR
Sadra Medical Lotus Valve System

Designed for optimized aortic valve replacement with a user-friendly delivery system

- Highly accurate, controlled prosthesis positioning
  - Self-centering
- Easy repositioning, distally or proximally
- Retrievability
- Minimal Perivalvular Leakage

Bovine Pericardium

Adaptive™ Seal
Lotus Valve – Accurate Positioning

• Control in the MD’s hands
  • Rate of deployment
  • Ability to pause, unsheath, re-sheath, lock, unlock
  • Fully repositionable, distally and proximally

• Accurate positioning facilitated by
  • Self-centering
  • Predictable locking around central marker
Procedure – Controlled Positioning
Clinical Experience to Date

- Clinical experience
  - 10 patients enrolled – July 2007 – October 2008
  - 6 patients implanted, 5 surviving

- Intra-procedural results
  - Procedure time <20 minutes
  - No perivalvular leaks
  - No migration issues

- Follow-up at 1 year to be presented
- European Trial with new Device started in April 2010
## Clinical Data Summary – Enrollment/Demographics

<table>
<thead>
<tr>
<th>Number of Patients Enrolled</th>
<th>10</th>
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<tbody>
<tr>
<td>Gender</td>
<td>80% Female</td>
</tr>
<tr>
<td>Age</td>
<td>84.2±5.9 years</td>
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</table>

| EuroScore (n=8) | 17.3%±7.8% (9.7 - 28.9%) |
| STS Score (n=8) | 9.6%±6.0% (2.3 - 22.1%) |

| Common Pre-existing Conditions | COPD, Hypertension, hyperlipidemia, CHF, PVD, mitral valve disease |

| Pre-op Annulus Diameter (per CT) (n=10) | 21.4±1.2 mm (20.1 – 23.7) |
| Pre-op Mean Gradient (n=10) | 55.7±15.6 mmHg (32 – 80) |
| Pre-op AVA | 0.58±0.08 cm² (0.4 – 0.85) |
Long Term Follow-up – Gradient

Mean Gradient (mmHg)

Preop  Discharge  30 Days  3 months  6 months  1 year

Patient 1  Patient 4  Patient 5  Patient 6  Patient 8  Patient 9
Long Term Follow-up – Valve Area

Effective Orifice Area (cm²)

- Preop
- Discharge
- 30 Days
- 3 months
- 6 months
- 1 year

Patient 1
Patient 4
Patient 5
Patient 6
Patient 8
Patient 9
Lessons from First Clinical Experience

• Lotus Valve Implant function is excellent, but opportunities identified to improve delivery system:
  • Valve attachment to and release from delivery system needed to be simplified.
  • Handle needed to be redesigned with ease of use a foremost consideration
  • Delivery System size limited use – needed to be reduced.
Simplified Attachment: 15 $\rightarrow$ 3 fingers

Previous 15 finger design

New 3 finger design
Redesigned Handle: 7 $\rightarrow$ 2 controls

- Fewer controls – easier to use
- Ensures correct deployment sequence
- Reduced force required to lock
Profile Reduction: 21 → 18 Fr

- Sadra-developed thin-wall introducer enables fully percutaneous procedure:
  - Same outer diameter as Cook 18Fr
  - Reinforced for excellent kink resistance
Timeline

• Multicenter European Trial started 13. April 2010 (PI. E. Grube)
  • Intl. Heart Center Rhein Ruhr (E. Grube)
  • University Hospital Essen (R. Erbel)
  • Heart Center Siegburg (R. Mueller)

• First 3 Patients enrolled with excellent acute hemodynamic and angiographic results
  • Zero Gradient
  • No Aortic Insufficiency
  • No Pacemaker Implant
  • Av. Implant Time 14 Minutes
The Direct Flow Medical (DFM) Aortic Valve Prosthesis

Ventricular and Aortic Rings
- Inflate independently so device can be repositioned
- Deflatable so that device can be fully retrieved

Slightly Tapered, Conformable Polyester Fabric Cuff

Position Fill Lumens (PFLs)
- Used to position/reposition valve
- Complete Inflation Media Exchange

Tri-leaflet Valve constructed of Bovine Pericardium

Multilumen
18F System Features

3 sizes matching valvuloplasty balloons

22F Design

18F Design
**European Feasibility Trial**

**Design:** Prospective, non-randomized clinical evaluation of the DFM PAV at two centers in Germany
- Hamburg University Cardiovascular Center (n=25)
- Siegburg, Helios Heart Center (n=6)

**Purpose:** Determine clinical feasibility and safety of treating patients high-risk for cardiac surgery:
- EuroSCORE $\geq 20\%$
- Age $\geq 70$
- Severe aortic valve stenosis
The DFM AV Prosthesis
European Clinical Trial

Mean Gradient (mmHg)

Mean EOA (cm²)
Next generation TAVR devices are rapidly evolving, providing substantial benefits over the first generation devices.

Issues addressed are repositionability, risk of paravalvular leakage, profile size etc.

Valve + platform durability still must be conclusively demonstrated!

Once durability is established, we can expand clinical trials and indications for TAVR to most (not all) patients with severe AS!
Aortic Atheroma: High Risk

- 268 of 3404 CABG patients (8%) had atheroma (≥ 5 mm, or mobile)
- Defined by epi-aortic ultrasound
- 15.3% of group had intra-operative stroke

- High Risk for:
  - Intra-operative stroke
  - Multiple morbidity
  - Prolonged hospital stay,
  - Death resulting from heart surgery.

- Risk Factors for Aortic Atheroma:
  - > 70 years old
  - Diabetes Mellitus
  - Hyperlipidemia
  - Arterial hypertension
  - Aortic calcifications on chest X-ray
  - Elevated serum levels of C-reactive protein
  - Other inflammatory markers
  - Activated coagulation

Cerebral Filter Protection

Claret

Filter in Truncus

Filter in left Carotid
Embolic Material
Embolic Material

Emboli
Claret Dual Filter

7 mm filter placed in left carotid
Embrella Embolic Deflector™

- Porous membrane designed to deflect embolic debris
- Nitinol® Frame & Shaft
- Polyurethane Porous Membrane
- Heparin Coating
- 3 Radiopaque Markers
- Suture; Monofilament Nylon
Brachiocephalic Artery

Left Common Carotid Artery

Embrella span width
Thank you for your attention!
Thank you
There Is a Higher Incidence of Pacemaker Implant Associated with CoreValve

New Permanent Pacemaker within 30 Days

<table>
<thead>
<tr>
<th>% patients</th>
<th>(n=30)</th>
<th>(n=102)</th>
<th>(n=34)</th>
<th>(n=91)</th>
<th>(n=1521)</th>
<th>(n=126)</th>
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<tbody>
<tr>
<td>Calvi (PACE 2009)</td>
<td>20</td>
<td>33</td>
<td>32</td>
<td>19</td>
<td>23</td>
<td>25</td>
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<td>Grube (Circ Interv 2008)</td>
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<td>Jilaihawi (Am Heart J 2009)</td>
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<td>Rotterdam</td>
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Weighted average = 23%
(n=1990 patients)
It is important to remember that pacemaker implantation may not mean pacing need.

New Permanent Pacemaker within 30 Days
18F Safety and Efficacy Study (n=126)

<table>
<thead>
<tr>
<th>Participating Centers</th>
<th>% patients</th>
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<tr>
<td>A</td>
<td>5</td>
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<tr>
<td>B</td>
<td>20</td>
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<tr>
<td>C</td>
<td>25</td>
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<td>D</td>
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<td>E</td>
<td>36</td>
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<tr>
<td>F</td>
<td>50</td>
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<tr>
<td>G</td>
<td>56</td>
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* 2 centers with < 5 implants excluded from the presentation; both centers had 0% 30-day permanent pacemakers

Physicians’ decision to prophylactically implant play a big role in the variability among centers.
Claret Dual Filter

The Device:

• **Must be easy to use!**
• The filter device should **not** be present in the aorta
• Catheter 6F (5F in development)
• 140 micron pore size
• Right radial/brachial delivery
• System will accommodate variable aortic anatomy
Claret Dual Filter Device
Claret Dual Filter Device
Embrella
Concept of Embrella
Product Requirements

- Separate access site from main procedure; radial or brachial artery
- Fits through a 6F sheath
- Minimal orientation
- Ease of use, no new techniques
- Low profile
- One size fits all
- Deflect debris
Concept of Embrella
Human Aorta

- Right Common Carotid Artery
- Left Common Carotid Artery
- Left Subclavian Artery
- Brachiocephalic Artery
- Descending Aorta
- Ascending Aorta
Brachiocephalic Artery

Aortic Arch
Embrella Device placed in outer curve of aortic arch
Passage of balloon along the Embrella Device