Percutaneous Ventricular Restoration using the Parachute® Device in Patients with Ischemic Heart Failure: Three-year Outcomes of the PARACHUTE First-in-Human Study

Costa et al: Three-Year Outcomes post Percutaneous Ventricular Restoration

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DOI: 10.1161/CIRCHEARTFAILURE.114.001127

Journal Subject Codes: Etiology:[7] Chronic ischemic heart disease, Heart failure:[110] Congestive
Abstract

Background—Left ventricle (LV) remodeling after anterior wall myocardial infarction leads to increased LV volumes, myocardial stress, and ultimately heart failure (HF). Treatment options are limited for these high-risk HF patients. A study was conducted to assess safety and feasibility of a percutaneous ventricular restoration (PVR) therapy using the Parachute® device in subjects with HF due to a cardiac ischemic event.

Methods and Results—Thirty-nine subjects with New York Heart Association (NYHA) Class II-IV ischemic HF, ejection fraction (EF) between 15% and 40%, and dilated akinetic or dyskinetic anterior-apical wall without the need to be revascularized, were enrolled in a prospective, non-randomized, multi-center investigation testing PVR using the Parachute device. The safety primary endpoint was defined as successful procedure without device-related major adverse cardiac events (MACE) over 6-months. Clinical and echocardiographic outcomes were obtained at 6, 12, 24 and 36-months post treatment. Echocardiographic and endpoint data were adjudicated independently. Of the 39 subjects enrolled, device implantation was attempted in 34 and successful in 31 patients. Twenty-three subjects reached 3-years post treatment with the device implanted. NYHA symptom class was improved or maintained in 85% of subjects. Left ventricle end-diastolic volume index (EDVi) and end-systolic volume index (ESVi) were reduced from 128·4±22·1 ml/m² and 94·9±22·3 ml/m² pre-implant to 115·2±23·1 ml/m² and 87·3±18·7 ml/m² at the 3-years follow-up (EDVi p=0·0056, ESVi, p=0·4719), respectively. The cumulative incidence of HF hospitalizations or death were 16·1%, 32·3% and 38·7% at 12, 24 and 36-months respectively. By 3-years follow-up, two (6·5%) of the 31 patients with successful implant had died from cardiac reasons, with no cardiac deaths occurring past 6-months post treatment.

Conclusions—The first series of ischemic HF patients treated with PVR using the Parachute device demonstrates feasibility and safety of the device up to 3-years post treatment.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifiers: NCT00573560 (US patients) and NCT01286116 (EU patients).

Key Words: ischemic heart failure, structural heart, left ventricle remodeling
The process of left ventricle (LV) dilatation and remodeling after MI has been well documented in experimental and clinical investigations. Progressive LV dilatation or remodeling post myocardial infarction occurred in 33% of patients enrolled in the GISSI-3 trial (n=13,679). Advances in the treatment of myocardial infarction may have reduced the incidence of LV dilation post MI, but once heart failure (HF) develops the overall one year mortality percentage remains unacceptably high at 32% in spite of modern pharmacological and mechanical approaches. Therapeutic efficacy depends, albeit not exclusively, on improvements in LV volumes and geometry. Left Ventricular end-systolic and end-diastolic volumes are surrogate measures of LV remodeling and have been shown to be independent clinical predictors of outcomes in HF patients. The treatment goal for this group of patients is to reduce LV volume thereby reducing wall stress and reshape the LV to improve flow dynamics.

The concept of percutaneous ventricular restoration (PVR) of the LV is based on the premise that a dedicated partitioning device delivered via a catheter-based approach may achieve LV volume reduction and geometric reconfiguration while minimizing the risk of a more invasive method. The Parachute device was designed with a conical nitinol frame covered with fluoropolymer (ePTFE) membrane that can be compressed into a delivery catheter and deployed into the LV apex to partition off akinetic or dyskinetic myocardium (Figure 1). Three-years echocardiographic and clinical outcomes of the first series of ischemic HF subjects treated with PVR using the Parachute device are presented in this manuscript.
Methods

Study Design

The PARACHUTE first-in-human study was a prospective, single-arm study conducted in 10 medical centers in the U.S. and Europe. The study was designed to assess the safety and feasibility of the Parachute device. Following implantation of the device, clinical and echocardiographic follow-up was performed at 6-months and annually out to 3-years.

Patient Selection

The study included subjects with symptomatic ischemic HF of the New York Heart Association (NYHA) Classes II-IV. The subjects had to be at least 18-years of age with LV wall motion abnormalities (anteroapical akinesis or dyskinesis) secondary to myocardial infarction, an LV ejection fraction between 15% and 40% and managed with stable doses of standard HF medical therapy for at least 3 months. Subjects with myocardial ischemia requiring revascularization within 60 days, those with revascularization or cardiac resynchronization therapy within 60 days, and those with significant valve disease were excluded from the study. All sites obtained approval from an Institutional Review Board (IRB) or Ethics Committee (EC) before study commencement and written informed consent was obtained for all subjects at the appropriate time prior to involvement in the study.

Study Device and Procedure

The Parachute system includes the device (Parachute), a delivery system, a balloon that facilitates expansion of the device, and a pre-shaped delivery catheter and dilator (Figure 1). The Parachute device is comprised of a self-expanding nitinol frame, an ePTFE impermeable membrane, and an atraumatic polymer foot. The nitinol frame has a conical shape with 16 struts. At the time of this investigation, the device had two sizes (75 and 85 mm). The tip of each strut
ends in a 2 mm anchor. The anchors engage the myocardium and help stabilize the device. The
distal atraumatic foot is radio-opaque and provides a contact point between the LV apex and the
Parachute device in addition to facilitating visualization to ensure proper placement.
The procedure (Figure 2) is performed in a catheterization laboratory, and subjects are under
conscious sedation. Per protocol, subjects were considered enrolled if they signed a consent
form, underwent a baseline evaluation, and had a successful placement of a 14 Fr or 16 Fr sheath
in the femoral artery. Device size selection was initially based on echocardiography assessment
of the LV mid-cavity at the intended site of device anchoring. After the first 15 cases, multi-
slice computed tomography was implemented to provide accurate measurements and rule-out LV
apical thrombus and severe calcification which would preclude safe deployment of the device.
The LV was accessed via femoral approach using a conventional pig-tail wire. A stiff 0·035
inch wire was positioned in the LV for support. The pre-shaped catheter was then placed near
the LV apex. The Parachute device was advanced through the sheath guided by fluoroscopy
until the foot was exposed. The delivery system was then advanced until the foot was in contact
with the LV apex. Proper position was confirmed by fluoroscopy and or trans-thoracic
echocardiography. The device was deployed by retracting the delivery catheter, exposing the
device frame. Self-expansion of the Parachute device was facilitated by inflating a low-pressure
contrast-filled 6-ml balloon with a nominal diameter of 24 mm until the anchors were fully
expanded and in contact with the LV wall. The device remained attached to the delivery system
after deployment and contrast LV angiography was performed to confirm correct positioning
before releasing the device. After device release, a final LV angiography was performed, all
catheters were removed, and when appropriate, the femoral access sheath was removed. All
subjects were required to receive 12-months of aspirin and 6-months of clopidogrel post device
implant. It was also recommended that subjects be placed on anticoagulation with warfarin for 3 months post device implant.

**Data Collection and Oversight**

All study related data were collected on standardized case report forms. All protocol-mandated echocardiograms were sent to an independent core laboratory (University of Pennsylvania Medical Center, Philadelphia, PA). Data management was performed by an independent contract research organization and an independent data safety monitoring board (DSMB) met frequently to oversee the trial and provide recommendations on study progress. An independent clinical events committee (CEC) adjudicated serious adverse events (AEs), cardiac and non-cardiac deaths, and heart failure hospitalizations, and determined the relationship with device and procedure.

**Study Endpoints**

The primary safety endpoint of the PARACHUTE study was defined as the successful delivery and deployment of the device without the occurrence of device related major adverse cardiac events (MACE) up to 6-months post-procedure. MACE was broadly defined and included the occurrence of any of the following: cardiac death, emergent cardiac surgery, erosion of the device through the LV, cardiac tamponade, peripheral embolization (including stroke), new or worsening heart failure, endocarditis or device infection, device migration or embolization, or placement of a mechanical support device. Worsening heart failure hospitalization was defined as an unplanned hospitalization that results in at least one overnight stay (i.e., where the admission date and the discharge date are different) that includes increased signs and/or symptoms of worsening heart failure including increased jugular venous pressure (JVP) and requires the administration or augmentation of intravenous heart failure therapy (e.g., inotropes,
diuretics, and/or vasodilators). Vascular complications were defined using an expanded Valve Academic Research Consortium (VARC) definition that includes damage of the aortic valve requiring surgery.\(^5\) Secondary efficacy endpoints included serial hemodynamic measurements determined by echocardiography (LV volume indices, EF, and stroke volume [SV]) and functional parameters. A sub study was performed in 10 patients measuring LVEDP at baseline and 6-month follow up with a Swan-Ganz catheter. In order to measure functional status and quality of life, subjects underwent a standardized 6-minute walk-test and Minnesota Living with Heart Failure (MLWHF) quality of life assessment at clinic visits up to 1-year post treatment.

**Statistical Analysis**

Baseline characteristics were summarized using mean ± SD for continuous variables and counts and percentages for categorical variables. Continuous variables assessed over time were evaluated using a linear mixed model with variance components covariance structure, controlling for baseline values and categorical visit. Least squares means and standard errors were presented for scheduled time points, and p-values presented for pairwise comparisons between visits and baseline. Death, stroke, end-stage heart failure utilization of LVAD or heart transplant, and heart failure re-hospitalizations were evaluated using Kaplan-Meier analysis. All analyses were performed using SAS version 9.3 (SAS, Cary NC).

**Results**

Between October 2005 and June 2009, 39 subjects were enrolled at 10 sites in the U.S. and Europe. Thirty-one subjects were discharged with the Parachute device and followed-up for hemodynamic, functional, and clinical outcomes. The mean follow-up time for this population was 2.6 years. The number of patients who completed three year follow-up is shown in Figure 3.
Procedural Outcomes

Of the 39 consented subjects, no attempt to deliver the Parachute device was made in 5 subjects due to anatomical reasons. Three of the 34 treated subjects (Table 1) had the device explanted prior to discharge due to: 1) the nitinol frame did not fully expand likely due to the thickness of ePTFE in the first generation device construct, 2) LV calcification prevented the device from being secured, and 3) unrelated splenic abscess with sepsis resulting in precautionary device removal at day 15 post implant. Minor vascular complications related to the femoral access site were noted in 14.7% (4/34) of subjects. There were no major vascular complications or aortic valve injuries.

Hemodynamic and Functional Outcomes

At the 3-year follow-up echocardiograms were available for 20 of the 23 active subjects. Figure 4 shows NYHA class distribution over 3 years post procedure. Symptomatic improvements were evident in 52% of the subjects, with no change in 33% and worsening in 15% of the subjects through 3-years follow-up. The MLWHF and 6-minute walk-test have been reported previously in the 12-months follow-up report. Complementary data supporting the hemodynamic and functional improvements were collected on a subset of patients. Invasive pressure monitoring data were available in 10 subjects showing a 29% reduction in LV end-diastolic pressure at 6-months post-procedure (p<0.05). Available serial echocardiographic data are reported in Table 2, Table 3, Figure 5, and Figure 6. Improvements in LV volume indices were sustained through the 3-year follow-up. In contrast to other interventions such as neurohormonal antagonists and CRT, the Parachute device reduction in LV volume occurs immediately post treatment with no further decrease over time.
Clinical Outcomes

The primary safety endpoint, defined as the successful delivery and deployment of the Parachute device through 6-month follow-up without the occurrence of Major Adverse Cardiac Events (MACE) related to the investigational device, was met by 29 of 34 patients (85.3%). The incidences of clinical adverse events for 12, 24 and 36-months are listed in Table 4. There were no strokes at 1-year follow-up, one ischemic stroke at 24-month follow-up and one ischemic and two hemorrhagic strokes at 36-month follow-up. No cardiac deaths occurred after 6-months post treatment and the overall 3-years incidence of death was 13.9%. Non cardiac deaths occurred in 2 subjects. One death, in relation to lung cancer, occurred at 28-months and the other death, related to cerebral hemorrhage occurred at 29-months. The 3-year cumulative incidence of HF hospitalizations was 33%. The combined measure of death or heart failure hospitalization was 38.7% (Figure 7).

Discussion

The PARACHUTE study introduces a novel approach, namely percutaneous ventricular restoration (PVR), to treat subjects with ischemic HF and akinetic or dyskinetic anterior-apical wall. The long-term outcomes observed in this first series of subjects treated with the Parachute device demonstrated the feasibility and safety of PVR. These preliminary results show reduction of left ventricle volumes for up to 3-years post implant, and concomitant improvements in HF symptoms. There were no cardiac deaths past 6 months and the risk of hospitalization between year 2 and 3 was <5%. In absence of a control group, these findings should be interpreted cautiously.

Medications such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, and aldosterone antagonists remain the cornerstone of HF therapy.7 Patients with
advanced HF and ventricular dyssynchrony are most likely to benefit from simultaneous pacing of both right and left ventricles. In addition, surgical interventions to repair dysfunctional cardiac valves, bypass coronary artery disease, left ventricular assist devices (LVAD), and ultimately heart transplantation are integral components of modern strategies to improve outcomes of subjects with HF. In spite of these advances in both pharmacological and mechanical therapeutic approaches to HF, the overall mortality remains high at 32% in the first year after a HF hospitalization. Five year mortality from Framingham Heart Study and Hillingdon Heart Failure Study after the onset of heart failure was 65%. A recent meta-analysis highlighted the critical role of LV end-systolic and end-diastolic volume reduction for the success of pharmacological and mechanical approaches to HF. However, the data reported in this report has to be interpreted with caution as the compiled data did not include mechanical or direct reduction of LV volume, such as produced by PVR therapy. Reduction in LV volumes in subjects with dilated cardiomyopathy has been the target of SVR, with promising results reported by experienced centers. Unfortunately, the ability to surgically reconstruct an elliptical shape of the LV cavity with appropriate degree of volume reduction may vary significantly among operators. Furthermore, the SVR approach is not without operative risk and it has been associated with malignant ventricular arrhythmias. A recent multicenter trial investigating the role of SVR combined with coronary artery bypass grafting (CABG) was unable to demonstrate clinical benefits when compared to CABG alone. Several hypotheses have been postulated to explain the failure of SVR in STICH, including the fact that 50% of the subjects did not have akinetic/dyskinetic wall motion, the study entry criteria were based on ischemic symptoms with 50% of subjects in NYHA class I-II HF, and thus reduction in LV volumes were relatively modest. A recent study using untagged magnetic resonance images to
create patient-specific mathematical left ventricular models before and after SVR provided a mechanistic explanation to the STICH trial results. The authors noted increase in left ventricular sphericity after SVR, which contributes to a depressed Starling relationship and diastolic dysfunction that likely counter-balanced the potential beneficial effects of LV volume reduction.17

A percutaneous approach to ventricle restoration may achieve volume reduction with a more reproducible reconfiguration of the conical shape of the LV cavity in a less invasive manner. The Parachute device is the first device designed specifically for PVR to treat subjects who have ischemic cardiomyopathy with akinetic/dyskinetic anterior wall motion and heart failure symptoms. The device shape was designed to partition the damaged, non-contractile myocardium while creating a new apex and restoring the elliptical shape of the LV cavity in a reproducible manner. The nitinol construct permits contraction of the underlying healthy myocardium. The percutaneous nature of the procedure, which is performed under local anesthesia, may minimize operative risk and avoid suture-related myocardial scar. There are several possible mechanisms by which the implant of the Parachute device may improve cardiac performance and explain these preliminary positive results: 1) Reduction of volumes and partition of non viable myocardium may reduce contractile wall stress; 2) the shape of the device and its nitinol framing may help restore the elliptical shape of the LV cavity and allow systolic torsion, respectively; 3) partition of the scarred anteroapical wall with a conical shaped nitinol frame covered with ePTFE may improve diastolic compliance. The ongoing, large, U.S pivotal trial, PARACHUTE IV, will examine paired echocardiographic data to further define this response to treatment and to assess the more subtle changes of myocardial performance such as strain analysis, E/E' and other measures of diastolic function.
Limitations

The study does have limitations given its small sample size and unblinded, single-arm nature. Because of this study design, one cannot rule out potential bias in the adjudication process and without a control group efficacy conclusions cannot be made.

Conclusions

The favorable long-term outcomes observed in this high-risk population are certainly not definitive, but provide reassuring safety and feasibility data to support further investigations. The ongoing large-scale, randomized clinical trial in the United States will be critical to validate the present results and establish the role of this novel therapeutic approach for patients with ischemic HF.

Appendix

Sinisa Gradinac, MD, PhD, FETCS³, Dragan Sagic, MD³, Petar Otasevic, MD³, Ayesha K. Hasan, MD, FACC², Thomas L. Goff, MD²; Nina Wunderlich, MD⁴, Venita DePuy, PhD⁵,⁶, and Frank Smart, MD⁷, and the PercutAneous Ventricular RestorAtion in Chronic Heart failUre PaTiEnts (PARACHUTE) Study Group

From the ³Dedinje Cardiovascular Institute, University of Belgrade School of Medicine, Belgrade, Serbia; ⁴CardioVascular Center, Sankt Katharinen, Germany; ⁵Bowden Analytics, Apex, North Carolina, ⁶Clinipace Worldwide, Morrisville, North Carolina ⁷Louisiana State University, New Orleans, LA
Sources of Funding

The PARACHUTE trial was funded by CardioKinetix, Inc. No extramural funding was used to support the creation of this manuscript. The authors are solely responsible for the design and conduct of this study, the study analyses, the drafting and editing of the paper and its final contents.

Disclosures

Marco A. Costa and William T. Abraham are paid consultants for CardioKinetix.

Venita DePuy is a statistician hired by CardioKinetix.

Sinisa Gradinac has been paid in the past to consult for CardioKinetix.

Horst Sievert has received stock options as compensation for consulting.

All other authors do not have any conflicts of interest.

References


## Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device Success</td>
<td>91% (31/34)</td>
</tr>
<tr>
<td>Age, years</td>
<td>56.4 ± 9.8</td>
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<tr>
<td>Gender, male</td>
<td>88% (30/34)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>94.2 ± 21.5</td>
</tr>
<tr>
<td>Height, cm</td>
<td>174.9 ± 7.4</td>
</tr>
<tr>
<td>Smoking History</td>
<td>75% (21/28)</td>
</tr>
<tr>
<td>History of Stroke</td>
<td>12% (4/34)</td>
</tr>
<tr>
<td>History of Hypertension</td>
<td>59% (20/34)</td>
</tr>
<tr>
<td>History of Diabetes</td>
<td>41% (14/34)</td>
</tr>
<tr>
<td>History of Dyslipidemia</td>
<td>79% (23/29)</td>
</tr>
<tr>
<td>Prior ICD Implantation</td>
<td>50% (17/34)</td>
</tr>
<tr>
<td>Prior CRT Device</td>
<td>12% (14/34)</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>53% (18/34)</td>
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<tr>
<td>Prior CABG Surgery</td>
<td>24% (8/34)</td>
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<tr>
<td>HF Hosp. 12M Before Enrolled</td>
<td>39% (7/18)</td>
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<tr>
<td>LV Wall Motion Types</td>
<td></td>
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<tr>
<td>Akinetic</td>
<td>56% (19/34)</td>
</tr>
<tr>
<td>Dyskinetic</td>
<td>26% (9/34)</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>18% (6/34)</td>
</tr>
</tbody>
</table>

Data is presented as either percent or mean ± SD for subjects where treatment was attempted.
Table 2. Least Square Means and Standard Error of Serial Echocardiogram Results for Treated Subjects

<table>
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<th>Baseline (N=30)</th>
<th>6M (N=29)</th>
<th>p-value†</th>
<th>12M (N=28)</th>
<th>p-value‡</th>
<th>24M (N=27)</th>
<th>p-value‡</th>
<th>36M (N=20)</th>
<th>p-value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV EDVi‡</td>
<td>127.7 (2.92)</td>
<td>105.8 (3.02)</td>
<td>&lt;.0001</td>
<td>108.7 (3.08)</td>
<td>&lt;.0001</td>
<td>112.8 (3.14)</td>
<td>0.0006</td>
<td>115.5 (3.67)</td>
<td>0.0103</td>
</tr>
<tr>
<td>LV ESVi‡</td>
<td>93.9 (2.49)</td>
<td>74.1 (2.58)</td>
<td>&lt;.0001</td>
<td>77.0 (2.62)</td>
<td>&lt;.0001</td>
<td>81.6 (2.67)</td>
<td>0.0009</td>
<td>89.4 (3.13)</td>
<td>0.2638</td>
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<tr>
<td>Cardiac Output</td>
<td>4.5 (0.24)</td>
<td>4.0 (0.25)</td>
<td>0.6986</td>
<td>4.0 (0.27)</td>
<td>0.1352</td>
<td>4.4 (0.26)</td>
<td>0.6844</td>
<td>3.5 (0.32)</td>
<td>0.0118</td>
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<tr>
<td>LV Length</td>
<td>10.1 (0.11)</td>
<td>8.8 (0.11)</td>
<td>&lt;.0001</td>
<td>8.6 (0.11)</td>
<td>&lt;.0001</td>
<td>8.6 (0.11)</td>
<td>&lt;.0001</td>
<td>8.6 (0.13)</td>
<td>&lt;.0001</td>
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<tr>
<td>EF</td>
<td>27.0 (1.13)</td>
<td>30.0 (1.17)</td>
<td>&lt;.0001</td>
<td>29.5 (1.19)</td>
<td>0.1390</td>
<td>27.8 (1.21)</td>
<td>0.6425</td>
<td>23.0 (1.42)</td>
<td>0.0269</td>
</tr>
<tr>
<td>Stroke Volume</td>
<td>69.0 (3.09)</td>
<td>64.7 (3.20)</td>
<td>0.3274</td>
<td>65.0 (3.26)</td>
<td>0.3674</td>
<td>64.4 (3.32)</td>
<td>0.3049</td>
<td>53.3 (3.90)</td>
<td>0.0019</td>
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<tr>
<td>Heart Rate</td>
<td>64.2 (1.50)</td>
<td>65.9 (1.56)</td>
<td>&lt;.0001</td>
<td>63.6 (1.67)</td>
<td>&lt;.0001</td>
<td>68.7 (1.63)</td>
<td>0.0424</td>
<td>67.0 (1.96)</td>
<td>0.2478</td>
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<tr>
<td>LV Mass</td>
<td>285.6 (8.39)</td>
<td>273.9 (9.27)</td>
<td>0.3497</td>
<td>289.2 (9.02)</td>
<td>0.7736</td>
<td>278.0 (9.54)</td>
<td>0.5525</td>
<td>279.1 (11.86)</td>
<td>0.6540</td>
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† p values indicate whether changes from baseline are significantly different from zero at each time point, and are for informational purposes only. No adjustments for multiple comparisons were performed. EF = ejection fraction (%), EDVi = end diastolic volume index (ml/M2), ESVi = end systolic volume index (ml/M2), Cardiac Output (L/minute), LV Length – diastolic longitudinal length (cm), Stroke Volume (ml), Heart Rate (beats per minute), LV Mass (grams)

‡The functional LV volume is used in the follow-up echo variables. The functional volume is defined as total LV volume less the partitioned volume by the Parachute Device (Figure 6).
Table 3. Least Square Means and Standard Error of Serial Echocardiogram Results for Treated Subjects with Complete 36 Month Longitudinal Data

<table>
<thead>
<tr>
<th></th>
<th>Baseline (N=19)</th>
<th>6M (N=19)</th>
<th>p-value†</th>
<th>12M (N=19)</th>
<th>p-value‡</th>
<th>24M (N=19)</th>
<th>p-value‡</th>
<th>36M (N=19)</th>
<th>p-value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV EDVi‡</td>
<td>125·7 (3·04)</td>
<td>109·4 (3·04)</td>
<td>0·0002</td>
<td>108·9 (3·04)</td>
<td>0·0001</td>
<td>108·9 (3·04)</td>
<td>0·0057</td>
<td>114·4 (3·04)</td>
<td>0·0095</td>
</tr>
<tr>
<td>LV ESVi‡</td>
<td>89·6 (2·60)</td>
<td>77·1 (2·60)</td>
<td>0·0009</td>
<td>76·7 (2·60)</td>
<td>0·0006</td>
<td>76·7 (2·60)</td>
<td>0·0130</td>
<td>87·0 (2·60)</td>
<td>0·4792</td>
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<td>Cardiac Output</td>
<td>4·4 (0·33)</td>
<td>4·4 (0·33)</td>
<td>0·9982</td>
<td>3·9 (0·33)</td>
<td>0·2672</td>
<td>3·9 (0·33)</td>
<td>0·8996</td>
<td>3·4 (0·33)</td>
<td>0·0299</td>
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<tr>
<td>LV Length</td>
<td>10·1 (0·11)</td>
<td>9·0 (0·11)</td>
<td>&lt;·0001</td>
<td>8·8 (0·11)</td>
<td>&lt;·0001</td>
<td>8·9 (0·11)</td>
<td>&lt;·0001</td>
<td>8·6 (0·11)</td>
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<tr>
<td>EF</td>
<td>28·9 (1·39)</td>
<td>29·7 (1·39)</td>
<td>0·7034</td>
<td>30·0 (1·39)</td>
<td>0·5737</td>
<td>30·0 (1·39)</td>
<td>0·8544</td>
<td>27·0 (1·39)</td>
<td>0·0132</td>
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<tr>
<td>Stroke Volume</td>
<td>73·6 (3·87)</td>
<td>65·8 (3·87)</td>
<td>0·1566</td>
<td>66·2 (3·87)</td>
<td>0·1791</td>
<td>66·2 (3·87)</td>
<td>0·3489</td>
<td>55·5 (3·87)</td>
<td>0·0012</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>63·3 (1·99)</td>
<td>65·6 (1·99)</td>
<td>0·4145</td>
<td>63·3 (1·99)</td>
<td>0·9794</td>
<td>63·73 (1·99)</td>
<td>0·3599</td>
<td>66·3 (1·99)</td>
<td>0·2893</td>
</tr>
<tr>
<td>LV Mass</td>
<td>290·1 (12·08)</td>
<td>279·1 (12·08)</td>
<td>0·5216</td>
<td>288·3 (12·08)</td>
<td>0·9160</td>
<td>288·3 (12·08)</td>
<td>0·1927</td>
<td>278·5 (12·08)</td>
<td>0·5020</td>
</tr>
</tbody>
</table>

† p values indicate whether changes from baseline are significantly different from zero at each time point, and are for informational purposes only. No adjustments for multiple comparisons were performed. EF = ejection fraction (%), EDVi = end diastolic volume index (ml/M2), ESVi = end systolic volume index (ml/M2), Cardiac Output (L/minute), LV Length – diastolic longitudinal length (cm), Stroke Volume (ml), Heart Rate (beats per minute), LV Mass (grams)

‡The functional LV volume is used in the follow-up echo variables. The functional volume is defined as total LV volume less the partitioned volume by the Parachute Device (Figure 6).
Table 4. Cumulative Percentages of Subjects Experiencing Clinical Outcomes by Time Period

<table>
<thead>
<tr>
<th></th>
<th>12 Month</th>
<th>24 Month</th>
<th>36 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=31</td>
<td>N=28</td>
<td>N=27</td>
</tr>
<tr>
<td>Mortality % (n)</td>
<td>6.5% (2)</td>
<td>6.5% (2)</td>
<td>13.9% (4)</td>
</tr>
<tr>
<td>Cardiac Mortality % (n)</td>
<td>6.5% (2)</td>
<td>6.5% (2)</td>
<td>6.5% (2)</td>
</tr>
<tr>
<td>Mortality + HFH % (n)</td>
<td>16.1% (5)</td>
<td>32.3% (10)</td>
<td>38.7% (12)</td>
</tr>
<tr>
<td>Heart Failure Hospitalizations % (n)</td>
<td>12.9% (4)</td>
<td>29.7% (9)</td>
<td>33.0% (10)</td>
</tr>
<tr>
<td>VAD or Transplant % (n)</td>
<td>3.5% (1)</td>
<td>6.9% (2)</td>
<td>13.8% (4)</td>
</tr>
<tr>
<td>Stroke % (n)</td>
<td>0% (0)</td>
<td>3.6% (1)</td>
<td>15.9% (4)</td>
</tr>
</tbody>
</table>

VAD = ventricular assist device, HFH = heart failure hospitalization. Three subjects did not complete the 12 month visit (2 deaths, 1 transplant). One subject did not complete the 24 month visit (1 transplant). Four subjects did not complete the 36 month time point (2 deaths, 2 VADs).
Figures Legends

Figure 1. Upper panels show an illustration of the Parachute device implanted in a dilated left ventricle (A) and an actual angiographic view of Parachute device implanted in a dilated left ventricle with apical wall motion abnormality (B). Lower panels show the Parachute device open (C) and various shapes of the delivery system to facilitate navigation in different morphologies (D).

Figure 2. Angiographic sequence of a Parachute implantation in the left ventricle (LV). Pigtail in the LV cavity to perform LV angiography (A), Device placement with foot exposed and in contact with the antero-apical wall (B), Balloon inflation to facilitate self-expansion of the device (C), Device fully expanded but still attached to the delivery system (D). Final positioning after release of the device (E).

Figure 3. Disposition of Patients Enrolled. The mean follow-up time was 2.6 years with 74% (23/31) completing 3 year follow-up.

Figure 4. Clinical Outcomes of Treated Subjects, N=31, according to New York Heart Association class (I-IV).

Figure 5. Echo image comparing baseline volume to two year follow-up functional volume.

Figure 6. LVEDVi and LVESVi mean±SD plotted over time. All volumes are significantly less than baseline (p < 0.05), except LVESVi at year three.
Figure 7. Kaplan Meier Curves for Mortality, Heart Failure Hospitalization, and the combination of Heart Failure Hospitalization and Mortality.
Percutaneous Ventricular Restoration using the Parachute® Device in Patients with Ischemic Heart Failure: Three-year Outcomes of the PARACHUTE First-in-Human Study
Marco A. Costa, Ernest L. Mazzaferri, Jr., Horst Sievert and William T. Abraham

Circ Heart Fail. published online July 18, 2014;
Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3289. Online ISSN: 1941-3297

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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