

# Improved Myocardial Energetics Following Chronic Treatment Using an Implantable Device in Resistant Hypertension: Results from European and United States Trials of the Rheos® System

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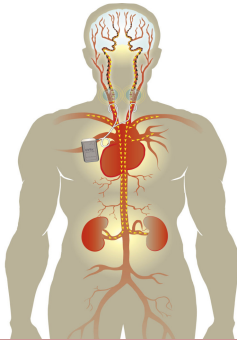
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## Introduction

- Patients with resistant hypertension often have increased left ventricular fibrosis and arterial stiffness which may be accompanied by increased left ventricular stroke work and increased myocardial oxygen demand.
- These adverse functional changes to the heart and systemic vasculature, as well as abnormalities in left ventricular structure, are associated with poor outcome and may contribute to reduced functional capacity.
- The Rheos® System uses Baroreflex Activation Therapy® (BAT®) to chronically activate the carotid baroreflex and has been shown to significantly reduce systolic and diastolic blood pressure in patients with resistant hypertension.
- It is unknown if BAT improves myocardial energetics and mechanical efficiency in resistant hypertension patients.

### Mechanisms of Rheos Therapy

The Rheos System is designed to electrically activate the carotid baroreceptors, the body's natural cardiovascular regulation sensors. When the baroreceptors are activated, signals are sent through neural pathways to the brain and interpreted as a rise in blood pressure. The brain works to counteract this perceived rise in blood pressure by sending signals to other parts of the body (heart, blood vessels and kidneys) that relax the blood vessels and inhibit the production of stress-related hormones. These changes enable the heart to increase output, while maintaining or reducing workload, thereby reducing blood pressure.

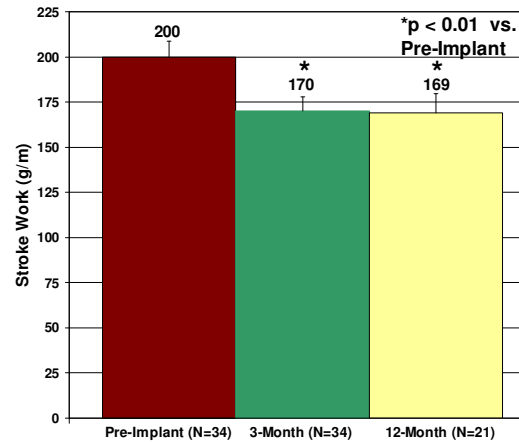


## Methods

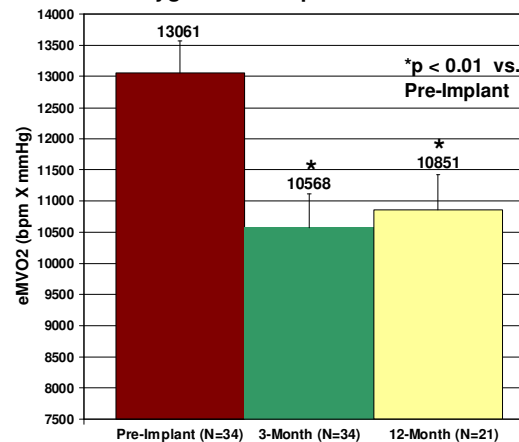
- Patients implanted with the Rheos system had Stage II Hypertension (systolic BP  $\geq 160$  mmHg) and were taking  $\geq 3$  anti-HTN drugs including at least one diuretic to treat their hypertension. The patients are from a subset of the DEBuT and US Feasibility studies of the Rheos device for whom complete echocardiographic data were available. The device was activated 1 month after implant to deliver BAT.
- Echocardiographic data were collected after 3 and 12 months of therapy initiation in a subset of patients and analyzed at a blinded core lab.
- Stroke work was calculated as systolic BP  $\times$  stroke volume  $\times 0.0144$  and eMVO<sub>2</sub> was defined as heart rate  $\times$  systolic BP. Myocardial mechanical efficiency was defined as the ratio of stroke work / (eMVO<sub>2</sub><sup>2</sup>/60).

## Results

### Sustained Reduction in Left Ventricular Stroke Work After BAT



### Improvement in Estimated Myocardial Oxygen Consumption After BAT



### Improvement in Cardiac Function and Structure

<u>Cardiac Function</u>	Pre-Implant (N = 34)	3-Month (N = 34)	12-Month (N = 21)
Myocardial Mechanical Efficiency (%)	0.94 $\pm$ 0.04	0.98 $\pm$ 0.04	0.95 $\pm$ 0.05
Midwall Fractional Shortening (%)	13.9 $\pm$ 0.05	14.9 $\pm$ 0.05*	15.6 $\pm$ 0.07*
<u>Cardiac Structure</u>			
Left Atrial Diameter (mm)	44.8 $\pm$ 1.1	43.6 $\pm$ 0.9*	41.9 $\pm$ 1.5*
LV Mass (g)	302 $\pm$ 16	262 $\pm$ 13*	235 $\pm$ 18*
LV Mass Index (g/m <sup>2</sup> )	138.9 $\pm$ 6.0	120.9 $\pm$ 5.3*	108 $\pm$ 7*
LV Septal Wall (mm)	14.4 $\pm$ 0.5	13.2 $\pm$ 0.5*	12.4 $\pm$ 0.5*

Data are mean  $\pm$  SE; \* P < 0.05 vs. Pre-Implant

### Other Findings

- No significant change in BMI was observed in the cohort over 12 months of follow-up.
- Patients with a NYHA  $\geq$  I had a significant improvement (438  $\pm$  153 m to 475  $\pm$  153 m,  $p = 0.01$ , N = 21) in 6-minute Walk Distance after 12 months of active therapy.
- Arterial compliance, defined as stroke volume/SBP, was significantly improved (1.12  $\pm$  0.1 to 1.33  $\pm$  0.1 mL/mmHg,  $p = 0.02$ ) after 12 months of BAT.
- Given the positive correlation of arterial compliance and LV diastolic pressures (Borlaug et al 2007), the improvements observed in arterial compliance likely contributed to improvements in diastolic function.

## Conclusions

- In addition to previously documented blood pressure reduction, chronic BAT improves myocardial energetics, as indicated by reduced stroke work and eMVO<sub>2</sub>, while maintaining normal myocardial efficiency in resistant hypertensive patients.
- Concomitant improvements in cardiac structure were also observed.
- These data suggest that BAT provides benefits beyond blood pressure reduction.

CAUTION: The CVRx Rheos System is an investigational device and is limited by Federal (or United States) law to investigational use only.

The Rheos System is CE Marked for the treatment of resistant hypertension. CVRx, Rheos, Baroreflex Activation Therapy, and BAT are trademarks of CVRx, Inc. © CVRx, Inc. 2009.