Update on Transcatheter Aortic and Mitral Valve Therapies

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Tower Health Cardiovascular Update
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Disclosure Statement of Financial Interest

Affiliation/Financial Relationship

• Grant/Research Support

• Consulting Fees/Honoraria

Company

• Edwards Lifesciences, Medtronic, LivaNova, W.L.Gore, Bolton Medical

• Microinterventional Device
TAVR and SAVR* Procedures In the TVT Registry and STS ACSD*

Source: STS/ACC TVT Registry Database and STS Database 2017 as of April 10, 2017
A Look Back Over the Beginning of TAVR at UPHS

TAVR November 2007 to November 2015

Volume

Year

2007

2

55

110

224

444

666

1271

CoreValve eSurTAVI

LOTUS

Jena

S3

PORTICO

Sapien Commercial Approved 2011

Sapien XT Partner II

Partner I

TA 9/2008

11/2009 PPMC

Nov 2007

11/2009 PPMC

PenStent

Lotus"
Penn TAVR Program

Penn Medicine Transcatheter Total Volume FY08-current

# TRANSCATHER CASES

<table>
<thead>
<tr>
<th>Year</th>
<th>Total FY08</th>
<th>Total FY09</th>
<th>Total FY10</th>
<th>Total FY11</th>
<th>Total FY12</th>
<th>Total FY13</th>
<th>Total FY14</th>
<th>Total FY15</th>
<th>Total FY16</th>
<th>Total FY17</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>10</td>
<td>27</td>
<td>39</td>
<td>79</td>
<td>193</td>
<td>212</td>
<td>270</td>
<td>324</td>
<td>391</td>
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</table>

~2000
U Penn
AVR / TAVR Volume

CY 2007 – September 2017

<table>
<thead>
<tr>
<th>Year</th>
<th>Open AVR</th>
<th>TAVR</th>
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<tbody>
<tr>
<td>2007</td>
<td>356</td>
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<td>2008</td>
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<td>2009</td>
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<td>2010</td>
<td>431</td>
<td>55</td>
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<tr>
<td>2011</td>
<td>419</td>
<td>114</td>
</tr>
<tr>
<td>2012</td>
<td>427</td>
<td>226</td>
</tr>
<tr>
<td>2013</td>
<td>539</td>
<td>218</td>
</tr>
<tr>
<td>2014</td>
<td>398</td>
<td>306</td>
</tr>
<tr>
<td>2015</td>
<td>448</td>
<td>323</td>
</tr>
<tr>
<td>2016</td>
<td>358</td>
<td>361</td>
</tr>
<tr>
<td>2017</td>
<td>294</td>
<td>349</td>
</tr>
<tr>
<td>Trial</td>
<td>Risk</td>
<td>Outcome</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Partner 1B</td>
<td>Inoperable</td>
<td>TAVR &gt; Medical Therapy</td>
</tr>
<tr>
<td>Medtronic</td>
<td>Extreme risk</td>
<td></td>
</tr>
<tr>
<td>Partner 1A</td>
<td>High Risk</td>
<td>TAVR = SAVR TAVR &gt; SAVR</td>
</tr>
<tr>
<td>Medtronic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partner 2A</td>
<td>Intermediate Risk</td>
<td>TAVR = SAVR TAVR = SAVR</td>
</tr>
<tr>
<td>SURTAVI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partner 3</td>
<td>Low Risk</td>
<td>TAVR vs. SAVR</td>
</tr>
<tr>
<td>Medtronic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• What is the future of TAVR?

• What will be the role of surgeons?
Heart Valve Team

- Repair
- TAVR
- Sutureless
- MIS
The Heart Team
A Powerful Paradigm for the Future Training of Cardiovascular Surgeons

Andrew J. feet. MD, John H. B. MD

An important milestone in the field of cardiovascular medicine was the advent of a new medical practice in the 1990s, known now as the "Heart Team." This team approach was developed to enhance the quality of patient care by bringing together specialists from various disciplines to address complex cardiovascular problems. The Heart Team consists of cardiologists, surgeons, intensivists, and other specialists who collaborate to develop a comprehensive treatment plan for each patient.

In this era of globalization and specialization, the Heart Team approach has become increasingly important. This approach allows for a more coordinated and individualized care plan, which can lead to better outcomes for patients. The Heart Team approach helps to ensure that the care provided is aligned with the latest evidence and best practices, and that patients' needs are met in a timely and efficient manner.

The Heart Team approach has been shown to be effective in various settings, including hospitals, cardiology clinics, and cardiothoracic surgery units. It has been endorsed by regulatory bodies and professional societies, and is now widely accepted as a standard of care.

In conclusion, the Heart Team approach is a powerful paradigm for the future training of cardiovascular surgeons. It provides a model for collaboration and interdisciplinary care, and has the potential to improve patient outcomes and enhance the quality of care provided in the field of cardiovascular medicine.
First TF case (Sapien)
Penn Nov 2007
First Transfemoral Implant At Penn 11/15/2007

Josep Rodes-Cabau
Joseph Bavaria
Howard Herrmann
Wilson Szeto
Samir Kapadia
A Decade of Change!
Hybrid ORs at Penn
All-Cause Mortality at 30 Days
Edwards SAPIEN Valves (As Treated)

PARTNER 1 and 2 Trials
Overall and TF Patients

<table>
<thead>
<tr>
<th>Valve Type</th>
<th>30 Days Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPIEN</td>
<td>6.3%</td>
</tr>
<tr>
<td>SAPIEN X</td>
<td>5.2%</td>
</tr>
<tr>
<td>SAPIEN X</td>
<td>3.7%</td>
</tr>
<tr>
<td>SAPIEN 3</td>
<td>4.5%</td>
</tr>
<tr>
<td>SAPIEN 3</td>
<td>3.5%</td>
</tr>
<tr>
<td>SXT</td>
<td>2.2%</td>
</tr>
<tr>
<td>S3HR (All)</td>
<td>1.6%</td>
</tr>
<tr>
<td>S3HR (TF)</td>
<td>1.1%</td>
</tr>
<tr>
<td>S3i (All)</td>
<td>1.1%</td>
</tr>
<tr>
<td>S3i (TF)</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

*P1B (TF) 175, P1A (All) 344, P1A (TF) 240, P2B (TF) 271, P2B XT (TF) 282, S3HR (All) 583, S3HR (TF) 491, S3i (All) 1072, S3i (TF) 947*
Evolution of the “Minimalist” Approach

- Femoral cutdown to percutaneous
- Postoperative recovery from ICU to fast track
- General anesthesia (GA) to conscious sedation (CS) / monitored anesthesia care (MAC)

Heart Team Is Intact
Penn TAVR Program: Continue Growth w/ MAC

Penn Medicine Transcatheter Total Volume FY08-current

~2000

“Minimalist” TAVR

<table>
<thead>
<tr>
<th>Series1</th>
<th>Total FY08</th>
<th>Total FY09</th>
<th>Total FY10</th>
<th>Total FY11</th>
<th>Total FY12</th>
<th>Total FY13</th>
<th>Total FY14</th>
<th>Total FY15</th>
<th>Total FY16</th>
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<td>391</td>
<td>414</td>
</tr>
</tbody>
</table>
TF Cases Completed with MAC or GA at Penn

Current use (2017) of MAC in TF cases: 90-95%
LOS with Fast-Track

HUP Fast Track LOS FY15-FY17
(thru 6/1/17)

<table>
<thead>
<tr>
<th>Fast Track postop LOS (days)</th>
<th>Fast Track total LOS (day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.86</td>
<td>4.25</td>
</tr>
<tr>
<td>3.41</td>
<td>4.95</td>
</tr>
<tr>
<td>2.73</td>
<td>4.05</td>
</tr>
</tbody>
</table>

FY15 FY16 FY17
TAVR: Tip of the Iceberg

Just the Beginning
TAVR Systems with CE Mark

All Comers
(including Low Risk)

TAVR vs SAVR?
High Number of US Patients with Severe Aortic Stenosis Remain Largely Undertreated

Prevalence of Mod+ AS\(^1\) ~1.6M
Prevalence of Severe AS\(^1\) ~548K
Prevalence through SAVR or TAVR ~88K
TAVR Cases ~18K

The PARTNER 3 Trial
Study Design

Symptomatic/Asymptomatic Severe Calcific Aortic Stenosis

Low Risk ASSESSMENT by Heart Team
(STS < 4%)

Alternative Access (n=100)
(TA/Taa/Subclavian)

1:1 Randomization (n=1228)

TF - TAVR
(SAPIEN 3)

CT Imaging Sub-Study (n=200)
Activity/QoL Sub-Study (n=100)

SAVR
(Surgical Bioprosthetic Valve)

CT Imaging Sub-Study (n=200)
Activity/QoL Sub-Study (n=100)

Follow-up: 30 day, 6 mos, 1 year and annually through 10 years

PARTNER 3 Registries

Bicuspid
(n=100)

VIV
(n=100)

Primary Endpoint:
Composite of all-cause mortality, all stroke, or re-hospitalization at 1 year post procedure
Medtronic TAVR in Low Risk Patients

TRIAL DESIGN & LEAFLET SUB-STUDY

- **Patient Population: Low Risk Cohort**
  - Determined by Heart Team to be low surgical risk

- **Primary Endpoint:**
  - Safety: Death, all stroke, life-threatening bleeding, major vascular complications, or AKI at 30 days
  - Efficacy: Death or major stroke at 2 years

- **Sample Size: ~1200 Subjects**

- **Follow-up Evaluations:**
  - 30-days, 6-month, 18-month, and 1 Through 5 years

- **Number of Sites: Up to 80 sites**
What is **Low** Risk?
**(All Comers)**

<table>
<thead>
<tr>
<th>Clinical Evaluation</th>
<th>STS - PROM</th>
</tr>
</thead>
<tbody>
<tr>
<td>82 yo male, LVEF 65% No other PMH</td>
<td>Low</td>
</tr>
<tr>
<td>74 yo female, LVEF 50%, HTN, DM, low grade CAD</td>
<td>Low</td>
</tr>
<tr>
<td>60 yo male, probable bicuspid valve Asc Aorta 4.8 cm</td>
<td>Low</td>
</tr>
</tbody>
</table>

**Heterogenous group**

**Different clinical implications with TAVR**
Lessons Learned: Why Not for Everyone Yet.....

Achilles Heel of TAVR

- Vascular Complications
- Stroke
- PPM
- Leaflet Thrombosis*
- PVL*
- Durability – long term outcome*

Limitations amplified in “younger” lower risk patients
Claret Medical™
Sentinel® Cerebral Protection System

Approx. 8 mm, captured in LCC

Baseline DWI  2-7 days DWI  Subtraction DWI
52.7mm²  34.3mm²

Baseline FLAIR #1  Baseline FLAIR #2  Baseline FLAIR #3
Cerebral Embolic Protection: Sentinel Procedural Animation
Cerebral Embolic Protection:

Claret Sentinel Cerebral Embolic Protection

- Two independent filters capture & remove embolic material
- Polyurethane filter, pore size = 140 µm
- Standard right trans-radial sheath access (6F)
- One size accommodates most vessel sizes; fits ~90% of anatomies
- Deflectable compound-curve catheter facilitates cannulation of LCC
- Minimal profile in aortic arch (little interaction with other devices)
Cerebral Embolic Protection:
"Claret Sentinel Cerebral Embolic Protection"

**SENTINEL Trial Design Overview**

- **Patients with Severe Symptomatic Aortic Stenosis undergoing TAVR**
  - Patients Randomized (1:1:1) (N=363)
    - SAFETY ARM: TAVR with Sentinel (N=123)
    - TEST ARM: TAVR with Sentinel (N=121)
    - CONTROL ARM: TAVR Only (N=119)
  - Histopathology & Morphometry
  - Clinical Follow-Up (Neurology Assessments in all patients)
  - Serial MRIs (Baseline, Day 2-7 & Day 30)
  - Serial Neurocognitive Assessment (Baseline, Day 30 & Day 90)

*Kapadia S et al, J Am Coll Cardiol 2017*
Debris Captured During TAVR
Cerebral Embolic Protection: Claret Sentinel Cerebral Embolic Protection: Stroke Reduction

- **Sentinel**
  - Day 1: 1.3%
  - Day 2: 0.4%
  - Day 3: 0.9%
  - Total*: 3.0%

- **Control**
  - Day 1: 4.5%
  - Day 2: 0.9%
  - Day 3: 1.3%
  - Total*: 8.2%

**p=0.05**

63% Reduction

*Fisher Exact Test
Durability / Long Term Outcome

No Data?
Longitudinal Hemodynamics of Transcatheter and Surgical Aortic Valves in the PARTNER Trial

Reintervention

SAVR  1 (0.3%)

TAVR  20 (0.8%)

Due to SVD  5
Mechanical Valves: Survival Benefits in Young Patients?

PRO: Excellent durability
CON: Life-long anticoagulation and risk of bleeding

PRO: No anticoagulation
CON: Limited durability requiring reoperation
Mechanical or Biologic Prostheses for Aortic-Valve and Mitral-Valve Replacement

Andrew B. Goldstone, M.D., Ph.D., Peter Chiu, M.D., Michael Baiocchi, Ph.D., Bharathi Lingala, Ph.D., William L. Patrick, M.D., Michael P. Fischbein, M.D., Ph.D., and Y. Joseph Woo, M.D.
Transcatheter Aortic Valve Replacement in Bicuspid Aortic Valve Disease

Postimplantation echocardiography

Aortic regurgitation, grade (1–4)* 1.1 ± 0.9

≥ Grade 2 38 (28.4)
≥ Grade 3 8 (6.0)

Aortic valve gradient, mm Hg* 11.4 ± 9.9

Aortic valve area, cm²* 1.7 ± 0.5

Contrast media, ml 174 ± 88

Fluoroscopy duration, min 20 (14–28)
The PARTNER 3 Low-Risk Trial (Bicuspid Registry)

University of Pennsylvania
Dr. Wilson Szeto and Dr. Robert Li
## CT Analysis (Core Lab): P3E-0009-035

<table>
<thead>
<tr>
<th>Aortic Root</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve Morphology</td>
<td>Bicuspid Sievers Type 0</td>
</tr>
<tr>
<td>Commissural Morphology</td>
<td>Bicuspid Sievers Type 0 lateral</td>
</tr>
<tr>
<td>Valve Calcification Along Raphe</td>
<td>N/A</td>
</tr>
<tr>
<td>Ascending Aorta Diameter</td>
<td>28.0 mm</td>
</tr>
</tbody>
</table>

### Core Lab Comments:

```
   SoV
   Asc aorta max diameter
```
TMVR V in V and V in R
TAVR in MAC
University of Pennsylvania
PI: Wilson Szeto
Co-PI: Matthew Gillespie
COMPASSION S3
Pulmonary Valve Assessment: 4/17/2018

<table>
<thead>
<tr>
<th>CT</th>
<th>Measure</th>
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</thead>
<tbody>
<tr>
<td>RV Pressure</td>
<td>Peak 72 mmHg // Mean 15 mmHg from 3/8/17 cath</td>
</tr>
<tr>
<td>PA Pressure</td>
<td>Peak 34 mmHg // Mean 22 mmHg from 3/8/17 cath</td>
</tr>
<tr>
<td>Landing Zone</td>
<td>24.2 mm x 23 mm</td>
</tr>
<tr>
<td></td>
<td><strong>AP</strong> 22.3 mm</td>
</tr>
<tr>
<td></td>
<td><strong>Lateral</strong> 22.4 mm</td>
</tr>
<tr>
<td>Valve Conduit Area</td>
<td>428 mm$^2$</td>
</tr>
</tbody>
</table>

**Other Findings:**
- Marked dilation of the right heart in keeping with prosthetic pulmonic valve dysfunction
- Atrophic occluded left PA with corresponding chronic fibrosis of the left lung base. Corresponding compensatory enlargement of the right pulmonary artery.
- Absent flow within the proximal right subclavian artery and right vertebral artery related to prior Blalock-Taussig shunt.

In Window $\leq$ 24 months (Previously Placed Valve)
Transcatheter Mitral Valve Therapies
Transcatheter Mitral / Tricuspid Repair: Device Landscape

**Edge to Edge**
- MitraClip NT*
- MitraFlex
- Cardica
- MitraClamp
- Neochord E2E

**Direct Annuloplasty**
- Valtech Cardioband*
- Millipede*
- Valcare*
- Cardiac Implants
- Mitralign*
- MitraSpan
- GDS Accucinch*
- MIA

**Chordal Replacement**
- Neochord*
- Harpoon*
- Valtech V-Chordal

**Indirect Annuloplasty**
- Carillon*
- Cerclage*

**LV Remodeling**
- VenTouch*
- BioVentrix Revivent-MR

**Tricuspid**
- MitraClip NT*
- TriCinch*
- 4-Tech*
- Trialign*
- Edwards Forma*
- Millipede*
- Valtech Cardioband*

**Other Approaches**
- MitraSpacer*
- Mitramaze
- Mitra-Plug
- MVRx*
- Mitral Bridge
- Mitral Butterfly
- Middle Peak Medical Neo-leaflet*
- MitraClip NT*
- TriCinch*
- 4-Tech*
- Trialign*
- Edwards Forma*
- Millipede*
- Valtech Cardioband*
Classification of MR

Type I

Type II

Type IIIa

Type IIIb
MitraClip® Therapy: >40,000 cases worldwide
2015 German Heart Report: MitraClip surpassed surgical volume!
US MitraClip Cases

Source: Abbott

2015 MitraClip Cases = 2,877
vs 2015 STS Isolated MV Repair = 8,881
No growth in surgery 2013-2015
# MV Disease Etiology & MitraClip Details

<table>
<thead>
<tr>
<th>Etiology - % of pts with:</th>
<th>2014 (n=1,023)</th>
<th>2015 (n=3,362)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degenerative Mitral Regurgitation (DMR) only</td>
<td>79.7%</td>
<td>75.5%</td>
</tr>
<tr>
<td>Functional Mitral Regurgitation (FMR) only</td>
<td>10.0%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Mixed (both FMR and DMR)</td>
<td>6.2%</td>
<td>10.1%</td>
</tr>
<tr>
<td>Neither DMR and FMR</td>
<td>4.2%</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Count of Leaflet Clips (used during the procedure)</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Leaflet Clip</td>
<td>51.8%</td>
<td>54.3%</td>
</tr>
<tr>
<td>2 Leaflet Clips</td>
<td>39.8%</td>
<td>38.4%</td>
</tr>
<tr>
<td>&gt;=3 Leaflet Clips</td>
<td>7.0%</td>
<td>6.9%</td>
</tr>
</tbody>
</table>
## Outcomes & Adverse Events at Discharge

<table>
<thead>
<tr>
<th>Post Procedure Events (at discharge)</th>
<th>2014 (n=1,023)</th>
<th>2015 (n=3,362)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial Infarction</td>
<td>0%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Acute Kidney Injury (stage 3)</td>
<td>1.2%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Bleeding (major)</td>
<td>1.3%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Bleeding (life threatening)</td>
<td>1.1%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Major Vascular Complication</td>
<td>0.2%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

Source: STS/ACC TVT Registry Data Mart 3,362 pt records from 2014-15, as of 4-24-16

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## Outcomes & Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>2014 ((n=1,023))</th>
<th>2015 ((n=3,362))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral Regurgitation ((&lt;=2+))</td>
<td>92.0%</td>
<td>92.0%</td>
</tr>
<tr>
<td>MV Mean Gradient (&lt;=8) mmHg</td>
<td>92.3%</td>
<td>93.8%</td>
</tr>
<tr>
<td>Single Leaflet Device Attachment</td>
<td>1.2%</td>
<td>1.6%</td>
</tr>
<tr>
<td>MV Re-intervention</td>
<td>0.4%</td>
<td>0.9%</td>
</tr>
<tr>
<td>ASD requiring closure</td>
<td>1.6%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Source: STS/ACC TVT Registry Data Mart 3,362 pt records from 2014-15, as of 4-24-16
# Post-Procedure Status

<table>
<thead>
<tr>
<th></th>
<th>2014 (n=1,023)</th>
<th>2015 (n=3,362)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Length of Stay</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total LOS (mean/median)</td>
<td>5.3/3 days</td>
<td>5.1/2 days</td>
</tr>
<tr>
<td>Post procedure LOS (mean/median)</td>
<td>3.7/2 days</td>
<td>3.5/2 days</td>
</tr>
<tr>
<td><strong>Discharge Location</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>84.2%</td>
<td>87.0%</td>
</tr>
<tr>
<td>Extended care facility</td>
<td>10.4%</td>
<td>7.9%</td>
</tr>
</tbody>
</table>

Source: STS/ACC TVT Registry Data Mart 3,362 pt records from 2014-15, as of 4-24-2016
US TVT MitraClip – NYHA Improvement

Source: STS/ACC TVT Registry Data Mart 2,339 pt records from 2015, as of 4-24-16

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Choral Replacement
NeoChord US Prospective Randomized Trial

• **Principle Investigators**
  - David Adams & Michael Borger

• **ReChord Trial**: Randomized, Controlled Design
  - Control → Standard of Care MV Repair
  - Treatment → Beating Heart MV Repair (NeoChord)

• **Inclusion Criteria**
  - Isolated segmental prolapse of P2 or A2

• Up to 450 subjects / Up to 20 centers / app. Q4/2016
1st case in US: Mount Sinai Medical Center, 11/3/2016
Mitral Valve Repair System

- Small 3mm shaft profile houses 21 gauge needle with pre-wound ePTFE suture
- Strong proprietary anchor, place cords anywhere, no need to “catch” the leaflet
- Dedicated 14 Fr hemostatic introducer minimizes trauma & blood loss

1. Simplified off-pump repair of degenerative MR
2. Image-guided placement & anchoring of ePTFE cords
3. Real-time titration of cords on the beating heart to maximize coaptation
Indirect Annuloplasty
Device Description: Carillon

Distal Anchor
(in great cardiac vein)

Implant lengths:
60 - 80 mm

Proximal Anchor
(in coronary sinus)

Anchor sizes:
Individually selected for each patient

Delivery System
Easily Implanted with a Minimally Invasive Procedure

1. Access
   Catheter inserted into the jugular vein

2. Placement
   Coronary sinus measured and device size selected

3. Reshape
   The Carillon device is anchored in place, reshaping the mitral annulus

Mitral valve coaptation after Carillon implant
Carillon® Mitral Contour System®

The Carillon® Mitral Contour System® is not approved for use in the United States. It is CE marked and approved for sale in the European Union and elsewhere in the world.
Multi-Center Clinical Studies

Study Design
- AMADEUS\(^1\): Prospective, single arm
- TITAN\(^2\): Prospective, non-blinded double arm
- TITAN II\(^3\): Prospective assessment of Carillon

Inclusion Criteria
- Dilated Ischemic or Non-ischemic Cardiomyopathy
- FMR moderate to severe ( 2+ to 4+ )
- EF < 40%
- NYHA Class II – IV
- Stable on heart failure meds
- No anatomical exclusions – enrolled all comers

Primary Endpoint
- Thirty-day rate of Major Adverse Events

N = 30
N = 53
N = 30
Total = 113
Direct Annuloplasty
Edwards Cardioband

1. Transseptal Puncture
2. System Insertion
3. Implant Deployment
4. Implant Size Adjustment
Edwards Cardioband System
MR Severity by Echo Core Lab

Grayburn, MD – Baylor University, Dallas, TX
Annular Reconstruction by Significant Reduction in Septolateral (A-P) Diameter (N=45)

30% average reduction in septolateral diameter

Baseline

<table>
<thead>
<tr>
<th>Septolateral Diameter [mm]</th>
<th>26±4 (18-35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge</td>
<td>26±4 (18-35)</td>
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</tbody>
</table>

p<0.01
Edwards Cardiband System ACTIVE Pivotal Clinical Trial

A prospective, multicenter, randomized, controlled pivotal trial to assess transcatheter mitral repair with Edwards cardioband System and guideline directed medical therapy (GDMT) compared to GDMT alone in patients with functional mitral regurgitation (FMR) and heart failure.

- Up to 50 Centers in North America
- Roll-in cohort: up to 3 patients per study site
- Pivotal cohort: approximately 375 patients
- Up to 525 patients
- Prospective, multicenter 2:1 randomized trial
  - Edwards Cardioband System + GDMT (Device group)
  - GDMT (Control group)
Future: A Combination of Techniques

=

Fully Percutaneous Mitral Repair
# Transcatheter Mitral Valves in Early Clinical Studies

<table>
<thead>
<tr>
<th></th>
<th>Both Transseptal and Transapical</th>
<th>Transeptal Only</th>
<th>Transapical Only</th>
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</thead>
<tbody>
<tr>
<td><strong>CardiAQ</strong></td>
<td>![CardiAQ Image]</td>
<td>![Caisson Image]</td>
<td>![Tendyne Image]</td>
</tr>
<tr>
<td><strong>Sapien M3</strong></td>
<td>![Sapien M3 Image]</td>
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<td></td>
</tr>
<tr>
<td><strong>Caisson</strong></td>
<td>![Caisson Image]</td>
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<tr>
<td><strong>Tendyne</strong></td>
<td>![Tendyne Image]</td>
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<td><strong>Intrepid</strong></td>
<td>![Intrepid Image]</td>
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<tr>
<td><strong>Tiara</strong></td>
<td>![Tiara Image]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Delivery System Size</strong></td>
<td>33 Fr</td>
<td>20 Fr</td>
<td>31 Fr</td>
</tr>
<tr>
<td></td>
<td>27mm</td>
<td>32 Fr</td>
<td>35 Fr</td>
</tr>
<tr>
<td><strong>Valve Size</strong></td>
<td>40 mm</td>
<td>29mm</td>
<td>27 mm</td>
</tr>
<tr>
<td></td>
<td>27 mm</td>
<td>27 mm</td>
<td>35, 40 mm</td>
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</tbody>
</table>
TMVR (vs TMVrepair) Potential Advantages

1. Agnostic to etiology of MR
2. Ease of implantation
3. Reliable elimination of MR
4. Less recurrence of MR
CardiAQ-Edwards Transcatheter Mitral Valve Replacement System

- Can be delivered transseptally
- Unique anchoring mechanism uses native valve anatomy
- Designed to minimize both LV and LA intrusion
- Beating heart procedure does not require circulatory support

Investigational device, limited by Federal (or United States) law to investigational use. Exclusively for clinical investigations. To be used by qualified investigators only. Not available for use until validly CE marked.
CardiAQ-Edwards Transcatheter Mitral Valve Replacement System

- Transseptal delivery system
- Trileaflet bovine pericardial tissue valve
- Nitinol frame
- Fabric skirt

Investigational device, limited by Federal (or United States) law to investigational use. Exclusively for clinical investigations. To be used by qualified investigators only. Not available for use until validly CE marked.
# CardiAQ-Edwards Transcatheter Mitral Valve Replacement System

## Strengths

- Transseptal delivery for safer procedure and better outcomes
- No rotational alignment required during implantation
- Unique anchoring mechanism preserves the native anatomy
- Low ventricular profile minimizes risk of LVOT obstruction
- Intra-annular sealing skirt to minimize PV leak

## Learnings

- Significant learnings occurred in parallel:
  - Early transapical experience enabled better understanding of patient selection
  - Introduction of new transseptal delivery system enabled further procedural learning
- Anticoagulation requirement for TMVR devices
Positive Trend in Outcomes Attributed to Clinical Learning
CardiAQ-Edwards Transcatheter Mitral Valve Replacement System

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CardiAQ-Edwards TMVR Case
Patient Demographics and Medical Hx

• Demographics
  • 86 year-old male
  • 83.4 kg (183 lbs.) x 180.3 cm (71 in)
  • BMI = 25.6 kg/m^2; BSA = 2.03 m^2 (Du Bois formula)
  • NYHA Class = II-III (DOE at 50 yards, stairs)

• PH: Hyperlipidemia, PUD, pulmonary hypertension, gout and MR

• No significant CAD
  • LV Function
    • Echo LVEF = 40-45%
  • Renal Function (Stage III CKD)
    • Creatinine: 1.21 mg/dL
    • eGFR: 54 mL/min
  • Pulmonary Function - No obstruction or restriction
CardiAQ-Edwards TMVR Case

Risk Stratification

• STS (MV replacement) → 4.01-6.8 % (Mortality) / 23.41-32.3 % (Morbidity) (varying EF and creatinine)

• EuroSCORE II → 3.01% (Mortality)

• Justification for surgical risk (high):
  • Age
  • CAD
  • Kidney Disease
  • LV dysfunction
CardiAQ-Edwards TMVR Case

TEE: 3+ FMR with multiple jet origins

- 3+ FMR due to restricted leaflet motion, no MAC, mild anterior leaflet calcification
- Mild to moderately decreased LVEF (LVEF = 40-45% by 3D echo)
CTA Cardiac
Annulus Diameter and LA Height
LVOT Analysis

Distance: 17.9 mm

<table>
<thead>
<tr>
<th>ID Type</th>
<th>Label</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Freehand Area</td>
<td>565.1 mm²</td>
</tr>
<tr>
<td></td>
<td>Perimeter</td>
<td>135.2 mm</td>
</tr>
<tr>
<td>2</td>
<td>Freehand Area</td>
<td>366.1 mm²</td>
</tr>
<tr>
<td></td>
<td>Perimeter</td>
<td>84.4 mm</td>
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</tbody>
</table>
The CardiAQ-Edwards™ Transseptal TMVR Procedure
Valve Deployment

Positioning

LVA Release
The CardiAQ-Edwards™ Transseptal TMVR Procedure

LAA Release

Valve Release
The CardiAQ-Edwards™ Transseptal TMVR Procedure

Delivery System

Completion
The CardiAQ-Edwards™ Transseptal TMVR Procedure
CardiAQ-Edwards Transcatheter Mitral Valve Replacement System Clinical Status

• Focused on transseptal and incorporating learnings to optimize procedure
• US Early Feasibility Study – increased enrollment cadence over the last several months
• Continued progress towards an optimized transseptal product and procedure
• Both Edwards transseptal TMVR programs continue enrolling (CardiAQ & SAPIEN M3) – early clinical experience is encouraging
Penn Heart Team

Thank You!