

SUNSHINE
HEART

Hemodynamics of C-Pulse: Aortic Counterpulsation and Beyond?

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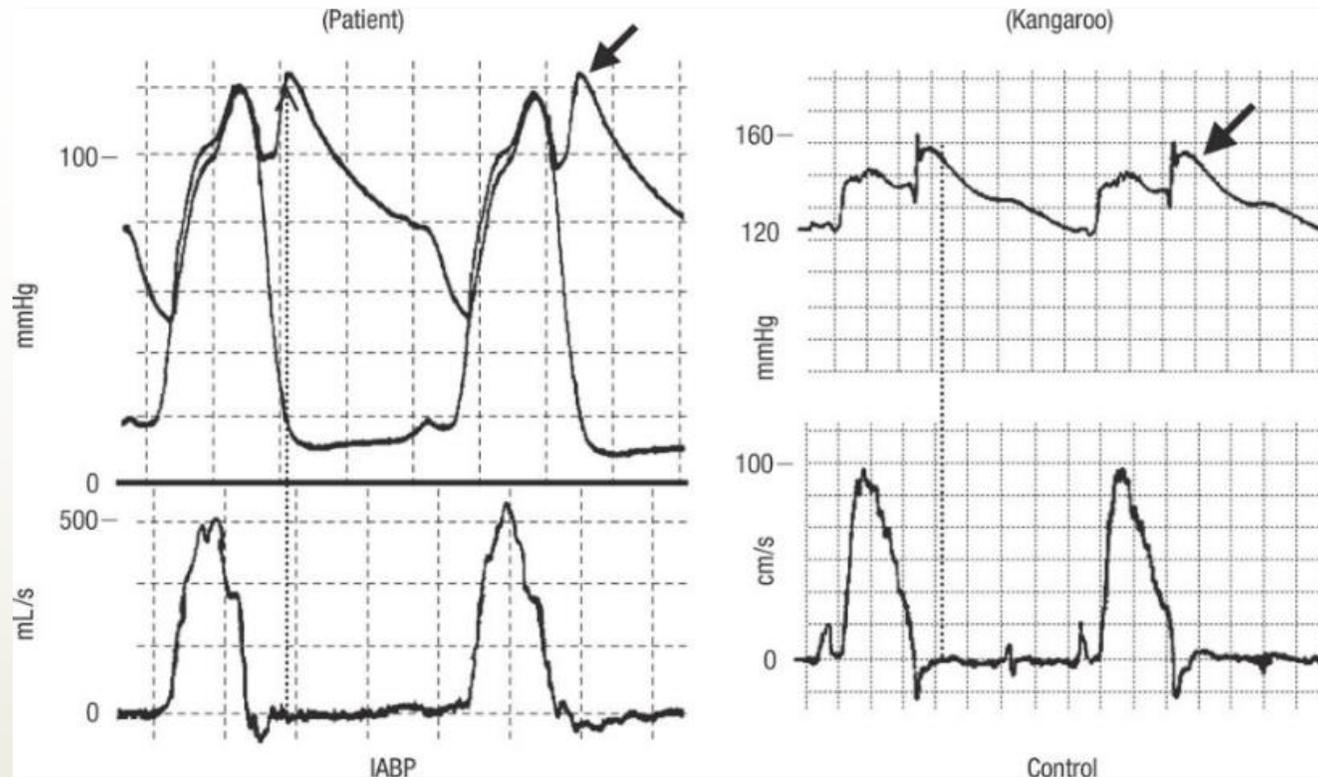
Dimitrios Georgakopoulos, PhD
CSO, Sunshine Heart Inc.

Forward Looking Statement



- This presentation contains forward-looking statements. All forward-looking statements are management’s present expectations of future events and are subject to a number of risks and uncertainties. Various factors could cause actual results to differ materially from these statements including timing, clinical enrollment, clinical results, financing availability, product sales and marketing or efficacy of products, and the other risks set forth under the caption “Risk Factors” and elsewhere in our periodic and other reports filed with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2014.
- Although the Company believes that the forward-looking statements are reasonable and based on information currently available, it can give no assurances that the Company’s expectations are correct. All forward looking statements are expressly qualified in their entirety by this cautionary statement.
- Caution: C-Pulse[®] is an investigational device. The device is limited by federal (United States) law to investigational use only.
- C-Pulse is a registered trademark of Sunshine Heart Inc.

Counterpulsation Mechanism Based On Physiologic Hemodynamics of Wave Travel in Arteries



McDonald's Blood Flow In Arteries. 6th Ed.

C Pulse Counterpulsation: 3D CT Clinical Example



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

25

C-Pulse Design: Unique Placement on Ascending Aorta

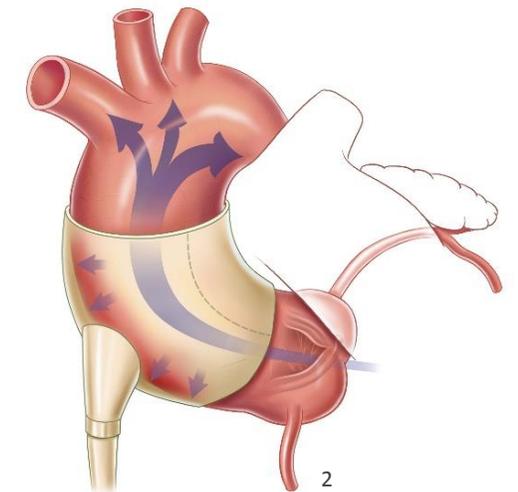
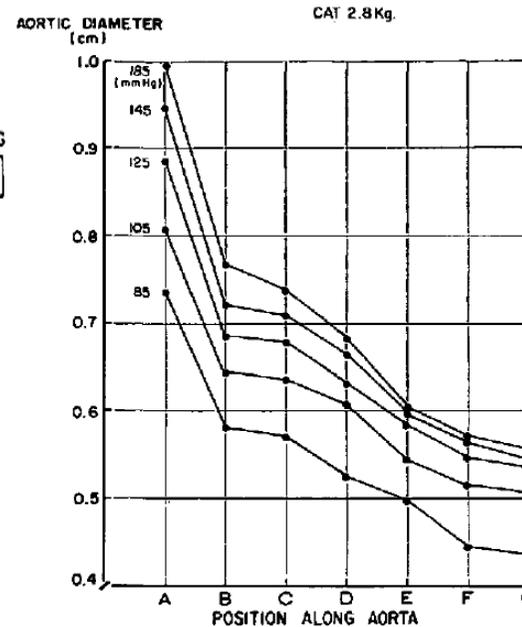
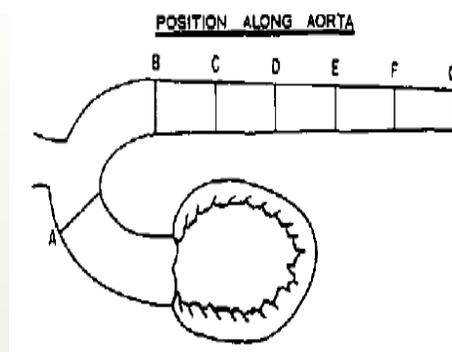
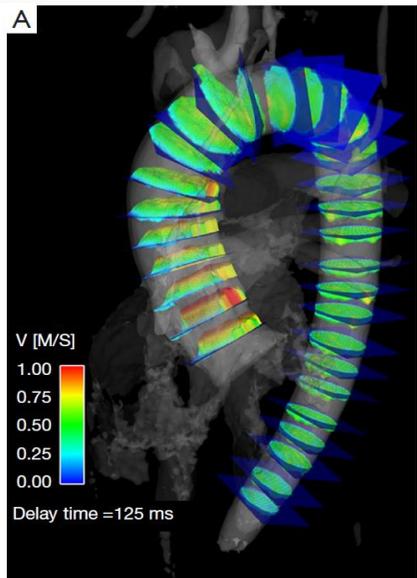
- **Proximal Aorta 70% of compliance in**

PROXIMITY TO AORTIC VALVE AND UNIDIRECTIONALITY AS PRIME FACTORS IN COUNTERPULSATION EFFECTIVENESS

S. Furman, R. Whitman, J. Stewart, B. Parker, and M. McMullen

An aortic occlusive balloon of small volume distal to the volume displacing balloon projected virtually the total displacement toward the heart and increased arch and coronary blood flow.

Vol. XVII Trans. Amer. Soc. Artif. Int. Organs



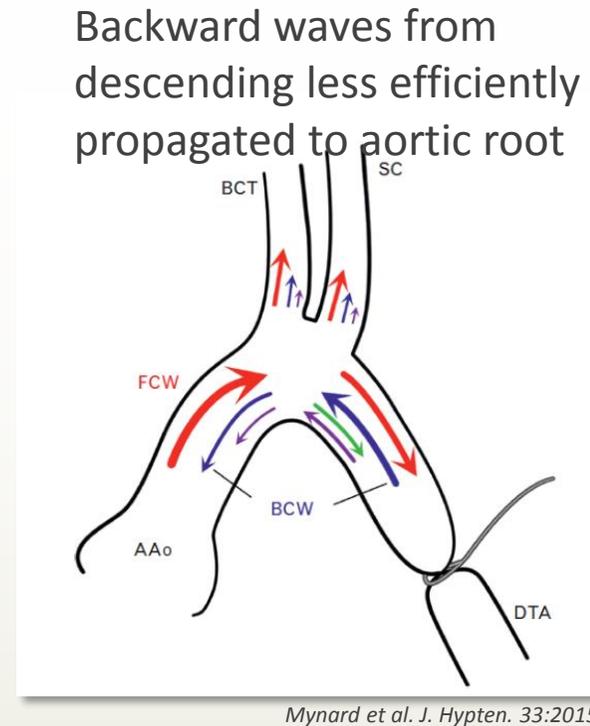
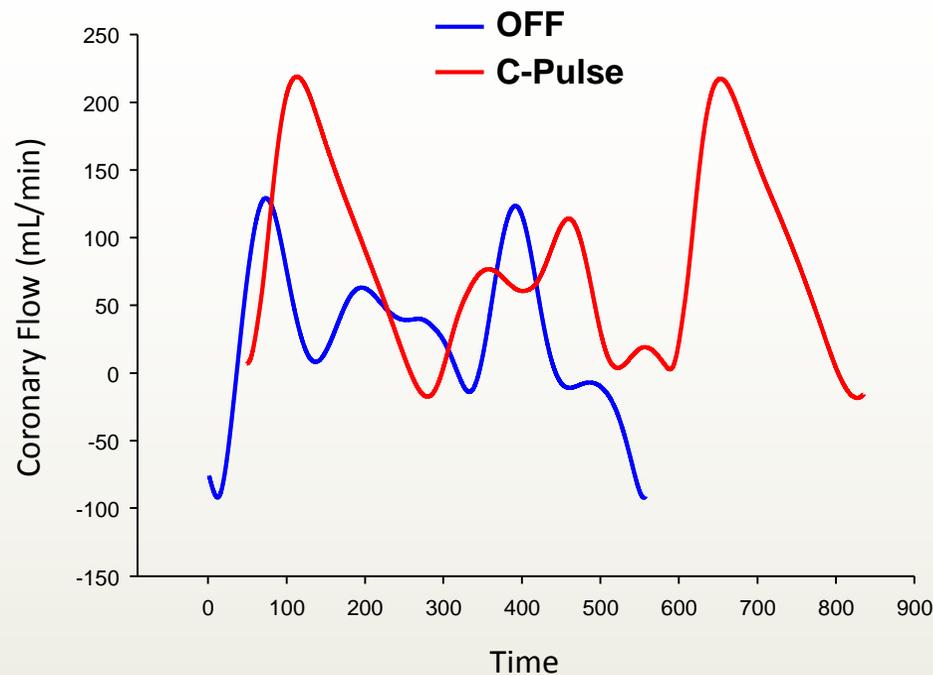
Arndt et al. Circ. Res. 28:1971

Counterpulsation and Myocardial Oxygen Consumption



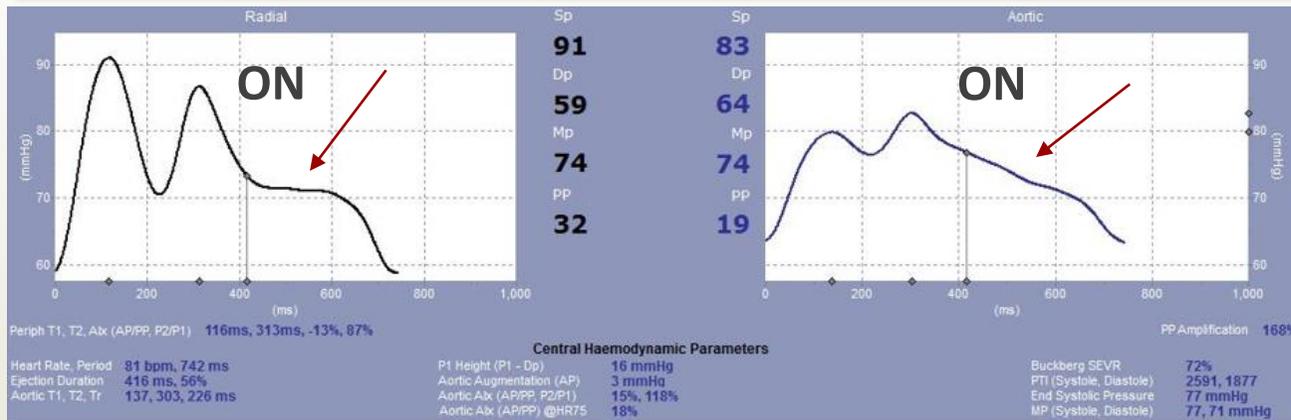
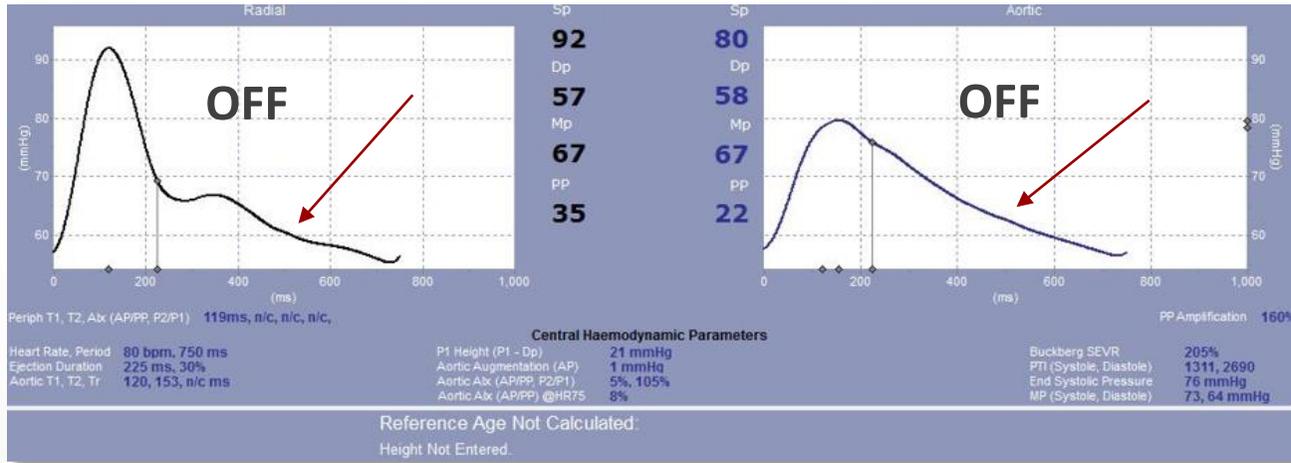
- The heart is especially **vulnerable** to ischemia, because its O₂ extraction ratio is 65% (vs. average of 25% for rest of body)
- Because the heart is near maximal O₂ extraction during increased demand, primarily accomplished by increasing blood flow

C-Pulse Effect on Coronary Hemodynamics in Normal Swine



“If you wanted to design a perfect sound absorber, you could hardly do better than a set of tapering and branching tubes ...such as the arterial tree. (DA McDonald 1960).”

Boost Diastolic Pressure: Reservoir for Coronaries to Fill



Counterpulsation and Coronary Perfusion and Oxygen Utilization at Rest and Exertion

Improvements in Myocardial Perfusion Observed in Patients Supported with the C-Pulse[®] Counterpulsation Device

Renzo Cecere¹, Marc Hickeson², Nadia Giannetti³

¹McGill University Health Centre, Cardiac Surgery, Montreal, Canada; ²McGill University Health Centre, Nuclear Medicine, Montreal, Canada; ³McGill University Health Centre, Cardiology, Montreal, Canada

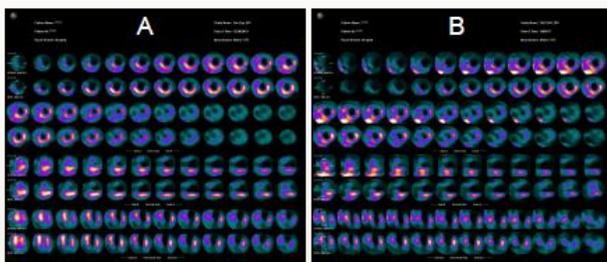


Figure 3. Patient 1. Ischemic cardiomyopathy. A. Baseline. B. 6-month.

MPI at baseline shows a perfusion defect involving the mid to distal anterolateral, anterior and antero-septal walls, the apex and the distal inferior and inferolateral walls with partial reversibility in the distal inferior and inferolateral walls at rest. At 6-months post-implant, there is improvement in perfusion in the distal inferior and inferolateral walls.

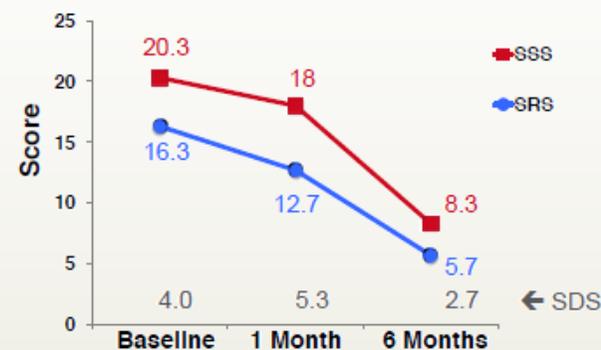


Figure 2. SPECT myocardial perfusion imaging (MPI) Stress-Rest scoring

What About Other Concept of Counterpulsation: Reduce Cardiac Afterload?

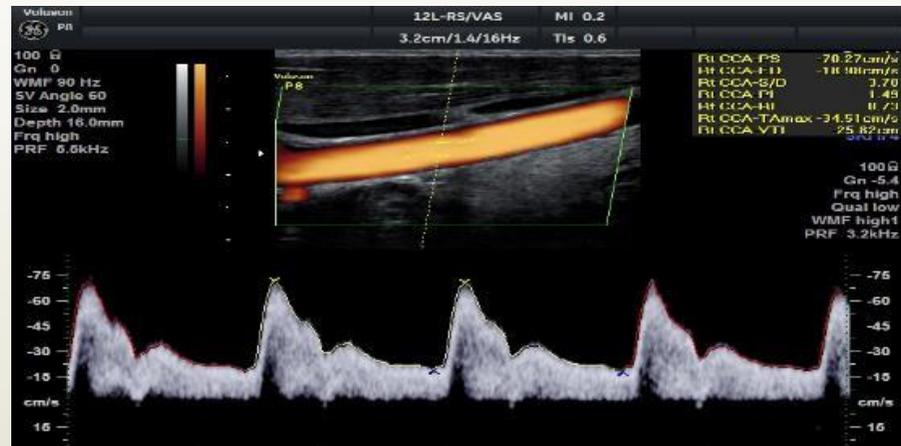
Play Video



LVOT

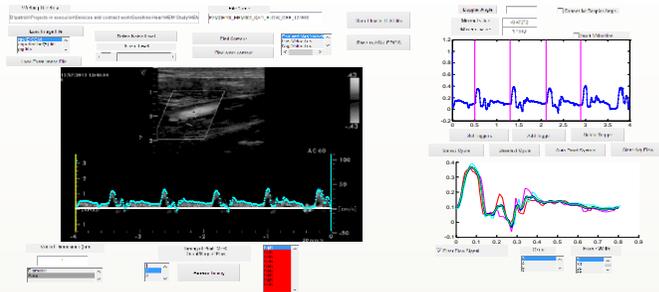


CCA

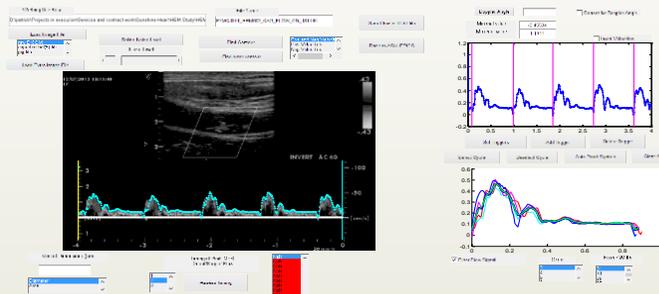


Ultrasound data – Ascending Aorta and Carotid Artery

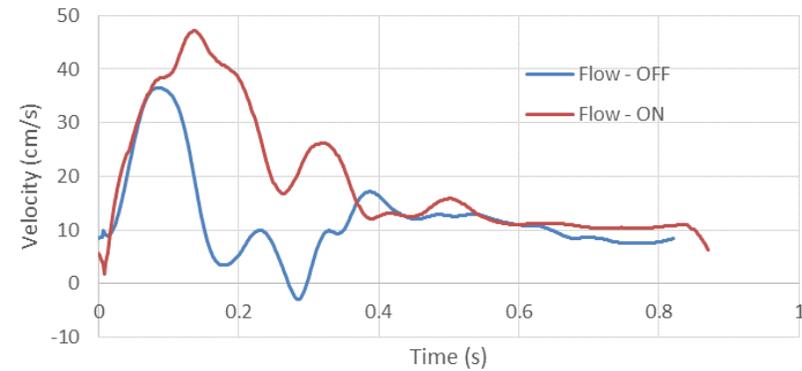
Device OFF



Device ON

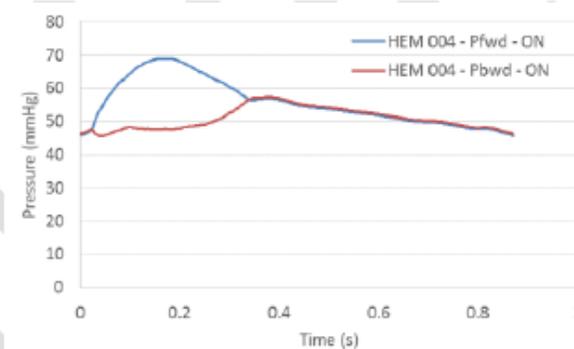
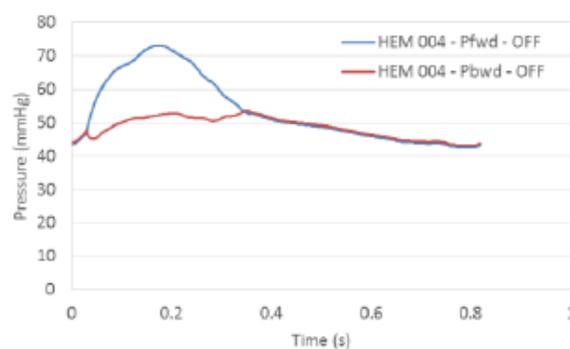
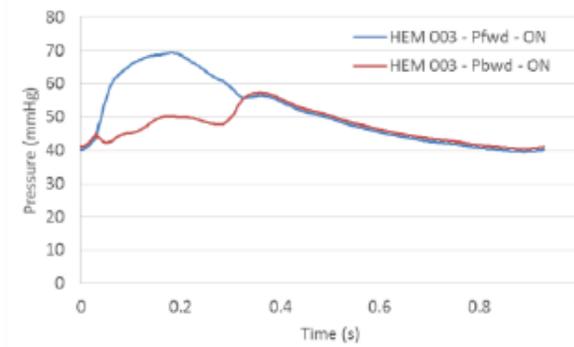
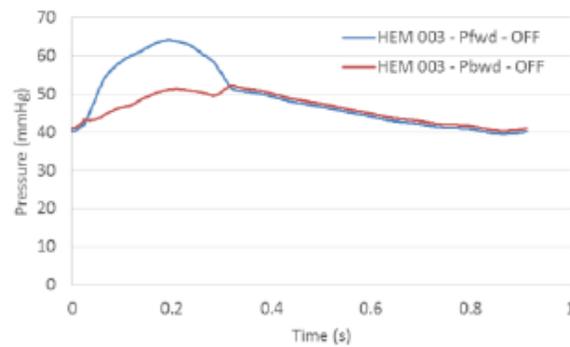
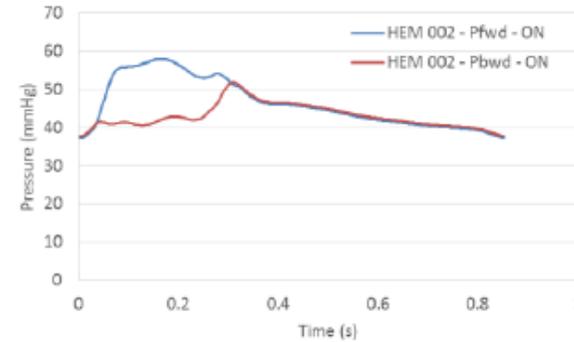
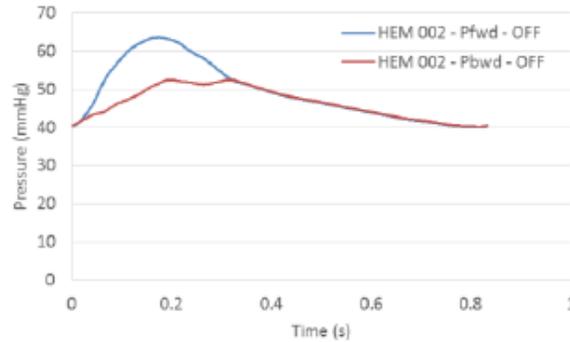


Carotid flow - HEM 002

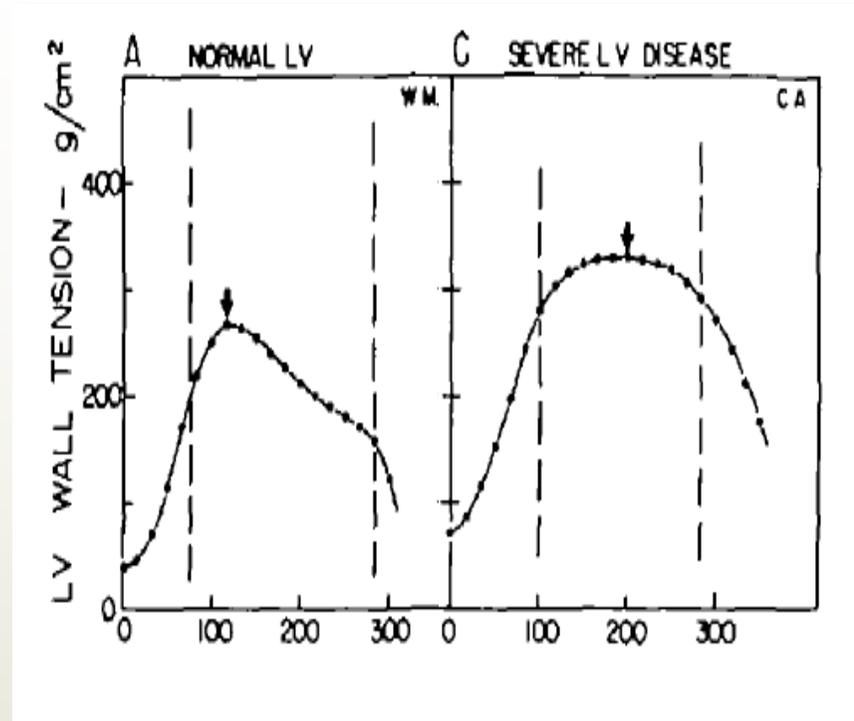
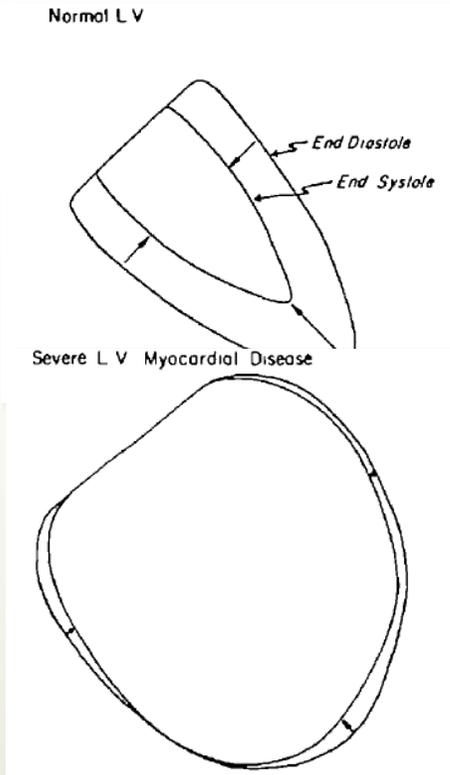


- Marked increase in carotid net flow (+57%)
- Increased flow in diastole
- Avg 30% increase in carotid flow

Forward and Backward Waves in Patients with C-Pulse: Ascending Aorta

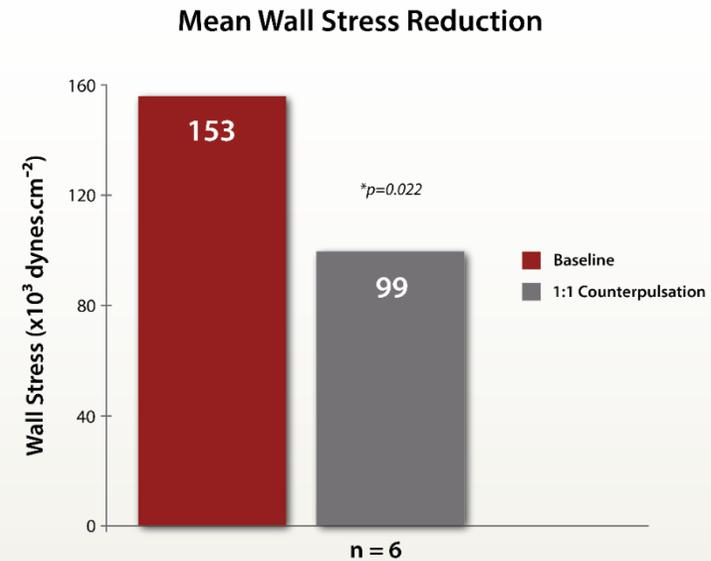
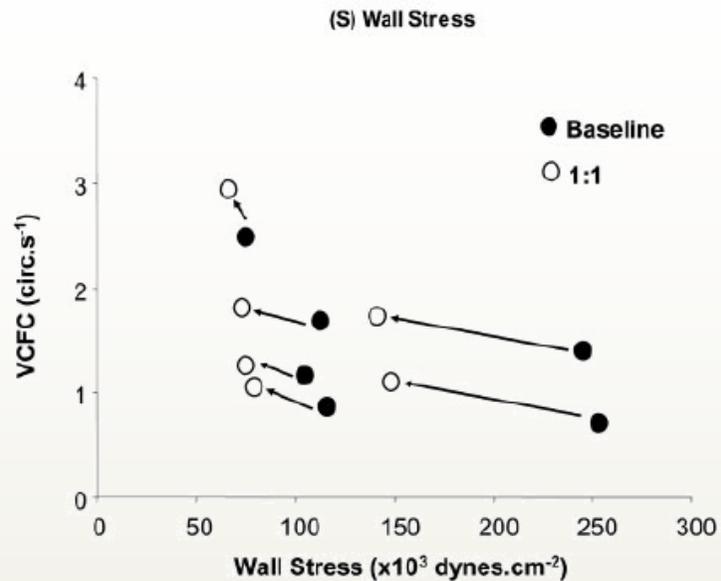


Wall Stress Peaks Late Systole in HF



Noordergraaf, A. Circulatory System Dynamics. Lea and Febiger (1976).

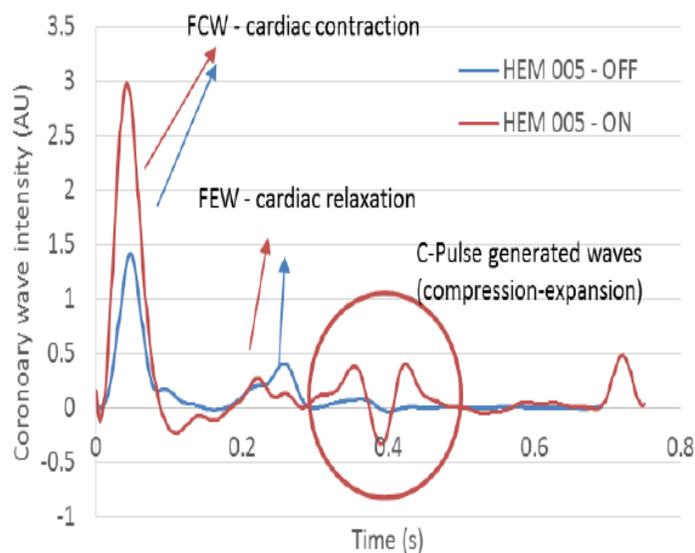
C-Pulse Reduces Wall Stress and Increases Shortening Velocity



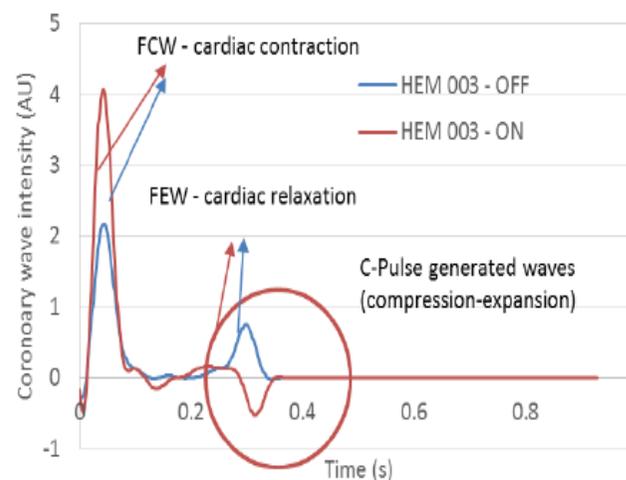
Leggett et al. *Circ.* 112:1-26. 2005

C- Pulse: Wave Intensity Analysis in Carotid and Aorta (N=3)

Carotid Artery

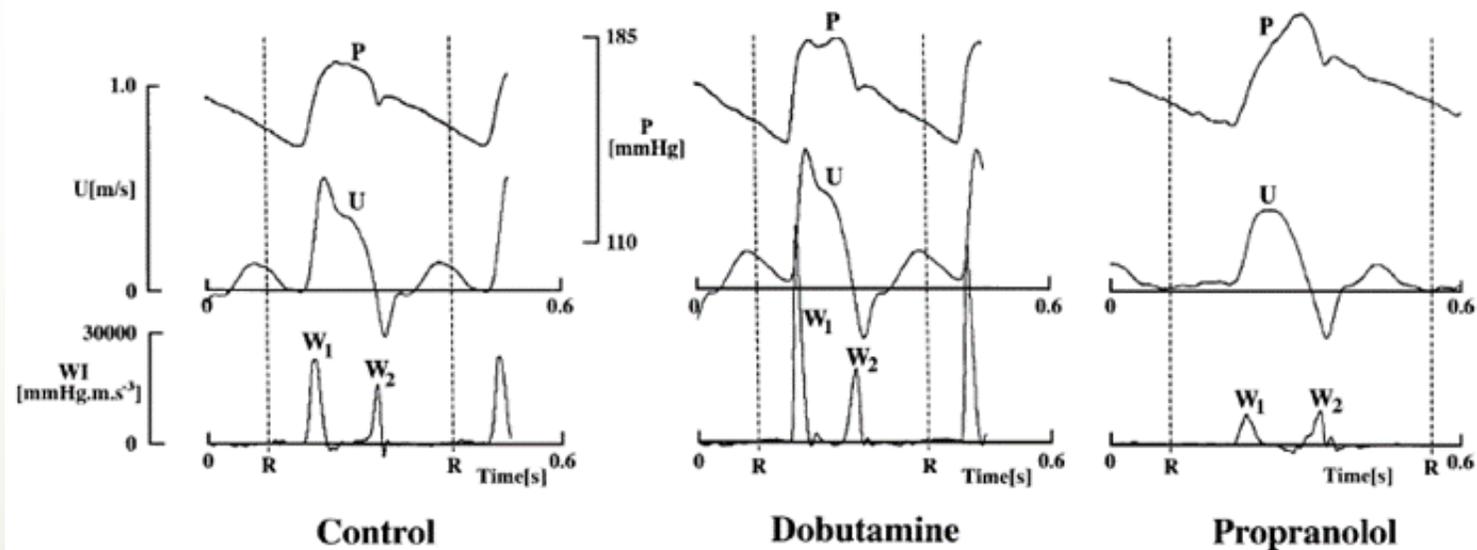


Ascending Aorta

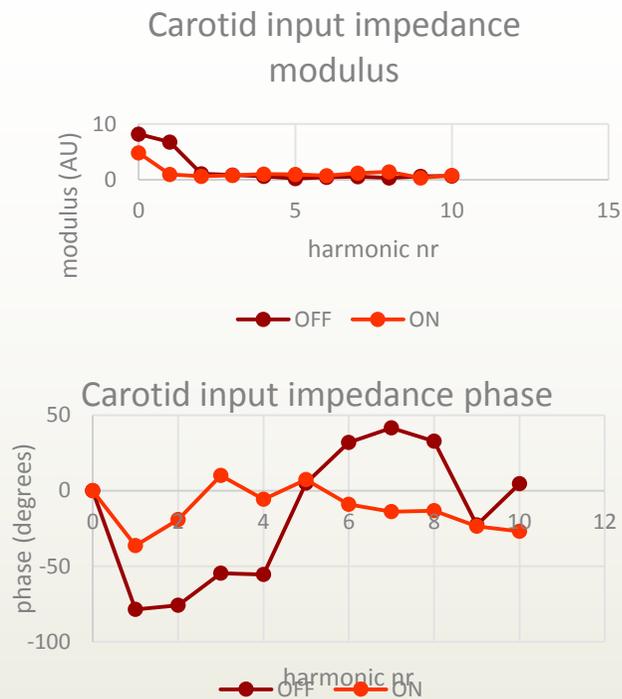


- Average Increase in Forward Compression Wave (Energy generated by LV): 65%
- Similar to positive inotrope with improved energetics profile

C-Pulse Hemodynamically Similar to Positive Inotrope



HEM 002 – Pressure and Flow – carotid artery



- Marked decrease in carotid bed resistance
- Marked decrease in impedance
- Impedance ~ reduced reflections

Avg. Reduction in DC
resistance: 30%

Clinical Importance of Wave Reflections and Late Systolic Load

Epidemiology/Population

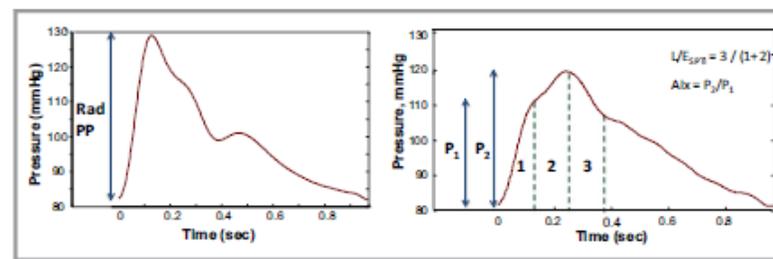
Reflection Magnitude as a Predictor of Mortality The Multi-Ethnic Study of Atherosclerosis

Payman Zamani, David R. Jacobs Jr, Patrick Segers, Daniel A. Duprez, Lyndia Brumback, Richard A. Kronmal, Scott M. Lilly, Raymond R. Townsend, Matthew Budoff, Joao A. Lima, Peter Hannan, Julio A. Chirinos *Hypertension 2014; 64: 958-964*

Late Systolic Central Hypertension as a Predictor of Incident Heart Failure: The Multi-Ethnic Study of Atherosclerosis

Julio A. Chirinos, MD, PhD; Patrick Segers, PhD; Daniel A. Duprez, MD, PhD; Lyndia Brumback, PhD; David A. Bluemke, MD; Payman Zamani, MD; Richard Kronmal, PhD; Dhananjay Vaidya, MBBS, PhD; Pamela Ouyang, MD; Raymond R. Townsend, MD; David R. Jacobs, Jr, PhD

(J Am Heart Assoc. 2015)



Hemodynamic Effects of Unloading with C-Pulse On Central Pressure and Wave Reflections



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 Pennsylvania, Philadelphia, PA; Dimitrios Georgakopoulos, David Pomfret, Sunshine Heart Inc, Eden Prairie, MN; Pavan Atluri, Hosp of the Univ of Pennsylvania, Philadelphia, PA; Phi Wieg, 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

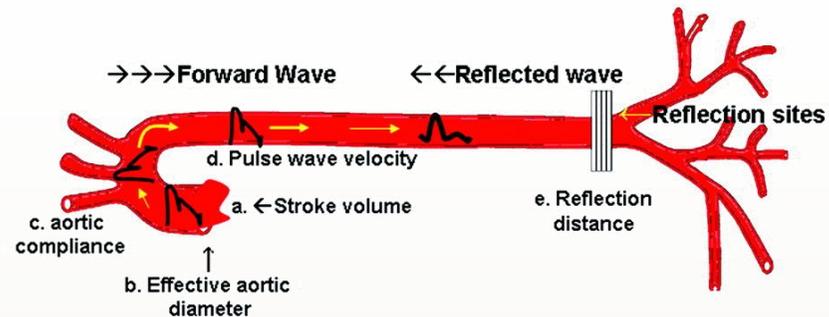
(N=6)	OFF	ON
Max Aortic BP (mmHg)	EMBARGOED	
Diastolic BP (mmHg)		
P1 (mmHg)		
Time to P2 (ms)		
SEVR		
Aix (P2/P1)		

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

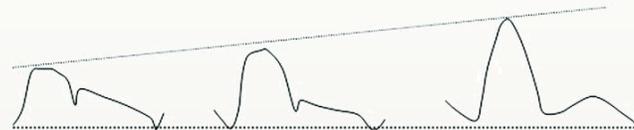
To be presented AHA 2015!

Wave Reflections Primarily Arise from Periphery: How Does C-Pulse Affect Peripheral Arteries?

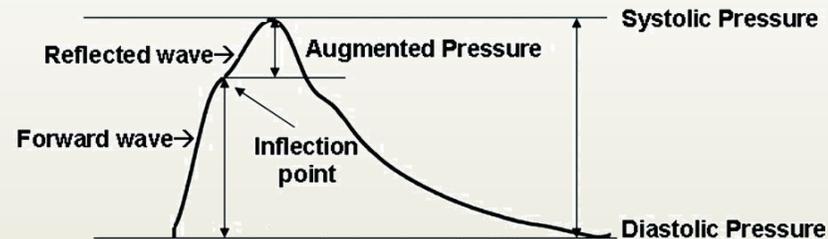
I. Correlates of Pulse Pressure



II. Peripheral Amplification of Pulse Wave



III. Summated Forward & Reflected Waves in the setting of a stiff aorta



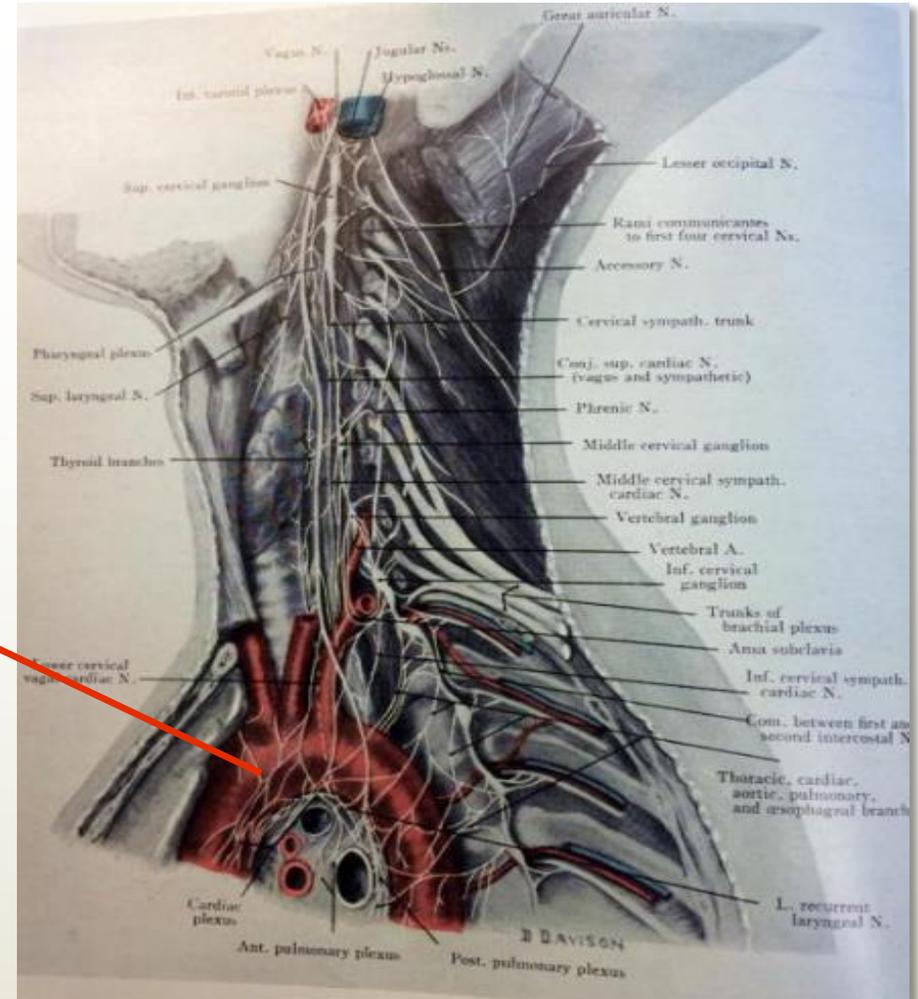
***HOW DOES A CUFF IN ASCENDING
AORTA INFLUENCE PERIPHERAL VESSELS?***

Large Unloading Effects Partly Due to Neural Reflexes?

Direct and reflex vascular effects of intra-aortic balloon counterpulsation in dogs

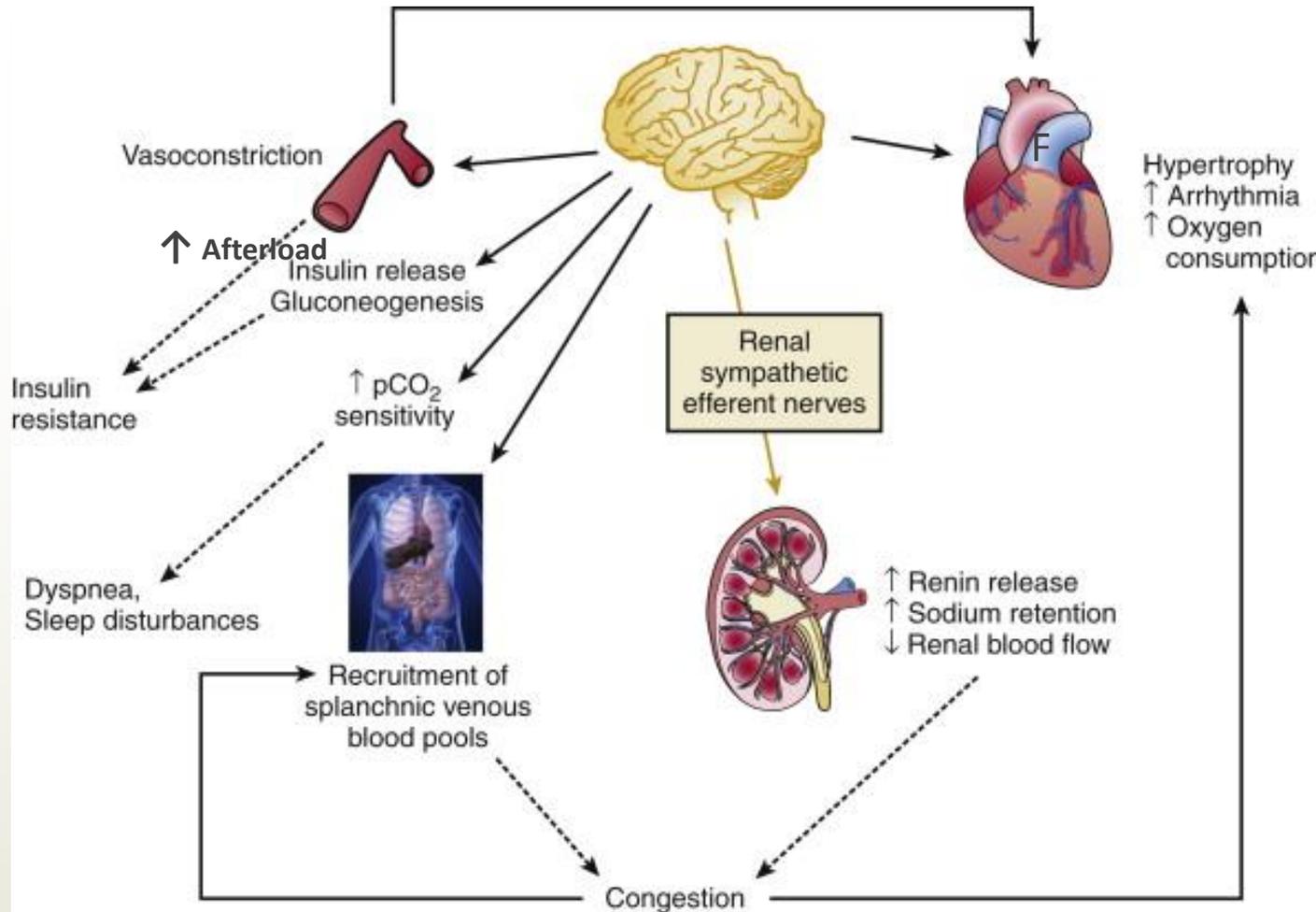
Am. J. Physiol. 221(3); 1971

**C-Pulse balloon placement
even more optimal location
to activate reflexes**

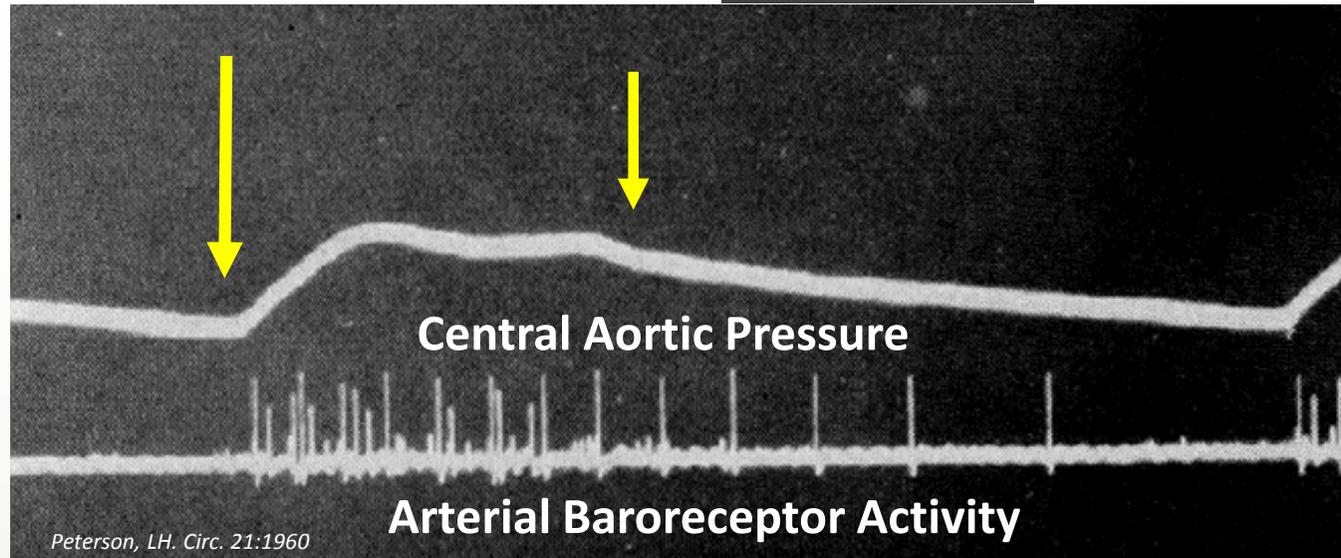


Mitchell GAG. *Anatomy Autonomic Nervous System.* 1953

Systemic Effects of Neural Reflex Modulation of Sympathetic Nervous System



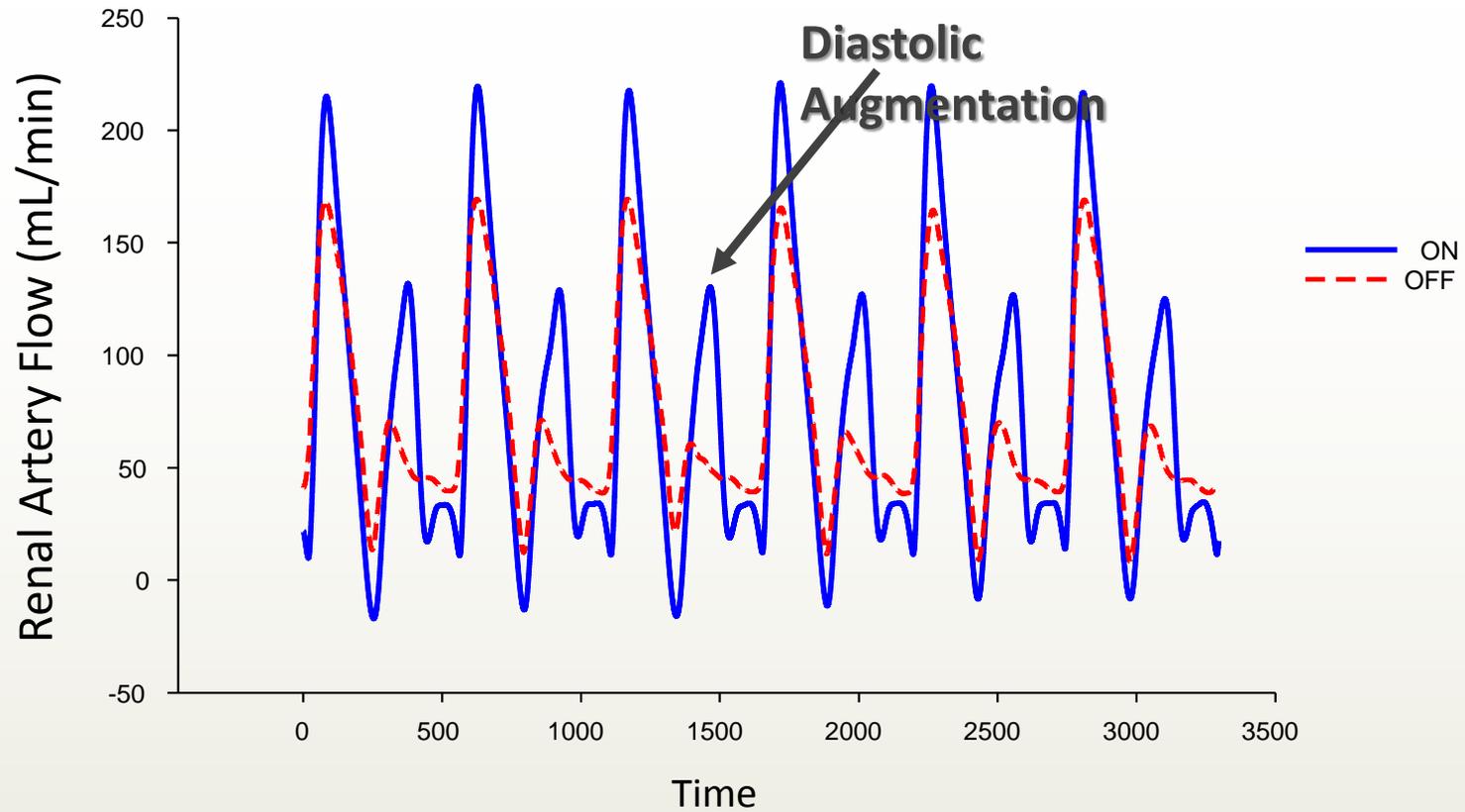
C-Pulse



Bronk and Stella. J Cell. Comp. Physiol. (1): 1932

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

C-Pulse Effects on Renal Blood Flow: Normal Swine



C-Pulse and Volume Management

Patient with C-Pulse Therapy and Cardiomechs

C-Pulse OFF



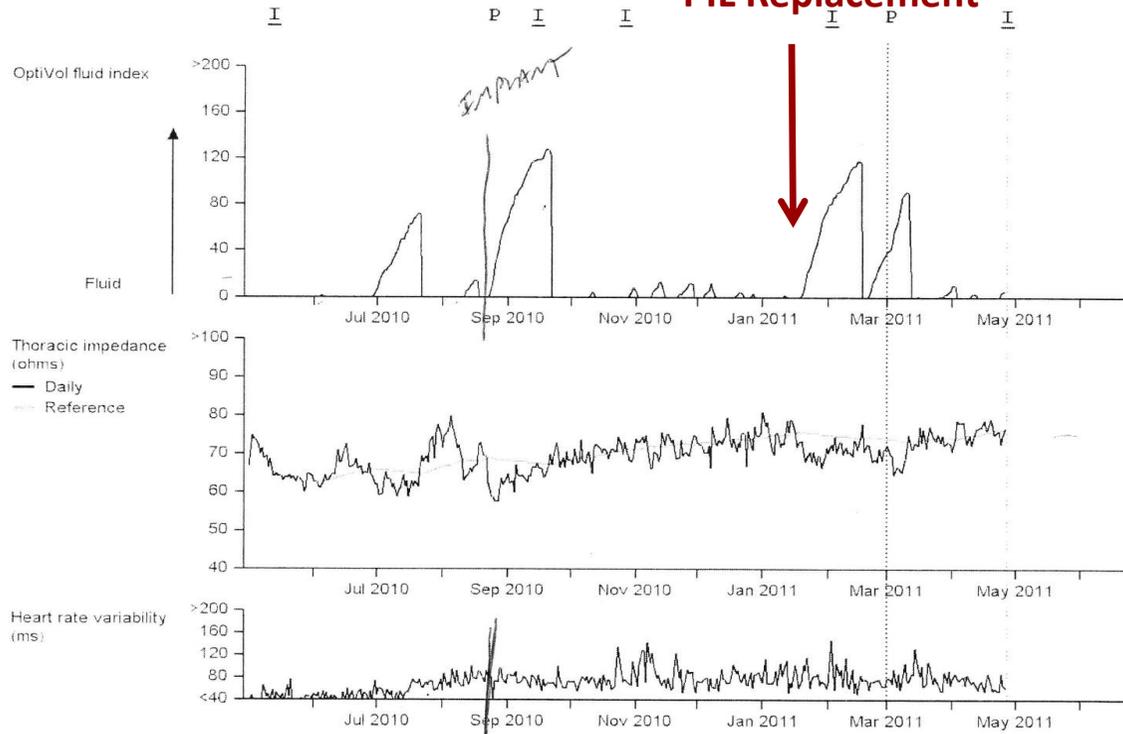
Submitted to HFSA 2015

C-Pulse and Heart Rate Variability: Clinical Case

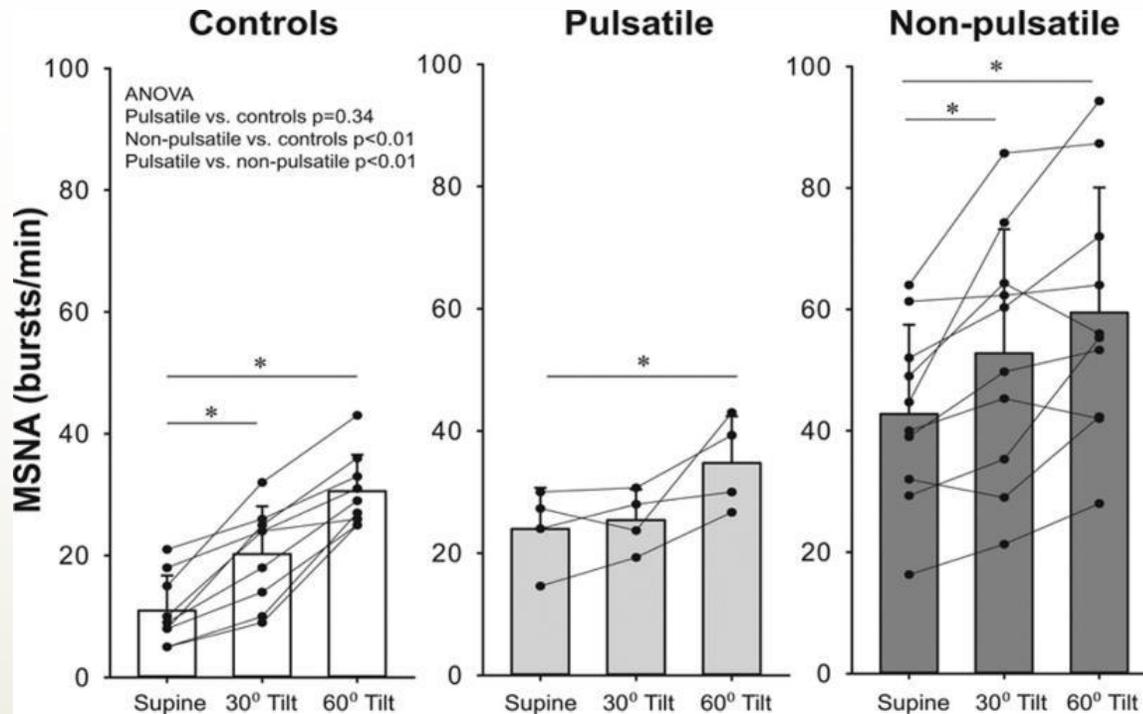


Cardiac Compass®

PIL Replacement



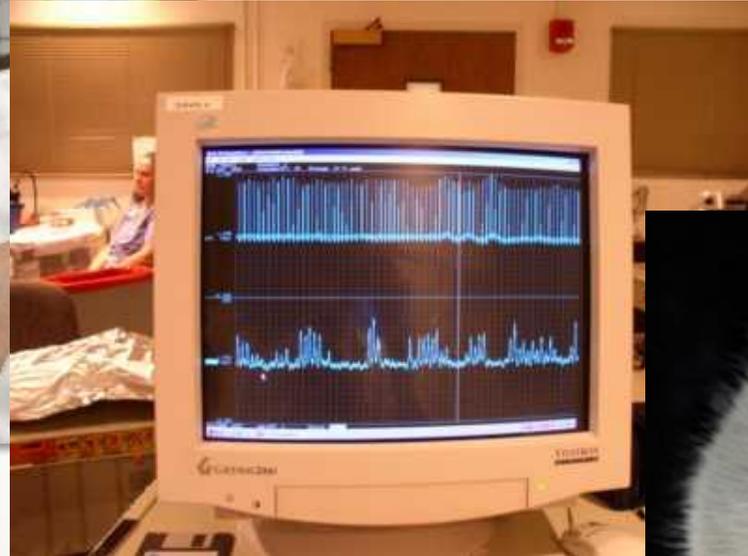
Pulsatility and Sympathetic Nervous System: Insights from LVAD Patients



Individual and mean muscle sympathetic nerve activity (MSNA) burst frequencies in healthy controls and patients with pulsatile and non-pulsatile left ventricular assist devices in the supine position and during upright tilt.

Markham D W et al. *Circ Heart Fail.* 2013;6:293-299
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C-Pulse and Studies to Assess Neuromodulation Effects: Multi-Disciplinary Approach



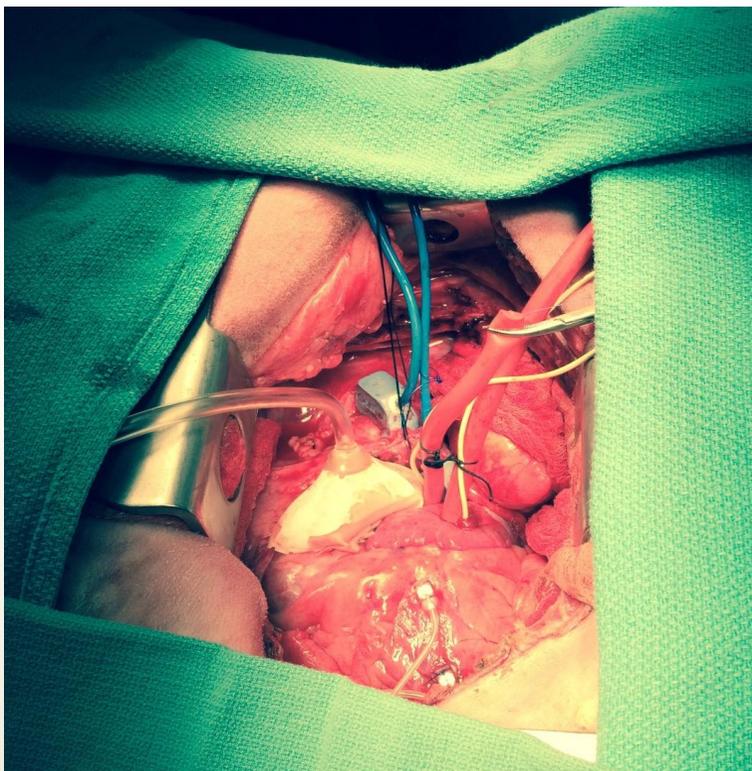
HEMODYNAMIC IMPACT OF THE C-PULSE CARDIAC SUPPORT DEVICE: A 1D ARTERIAL MODEL STUDY

D. Campos Arias¹, T. Rodriguez, N. Stergiopoulos², P. Segers³

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

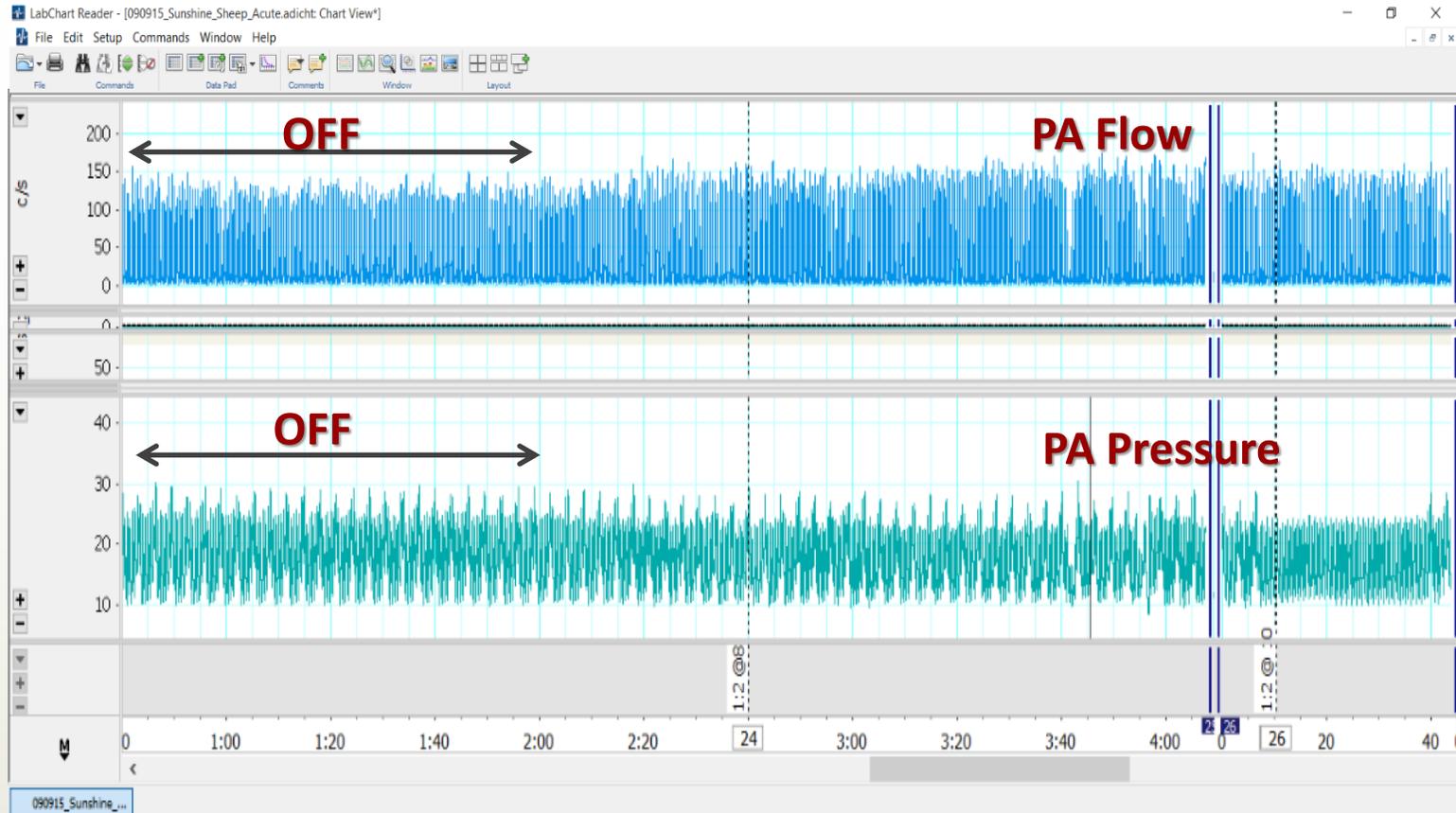


Animal Studies: Pulmonary Artery Counterpulsation

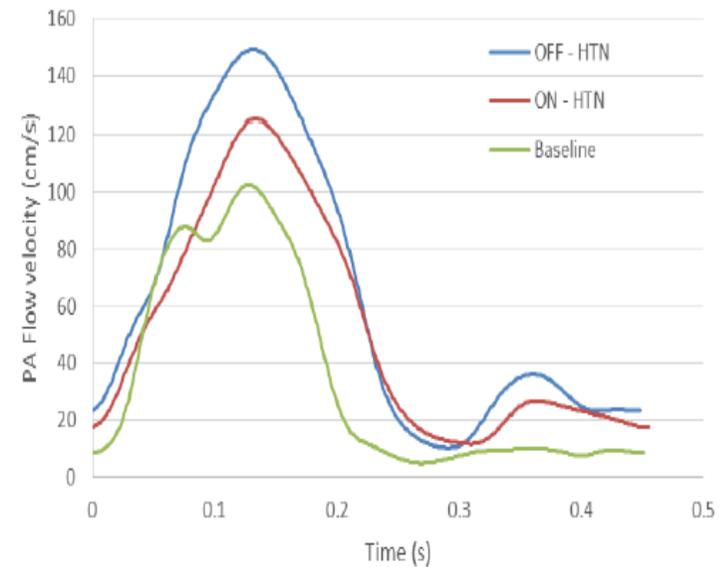
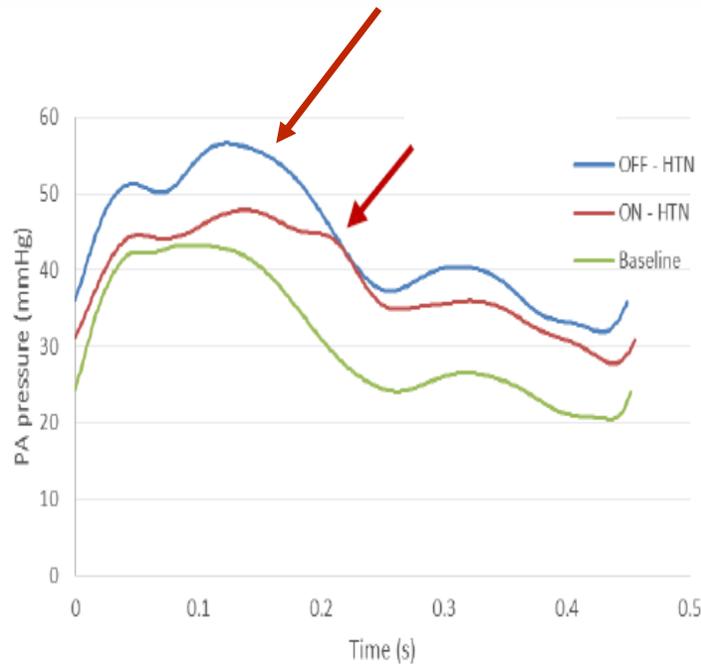


- Pulmonary HTN
- RV Failure Secondary to LVAD
- Congenital Defects (Tetralogy of Falot)

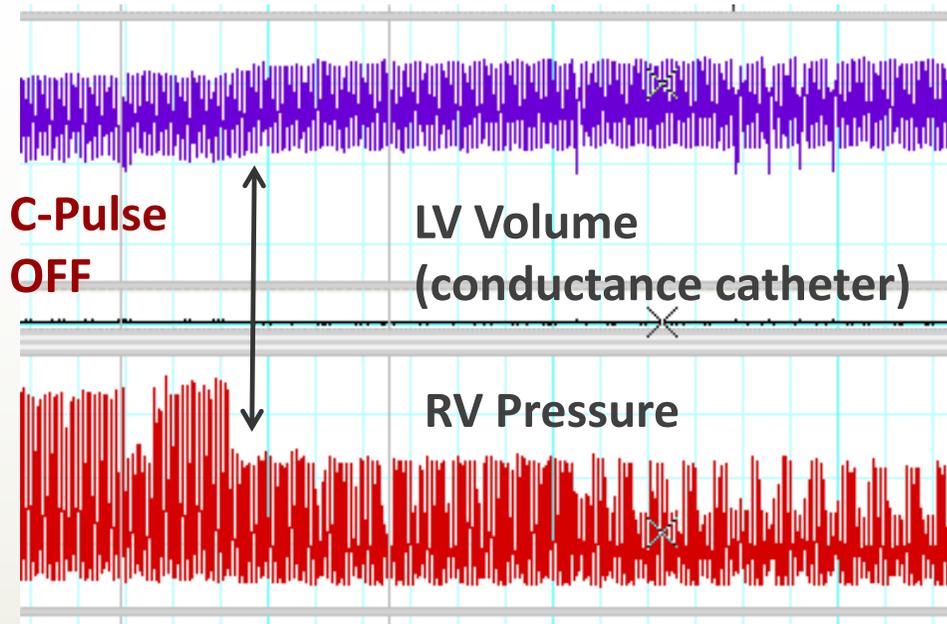
C-Pulse Counterpulsation on Pulmonary Artery



Pulmonary Pressure and Flow in PA HTN: C Pulse Acutely Reverses Elevated PA Pressure

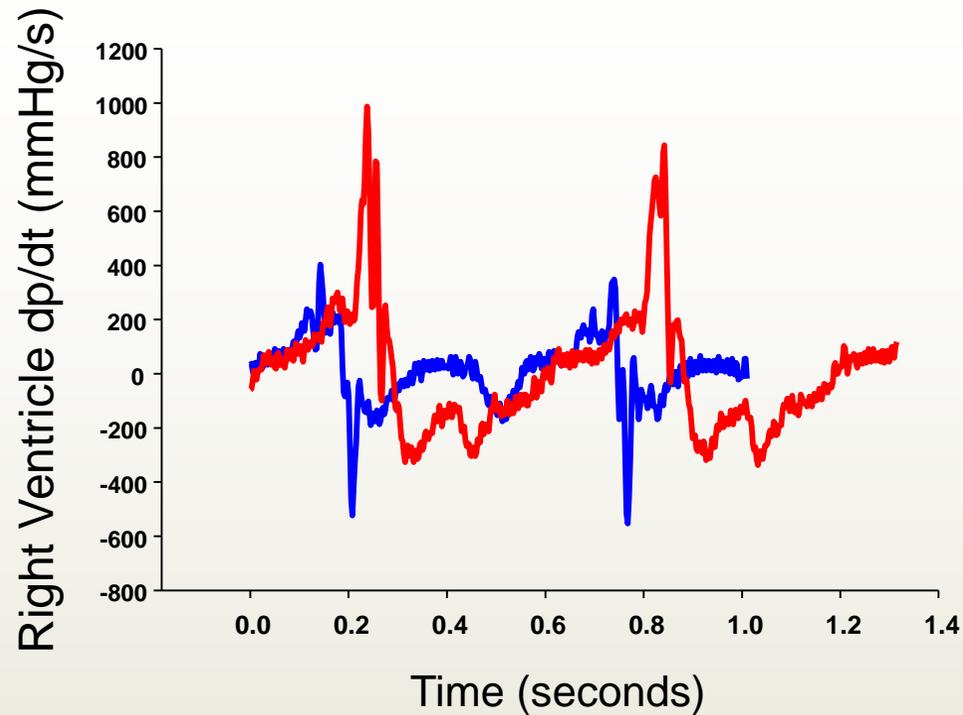


C-Pulse Unloads RV during Right Heart Failure and Simultaneously Reduces LV Dilation



- C-Pulse restores RV function in setting of pulmonary hypertension and acute RV failure
- Reduces dilation of LV during right heart failure

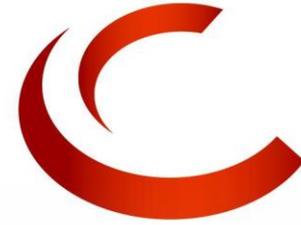
Counterpulsation on PA Improves RV Function In Acute Right Heart Failure due to Embolism



Summary

- C pulse provides based on traditional concepts of counterpulsation: increase coronary perfusion and afterload reduction.
- Advanced hemodynamic analysis from patients indicates afterload reduction in late systole not onset of ejection related to balloon deflation.
- Late systolic reduction associated with marked vasodilation in carotid artery and distal arterioles. What is mechanism????
- Hypothesis of mechanical stimulation of aortic and carotid baroreceptors. Stimulation due to nature of counterpulsation timed during cardiac cycle mimics physiologic stimulation pattern
- Chronic neuromodulation and enhanced coronary perfusion may provide substrate for chronic remodeling and myocardial recovery.

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Thank You!

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