Bud Frazier's 1,000th LVAD at THI

The 1,000th VAD, the Great Rivalry, and the Grand Experiment of the Texas Medical Center

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In the closing days of 2013, Dr. O.H. "Bud" Frazier and the Texas Heart Institute (THI) team performed their 1,000th ventricular assist device (VAD) implantation. This landmark achievement occurred barely more than half a century after Dr. Denton A. Cooley founded THI in 1962 as an institution dedicated to reducing the "devastating toll of cardiovascular disease through innovative programs in treatment, education, and research."[1] The 1,000th VAD implantation occurred almost exactly 50 years after the original 1964 National Heart Institute (NHI) grant was awarded to Dr. Michael E. DeBakey and the Baylor College of Medicine for the development of an artificial heart. The juxtaposition in time of these 2 auspicious events would begin a unique and remarkable story—one that would ultimately lead to the realization of VAD implantation as a standard of care after more than 5 decades of ceaseless effort and unrelenting innovation.

The saga of the 1,000th VAD is a testament to the perseverance of Dr. Frazier and his colleagues at THI, under the leadership of Dr. Cooley, in designing and perfecting circulatory assist devices. However, as noted by Dr. Frazier, the saga is also firmly rooted in foundations first laid at Baylor, including the pioneering work of DeBakey protégés such as Dr. George P. Noon. After 1969, these key players found themselves working at rival institutions located a stone's throw from each other on the Texas Medical Center (TMC) campus. The 1,000th VAD implantation therefore highlights an intriguing story of medical progress and scientific collaboration borne of conflict and competition.

Bud Frazier's Initial Interest

The field of assisted circulation first attracted Frazier in 1965, when, as a 2nd-year medical student at Baylor, he joined Dr. Domingo Liotta in the Baylor laboratories in research involving the total artificial heart (TAH) project. Upon Frazier's graduation in 1967, he received the DeBakey Award as Outstanding Surgical Student. However, instead of staying at Baylor after his general surgery residency, Frazier moved to THI in 1974 for his cardiac training, because VAD research by that time had moved primarily to the THI laboratories. During his 40 ongoing years at THI, Frazier would lead the development of the pulsatile HeartMate I pneumatic device (first clinically implanted in 1986); the first intravascular implantable continuous-flow VAD, the Hemopump (1988); the HeartMate XVE (first clinically implanted in 1991); the Jarvik 2000 heart (2000); the AbioCor TAH (2001); and the continuous-flow HeartMate II (2003). Remarkably, except for the AbioCor, Frazier was the first to implant these devices clinically. He initiated research to develop the HeartWare VAD in 1994. That same year, he reported the first hospital discharge of a patient with a VAD and the first long-term clinical use of a VAD (505 days).[2] The HeartWare and the HeartMate II are currently the most widely used VADs in the world.

Dr. George Noon worked with the National Aeronautics and Space Administration to develop the MicroMed DeBakey Noon axial-flow pump (1998) and helped to pave the way for the important role that would be played by continuous-flow devices as long-term VADs.[3] Noon observed that Frazier's commitment to "getting it right" has been as important as all the milestones that Frazier has achieved. For example, when

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thrombotic complications with the HeartMate II were encountered early after its clinical deployment, Frazier led the redesign efforts that resulted in a substantially improved device and helped to make it the most frequently implanted VAD in the world. As significant as these many accomplishments are in themselves, they are even more meaningful within the context of the 50-year effort of THI and Baylor researchers to develop the artificial heart and circulatory assist devices.

Setting the Stage for Assisted Circulation

As DeBakey explained in 2005,[4] the determination to develop VADs and a TAH was inspired by the high mortality rate associated with the use of the early heart-lung machine and the observation that some patients undergoing prolonged support with aid of that machine would recover their cardiac function. This led to the conclusion that more prolonged support of the failing heart would improve cardiac recovery. Accordingly, DeBakey remembered, the dawn of the "open-heart" era in the 1950s created a *zeitgeist* that stimulated the pursuit of assisted circulation[4] and motivated DeBakey to establish an experimental laboratory. This laboratory, complete with a machine shop for building mechanical prototypes, is still in use (currently for nanotechnology research), on the 4th floor of the Baylor College of Medicine. Artificial-heart development efforts at Baylor accelerated in the early 1960s after DeBakey recruited a promising young Argentine researcher, Dr. Domingo Liotta, from the Cleveland Clinic. Liotta had presented his work on artificial-heart technology in 1961 at the annual meeting of the American Society for Artificial Internal Organs.[2] Soon thereafter, DeBakey's testimony to the United States Senate led to the 1964 NHI funding for an artificial-heart program at Baylor. DeBakey also forged a research collaboration with the engineers at neighboring Rice University—another TMC institution—to lay the final building block in a solid foundation for pursuing assisted circulation.

During the boom in cardiovascular surgery in Houston led by Cooley and DeBakey, an opportunity soon arose to use the assist devices that were being engineered in the Baylor laboratories. In July 1963, a patient of Stanley Crawford, named George Washington, had a cardiac arrest after undergoing aortic valve replacement and became the first human recipient of a VAD. Mr. Washington died after 4 days; however, this experience prompted further innovation. After several more attempts, the first successful clinical VAD implantation was performed on 6 August 1966, in Esperanza del Valle Vasquez, a patient from Mexico who could not be weaned from cardiopulmonary bypass (CPB) after a double valve replacement. She was weaned from the VAD after 10 days and lived for many years. More setbacks were to come, but there was no turning back after this pioneering accomplishment.

The Artificial Heart and the Great Rivalry

According to Liotta,[5] a case at St. Luke's Episcopal Hospital prompted the first clinical TAH implantation. In 1968, one of Cooley's patients developed a "stone heart" after aortic valve replacement and could not be weaned from CPB (this problem was not infrequent in that era, when cardioplegia was seldom used). In those heady days of the first heart transplantations, Cooley sought desperately to buy time for a human transplant by temporarily implanting a xenograft into his patient. The heart was rejected almost instantly; however, this event stimulated collaboration between Cooley and Liotta to perfect a TAH that could be used clinically.

Because DeBakey was focusing largely on VAD technology in the belief that the TAH would take longer to develop, Cooley and Liotta feared that their TAH research would be immutably blocked.[6] Nevertheless, Cooley helped to conduct the animal studies needed to test the TAH prototypes that Liotta was engineering, thereby sustaining hope of advancing the TAH. The events that transpired soon thereafter, in ways that were then unforeseeable, would have major consequences for the protagonists at Baylor and would set the stage for the decades-long effort to develop a reliable VAD.

The fateful day was 4 April 1969. Cooley had agreed to perform a ventricular aneurysmectomy in a desperate attempt to save Haskell Karp, a 47-year-old man dying of heart failure while awaiting a transplant at St. Luke's Episcopal Hospital. In the operating room, Cooley found that Karp's heart was extensively scarred; after the aneurysmectomy, he could not be weaned from CPB. Having gained the approval of Karp and his family beforehand, Cooley proceeded to implant the TAH that he and Liotta had been testing.[6] In that era before cell phones, e-mails, and text messages, DeBakey—on a trip to the National Institutes of Health in Washington—was unreachable. Upon learning of the events in Houston, DeBakey was outraged, accusing Cooley of exceeding his medical authority and using his device without permission. Thus began the feud that would last for nearly 40 years.

Mr. Karp died on 8 April 1969, 4 days after receiving the TAH and 2 days after the TAH was exchanged for a donor heart. Amidst the subsequent controversy, Cooley resigned from Baylor and completed his move to THI. The stage was set for the famous rivalries between Cooley and DeBakey and between THI and Baylor. Frazier joined THI a few years later, and Cooley recruited other innovators such as John Norman who, with Cooley and George Reul, implanted the first VAD as a bridge to transplantation (1978). The TMC became a bipolar hub for cardiac surgery—led by 2 giants in the field who were always in eye's view of each other.

The rivalry between DeBakey and Cooley yielded a paradoxical and important result: the talents and re-

sources of the juxtaposed Baylor–THI powerhouses were mutually energizing, and a new degree of medical creativity flourished on the TMC campus. This critical mass of competing talents would eventually contribute to the growth of the TMC, its other programs, and its other institutions, such as the MD Anderson Cancer Center and Texas Children's Hospital. As a result, the TMC became the largest medical center in the world.

It is intriguing to speculate in the context of historical perspective. Might the outcome have been vastly different if the lines of reporting and communication had been better in the 1960s? What if DeBakey had left more "oxygen in the room" for talented and energetic younger faculty members such as Cooley? What if Cooley and Liotta had not acted on their convictions or had not feared for the viability of their TAH efforts? It is impossible to know whether the energies of the THI and Baylor surgeons and scientists would have flagged without the healthy competition fostered by the proximity of DeBakey and Cooley. Regardless, Frazier, Noon, and others express their indebtedness to the power of that competition.

Rapprochement

In 2007, rapprochement between DeBakey and Cooley brought a welcome end to their rivalry.[7] Today, the dynamic has come full circle. Dr. Cooley has rejoined the faculty of the Baylor College of Medicine as a Distinguished Professor Emeritus. Dr. Frazier and a younger generation of surgeon-scientists at THI—led by Drs. Hari Mallidi and William Cohn—are also active members of the Baylor faculty, rejoining DeBakey's protégé George Noon and others. Baylor, THI, and St. Luke's have recently formed a unique and historic corporate partnership.

The formation of this partnership and the milestone of the 1,000th VAD implantation prompt reflections on what has been learned from this half-century of progress. The crucial contributions of industrial partners—such as Thermo Cardiosystems and its successors, Thoratec Corporation and HeartWare, Inc.—cannot be ignored. However, the success story symbolized by the 1,000th VAD implantation is chiefly one of personal passion, thoughtful perseverance, and professional competition—with transparency and collegiality, which are core principles of medical science and cornerstones of medical progress.

We are indebted to Dr. Cooley, Dr. Frazier, and their colleagues at THI, and to Dr. DeBakey, Dr. Noon, and their colleagues at Baylor, for their historic contributions. It is hoped and expected that the innovation embodied in their work will give rise to even more elegantly miniaturized and internalized long-term VADs. In addition, perhaps the lessons learned from the great rivalry and the grand experiment that culminated in the 1,000th VAD implantation will translate into successful collaborations in the future.

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Comment

As I reflect on the circumstances and events that led up to the 1,000th VAD implantation, I would like to add my congratulations to those of Dr. Rosengart and others in honoring Dr. O.H. "Bud" Frazier in this special section of the *Texas Heart Institute Journal*. I feel enormous pride and gratitude for what this milestone represents—both to the Texas Heart Institute and to heart-failure patients worldwide. I applaud Dr. Frazier for his many accomplishments, which reveal his remarkable capacity for innovation and leadership and his lifelong commitment to the alleviation of heart disease.

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