Clinical Experiences with Pi-Cardia Leaflex
Aortic Valve Remodeling:
An Alternative to TAVR in Some Patients?

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8 mins
Within the past 36 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>• Research Support</td>
<td>Abbott, Boston Scientific, Edwards Lifesciences, Medtronic</td>
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<tr>
<td>• Consulting Fees*</td>
<td>Abbott, Boston Scientific, Gore, Medtronic, Meril Life Sciences</td>
</tr>
<tr>
<td>• Equity</td>
<td>Ancora, Valve Medical</td>
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*Medical or scientific advisory boards
Background:

BAV - Case Example

88yo fully active until 1 mo prior to admission; presents with class IV heart failure; 15 lb weight gain; EF 15%; AKI

Pre-BAV Echo
AVA - 0.32 cm$^2$
Mean PG - 44.2 mmHg

Post BAV
Mean PG - 30.7 mmHg

F/up Echo 1 week later
AVA - 0.49 cm$^2$
Leaflex Aortic Valve Remodeling

Current patient populations who might benefit

• Patient who are not candidates for TAVR – clinical and anatomic considerations (cohort “C” and some extreme risk patients)
• Patients with acute decompensation who after stabilization may be TAVR candidates (bridge to TAVR)
• Patients with symptoms which may or may not be AS-related, as a therapeutic trial to see if TAVR is indicated (e.g. AS + severe COPD)
• Geographies where economic constraints limit access to TAVR
Technology:
Leaflex™ – Vision

To provide a safe and effective non-implant based repair of Aortic Stenosis by addressing the fundamental issues – calcification and leaflet rigidity
Background:
10-year Research into Valve Calcification

- Valve calcification studied in **over 2,500** surgically excised human valves
- Leaflets imaged and tested to measure calcium distribution, thickness and mechanical properties
- Developed bench models using reconstructed human valves in pulse duplicators to study effect of repair techniques on hemodynamics

![Photo](image1.png)
![Back-light](image2.png)
![X-Ray](image3.png)
Technology:
Calcium Segmentation Restores Mobility

- Leaflet motion hindered when calcium covers natural folding lines ("hinges")
- When calcium is segmented/scored – mobility is restored
Technology:
Multiple scoring lines improves mobility

AVA - 0.65 cm²
AVA - 0.83 cm²
AVA - 1.03 cm²
AVA - 1.12 cm²
AVA - 1.15 cm²
AVA - 1.32 cm²
AVA - 1.49 cm²
AVA - 1.64 cm²
Technology: Scoring Mechanism of Action

- **Calcium** is encapsulated especially on the ventricular surface of the leaflet and is **brittle** and **easy to score** on the aortic surface.
- The ventricular layer maintains valve structure, is **elastic** and **resistant to cutting**.
- Applying a controlled force between Frame and Expander achieves scoring of calcium without lacerating the ventricular surface.
- Differential cutting widely applied in the treatment of vascular diseases.
Technology:
Leaflex™ Procedure
Technology:
Controlling Scoring Position and Depth

- Angular Alignment
- 27mm expansion
- Axial stopper
- Annular Plane
- 23-26mm annulus diameter
- 3mm depth
Clinical Experience:
Intra-Operative OUS Clinical Study, N=5

- Single-center: Krakow, Poland
- Objective - assess safety and acute performance of Leaflex™ in patients undergoing SAVR (intra-operative)
- 4 scorings per patient
- Force gauge used to assess change in valve resistance
- Leaflets then excised for visual, micro-CT and histological assessments
Clinical Experience:
Gross Pathology and Radiograph in a Clinical Case

Radiograph  Aortic view  Ventricular view

Figure showing the radiograph and corresponding aortic and ventricular views of the aortic valve, note the intact ventricular surface of the valve
Clinical Experience: Micro-CT and Histologic Analysis
Clinical Experience: Transfemoral OUS Clinical Experience

- **Study Objectives** - Safety, feasibility and acute performance when used in conjunction with TAVR in aortic stenosis patients

- **Safety Endpoint**
  - All-cause mortality and stroke at 30 days
  - Complications post Leaflex (observed prior to TAVR)

- **Performance Endpoint**
  - Successful Leaflex introduction, positioning, operating and withdrawal
  - Improvement in $\Delta P$ and/or AVA post Leaflex
  - Final valve implantation assessment

- **Patients** enrolled – 16 in 6 sites

- **Procedure** – Sentinel > four scoring cycles > TAVR

- **FU** at pre-discharge, 1 month and 3 months*

*IO-TF study includes 1 month FU only
Clinical Experience:
Example of Individual Patient Performance

- 81 y/o male
- NYHA Class II, LVEF – 48%
- Hypertension, diabetes, renal impairment, pulmonary hypertension
- Four scorings performed

<table>
<thead>
<tr>
<th>Aortic Valve Area (cm²)</th>
<th>Pre Leaflex</th>
<th>Post Leaflex</th>
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<tbody>
<tr>
<td>Pre</td>
<td>0.8 cm²</td>
<td></td>
</tr>
<tr>
<td>Post</td>
<td></td>
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Pre Leaflex

Post Leaflex
Clinical Experience:
Significant Improvement in Leaflets Mobility

Pre Leaflex™

Post Leaflex™
Clinical Experience:
Transfemoral OUS Clinical Study

Pi-Cardia’s Transfemoral Clinical Experience OUS

Patients Enrolled
N=16

No treatment/No scoring, N=5
N=4 Friction, modified
N=1 Friction, modified

Treated/Scoring, N=11

Effectiveness analysis - treated (scoring) patients, N=11

Safety analysis - all patients, N=16
Clinical Experience:
Summary of Treated Patients

**Aortic Valve Area (cm²) - Echo**

- Pre Leaflex™: 0.7
- Post Leaflex™: 1.2
- P = 0.001

**Mean Pressure Gradient (mmHg) - Echo**

- Pre Leaflex™: 33
- Post Leaflex™: 17
- P = 0.001

**Peak-to-Peak Pressure Gradient (mmHg) - Invasive**

- Pre Leaflex™: 51
- Post Leaflex™: 21
- P = 0.001

N = 10 for all graphs.
Clinical Experience:
Safety Summary

- All devices safely retrieved
- No injury of aortic valve leaflet
- Six patients had SAEs of interest:

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<th>Safety Population</th>
<th>Details</th>
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<tr>
<td>Non- Cardiac Death</td>
<td>Day 16 – found dead at home; dehydration</td>
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<tr>
<td>Stroke/LV perf</td>
<td>Secondary to LV perforation of GW between 3rd and 4th scoring; unrelated to device but related to procedure</td>
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<tr>
<td>Stroke/hypotension</td>
<td>Day 1 – in the setting of prolonged procedure with hypotension, due to inability to re-sheathe the device</td>
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<tr>
<td>Aortic regurgitation</td>
<td>Core-lab noted increase from mild to severe before TAVR without damage to the leaflet (wire across valve)</td>
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<tr>
<td>LBBB/PPM</td>
<td>Noted after Leaflex treatment/assessed as TAVR (CoreValve) procedure related</td>
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<tr>
<td>AV Block/PPM</td>
<td>Noted after Leaflex introduction/assessed as device related</td>
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Clinical Experience:
Lessons Learned & Integrated in Next Revision

**REV06**
- Narrower Frame for easy maneuvering
- Multiple sizes to cover larger range of annulus diameters
- Robust calcium scoring
- More scoring cycles with real time PG feedback
- Shorter LV section
- Lower axial forces

**REV07 – Target for EFS**
- 23mm
- Ø24mm
- Ø28mm
- 7mm
There is a growing population of patients with severe AS who might benefit from a safe and effective aortic valve remodeling technology.

The Leaflex device provides a precise pattern of leaflet scoring (aortic surface) which improves leaflet flexibility and increases AVA in bench models and in intra-operative proof-of-concept human studies.

In a feasibility study prior to TAVR, the transfemoral Leaflex procedure was successfully performed in 11 patients in EU with hemodynamic improvement (intra-procedure echos) in most patients.
A U.S. early feasibility study using Leaflex as sole therapy in patients who are not candidates for TAVR is planned to begin in 2020.
Clinical Role: Leaflex™ Along the Spectrum of AS Disease

<table>
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<tr>
<th>Severe Symptomatic AS</th>
<th>Intermediate / Low risk &gt; 75yrs</th>
<th>Low risk &lt; 75yrs</th>
<th>Severe Asymptomatic / Moderate AS</th>
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<td>Inoperable/High risk</td>
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**Favorable reimbursement for TAVR: US, Germany**

**TAVI Unfavorable**
- Pts. with comorbidities* where TAVI is excluded or of limited benefit
- Bridge to TAVI for patients undergoing another surgery/therapy
- Diagnostic means to understand if symptoms are due to AS

**Ideal for TAVI**
- Pts. with:
  - Definitive severe symptomatic AS
  - Reasonable comorbidities
  - Life expectancy >1yr but < TAVI durability

**Defer TAVI**
- Pts <75yrs to defer the need for TAVI and avoid complications of future Valve-in-Valve

**Early stage AS**
→ delay disease progression

**Less favorable / No reimbursement for TAVR: Canada, Belgium, Eastern EU, China, India, South America...**

Limited reimbursement for TAVR means no, or limited, access to TAVR

*Short life expectancy, COPD, acute pulmonary edema, infection, LFLG