OCTOBER 2024 | Vol. 11, No. 9

# MedTech STRATEGIST

### DEVICES FOR MANY-FACETED HEART FAILURE

### Corlnnova:

A Versatile Device Serves Many Heart Failure Patients

**Mary Stuart** 



MYSTRATEGIST.COM/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 longterm 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 Only a small percentage of patients with late-stage heart failure can benefit from existing support devices.

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 longerterm applications, according to Altman. "We believe we have nailed the design principles to make a permanent or semipermanent implantable device in the next generation."

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 longterm 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 cardiacassist 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 shortterm 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."

Posted on MyStrategist.com Oct. 16, 2024