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Heart Failure: Start-Ups Harness Natural Pathways

Mary Stuart

Ireland: A Quarter-Century of Medtech Innovation

Reed Miller

Conformal Joins Gore Amid LAAO Trials

Colin Miller

Personalized Medicine Is Coming to Chronic Low Back Pain

Wendy Diller

MyStrategist.com/medtech-strategist

INNOVATING HEART FAILURE: START-UPS HARNESS NATURAL PATHWAYS

Heart failure isn't just a failing heart—it's a system in revolt, where heart, lungs, kidneys, lymphatics, and blood vessels conspire to fuel decline. Next-gen heart failure start-ups tap into physiological mechanisms to bring order back to the system.

MARY STUART

Heart failure still represents one of the greatest unmet needs in medicine. The lifetime risk of this degenerative and life-threatening disease has risen to almost one in four, and according to the Heart Failure Society of America's "HF Stats 2025: Heart Failure Epidemiology and Outcomes Statistics," in the US approximately 6.7 million people over the age of 20 have heart failure. That prevalence is rapidly rising.

In 2022, heart failure was a contributing cause of almost half of all cardiovascular deaths, and within two decades, the costs of managing this challenging condition are projected to reach $858 billion, with 50% of that sum due to frequent episodes of hospitalization.

Long seen by therapy innovators as primarily a problem of the heart's pumping—mechanical and electrical dysfunctions that could be fixed in isolation—today's heart failure innovators understand it as a systemic condition: a complex interplay between the heart, lungs, kidneys, lymphatic system, and vasculature, where each component can amplify—or worsen—the others in a doom loop.

Medical device strategics are showing keen interest in this space, evidenced by recent acquisitions such as **Johnson & Johnson**'s purchase of V-Wave, the developer of a minimally invasive interatrial shunt for heart failure patients who experience elevated left atrial pressure, in a deal worth $1.1 billion when up-front and commercial payments are added up.

This degenerative disease often starts long before patients are aware of symptoms, yet once structural changes happen, cardiorenal and cardiopulmonary systems go out of whack, further intensifying the disease progression. For that reason, one of the major clinical goals today is catching early signs of the disease, and for those patients already in the loop, detecting signals of deterioration before they find themselves in a full-blown episode of acute decompensated heart failure (ADHF) requiring hospitalization.

In this space, we've discussed **Acorai** before; the start-up is in the business of detecting these early signs of deterioration noninvasively. (*See "Acorai Serves Up Long-Desired Noninvasive Pulmonary and Cardiac Pressure Sensing,"* MedTech Strategist, *October 22, 2024*.) Acorai has raised about $24 million to date for its FDA-designated Breakthrough Device. Having validated its noninvasive approach as compared to the gold standard (invasive right heart catheterization) in the 1,600 patient clinical study CAPTURE, Acorai is now conducting a 1,000 patient pivotal study aiming to demonstrate the health economics benefits of its scalable tool.

In this article, we interview **Ventric Health**, which aims to bring an early heart failure screen to primary care, the setting of the physicians most likely to see patients when they're in the earliest stages of disease. The company's FDA-cleared noninvasive device works to detect both HFrEF (heart failure with reduced ejection fraction, or a dysfunction of pumping) and HFpEF (heart failure with preserved ejection fraction, a dysfunction of heart filling).

Indeed, the ability to address both heart failure patient populations is a feature of many of the next-generation heart failure companies. Not long ago, HFpEF was left behind in terms of effective diagnostics and treatment options, but the advent of new and effective pharmaceuticals for this group of patients, such as the class of SGLT2 inhibitors, creates an imperative to find and treat them early.

Natural Mechanisms to Decompensation

Many companies have clustered around the goal of improving the treatment of ADHF, one, because it's responsible for the costly hospitalizations noted above, and two, because each episode worsens a patient's heart failure (*see Figure 1*). Thus, an important goal is to detect exacerbations early enough to prevent such hospitalizations.

Aligned with that theme were the **Edwards Lifesciences** acquisitions of Endotronix and Vectorious Medical. The structural heart leader acquired Endotronix, maker of the *Cordella* implantable pulmonary artery pressure sensor, in July 2024, and Vectorious, which developed the *V-LAP* implantable left atrial pressure sensor, in September 2025, in a transaction that valued the start-up at almost $500 million. These tools allow clinicians to catch episodes of ADHF early and proactively manage patients.

What's particularly interesting about next-generation start-ups is their focus on intervening not directly on the heart itself, but along the physiological pathways that contribute to ADHF, and by working with or repairing innate mechanisms along the entire interconnected system involved in cardiac health. We interview two such companies.

Discussed below, **WhiteSwell** takes advantage of the large fluid-removing capacity of the lymphatic system to quickly and safely move ADHF patients to a healthier state. Its efficacy will lean on not just fluid removal itself, but also the way in which that engages the kidneys to work better for a long-lasting result.

We also discuss **Levron Cardiovascular**, which has a novel pacing approach to help the heart by coordinating breathing cycles with pumping cycles.

Taken together, these emerging technologies reflect a broader shift in how innovators think about heart failure—not as a single organ failure, but as a breakdown of the body's integrated fluid and pressure management systems. By sensing earlier, intervening along physiological pathways, and restoring the natural mechanisms that regulate circulation, breathing, and fluid balance, innovations of next-generation companies are reframing the therapeutic playbook. If successful, this systems-level approach could not only reduce costly hospitalizations for acute decompensated heart failure, but it could also slow the disease's relentless progression—bringing heart failure care closer to prevention and long-term stability rather than repeated rescue.

Figure 1

Heart Failure Innovators Work With the System

Approach	Representative Companies
Office-Based Early Detection	Ventric Health
Addressing ADHF by Novel Mechanisms	Axon Therapies (splanchnic ablation) Cardionomic, now part of Catheter Precision (cardiac pulmonary nerve stimulation) Precardia, part of the Abiomed division of Johnson & Johnson (intermittently occludes the superior vena cava to lower cardiac filling pressure) Procyrion (percutaneous pump boosts blood flow in the aorta and reduces aortic root pressure) Relief Cardiovascular (implant modulates venous return, preload) Revamp Medical (percutaneous, temporary central venous catheter reduces venous congestion and unloads renal system) Selera Medical (minimally invasive device offloads lymphatic system) Sequana Medical (direct sodium removal) VisCardia (modulates the diaphragm) WhiteSwell (pressure-lowering device procedure improves lymphatic drainage)
Reversing Cardiac Remodeling	Berlin Heals (implantable device delivers constant low-level electricity to the heart)
Modulating Stress Response	CVRx (implantable device regulates autonomic system to reduce adrenaline overload)
Novel Cardiac Pacing Approaches	Ceryx Medical, EBR Systems, Impulse Dynamics, Levron Cardiovascular
Pulmonary Pressure Monitoring for Signs of Deterioration	*Noninvasive:* Acorai, Cardiosense *Implantable:* Abbott's CardioMEMS, Edwards' Vectorious and Endotronix, Fire1

Source: MedTech Strategist

Ventric Health: Expanding Access to Early Heart Failure Detection

Heart failure is a complex clinical syndrome that evolves across stages and presents with diverse symptoms arising from multiple underlying causes. Yet one principle is universal: the earlier heart failure is identified and treated, the better the patient's quality of life and long-term outcomes. Early detection is the mission of Ventric Health, whose FDA-cleared, office-based system, *Vivio*, is designed to help primary care physicians identify and triage patients with early-stage heart failure—before structural damage and overt symptoms fully manifest.

Primary care clinicians are most likely to encounter patients harboring early, subclinical cardiac changes. Historically, however, they have lacked objective tools to identify such patients. Instead, clinicians rely on risk factors, comorbidities, and symptom reports—an approach complicated by overlapping complaints such as fatigue, dyspnea, or chest discomfort, if symptoms are reported at all.

Comorbid conditions in patients over age 65, for example, diabetes, sleep apnea, or chronic kidney disease, may prompt referral for echocardiography. Echocardiography is most informative in patients with heart failure with HFrEF, in which systolic pumping function is impaired. But roughly half of heart failure patients, however, have heart failure with HFpEF, a condition characterized by elevated filling pressures due to ventricular stiffness. In its earlier stages, HFpEF often lacks the structural abnormalities that echocardiography can detect. Ventric Health's clinical data shows *Vivio* can identify physiological changes associated with both forms of heart failure.

Scientific Foundations

Ventric Health was founded in 2014 by a team that includes CEO Sean Brady (a lawyer, he came to the company with experience in licensing intellectual property from universities and their investors); chief technical officer and Caltech engineering alum Derek Rinderknecht, PhD; Niema Pahlevan, whose Caltech PhD is in bioengineering and biomedical engineering; and Mory (Morteza) Gharib, PhD, the Hans W. Liepmann Professor of Aeronautics and Medical Engineering at Caltech. The company's origins trace back to foundational research conducted in Gharib's laboratory.

Gharib's group studied cardiac embryology and fluid dynamics in zebrafish, a model organism widely used in cardiovascular research because its transparent body permits high-speed confocal imaging of cardiac function. The team discovered that in the earliest stages of development—before valves form—the embryonic heart pumps blood via elastic pressure waves traveling along the heart tube. These waves create dynamic suction that drives flow. Importantly, elements of this primitive pumping mechanism persist in the mature heart.

The researchers further demonstrated that waveforms generated by this phenomenon could be measured noninvasively. The founders recognized that heart failure—particularly the elevation of filling pressures—represented a compelling clinical application.

Targeting LVEDP

The team focused on estimating left ventricular end-diastolic pressure (LVEDP), widely regarded as a physiological hallmark—and one of the earliest signs—of heart failure. Elevated LVEDP reflects impaired ventricular function and the inability of the heart to meet systemic demands in the setting of increased filling pressures. These pressure elevations often precede structural remodeling and clinical symptoms.

Historically, LVEDP measurement required invasive left heart catheterization or implantable sensors. *Vivio* estimates LVEDP noninvasively.

The system includes a modified pneumatic blood-pressure cuff applied to the upper arm, a synchronized single-lead ECG, and an electronics module. After obtaining standard brachial blood pressure measurements, the cuff reinflates to suprasystolic pressure and records approximately 40 seconds of brachial pulse waveform data synchronized with ECG signals. The exam takes about five minutes.

From the user's perspective, the device resembles a conventional blood pressure cuff (*see Figure 2*). Data streams to an *iPad* running the *Vivio* software, and results are returned within seconds via a cloud-based analysis. The workflow fits naturally into routine vital sign collection during patient intake.

Brady emphasizes that the approach is physics-based rather than a "black box" machine learning system.

Brady emphasizes that the approach is physics-based rather than a "black-box" machine learning system. Using a three-parameter cardiovascular model reflecting preload, afterload, and contractility, the system reconstructs left ventricular pressure dynamics to estimate LVEDP.

Vivio received FDA 510(k) clearance in October 2023.

A validation study published in the *Journal of the American Heart Association* in December 2025 compared *Vivio*'s estimates with invasive LVEDP measurements obtained during left heart catheterization using high-precision Millar catheters. The invasive cohort included 407 patients undergoing non-emergent catheterization; 321 healthy participants served as controls.

Vivio identified elevated LVEDP (>18 mm Hg) with a sensitivity of 0.80 and specificity of 0.83. This performance is particularly

Figure 2
***Vivio* in Primary Care**

Source: Ventric Health

relevant for HFpEF, where conventional diagnostics—including BNP (B-type natriuretic peptide) testing and echocardiography—may lack sensitivity in early disease.

Real-World Implementation

A separate real-world study published in the *Journal of the American College of Cardiology* (*JACC*) in July 2025 evaluated *Vivio* screening across three primary care practices. Among 2,040 patients without prior heart failure diagnosis—but with diabetes, chronic kidney disease, or clinical suspicion—38.5% tested positive (LVEDP >18 mm Hg).

Results of the Vivio real-world study suggest that it can find many patients that might otherwise have remained undiagnosed until at a more advanced stage of disease.

Patients also completed the KCCQ-12 questionnaire to assess symptom burden and functional status. Among those with positive findings, more than one-third were asymptomatic (Stage B heart failure), approximately 42% were New York Heart Association (NYHA) Class I, and about 27% were NYHA Classes II–IV, the latter living with substantial symptoms and impaired health status associated with higher risks of heart failure hospitalization and death. These results suggest many patients might otherwise have remained undiagnosed until at a more advanced stage of disease.

In practice, says Brady, "If patients come back positive, you can run through the KCCQ-12 questionnaire to assess symptom burden to determine if they are really sick, asymptomatic, or somewhere in the middle. It allows primary care providers to institute workflows, including the initiation of guideline-directed medical therapy and specialty referral at the time of diagnosis." Primary care practices are often quite comfortable managing patients in the asymptomatic or mildly symptomatic stages of heart failure, but they would otherwise refer the patient for a near-term cardiology visit so they can access more advanced care.

A Population Health Tool

Up to half of heart failure patients remain undiagnosed, and many Medicare beneficiaries receive their first diagnosis during an emergency room visit or hospitalization. Delays in recognition contribute to avoidable costs and morbidity.

Vivio is positioned as a population health tool—deployable in primary care settings to identify at-risk individuals during routine visits. Early detection enables timely initiation of therapies, including SGLT2 inhibitors and aggressive blood pressure management, which have demonstrated outcome benefits across heart failure phenotypes.

For health systems operating under value-based care arrangements, earlier diagnosis may translate into reduced hospitalizations and improved quality metrics. Brady estimates that about 70% of Medicare is under value-based arrangements, across Medicare Advantage, the Medicare Shared Savings Program, or Accountable Care Organizations, for example. "CMS is rolling out new models all the time, and its goal is to transition Medicare to 100% value-based arrangements by 2030." Going forward, an increasing number of patients will be under these arrangements.

Ventric Health operates under a per-test revenue model, providing devices and training at no additional cost—an approach designed to align with value-based organizations. "There is no up-front cost, and they're able to use it on an ongoing basis to see how it impacts their practice," Brady says.

Reframing Heart Failure

Heart failure is often perceived as a late-stage condition marked by edema, dyspnea, and recurrent hospitalizations. But it is a progressive disease that begins months—or years—before overt decompensation.

Reframing heart failure as a condition that can be detected and treated earlier is central to Ventric's thesis. Early physiological identification offers the possibility of intervening before irreversible remodeling occurs.

As *Vivio* enters broader clinical use, anecdotal reports describe patients who, after positive screening and initiation of therapy, return with improved symptoms—sometimes only then recognizing how much their baseline had shifted over time.

This scenario is emblematic of the challenges of diagnosing elderly people who have many co-morbid conditions; subtle declines often go unnoticed. Brady says. "They adjust, and they just expect to have these things happening, but you really can take care of them."

Objective physiological assessment may help restore visibility to a disease that too often advances quietly.

WhiteSwell's Lymph-Targeted ADHF Therapy Aims for System-Wide Improvements

Fluid overload, which usually appears relatively late in the heart failure trajectory, is the bane of heart failure. It kicks off a vicious cycle of kidney fluid retention, venous and tissue congestion, and respiratory distress, which, each year, lands more than a million patients (in the US) in the hospital with a primary diagnosis of acute decompensated heart failure (ADHF).

These ADHF hospitalizations account for the single most expensive component of heart failure care in the US, costing roughly $18 billion each year, a number that will rise steeply in coming years due to an increase in heart failure diagnoses and the fact that hospitalizations beget more hospitalizations.

Each episode of ADHF worsens the patient's condition because fluid overload exerts high wall stress on the ventricle, and the heart's ability to pump is diminished, resulting in poor perfusion of the kidneys. Patients at risk of worsening renal function, which affects more than 30% of ADHF patients, face a particularly poor post-discharge diagnosis.

According to the American Heart Association, the 30-day readmission rate for a hospitalized ADHF patient is between 18% and 25%. At 90 days it's more than 30%, and 61% will have been rehospitalized within one year.

And there is another reason why previously hospitalized patients return so soon; despite optimal diuretic and other therapies, many leave the hospital with lingering congestion that compromises the workings of the heart, lungs, and kidneys. Addressing this specific cause of ill health is the goal of Galway-Ireland based WhiteSwell, which is developing a device therapy that achieves greater decongestion by supporting the most naturally effective pathway, the lymphatic system.

The oxygen-rich blood that provides nourishment to interstitial tissue relies upon the lymphatic system to drain that interstitial fluid back into the venous system, playing a key role as an agent of the immune system, and maintaining fluid balance. The interstitium normally holds three to four times more fluid (approximately 12 liters) than intravascular plasma (approximately 3 liters) in the body.

While diuretics act directly on the fluid-overloaded vascular compartment, WhiteSwell believes that during episodes of ADHF, to effectively restore balance, interstitial fluid must be moved out of the congested tissues, drained back into circulation, then excreted. The start-up plans to accomplish this with a device called the *eLym* System, now being studied in a multicenter, prospective single-arm study called DELTA-HF.

Making a Decades-Old Insight Practicable

During episodes of ADHF, tissues hold three to four times more interstitial fluid than they do under normal circumstances, because high central venous pressure causes capillaries to leak fluid into the interstitial space faster than the lymphatic system can drain that fluid back to the venous system. That same elevated venous pressure creates a pressure head that resists lymph drainage via the thoracic duct (the main conduit for lymphatic fluid, which drains 75% of the body's fluid) into the great veins above the heart.

These dynamics point to the lymphatic system as an obvious point for intervention in ADHF. Indeed, Eamon Brady says that when he joined WhiteSwell as CEO in 2018, he did initially wonder why this hadn't been tried before, but he learned that in fact, going back to the '60s, a couple of publications reported on efforts to cannulate the thoracic duct and remove fluid outside the heart failure patient.

Such studies did demonstrate that doing so improved heart failure symptoms and hemodynamic measures (see, for example, "Lymph Circulation in Congestive Heart Failure: Effect of External Thoracic Duct Drainage," Witte, Dumont, et al., *Circulation*, June 1969).

However, directly cannulating the thoracic duct is risky and not clinically practicable because of the chance of perforating that conduit, which cannot be easily or safely repaired. Such a breech would also cause lymphatic fluid to go where it shouldn't, with the potential for local damage. Further, removing the fluid to the exterior of the patient robs the body of the nutritional and immune-system benefits of the lymphatic system.

It was WhiteSwell founder Yaacov Nitzan who found a way to increase clearance through the thoracic duct without direct cannulation. The transcatheter therapy of WhiteSwell, which he founded in 2014, would increase fluid clearance by lowering pressure in the central vein that connects to the thoracic duct, with the goal of increasing lymphatic flow and relieving interstitial congestion. A Technion-trained biomedical engineer who worked at Biosense Webster, Given Imaging, and Edwards Lifesciences, Nitzan also founded V-Wave, which is now part of Johnson & Johnson by way of acquisition, in addition to several other medical device companies.

When Eamon Brady was recruited to lead the company in 2018, he also brought a depth of medtech innovation experience, being fresh off the sale of Neuravi, the neurovascular start-up he led

up to its acquisition by Johnson & Johnson. He was previously involved with R&D and new ventures at Abbott Vascular. The former director of R&D at MedNova, he became part of Abbott when the large strategic acquired his company in 2005.

Upon joining WhiteSwell as CEO, Brady spearheaded the raising of the company's Series B round, a hefty $30 million sum, from a group of investors led by RA Capital Management and InCube Ventures syndicate, with participation from other unnamed investors.

"It's well known in the literature that if you do not fully decongest the patients, they are at a high risk for rehospitalization." ***–Eamon Brady***

Draining the Swamp

The *eLym* System treats congestion in acute heart failure by helping the lymphatic system drain fluid from tissues back into the bloodstream, where it can then be removed by the kidneys. It comprises a sheath, a catheter incorporating an inflatable balloon and a microaxial decompression pump, and a bedside console that drives the pump in response to pressure readings.

It works by creating a controllable lower pressure zone at the thoracic duct outflow in an area called the left venous angle, the convergence of the left internal jugular vein (the main vein issuing from the brain), and the subclavian (the main vein coming from the arm).

To start, the interventionalist advances a guidewire through the neck to access the internal jugular vein, a common entry point used to place many millions of central venous catheters each year, Brady points out.

The *eLym* procedure brackets a zone at the venous angle by placing a flow-reducing balloon in the jugular and a balloon in the innominate vein and inflating both. A pump underneath the distal balloon moves fluid out of that region, and by doing so, reduces the pressure locally, creating a pressure differential near the thoracic duct outflow. Normal blood flow into that region continues; *eLym* is simply controlling the pressure at the outflow.

The interstitial fluid (or lymph) mixes with plasma then circulates throughout the system, eventually reaching the kidneys, where it is filtered and passed out as urine. Says Brady, "The lymphatics return plasma proteins that have leaked into the interstitium, which are important for a lot of functions, including creating oncotic pressure in the capillaries, which helps to hold fluid in the capillaries and prevents further tissue fluid accumulation and swelling."

According to Brady, while the company initially felt therapy delivery would require up to 72 hours, "We will probably bring that down to 60 hours as we go forward because we think that's enough. But we believe that lymph from organs such as the kidneys and heart may mobilize earlier in the process, and we have found clinically that *eLym* has facilitated significant decongestion in 24 hours of therapy, and a shorter treatment means that the patient is comfortable much more quickly."

In practice, as soon as patients enter the hospital, they would be put on *eLym* to begin the process of moving fluid out of tissue, in conjunction with IV diuretics, because, says Brady, "It takes time to draw fluid out of tissues. It's not like emptying a lake, it's like draining a swamp."

By starting therapy early, the goal is for *eLym* to promote lymph drainage to relieve pressure that has built up in the organ systems, particularly the heart and kidneys, which is important for organ function. "Getting the kidneys working well early on in therapy has a potentially powerful impact, as does simultaneously decongesting the two compartments, the vascular compartment and the interstitial compartment."

Anecdotally, Brady continues, very quickly, patients report that they feel better. "Maybe too much so," he jokes, "because they say, 'I don't think I need this device anymore!'" According to Brady, the company is seeing substantial fluid loss in patients in a day or two after treatment because their kidneys are working better. "But decongesting the patient during that episode isn't the company's only goal," he points out. "We want to keep the patient out of the hospital for the next three to six months or longer. And it's well known in the literature that if you do not fully decongest the patients, they are at a high risk for rehospitalization."

Longer-lasting effects may be achieved when the lymphatics are working properly. "That's what we're focused on. We want to do trials on the basis that the patient stays out of the hospital and has a reduced risk of dying in the follow-up period," Brady emphasizes.

Validating a Novel Mechanism

The company believes it has uncovered a sweet spot for patient selection. Brady explains, "To start with, the FDA is very clear that they want early heart failure device trials to be focused on patients who are not responding well to diuretic therapy and are

not likely to. So straight away, that is a rich patient population in need of a better treatment option." Among these patients, WhiteSwell will study those who are substantially congested.

WhiteSwell's non-randomized safety and feasibility study, DELTA-HF, is ongoing in Poland, Spain, and the Republic of Georgia. Up to 70 subjects may be enrolled and treated. Inclusion criteria include the presence of congestion, a home diuretic dose greater than or equal to 80 mg furosemide (or equivalent), and elevated natriuretic peptides.

Clinical investigator Jan Biegus, MD, PhD, of the Department of Cardiology, Clinical Department of Intensive Cardiac Care at Wroclaw Medical University (Wroclaw, Poland), presented 90-day data on the first 21 patients treated, at the THT (Technology and Heart Failure Therapeutics) Conference in 2025.

According to his report, there was 100% technical success, a mean therapy time of 23.2 hours, all patients lost weight with a mean decrease of 10.7 pounds at 90 days, all enjoyed stable kidney function, and nearly all were optimally decongested by discharge, as well as at 30 and 90 days post-discharge. Markers of wall stress and congestion improved, and rehospitalization rates were low, with one patient coming back within 30 days, and two by 90 days. Within the 90-day follow-up period, there were no deaths.

The next milestone for the company will be the initiation of a randomized controlled trial in the US, Canada, Europe, and Israel.

Distinguishing WhiteSwell from other new heart failure start-ups also aiming to enhance decongestion in ADHF, Brady notes, "We are essentially going into the lowest pressure veins in the vascular system and that inherently means that the risk is lower than an arterial-based approach." *eLym* patients can also get up and move around, which is important he says, and is not a feature of some other therapies. "If you are using femoral access, your patients can't mobilize. And that's an important part of care."

Finally, he says, many other devices create a condition, whether reducing venous outflow pressure or increasing arterial pressure, that goes away when the device therapy is removed. "Whereas we're helping the lymphatic system get back into balance, so it continues to operate after the therapy." In heart failure, that natural mechanism is simply overwhelmed, Brady states. "We're helping it get past that overwhelm. We're tapping into this vast network and helping it do what it does very well under normal conditions, and it continues to operate."

Levron Cardiovascular Harnesses the Body's Own Mechanism to Relieve Heart Failure

Levron Cardiovascular has invented a new category of devices that treats heart failure by leveraging innate physiological mechanisms to shift fluid out of the lungs and reduce the workload of the heart. It thus presents a relatively low-risk proposition, according to CEO Amir Ronen. "We're taking an approach that is simple, low risk, and elegant to help patients," he says.

It all starts with the cardio-respiratory system and so-called "respiratory pump," that is, the relationship between the lungs and heart, or rather, how breathing cycles naturally assist the heart. The respiratory pump modulates the intrathoracic (pleural) pressure, and in an intriguing contrast, the right and left ventricles respond oppositely to changes in intrathoracic pressure.

When you inhale strongly, the diaphragm moves down, creating negative pressure in the chest (relative to the ambient pressure). That negative pressure acts like suction, pulling blood from the systemic veins into the right ventricle. As a result, the right ventricle fills more, and the right ventricle pumps more blood into the lungs.

At the same time, the negative pressure surrounding the left ventricle increases the pressure gradient across the left-ventricle wall, increasing the effort required for ejection, and thus causing the left ventricle to pump less blood out. The opposite occurs during exhalation, when higher intrathoracic pressure helps increase left heart output while decreasing right ventricle filling and inflow into the lung.

Levron's scientific founder Amir Landesberg, MD, PhD is an electrical engineer and physician and a professor and the former dean of biomedical engineering at Technion (Israel Institute of Engineering). He's also an inventor with many medical patents to his name. Landesberg wondered if it might be possible to harness this innate respiratory pump to ease the burden of heart failure patients.

He conceived a way of using conventional pacemakers to synchronize the heart and lung cycles in a particular way that increases the heart rate during the time of higher intrathoracic pressure (relative to the heart rate at low intrathoracic pressure), to shift fluid out of the lungs and boost outflow from the left ventricle. In essence, the concept turns a physiological interaction that normally exists in the body into a therapeutic advantage.

Turning Pacemakers Into Cardiac Assist Devices

To bring that concept to patients, Landesberg co-founded Levron Cardiovascular in 2021, alongside Shimon Eckhouse, PhD, physicist, inventor, and notable serial entrepreneur, who has founded or co-founded at least 16 medical device companies across diverse clinical fields. To lead the company, the founding team recruited Amir Ronen, an experienced CEO who has done this before, as the former head of the still-active heart failure company Sensible Health Medical Innovations, which developed a platform for noninvasive fluid monitoring.

Levron's novel therapy is called CRPA (Cardio-Respiratory Physiological Assist) and is branded as *Soulmate*. With a standard pacemaker, says Ronen, "We synchronize the heart, lungs, and the pacemaker. We slightly modulate the heart rhythm in cadence with the respiratory dynamic, correcting the imbalance that leads to lung congestion and improving pulmonary hemodynamic and left ventricle output."

For its first product, the company has chosen a lower-risk go-to-market strategy. *Soulmate 1.0* is targeted at the 20-30% of heart failure patients who already have pacemakers. "We will focus on the patients in this group by adding more functionality to the pacemaker, thus reaching the market much faster," Ronen explains. The first-generation product is now undergoing first-in-human clinical studies. Sixteen patients have been enrolled at four hospitals in Israel (Sheba Medical Center, Tzafon Medical Center, Sha'are Zedek Medical Center and Rabin Medical Center).

Soulmate 2.0 will be an implantable device that increases the functionality of implanted pacemakers. Ronen says, "Ultimately we want every pacemaker to have the Levron secret sauce inside!"

After presenting first-in-human results at the ICI (Innovations in Cardiovascular Interventions) start-up competition in December 2024, the company won a $200,000 award. Anecdotally, Ronen reports that the results are promising. "The genius is in the simplicity and the immediate response. Patients experience symptom relief, lung fluid is reduced, and we noticed a decrease in the pulmonary artery pressure and an improvement in respiratory makers such as tidal volume."

Levron recently raised $4 million in a funding round led by Shoni Ventures, with participation from Shimon Eckhouse, Alon MedTech Ventures, the Technion, and additional investors.

It's often reported that heart failure affects 6.7 million people in the US, and the population continues to grow. However, it is a complex condition that occurs in patients with comorbidities. For a heart failure start-up, it's important to clearly define which patients the new therapy is intended to treat and at which stage of the disease. One advantage for Levron, says Ronen, is that "our technology is agnostic to etiology. We serve both HFrEF and HFpEF, because these cardio-respiratory interactions affect all types of heart failure."

From a practical regulatory standpoint, however, he points out that the company is focusing first on NYHA Class III patients, who are sick and whose frequent hospitalizations are primarily driven by severe dyspnea due to progressive lung congestion. That's our sweet spot to start with, and we'll expand further."

Since the device appears, at this stage, to present little risk, might it eventually be used earlier in the heart failure cascade to prevent deterioration? "Economically and clinically, it is easier to prove benefit patients who experience more severe dyspnea and acute decompensation," Ronen answers. "But there is no reason why we can't treat earlier, and addressing Class II is part of the longer-term plan." With an estimated 1.5-2 million Class III patients in the US and with hospitalization rates of 25-30%, "there are plenty of patients to start with." MTS