

Introducing a new minimally invasive investigational  
treatment for patients with heart failure  
**AUTONOMIC REGULATION THERAPY (ART)**



**LivaNova**

Health innovation that matters

[ARTforHeartFailure.com](http://ARTforHeartFailure.com)

[VITARIAsystem.com](http://VITARIAsystem.com)

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OVER

25 MILLION

LIVING WITH HEART FAILURE WORLDWIDE<sup>1</sup>

SEVERAL  
MILLION

NEW DIAGNOSES EACH YEAR<sup>1</sup>

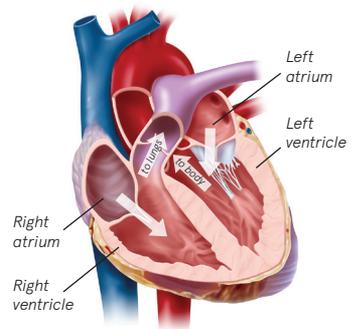


# UNDERSTANDING HEART FAILURE

Heart failure does not mean your heart has stopped working. Heart failure is a condition in which the heart cannot pump enough blood to meet your body's needs. If you or a loved one have heart failure, you are not alone. Over 25 million people worldwide have this condition with **several million** new diagnoses per year.

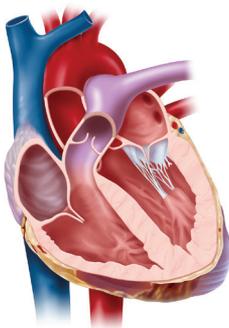
## GETTING TO KNOW YOUR HEART

The heart is a fist-sized organ that acts as a pump to send oxygen-rich blood throughout the body. In a healthy heart, each chamber contracts (squeezes) in a coordinated effort – the upper chambers (atria) of the heart contract first, then the lower chambers (ventricles) contract. These coordinated contractions circulate blood between the lungs and heart and to the rest of the body.

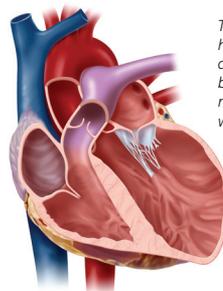


## THE FAILING HEART

During heart failure, the heart attempts to compensate for lost pumping power, and the heart may change its shape and result in an uncoordinated and inefficient heartbeat.



Normal heart



*The walls of the heart become thin, and the chambers become enlarged, making the heart weak and inefficient*

Heart failure



Heart failure

# MAY WORSEN OVER TIME

EVEN WITH CURRENTLY AVAILABLE TREATMENT

## HEART FAILURE CAUSES

Heart failure is typically a progressive condition, meaning it worsens and shortens life expectancy. There is no single cause, and sometimes the cause is unknown. Some of the most common causes of heart failure are:

- Heart attack
- Coronary artery disease
- High blood pressure
- Defective heart valves
- Heart infection (i.e., virus)
- Alcohol addiction
- Illicit drug use
- Diabetes

## HEART FAILURE SYMPTOMS

At first you might not experience any symptoms. However, over time you may experience some, or all, of the following symptoms:

- Chronic lack of energy
- Interrupted sleep at night due to breathing difficulties
- Confusion and/or impaired memory
- Increased urination at night
- Swelling of feet and legs
- Shortness of breath
- Abdominal swelling or tenderness with loss of appetite
- Cough with saliva/mucus

EVERY

# 30 SECONDS

SOMEONE WITH HEART FAILURE IS HOSPITALIZED<sup>2</sup>

## HEART FAILURE TREATMENT OPTIONS

Treatment can help to relieve the symptoms of heart failure and may help you live longer. There are several ways that heart failure can be treated.

Less Invasive

More Invasive



### Lifestyle Modifications

Certain lifestyle changes such as increasing physical activity, decreasing emotional stress, weight loss, stopping smoking and eating less salt/fat may reduce heart failure symptoms.



### Medications

Doctors usually treat heart failure with a combination of medications. Depending on your symptoms, you might take one or more medications including beta-blockers, ACE inhibitors, angiotensin receptor blockers (ARBs), blood thinners and diuretics.



### Medical Devices or Surgery

In some cases, doctors recommend interventions such as bypass or valve replacement surgery, implantation of a cardioverter-defibrillator or cardiac resynchronization device, or a heart transplantation.



## AN INVESTIGATIONAL APPROACH

A new form of therapy is being evaluated for patients with heart failure. It is called Autonomic Regulation Therapy (ART) delivered through Vagus Nerve Stimulation (VNS). ART is investigational and being studied in a clinical trial called ANTHEM-HFrEF. This trial is currently enrolling patients who are eligible to participate to determine the long-term benefits of ART on patients suffering from heart failure. All patients who participate in the trial are receiving one of two equally valid and important treatments until the results of the trial are known.

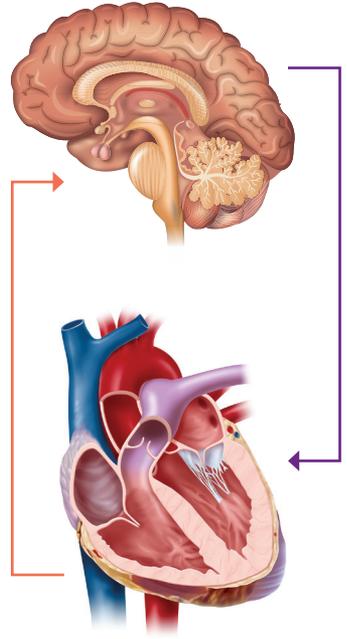


# THE 'HEAD-HEART' CONNECTION IN NORMAL HEALTH

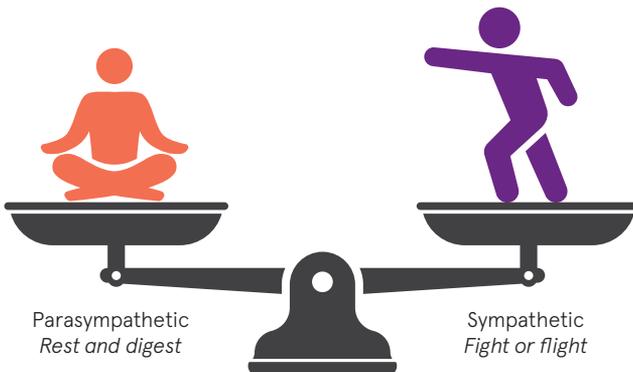
The autonomic nervous system plays a large role in heart failure. The brain controls the function of the heart through two branches of the autonomic nervous system.

The first is the **sympathetic branch**, which acts as the body's 'accelerator' and is responsible for the 'fight or flight' response during stress.

The second is the **parasympathetic branch**, which acts as the body's 'brake' and allows the body to rest and digest. The parasympathetic branch acts through a special nerve in your body called the **vagus nerve**. In normal health, the two branches are said to be 'in balance.'

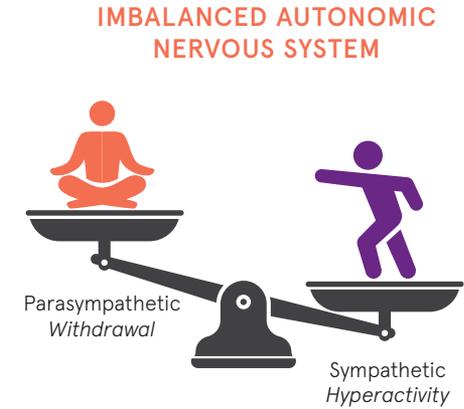


## BALANCED AUTONOMIC NERVOUS SYSTEM



# AN AUTONOMIC IMBALANCE IN HEART FAILURE

In heart failure there is an imbalance in the autonomic nervous system. The sympathetic branch is overactive while parasympathetic activity is under-active. In other words, the body is continually in a state of 'fight or flight' therefore not allowing the body to 'rest and digest.' While some heart failure medications may help to treat sympathetic overactivity, there are currently no proven treatments to effectively treat the underlying cause.



## RESTORING THE BALANCE WITH ART

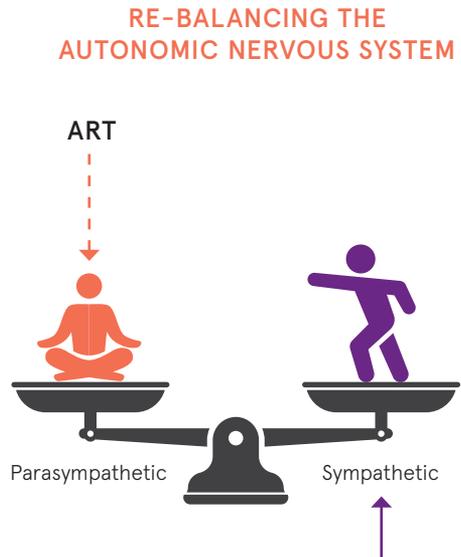
### How it works:

Autonomic Regulation Therapy (ART) applies mild electrical impulses to the vagus nerve to activate the parasympathetic branch and restore balance. LivaNova uses a unique approach that tailors therapy to individual patient needs.

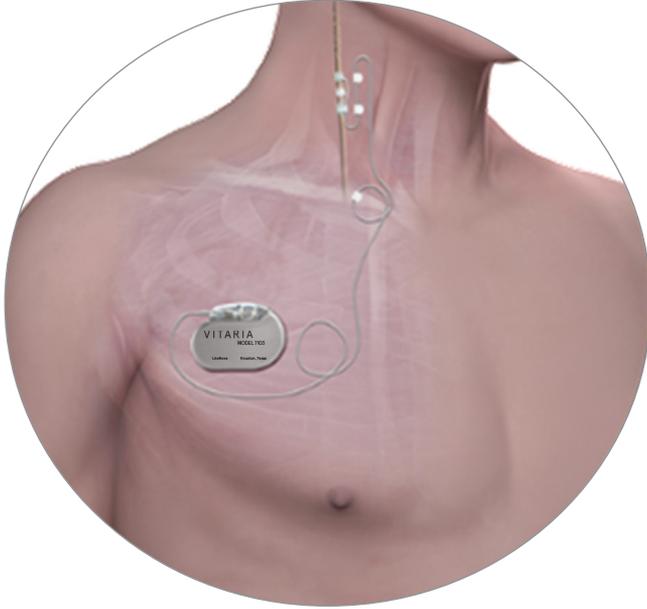
### A new therapy, but a proven approach:

While vagal nerve stimulation is new for heart failure, the approach has been successfully used for over 20 years in the treatment of epilepsy with over 150,000 implants worldwide.

Additionally, ART has been tested in the treatment of heart failure in two small human pilot studies that led to FDA and Health Canada Approval of the ANTHEM-HFrEF clinical trial.



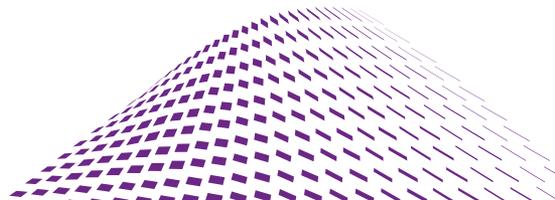
# THE ART SYSTEM AND PROCEDURE



## ART IS DELIVERED THROUGH VNS BY THE VITARIA™ SYSTEM FROM LIVANOVA, WHICH CONSISTS OF:

1. **Lead:** a flexible insulated wire that transmits tiny electrical signals from the generator to the nerve.
2. **Pulse Generator:** a device similar to a pacemaker that is implanted just under the skin and sends the energy to the vagus nerve through the lead.

The VITARIA System is placed during a minimally invasive outpatient procedure lasting about an hour.



## HAVE YOU BEEN DIAGNOSED WITH HEART FAILURE?

If yes, you may consider participating in the FDA and Health Canada approved clinical study called ANTHEM-HFrEF, which is evaluating the safety and efficacy of Autonomic Regulation Therapy.

A clinical trial is a research study to answer specific health related questions. The ANTHEM-HFrEF clinical trial will determine whether Autonomic Regulation Therapy (ART) plus medical therapy is safe and more effective than medical therapy alone for the treatment of heart failure. The trial is seeking up to 1,000 adult men and women with heart failure at selected medical centers in the United States, Canada, and Europe. The investigators are doctors who specialize in treating heart failure.

## AM I ELIGIBLE?

**Are you 18 years or older with:**

- Stable symptomatic heart failure NYHA class III; or NYHA class II with a heart failure hospitalization in the previous 12 months
- Left ventricular ejection fraction (EF)  $\leq$  35%, as confirmed by core echocardiography laboratory during screening
- Physically capable and willing to perform repeated 6-minute walk tests associated with the study, and having a baseline distance of between 150 and 450 meters

If you answered 'YES' to these questions you may be eligible to participate depending upon other inclusion and exclusion criteria.

## SPEAK TO YOUR DOCTOR TO LEARN MORE

## WHY SHOULD I VOLUNTEER?

By participating<sup>†</sup> in a clinical study you can:

- Take an active role in your own health care
- Obtain expert medical care at leading health care facilities during the clinical trial
- Help others by contributing to medical research

*†Before you join a clinical study you should know as much as possible about the study. It is important for you to feel very comfortable asking questions and receiving complete answers prior to deciding to participate or not in the study. You should feel comfortable not participating in the study if you so choose.*

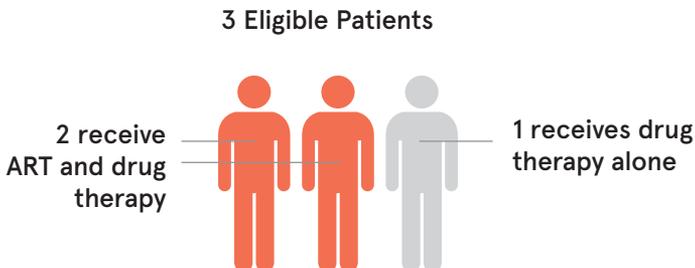
## WHAT IS EXPECTED OF ME IF I PARTICIPATE?

- 1. SIGN THE CONSENT FORM** after understanding details about the study including risks, benefits and your responsibility as a participant
- 2. COMPLETE ENROLLMENT AND EVALUATION STEPS**, which will likely include:
  - Medical history and physical examination
  - Tests to check your overall health status (echocardiogram, blood and Holter Monitor)
  - Questionnaires
- 3. PARTICIPATE IN FOLLOW-UP VISITS**  
Return for clinical visits throughout the study. You will be reimbursed for travel associated with follow-up visits, which will include:
  - ART stimulation adjustments until therapy target established
  - Subsequent follow-up visits consisting of scheduled visits every 3 months after therapy adjustment during the first 12 months and scheduled visits every 4 months thereafter.

## HOW LIKELY AM I TO RECEIVE INVESTIGATIONAL THERAPY?

### YOU ARE MORE LIKELY TO RECEIVE ART THAN NOT RECEIVE ART IN THE CLINICAL TRIAL

Everyone in the clinical trial will continue receiving the best medical (drug) therapy available for heart failure from their doctor. **In addition, 2 out of every 3 eligible patients will receive ART.**





Health innovation that matters

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### REFERENCES

1. Card Fail Rev. 2017 Apr; 3(1): 7–11. doi: 10.15420/cfr.2016:25:2.
2. Blecker S, Agarwal SK, Chang PP, et al. Quality of care for heart failure patients hospitalized for any cause. J Am Coll Cardiol. 2014;63(2):123–30.

(US) **CAUTION** Investigational device. Limited by Federal (or United States) law to investigational use.

(CANADA) **CAUTION** Investigational device. To be Used by Qualified Investigators Only.

### CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

The VITARIA System cannot be used on patients with a bilateral vagotomy.

The VITARIA System cannot be used on patients with a history of AV block.

Do not use shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with a VITARIA System. Diagnostic ultrasound is not included in this contraindication.

Magnetic Resonance Imaging (MRI) – If MRI is required in a patient with the VITARIA System, consult the VITARIA Physician's Manual.

Patients with existing ulcers (gastric, duodenal or other) may have their condition aggravated by ART. Patients with ulcers should be evaluated prior to implantation and monitored following initiation of stimulation.

Potential surgery-related adverse events include hematoma, infection, pain and voice alteration (hoarseness). Potential stimulation-related adverse events include dyspepsia (indigestion), dysphagia (difficulty swallowing), dyspnea (difficulty breathing, shortness of breath), increased coughing, laryngismus (throat, larynx spasms), pain, paresthesia (prickling of the skin), pharyngitis (inflammation of the pharynx, throat), satiety (reduced appetite), sensation of stimulation, and voice alteration (hoarseness).

