

# ArrhythmiaNEWS

*From the Arrhythmia Service of St. Luke's-Roosevelt Hospital Center*

*Arrhythmia News* is a physician bulletin providing arrhythmia updates and information on services at **St. Luke's-Roosevelt Hospital Center** which may benefit your practice and your patients.

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## The OPTIMIZER II System – An Innovative New Treatment for Congestive Heart Failure

Congestive heart failure (CHF) resulting from systolic dysfunction accounts for a large proportion of health care expenditure and resource allocation. An estimated **five million** Americans suffer from congestive heart failure with almost 500,000 new cases of congestive heart failure diagnosed each year. Despite many advances in the treatment of CHF, it remains the leading cause of hospitalization in the United States.

CHF is a condition in which the heart can't pump enough blood to the body's other organs. This can result from a variety of causes such as coronary artery disease, high blood pressure, heart valve disease or primary disease of the heart muscle itself. The "failing" heart keeps working but not as efficiently as it should.

Medical therapy for CHF combines several classes of medications including **diuretics, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta-blockers, digoxin** and often **spironolactone**. In patients with electrocardiographic evi-

dence of intra-ventricular conduction system delay and ventricular dyssynchrony, pharmacologic therapy is often augmented by the addition of bi-ventricular pacing (cardiac re-synchronization therapy).

## Improved Systolic Performance

Evidence from *in-vitro* experiments on heart muscle preparations suggest that the application of non-excitatory electrical signals to heart muscle affects intra-cellular calcium homeostasis, and thus modulation of cardiac contractility can be accomplished. When non-excitatory cardiac contractility modulation (CCM) signals were studied in animals and humans, these electrical signals **enhanced hemodynamic parameters** and improved systolic performance. Intra-cellular microelectrode recordings showed that improved contractility was associated with prolongation of the action potential and not related to recruitment of additional myocardial fibers.

Experimental evidence suggests that CCM signal application to either the right or left ventricle can improve myocardial contractility, but the effects are greatest when the signals are delivered simultaneously from two electrodes inserted into the right ventricular septum. In a pilot study, CCM signals delivered through a catheter placed in the great cardiac vein of patients, enhanced hemodynamic parameters that were additive to the effects of bi-ventricular pacing (cardiac re-synchronization therapy).

## Studies Produce Promising Results

Examination of the effects of CCM application on myocardial structure and function revealed no apparent alteration in appearance (microscopic or gross) of the myocardium either at the site of implantation or remote from it. Additionally, the myocardium maintained normal inotropic reserve as evidenced by normal resting function and response to dobutamine infusion.

Given the promising results of preliminary animal and human studies, along with the safety profile of this system, a clinical investigation was performed to evaluate the safety and functionality of this system in subjects with New York Heart Association (NYHA) class III heart failure. Data from this study indicated that there was a **statistically significant** improvement in symptoms and ejection fraction in the 22 subjects studied.

There was no significant change in heart rate, number of PVC's or PAC's per hour or number of runs of non-sustained ventricular tachycardia in the patients studied. These promising initial results have prompted the interest in conducting a larger, multi-center, randomized, blinded trial.

**The Arrhythmia Service**, in conjunction with the **Congestive Heart Failure Program** at St. Luke's-Roosevelt Hospital Center will be one of only 30 study sites in the U.S. set to enroll 340 patients for this randomized double-blind trial.

**About OPTIMIZER II**

The CCM system to be evaluated and implanted in this trial is comprised of four major components: three standard pacemaker leads and a pulse generator. The three leads are placed in the heart; one in the right atrium to sense right atrial activity and two in the right ventricle to sense ventricular activity and deliver CCM signals. The non-excitatory electrical signals are applied to the heart using a novel pulse generator system, **The OPTIMIZER II System**. Leads can easily positioned in the right ventricle through a procedure similar to that of permanent pacemaker implantation and the pulse generator is placed in a similar fashion to a permanent pacemaker generator.

**Trial eligibility criteria include:**

- Age > 18
- Ejection fraction  $\leq$  35%
- NYHA Class III-IV CHF on appropriate medical therapy

This innovative treatment may be particularly appealing for use in patients with progressive CHF, reduced LVEF, on optimal medical therapy, who do not meet criteria for bi-ventricular pacing (cardiac re-synchronization therapy) because of a narrow QRS on the surface EKG. Additionally, this system

is safe for use in patients who have existing defibrillators or who are candidates for ICD implantation.

The primary endpoints of the trial, to be assessed six months after implantation, are comprised of a variety of clinical CHF endpoints such as NYHA class improvement, quality of life and exercise tolerance. Secondary endpoints include left ventricular size and function as well as the need for changes in the medical treatment for heart failure. Additionally, several safety endpoints such as mortality and hospitalizations will be examined.

For more information about this trial, please contact the Arrhythmia Service at one of the numbers listed below.

**References:**

1. Burkhoff D, Shemer I, Felzen B, Shimizu J, Mika Y, Dickstein M, Prutchi D, Darvish N, Ben-Haim SA. *Electric currents applied during the refractory period can modulate cardiac contractility in vitro and in vivo*. Heart Fail Rev. 2001;6:27-34.
2. Ellison K. *Nonexcitatory stimulation: 2002: a pace odyssey*. J Cardiovasc Electrophysiol. 2002;13:696-7.

3. Marrouche NF, Pavia SV, Zhuang S, Kim YJ, Tabata T, Wallick D, Saad E, Abdul-Karim A, Schweikert R, Saliba W, Tchou P, Natale A. *Nonexcitatory stimulus delivery improves left ventricular function in hearts with left bundle branch block*. J Cardiovasc Electrophysiol. 2002;13:691-5.

**The Arrhythmia Service  
of St. Luke's-Roosevelt  
Hospital Center**

Jonathan Steinberg, MD, Director

Frederick Ehlert, MD

Avi Fischer, MD

Walter Pierce, MD

Margot Vloka, MD

Private Office: (212) 523-8353

Hospital Office: (212) 523-4007

Ridgewood, NJ: (201) 251-9080

Staten Island: (718) 981-0396

Goshen, NY: (845) 373-7400

FAX: (212) 523-3915

**St. Luke's  
Roosevelt**

Continuum Health Partners, Inc.

St. Luke's-Roosevelt Hospital Center  
1111 Amsterdam Avenue at 114th St.  
New York, NY 10025

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