HARPOON
Beating Heart
Mitral Valve Repair System

Envision a new way forward in surgical mitral valve repair
In the treatment of severe DMR*: the challenges are known, the future is clear

Surgeons are consistently seeking to improve the outcomes of DMR repair with simplicity, reproducibility, and reliable results.

Patients are looking for a less disruptive, low-risk option that can get them back to their lives more quickly.

We are focused on redefining the surgical experience for patients and surgeons, turning procedural challenges into new opportunities for better outcomes.

*DMR: Degenerative Mitral Regurgitation
Mitral disease is the most common valvular disease

- DMR covers a spectrum of lesions, involving single or multiple segments
- Most common finding in DMR is leaflet prolapse due to chordal elongation / rupture

- Treatment is highly complex, specialized
  - Multiple resectional / non-resectional techniques to achieve functional valve
  - Annuloplasty rings routinely used to provide stability and support to repair
The majority of severe Degenerative Mitral Regurgitation patients are untreated

Reasons eligible patients do not receive mitral surgery include:

- Asymptomatic
- Symptomatic but not diagnosed
- Not referred
- Patients refuse surgery

Reprinted from Head et al, EuroIntervention 2014
Mitral surgery patients are relatively young, at low-risk for surgery. DMR is the most common disease etiology.

Mean Age
(STS 2007-2010, n=40,093, isolated)\(^1\) 60 years

STS Risk
(STS 2007-2010, n=40,093, isolated)\(^1\) 82% low-risk

DMR
(Split of surgical mitral procedures today)\(^2\) 62% DMR

US Hospitals by Annual Mitral Volumes
(Gammie, Circulation, 2007)

Mitral cases / yr:
- 1-35
- 36-70
- 71-140
- >140

Repair rate:
- 47.7%
- 77.4%

Greater Volumes Associated with Better Outcomes for Patients
(Chikwe, JACC, 2017)

- Higher rates of repair (p<0.001)
- More durable outcomes (p=0.003)
- Improved patient survival (p<0.001)

2 Multiple sources (Gammie et al, Ann Thorac Surg 2018;106:716–27; Bach et al., JACC 2009;54:860-5; BCG; Junicon)
Mitral repair is associated with better outcomes than replacement.

For patients with degenerative leaflet prolapse undergoing surgical treatment, repair rates have been stable between 2011 and 2016 and approximated 80%.

Individual surgeon volume influences Mitral Valve repair rate and outcomes

5,475 DMR patients underwent MV operations in NY state

MV repair rate in Degenerative MV disease 67%

Higher total annual surgeon volume associated with
  - Increased repair rates
  - Steady decrease in reoperation risk
  - Improved 1-year survival

Surgeons perform median of 10 mitral valve procedures / year

Chikwe et al, J Am Coll Cardiol 2017;69:2397–406
Although mitral repair is the gold standard for severe DMR, challenges remain

**Cleveland Clinic Experience**

- 2,575 patients with isolated posterior leaflet repair
- Recurrent MR at 2 weeks:
  - Moderate: 6%
  - Severe or moderate-severe: 5%
- 89% of patients with ≤ mild MR at 2 weeks

**Surgical Arm of EVEREST II**

- 80 patients with surgical repair
- Replacement 14%
- One year surgical treatment results:
  - Death: 6%
  - Reoperation 1%
  - Recurrent moderate or severe MR: 17%
- 76% of patients with ≤ mild MR at 1 year

*Johnston et al, Ann Thorac Surg 2010;89:1385–94*  
*N Engl J Med 2011;364:1395-406*
Introducing reproducible, beating-heart, off-pump surgical mitral repair

A new procedure designed to improve outcomes in DMR repair

- **Performed off pump on a beating heart**
  - no cardiopulmonary bypass required, significantly reducing patient impact

- **Based on familiar surgical principles**
  - enables multiple chords to be deployed in mitral valve repair

- **Options preserved**
  - preserves the ability to perform future mitral valve repair

- **Guided by Echocardiography**
  - enables real-time chordal adjustment and confirmation of results

- **Elegant Simplicity**
  - in the least-invasive surgical procedure

- **Reliable Reproducibility**
  - with real-time confirmation of results
Re-envisioning the surgical experience

1. Reproducible Results
   - Simple delivery, Familiar surgical principles, Standardized procedure, No bridges burned

2. Elevate the surgical experience
   - Intuitive, Real-time confirmation of results; Echo-guided

3. Improving the patient experience
   - Off-pump, Beating-heart, 4-5 cm incision, Facilitates excellent safety and rapid patient recovery

Hemostatic Introducer
- Minimizes Blood Loss

Low Profile Delivery
- 9 Fr Shafted Instrument

Secure Anchoring
- Self Forming ePTFE anchor
HARPOON Beating Heart Mitral Valve Repair System

**TSD-5**
Delivery System

- Pre wound with ePTFE chord; single use device
- 9 Fr shaft; end effector to assist leaflet stabilization
- Device tip visible under echo guidance

**TAV-5**
Introducer

- Hemostatic; 3 chord pairs + device
- 12 Fr I.D., 14 Fr O.D.
- Dilatator and flush port equipped
HARPOON Delivery System (TSD-5)
HARPOON Introducer and Dilator (TAV-5)
Improving the patient experience

Least-invasive surgical procedure for mitral valve repair; facilitates excellent safety and rapid patient recovery

No cardiopulmonary bypass or sternotomy Required; < 5 cm left thoracotomy incision.

Ability to perform procedure through a non–rib-spreading technique in a 1- to 2-hour time frame, enabling faster return to normal activity.
For reliable repair, seeing is achieving; know before you close

<table>
<thead>
<tr>
<th>Place</th>
<th>Adjust</th>
<th>Confirm</th>
</tr>
</thead>
</table>
| • Accurate placement of knot anchors  
  • Placement of multiple chords | • Titration of chordal length and tensioning | • Confirmation of results prior to closure |

Collaborative echo guidance allows real-time chordal adjustment on the beating heart, ensuring optimal leaflet coaptation and reduction of MR.
TTE to identify optimal intercostal space; typically between 4th and 5th rib
Placement of soft tissue retractor
Finger ballottement performed on proposed entrance site
Incision between LAD and Diagonal, 2-4 cm basal to true apex
Targeting and deployment

- Device navigated to target on leaflet, per preoperative plan
- Leaflet stabilized with device tip
- Confirmation of desired location with 3D echo assessment
Tensioning under echo guidance; real time confirmation of results

- Stiff Teflon pledget used for secure anchoring
- Sutures tensioned together, removing any excess slack
- Knots visualized on leaflet free edge under TEE
- Progressive tensioning of chords to ensure coaptation; confirmation or results
Two prospective, multicenter, single-arm trials

- Patients with severe mitral regurgitation due to isolated posterior leaflet prolapse were treated with HARPOON system*
- Follow-up ongoing to 5 years
- Serious Adverse Events adjudicated by a Clinical Events Committee
- Echocardiographic analyses: Independent Core Laboratory (Massachusetts General Hospital – Judy Hung, M.D.)
- Aggregated experience from EFS and CE studies are reported here

*For EFS, patients with moderate-to-severe MR were included

**Early Feasibility Study (EFS)**
- N=13
- 2 Sites in Poland
- Patients enrolled Feb 2015-Feb 2016

**TRACER CE Mark Trial**
- N=52
- 6 Sites in Europe
- Patients enrolled Mar 2016-Nov 2017
Inclusion and exclusion criteria

**Key Inclusion Criteria**
- ≥18 years of age
- Severe degenerative mitral regurgitation*
- Isolated posterior leaflet prolapse
- Good predicted surface of coaptation

**Key Exclusion Criteria**
- Anterior or bileaflet prolapse
- Functional mitral regurgitation
- Infective endocarditis
- Severely calcified mitral leaflets
- Severe left ventricular dysfunction
- Renal insufficiency
- STS risk score* >6% or EuroSCORE II >8%

*For EFS, patients with moderate-to-severe DMR were included
*For mitral valve repair
Participating sites

EFS

John Paul II University Hospital, Krakow, Poland (n=10)
Institute of Cardiology, Warsaw, Poland (n=3)

TRACER CE Trial

John Paul II University Hospital, Krakow, Poland (n=11)
Institute of Cardiology, Warsaw, Poland (n=15)
The Royal Brompton Hospital, London, UK (n=8)
Southampton General Hospital, Southampton, UK (n=8)
Ospedale San Raffaele, Milan, Italy (n=4)
University of Padova Hospital, Padova, Italy (n=6)
Patient enrollment and follow-up

Enrolled (Intent to Treat)
N=65

Converted to open surgery n=2
Procedure aborted n=1

Implanted (As Treated)
N=62 (95.4%)

Death n=2
Study exit due to secondary intervention n=8

1-Year Follow-Up
N=52

Mean study follow up is 1.4 ± 0.6 years
One year clinical follow up was 100%
One year Echo core lab follow up for the 52 patients at 1 year was 100%

Data lock: Apr 2nd, 2019
<table>
<thead>
<tr>
<th><strong>Patient demographics</strong></th>
<th>% or Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>61 ± 12</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>76%</td>
</tr>
<tr>
<td><strong>STS PROM</strong></td>
<td>0.6 ± 0.6%</td>
</tr>
<tr>
<td><strong>EuroSCORE II</strong></td>
<td>1.2 ± 1.1%</td>
</tr>
<tr>
<td><strong>NYHA Functional Class I / II / III / IV</strong></td>
<td>41 / 41 / 19 / 0%</td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td>69 ± 6%</td>
</tr>
<tr>
<td><strong>Atrial Fibrillation</strong></td>
<td>19%</td>
</tr>
<tr>
<td><strong>LVEDD (mm)</strong></td>
<td>53.2 ± 5.2</td>
</tr>
</tbody>
</table>
# Intraoperative characteristics

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD (Range)</th>
</tr>
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<tbody>
<tr>
<td><strong>Total Procedure Time</strong> (minutes)</td>
<td>126 ± 36 (72-222)</td>
</tr>
<tr>
<td><strong>Introducer Time</strong> (minutes)</td>
<td>42 ± 18 (18-126)</td>
</tr>
<tr>
<td><strong>Intraoperative Blood Loss</strong>*(mL)*</td>
<td>272 ± 182 (50-949)</td>
</tr>
<tr>
<td><strong>Chords Implanted</strong></td>
<td>4.0 ± 1.1 (0-7)</td>
</tr>
</tbody>
</table>

* Data collected for TRACER CE Mark study only, N=51

EFS+CE ITT cohort
## Operative outcomes*

<table>
<thead>
<tr>
<th>Condition</th>
<th>% (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0% (0/62)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0% (0/62)</td>
</tr>
<tr>
<td>Reintubation**</td>
<td>0% (0/49)</td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>0% (0/62)</td>
</tr>
<tr>
<td>Atrial Fibrillation***</td>
<td>18% (9/50)</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>0% (0/62)</td>
</tr>
</tbody>
</table>

* Operative is defined as new onset complications from procedure through discharge

** Data collected for TRACER CE Mark study only

***Atrial Fibrillation only summarized for those without baseline Atrial Fibrillation
## Safety outcomes at 1 year

<table>
<thead>
<tr>
<th>Event</th>
<th>Cumulative Events</th>
<th>Probability Event Free (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>2</td>
<td>0.967 (0.922-1.000)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1</td>
<td>0.983 (0.950-1.000)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>1</td>
<td>0.984 (0.952-1.000)</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>0</td>
<td>1.000 (1.000-1.000)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>8</td>
<td>0.867 (0.781-0.953)</td>
</tr>
</tbody>
</table>
Severity of mitral regurgitation*

- Baseline: 93% None/Trace, 7% Moderate
- Discharge: 74% None/Trace, 21% Mild, 3% Moderate
- 30 Day: 62% None/Trace, 23% Mild, 13% Moderate
- 6 Month: 52% None/Trace, 29% Mild, 10% Moderate
- 1 Year: 52% None/Trace, 23% Mild, 23% Moderate

*Three patients had moderate MR at baseline per TTE but pre-procedure TEE showed severe MR
98% of patients in NYHA functional class I/II at 1 year

Baseline
N=59
30 Day
N=58
6 Month
N=57
1 Year
N=52

- NYHA Class I
- NYHA Class II
- NYHA Class III
Cardiac remodeling improvements sustained at 1 year

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>30 Day</th>
<th>1 Year</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD (mm)</td>
<td>53 ± 5</td>
<td>49 ± 5</td>
<td>47 ± 6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>69 ± 6</td>
<td>61 ± 5</td>
<td>62 ± 6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>153 ± 41</td>
<td>120 ± 28</td>
<td>120 ± 28</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MV Annular Diameter (mm)</td>
<td>35 ± 5</td>
<td>32 ± 5</td>
<td>31 ± 5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MV Gradient (mmHg)</td>
<td>NA</td>
<td>1.3 ± 0.5</td>
<td>1.4 ± 0.7</td>
<td>NA</td>
</tr>
</tbody>
</table>

* P-values were based on testing of baseline versus 1 year

EFS+CE AT cohort
Welcome to the future of surgical mitral valve repair

Elegant simplicity and reliable repair

Least-invasive surgical procedure

Real-time confirmation of results

Edwards continues its legacy of elevating surgical care in meaningful and lasting ways with the HARPOON Beating Heart Mitral Valve Repair System.
Thank you

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Edwards devices placed on the European market meet the requirements for bearing the CE marking of conformity.

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