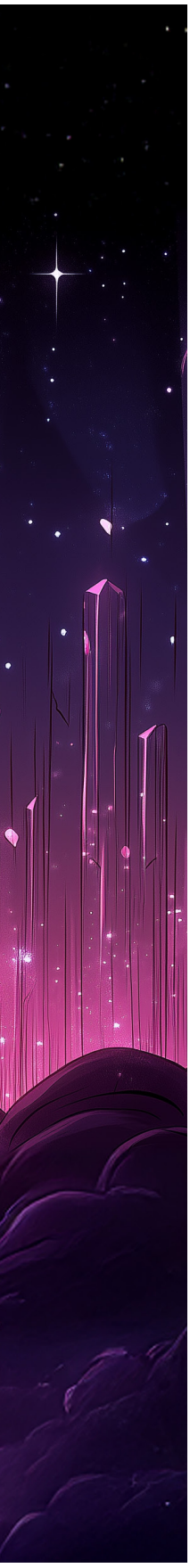
DEVICES FOR MANY-FACETED HEART FAILURE

Heart failure has come to the fore as an innovation and acquisition target for medical device companies at a time when the Heart Failure Society is working to create guidelines that support the use of devices in many groups of heart failure patients. The challenge remains: characterizing patients and understanding the best approach for them.

MARY STUART



What's the biggest unmet need in cardiovascular disease? Heart failure, at least from the perspective of medical device company representatives who spoke on the panel "New Opportunities and Directions in Cardiovascular Medical Devices," which took place in April at the MedTech Strategist Innovation Summit in Dublin. Executives from **Edwards Lifesciences**, **Johnson & Johnson**, and **Medtronic** agreed that many patients with heart failure don't yet have access to the right therapy, because the disease is complicated in ways that we're only beginning to address.

Bruce Rosengard, MD, vice president and global lead for medtech for Johnson & Johnson's External Innovation group (and a cardiac surgeon), noted that, to begin with, "It's not one disease. It's really a syndrome, and in fact, heart failure is the end state of every form of cardiac disease: valvular disease, coronary disease, congenital disease, infectious disease, inflammatory disease, arrhythmic disease. All of them can lead to heart failure."

There are two major categories of heart failure between which patients are split about 50-50: heart failure with reduced ejection fraction (HFrEF), also known as systolic heart failure, and heart failure with preserved ejection fraction (HFpEF), or diastolic heart failure. But within those high-level distinctions are many gradations of disease, taking into account how, exactly, the heart is dysfunctional, and how the patient got there. Heart failure usually begins with some other condition—an earlier damaging myocardial infarction, an untreated arrhythmia or sleep apnea, or the slow accumulation of comorbidities like hypertension, coronary artery disease, and diabetes, which lead to vascular resistance.

Panelist Virginia Giddings, vice president of exploration for Edwards Lifesciences, pointed out that heart failure develops over many years, and it "is a very complex disease presenting with different phenotypes." Within the pathological state in which the heart is failing, there might be problems with the pump, the ventricles, the heart's muscle, or the valves, she said. There is right or left heart failure, and biventricular failure. Heart failure manifests in so many phenotypes because it arises from the interplay of structural and biological changes influenced by aging, one's genetic background, comorbidities, and lifestyle. "The physiology can be very different from one patient to another," Giddings said.

Also on the panel was Chris Eso, vice president of corporate development for Medtronic, who said, "It is inevitable that companies that come to present to us say they're in heart failure. Our initial follow-up question is, 'Well, what patient type?' Because at the end of the day, there probably isn't one heart failure solution. It's a question of addressing all the different disease states that lead to heart failure."

In terms of the therapeutic development possibilities around heart failure, Giddings said, "The sky is the limit," and, she added, "the patient population is enormous."

Tailwinds for Heart Failure Innovators

In September, the Heart Failure Society of America reported that in 2021, heart failure, which affects approximately 6.7 million people over the age of 20, was responsible for 45% of all cardiovascular deaths, and the situation is worsening (*see box, "In 2024, Heart Failure Has Become an Even Bigger Problem"*).

That same month, the society also issued a consensus document in the *Journal of Cardiac Failure*, to begin the process of creating guidelines for the use of medical devices in heart failure—not necessarily as a second-line alternative after guideline-directed medical therapy (GDMT) fails or is precluded, but right alongside medical therapy in the appropriate sets of patients. The authors make the case that devices can be beneficial because they might target specific physiological mechanisms of disease in ways that drugs can't, and they're also not, usually, subject to issues of adherence or metabolism the way drugs are.

The Heart Failure Society felt it necessary to take this step because device therapies, even when approved with evidence that they work, are underused or not used early enough. Thus the society wants to create, for heart failure device therapies, the kind of standardized, guidelines-based approach that governs drug therapy.

The authors contend that even when heart failure patients are managed by medical therapy, the residual risk of events (hospitalizations due to episodes of decompensation and death) is high enough to support combination approaches that include devices. But that's not the whole problem. The scientific statement cites real-world studies showing that 43% of eligible heart failure patients don't benefit from guideline-directed medical therapy for many reasons, including intolerance, nonadherence, inconsistent delivery, and the long-term cost of recurrent usage.

Given that inadequate medical therapy confers an excess risk of all-cause mortality of 29% over two years (or higher—37% when the comparison includes only concurrent medication refills), the society has set out to create a care pathway and guidelines for the timely and judicious use of devices that target specific pathophysiological mechanisms, some already approved, and many more making their way through development.

This provides tailwinds for heart failure device developers, as do recent acquisitions by the some of the strategics mentioned above, whose spokespeople were clearly not talking through their hats when they said heart failure was a priority. In August, Edwards acquired, from **Genesis MedTech**, JC Medical, the maker of a transcatheter valve for the treatment of aortic regurgitation, a condition that drives the progression of heart failure, after previously announcing in July that it paid $1.6 billion to acquire two other companies in the space (without disclosing what it paid for each). In the bundle was JenaValve, which Edwards bought for the potential of its transcatheter valve to treat aortic regurgitation, with FDA approval anticipated in late 2025 (see *"TAVR Update: Market Leaders Medtronic and Edwards Look to Conquer New Indications and Solve Old Problems"*, MedTech Strategist, *September 4, 2024*). Endotronix was the second company purchased. It's *Cordella* sensor for monitoring pulmonary arterial pressure, which the FDA approved in June, provides an early warning of heart failure so clinicians can intervene in a timely fashion.

Johnson & Johnson had already staked a major claim to the space in December 2022 by acquiring Abiomed, the leader in mechanical circulatory support, in a deal that valued the acquisition target at almost $17 billion. In August, it entered into a new device category for heart failure treatment by acquiring V-Wave for $600 million up front with the possibility of additional regulatory and commercial milestone payments totaling $1.1 billion. V-Wave is a leading player in the interatrial shunt space, having reported early results from its pivotal trial in April.

These events are giving a much-needed boost to a medtech development category that, while offering compelling products for an enormous market, is extremely challenging.

Figure 1

Mechanical Circulatory Support for Heart Failure

Category	Selected Company Examples
Left ventricular assist devices	FDA cleared: Abbott (*HeartMate 3*) In development: CorWave, Corvion Medical, EvaHeart
Total artificial heart (TAH)	SynCardia, only approved TAH in US. Carmat (*Aeson*) has CE mark. In development: BiVACOR (*BiVACOR*), Scandinavian Real Heart (*Realheart*)
Intraventricular flow accelerator	FineHeart (*FlowMaker*)
Balloon pump for counterpulsation	NuPulseCV (*iVAS* intravascular assist system)
Non blood-contacting biventricular support	CorInnova, Adjucor
Percutaneous ventricular assist devices	Abbott (*Impella*) Devices in development migrating from temporary support during high-risk PCI to heart failure: BrioHealth Solutions (*BrioVAD*), Magenta Medical (*Elevate*), Procyrion (*Aortix*), Puzzle Medical, Supira Medical

Source: "HFSA Scientific Statement: Update on Device Therapies in Heart Failure," *Journal of Cardiac Failure*, September 10, 2024; *MedTech Strategist*

The Different Faces of Heart Failure: Opportunities and Challenges

Once, devices for heart failure fell into three basic categories: implantables for cardiac rhythm management (implantable cardioverter defibrillators or ICDs, and devices for cardiac resynchronization therapy or CRT); devices to manage fluid overload during acute decompensated heart failure; and mechanical circulatory support (artificial hearts or ventricular-assist devices) to sustain late-stage patients until a decision is made about a next step, such as a heart transplant.

The classic image of heart failure was the decompensated patient, breathless, swollen, and hospitalized frequently. While

decompensation is a common late-stage feature of all types of heart failure when it isn't under control, we now know that depending on the patient's disease, there are many more potential pathophysiological points of intervention, which device companies are now targeting.

There are programs addressing heart failure from a structural angle by repairing mitral or other damaged heart valves that exacerbate the problem, and others that attempt to reshape and/or remodel enlarged ventricles. Many companies are working to electrically modify pathways relevant to disease, at the level of cardiac cells, for example, to increase contractility, or by stimulating the autonomic nervous system or the respiratory system. Others are creating new heart pressure monitoring systems (Endotronix, for example) to signal worsening trends of heart failure to allow timely intervention, and, ultimately, a greater understanding of disease processes. (see *Figures 1-3*).

In addition, work is being done by companies on the front end of the problem, to diagnose and characterize heart failure patients, an unmet need that makes therapy development all the more challenging.

For example, while HFrEF, which is a dysfunction of the heart's pumping action, is easily diagnosed by the ejection fraction or how much blood is pumped out with each heart contraction, HFpEF, which represents at least half of all heart failure, is difficult to diagnose. HFpEF patients have a normal ejection fraction, but a dysfunction in the filling cycle of the heart. The current criteria for diagnosing HFpEF, in patients having shortness of breath during exertion and other signs of heart failure, include a normal left ventricular ejection

Figure 2

Selected Physiological Therapeutic Devices for Heart Failure

Physiological Approach	Selected Company Examples
Interatrial shunts	Adona Medical, Alleviant (*Alleviant System*), Corvia (*Corvia* Atrial Shunt), Edwards (*APTURE*), InterShunt Medical (*PAS-C Catheter*), NoYA MedTech (*NoYA*), Occlutech (*Atrial Flow Regulator*), V-Wave (*Ventura*)
Heart valves	Devices for the repair or replacement of heart valves, SAVR, and TAVR: Abbott (*Navitor*), Edwards (*Sapien S3*), Medtronic (*Evolut FX*) Transcatheter valves in development for aortic regurgitation: Edwards (JC Medical and JenaValve) Transcatheter edge-to-edge mitral valve repair: Abbott (*MitraClip*), Edwards (*PASCAL*) Tricuspid valve repair or replacement: Abbott (*TriClip*), Edwards (*EVOQUE*)
Neuromodulation, various	Baroflex activation: CVRx (*Barostim Neo*) Vagus nerve stimulation: LivaNova (*VITARIA*) Splanchnic nerve ablation: Axon Therapies (for HFpEF) Immunomodulation: Humanitas Research (*HF-ImMod*)
Electrophysiology modulation	Cardiac resynchronization therapy: Abbott, Biotronik, Boston Scientific, Medtronic. Cardiac contractility modulators: Berlin Heals (*C-MIC*), Impulse Dynamics *(IMPULSE Optimizer*)
Respiratory modulation	Phrenic nerve stimulation: Respicardia
Fluid volume management	Reprieve Cardiovascular
Reduction of pulmonary hypertension	Aria CV
Ventricular reshaping	Ancora Heart (*AccuCinch*); BioVentrix (*Revivent TC*), Cardiac Success (*VSling*)

Source: "HFSA Scientific Statement: Update on Device Therapies in Heart Failure," *Journal of Cardiac Failure*, September 10, 2024; *MedTech Strategist*

fraction (≥ 50%), evidence of abnormal left ventricular filling, increased filling pressures, and elevated levels of natriuretic peptides.

While transthoracic echocardiography is used to estimate intracardiac filling pressures, it requires expertise and is subject to intraoperator variability. Natriuretic peptides are easy to measure, but it's estimated that one-third of HFpEF patients have normal levels. Right heart catheterization is the gold standard in determining increased left ventricle pressure, but it's not undertaken lightly in a frail, elderly patient. The noninvasive diagnosis of HFpEF is an innovation target that one UK-based company, **Ultromics**, has taken on successfully with an AI application for echocardiography (*see sidebar, "Ultromics: Successful Treatment Begins With Accurate Diagnosis"*).

The Swedish start-up **Acorai** is also developing an AI-enabled solution for heart failure; the company has developed a cluster of sensors for noninvasive pulmonary and cardiac pressure monitoring, which, as its founder Filip Peters says, "has been the Holy Grail of cardiology and particularly heart failure, for decades." We discuss Acorai below.

But Who Are the Patients?

With so much heterogeneity among patients, many unanswered questions remain. Which patients are right for the mechanism of action of which therapy? And in the end, how large is the market for that particular approach? How do you characterize patients and study them in clinical trials for the purpose of demonstrating benefit? Speaking at the Innovation Summit meeting mentioned above, Medtronic's Chris Eso said, "Any one of the new solutions might only be suitable for a smaller patient population. But we have to identify the right patients, period." This is an opportunity in and of itself; heart failure is ripe for innovation in the space of phenotyping tests.

The clinical experience of **Corvia** and V-Wave are illustrative of the challenges heart failure device developers face, as the first two companies in a new class of devices called interatrial shunts, a popular innovation space that has attracted at least seven start-ups so far. Elevated left atrial pressure is a feature in many heart failure patients and interatrial shunts create an opening in the septum between the left and right atria to shunt blood into the larger reservoir of the right atrium to relieve

In 2024, Heart Failure Has Become an Even Bigger Problem

The lifetime risk of heart failure has increased to 24%

- Approximately 6.7 million Americans over 20 years of age have heart failure (HF), and the prevalence is expected to rise to 8.7 million in 2030, 10.3 million in 2040, and 11.4 million by 2050.
- One in four will develop HF in their lifetime; the risk increases with obesity, hypertension, and clusters of comorbidities.
- The proportion of younger patients with HF is increasing more than the share of older patients.
- 24-34% of the US population has pre-heart failure.
- The incidence and prevalence of HF is higher among Black individuals compared with other racial and ethnic groups. The prevalence of HF has increased among Black and Hispanic individuals over time.
- HF mortality rates have been increasing since 2012. In 2021, HF contributed to more than 425,000 deaths in the US and accounted for 45% of cardiovascular deaths.
- Black, American Indian, and Alaskan Native individuals have the highest all-cause age-adjusted HF mortality rates compared with other racial and ethnic groups. From 2010 to 2020, HF mortality rates have increased for Black individuals at a rate higher than for any other racial or ethnic group, particularly for individuals below the age of 65.
- A greater relative annual increase in HF-related mortality rates has been noted for younger (35-64) compared with older (65-84) adults.
- Rates of HF hospitalizations have increased since 2014. This increase was consistent between age groups and sexes, with the highest rates being among Black patients.

Source: Heart Failure Society of America, reported on September 24, 2024

the pressure. Both companies ran well-powered, high-quality randomized clinical trials, and both failed to prove their primary endpoints (of a reduction in heart failure events).

First, Corvia enrolled 626 patients in REDUCE-LAP HF II and randomized patients to either the *Corvia* Atrial Shunt, or a sham procedure. At two years, there was no difference in primary outcomes between the two groups. However, certain subsets of patients responded well to the therapy. Hence, Corvia is now running a second double-blinded, randomized, sham-controlled trial, RESPONDER-HF, and will study another 260 patients for two years, this time recruiting only certain patients with HFpEF (with an ejection fraction ≥ 40% and further qualified by their hemodynamics during exercise) and HFmrEF (heart failure with mid-range ejection fraction), to try to determine which heart failure patients benefit from shunting.

Likewise, V-Wave enrolled 508 patients in its pivotal trial RELIEVE-HF. Heart failure patients with any ejection fraction were admitted, but randomization was stratified across patients with either reduced or preserved ejection fraction. As noted, the trial failed to achieve primary endpoints around the reduction of heart failure events, but demonstrated a 45% reduction in adverse cardiovascular events for HFreF patients, and a higher rate of harm to those with HFpEF.

The clinical community remains positive about the potential for these devices, although not enough patients have been studied yet to make pronouncements. Both **Occlutech** (with its *Atrial Flow Regulator*) and **Alleviant** (which creates a shunt without leaving a device behind) are currently enrolling for equally large and robust clinical trials, so we can expect some clarification within the next five years or so.

While incumbents are focused on determining which kinds of heart failure patients respond to interatrial shunting, Brian Fahey, PhD, the co-founder, president, and CEO of interatrial shunt newcomer **Adona Medical**, believes that's not the only challenge, and that today's "one-size-fits-all" approach to interatrial shunts isn't likely to be broadly effective for such a heterogenous patient population. Further, current developers are challenged by the lack of a window into what, precisely, is happening with cardiac filling pressures as patients go about their lives. Adona Medical, profiled below, has designed its platform to address both shortcomings.

> Depending on the patient's disease, there are many more potential pathophysiological points of intervention, which device companies are now targeting.

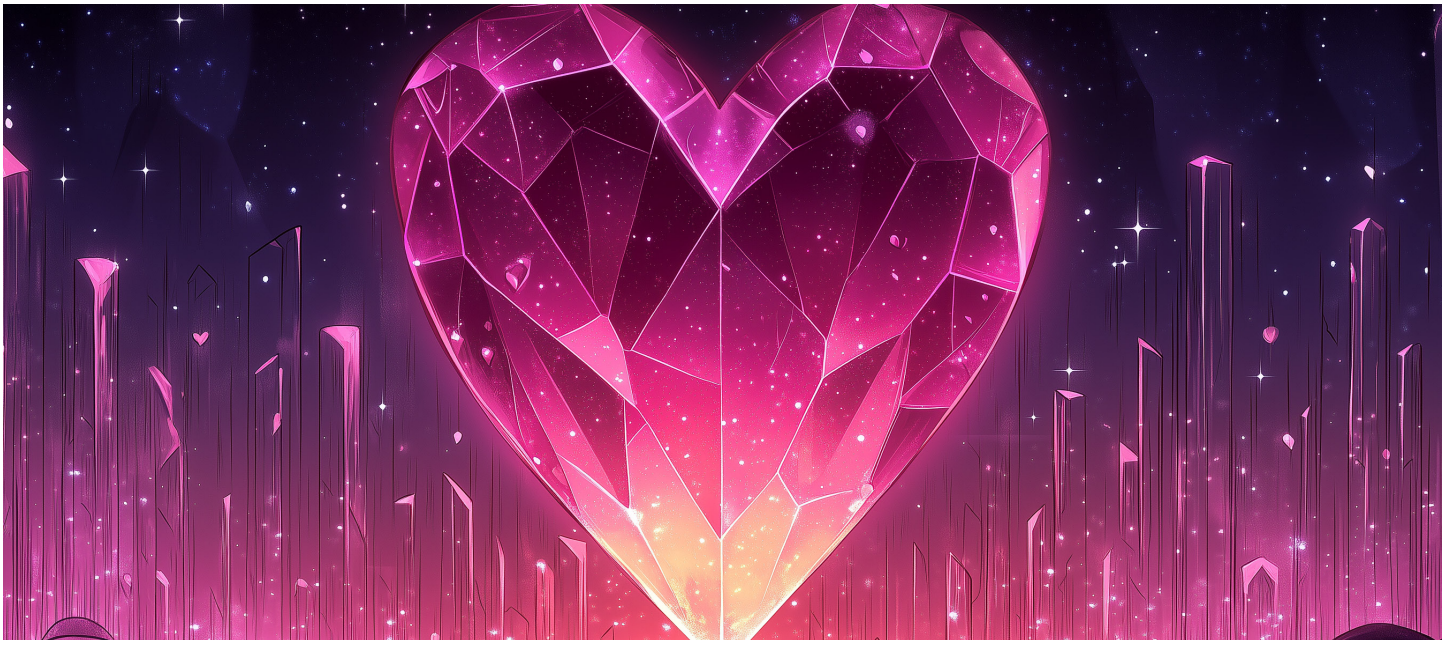
Addressing late-stage heart failure and cardiogenic shock, **CorInnova** hopes to disrupt the space with a novel, physiological, and non-blood contacting device. The start-up faces the rigorous PMA pathway for a first-of-its-kind device, but its CEO believes that the patient population it is initially targeting is well defined and large, with more to follow. We interview CorInnova below.

Figure 3

Selected Heart Failure Monitoring Companies

Category	Selected Company Examples
Invasive monitoring of surrogates for cardiac pressure (predicting congestion)	Two FDA-cleared stand-alone products: Abbott (*CardioMEMS*), Edwards (*Cordella*) Diagnostic companions to implanted CRT or ICD devices: Medtronic (*TriageHF*), Boston Scientific (*HeartLogic*), Biotronik (*HeartInsight*) In development: Fire1, Vectorious
Noninvasive surrogates for cardiac pressure monitoring	Acorai (*SAVE* sensor), Analog Devices (*Sensinel*), Bodyport, Cardiosense (*Cardiotag*), Zoll (*Heart Failure Management System*)

Source: "HFSA Scientific Statement: Update on Device Therapies in Heart Failure," *Journal of Cardiac Failure*, September 10, 2024; *MedTech Strategist*



CorInnova: A Versatile Device Serves Many Heart Failure Patients

Now, on the eve of its first-in-human studies, CorInnova has developed a minimally invasive mechanical circulatory-assist device that respects the natural physiology of the heart. It is disruptive because it provides active cardiac support without requiring contact with blood, a source of complications for existing left ventricular assist devices (LVADs) and other mechanical circulatory support devices for heart failure.

The device was conceived by its inventor, John Criscione, MD, PhD, a biomedical engineer and a professor in the Department of Biomedical Engineering at Texas A&M University, to restore healthy motion to the hearts of patients after a damaging myocardial infarction (MI), to prevent them from progressing to heart failure. Since then, the company has uncovered many other valuable opportunities in heart failure, where its current device has the ideal attributes for temporary cardiac assist, and the potential to be developed for long-term heart support.

Myocardial infarction is one pathway to heart failure. Epidemiological studies suggest that 15-20% of patients develop heart failure as a complication of a heart attack while in the hospital, and 10-12% of all MI patients subsequently develop heart failure after leaving the hospital. The risk is greatest in the year following the heart injury, when 45% of the post-MI patients present with chronic heart failure.

Heart failure develops in these patients because the infarcted section of the heart becomes pliable and spongy immediately following the injury to the tissue, prior to the formation of scar tissue. It bulges outward, whereas the healthy areas remain firm, and this leads to dyskinetic motion. That in turn starts the cytokine-signaling cascade that causes the heart to enlarge to compensate for the damage, which makes things worse.

Criscione started with the known efficacy of direct cardiac massage, which, when done by surgeons during open heart surgery, is known to effectively restore cardiac biomechanics. He went to the drawing board to create a device that could go around the heart and gently massage it in a physiologically correct manner, improving hemodynamics and correcting dyskinetic motion after MI to prevent the cytokine signaling cascade that leads to heart failure.

With money from the Texas Emerging Technology Fund and NIH grants, Criscione founded CorInnova in 2004 and spent five years developing the device to the point of its first successful proof-of-concept study in a large animal.

Creating a Pipeline

CorInnova CEO William Altman met Criscione when he was an "entrepreneur-at-large" looking for a start-up to run, after a 30-year career building healthcare companies. He approached his alma mater, Texas A&M, to see if any medical device start-ups under its aegis were in need of experienced leadership. Criscione's company resonated with Altman, although it would necessarily go through the riskier and long-term development process of a PMA device. "Both my father and father-in-law died of heart failure," says Altman, "so I figured if I'm going to put a lot of sweat equity into an early stage medtech company, it should be one with the potential to have a huge impact."

Putting together a team that includes VP of product development Boris Leschinsky, the former chief technology officer of Datascope, Altman approached Wellcome Trust in the UK and was invited to enter CorInnova into the competitive process for its Translation Fund, which supported breakthrough technologies. Over the course of a year, Altman made several pitches. For the final event, he asked his company advisor Billy Cohn, MD, the renowned heart surgeon at the Texas Heart Institute, to accompany him. The $6 million the company won got it to the point of an optimized device, short-term preclinical studies in a drug-induced model of heart failure, and experience in chronic models of heart failure.

Designing Around Ease of Implantation and Removal

CorInnova set out to create a solution that would be extremely small, lightweight, and easy to implant. The device, which encircles the ventricles of the heart within the pericardial space (where it doesn't contact blood) applies gentle compression to the heart by cycling fluids (air and saline) in and out of two concentric sets of thin polyurethane bladders, driven by a portable pneumatic drive/controller.

The fluid-filled inner bladder is adjusted upon implant to accommodate for any gaps between the device and the heart wall, and the outer bladder applies compression to the heart using air pressure in synchrony with systole. "In doing so, we increase cardiac output in rhythm with the native heartbeat," Altman says. He notes that the polyurethane is smooth and doesn't stick to the heart. "In our studies, we have been able to easily remove the device."

The major challenge that had to be overcome with such a thin film, low-profile device was durability, Altman recalls. But after many iterations, the company has finally reached a design freeze. "Moving from manufacturing by hand to outsourcing the manufacturing, durability went from 20 days to 60, and we only need 10 days of durability for a 5-day use indication." This level of durability also opens the possibility for the device to be used in longer-term applications, according to Altman. "We believe we have nailed the design principles to make a permanent or semipermanent implantable device in the next generation."

> Only a small percentage of patients with late-stage heart failure can benefit from existing support devices.

Designed to be implanted in a minimally invasive manner, the cardiac-assist device, which consists of thin film polyurethane held by thin wire struts in a cup-like shape, collapses into a tube. The cardiothoracic surgeon gains access to the heart via a mini-thoracotomy and the cardiologist pushes the device in, over the heart. This heart team approach to cardiac device implantation is a familiar technique used to implant the latest *Impella 5.5* left ventricular assist device manufactured by Johnson & Johnson's Abiomed.

Upon deployment, the CorInnova device expands like a flower around the heart. According to Altman, it takes less than 20 seconds to deploy. Based on large animal studies, CorInnova's surgical advisors expect that it will take as little as 10 minutes from the start of surgery to device activation. In large animals, the company has had 100% success in more than 55 deployments.

The company first demonstrated the efficacy of its device in a one-day large-animal study (four sheep) published in 2019 in the *Journal of Cardiovascular Translational Research*. In a model of esmolol-induced cardiogenic shock, use of the CorInnova cardiac-assist device recovered healthy baseline hemodynamics by an average of 74% and the left ventricular stroke volume by 86%. Study authors noted that the

hemodynamic improvements were on par with or better than several existing mechanical circulatory devices, including the *Impella 2.5* and intra-aortic balloon pumps.

CorInnova is now preparing for the publication of a chronic (14-day) heart failure study in large-animal models more predictive of human heart failure (plastic microspheres were delivered into the left circumflex artery to induce a heart attack, resulting in cardiac remodeling and dilatation over six to eight weeks and low ejection fraction). Six animals had surgery, and only half got the device, explains Altman. All three device-implanted animals survived to the final day, and there were no adverse events in terms of bleeding, thrombosis, or stroke.

In the treated animals, the ejection fraction improved over 14 days, starting with 20% after the induction of heart failure and rising to 31% after two weeks of device support. "Even when the device was turned off, it stayed at 25%, which indicates heart recovery for those animals," reports Altman. The potential to stop and start the device safely would allow patients to walk around and do physical therapy without wearing the pneumatic driver and sleep with the device off. That's not the case for LVADs or other blood-contacting pumps, which must always remain on to avoid the formation of thrombus in the device and a potentially fatal stroke. "If an LVAD loses power, this is a medical emergency, and the patient will have to be closely evaluated before risking re-starting the LVAD," he notes.

Lower Barriers to Adoption

The CorInnova platform has many attributes that make it ideal for short-term indications in bridging patients to long-term chronic device therapy or recovery. If it works as well in humans as it does in animals, it will improve hemodynamics and end-organ function, so patients are healthier for longer-term mechanical circulatory support. A mini-thoracotomy preserves the option for a future sternotomy, if required later to implant long-term ventricular-assist devices. Implantation of the device doesn't require suturing or the heart or vessel cannulation that could result in myocardial or vascular damage.

Such ease of use presents low barriers to adoption, Altman believes, by enabling even secondary medical centers to deliver the device as a bridge to long-term chronic device therapy that might be later provided at a more specialized center. "A general surgeon should be able to do this fairly easily," says the CEO, who also points out that the CorInnova device accomplishes biventricular support, which only artificial hearts and venoarterial extracorporeal membrane oxygenation (VA-ECMO) can provide today. "Many secondary hospitals don't have the capabilities to offer these other devices. At conferences, doctors have told us they're excited about doing this at secondary centers."

The company is ready to begin human studies. It has a manufacturing partner for its driver, "a top manufacturer of VAD controllers and pneumatic drivers," emphasizes Altman, and it promises to be "the quietest driver on the market for cardiac-assist devices." The driver's design calls for it to be lightweight, weighing roughly five pounds plus a few extra pounds for batteries, and to be worn in a backpack.

Defining the Market Opportunities

There is a great variety of devices for supporting patients with late-stage heart failure—temporary and long-term left ventricular devices, artificial hearts, intra-aortic balloon pumps, and VA-ECMO. However, only a small percentage of patients can benefit from them, and for some who can, there are disadvantages to living with the implanted devices, for example, as already noted, the fear and danger of the mechanical failure of LVADs and stroke risk. CorInnova defines its initial market opportunities in terms of patients who are unable to be helped by LVADs, or other existing mechanical circulatory support devices.

Certain patients with heart failure categorized as Class IV (end stage), according to the New York Heart Association classification system, are eligible for chronic LVADs for destination therapy (long-term use). In the US and EU combined, that's 600,000 end-stage heart failure patients who are potentially eligible, but in 2018 the number of patients who received chronic LVADs was only 10,000. Since 2018, that number has been steadily dropping because the US UNOS (United Network of Organ Sharing) changed its criteria for the allocation of donor hearts in an effort to prioritize the sickest patients and reduce the number of patients dying while in line for a new heart.

Chronic LVADs have established a good record for keeping patients alive, but since the criteria change, patients with chronic LVADs have been moved further down the priority list. Now, doctors must ask themselves whether the decision to implant an LVAD means their patient will never get a human heart.

Besides that, though, there is an extensive list of reasons why 50% of patients in need of cardiac support don't get long-term and short-term heart assist devices. Many patients are ineligible;

some examples include those who are elderly and too frail for a sternotomy; have calcified or small arteries, aortic insufficiency, or stenosis; cannot take anticoagulants because of a previous bleed or stroke risk; have a body size too small for existing devices; or need biventricular support (since LVADs only support one ventricle).

Then there is a whole host of risks associated with the fact that existing pumps come into direct contact with blood, including GI bleeding, a 5-60% rate of bleeding at the access site, a 2-15% rate of stroke within 5 days of use, a 5-13% rate of red blood cell destruction, and a 21-47% rate of kidney dysfunction (according to the company's estimates from published sources).

All existing mechanical circulatory support systems have been designed for HFrEF, but Altman also sees a potential opportunity for his company in HFpEF, where the heart filling or diastolic phase of the cardiac cycle is dysfunctional. During deflation, the CorInnova device provides a low-grade negative pressure to the outside of the heart, which increases the amount of blood volume that flows into the heart during relaxation. "When the heart pumps, the wire frame is drawn inwards, and when the heart relaxes, the wire frame provides suction to pull the heart open," he explains. For now, an unpowered device for HFpEF is a secondary project, which the company has funded through NSF grants.

Because CorInnova's device intrinsically avoids the contraindications that apply to blood-contacting devices, Altman believes that the company's initial opportunity in short-term (less than 5 days' use) cardiac assist is 150,000 patients ineligible for short-term LVADs. These initial short-term cardiac assist markets include acute heart failure or cardiogenic shock, which occur frequently after an MI, and, less frequently, due to other conditions, for example, COVID-19 or post-partum cardiomyopathy. Patients suffering from acute decompensated heart failure could also benefit from minimally invasive mechanical support.

Among those who are medically eligible for support but ineligible for LVADs are many women who are underserved by existing devices because they have smaller femoral arteries, which can preclude them from existing short-term devices. Altman notes that although women represent 50% of heart failure (or 67%, when talking about HFpEF), only one in four receives an LVAD. CorInnova's device can be sized for smaller patients, including women.

Altogether, the company will be serving a $5 billion market in which it is not directly competing with any company, he notes.

Looking ahead, the company's future market in chronic cardiac support for end-stage heart failure patients is worth at least another $5 billion. "Ours is the only device that increases output by helping the heart itself pump and do its job better," as opposed to other devices which pump blood through the device and essentially replace the heart's function. "That makes our device much safer and more likely to promote heart recovery, and its market should extend beyond short-term use," asserts Altman.

CorInnova has raised just over $20 million to get to this point, from, as noted, Wellcome Trust, the Texas Emerging Technology Fund, the NSF and NIH, as well as the Texas Medical Center Venture Fund, family offices and angels. Now, the company is beginning to raise $30 million to execute its first human clinical efficacy trial, which will be designed by a team led by cardiologist Joseph G. Rogers, MD, president and CEO of the Texas Heart Institute and a thought leader in heart failure, heart transplantation, and mechanic circulatory assist devices.

Altman pitches future investors: "Our device provides gentle, direct cardiac compression; it gently squeezes the heart, just like a surgeon does," that is, it works by a proven therapeutic mechanism. "It is a breakthrough versus prior art because it is an active device providing systolic and diastolic assist to both ventricles." The company's innovation is protected by 18 issued US patents and three more pending. "We are targeting a large underserved market. We have completed preclinical animal studies demonstrating excellent efficacy and safety, achieved design transfer, and have the assistance of the world's leading heart failure experts to design the clinical trials." The market is large and existing reimbursement is high, he states, adding, "We have a rapid path to human trials and the clinic." And, given that the company is targeting patients who need a short-term device for up to 5 days of use, Altman believes clinical trials will be short and much less expensive than those for other cardiac devices.

A bittersweet testament to the importance of CorInnova's mission came from his father-in-law's cardiologist at Massachusetts General Hospital, who told Altman, "If we'd had this device, instead of having to live on the ground floor and huff and puff up the stairs, your father-in-law could have gone on as he wished for perhaps several years." Like many a medical device innovator before him, Altman says "That's why I get up in the morning." MTS

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