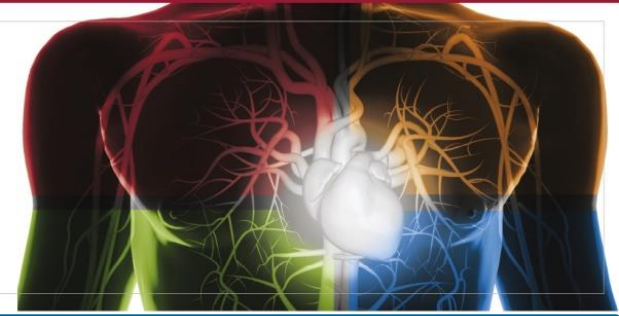


The Ohio State University
Division of Cardiovascular Medicine



Reversing Coronary Artery Disease and Heart Muscle Damage

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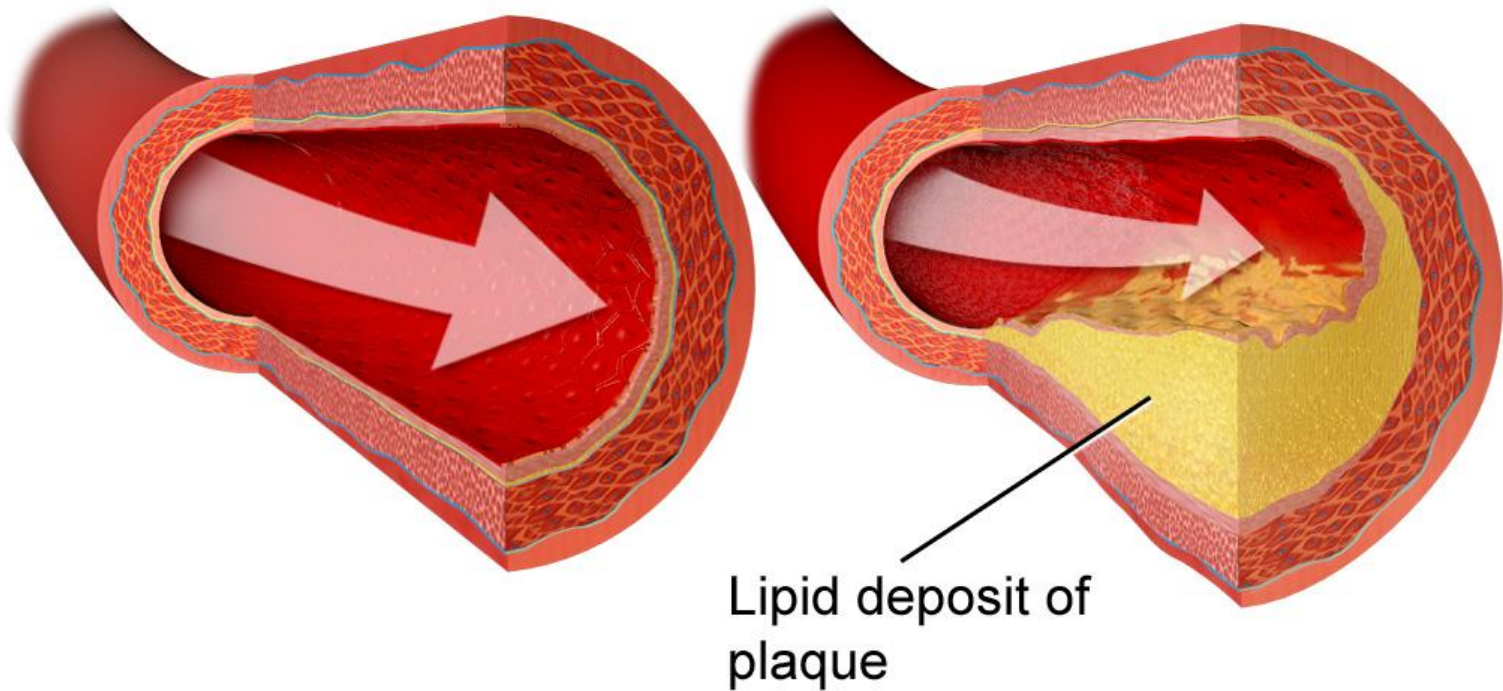


Wexner
Medical
Center

Coronary Artery Disease (CAD)

Normal Artery

Narrowing of Artery



Major Risk Factors for CAD

Modifiable	Non-Modifiable	Emerging Risk Factors
High blood pressure	Family history	Homocysteine
Abnormal cholesterol levels	Age	Elevated lipoprotein (a) levels
Diabetes		High CRP
Cigarette smoking		Low HDL
Obesity		High TG
Physical inactivity		Metabolic Syndrome
Poor diet		Depression
		Obstructive Sleep Apnea

Major Risk Factors You Can Modify, Treat, or Control by Changing Your Lifestyle or Taking Medicine

- Tobacco smoke — Smokers' risk of developing coronary heart disease is 2-4 times that of nonsmokers. Cigarette smoking is a powerful independent risk factor for sudden cardiac death in patients with coronary heart disease; smokers have about twice the risk of nonsmokers. Cigarette smoking also acts with other risk factors to greatly increase the risk for coronary heart disease. Exposure to other people's smoke increases the risk of heart disease even for nonsmokers.

Major Risk Factors You Can Modify, Treat, or Control by Changing Your Lifestyle or Taking Medicine

- High blood cholesterol — As blood cholesterol rises, so does the risk of coronary heart disease. When other risk factors (such as high blood pressure and tobacco smoke) are present, this risk increases even more. A person's cholesterol level is also affected by age, sex, heredity, and diet.

Major Risk Factors You Can Modify, Treat, or Control by Changing Your Lifestyle or Taking Medicine

- High blood pressure — High blood pressure increases the heart's workload, causing the heart to thicken and become stiffer. It also increases your risk of stroke, heart attack, kidney failure, and congestive heart failure. When high blood pressure exists with obesity, smoking, high blood cholesterol levels, or diabetes, the risk of heart attack or stroke increases several times.

Major Risk Factors You Can Modify, Treat, or Control by Changing Your Lifestyle or Taking Medicine

- Physical inactivity — An inactive lifestyle is a risk factor for coronary heart disease. Regular, moderate-to-vigorous physical activity helps prevent heart and blood vessel disease. The more vigorous the activity, the greater your benefits. However, even moderate-intensity activities help if done regularly and long term. Physical activity can help control blood cholesterol, diabetes, and obesity, as well as help lower blood pressure in some people.

Major Risk Factors You Can Modify, Treat, or Control by Changing Your Lifestyle or Taking Medicine

- Obesity and overweight — People who have excess body fat, especially if a lot of it is at the waist, are more likely to develop heart disease and stroke even if they have no other risk factors. Excess weight increases the heart's work. It also raises blood pressure and blood cholesterol and triglyceride levels, and lowers HDL ("good") cholesterol levels. It can also make diabetes more likely to develop. Losing even as few as 10 pounds, you can lower your heart disease risk.

Major Risk Factors You Can Modify, Treat, or Control by Changing Your Lifestyle or Taking Medicine

- Diabetes mellitus — Diabetes seriously increases your risk of developing cardiovascular disease. Even when glucose (blood sugar) levels are under control, diabetes increases the risk of heart disease and stroke, but the risks are even greater if blood sugar is not well controlled. About three-quarters of people with diabetes die from some form of heart or blood vessel disease.

A Heart Attack Waiting to Happen



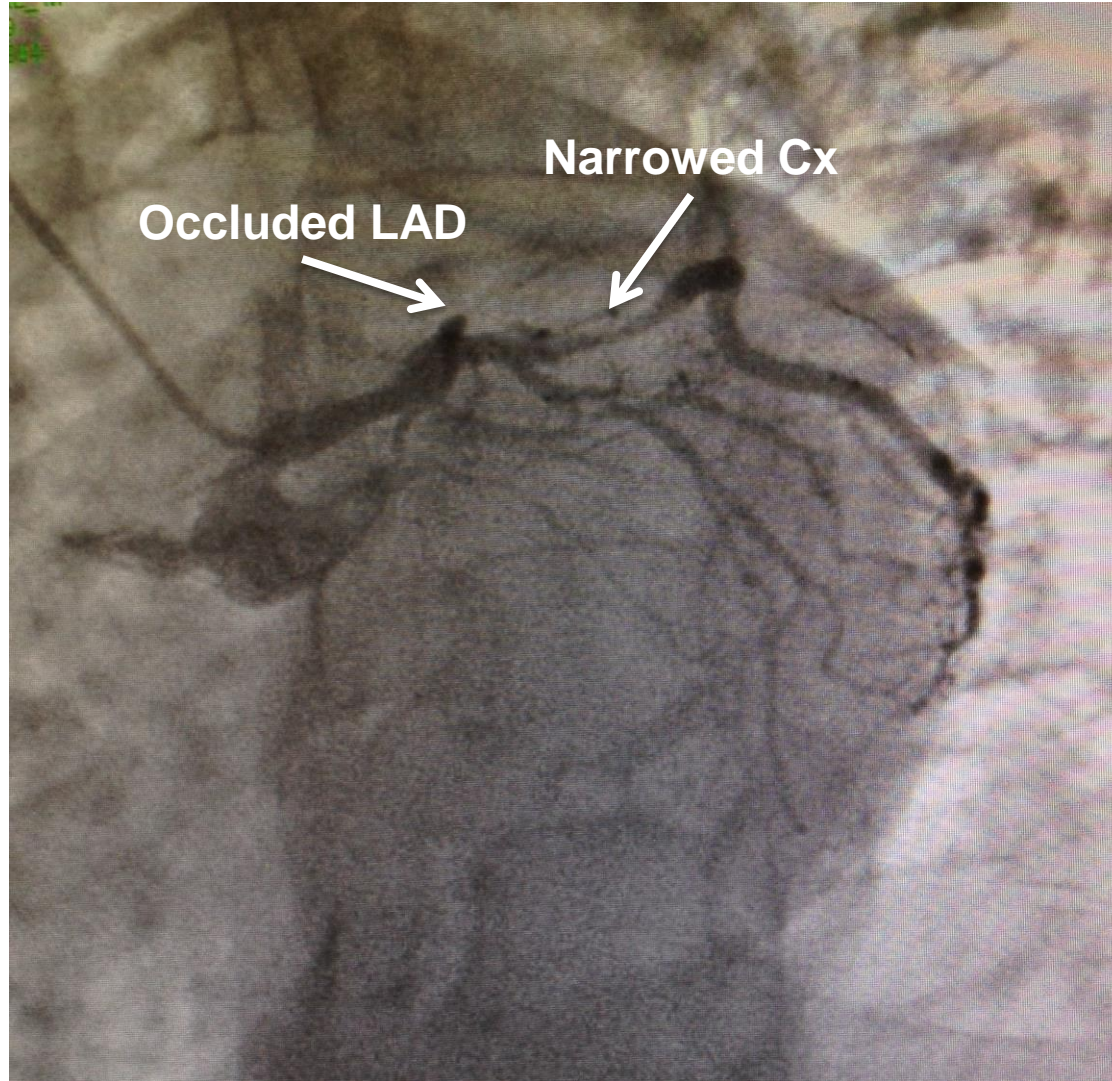
*This is not a photo of Carl

Major Risk Factors for CAD: Carl Then

Modifiable	Carl Then
High blood pressure	✓
Abnormal cholesterol levels	✓
Diabetes	✓
Cigarette smoking	
Obesity	✓
Physical inactivity	✓
Poor diet	✓

In addition, Carl had obstructive sleep apnea.

Carl Then: Coronary Angiogram



What Can We Do to Eliminate CAD?

- 80% of heart disease is preventable
- Less than 5% of the U.S. population is doing what they need to do to prevent it
- Lifestyle change is the key

Prevention of CAD

- Quit smoking
- Increase Physical Activity
 - Minimum of 30 minutes of moderate intensity physical activity \geq 5 days per week
 - For those who need to lose weight or sustain weight loss, 60-90 minutes of moderate intensity physical activity \geq 5 days per week
- Achieve / Maintain Ideal Weight
 - BMI between 18.5 and 24.9
 - Waist circumference $<$ 35 inches

Prevention of CAD

- Improve Diet
 - Fruits and vegetables
 - Whole grain, high-fiber foods
 - Fish, at least twice a week
 - Saturated fats < 10% of calories, < 300mg cholesterol/d
 - Limit trans fatty acid intake (<1% of calories)
 - Limit salt and sodium intake (<2.4 g/d)
 - Alcohol no more than 1 drink per day
 - Limit portion sizes

Prevention of CAD

- Lower Blood Pressure
 - goal $\leq 120/80$ mmHg
- Treat Dyslipidemia (Lower High Cholesterol)
 - Total Cholesterol goal < 200 mg/dL
 - LDL goal < 100 mg/dL (or < 70 for established CAD)
 - Triglycerides goal < 150 mg/dL
 - HDL goal > 50 mg/dL
- Treat Diabetes Mellitus (Lower Blood Sugar)
 - $\text{HbA}_{1c} < 7\%$

Key Medications for CAD Treatment

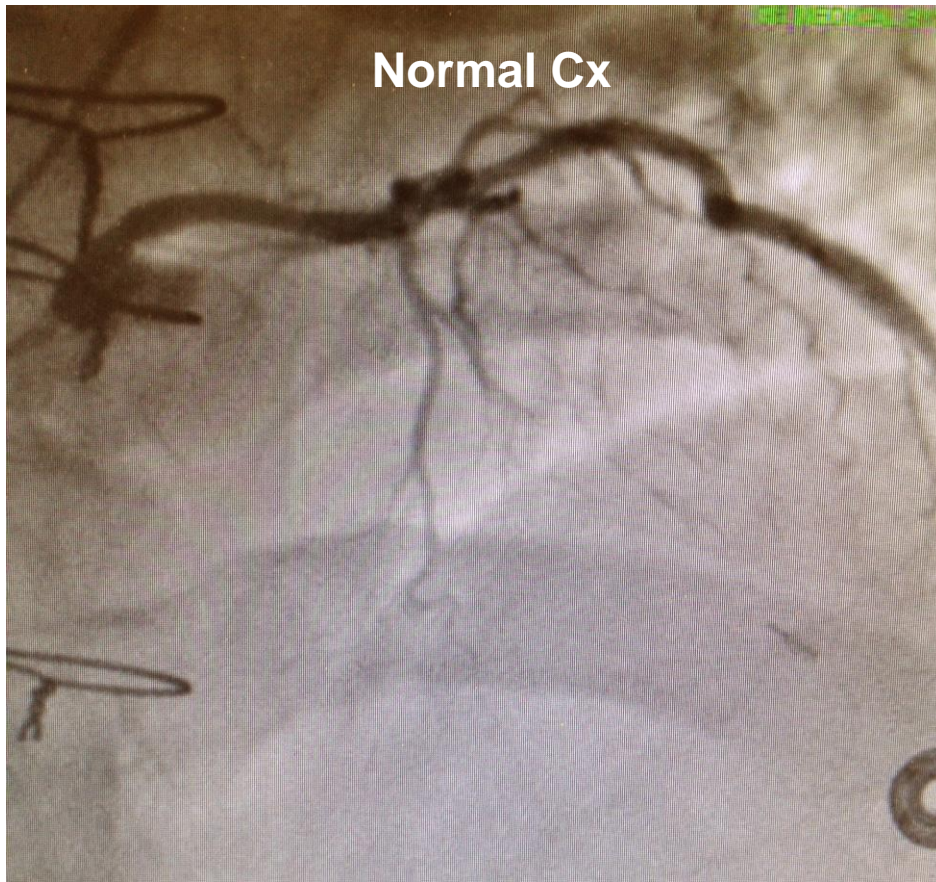
- Angiotensin Converting Enzyme (ACE) Inhibitors
- Beta-Blockers
- Aspirin
- Statins
- Others

Major Risk Factors for CAD: Carl Now

Modifiable	Carl Then	Carl Now
High blood pressure	✓	Blood pressure 110/80
Abnormal cholesterol levels	✓	Cholesterol 102, LDL 47, Triglycerides 58
Diabetes	✓	Off of insulin
Cigarette smoking		
Obesity	✓	BMI from 28.6 to 24.2
Physical inactivity	✓	Very active
Poor diet	✓	Better diet

In addition, Carl's obstructive sleep apnea has completely gone away with weight loss. Carl is taking the essential medications to treat CAD.

Carl Now: Coronary Angiogram



Getting Enough Sleep Might Just Save Your Heart

- Sleeping **<5 hours of sleep/night** is associated with more blockages in heart arteries vs those getting **>5 hours** of sleep
- **Each additional hour of sleep = lowering systolic blood pressure by ~17mm Hg**
- Insufficient sleep linked to increased risk for heart disease, colon cancer, breast cancer, and diabetes

In Summary, What Can You Do to Protect Your Heart?

- Don't Smoke / Quit Smoking
- Know your Blood Pressure / Control your Blood Pressure
- Know your Cholesterol / Control your Cholesterol
- Maintain a Low Fat Diet
- Maintain a Healthy Weight
- Control your Stress / Sleep > 5 hours/night
- Exercise Regularly / Not Optional, Daily Dose
- Prevent or Control diabetes
- Know your Family History
- Be Aware of Chest Pain
- Be Screened for Heart disease

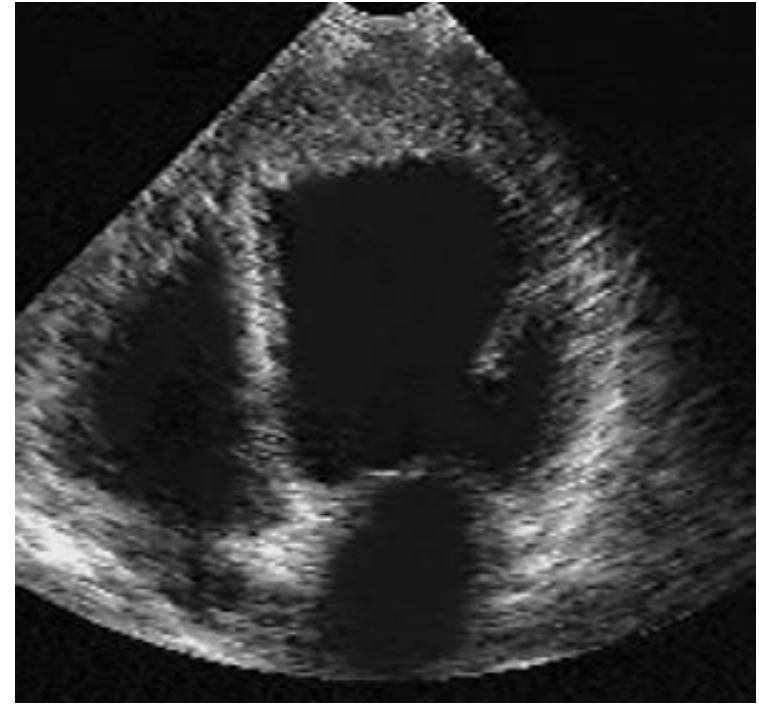
Adverse Changes in Heart Structure and Function After a Heart Attack

1 week



**EDV 137 mL ESV 80 mL
EF 41%**

3 months



**EDV 189 mL ESV 146 mL
EF 23%**

Apical 4 Chamber View

This process is reversible!

- Weak hearts can get stronger
- Large hearts can get smaller
- These changes improve quality of life and longevity

Approved Treatments Promoting Reverse Remodeling of the Failing Heart

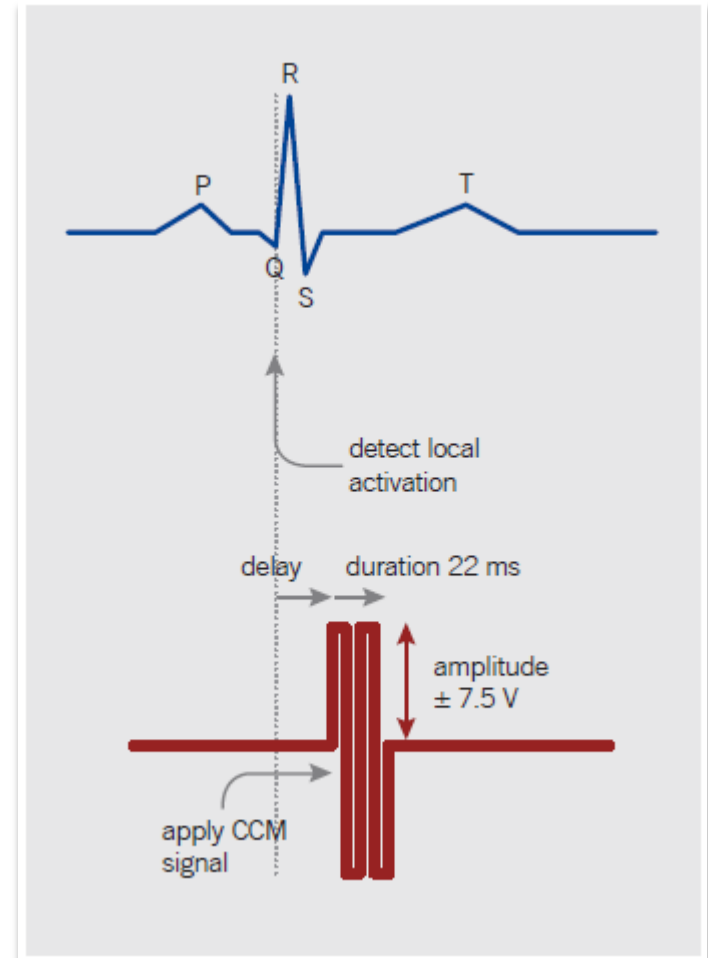
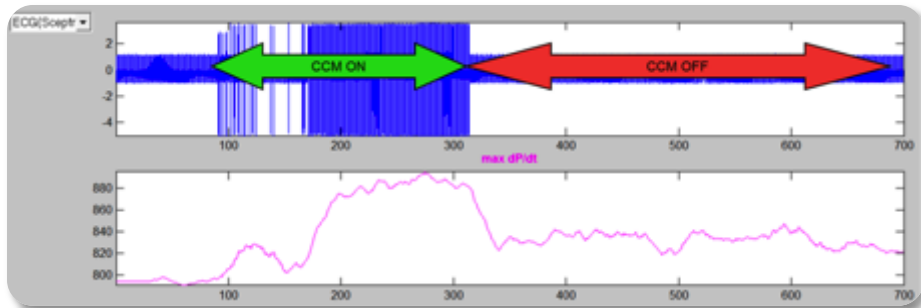
- ACE Inhibitors/Angiotensin Receptor Blockers*
- Beta-Blockers*
- Aldosterone Antagonists*
- Cardiac Resynchronization Therapy*
- Surgical Approaches/Devices
 - LVADs*
 - Mitral valve repair
 - Others

*These therapies save lives!

Investigational Devices to Improve Heart Function

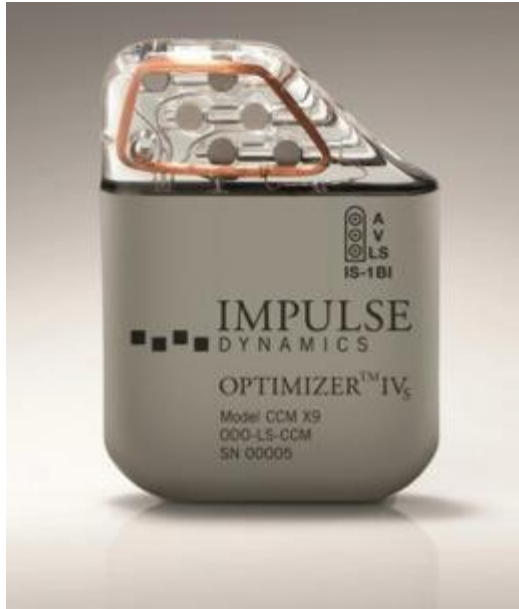
What is Cardiac Contractility Modulation?

- Non-excitatory electrical signals delivered to the ventricles
- Applied during the absolute refractory period of the heart contraction
- Increases cardiac contractility without an increase in myocardial work (increases efficiency of the heart as a pump)



OPTIMIZER IVs: Delivers CCM Signals to Heart

IPG



**Small,
Rechargeable battery,
Flexible positioning**

Charger



**Portable,
Battery driven,
Integrity test**

Programmer

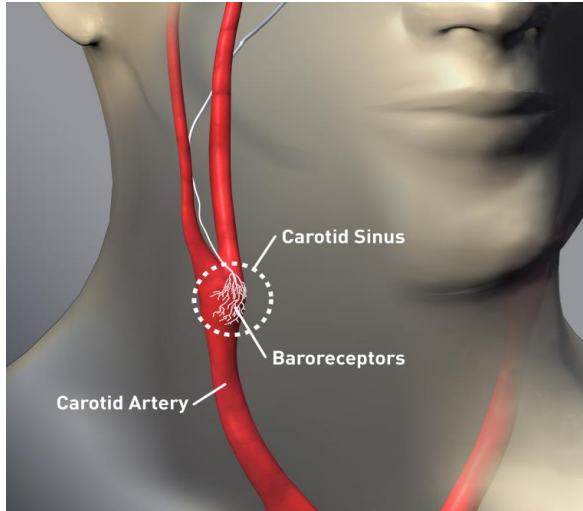


**Intuitive user interface,
Remote support**

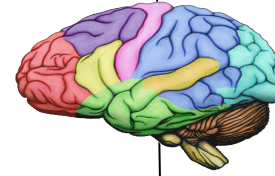
Cardiac Contractility Modulation

- Studies show that CCM:
 - Increases heart function and structure
 - Improves quality of life, exercise capacity, and functional status
 - May prolong life

The Baroreflex as a Therapeutic Target

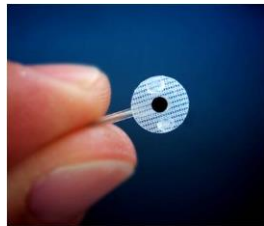


Carotid Baroreceptor Stimulation



Integrated Autonomic Nervous System Response

Inhibits **Sympathetic** Activity
Enhances **Parasympathetic** Activity



↓ HR
↓ Remodeling



↑ Vasodilation
↓ Elevated BP



↑ Diuresis
↓ Renin secretion

CLINICAL RESEARCH

Baroreflex Activation Therapy for the Treatment of Heart Failure With a Reduced Ejection Fraction



William T. Abraham, MD,* Michael R. Zile, MD,†† Fred A. Weaver, MD,§ Christian Butter, MD,||
Anique Ducharme, MD, MSc,¶ Marcel Halbach, MD,# Didier Klug, MD,** Eric G. Lovett, PhD,††
Jochen Müller-Ehmsen, MD,‡‡ Jill E. Schafer, MS,§§ Michele Senni, MD,|||| Vijay Swarup, MD,¶¶
Rolf Wachter, MD,## William C. Little, MD***

BAT for HFrEF Trial Results: Summary

	Difference	p value	Favors
NYHA (% improved)	31	< 0.01	BAT
MLWHF QoL Score (points)	20	<0.001	BAT
6-MHW Distance (m)	58	<0.01	BAT
NT-proBNP (pg/ml)*	342	0.02	BAT
LVEF (absolute %)	2.5	0.15	BAT
Hospitalization Days for Worsening HF (days/pt/yr)	6.4	0.05	BAT

* Median

Parachute Ventricular Partitioning Device

PARACHUTE IMPLANT

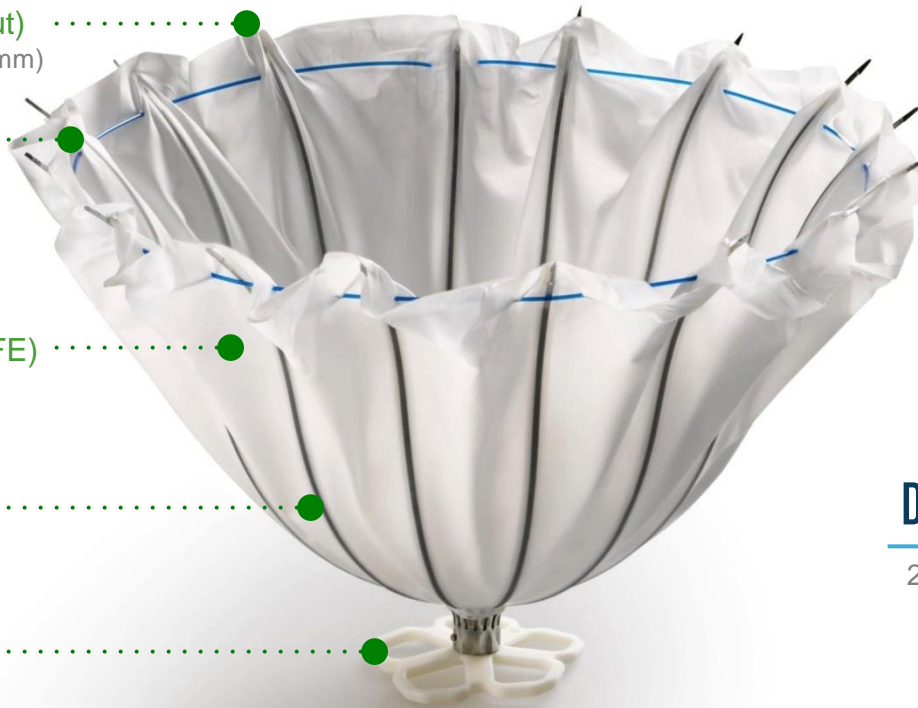
Anchor (Laser Cut) ●
Engages LV Wall (2mm)

Suture (Polypropylene) ●
Collapses Device.
Supports ePTFE at the Edge

Membrane (ePTFE) ●
Dual layer occlusive membrane. Allows tissue growth.

Frame (Nitinol) ●
16 Arms Laser Cut from a Single Tube

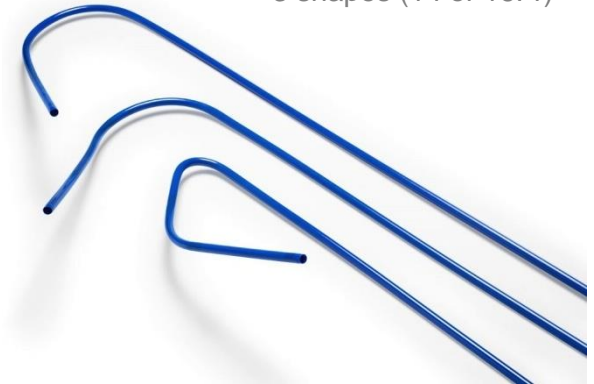
Foot (Urethane) ●
Radiopaque. Shock Absorber



	65mm	75mm	85mm	95mm
Standard (+3mm)	X	X	X	X
Short	X	X	X	X

GUIDE CATHETER

3 shapes (14 or 16Fr)

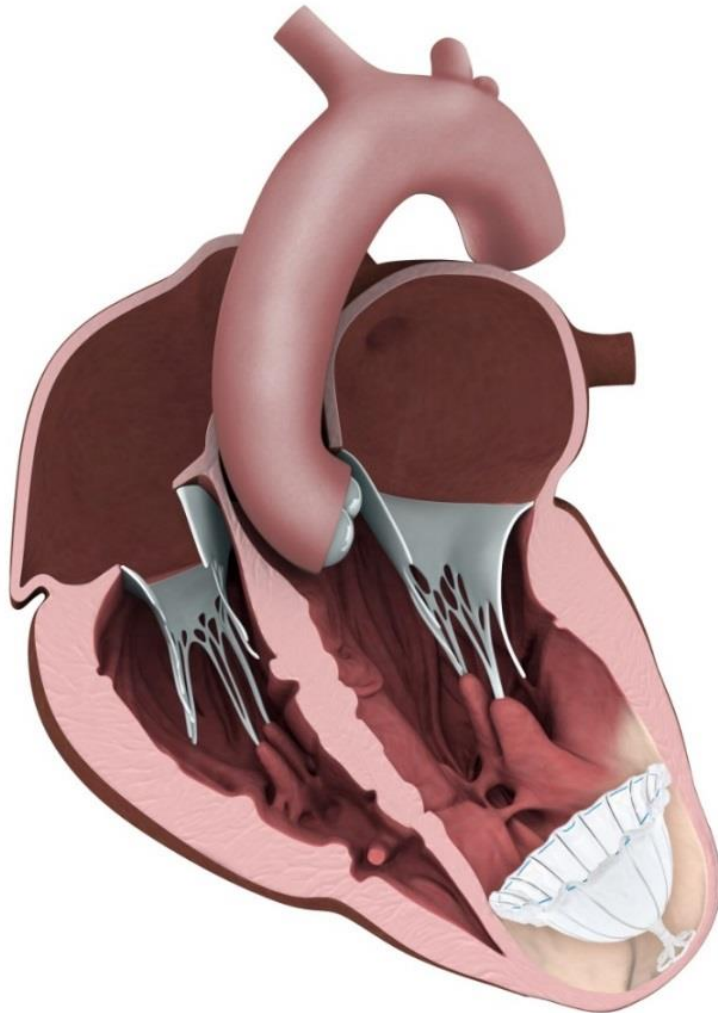


DELIVERY SYSTEM

20cc balloon is inflated to anchor device



Parachute Ventricular Partitioning Device: Mechanism of Action



(1) “RESTORING EFFECT”

Reduces wall stress in the upper chamber by changing LV geometry and reducing volume

(2) “TRAMPOLINE EFFECT”

Replaces the stiff/rigid scar with a more compliant Parachute that provides outward force by the anchors to aid in diastolic filling

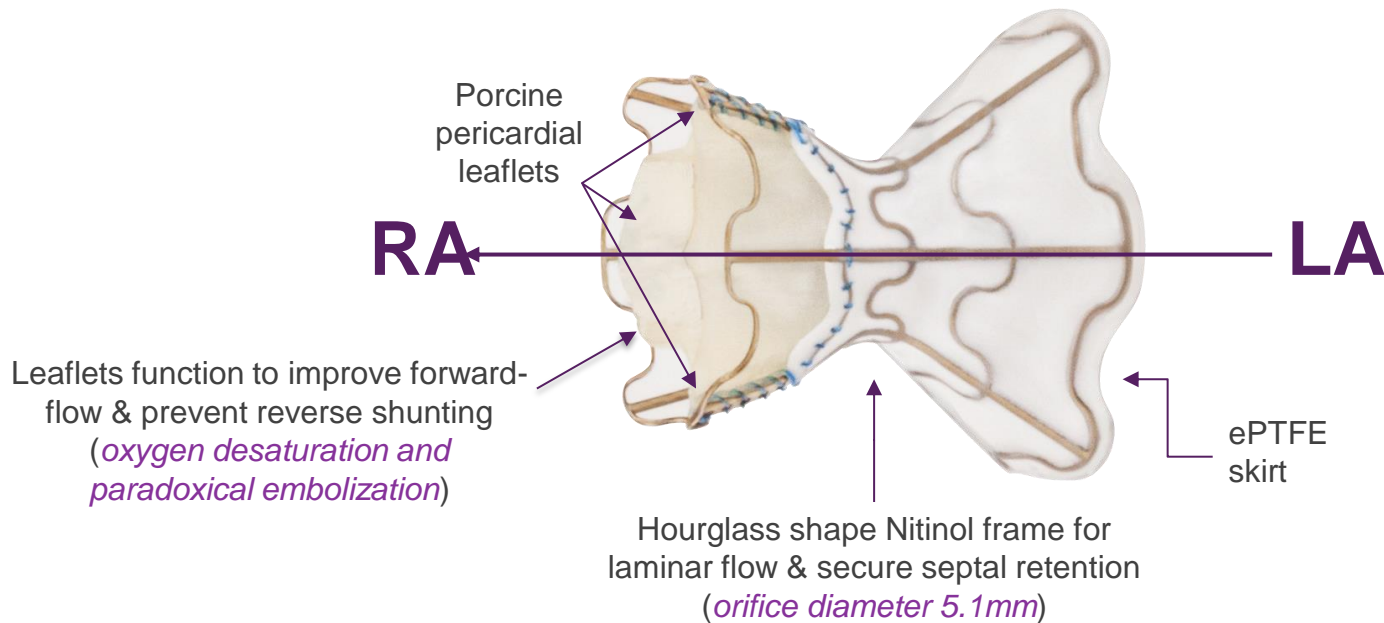
Improves diastolic compliance that reduces end diastolic filling pressures

Parachute Clinical Effects in Trials to Date

- Improves in functional status, quality of life, and exercise capacity
- Lower than expected rates of morbidity and mortality suggested by totality of study data

Intra-Atrial Shunt Device

L to R shunting self regulates LAP elevations preventing pulmonary congestion and hospitalization



V-Wave Clinical Experience Summary

- More than 25 patients implanted to date
- HF patients with both reduced and preserved EF (*75% with reduced-EF*)
- Marked improvement in quality of life and exercise capacity
- No worsening in RV function
- No device related adverse events
- No device malfunctions; no migrations or embolization

Bottom Line

- Coronary artery disease and heart muscle damage are potentially reversible
- Lifestyle changes and medications are key
- Future devices may add incremental value to currently available therapies