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Development of a Small, Implantable Right Ventricular Assist Device

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Abstract

Purpose—The purpose of this program is to design, develop, and clinically evaluate a new, implantable right ventricular assist device (RVAD) that can be used as a component of an implantable biventricular assist device for patients with severe biventricular heart failure.

Methods—The initial phase of this program resulted in a prototype RVAD, named DexAide, a modified version of the CorAide™ left ventricular assist device. *In vitro* testing was performed in a stand-alone circuit as well as in a true RVAD mode to evaluate pump performance. Pump flow and power were measured under various afterload and pump speed conditions.

Results—The pump performance requirements of 2 to 6 L/min and a pressure rise of 20 to 60 mm Hg were successfully met with the pump speeds between 1,800 and 3,200 rpm. The nominal design point of 4 L/min and 40 mm Hg pressure rise was achieved at $2,450 \pm 70$ rpm with a power consumption of 3.0 ± 0.2 watts.

Conclusion—The initial *in vitro* testing met the design criteria for the new DexAide RVAD. Initial *in vivo* testing is under way, which will be followed by preclinical readiness testing and a pilot clinical trial in this 5-year program.

Keywords

ventricular assist device; right ventricular failure; circulatory support

Introduction

The use of implantable left ventricular assist devices (LVADs) has been increasing to serve the growing population of patients with end-stage congestive heart failure. The currently available implantable LVADs used as a bridge to transplant have produced improvements in multiorgan function. Patients implanted with a portable, electrically powered device can become outpatients and enjoy an acceptable quality of life.^{1–3} Recently, the Food and Drug Administration (FDA) granted permission for the permanent use of an implantable LVAD in patients who are not candidates for cardiac transplantation. However, up to 40% of LVAD patients have significant right ventricular (RV) failure that may limit the success of the LVAD

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therapy.⁴ The RV failure leads to two problems: decreased RV output, thus low LVAD flow, and high central venous pressures that result in passive congestion of the liver, kidneys, and abdominal organs. Both factors contribute to multiorgan failure, the leading cause of death after LVAD implant. Such patients commonly require prolonged inotropic support or support with a right ventricular assist device (RVAD). Clinically available RVADs, such as the Bio-Pump® (Medtronic, Inc., Minneapolis, MN), BVS 5000 (ABIOMED, Inc., Danvers, MA), Thoratec® VAD (Thoratec Corp., Berkeley, CA), and CentriMag® (Levitronix GmbH, Zurich, Switzerland) are extracorporeal devices and have several limitations, such as need for anticoagulation, need for a hospital stay, and a less than ideal quality of life.

The purpose of this new program, funded by a National Heart, Lung, and Blood Institute (NHLBI) Bioengineering Research Partnerships (BRP) grant, is to design, develop, and clinically evaluate an implantable RVAD that can be used as a component of an implantable biventricular assist device for patients with severe biventricular heart failure. This article describes the initial phase of this program, including the pump design and *in vitro* test results.

Methods

The DexAide Design

The basic design of the new RVAD, named DexAide, is that of the CorAide™ LVD-4000 Assist System (Arrow International, Reading, PA) developed at the Cleveland Clinic Foundation.^{5–9} Figure 1 shows the CorAide LVAD and DexAide RVAD, both of which consist of three sub-assemblies: the volute housing, the rotating assembly, and the stator assembly. The cast titanium volute housing contains the threaded blood inlet and outlet ports. The pumping element is a cylindrical rotating assembly, containing a permanent magnet ring and impeller vanes on each axial end of the assembly. The stator assembly contains the motor windings surrounded by a thin walled titanium cylinder. This cylinder forms the post around which the rotating assembly spins. The rotating assembly is supported passively by magnetic forces in the axial direction and by a stable, blood-lubricated fluid film bearing in the radial direction. With the rotating assembly levitated, there is no surface contact in the bearing, thus no wear during operation.

If the CorAide LVAD in its current design were used to assist the RV, a much lower rotational speed would be needed to produce the same pump flows as an LVAD due to the lower pulmonary arterial pressure compared with the systemic arterial pressure. Speeds less than 1,800 rpm would cause sliding contact between the rotating assembly and the stator assembly. To address this issue, we reduced the diameter of the primary impeller blades and also reduced the blade count from seven to five in the DexAide, which allowed a nominal operating speed range of 1,800 to 3,200 rpm. The smaller diameter impeller, which has a larger blade height at the tip, also allowed a more simplified machining of the volute housing from a single piece of barstock or casting. The CorAide and DexAide stator assemblies are identical. The CorAide LVAD's favorable features of reduced thrombogenicity and long durability will be retained in the DexAide RVAD.^{5–9}

Pump Performance Requirements

DexAide pump performance requirements were set as follows: (1) range of nominal flow (excluding pulsatile transients) of 2 to 6 L/min, (2) range of nominal pump pressure rise of 20 to 60 mm Hg, and (3) a linear normalized power vs. flow characteristic over nominal speed range.

Mock Circulatory Systems

In vitro testing was performed using two different mock circulatory systems: (1) a nonpulsatile (steady-state) mock circulatory system as a stand-alone circuit and (2) a pulsatile mock circulatory system to simulate a true RVAD mode (Figure 2). The nonpulsatile mock circulatory system is a simple loop that includes an inflow reservoir, the DexAide pump, compliance and resistance elements simulating pulmonary vascular characteristics, fluid-filled pressure lines to measure inlet and outlet pressures, and an ultrasonic flow probe (Transonic Systems, Inc., Ithaca, NY) to measure the pump flow. The pulsatile mock circulatory system included a pneumatic, pulsatile ventricular assist device (VAD) with inflow and outflow valves simulating the native right ventricle, compliance and resistance elements simulating pulmonary vascular characteristics, fluid-filled pressure lines to measure inlet and outlet pressure, and flow probes (Transonic Systems, Inc.) to measure the DexAide flow and total flow. The mock circulatory loop compliance and resistance elements were adjusted to produce physiologic cardiac outputs and pulmonary arterial pressure waveforms (both mean and pulse pressure) with the pneumatic pulsatile pump operating alone. Next the DexAide pump was added to the circuit receiving flow and pressure inputs from the pulsatile VAD chamber and output distal to the outflow valve of the pulsatile VAD. This set-up simulated the DexAide RVAD ventricular inflow cannulation and outflow graft anastomosis to the pulmonary artery.

The solution used in the mock circulatory loop was glycerin and water (approximately 20% glycerol, 80% water) to produce a specific gravity of 1.06 g/mL and viscosity of 2.0 cP at 20 °C.

In Vitro Test Protocol

We fabricated prototypes DexAide pumps for initial evaluation using four RVAD rotating assemblies, three RVAD volute housings, and four CorAide LVAD stator assemblies. Five different combinations of the DexAide pump components were tested in six trials (one combination was used twice but on separate dates) in the nonpulsatile mock circulatory system. The results were expressed as the average and standard deviation of the six trials. The DexAide pump was operated under various afterload (between 10 mm Hg and 80 mm Hg) and pump speed conditions (between 1,800 rpm and 3,200 rpm). The pressure rise, pump power, hydraulic power, pump efficiency, and normalized pump power were calculated using the following equations:

$$\text{Pressure rise [mm Hg]} = (\text{Outlet pressure}) - (\text{Inlet pressure})$$

$$\text{Pump power [Watts]} = (\text{Motor driver voltage}) \cdot (\text{Motor current})$$

$$\text{Normalized pump power [Watts / krpm}^{1.8}] = (\text{Pump power}) / (0.001 \cdot (\text{Pump speed}))^{1.8}$$

$$\text{Hydraulic power [Watts]} = 0.00222 \cdot (\text{Pump flow}) \cdot (\text{Pressure rise})$$

$$\text{Pump efficiency [\%]} = (\text{Hydraulic power}) / (\text{Pump power})$$

We obtained the relationships between the pressure rise and pump flow, between the pump power and pump flow, between the normalized pump power and pump flow, and between the pump efficiency and pump flow, with various pump speed.

A DexAide pump was tested in the pulsatile mock circulatory system as well, operating at 2,400 rpm, while the pneumatic VAD was operated at 70 bpm and 120 bpm. We measured the DexAide pump flow, inlet pressure, and outlet pressure, and obtained the instantaneous relationship between the pressure rise and pump flow at each condition. The mean pressure rise and mean pump flow were calculated during the pulsatile VAD cycle. These data were

compared with the data obtained from the nonpulsatile circulatory system with the DexAide pump operating at 2,400 rpm.

Results

Figure 3 presents plots of pressure rise vs. pump flow relationship under various pump speeds. The reproducibility of DexAide pump performance and the interchangeability of the three main pump components were demonstrated by the small standard deviation in pump performance for the 5 combinations. The pressure rise and pump flow exhibit an inverse relationship as commonly observed with rotary blood pumps. The shaded area shows our target operating range of 2 to 6 L/min pump flow and 20 to 60 mm Hg pressure rise. This range was covered with pump speeds between 1,800 and 3,200 rpm. The nominal design point of 4 L/min and 40 mm Hg pressure rise was met at $2,450 \pm 70$ rpm.

The corresponding pump power vs. pump flow plots are presented in Figure 4. Power consumption increased linearly with increasing pump flow, and the slope of the relationship is higher at higher pump speed. Power consumption was 1.6 ± 0.1 watts at the minimum operating condition of 2 L/min and 20 mm Hg pressure rise and 5.1 ± 0.3 watts at the maximum operating condition of 6 L/min and 60 mm Hg pressure rise. Power consumption at the design point of 4 L/min and 40 mm Hg pressure rise was 3.0 ± 0.2 watts. The normalized pump power vs. pump flow relationship is shown in Figure 5. The linear relationships are almost identical in various pump speeds except for those at 1,800 rpm.

As shown in Figure 6, the reduced impeller size resulted in reduced efficiency. Overall pump efficiency at the nominal design condition was about 10% in the DexAide, compared to 20% for the CorAide. This reduction in efficiency occurs because the pump losses (bearing, secondary impeller, rotating assembly windage) are nearly the same as for the CorAide LVAD while the nominal hydraulic output is about one third of the LVAD's.

Figure 7 shows the instantaneous relationship between pressure rise vs. pump flow in the pulsatile mock circulatory system for three cardiac cycles of the pneumatic, pulsatile VAD at a beat rate of 70 bpm with the DexAide pump speed set at 2,400 rpm. Although the data showed some hysteresis (thin line), both the maximum flow data point (ejection phase of the pneumatic VAD) and minimum flow data point (filling phase of the pneumatic VAD) were the same as that was obtained in the nonpulsatile circulatory system (thick line). Furthermore, the mean pressure rise vs. mean pump flow for the three pulsatile cardiac cycles (a closed circle) was almost on the line that was obtained in the nonpulsatile circulatory system. Figure 8 shows similar data but with a pneumatic VAD beat rate set at 120 bpm. Again, the data obtained from the pulsatile mock circulatory system were very similar to those obtained in the nonpulsatile circulatory system. The swing of the pump flow (between 4.6 L/min and 6.5 L/min) during the cardiac cycles of the pneumatic, pulsatile VAD was much less than that observed with the VAD at a beat rate of 70 bpm (between 2.7 L/min and 7.0 L/min).

Discussion

The results indicated that the pump performance requirements of 2 to 6 L/min and a pressure rise of 20 to 60 mm Hg were successfully met with the pump speed between 1,800 and 3,200 rpm using prototypes of the DexAide. The nominal design point of 4 L/min and 40 mm Hg pressure rise was achieved at $2,450 \pm 70$ rpm with a power consumption to the motor driver of 3.0 ± 0.2 watts.

Rapid strides have been made in the management of end-stage heart failure with an LVAD as a bridge to transplant,¹⁰ in post-cardiotomy shock,¹¹ potentially as a bridge to recovery,¹² and as an alternative to transplant.¹³ Several LVADs have been shown to improve end-organ

dysfunction, allow patients to be sent home, and provide a reasonable quality of life. As a result, the LVAD will continue to play an increasingly important role in the management of severe heart failure. However, RV failure remains a serious complication in the LVAD recipients. We have reported a poor prognosis for patients with LVAD support who also required external RVAD support.^{14,15} The survival to transplantation rate was very low (14.7%) in these patients. We also recently analyzed the prognosis for patients who did not require RVAD support but required inotropic support of 14 days or more after the LVAD implantation. The survival to transplantation rate in these patients was only 41% versus 89% ($P = 0.0001$) for those patients with shorter duration of inotropic support (unpublished data). If a reliable, implantable RVAD was available, we could save the lives of these patients with RV failure. Currently, surgeons are reluctant to use RVADs because of the bleeding and anticoagulation complications, device-related complications, need for a prolonged hospital stay, and relatively primitive technology (the clinically available RVADs are all extracorporeal devices). Therefore, the decision is made to “get by” with inotropic support for RV contractility, while some patients have very poor contractility, become dependent on inotropes, and frequently have marginal LVAD filling and prolonged high right heart pressures. These patients are at risk for multiorgan failure and death. Therefore, it is very important to develop a small, safe, durable, and implantable RVAD that can be employed early before a patient suffers from severe RV failure. Surgeons would be more inclined to utilize such technology, and patient survival and quality of life should consequently improve. An implantable RVAD combined with an LVAD would be clinically useful in several scenarios: 1) for patients with severe RV dysfunction who are not able to fill the LVAD; 2) patients with high pulmonary vascular resistance limiting pulmonary venous return to the LVAD; 3) patients with frequent ventricular arrhythmias; and 4) patients who would otherwise require total artificial heart (TAH) support. An implantable RVAD can also be used in patients with isolated severe RV failure, although its incidence is not common.

Several devices are under development as an implantable RVAD. The Baylor College of Medicine group has been developing the Gyro centrifugal pump that can be used as an implantable biventricular assist device (BVAD).^{16–18} Clinically available, implantable LVADs have also been adapted to be used as an implantable RVAD. The Jarvik 2000 LVAD (Jarvik Heart, Inc. New York, NY) is a titanium axial flow impeller pump implanted into the apex of the failing LV.¹⁹ The rotor constitutes the only moving part of the device and is supported at each end by 1 mm diameter, blood-immersed ceramic bearings.^{20,21} Satisfactory biventricular support with two Jarvik 2000 pumps was demonstrated in two acute animals,²² one 30-day animal,²³ and one patient.²⁴ An animal study of total heart replacement with two HeartMate® III pumps (Thoratec Corp., Pleasanton, CA) was also reported.²⁵

The DexAide was designed to meet pump performance requirements for RVAD use following modification of the CorAide LVAD. The diameter of the primary impeller blade was reduced along with a reduction in the number of the blades, and the volute housing was simplified to improve manufacturability. Since there are no fundamental changes in the core design, we expect that the DexAide maintains the advantages of reduced thrombogenicity and long durability of the CorAide LVAD. There are no stator vanes at the inlet or outlet (as required with axial pump devices), which, at off-design flow, can become areas of recirculation and surfaces for deposition. There are also no pivot bearings or other dead-ended crevices to serve as a nidus for deposition. The rotating assembly and stator assembly are coated with amorphous carbon, and then an overcoat of fluorinated ethylene propylene (FEP) is applied to make the pump more resistant to thrombosis, as well as impervious to startup transients and shock loads. The inlet cannula and volute housing, which are not coated, are made of a highly polished titanium alloy. Long durability is expected, as there is only one moving part that has no surface contact or mechanical wear during operation.

A study limitation is that we evaluated pump performance using mock circulatory systems that may not accurately reflect *in vivo* pump performance. A series of *in vivo* studies in calves without any anticoagulation therapy is under way to validate *in vivo* pump performance and biocompatibility of the DexAide. Portable external electronics are being developed for a stand-alone RVAD Portable Electronics Module (RPEM) and RVAD System Interface (RSI) with a fixed flow control algorithm. External electronics to control a BVAD comprised of both a CorAide LVAD and a DexAide RVAD will also be developed. The future goal of a clinical BVAD is illustrated in Figure 9. Human fitting studies are under way to develop the inflow and outflow conduits for our initial pilot clinical trial.

Conclusion

The initial *in vitro* testing met the design criteria for the new, implantable DexAide RVAD. Initial *in vivo* testing is under way, which will be followed by preclinical readiness testing and a pilot clinical trial in this 5-year program.

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Figure 1.

A comparison of the CorAide™ LVAD (Left) and DexAide RVAD (Right). Both pumps consist of three sub-assemblies: the volute housing, the rotating assembly, and the stator assembly (from top to bottom).

Figure 2.
Schematic drawings of nonpulsatile and pulsatile mock circulatory systems. F : DexAide pump flow, P_{in} : Inlet pressure, P_{out} : Outlet pressure, VAD: ventricular assist device.

Figure 3. Pressure rise vs. pump flow relationship under various pump speeds. The shaded area shows our target operating range. The upward bars indicate standard deviation.

Figure 4. Pump power vs. pump flow relationship with various pump speeds. The upward bars indicate standard deviation.

Figure 5. Normalized pump power vs. pump flow relationship under various pump speeds. The upward bars indicate standard deviation.

Figure 6. Pump efficiency vs. pump flow relationship under various pump speeds. The upward bars indicate standard deviation.

Figure 7.

Instantaneous relationship between pressure rise vs. pump flow (thin line) in the pulsatile mock circulatory system with a DexAide pump speed set at 2,400 rpm and a pneumatic VAD beat rate set at 70 bpm. The mean pressure rise vs. mean pump flow data in the pulsatile mock circulatory system is plotted as a closed circle. The data in the nonpulsatile circulatory system with the DexAide pump speed of 2,400 rpm are also plotted (thick line) for comparison.

Figure 8.

Instantaneous relationship between pressure rise vs. pump flow (thin line) in the pulsatile mock circulatory system with the DexAide pump speed set at 2,400 and the pneumatic VAD beat rate set at 120 bpm. The mean pressure rise vs. mean pump flow data in the pulsatile mock circulatory system is plotted as a closed circle. The data in the nonpulsatile circulatory system with the DexAide pump speed of 2,400 are also plotted (thick line) for comparison.

Figure 9.
Percutaneous BVAD with CorAide LVAD and DexAide RVAD.