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

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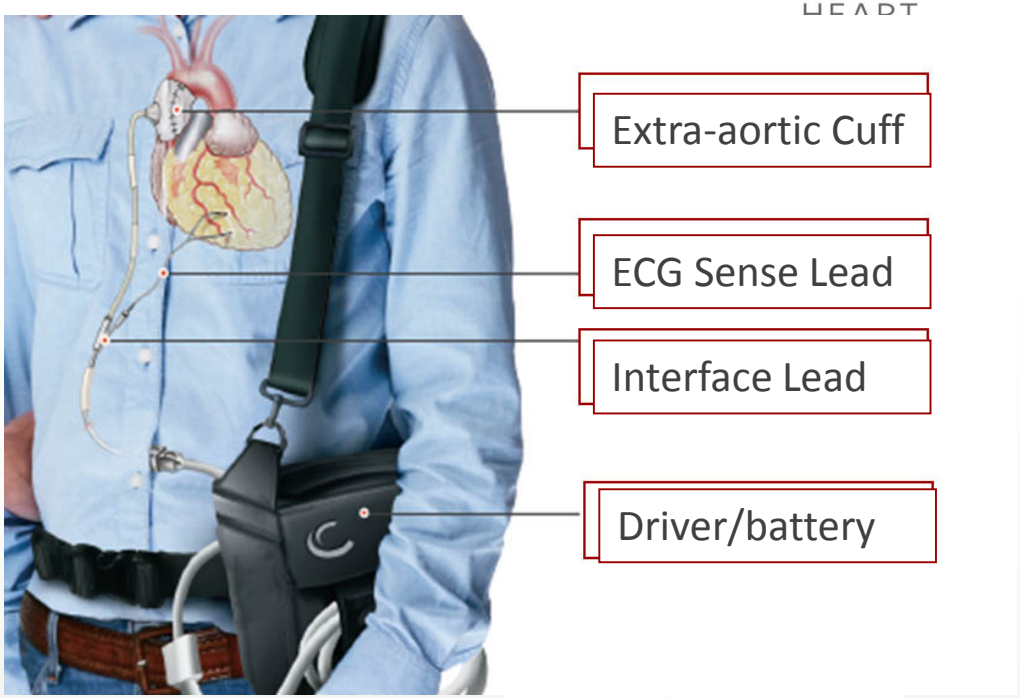
Relevant Financial Relationship Disclosure Statement

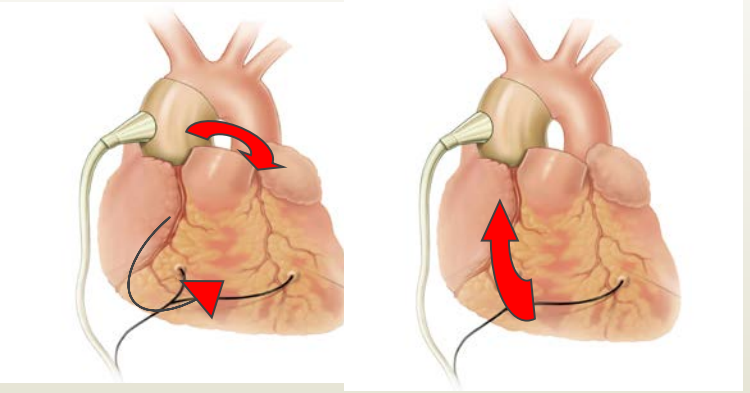
The following relevant financial relationships exist related to this poster presentation:

- Francisco Javier Londono Hoyos, None
- Dimitrios Georgakopoulos, Ph.D.; Employee
- Oliver Fey, Employee
- Dori Jones, MS, Employee
- Christian Schlensak, MD; None
- David Schibilsky, MD; None
- Michael Weyand, MD; None
- Daniel Bujnoch, MD; None
- 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

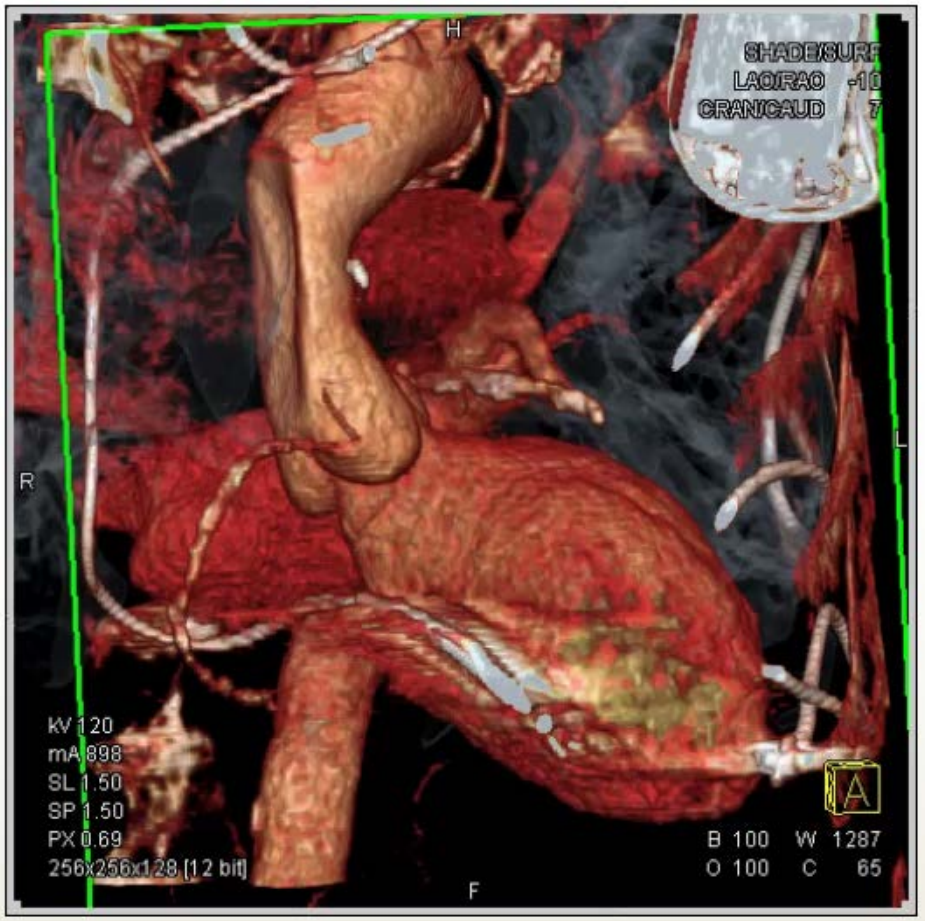




C-Pulse Counterpulsation: 3D CT Clinical Example

To view C-Pulse in 3D:

[View Video >]



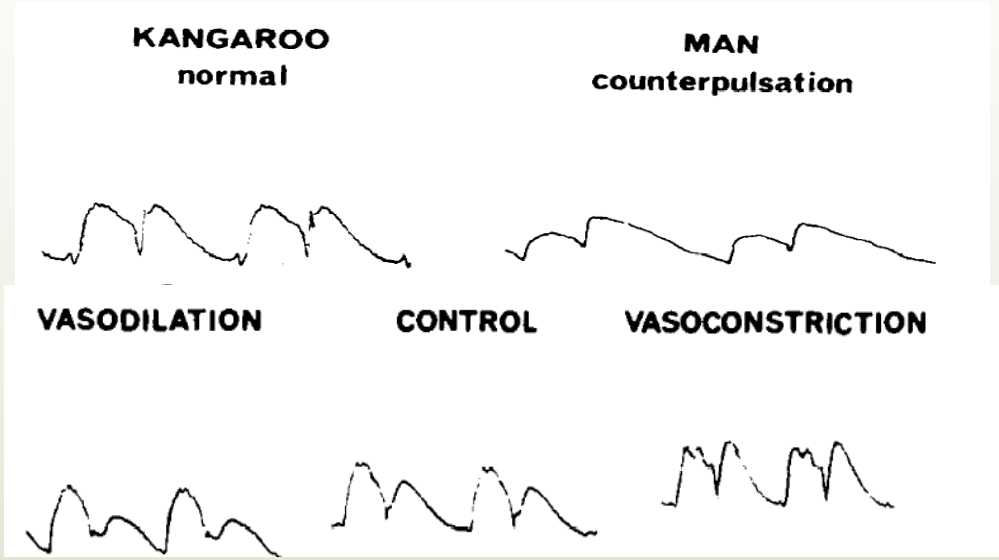
Courtesy Dr. Daniel Bujnoch; Department of Cardiac Surgery, University of Erlangen, Germany

Counterpulsation: Physiologic Phenomenon of Wave Reflection in Arterial System

Exaggerated wave reflection in the kangaroo simulates arterial counterpulsation

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**



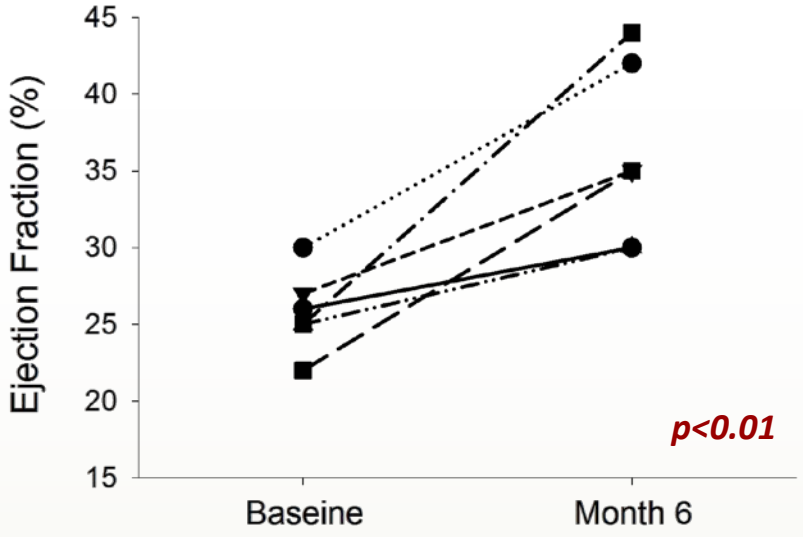
AJP 246: R267. 1984

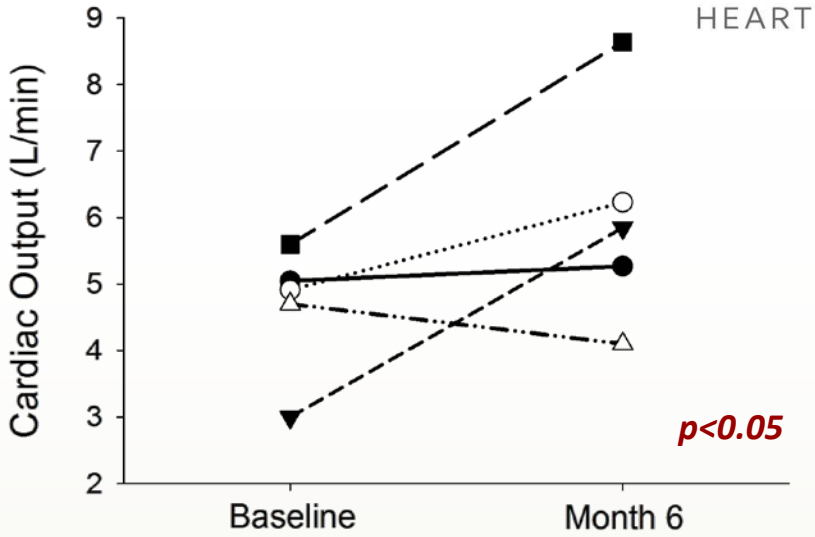
CLINICAL EXPERIENCE: FEASIBILITY AND OPTIONS HF

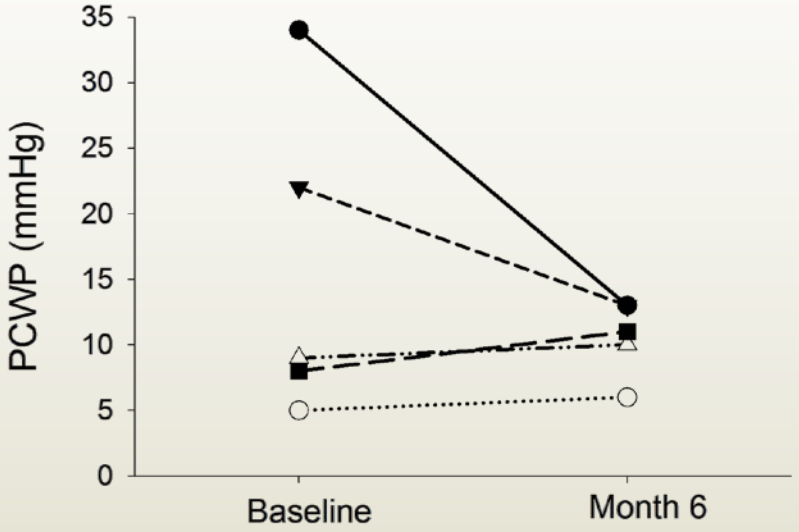
Weaned Medications

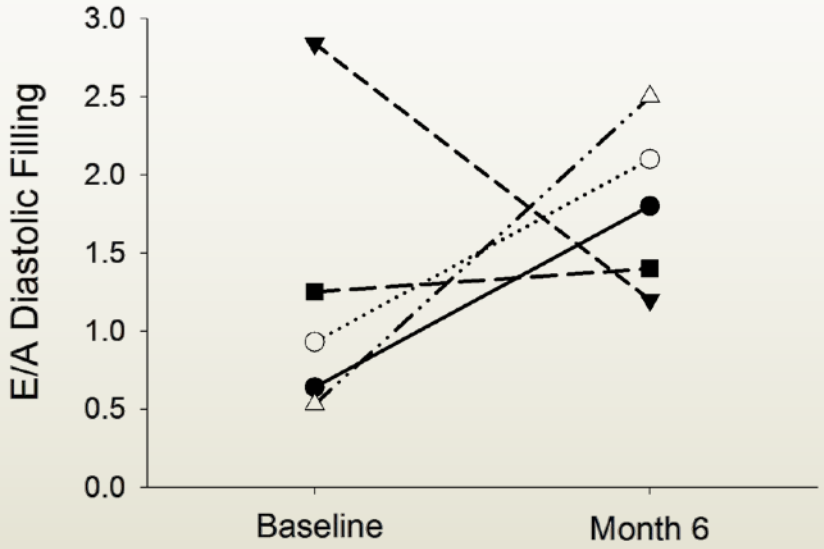
- 4 pts weaned from inotropes
- 9 patients reduced diuretic load
- 1 patient increased beta blocker (50mg→200mg Toprol)

Weaned C-Pulse: Hemodynamics (N=6)

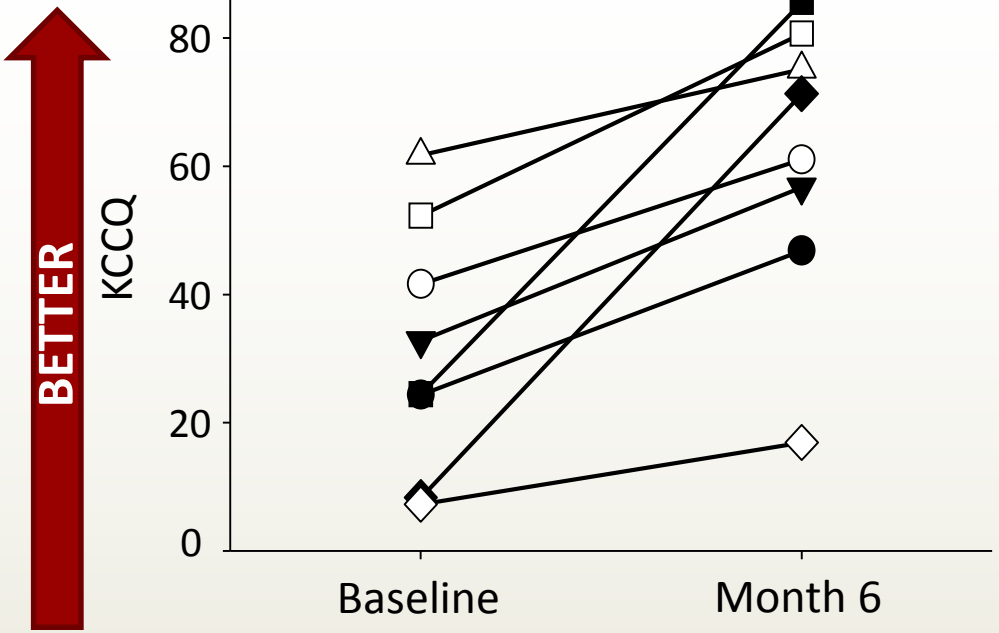


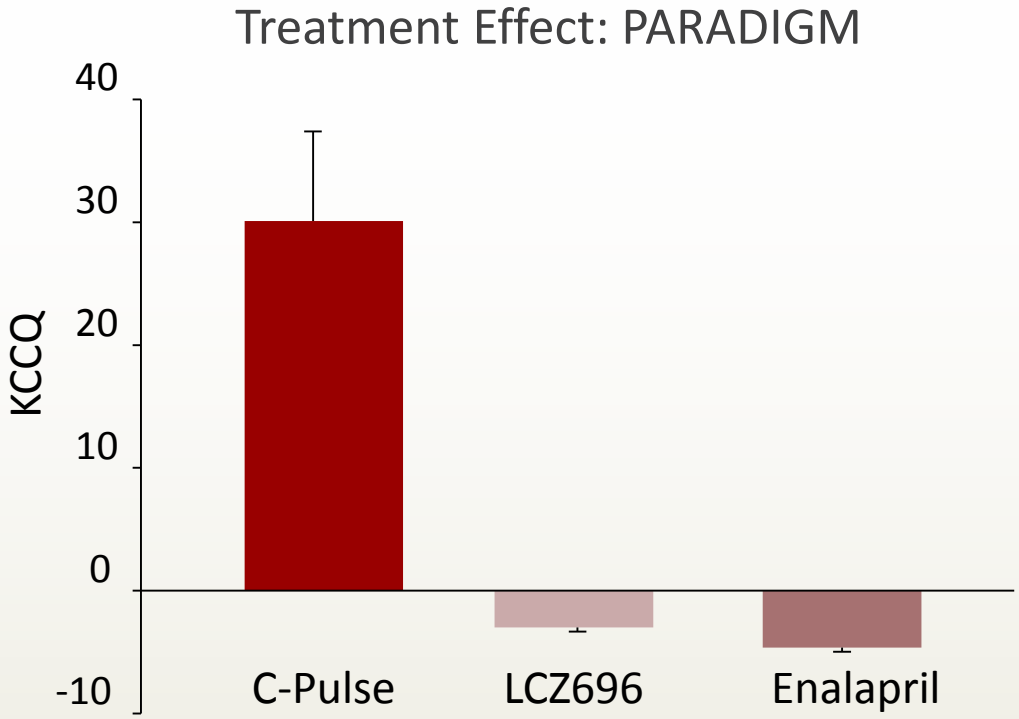




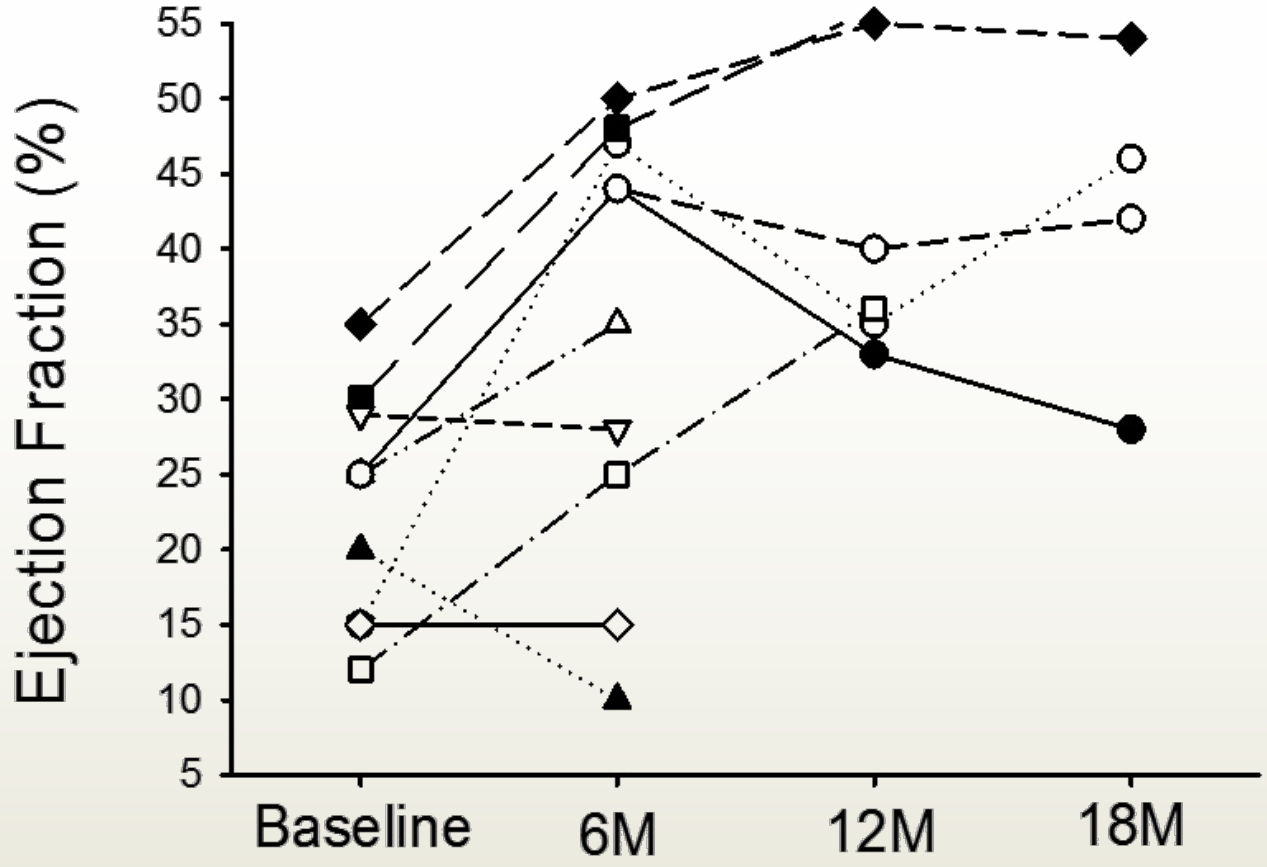


OPTIONS HF Efficacy: Improved Overall Score In Kansas City Cardiomyopathy Questionnaire (KCCQ)

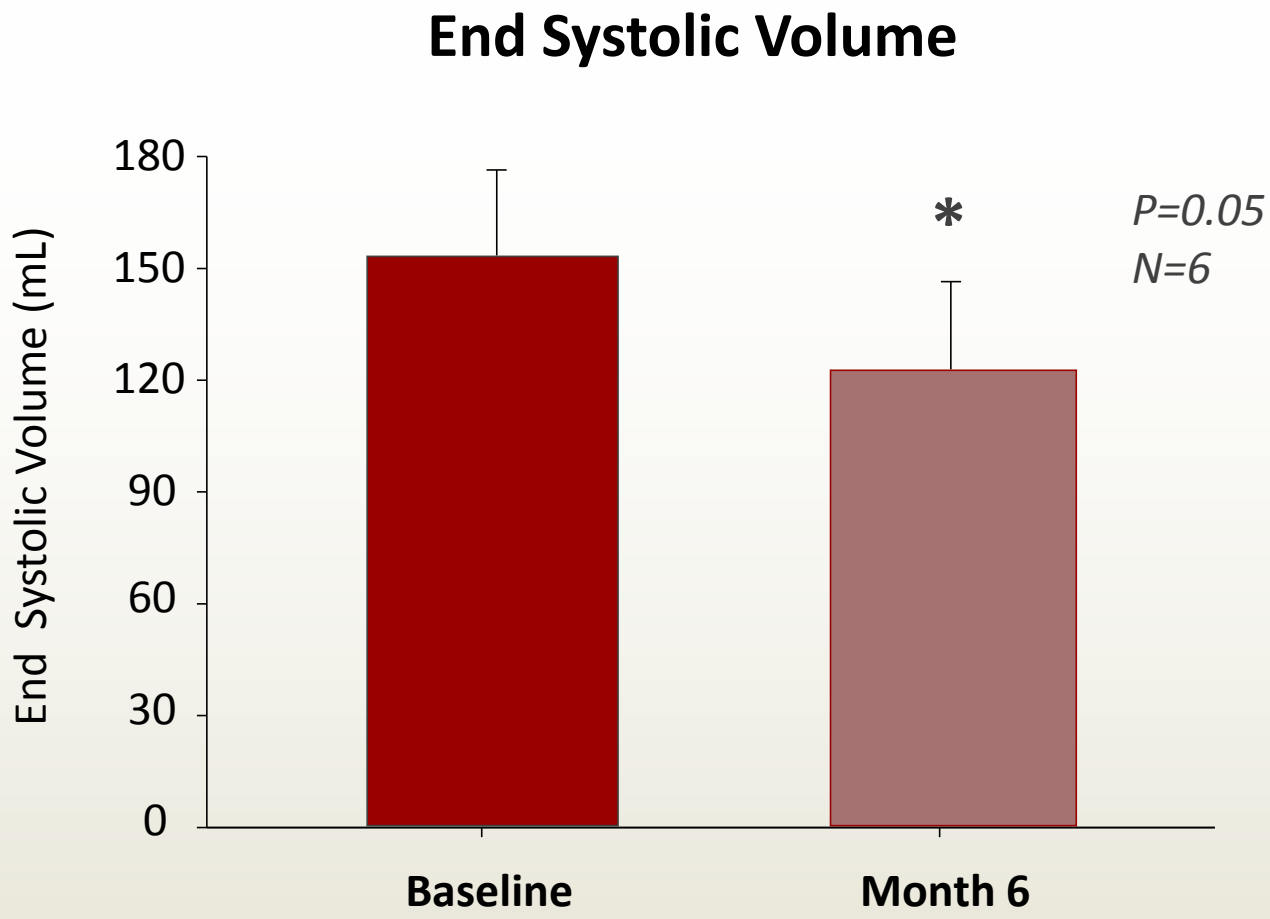




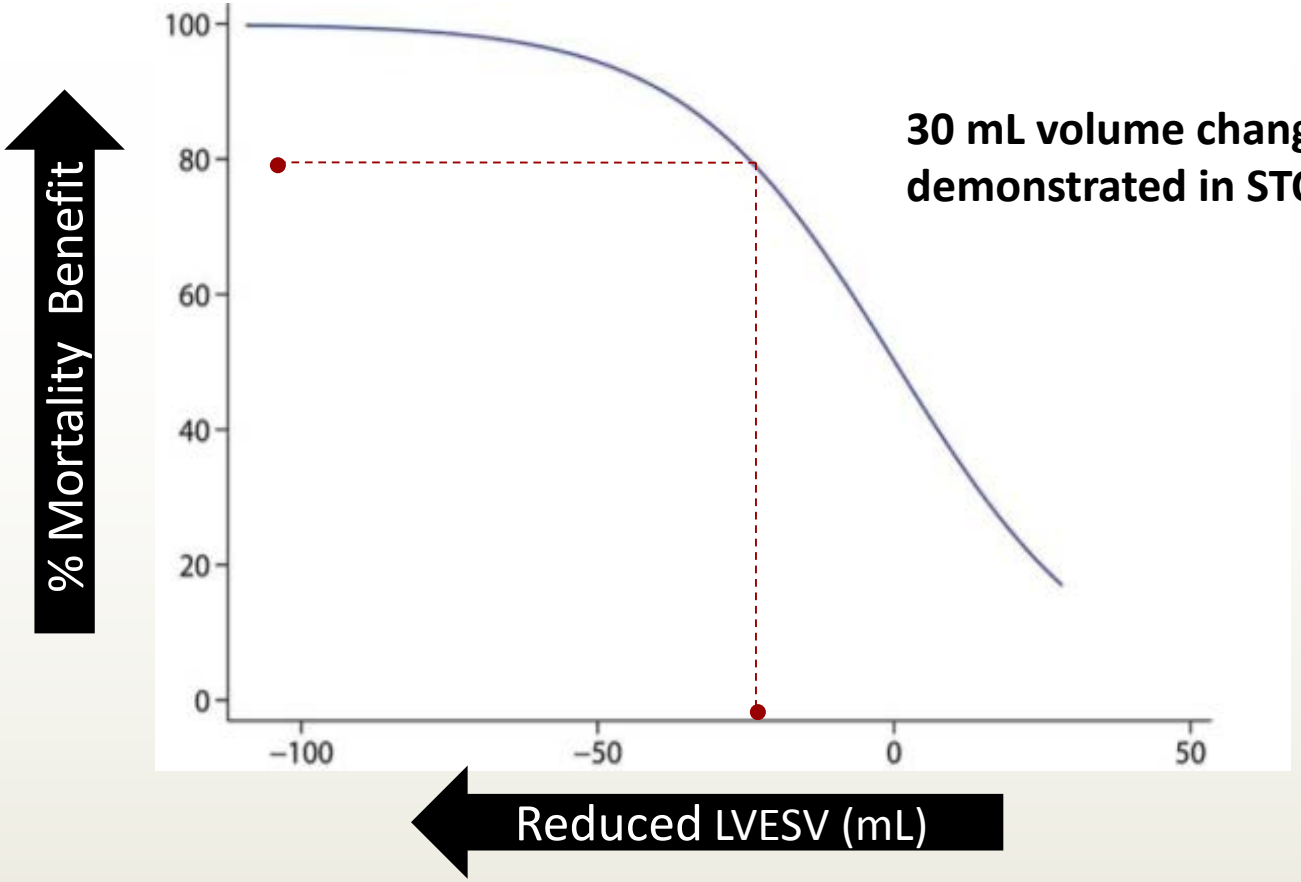
OPTIONS HF Efficacy: Structural Remodeling



OPTIONS HF Efficacy: Cardiac Function and Structural Remodeling



LVESV is Correlated with Mortality Meta Analysis of 30 trials*

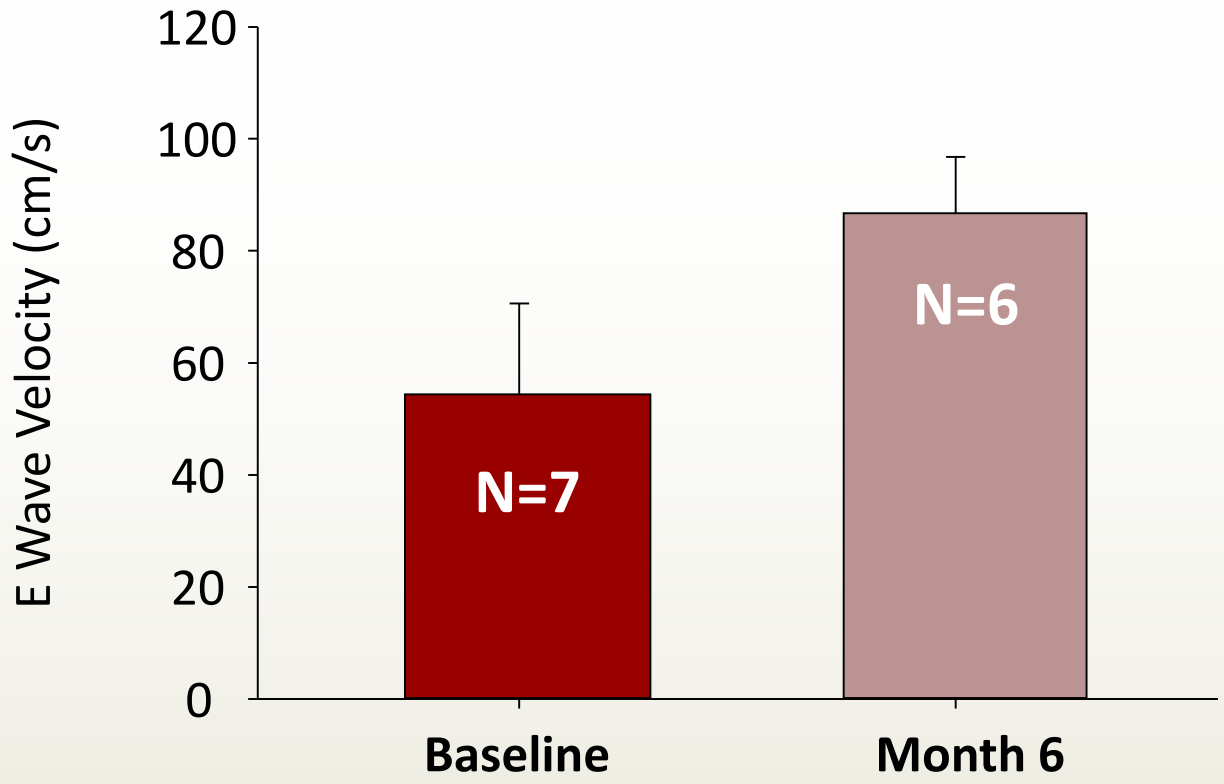


30 mL volume change demonstrated in STOP-HF

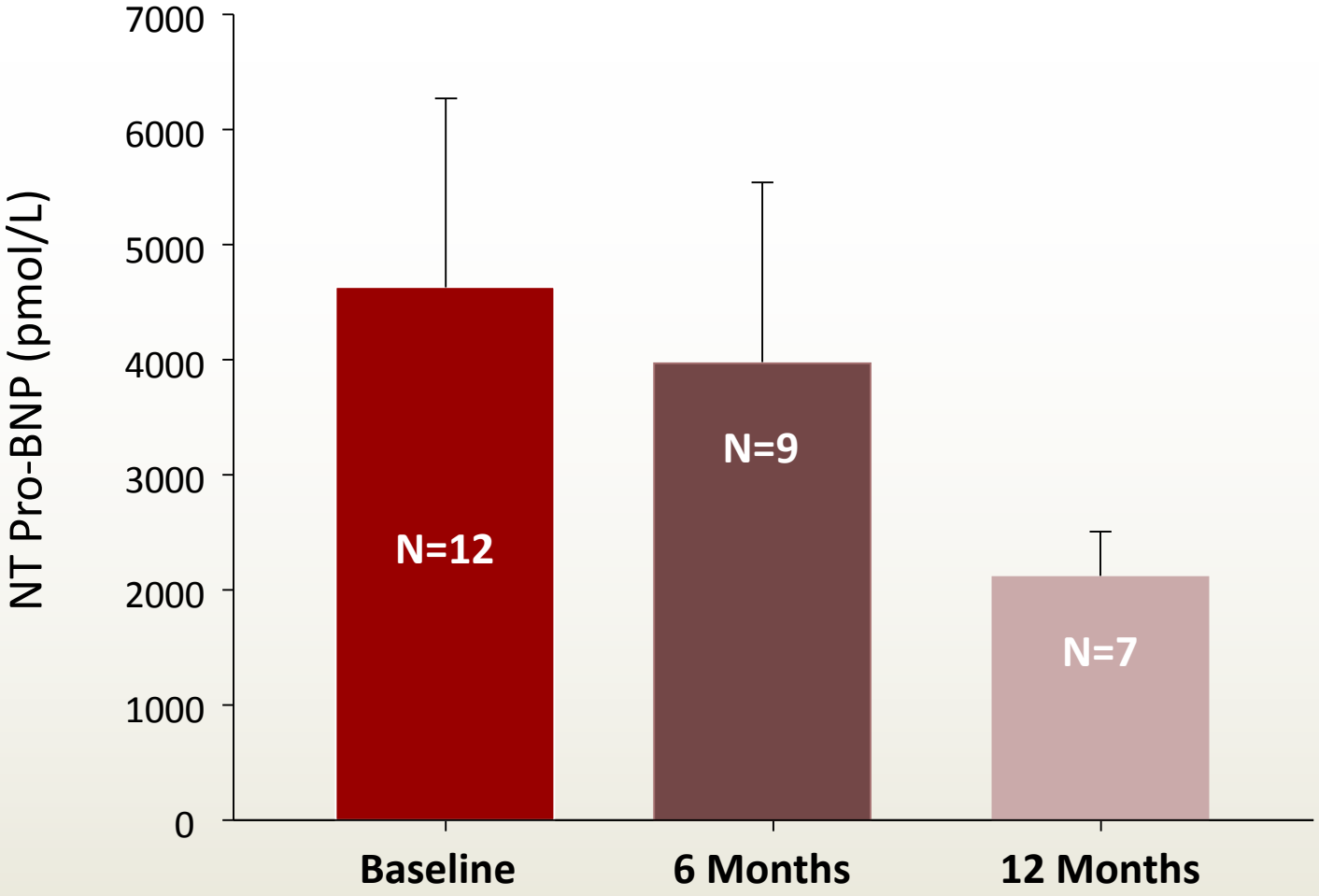
Studies indicate that a 30 mL LVESV change correlates with~80% improvement in mortality.

*Kramer DG. JACC 2010; 56(5)

OPTIONS HF Efficacy: Diastolic Function

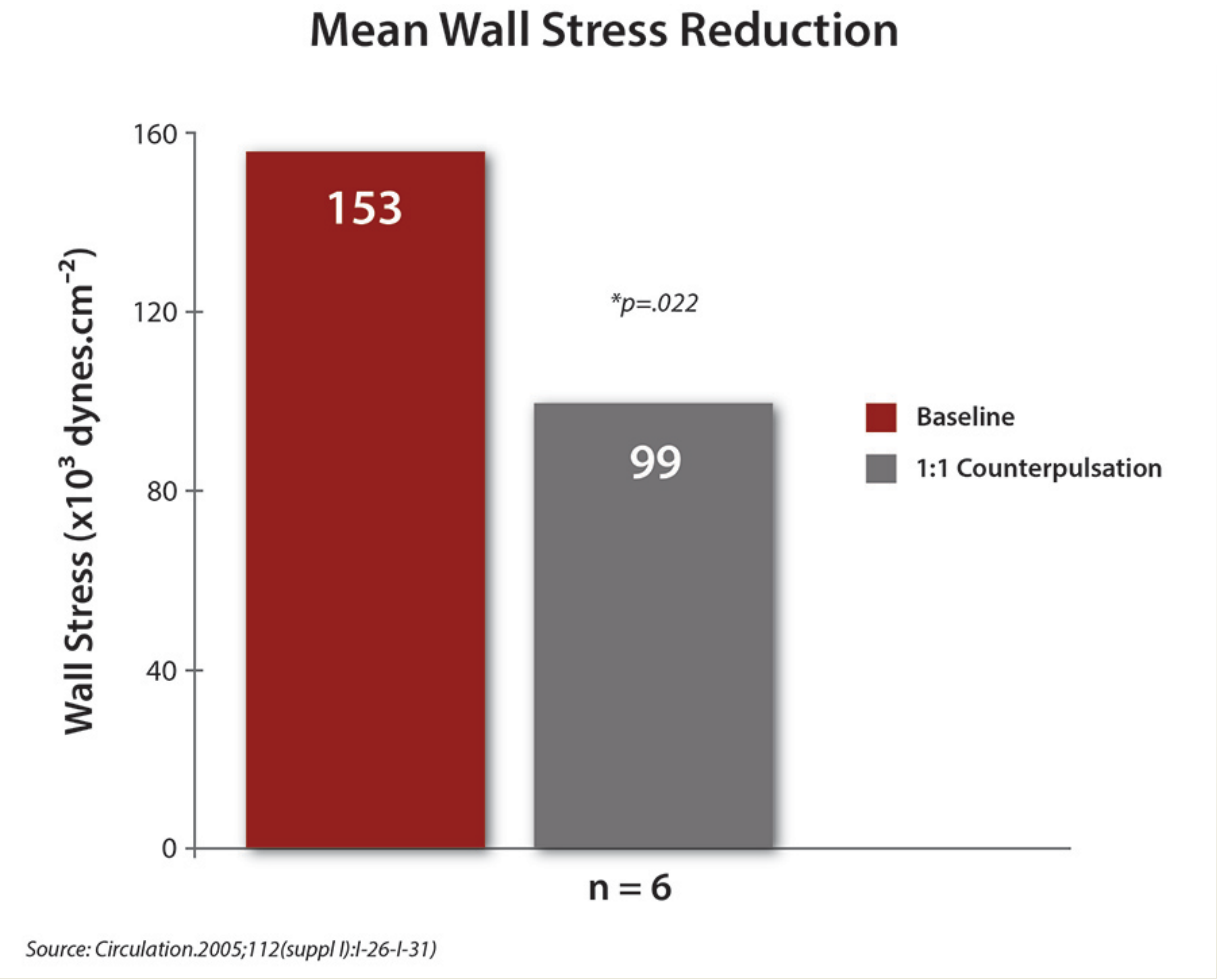


OPTIONS HF Efficacy: Neuro-hormones NTproBNP

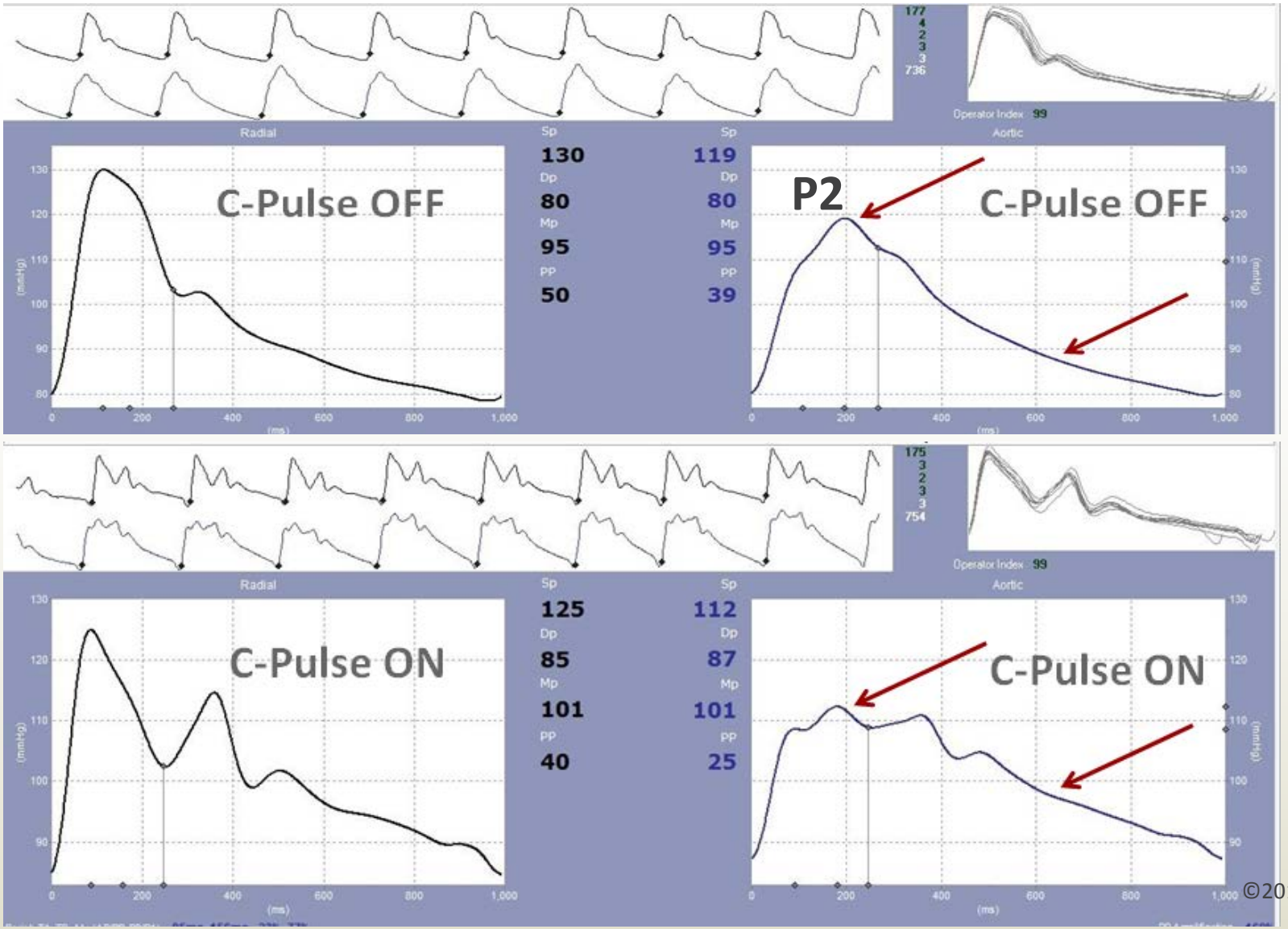


C-PULSE: QUANTIFYING LV UNLOADING

C-Pulse Acute Afterload Reduction: Wall Stress



Augmentation Index (P2): Index of Wave Reflections



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

Author Block: J. Eduardo Rame, Hosp of the Univ of Pennsulvania, Philadelphia, PA; Dimitrios Georgakopoulos, David Pomfret, Sunshine Heart Inc, Eden Prairie, MN; Pavan Atluri, Hosp of the Univ of Pennsulvania, Philadelphia, PA; Phi Wiegn, VA North Texas Health Care System: Dallas VA Medical Ctr, Dallas, TX; Patrick Segers, Ghent Univ, Gent, Belgium; William T Abraham, The Ohio State Univ, Columbus, OH

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

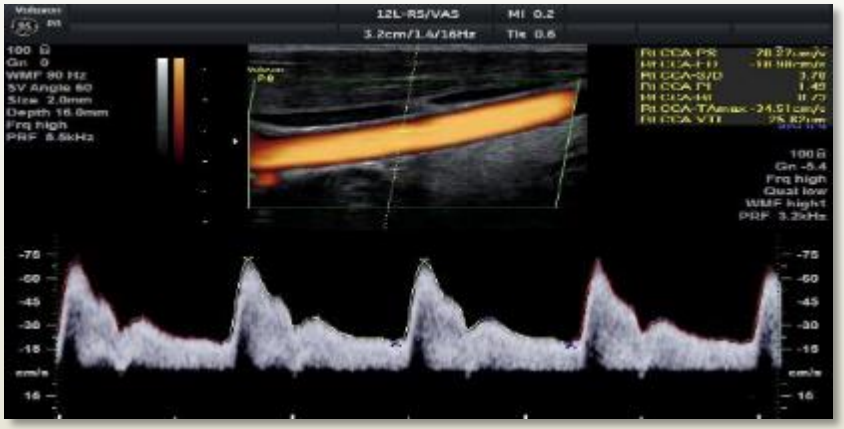
Mean±SD. Paired t-test. † p<0.01; * p=0.01; ‡ p<0.05

Data presented at AHA 2015

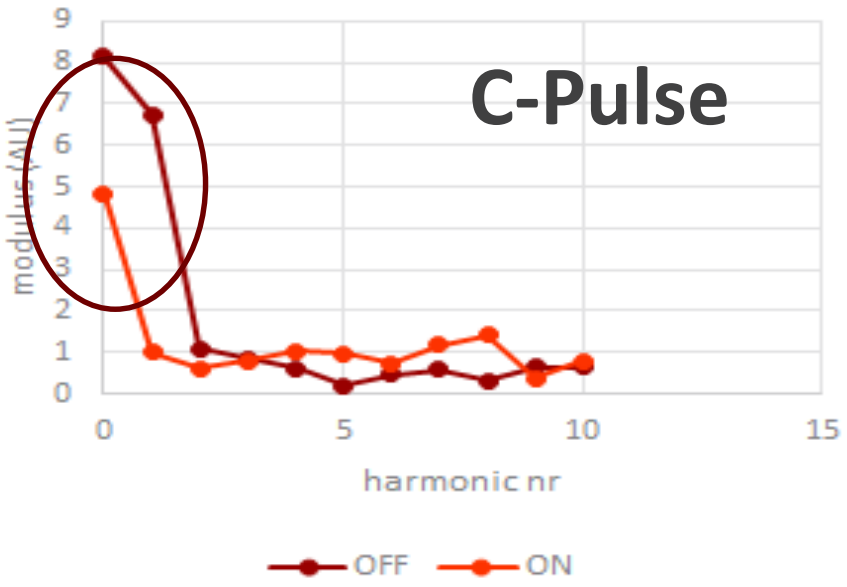
Non-Invasive Measures Pressure and Flow to Study Peripheral Vascular Effects of C-Pulse in Patients

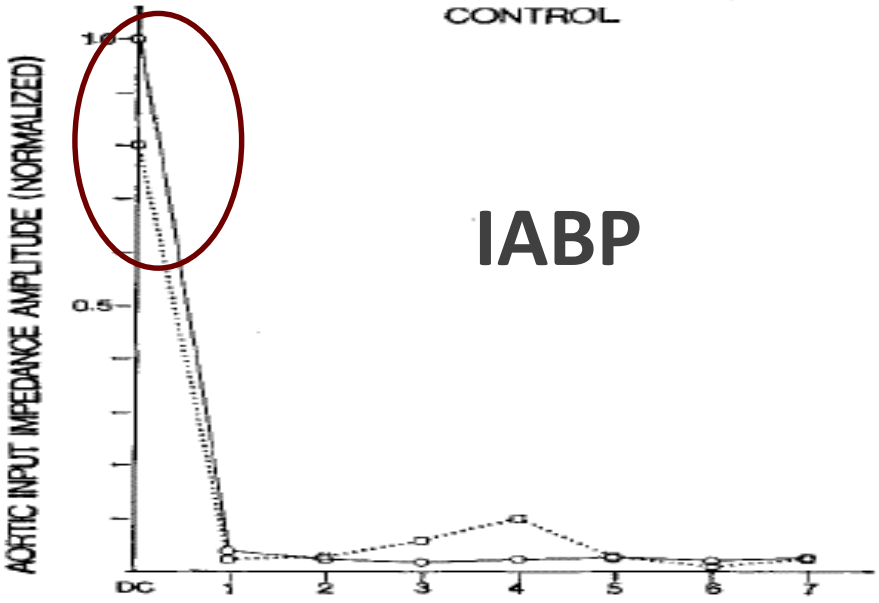
LVOT

CCA



C-Pulse and Impedance Analysis: Marked Reduction in Peripheral Resistance (n=3)

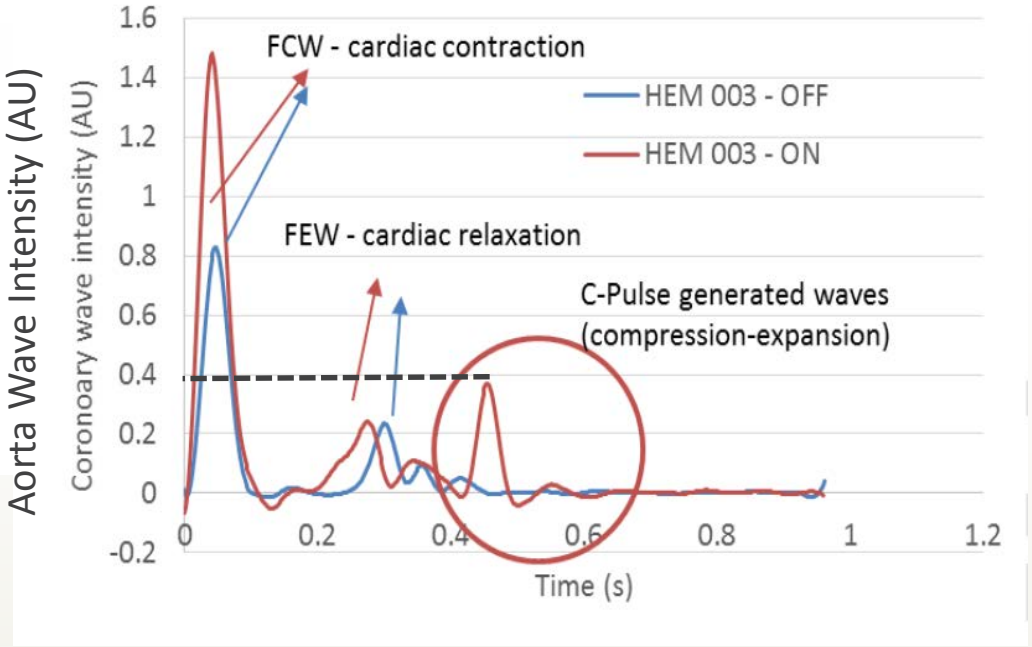


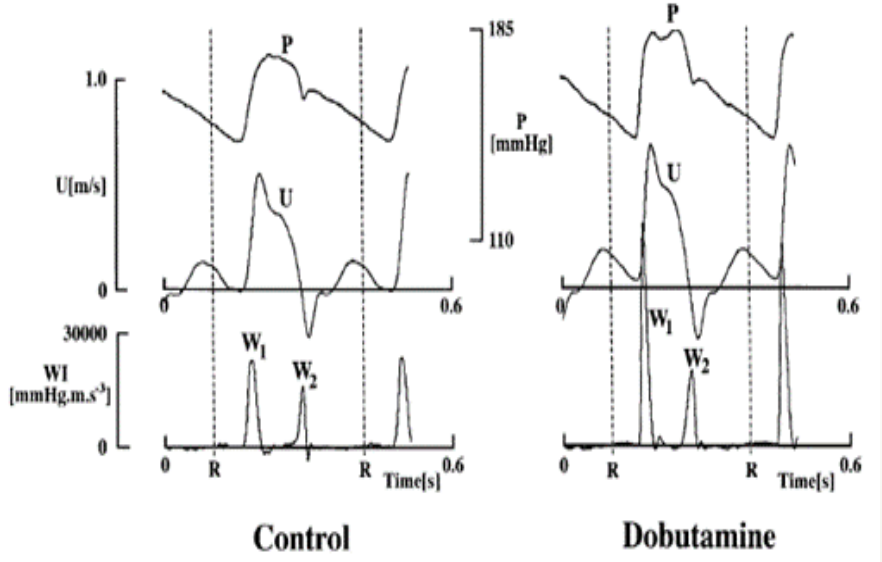


Jaron, D. Ann. Biomed Eng. 5: 1977

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

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



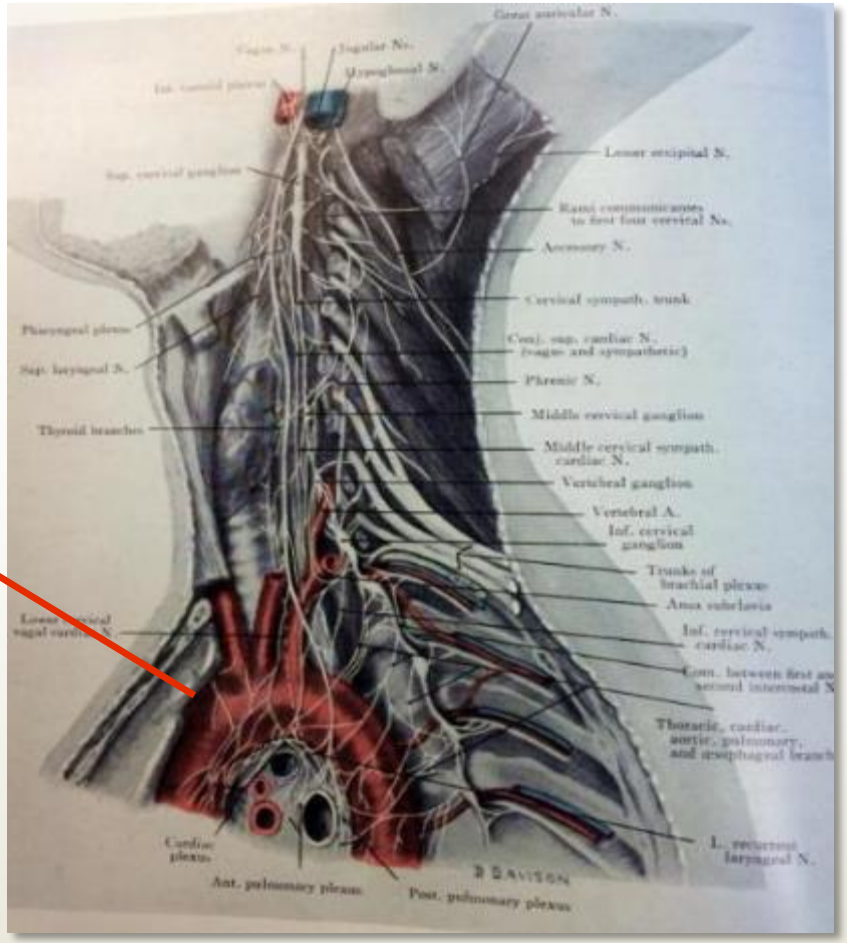


- **Average Increase in Forward Compression Wave (Energy generated by LV): 71% due to decreased peripheral resistance**
- **C-Pulse augmentation during diastole 50% total energy generated by un-assisted LV**
- **Quantitatively similar to positive inotrope with better energetics profile**

Large Unloading Effects Due to Neural Reflexes?

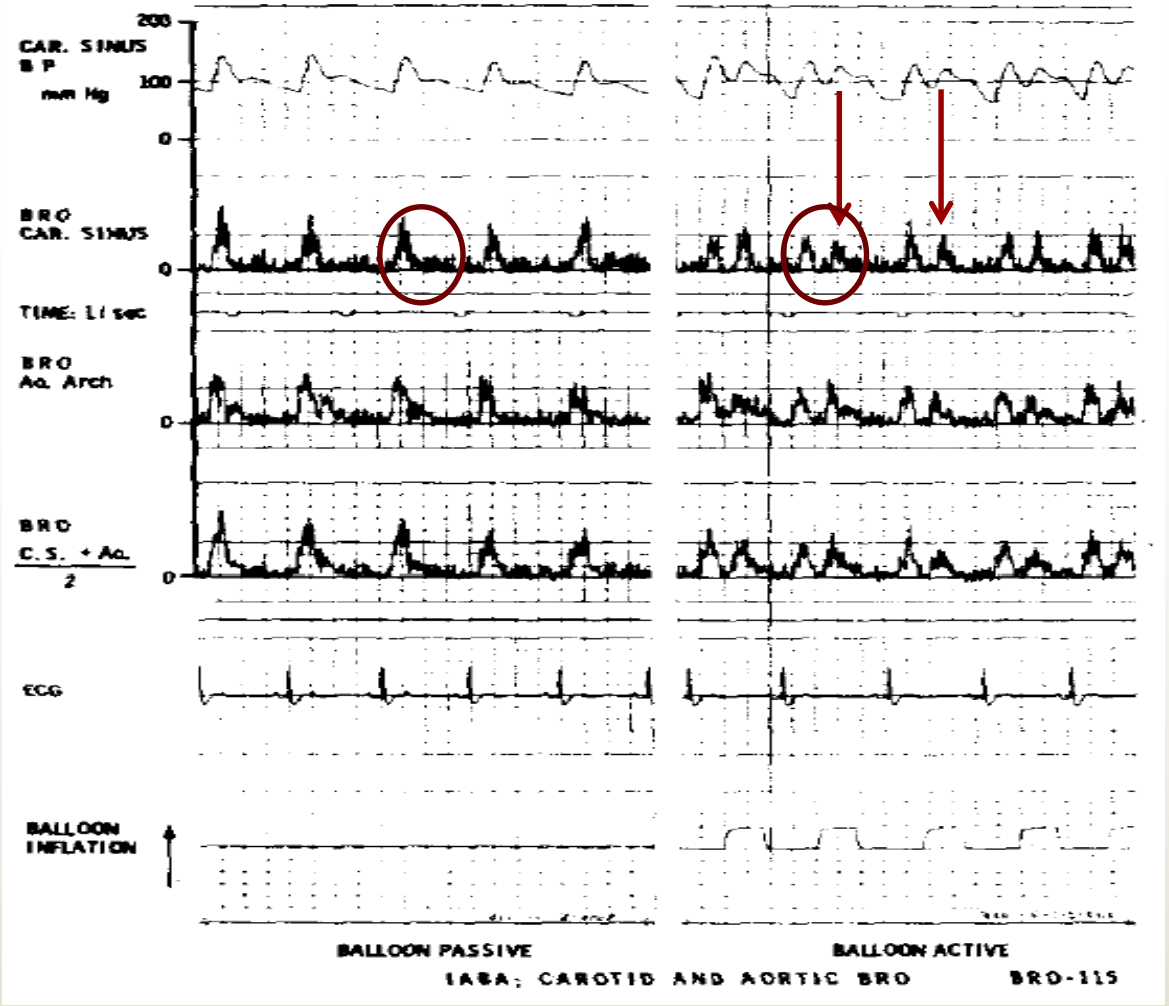
Location, Location, Location

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



Mitchell GAG. Anatomy Autonomic Nervous System. 1953

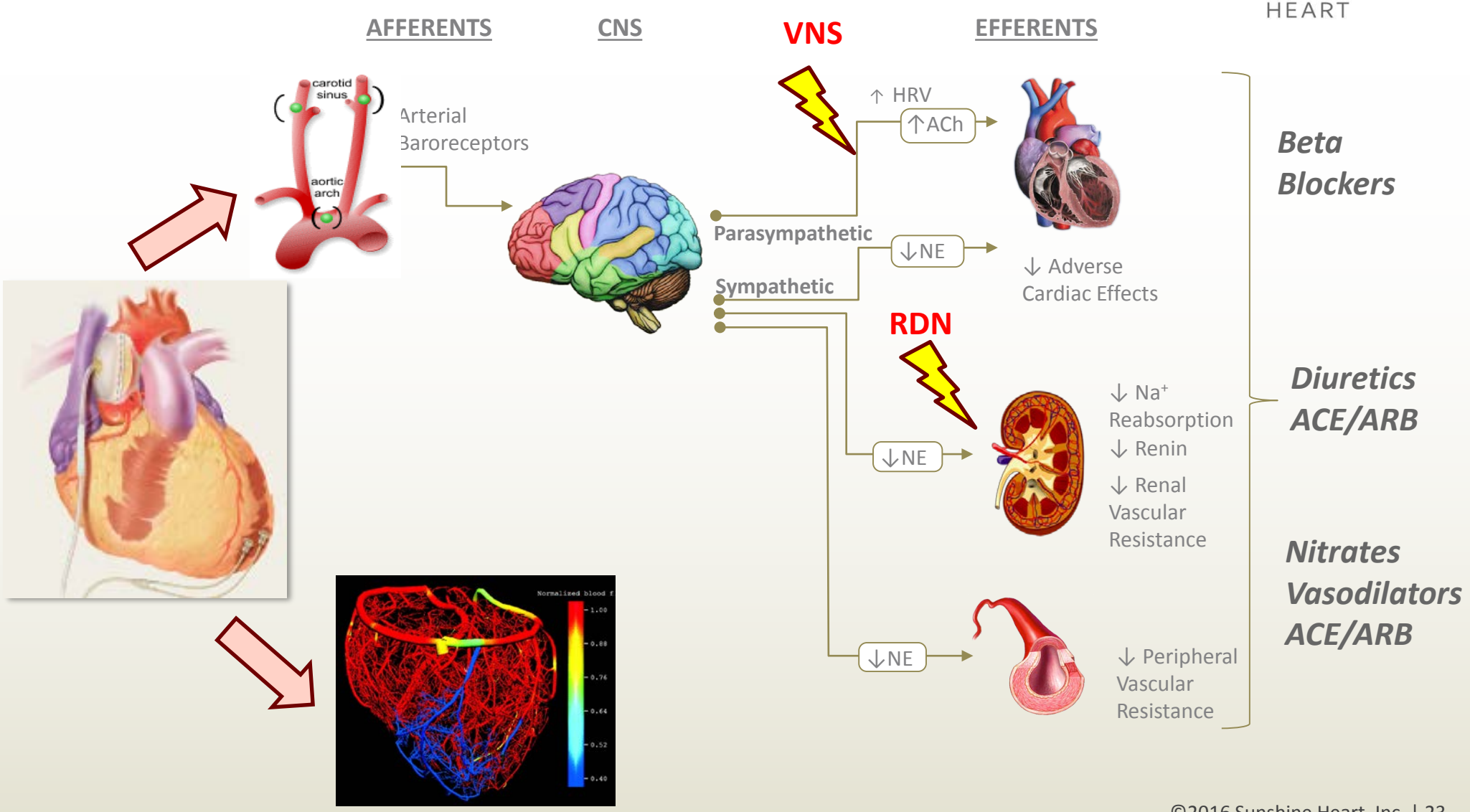
Arterial Baroreceptor Response to Intra-aortic Balloon Assistance: Baroreceptor Afferent Signaling Doubled



Diastolic Augmentation ↑ Baroreceptor Activity

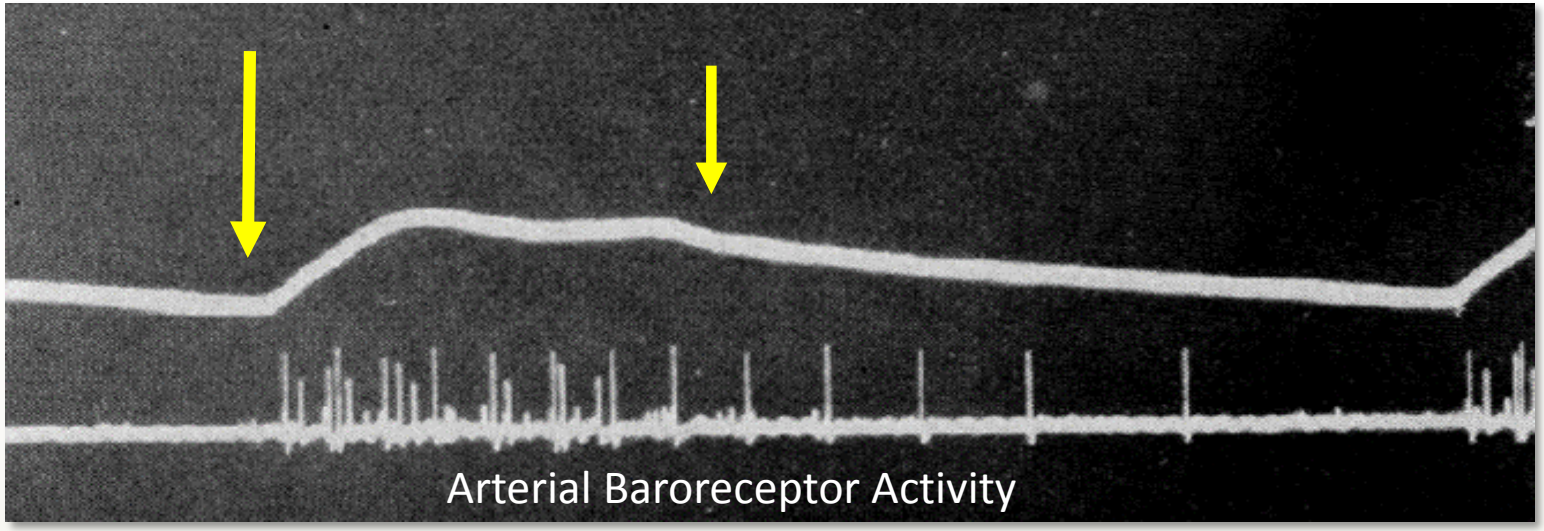
J. Surg. Res. 11(8); 396. 1971

Potential Mechanism Of Action – Counterpulsation and Neuromodulation Targets Key Pathologies in HF: Coronary Perfusion and Neurohormonal



Heart Failure: Companion to Braunwald's Heart Disease. 3rd Edition. D.L. Mann and G. M. Felker. 2016.

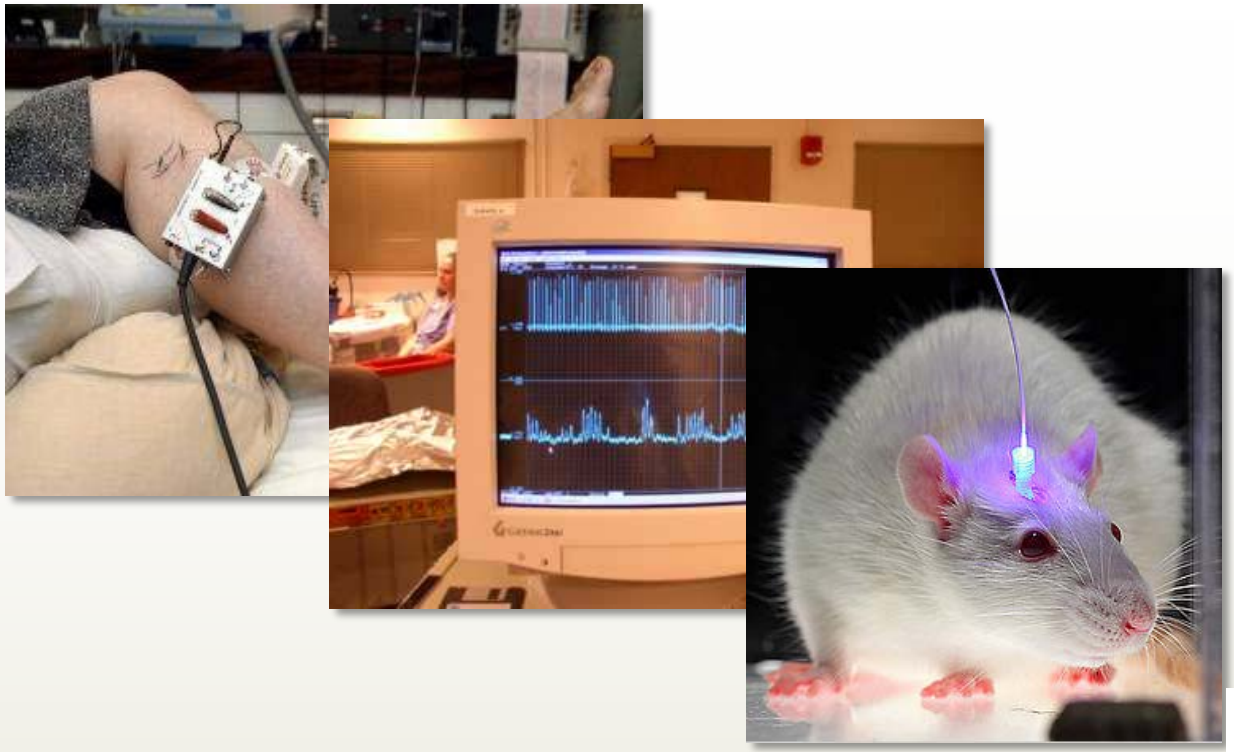
C-Pulse and Counterpulsation

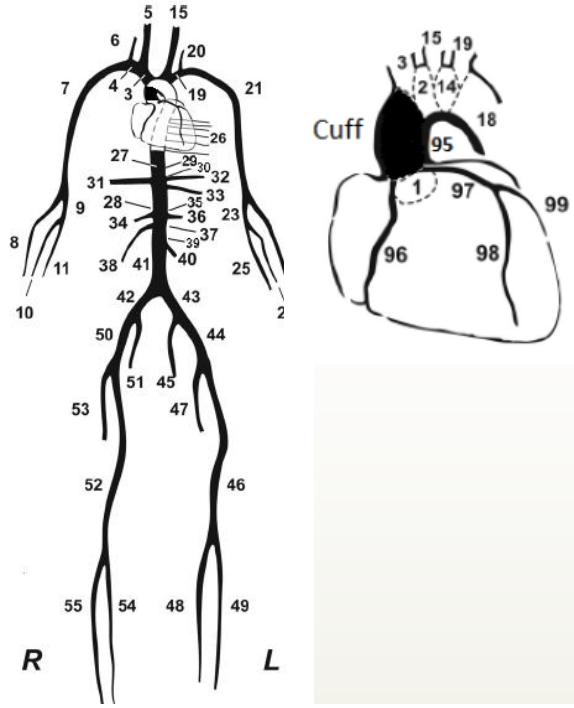


Peterson, LH. Circ. 21:1960

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

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 Arias[1], T. Rodriguez, N. Stergiopulos[2], P. Segers[3]

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

$$\frac{\partial P}{\partial t} = -\frac{1}{C}\frac{\partial Q}{\partial x} + \frac{\partial P_{ext}}{\partial t}$$

$$\frac{\partial Q}{\partial t} + \frac{\partial}{\partial x}\left(\int_A u^2 dA\right) + \frac{A}{\rho}\frac{\partial P}{\partial x} = \frac{A}{\rho}\frac{\partial P_{ext}}{\partial x} - 2\pi R\frac{\mu}{\rho}\frac{\partial u}{\partial r}\Big|_{r=R} \quad (18)$$

values of the external pressure at the time of diastole for these si
tion is assumed.

$$P_{ext}(x,t) = \begin{cases} 0 & \text{during systole} \\ a \cdot exp\left(-\left(\frac{t-b}{c}\right)^2\right) & \text{during diastole} \end{cases} \quad (19)$$

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.