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My Journey with the HeartWare Ventricular Assist Device- An Obituary

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In June 2003, the intended re-launch of the European clinical study of the HeartMate II (Thoratec, Inc, Pleasanton, CA, USA) at my institution, the Medical University of Vienna, was aborted due to technical considerations. A friend of mine, Jane Reedy, then contacted me and asked if I would be interested in meeting with a start-up company to set up a roadshow for a new, striking left ventricular assist device (LVAD) pump during the upcoming American Heart Association (AHA) meeting in Orlando, Florida later that year. Without having more detailed information about this pump, I immediately agreed and set up an appointment to meet. At this time, our institution was mainly using the MicroMed-DeBakey Pump (MicroMed, Inc, Houston, USA) as the workhorse for clinical LVAD implants. The MicroMed-DeBakey-pump was the first implantable, miniaturized axial-flow pump to be implanted in patients at our institution in November 1998. Although the first implants were performed at the German Heart Center in Berlin 3 days before our implants, our two patients were the first long-term survivors in the world with a completely nonpulsatile blood pressure. For biventricular support, we still used the pulsatile Thoratec p-VAD (Thoratec, Inc, Pleasanton, CA, USA) in those days. In addition, we started to prepare an institutional review board (IRB) application and sought a competent authority approval for the European clinical trials for the first fully-Maglev centrifugal pump, the DuraHeart (Terumo, Inc, Ann Arbor, MI, USA), and the Berlin-Heart Incor (Berlin Heart, Inc, Berlin, Germany)—the first fully magnetically levitated axial-flow pump.

During the AHA meeting in Orlando, I met with this new start-up company called HeartWare, Inc. with great excitement. HeartWare was formed out of a bankrupted company named Kriton, Inc. (Sacramento, California). Richard Wampler, the



inventor of the famous Hemopump, was working with Kriton on a prototype of a blood pump with a hydromagnetic suspension. I met with three people at the proposed roadshow who showed me a prototype of a miniaturized centrifugal pump, weighing only 145 grams.¹ Jeff LaRose, the engineer behind the pump, explained the striking technology - a combination of hydrodynamic and passive magnetic bearings, which resulted in a wear-less blood pump with a very thin and flexible driveline with only five leads. Another great feature was the integrated inflow cannula into the pump housing, which dramatically reduced the size of the pump.

I was fascinated by the concept of the pump and expressed my great excitement to Seth Harrison, who was the financial brain behind this start-up. Being an electrical engineer by training and having worked with my close friend and bioengineer, Heinrich Schima, on different miniaturized centrifugal pump concepts with different bearing configurations in our own bioengineering/animal lab at the Medical University in Vienna, I started a very detailed technical conversation with Jeff LaRose and Brian Gore, a mechanical engineer from the Navy. I insisted that an LVAD in a clinical setting consists not only of a pump but also requires a control/driving unit that is of equal importance. I was assured that the controller already existed but was not part of the roadshow. I left this meeting with these three gentlemen with the impression that I had seen a great piece of technology, and I was excited to hear more in the near future. Completely unexpectedly, I received a phone call later that day from Seth Harrison, who asked to meet the very next day. During this meeting, we talked again about the possibilities for such a technology to be implemented into clinical practice, and he invited me to visit their new setup facility in Miramar, Florida. Unfortunately, I had to leave for Vienna again, but he promised to stay in contact.

Several weeks later, Seth Harrison contacted me and told me that he had business in Europe and wanted to meet in Vienna. During this follow-up meeting, I agreed to a consultancy role with the company. I would travel every month for the coming years to Florida and work with the team to bring this technology to market. Two weeks later (December 2003), I made my first clinical consultant trip to meet with Jeff LaRose, Jane Reedy, Carlos Reyes, and Chris Owens in Florida. It was an extremely exciting time for me because, after many years of endless hours and hard work in a university-funded research/animal lab facility, I was working in a professional start-up environment with a preset business plan and clearly defined timeline goals.



The early HeartWare team in 2004; Jane Reedy, Jeff LaRose, Georg Wieselthaler, Carlos Reyes (from left to right)

As expected, the frozen prototype of the pump was available but a clinically applicable driving/control-unit was not ready. However, this made it even more exciting, because we spent the next couple of months brainstorming on how we could develop something brand-new, something that was not available at this point, and something that would make the system as user-friendly as possible.

Unlike my American surgical colleagues, I deal with heart failure patients for many years—from the very early moment in which they receive an LVAD to the time they are transplanted or expired. I saw patients on LVAD support every single day in my outpatient clinic and learned all the needs and threats these patients experienced while being on pump support. I also saw the needs of physicians taking care of these patients while being on LVAD support. Specifically, I knew the need for information from the LVAD-system to guide treatment. In this way, I was able to bring my years of clinical experience with VAD patients to concept meetings, and it was fascinating for me to be able to discuss the "crazy" new ideas with professionals who were willing to bring these ideas into reality. Thus, we created a controller/driving unit with new features that were not available in any other pump system at that time. Unfortunately, we were naturally limited by the money. The start-up company funding was supposed to last until the first clinical implant was completed. Nevertheless, we were able to implement quite a few novel features that could help patients with LVADs as well as the physicians taking care of them.

First, the controller/driving unit was miniaturized and lightweight to give patients the maximum comfort possible while wearing the device. For the first time, a controller had a little display on it where all-important pump parameters could be visualized by the patient at home, and all critical alarm conditions were visually displayed. The patient was provided information on how to react to these alarms or even mitigate them—a clear precursor of an interactive "smart controller." We implemented, for the first time, a storage media into the controller that retained



pump data for a period of 30 days. When the patient was seen as an outpatient in the clinic, the physician or coordinator could download the data on the monitor and have a clear overview of the patient's pump data for the previous month. We also replaced the heavy, old-fashioned lead batteries with smaller and lightweight lithium-ion batteries to reduce the overall weight the patients had to carry, which made the controller/battery pack the lightest pack at that time.

Another important new feature was that the monitor was not a large laptop computer mounted on a cart on wheels. These carts take up a lot of space, especially when a patient is in the intensive care unit (ICU) where the rooms are jam-packed with other devices and monitors. We came up with the idea to use a touch screen tablet as a monitor. The monitor-screen needed to be a good size where the vital pump parameters were displayed in large numbers, so they could be seen even from a distance. This gives the nurses and ICU attendings the opportunity to check on patients on LVAD support even from outside the room. An additional new feature was that the monitor displayed in real-time LVAD power-uptake and calculated LVAD-flow waveforms. This feature turned out to be the most valuable tool for physicians because out of the waveforms many physiological and pathological patterns could be detected. With more and more knowledge about the waveforms and more detailed interpretation of them, several important diagnostic pump conditions could be determined: heart rate, arrhythmias, left ventricular volume filling, ventricular suck-down, the opening of the aortic valve, pulsatility, contractility of the left ventricle, beginning of clot formations, and more. One major feature we, unfortunately, were not able to accomplish was the idea to connect the monitor with the pump-controller via Bluetooth. This would have been very convenient for the nurses and coordinators to handle the monitor. Nevertheless, this was extremely complex in 2004 and surpassed the financial abilities of our start-up company, so we ended up with a regular physical cable connection of the controller with the monitor.

The intention of our team was to develop the best and most user-friendly pump with a wear-less pump technology so that patients could be supported for years and years. To increase the durability of the LVAD-system, we intended the pump-driveline to be as flexible and fracture-resistant as possible; therefore, we used the more expensive pacemaker-lead alloy instead of copper leads that have lower fatigue limits and were routinely used by other companies.

During the early days with HeartWare in Miramar, I was still working on a small, miniaturized centrifugal pump in our university-based lab in Vienna. I did multiple animal experiments with different rotor configurations that my technical team, with my bioengineer Heinrich Schima, wanted to investigate. After one of these extremely long and tiring days in the operating room and then in the bioengineering and animal lab, I returned home and had a horrible nightmare the following night. I dreamt that all our experiments with our university-based pump were so successful that we intended to go for the first human implants, and I personally volunteered for it demonstrating how well this pump was functioning. After the pump was successfully implanted into me, I was asked to give a talk in



front of the entire University faculty, which was very prestigious and filled me with lots of pride that our year-long work in the bioengineering and animal lab had come to such fruition. Unfortunately, on the way back home after this big moment, I was driving in my car and realized that my batteries were running out of power and no more spare batteries were left. This was such a stressful situation that I immediately woke up drenched in sweat. Based on this strange nightmare, I discussed this situation with the HeartWare team, and we decided to develop a car charger system for the HeartWare ventricular assist device (HVAD) to add usability and safety for patients to travel long distances in cars. To date, the HVAD is still the only LVAD system that provides this feature.

From 2004 to early 2005, the HeartWare team was growing, and everybody was working hard to accomplish all the goals we had set for ourselves. The first animal experiments were performed at Dr. Denton Cooley's lab at the Texas Heart Institute in Houston by "Bud" Frazier and his team. Dan Tamez was working in Dr. Cooley's lab at the time and took care of the animals with the implanted HeartWare pumps; he was later hired as a valuable addition to the HeartWare team. In late 2004, Stuart McConchie was appointed chief executive officer (CEO) of Heartware, Inc., and the company received a large financial boost from an Australian investor. At the end of 2005, after successfully finishing the good laboratory practice animal experiments, we started to prepare everything for the first human implantation.



HeartWare team at first implant in Vienna on March 22, 2006; Georg Wieselthaler, Jeff LaRose, Stuart McConchie (back, from left to right), Jane Reedy, Dan Tamez (front, from left to right)

When I signed my consultancy contract with Seth Harrison in 2003, I got his word that if we ever reached clinical implantation, it would be at my home institution in Vienna. Being the Clinical Director for Mechanical Circulatory Support at the Medical University in Vienna, I received IRB and competent authority approval for an implant in February 2006, and in March, I found the perfect patient. A 48-year-old former opera singer with end-stage heart failure, who suffered from non-ischemic cardiomyopathy, was the first patient to receive HeartWare's HVAD on March 22, 2006. The operation was successful; it was fast and uneventful. The patient was extubated seven hours after surgery and moved to the floor after four days. Although the patient was bed-ridden before surgery, he recovered quickly and was put on a very intense mobilization program by our well-trained physical therapy staff. He was the first patient of the European/Australian HeartWare CE-mark clinical trial with three centers in Europe (Vienna, Hannover, Harefield) and



two centers in Australia (Perth, Sydney). While on the HVAD support he started singing once again and went back on stage to perform professionally. He was successfully transplanted after a year on the pump and is still alive and doing extremely well. A month after this first patient, I implanted the second HeartWare pump into a 35-year-old patient, who also did very well. An additional two more implants followed in 2006. Overall, 23 patients were enrolled in this clinical trial, and excellent results were achieved. Specifically, a 91% survival rate at 6-months and an 89% 1-year survival were reported—the best results in a clinical LVAD trial at that time.² One of the patients from the Hannover site suffered an unfortunate intracranial bleed, and extensive blood work was performed. Coincidentally, diminished Von-Willebrand factor multimeres were found in his blood. For the first time, it was demonstrated that patients on rotary blood pumps can develop a clinical situation similar to the acquired Von-Willebrand's syndrome due to the high shear stress.³



Georg Wieselthaler (left) and the first patient to receive a HeartWare device (right)

In 2007, Doug Godshall was introduced as the new CEO of HeartWare, Inc., and he hired Jim Schurman as the new Director of Marketing and Sales. HeartWare's manufacturing facility moved from Miramar, Florida to Miami Lakes, Florida, where a larger space was available.

After achieving the CE-mark in Europe, the HVAD was immediately adopted at many centers in Europe, Australia, and Asia Minor as the primary LVAD to be used. It was in clear competition with the HeartMate II, which was an established pump in clinical use. For the next three years, I proctored HVAD implants all over Europe, Turkey, and Israel.

In 2011, I moved from Vienna to the United States and started working at the University of California-San Francisco (UCSF). It took until December of 2012 for the FDA to approve the HeartWare pump; with that commercial approval, the device was released for purchase in the United States. Meanwhile, a less invasive



implantation method for the small HVAD pump was evaluated for selected patients in Europe. Immediately after commercial approval in the US, I successfully implanted the first HVAD at UCSF with this less invasive surgical technique. HeartWare, Inc. initiated the LATERAL trial for evaluation of this new implantation method and enrolled 144 consecutive patients in 26 US centers.^{4,5} I was able to enroll 35 patients from my own institution, and the study proved that this implantation method is safe and can have advantages over the standard sternotomy procedure in selected patients.

Over the years, the HVAD gained market shares all around the world. Interestingly enough, a larger proportion of the Europe market used the HVAD when compared to the United States. Thoratec, Inc. attempted to acquire HeartWare, but in the end, Medtronic successfully bought HeartWare, Inc. in August 2016. Most of the original HeartWare staff left; David Steinhaus and Tom Vasiliades become the new leadership for the device. Initially, big plans were made to further improve the system and upgrade the technology. At this point, I was just involved as a distant consultant and, unfortunately, this was completely disrupted with the start of the pandemic in early 2020.

In the last few years, LVAD implant numbers soared worldwide; however, the HVAD market shares were dropping, and technical issues arose with the pumps. The FDA began issuing warning letters. On June 3, 2021, at 6:00 am Medtronic announced, without any warnings ahead of time, that it would stop the distribution and sale of HVAD. The company recommended no further implantations of the device. With this decision, a nearly 20-year story of a novel pump and a very sophisticated pump concept and more than 20,000 clinical implants came to an abrupt stop.

For me, personally, it was a very exciting journey over a large portion of my professional life as a cardiothoracic surgeon, engineer, and researcher. I personally implanted several hundred of these pumps and saved uncounted lives with its support. I am extremely pleased and honored that I was part of this extremely exciting endeavor. I do believe that we, as a team of engineers and dedicated clinicians, made some great achievements with the HVAD - for the field of mechanical circulatory support, as well as for our community, but mainly for our patients that suffer from a deadly disease.⁶



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