The Cleveland Clinic–Nimbus total artificial heart

Design and in vitro function

We describe the design and in vitro testing of the Cleveland Clinic-Nimbus electrohydraulic permanent total artificial heart as it nears completion of development. The total artificial heart uses an electric motor and hydraulic actuator to drive two diaphragm-type blood pumps. The interventricular space contains the pump control electronics and is vented to an air-filled compliance chamber. Pericardial tissue valves and biolized blood-contacting surfaces potentially eliminate the need for anticoagulation. In vitro studies on a mock circulatory circuit demonstrated preload-sensitive control of pump output over the operating range of the blood pump: 70 to 160 beats/min and 5 to 9.6 L/min at right and left atrial pressures of 1.0 to 7.0 mm Hg and 5.0 to 12.0 mm Hg, respectively. The pump output was found to be insensitive to afterload over a range of 15 to 40 mm Hg mean pulmonary artery pressure and 60 to 130 mm Hg mean systemic pressure. The left master alternate control mode balanced the ventricular outputs during simulated bronchial artery shunting of up to 20% of cardiac output. A 10% to 15% right-pump, stroke-volume limiter balanced ventricular outputs during maximum output of 9.6 L/min. In response to a sustained increase in systemic venous return, the pump increased output by 2 L/min (29%) in 35 seconds. Thus the Cleveland Clinic–Nimbus total artificial heart meets the National Heart, Lung, and Blood Institute hemodynamic performance goals for devices being developed for permanent heart replacement. The biolized blood-contacting surfaces should decrease the risk of thromboembolism associated with circulatory assist devices. (J THORAC CARDIOVASC SURG 1994; 108:412-9)

Alex Massiello, ME,a Raymond Kiraly, MSME,a Kenneth Butler, MS,c Steve Himley, MSME,a Ji-Feng Chen, BS,a and Patrick M. McCarthy, MD,b Cleveland, Ohio, and Rancho Cordova, Calif.

The number of heart transplants performed in the United States has plateaued at approximately 2100 per year.1 Yet, by the year 2010 up to 70,000 patients per year may be candidates for some type of circulatory support device, including the total artificial heart (TAH).2 The availability of the pneumatic TAH technology is limited to bridge to cardiac transplantation at a few clinical centers, and it may not provide a practical alternative for permanent circulatory support.

Clinical experience with the pneumatic TAH for both "permanent" implantation and as a bridge to heart transplantation has many useful lessons. Problems identified included proper patient selection (before irreversible end-organ dysfunction), acceptable fit in the patient without vascular compression, postoperative bleeding, infection, and thromboemboli.3,4 Despite these complications, the devices functioned well in the majority of patients, and the International Registry of Mechanical Devices reported that 71% of patients successfully received a transplant. Of these, 50% survived the transplant hospitalization.5

Patients supported with a pneumatic TAH, however, are tethered to an external drive console that limits their mobility and quality of life. Thus the National Heart, Lung, and Blood Institute (NHLBI) currently supports three U.S. programs in developing electrically powered

From the Departments of Biomedical Engineeringa and Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio, and Nimbus, Inc.c Rancho Cordova, Calif.

Supported by the National Institutes of Health contract N01-HV-88103.

Received for publication Aug. 4, 1993.
Accepted for publication March 13, 1994.
Address for reprints: Patrick M. McCarthy, MD, The Cleveland Clinic Foundation, Department of Thoracic and Cardiovascular Surgery, 9500 Euclid Ave., Cleveland, OH 44195.
Copyright © 1994 by Mosby-Year Book, Inc.
0022-5223/94 $3.00 + 0 12/1/56817
TAHs that can be completely implanted. The goal is to provide the patient a quality of life such that the TAH would be an alternative to heart transplantation or medical therapy for end-stage heart failure.

At The Cleveland Clinic, work on the TAH began in 1957, and work on the electrically powered TAH began in 1988. The program's clinical goal is to develop a totally implantable permanent TAH and, in tandem, a percutaneous electrically powered and vented version requiring only an external battery for operation.

The blood pump must meet the following clinical criteria: (1) a minimal risk of thromboemboli, (2) a size small enough to be safely implanted in most patients, (3) a low risk of infection, (4) accommodation of the inherent differences caused by pulmonary circulation between right- and left-sided cardiac output, and (5) 5-year reliable function.

The engineering challenges are formidable. Such a circulatory device must operate for 40 to 80 million cycles per year with no replacement or service of implanted components. The device must be manufacturable, reproducible, and have a cost/benefit ratio exceeding that of hospital care and pharmacologic support for patients with end-stage heart failure. The "totally implanted" TAH would have no percutaneous drivelines or connections and would allow the patient a tether-free existence acceptable for living and working outside the health care environment.

To eliminate skin penetration with the totally implanted system, auxiliary components are required that include a transcutaneous energy transmission system (TETS) to transmit external battery power across the intact skin, an internal battery to temporarily power the system independently of the TETS, and a compliance chamber to compensate for variable interventricular air volumes. The patient need only wear a battery belt to drive the primary TETS coil, which lies on the patient's skin over the implanted secondary coil shown in Fig. 1. A simpler, percutaneous version, designed for temporary bridge to transplantation, requires a percutaneous electric cable and vent tube for the interventricular space but eliminates the need for the aforementioned auxiliary components (TETS coil, internal battery, compliance chamber).

This is one of two articles describing the progress of The Cleveland Clinic Foundation (CC) and Nimbus (N), Inc. (Rancho Cordova, Calif.) in their collaboration (NHLBI contract No. I-HV88103) in developing the CC-N electrohydraulic permanent TAH. This article describes the device design and reports on in vitro performance characteristics. A second article describes the completed and ongoing in vivo experiments, early preclinical studies, and foreseeable clinical uses of the TAH.6

System description

Device design. The design details for this device have been described elsewhere7 and so are summarized here. This design meets the NHLBI performance goals: 8 L/min maximum output pumping into a mean systemic arterial pressure (aortic pressure, AoP) of 110 mm Hg and a mean pulmonary arterial pressure (PAP) of 25 mm Hg; left atrial pressure (LAP) and right atrial pressure (RAP) below 15 mm Hg and 10 mm Hg, respectively.8 The pump module ventricles are pusher-plate diaphragm pumps surrounding a centrally located, hydraulic actuator (Fig. 2). A continuously running brushless direct-current motor drives a positive displacement gear pump that forces hydraulic fluid to flow alternately between the ends of the hydraulic cylinder. The hydraulic fluid flow is controlled by spool valves that automatically reverse the direction of flow when the piston reaches either end of the cylinder. The drive piston is a magnet coupled to a follower magnet surrounding the hydraulic cylinder. This arrangement allows the entire hydraulic system to be hermetically sealed. The follower assembly continuously
Fig. 2. Cross section of blood pump-energy converter unit.

reciprocates through a stroke of 13.2 mm to eject blood from alternate ventricles at a pulse rate determined by the motor speed. While the actuator drives the pusher plate of one ventricle to eject blood, the opposite ventricle is free of the actuator, so that passive filling occurs at a rate determined by the corresponding atrial pressure.

The interventricular space connects with an air-filled compliance chamber to eliminate any significant interventricular pressure variations resulting from differences between the ejection and fill rates of the two diaphragms. Periodic replacement of the gas lost by diffusion through the compliance chamber walls is accomplished through a subcutaneous refill port (see Fig. 1) accessed by needle puncture. The compliance chamber enables pump filling in response to atrial pressures alone. The high-pressure hydraulics and strong magnetic coupling result in complete ejection at each stroke. The system is therefore inherently afterload insensitive.

The housing, diaphragms, and pusher plates are conical to minimize external dimensions. The maximum displacement stroke volume of both ventricles is 64 ml, but a mechanical stop limits the right stroke to compensate for its higher volumetric efficiency. The resulting effective stroke volume of each ventricle is approximately 60 ml, which accounts for valve losses. The motor-gear pump assembly is outside the blood pump, adjacent to the left blood-pump housing. This location allows motor heat to be directly conducted into the left ventricle housing for effective dissipation to the blood without a significant rise in the blood-interface temperature.

The control electronics, hydraulic switching spool valves, drive magnet, follower magnet assembly, and a load-biasing spring are located in the interventricular space. During ejection from the left side, the spring assists the follower assembly to work against systemic arterial afterloads. Also, work is required to compress the spring during ejection from the right side against lower PAPs. As a result, the electrical, hydraulic, and magnetic coupling loads are balanced during ejection.

The blood-pump housings are made of a carbon fiber-epoxy composite material. The diaphragms are compression molded from Hexsyn rubber, a high-flex-life polymer developed by the Goodyear Tire & Rubber Co., Akron, Ohio. Hexsyn rubber has been used for pump diaphragms and other components for TAHs and left ventricular assist devices for more than 15 years. Fig. 3 shows the assembled blood pump-energy converter module.

The blood-contacting surfaces of both the diaphragms and housings are textured and then coated with a "biolized" layer consisting of glutaraldehyde cross-linked, collagen-based gelatin. The trileaflet inflow and outflow valves are fabricated from bovine pericardium. Future implants will use customized bovine pericardial valves already in clinical use and in the Novacor left ventricular assist device (Baxter Healthcare Corp., Edwards CVS Division, Irvine, Calif.). The use of natural tissue valves and the biolization layer has eliminated the need for anticoagulation in animal experiments. This biolized layer is unique to circulatory assist devices, and it is hoped that it will minimize the problems of thrombosis and thromboembolism associated with smooth blood-contacting surfaces. Therefore, currently we do not plan to use more than antiplatelet agents for clinical implants, similar to the HeartMate ventricular assist device experience (ThermoCardiosystems, Inc., Woburn, Mass.).
Control system. The left master alternate control adjusts the motor speed and, consequently, pulse rate in response to the percent filling of the left blood pump. The left master alternate controller is set to drive the pump at a rate that keeps the left pump filling at 90% of its stroke. This setting produces preload-sensitive pump outputs that are controlled by left atrial filling pressures and has the advantages of minimizing LAPs and protecting pulmonary function. The 90%-of-fill point allows the remaining 10% of the left blood-pump volume to be used for handling instantaneous increases in atrial pressures.

The left master alternate controller requires no physiologic or intrapump pressure feedback. Two on/off hall effect switches detect the 90%-of-fill position and the switching spool valve end-of-travel position. The spool valve signal provides timing information concerning completion of the actuator stroke. The hall effect switches and the hybrid circuit electronic motor controller are in the interventricular space; they require only a 15 and 5 V direct-current power supply, respectively, to operate the blood pump.

Adjustments in pulse rate are based on the average left pump fill during 10 beats. A 4-beat stabilizing period then follows any rate adjustment, for a total of 14 beats. This 14-beat controller response filters out cyclic respiratory effects on LAP and any transient changes in atrial pressure as a result of coughing or physical exertion. Each rate adjustment is proportional to the change in average fill, up to a maximum change of ±5% in the current beat rate.

Whereas rate adjustments occur only every 14 beats, the individual ventricular output can vary on a beat-to-beat basis in response to increases or decreases in atrial pressure. To respond to LAP elevations, the 10% left stroke volume reserve shifts more volume to the systemic side. Likewise, the free-filling diaphragms allow the blood pumps to fill to less than 90% in response to transient decreases in atrial pressures.

Any changes in RAP resulting from changes in circulating blood volume or venous return produce corresponding changes in right ventricular filling and, consequently, right ventricular output. The resulting increase or decrease in LAP then alters pump rate if the change is sustained during the 14-beat controller response. Any transient changes in RAP, which are reflected on a beat-to-beat basis into the LAP, will also be filtered out by the 14-beat response.

To maintain physiologic atrial pressures, any TAH automatic controller and actuating mechanism must balance ventricular outputs. That the right blood pump is volumetrically more efficient than the left has been documented in artificial heart research and verified for the TAH. The inertial flow-through in the right pump and greater afterload-dependent valve loss in the left pump make the effective output of the right pump greater than that of the left. Physiologic bronchial artery shunting further decreases the net output of the left pump. Because of these factors, when the TAH is balancing ventricular output and the left pump is filling at 90%, the right blood pump always fills to some value less than 90%. Therefore, at least 10% of the right stroke volume is available to respond to transient changes in RAP. The amount of bronchial artery shunting and the difference in volumetric efficiencies between the two ventricles determine how much the right blood pump must fill relative to the left to balance ventricular outputs.
**In vitro system performance characterization**

**In vitro test loop.** The CC-N TAH was tested in vitro on a four-chamber mock circulatory system. The systemic and pulmonary venous beds are simulated by open chambers connected to the blood-pump inlet ports. Fluid height in the chambers is recorded as the blood-pump filling pressures and the chamber areas can be adjusted to simulate a range of venous compliances. The blood-pump outputs are connected to sealed fluid-filled chambers with adjustable air volumes to simulate systemic and pulmonary compliances. Conduits connecting the arterial compliance chambers to the venous chambers contain restrictions to provide adjustable arterial resistance.

A left-to-left shunt is included to simulate bronchial artery circulation. A conduit connecting the systemic arterial compliance chamber to the pulmonary venous compliance chamber simulates the physiologic shunt and can be adjusted to achieve shunt flows of up to 20% of the left pump output.

In vitro mock loop atrial and arterial pressures are measured by fluid-filled catheters connected to Trantec model 60-80 pressure transducers (Bentley Labs Inc., Irvine, Calif.). All mock loop pressures are measured at pressure taps in the four chambers. The CC-N diagnostic monitor generates analog outputs proportional to the right and left diaphragm positions, motor current, motor frequency, and spool valve position. Mock loop flow is measured by a clamp-on transit time ultrasonic probe (model 28C Transonic Systems Inc., Ithaca, N.Y.).

The in vitro data presented are representative of those that characterize and validate system design. Controlled mock loop flow impedance characteristics and simple left master alternate control function resulted in no significant variability in test data for any combination of blood-pump components and hydraulic actuators. We tested the CC-N TAH venous preload sensitivity, afterload sensitivity, ventricular balance, response rate to increased venous return, and the maximum cardiac output state.

**Venous preload sensitivity.** The left master alternate controller primarily protects pulmonary function by adjusting the pump output to maintain the left blood pump at 90% of filling. Atrial pressure-dependent, passive-filling blood pumps combined with the left master alternate controller allow only the LAP to control output flow. Typical data from mock-loop in vitro testing demonstrates this venous preload sensitivity (Fig. 4). For this testing, mock loop AoP and PAP were held constant at 100 mm Hg and 20 mm Hg, respectively, and a simulated bronchial artery shunt of 5% of the pump output was used. Mock loop atrial pressures and individual pump outputs were recorded for varying mock loop circulating volumes. At RAPs ranging from 1.0 mm Hg to 7.0 mm Hg and LAPs from 5.0 mm Hg to 12.0 mm Hg, the corresponding pump output is 5 L/min to 9 L/min, simulating the Frank-Starling-like response of the natural heart. 19

**Afterload insensitivity.** The CC-N TAH actuator completely ejects the blood-pump volume on each beat at a constant ejection velocity. Complete ejection makes the CC-N TAH insensitive to afterload, as demonstrated by in vitro data obtained for right and left blood-pump output versus a range of mean mock loop PAPs and AoPs (Fig. 5). Afterload insensitivity simplifies automatic controller function. No typical afterload feedback signals,
such as pressure transducers or motor current, are required.

The constant pusher-plate ejection velocity, as well as an ejection duration equal to 50% of the cardiac cycle, helps to minimize the rate of rise in intrapump pressure and so theoretically will promote tissue valve durability and reduce hemolysis. Afterload insensitivity could be a disadvantage in some clinical settings because pump output is not self-limiting in response to increasing arterial pressures. The CC-N afterload insensitivity has potential clinical benefits for those patients with elevated pulmonary vascular resistance resulting from chronic left heart failure or other disease processes in the pulmonary vasculature.

Ventricular balance. Left-right flow differences in TAH blood pumps from 10% to 20% of cardiac output have been reported. Previously, we reported that balance of the CC-N ventricular outputs controlled by the left master alternate controller was independent of variability in physiologic shunting and individual blood-pump volumetric efficiencies. In vitro data from the present study also demonstrate this control capability, as described later. Mock loop AoP and PAP were held constant at 100 mm Hg and 20 mm Hg, respectively; the mock loop circulating volume was unchanged; and initial operating conditions were set at a pump output of 6.3 L/min, and RAP and LAP were set at 2.0 mm Hg and 8.7 mm Hg at 0% versus 8.7 mm Hg, and PAP 20 mm Hg. With rapid volume loading to the systemic venous reservoir, the RAP and LAP increased to 6.0 mm Hg and 8.5 mm Hg, respectively, in 15 seconds and stabilized at 5.5 mm Hg and 8.0 mm Hg within 35 seconds. The left master alternate controller allowed a maximum 5% increase in beat rate every 14 beats to 152 beats/min, at which point the left pump was again filling at the 90% control point. Within 35 seconds, cardiac output increased from 7 to 9 L/min (29% increase) in response to significantly increased venous return. This response is analogous to that occurring during initiation of exercise or during an emotional response. TAHs must be able to handle a sudden increase in venous return to prevent transient elevations of LAP to levels that can impair pulmonary function.

Maximum cardiac output state. At its maximum beat rate, 160 beats/min, the TAH operates at a fixed cardiac output delivering approximately 10 L/min. As venous return increases at maximum pump output, the left blood pump fills to 100%, after which further increases in right ventricular output result in a rapid LAP rise. The possibility of exercise-induced pulmonary edema resulting from rapidly elevated LAP at maximum pump output is not acceptable. Therefore, during operation in the maximum fixed cardiac output state, a mechanism to maintain physiologic atrial pressures is required.

A right pump stroke volume limiter achieves this goal. This is a mechanical stop that limits the end of right blood-pump filling and consequently reduces the right ventricular stroke volume relative to the left. Because the right ventricular filling is significantly less than the left in normal left master alternate operation, moderate limiting of the maximum stroke of the right ventricle is not expected to affect automatic control function. However, such limiting will prevent uncontrolled high LAP at the maximum pulse rate after the left ventricle fills to 100%.

Our studies showed that reducing the maximum right stroke volume by 10% to 15% effectively stabilized both
atrial pressures while maintaining ventricular balance in the fixed maximum cardiac output state (Fig. 6). Testing was initiated at LAP 4.0 mm Hg and RAP 1.0 mm Hg. Steady-state atrial pressures were then recorded after successive increments in mock circulatory loop volume. When the LAP and RAP reach approximately 13 mm Hg and 6 mm Hg, respectively, the system has reached its maximum output; if there were no stroke volume limiter on the right pump (0% stroke volume limiter, Fig. 6), any increase in venous return or circulating blood volume would be reflected primarily in significant elevation of LAPs only. Testing showed that limiting the right pump stroke volume by more than 20% (not shown) decreased both the maximum cardiac output and the right venous preload sensitivity during normal left master alternate control operation at rates between 80 and 160 beats/min.

Summary and comments

The CC-N electrohydraulic actuator is a sealed system that is magnetically coupled to the actuating mechanism of the blood pump chambers; thus hydraulic fluid cannot leak on or through the blood-pump diaphragms and chambers (see Fig. 2). The actuator moving parts (motor rotor, gear pump, switching logic valves, and drive piston) operate in the hydraulic fluid, resulting in minimal mechanical contact and wear, and require no highly loaded bearings or cams. This design provides a significant advantage because it achieves an energy conversion and actuation system ultimately capable of running continuously for many years without service or repair. Although work remains to solve problems identified in the current developmental hardware, the studies reported here show that the design meets the NHLBI performance goals.  

The preliminary in vitro data demonstrate good preload sensitivity control of cardiac output to almost 10 L/min at physiologic atrial pressures. Afterload insensitivity allows the device to maintain right pump output despite elevated pulmonary vascular resistance. The left master alternate control balances ventricular outputs irrespective of variability in physiologic shunt or afterload. Transient changes in atrial pressures of a few seconds do not affect pump output, yet the capability for significantly increased cardiac output is apparent within 35 seconds of a sustained increase in venous return. A 10% to 15% right pump stroke volume limiter balances ventricular outputs during both operation at maximum output and with a sustained increase in venous return.

Progress made by the Cleveland Clinic Foundation and Nimbus, as well as the other phase I TAH contractors (Abiomed, Inc. [Danvers, Mass.] and the Texas Heart Institute, Pennsylvania State University, and Sarns/3M Healthcare [Ann Arbor, Mich.]) in developing these systems has reached the stage of initial animal in vivo trials. The technologic jump from externally powered systems is substantial and requires well-planned and supported development programs that include funding from both the NHLBI and private industry. Building a device that generates the total cardiac output within physiologic hemodynamic parameters, fits within the thoracic cavity, operates at 40 to 80 million cycles per year for a minimum of 5 years without service or replacement, minimizes the likelihood of infection and thromboembolism, and operates by power transmission across the intact skin is a tremendous clinical, engineering, and biomaterials challenge. Research and development efforts to bring these devices to reliability and performance levels suitable for clinical trials continue.

We thank C.R. Bard, Inc., Cardiosurgery Division, Billerica, Massachusetts, for donation of fabrics and grafts used in this project.

REFERENCES


