Mechanical circulatory assist device development at the Texas Heart Institute: A personal perspective

O. H. Frazier, MD

In December 2013, we performed our 1000th ventricular assist device implantation at the Texas Heart Institute. In my professional career, I have been fortunate to see the development of numerous mechanical circulatory support devices for the treatment of patients with advanced heart failure. In fact, most of the cardiac pumps in wide use today were developed in the Texas Heart Institute research laboratories in cooperation with the National Heart, Lung and Blood Institute or device innovators and manufacturers and implanted clinically at our partner St. Luke's Episcopal Hospital. My early involvement in this field was guided by my mentors, Dr Michael E. DeBakey and, especially, Dr Denton A. Cooley. Also, many of the advances are directly attributable to my ongoing clinical experience. What I learned daily in my surgical practice allowed me to bring insights to the development of this technology that a laboratory researcher alone might not have had. Young academic surgeons interested in this field might be well served to be active not only in laboratory research but also in clinical practice. (J Thorac Cardiovasc Surg 2014;147:1738-44)

I first became involved in the field of mechanical circulatory support in 1965 as a student at Baylor University Medical School. The previous year, Dr Michael DeBakey had been awarded the first federal grant for establishing a program at Baylor to develop a total artificial heart (TAH). For my second-year research project, I worked with Dr Domingo Liotta, under DeBakey’s supervision, to develop and test the TAH. At that time, Dr Denton Cooley was on the faculty at Baylor, and he was also interested in artificial devices.

As a senior medical student at Baylor, I had an experience that further focused my interest on artificial hearts. I scrubbed in for an aortic valve replacement in a young Italian boy whose case I had worked up earlier. He seemed to be doing well after the operation. But the night of the surgery, his heart fibrillated. We opened his chest in the recovery room, and I began massaging his heart. As long as I massaged his heart, he was alive… awake… looking at me. But despite our efforts, he died. It occurred to me then that if my hand could keep this young boy alive, why couldn’t we make a pump that would keep him alive?

The next year, in 1969, Dr Denton Cooley implanted a TAH in a human for the first time, with the assistance of Dr Liotta. Because that operation resulted in considerable controversy, Cooley and Liotta resigned from Baylor, and the device program there was discontinued. Dr DeBakey did not speak to Cooley for the next 38 years. Dr Cooley started his own device program at the Texas Heart Institute (THI), which he had founded in 1962. Although Cooley had the world’s largest heart transplant program, his outcomes and those of others were poor, so by 1971, he and most other surgeons had stopped doing transplants. As a result, the Devices and Technology Branch of the National Heart and Lung Institute under the direction of John Watson—now the National Heart, Lung and Blood Institute (NHLBI)—changed its focus to support development of a long-term (destination) left ventricular assist device (LVAD). This became the main goal of THI’s Surgical Research Laboratory, which Cooley established at THI in 1972. The laboratory was initially directed by Dr John Norman, who had come from Boston.

I began my cardiac training at THI under Dr Cooley in 1974, after completing my general surgery residency under Dr DeBakey. I made the decision to go to THI to continue device research. Although I thought my decision to leave Baylor for THI would go unnoticed, Dr DeBakey did not speak to me for another 10 years.

In 1981, when Dr Norman left THI, I was appointed director of the research laboratory. I have now been involved in the research and clinical development of mechanical circulatory support for nearly half a century.

ABDOMINAL LVAD

With NHLBI support, our THI laboratory worked on developing an abdominally positioned, pulsatile-flow LVAD. Between 1975 and 1980, 22 patients were supported with this device, and the series included the first bridge-to-transplant with an LVAD in 1978. The device was indicated mainly for postcardiotomy shock, to provide support until the heart could recover. Although the LVAD functioned well, the delay before implantation was so long that the
patients were already too sick to recover, and there were no long-term survivors.

In our laboratory, research was also underway to develop a destination-therapy LVAD. Our primary engineering partner was Boston-based Thermo Cardiosystems. The request for proposal called for a device with primary goals of reliable 2-year durability, transcutaneous power, and up to 12 L/min of flow. In pursuing these goals, we encountered 2 important barriers: compliance-chamber performance and inflow-graft occlusion. The compliance chamber was necessary to compensate for volume displacement behind the pump diaphragm. Despite extensive research, we could not achieve 2-year compliance-chamber durability. To solve this problem, I suggested simple percutaneous venting to the atmosphere, an idea that was based on my experience with chronic venting of bronchopleural fistulas in tuberculosis patients. With percutaneous venting, transcutaneous power became unnecessary.

The other problem that nearly led to failure of our LVAD program was inflow-graft occlusion. Possibly, Dr DeBakey should be credited for solving this problem. When I was an intern, he reprimanded me for asking him why a patient’s femoral-popliteal graft kept occluding. After “frogging” me in the chest (a common occurrence in those days), he said and made me repeat, “When blood stops moving, it clots. Got that? When blood stops moving, it clots.” I never forgot that incident. Because the early LVAD design included a long inflow graft, blood stoppage occurred during systole, a condition that led to accelerated pannus formation and graft occlusion. I solved this problem by simply shortening the inflow graft so that the pump was juxtaposed to the heart, minimizing stasis and controlling pannus.3

In 1994, this pump (the pneumatic HeartMate) became the first implantable device to be approved by the Food and Drug Administration (FDA) as a bridge to transplantation.4,5 Without the solution of these 2 problems, which represented finite barriers to further pump development, this milestone would not have been achieved.

BRIDGE TO TRANSPLANTATION
The world’s first 3 clinical bridge-to-transplant experiences (2 TAHs and 1 LVAD) occurred at THI.6,7 All 3 patients died of septic complications. After cyclosporine was introduced (a more forgiving immunosuppressant), we and others had renewed interest in cardiac transplantation. Our early transplant experience was favorable, even in patients with active sepsis.8 This also encouraged us to begin a new bridge-to-transplant program.

In 1986, I implanted the first HeartMate as a bridge to transplantation. Although developed for destination therapy, it was clearly satisfactory as a bridging device. Our favorable initial experience with this device as a bridge to transplantation is what led to its widespread use and ultimate FDA approval.4

In 1991, I implanted the first electrically powered HeartMate LVAD. After more than 500 days of support, that patient became the first to be discharged from the hospital with an LVAD (Fig 1).9 In 1999, the untethered HeartMate XVE was selected for the REMATCH trial (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure).10,11 That trial, led by Dr Eric Rose, resulted in the first FDA approval of an LVAD for destination therapy, thus achieving the original goal of the NHLBI request for proposal issued more than 20 years earlier.

BIOMEDICUS CENTRIFUGAL-FORCE LVAD
I became interested in a continuous-flow assist device for ventricular support early in my professional career. I had used the extracorporeal BioMedicus centrifugal-force pump for both a short-term LVAD and an extracorporeal membrane oxygenator, and this experience convinced me that continuous flow might also work for long-term support. I also remembered being fascinated by an embryology demonstration during an undergraduate biology course. The professor showed how blood flow in the capillaries of the chick embryo is continuous.

We continued to develop the BioMedicus pump as an implantable pump, and in 1984, I successfully implanted a short-term device in an acute experiment. To my knowledge, this was the first experimental implantation of
a continuous-flow pump. My presentation of the results at the American Society for Artificial Internal Organs was met with skepticism. At the time, we seemed to be the only “research center” investigating long-term, implantable, nonpulsatile devices.

THE HEMOPUMP
Because of my interest in nonpulsatile flow, Dr Richard Wampler, whom I had not known before, approached me at a conference in 1986 with his design for a small, axial-flow pump for temporary support of the failed ventricle. This promising device, called the Hemopump, spun at 25,000 rpm and was being manufactured by the Nimbus Company (Rancho Cordova, Calif). I was concerned that this pump might act like a Waring blender and injure the fragile blood cells. However, in animal experiments we began that same year, Wampler and I confirmed its safety. In 1988, I successfully implanted the Hemopump in a patient—the first continuous-flow LVAD implanted (Fig 2).12,13 This experience showed that, contrary to conventional wisdom, a high-rpm, continuous-flow intravascular pump was well tolerated by the circulatory system. In my opinion, this was the single most important event in the development of continuous-flow blood pumps. However, due to lack of funding, manufacturing was discontinued. Nevertheless, the Hemopump experience ultimately led to the development of other axial-flow blood pumps.

JARVIK 2000
At the 1986 meeting where I met Rich Wampler, I was also approached by Dr Robert Jarvik, who shared with me his concept of a long-term, implantable, continuous-flow LVAD. I was intrigued by his device’s potential and suggested that it be placed directly in the left ventricle, thus eliminating the necessity for an extracardiac inflow conduit. However, because this LVAD would be a long-term device, it would need implantable, blood-washed bearings. At that time, research experience indicated that bearings required lubrication, making blood-washed bearings a barrier to the clinical application of such a pump. And, in fact, in our initial laboratory experiments, we encountered hemolysis and bearing seizure. However, encouraged by the success of axial flow in the Hemopump, we persevered, and by the late 1980s, Jarvik had constructed a device with blood-immersed bearings that worked well in longer-term animal experiments. This important contribution by Dr Jarvik was vital to the success of implantable, axial-flow blood pumps.

The first successful clinical implantation of the Jarvik device occurred in April 2000 (Fig 3).14 We began a destination-therapy trial in Oxford, England, 2 months later. Dr Steve Westaby and I implanted the pump, and the patient survived for 7.5 years (Fig 4).15

The investigative and clinical success of these 2 pumps formed the foundation for further developments in continuous-flow pump technology. The main obstacles to the clinical use of these devices (blood damage from the high-rpm pump [Hemopump] and the perceived barrier of blood-washed bearings [Jarvik 2000]) were overcome by the combined efforts of Wampler and Jarvik, working with the THI laboratory and me. Because of THI’s affiliation with St. Luke’s Episcopal Hospital in Houston, where Dr Cooley had his clinical practice, we had unique access to what was then the world’s largest cardiovascular program. This allowed us to quickly
accumulate the largest series of patients for both of these pumps. The importance of this partnership cannot be underestimated.

HEARTMATE II VAD

The clinical success of the Hemopump stimulated the Nimbus Company to begin developing another pump, which ultimately became the HeartMate II. This device would also be an implantable, axial-flow blood pump for long-term use. At the time, I was the only surgeon actively involved in implantable continuous-flow pump research, so I consulted for both Nimbus and Jarvik Heart (New York City, NY). John Moise, at Nimbus, was leading the team to develop the pump but encountering difficulties with magnetic suspension of the rotor. I asked Moise, “Why don’t you just make a bigger Hemopump with bearings?” He laughed and said, “Bud, you don’t know anything about bioengineering. You can’t have non-lubricated bearings in the bloodstream.” I replied, “Rob and I don’t know that you can’t have blood-washed bearings. In fact, a calf in Houston has had a pump with blood-washed bearings for 8 months; that calf doesn’t seem to know either.” Had I not been working with both Jarvik and Wampler and had there not been collegiality among the researchers involved in the early development of these devices, the future of axial-flow blood pumps might have been different. When Nimbus could no longer fund development, Bartley Griffith and the University of Pittsburgh and, subsequently, Thoratec intervened and saved the HeartMate II.

Beginning in 2001, the HeartMate II was implanted in European patients, but early pump thrombosis occurred. Because of my familiarity with this pump and longstanding experience in the field, I was contacted for my opinion. The device had been manufactured with pump stators that had been textured with sintered titanium, a technology we developed in the 1970s for use in the early, large pulsatile pumps. This texture resulted in tissue proliferation on the textured surface, which, although an asset in the pulsatile pumps, was a liability in the narrowed blood pathway of the nonpulsatile pumps. We recommended removing the texturing, which solved this problem. We implanted the redesigned pump in the first patient in November 2003 (Fig 5). Since then, more than 15,000 HeartMate II pumps have been implanted worldwide, and this device remains the most widely used implantable LVAD. (Recently, I made a presentation in the Central Asian country of Kazakhstan and was somewhat surprised to learn that more than 100 of these pumps have been implanted there.)

HEARTWARE LVAD

The engineering of what would become the HeartWare LVAD began in 1994 when Dr Robert Fine, an early supporter of blood pump technology, asked my advice for developing the next-generation pump. I said that I believed continuous-flow VADs were “the future” but that 3 improvements had to be made. First, blood-washed bearings needed to be replaced by a magnetically suspended rotor. At the time, I was concerned about long-term bearing durability (in fact, patients have now lived more than 9 years with bearing pumps). Second, the pump needed to be a flat-surface, centrifugal-force pump, so that it would fit on the diaphragmatic surface of the heart and be able to function as both a left and a right VAD. To date, this is the only device that was designed specifically for use as a right VAD. Third, the pump needed to fit inside the pericardial sac to eliminate the need for a pump pocket, which contributed to an
increased infection rate. We began working with Rich Wampler and by 2001 had completed the basic design. However, before clinical trials could begin, the company (Kriton) declared bankruptcy and was reformed by other investors under the name HeartWare (HeartWare International, Inc, Miami Lakes, Fla). The HeartWare pump was first implanted in European and Australian patients and is now the second most widely used continuous-flow pump. I am gratified that the 3 original goals I proposed more than 20 years ago have been clinically validated (particularly as shown by the widespread use of this pump for rightsided heart failure in Europe).

RESTING THE HEART
In my initial experience with the HeartMate, I found that native ventricular function physiologically and anatomically improved in hearts unloaded with this pump. In 1992, we published a paper that showed histologic evidence of this improvement, and in 1994, I presented a paper on the results of ventricular unloading. The longer durability and safety of the newer, continuous-flow VADs now gives us an even greater opportunity to rest the heart and potentially discontinue support and, perhaps, avoid transplantation altogether.

TOTALLY IMPLANTABLE ARTIFICIAL HEART
In 1985, I was selected to be on the NHLBI Advisory Council. At that time, the National Institutes of Health were not directly involved in artificial heart research, and I was asked to make recommendations for TAH research. That talk was attended by 300 NHLBI faculty members, including Dr DeBakey. Afterward, he came up to me. I was surprised as he had not spoken to me for more than 10 years. He said, “Bud, you failed to emphasize the importance of the blood-biomaterial interface.” He was right, I had barely mentioned it, but it didn’t seem important for a mostly lay audience. He then said, “You know, inattention to detail is the hallmark of mediocrity” and walked off. Even though his words sounded negative to others with me, knowing him, I realized that this comment meant I was back in his “good graces.” And after that, he spoke to me every time we met.

I proposed that NHLBI develop a pump that would be transcutaneously powered and, therefore, untethered, and be potentially durable enough so that patients could return to meaningful lives. This proposal resulted in the funding of what eventually became the AbioCor TAH. In the THI laboratory, I implanted more than 50 of these devices, which supported calves successfully for up to 3 months, thereby confirming feasibility. Further research in collaboration with the Jewish Hospital in Louisville resulted in the first clinical implant of this pump there in July 2001. I subsequently implanted 5 of these pumps clinically. One of the Louisville patients survived for more than 17 months. Although this technology appeared promising, economic and administrative issues limited its subsequent clinical use.

CONTINUOUS-FLOW TAH
My clinical experience with continuous-flow pumps convinced me that the same technology could be utilized to develop a long-term TAH. Compared with pulsatile devices, a continuous-flow TAH would have a huge advantage, as it would be inflow-sensitive and, thus, like the native heart, automatically adjust right- and left-flow imbalances. The first patient in whom we implanted a HeartMate II did not have a pulse for more than a year yet remained in New York Heart Association functional class I. This experience indicated that a pulse was not necessary for effective long-term cardiac support. Encouraged by this result, in December 2005, we successfully excised the heart in a calf and replaced it
with 2 continuous-flow pumps; this was the first chronic experimental procedure to use implantable, continuous-flow pumps for total circulatory support. Since then, we have demonstrated in more than 30 cases that calves can be well sustained (even walking on treadmills) for up to 90 days without pulsatile blood flow.22 This experience led me to use this total heart replacement technology in a 55-year-old man dying of severe cardiac amyloidosis.23 Clinically, the patient did well. He awoke from his surgery and was active mentally and physically, but the amyloid was found to involve the liver, lungs, and kidneys, so support was electively discontinued after 5.5 weeks (Fig 6).

We are currently developing a totally implantable continuous-flow TAH (the Bivacor) that has shown feasibility in animal experiments, and we hope that this pump will finally translate into a totally contained and durable cardiac replacement device (Fig 7). It is being further developed in the THI laboratories under the leadership of Daniel Timms, an outstanding young engineer. The device has only 1 moving part and no bearings or valves, so we anticipate that it has the potential for years of sustained use.

CONCLUSIONS

In December 2013, we performed our 1000th VAD implantation at the THI. In my professional career, I have been fortunate to have embarked on the challenging but rewarding care of patients with advanced heart failure. I began this journey during the idealistic Kennedy era, which had the goals of going to the moon, curing hunger and poverty, as well as creating an artificial heart. Except for reaching the moon, these laudable goals have remained elusive. It is personally gratifying to see that most of the cardiac pumps that are widely used today initially came to light initially in the Baylor and then in the THI research laboratories. None of these breakthroughs would have happened without the guidance of my mentors, Dr DeBakey and, especially, Dr Cooley (Fig 8). Also, many of the advances were directly attributable to my ongoing clinical experience, as I never stopped being an active surgeon and practicing physician throughout my career. My clinical experience was extremely important to my research contributions, and this dual approach is likely valuable for current, young clinical investigators.

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References