

JULY 22, 2020 | Vol. 7, No. 8

MedTech STRATEGIST



RefleXion and Merck: Is the Promise of Combining Drug and Device Therapy About to Be Realized?

David Cassak

COVID-19 Testing Strategies: Experts Weigh In

Wendy Diller

ADA 2020: Closed-Loop Insulin Delivery Systems, CGM for Type 2s

Mary Thompson

COVID-19: An Accelerator of Existing Trends

Jonas Funk, Monish Rajpal, Ilya Trakhtenberg,
and Sheila Shah, L.E.K. Consulting

Smart Orthopedic Implants' MOMENT TO SHINE

Mary Stuart



Pessac, France

Contact: Arnaud Mascarell, Co-Founder & CEO

Arnaud.mascarell@fine-heart.com

FineHeart: An LVAD Works in Synchrony with the Heart

Founded by electrophysiologists, FineHeart has developed an LVAD that is like no other. It resides inside the left ventricle of the heart where it times the blood flow it generates with the opening and closing of the aortic valve, thus achieving a physiologic and pulsatile flow.

► MARY STUART

To a decades old \$1.9 billion global market for left ventricular assist devices (LVADs) French start-up **FineHeart SA** is bringing a new and intuitive product that is unlike any other on the market.

To date, LVAD development has largely centered on the notion that heart failure is a mechanical problem, the breakdown of a pump designed to supply end organs, and that has historically influenced device development. Most LVADs are continuous flow pumps designed to get blood where it's needed to augment the efforts of the failing heart.

But FineHeart has a different take on the requirements for an LVAD, perhaps because it was founded by electrophysiologists steeped in cardiac resynchronization therapy (CRT), rather than surgeons or engineers with a more mechanical focus.

Co-founder Philippe Ritter, MD, of the Hôpital Cardiologique du Haut-Lévêque (CHU, in Pessac, France) is a luminary in the field of CRT; he's a pioneer who helped bring cardiac resynchronization to light in the mid 1990s, a leader of electrophysiology societies, and an author of the textbooks on the subject. Co-founder and chief science officer Stéphane Garrigue, MD, PhD, is a

researcher in cardiology at the Bordeaux Medical University and is a practicing electrophysiologist at the St. Augustin heart center in Bordeaux. CEO Arnaud Mascarell came to know these physicians during his 20 years in the cardiac vascular group at Medtronic France.

FineHeart's founding team considered the electrical and rhythmic patterns of the heart, which ebbs and flows as its four chambers alternately contract and dilate, opening and closing valves in turn. Blood does not move in a steady flow throughout the body, rather there are specific patterns to the way it is delivered, and it seems that the end organs and vessels through which blood is transported require those patterns. FineHeart's founders believe that the synchronization of the heart's natural rhythm with the workings of an adjunctive LVAD is integral to its success.

FineHeart was thus founded in 2010 to develop the *ICOMS* (short for Implantable Cardiac Output Management System), which, uniquely placed entirely inside the ventricle of the heart, is the first LVAD capable of sensing then supporting the hemodynamics of the heart.

To date the company has raised €20 million through a tranché Series A

round, the majority of funds provided by venture capitalists, including lead investor Broadview Ventures and Longview Ventures (Boston, MA), industrial investor Doliam SA (Maisons-Lafitte, France) and regional investors based in France, including IRDInov, M Capital, Aquiti Gestion, SOFIMAC Partners, and Galia Gestion. European and regional grants as well as loans from BPI France make up about a third of the total funding, according to Arnaud Mascarell.

Continuous Flow is Practical, But Not Physiologic

After 50 years of debate, there is a consensus in the field that the ideal pump for the support of late stage heart failure would achieve pulsatile blood flow that mimics the heart. However, most LVADs on the market offer continuous, not pulsatile flow, for practical reasons.

Early on, pulsatile pump designs were attempted, but these were bulky and had many moving parts susceptible to wear and tear. First generation pulsatile devices weren't durable, and external components joined to the implants via transcutaneous leads encouraged infection. Industry abandoned pulsatile pumps in favor of simpler and smaller

continuous flow devices, the essential component of which is a rotating impeller.

These continuous flow pumps have proven that they can extend the short life expectancy of advanced heart failure patients by at least two years and more. Indeed, **Abbott Laboratories Inc.**, which sells the most widely used LVAD in the world—the *HeartMate II* axial flow device (the device has been implanted in more than 26,600 patients to date)—has reported a rate of two year survival free from disabling stroke (or reoperation to replace or remove a malfunctioning device) of 65%. As of June 19, 2020, the company reported that 100 of its *HeartMate II* patients were survivors at 10 years, some for even longer.

Abbott introduced a next generation pump that is pulsatile, the *HeartMate 3* centrifugal left ventricular assist system, after the largest LVAD study ever undertaken led to its FDA approval in 2018.

Abbott's pivotal study Momentum 3, a multicenter, prospective, randomized study of 1028 patients at 60 study sites, randomized patients approximately equally between implantation of the *HeartMate II* or *HeartMate 3*, and demonstrated the superiority of the new device design over its previous platform.

The *HeartMate 3* achieves pulsatility by varying rotor speeds, offers larger blood pathways to reduce shear stress on red blood cells, and has a magnetically levitated self-centering rotor that eliminates points of friction such as mechanical bearings. *HeartMate 3* achieved the study endpoint of two-year survival free of disabling stroke (or reoperation to replace or remove a malfunctioning device) in almost 77% of patients.

These are the best LVAD results seen to date. At the same time, the complication rates noted in the Momentum 3 results highlighted that there remain serious problems to solve here: 58.8% rates

of major infection, 43.7% of patients experienced bleeding (gastrointestinal bleeding accounted for 24.5%); and stroke rates of 9.9%, among others.

The founders of FineHeart argue that all of the current LVADs don't deliver blood in a physiological manner and that leads to high rates of serious complications—approximately 60% of LVAD patients will experience at least one with the first two years. Specifically, the high pressures required to move blood by current designs shear and cleave red blood cells, leading to thrombosis and a bleeding disorder known as acquired von Willebrand syndrome, and place unnatural stress on vessel walls, activating, for example, baroreceptors (blood pressure-regulating cells in the aortic arch).

FineHeart's thesis, borne out in preclinical studies so far, posits that the radically different design of its LVAD might reduce if not eliminate some of these complications.

Going with the Flow

Simply put, the *ICOMS* doesn't change the workflow of the heart.

"Our founders believed that if we wanted to achieve the support of patients who

need a long-term destination therapy and treat the majority of patients, we would have to respect physiology," says Mascarell. Commercially-available LVADs don't. In a healthy heart, as the left ventricle contracts, the aortic valve (which is at the top of the ventricle) opens, and blood, moved by the contraction, moves up into the aorta (again, above the heart).

An LVAD is implanted in the space below the heart. Oxygenated blood flows down the ventricle to an inflow valve to the pump outside the heart. The blood is pumped out of the LVAD through an outflow valve and up through an aortic graft into the aorta. "Today, all LVADs bypass the heart. They suck blood in the wrong direction before redirecting it up towards the aorta, and that is definitely not physiologic," says Mascarell. Furthermore, in 25-35% of patients, blood projected into the aorta flows back down into the left ventricle, an altered pathway for the native heart, which gradually becomes LVAD dependent, Mascarell explains.

FineHeart instead places its *ICOMS* inside the left ventricle, the only company ever to do so, describing its approach as an "intraventricular flow accelerator" (see *Figure 1*). Using pacemaker technology



Figure 1
The ICOMS LVAD

Source: FineHeart

it senses the opening of the aortic valve, and times the pumping action in synchrony with valve opening. "It subordinates to the native contraction and enhances native blood flow," says Mascarell.

To the question, "If such a simple approach works, why hasn't anyone done it before?" Mascarell responds that this concept depends on synchronizing the pump with the electrophysiology of the heart. "It was that one piece that perhaps hadn't been explored before," he says.

Mascarell emphasizes that both the inlet and outlet valves of the *ICOMS* are inside the ventricle, while for other LVADs the inlet is inside the left ventricle and the outlet is outside of the heart. The pressure existing LVADs require to move blood depends on overcoming the pressure gradient—the difference in pressure between the two cavities. "All other LVADs have to fight against the pressure gradient, which means that they have to generate pressure before they generate flow." And perhaps these unnaturally high pressures are responsible for damaging red blood cells and overstretching the aorta.

"This is key," says Mascarell, "because the two parts of our pump are in the same chamber, which means the pressure gradient is zero. Just by rotating the impeller, without generating high pressure we can generate flow."

A Familiar Surgical Approach

ICOMS will enter the body through a traditional percutaneous transseptal route, or through a mini-thoracotomy and up through the apex of the beating heart (the latter is its current approach), both tried-and-true routes for the implantation of transcatheter aortic valves.

Of course, as the first company to place its device inside the left ventricle, FineHeart has to address concerns that the such a long device might dislodge

and damage heart muscle, or shift and lose alignment with the aortic valve. "We have spent a lot of time on this," says Mascarell. "We are now confident that we have a simple and reliable way of fixating the pump so that it maintains alignment with the valve and maintains its stability within the left ventricle."

Furthermore, preclinical studies in healthy animals with much smaller hearts and more contractile force than heart failure patients with weak and dilated hearts, suggest that the device won't damage the heart wall. "There is a lot of room around the pump, so even if a patient is active and engaging in the normal activities of life, the surrounding space will keep it from damaging heart structures."

In May 2020 the company completed its first chronic seven-day *in vivo* study, which confirmed the feasibility of the mini-thoracotomy through a transapical approach into a beating heart. The study demonstrated preserved pulsatility, reduced shear stress on red blood cells, and low levels of hemolysis.

FineHeart is about 18 months away from its first-in-human studies, and is completing late-stage preclinical work. Next up is a €20 million Series B round to take *ICOMS* through its 12-month first-in-human study.

"Our device is certainly very complex with many parts—an implanted battery, embedded software, and a transcutaneous recharging system, so I'm not saying it's going to be quick," notes Mascarell, who expects the company to raise at least one more round of funding (in addition to the one now in progress) before the device can get to market.


A Virtuous Cycle

Many benefits accrue to the design of the *ICOMS* and its placement inside the left ventricle. For example, it will be much easier to explant and or replace, if

necessary, than current LVADs, which are grafted by an anastomosis to the aorta. "The pump itself is placed and fixed at the apical area. We don't touch a valve, we don't touch the aorta," he says, so under the optimistic scenario that a patient's heart remodels and the patient's health improves, it could be removed and the heart wall closed with a patch.

Fundamentally, the energy requirements of the *ICOMS* are much lower than those of conventional LVADs because, as mentioned, the pump isn't fighting an uphill battle against a pressure gradient. "Our energy requirements are four to five times lower than any other cardiac pump on the market today," says Mascarell, who notes that the FineHeart pump can be powered without a percutaneous drive line, which would go a long way towards avoiding the high infection rates seen with current devices. "We are able to use an implantable pacemaker-type rechargeable battery, and recharge it through the skin without any skin contact."

FineHeart will go the traditional route of applying for a bridge-to-transplant indication with the FDA, by demonstrating the ability to support patients in the short term (180 days). The potential advantages of the *ICOMS*, however, make it very suitable for a destination therapy—the support of patients for two years or more, a label FineHeart will seek in time.

The company hopes to help some 200,000 patients per year in advanced stages of heart failure, some on the transplant list and waiting for a new heart, others who, suffering greatly from fluid overload and pulmonary edema, are making many unplanned visits to the hospital. "We need something for these patients. We want to save them with our innovation," says Mascarell. 

Posted on MyStrategist.com July 13, 2020