IN VIVO ASSESSMENT OF CENTRAL AND PERIPHERAL HEMODYNAMIC IMPACT OF THE C-PULSE® SYSTEM

Francisco Javier Londono Hoyos, PhD; Dimitrios Georgakopoulos, PhD; Oliver Fey; Dori Jones, MS; Christian Schlensak, MD; David Schibilsky, MD; Michael Weyand, MD; Daniel Bujnoch, MD; Holger Hotz, MD; Patrick Segers, PhD; Leslie Miller, MD; J. Eduardo Rame, MD, M.Phil.

CAUTION: C-Pulse is an investigational device. The device is limited by Federal (or United States) Law to investigational use only. C-Pulse is a registered trademark of Sunshine Heart Inc. ©2016 Sunshine Heat Inc.
The following relevant financial relationships exist related to this poster presentation:

- Francisco Javier Londono Hoyos, None
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- Dori Jones, MS, Employee
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- Holger Hotz, MD; None
- Patrick Segers, PhD; Consulting Fees
- Leslie Miller, MD; Consulting Fees/Honoraria
- J. Eduardo Rame, MD, M.Phil. Consulting Fees/Honoraria
The C-Pulse System

- Balloon inflates – increases diastolic pressure & coronary perfusion – ‘second pulse’
- Balloon deflates – unloads LV
- Procedure can be performed in 90 minutes (minimally invasive)
- Non blood contacting
- Ability to disconnect – patient comfort and convenience
C-Pulse Counterpulsation: 3D CT Clinical Example

To view C-Pulse in 3D:
View Video >
Countercpulsation: Physiologic Phenomenon of Wave Reflection in Arterial System

Exaggerated wave reflection in the kangaroo simulates arterial countercpulsation

A. P. Avolio, W. W. Nichols, and M. F. O’Rourke
Saint Vincent’s Hospital, Darlinghurst 2010; and The University of New South Wales, Kensington, New South Wales 2033, Australia

- Preserve Coronary Blood Flow
- Maintenance of mean aortic pressure
- Optimize left ventricular coupling with the arterial system

AJP 246: R267. 1984
CLINICAL EXPERIENCE:
FEASIBILITY AND OPTIONS HF
Weaned Medications

- 4 pts weaned from inotropes
- 9 patients reduced diuretic load
- 1 patient increased beta blocker (50mg → 200mg Toprol)
Weaned C-Pulse: Hemodynamics (N=6)

- **Ejection Fraction (%)**
  - Baseline vs Month 6: \( p<0.01 \)

- **Cardiac Output (L/min)**
  - Baseline vs Month 6: \( p<0.05 \)

- **PCWP (mmHg)**
  - Baseline vs Month 6

- **E/A Diastolic Filling**
  - Baseline vs Month 6
OPTIONS HF Efficacy: Improved Overall Score In Kansas City Cardiomyopathy Questionnaire (KCCQ)

Treatment Effect: PARADIGM
OPTIONS HF Efficacy: Structural Remodeling

Ejection Fraction (%)

Baseline  6M  12M  18M

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OPTIONS HF Efficacy: Cardiac Function and Structural Remodeling

End Systolic Volume

End Systolic Volume (mL)

Baseline

Month 6

* $P=0.05$

$N=6$
Studies indicate that a 30 mL LVESV change correlates with ~80% improvement in mortality.

Kramer DG. JACC 2010; 56(5)
OPTIONS HF Efficacy: Diastolic Function

E Wave Velocity (cm/s)

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<tr>
<th></th>
<th>Baseline</th>
<th>Month 6</th>
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<tbody>
<tr>
<td>N</td>
<td>7</td>
<td>6</td>
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<tr>
<td>Value</td>
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C-PULSE: QUANTIFYING LV UNLOADING
C-Pulse Acute Afterload Reduction: Wall Stress

Mean Wall Stress Reduction

![Graph showing wall stress reduction](Image)

- **Baseline**: 153, *p*=.022
- **1:1 Counterpulsation**: 99

*n = 6

Source: Circulation.2005;112(suppl I):i-26-i-31
Augmentation Index (P2): Index of Wave Reflections

C-Pulse OFF

<table>
<thead>
<tr>
<th>Sp</th>
<th>Dp</th>
<th>Vp</th>
<th>Pp</th>
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<td>130</td>
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P2

C-Pulse OFF

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C-Pulse ON

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C-Pulse ON

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<tr>
<td>112</td>
<td>87</td>
<td>101</td>
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</table>
Hemodynamic Effects of Unloading with C-Pulse: Reduction in Peripheral Wave Reflections Similar to Vasodilators

Control/Tracking Number: 2015-SS-A-15860-AHA  
Activity: Abstract  
Current Date/Time: 6/10/2015 2:10:27 PM

**Arterial and Cardiac Hemodynamics in Advanced HF Patients Implanted with the C-Pulse Counterpulsation Device: Implications for Myocardial Recovery**

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<table>
<thead>
<tr>
<th>(N=6)</th>
<th>OFF</th>
<th>ON</th>
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</thead>
<tbody>
<tr>
<td>Max Aortic BP (mmHg)</td>
<td>114.4±4.4</td>
<td>114.3±4.9</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>68±13.4</td>
<td>65.7±14.7</td>
</tr>
<tr>
<td>P1 (mmHg)</td>
<td>106.5±6.0</td>
<td>109.3±4.9†</td>
</tr>
<tr>
<td>Time to P2 (ms)</td>
<td>182±20.8</td>
<td>161±29.5*</td>
</tr>
<tr>
<td>SEVR</td>
<td>1.70±0.45</td>
<td>1.99±0.53†</td>
</tr>
<tr>
<td>Aix (P2/P1)</td>
<td>1.23±0.13</td>
<td>1.04±0.06†</td>
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</table>

Mean±SD. Paired t-test. † p<0.01; * p=0.01; ‡ p<0.05

Data presented at AHA 2015
Non-Invasive Measures Pressure and Flow to Study Peripheral Vascular Effects of C-Pulse in Patients
C-Pulse and Impedance Analysis: Marked Reduction in Peripheral Resistance (n=3)

Avg. Reduction in DC (peripheral) resistance with C-Pulse: 30%

C- Pulse: Wave Intensity Analysis In the Aorta (N=3)

- Average Increase in Forward Compression Wave (Energy generated by LV): 71% due to decreased peripheral resistance
- C-Pulse augmentation during diastole 50% total energy generated by un-assisted LV
- Quantitatively similar to positive inotrope with better energetics profile
Large Unloading Effects Due to Neural Reflexes?
Location, Location, Location

C-Pulse cuff placement even more optimal location to activate reflexes than IABP

Mitchell GAG. Anatomy Autonomic Nervous System. 1953
Arterial Baroreceptor Response to Intra-aortic Balloon Assistance: Baroreceptor Afferent Signaling Doubled

Diastolic Augmentation ↑
Baroreceptor Activity
Potential Mechanism Of Action – Counterpulsation and Neuromodulation
Targets Key Pathologies in HF: Coronary Perfusion and Neurohormonal

CNS

AFFERENTS

Arterial Baroreceptors

↓ HRV

↑ ACh

Parasympathetic

↓ NE

Sympathetic

RDN

↓ Na⁺ Reabsorption

↓ Renin

↓ Renal Vascular Resistance

↓ Peripheral Vascular Resistance

VNS

Beta Blockers

Diuretics

ACE/ARB

Nitrates

Vasodilators

ACE/ARB

C-Pulse and Counterpulsation

**Counterpulsation Times to Most Sensitive Phases of Cardiac Cycle for Baroreceptor Stimulation**

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Arterial Baroreceptor Activity

Peterson, LH. Circ. 21:1960
C-Pulse Studies to Assess Neuromodulation Effects: Multi-Disciplinary Approach

HEMODYNAMIC IMPACT OF THE C-PULSE CARDIAC SUPPORT DEVICE: A 1D ARTERIAL MODEL STUDY

D. Campos Arias¹, T. Rodriguez, N. Stergiopolus², P. Segers³

¹Cujae, Research Group of Biomechanics and Biomaterials, Cuba; ²LHTC, EPFL, Lausanne, Switzerland; ³IBiTech-bioMMeda, iMinds Medical IT, Ghent University, Belgium

\[ \frac{\partial p}{\partial t} + \frac{\partial}{\partial x} \left( \int_A u \, dA \right) + \frac{\partial P}{\partial x} = \frac{\partial P_{\text{ext}}}{\partial x} - 2\pi R \frac{\partial \delta R}{\partial \delta x} \mid_{R=R} \] (18)

values of the external pressure at the time of diastole for these situations are assumed.

\[ P_{\text{ext}}(x,t) = \begin{cases} 0 & \text{during systole} \\ \alpha \cdot \exp \left( - \left( \frac{t-t_0}{\tau} \right)^2 \right) & \text{during diastole} \end{cases} \] (19)
Summary

- Hemodynamic analysis from patients indicates afterload reduction due to peripheral effects.

- Late systolic reduction associated with marked vasodilation hypothesized mediated by aortic and carotid baroreceptors.

- Chronic therapy with enhanced coronary perfusion, peripheral vascular unloading, and neurohormonal modulation may provide substrate for chronic remodeling and/or myocardial stabilization.

- Ideal system to implement weaning protocol due to modular nature, non-obligatory therapy, extravascular implant.