First-in-human experience with percutaneous ventricular restoration therapy in patients with ischemic heart failure and dilated left ventricle: multi-slice computer tomography and 3-year outcome

Marco A. Costa, MD, PhD, FACC, FSCAI
Professor of Medicine, Director Interventional Cardiovascular Center
Director Research and Innovation Center
University Hospitals, Case Western Reserve University, Cleveland, OH

On Behalf of
Sinisa Gradinac, Ernest Mazzaferri, Horst Sievert, Igor Gregoric, Charlie Davidson, Peter Berger, Sinisa Gradinac, Albrecht Elsasser, Ron Waksman, Frank Smart, William Abernethy, Hiram Bezerra, William Abraham
Presenter Disclosure:

Advisory/Speaker Bureau: Boston Scientific, St Jude LightLab, Cordis, Abbott, Medtronic, Scitech, CardioKinetix

Institutional research support: St Jude LightLab, Cordis, Abbott, Medtronic
Rationale: **LV Volume and Geometry Link to Outcomes**

Konstam et al, JACC 2011

Kramer et al, J Am Coll Cardiol 2010
Percutaneous Ventricular Restoration

**Treatment Goal**

Improve heart function by:

- LV Volumes Reduction
- LVED Pressure Reduction
- Restoring LV Conical Shape
- Preserving Torsional Contraction
- Increase LV Apical Ejection
- Minimize risk of scar-related ventricular arrhythmias
Parachute Implant

- The Parachute™ device is comprised of a fluoropolymer (ePTFE) membrane stretched over a nitinol frame.
- Nitinol frame to support torsional contraction and optimize LV outflow ejection.
- Shape was designed to restore conical/longitudinal geometry.
- The device is deployed into the apex of the left ventricle and partitions off non-contractile damaged myocardium to reduce LV volume and optimize performance of contractile, healthy myocardial.

<table>
<thead>
<tr>
<th>Size Matrix</th>
<th>65</th>
<th>65s</th>
<th>75</th>
<th>75s</th>
<th>85</th>
<th>85s</th>
<th>95</th>
<th>95s</th>
</tr>
</thead>
</table>

CE Mark approval for 75, 75s, 85, and 85s. In the U.S., the Parachute system is an investigational device limited by federal law to investigational use only and is not available for sale.

#esc2012  www.escardio.org
Parachute Guide Catheters

- 3D MSCT Modeling (Ao Arch, LVOT, LV Apex)
- 14Fr and 16Fr Delivery systems (multiple shapes)
- Kink Resistant construct
Parachute Pre-Clinical Data
Mechanism of Action

Mechanical Efficiency Improved by 22%

External Work
[External Work + Potential Energy]

Westerhof N Cardiovasc Res 2000;48:4-7
Present Study Aims: To evaluate percutaneous ventricular restoration (PVR) therapy utilizing a partitioning device, Parachute, by Computer Tomography (CT) and assess long-term 3-year clinical outcomes.
### Parachute: First-in-Human Trials

<table>
<thead>
<tr>
<th></th>
<th>EU FIH (Cohort A)</th>
<th>US FIH</th>
<th>EU (Cohort B)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled</td>
<td>19</td>
<td>20</td>
<td>44</td>
<td>83</td>
</tr>
<tr>
<td>Implanted per Protocol</td>
<td>16</td>
<td>18</td>
<td>44</td>
<td>78</td>
</tr>
<tr>
<td>Discharged with Device</td>
<td>14</td>
<td>17</td>
<td>44</td>
<td>75</td>
</tr>
<tr>
<td>6M FU</td>
<td>14</td>
<td>15</td>
<td>20</td>
<td>49</td>
</tr>
<tr>
<td>1Y FU</td>
<td>14</td>
<td>14</td>
<td>4</td>
<td>32</td>
</tr>
<tr>
<td>2Y FU</td>
<td>14</td>
<td>13</td>
<td></td>
<td>27</td>
</tr>
<tr>
<td>3Y FU</td>
<td>13</td>
<td>12</td>
<td></td>
<td>25</td>
</tr>
</tbody>
</table>

### Patient Population

- NYHA Class II-IV, EF >15% and ≤ 40%, Post LAD MI
- Dilated apical region with akinetic or dyskinetic wall motion abnormality
- Warfarin and ASA 1yr post implant

*Independent Clinical Event Adjudication*

*Independent Echocardiographic, EKG, and MSCT Core Labs*
LV Volume and Segmental function

PRE

Post Parachute implant
LV Geometric Analysis

Sphericity Index (SPI)

SPI = \frac{\text{Volume cavity (EDV or ESV)}}{\text{Volume of a sphere}}
(derived from LV long axis Length)

SID = 0.49
LAx = 94mm
EDV = 214
LV Geometric Analysis

Sphericity Index (SPI)
SPI = Volume cavity (EDV or ESV)
Volume of a sphere
(derived from LV long axis Length)

SID = 0.29
LAx = 109mm
EDV = 198ml
Parachute Implantation Assessment

✓ Foot distance from Apex
✓ Wall Apposition
✓ Device Orientation/Angulation:

**Angle measurements:**
Parachute “landing zone” and the LV short-axis at the highest level of the device landing zone (B).

- **Lateral Angle:** (A)
  Calculated in the 4 chamber view

- **Inferior angle:** (C)
  Calculated in the 2 chamber view
Parachute Safety Summary

• Procedural – All aspects similar to a standard PCI\textsuperscript{1,2}
  – Procedure duration – 80 minutes / Fluoroscopy time – 20 minutes
  – 2 Inadequate Attachments
    • Corrective actions (MSCT screening, ePTFE membrane improvements)

• Procedure Complications\textsuperscript{3}
  – Major Vascular Complications – 0%
  – Minor Vascular Complications – 14.7%

• 0% device related Death or Stroke by 1 Year

3-Year NYHA

Baseline 6M 12M 24M 36M

p < 0.0001
3-Year Cardiac Death

6.5%
3-Year Repeat HF Hospitalization

Time (Days from Procedure)

0 365 730 1095

0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1

29.7% 33.0%

HF Hospitalization

Repeat

Year
3-Year Repeat HF Hosp. + Death


#esc2012 www.escardio.org
Calcium assessment

60 patients treated with Parachute

Calcium at the landing zone = 15%
> 90 degrees = 8.3%

No impact on device anchoring or stability
Parachute Optimal Implant
Parachute Sub-Optimal Implant

Foot Away from Apex

Wall Malapposition

High Inferior Angulation

High Lateral Angulation
Segmental Wall Motion by MSCT

- Sub-study (N=14), Baseline and 6M FU
- Anterior Wall Segmental EF%
  - Baseline – 22.8%
  - 6M Follow-up – 22.6%

- Non-Anterior Wall Segmental EF%
  - Baseline – 25.6%
  - 6M Follow-up – 28.6%
  +12% p=NS
Baseline MSCT Parameters and Cardiac Death or Worsening HF @ 3y FUP

Volumes expressed in mm\(^3\), areas in mm\(^2\), diameters/perimeter in mm.
Ejection Fraction expressed in %, angles expressed in degrees (°)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HF Event n=10</th>
<th>NO HF Event n=10</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV</td>
<td>262.2</td>
<td>225.3</td>
<td>0.1963</td>
</tr>
<tr>
<td>EDV Sphericity Index</td>
<td>0.4234</td>
<td>0.374</td>
<td>0.1724</td>
</tr>
<tr>
<td>EF</td>
<td>28.125</td>
<td>30.693</td>
<td>0.5793</td>
</tr>
<tr>
<td>ESV</td>
<td>190.4</td>
<td>156</td>
<td>0.1896</td>
</tr>
<tr>
<td>ESV Sphericity Index</td>
<td>0.3447</td>
<td>0.3094</td>
<td>0.2233</td>
</tr>
</tbody>
</table>
MSCT 6-Month Post Parachute Implant and Cardiac Death or Worsening HF @ 3y FUP

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HF Event</th>
<th>NO HF Event</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=7</td>
<td>n=14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Device Inferior Angle</td>
<td>24.4571</td>
<td>17.4171</td>
<td>0.0701</td>
</tr>
<tr>
<td>Device Lateral Angle</td>
<td>13.0671</td>
<td>8.4864</td>
<td>0.1781</td>
</tr>
<tr>
<td>Device Malapposition area</td>
<td>4.6594</td>
<td>3.0039</td>
<td>0.1445</td>
</tr>
<tr>
<td>Difference of Landing Zone Area (EDV-ESV)</td>
<td>1.0833</td>
<td>8.1556</td>
<td>0.0395</td>
</tr>
<tr>
<td>Difference of Landing Zone Max Diameter (EDV-ESV)</td>
<td>0.8667</td>
<td>11.5818</td>
<td>0.0696</td>
</tr>
<tr>
<td>Difference of Landing Zone Perimeter (EDV-ESV)</td>
<td>3.5</td>
<td>32.1818</td>
<td>0.0954</td>
</tr>
<tr>
<td>Foot Distance from Apex</td>
<td>8</td>
<td>1.7207</td>
<td>0.0712</td>
</tr>
<tr>
<td>EDV</td>
<td>230.9</td>
<td>183.7</td>
<td>0.0934</td>
</tr>
<tr>
<td>EDV Sphericity Index</td>
<td>0.7454</td>
<td>0.4732</td>
<td>0.0259</td>
</tr>
<tr>
<td>EF</td>
<td>33.168</td>
<td>36.4156</td>
<td>0.7054</td>
</tr>
<tr>
<td>ESV</td>
<td>153.1</td>
<td>118.3</td>
<td>0.1929</td>
</tr>
<tr>
<td>ESV Sphericity Index</td>
<td>0.5382</td>
<td>0.3299</td>
<td>0.0037</td>
</tr>
</tbody>
</table>
Changes in MSCT Parameters 6-Month Post Parachute and Cardiac Death or Worsening HF @ 3y FUP

HF EVENT (n=5)  
NO HF EVENT (n=9)

Δ EDV
Δ EF
Δ ESV

Sphericity Index

P=0.035
P=0.098

Δ ESV
Δ EDV

-60 -40 -20 0 20

Delta = follow-up – baseline

Volumes expressed in mm³, Ejection Fraction expressed in %

ESC Congress 2012
#esc2012 www.escardio.org
PARACHUTE Outcomes in Perspective

1-Year Repeat HF Hosp. + Death

Aggregate data from CHAMPION, MIRACLE, COMPANION, MIRACLE ICD, RETHINQ, CRT-HF, FIX, CARE, and PARACHUTE. 12M estimates were made if only 6M data was published (6M x 1.5 = 12M)
Conclusions

✓ The first series of ischemic HF patients treated with Percutaneous Ventricular Restoration (PVR) using the Parachute™ device had a relatively low incidence of clinical events up to 3 years suggesting a plateau of the progression of heart failure.

✓ MSCT analysis provided important insights on factors that may impact outcomes after PVR therapy in the future. In particular, the present pilot data highlights the importance of patient selection and optimal device implantation.

✓ Recent enhancements in delivery system, availability of multiple shapes and device sizes, and use of MSCT for screening and procedure planning may further improve overall outcomes, which requires confirmation in the large scale PARACUTE III (EU) and PARACHUTE IV Pivotal (USA) Trials already underway.