COO-E(11-1)-2155-15

QUARTERLY PROGRESS REPORT

BIOMEDICAL ENGINEERING SUPPORT

Contract E(11-1)-2155-15

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Co-Investigator and Prepared by:

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Second Quarterly Report

for

November 16, 1974 to February 15, 1975

Institute for Biomedical Engineering and

Division of Artificial Organs

Building 518

University of Utah

Salt Lake City, Utah 84112

MASTER

DISCLAIMER

SUMMARY:

During the quarter covered by this progress report (November 16, 1974, to February 15, 1975), two implantation experiments were conducted to further develop surgical procedures as well as to assess the overall performance and adequacy of the AEC Blood Pump and ventricles. Both experiments were directed primarily at determining and improving pump and ventricular efficiency, improving surgical procedures and evaluating the reliability of the blood pump components, which include the flexible drive shaft, the blood pump drive mechanism and the blood handling components.

Experiment No. 16 (AEC) was scheduled as a long term experiment in a 112 kg female Hereford calf. The electric motor was implanted in the abdomen which powered AEC Blood Pump No. 2 via a 1/8" flexible drive shaft. Surgical implantation required 3¼ hours.

Three hours after surgical implantation the electric motor torque was 9 oz. inches at 900 r.p.m. Aortic pressures were 130/90 mm Hg and atrial filling pressures were 4 mm Hg (left side) and 3.5 mm Hg (right side). With movement of the animal in the cart, it was observed that arterial pressures varied with animal position. Because atrial filling blood pressures varied significantly, ranging from 0-35 mm Hg, the animal was surgically reopened at 23 hours to correct Blood Pump alignment in the thorax. After surgery the atrial pressures were 1 mm Hg (left) and -1 mm Hg (right) with aortic pressures of 100/35 mm Hg. However, it was not possible to maintain adequate arterial pressures and with the onset of hyperthermia the animal was terminated at 28 hours after implant. Autopsy of the animal indicated that some pressure necrosis resulting from the Blood Pump had occurred and that hyperthmia was possibly due to pyrogen leaching from the ventricles.

Experiment No. 17 (ERDA) was also scheduled as a long term experiment in a 106 kg. male Holstein calf. The electric motor was implanted in the abdomen and powered ERDA (AEC) Blood Pump No. 2 which was fitted with Avcothane Elastomer - 51 ventricles. Surgery required 3¼ hours and 6 hours later the animal was standing. All physiologic parameters were near normal and except for two temperature spikes, the animal was near normal until the animal suffered a stroke and was terminated at 266 hours (11 days - 2 hours). This was an excellent experiment which demonstrated the reliability of the Blood Pump and drive train (flexible drive shaft). With further improvements in ventrical design and materials to reduce blood damage it should be possible to sustain experimental animals many weeks in the near future.

Mr. Lee Smith has devoted 80% of his time to this project during the reporting period. Furthermore, Dr. Gary Sandquist has devoted 33% of his time to the project during the quarter and Dr. Don Olsen has devoted 25% of his time to the project during the quarter. Contract requirements are thus being filled.

I. SUMMARY REPORT ON AEC TOTAL ARTIFICIAL HEART REPLACEMENT EXPERIMENT AEC 16

Experiment (TH75 C6 AEC 16 A1): Conducted on February 11, 1975

Experiment No. 16 was planned as a long-term sterile experiment to evaluate the AEC blood pump driven by a water cooled electric motor implanted in the abdomen, with a reinforced flexible drive shaft and casing, with ventricles constructed of Avcothane Elastomer-51.

Surgical procedure: A sternal split surgical procedure was performed by Drs. Don Olsen, Jack Kolff and Clifford Kwan-Gett. The experimental animal was a female Hereford approximately 112 kg in weight. AEC Blood Pump No. 2 was used with Avcothane Elastomer-51 ventricles and a smooth intimal surface. The blood pump was fitted with Bjork-Shiley pyrolytic carbon valves. The AEC blood pump mechanism and Avcothane ventricles were gas sterilized 72 hours prior to surgery using ethylene oxide. The flexible drive shaft was also gas sterilized. The animal was anesthetized with Brevane followed by fluothane. Parameters monitored during the course of the experiment were aortic pressure, central venous pressure, left arterial pressures, right arterial pressures and pulmonary arterial pressures. Mechanical parameters measured were motor speed, torque, electric motor temperature and the vacuum maintained on the blood pump mechanism.

Twenty-four hours prior to surgery the experimental animal had pre-operative lung function measurements made which indicated normal lung function for that size of animal. The surgery lasted approximately 3¼ hours, with the animal on heart-lung bypass for approximately 130 minutes.

Postoperative recovery: At three hours into the experiment with the animal lying down in the postoperative recovery cart, the average motor torque was approximately 9 oz. inches at a speed of 900 r.p.m.; vacuum was 5 mm Hg; aortic pressure 130/90 mm Hg with a left side filling pressure of

4 mm Hg and a right filling pressure of 3.5 mm Hg. The animal was assisted with the mechanical respirator on 80% oxygen, breathing at 16 breaths per minute. There was a large amount of bleeding from the test drainage tubes. At 3 hours into the experiment approximately 2600 cc of chest drainage had accumulated. At 4 hours into the experiment the animal began to move around in the cart. This was the first time that arterial pressures were observed to vary with the position of the calf's body. At 7 hours into the experiment the animal was making attempts to stand. At 20 hours postoperatively the motor speed was still at 900 r.p.m. with an arterial pressure of 130/110 mm Hg. Left filling pressures had risen to 32 mm Hg because of the particular position that the animal had maintained. The filling pressure on the left side would vary tremendously from 0-35 mm Hg depending upon the animal's position. At 23 hours into the experiment it was decided to put the animal back on the operating table and reopen the chest in an attempt to correct the position sensitive condition that had been seen earlier in the experiment. At 24 hours the chest was again closed and the animal placed back into the postoperative cart. During the second operation the blood pump was loosened from its tethers, maintaining it against the sternum, and moved slightly to the right side of the animal. During the second operation there were no gross alignment problems noticed. However, it did appear that the blood pump may have been positioned a little more to the left than necessary.

At 25 hours into the experiment, 2 hours after a second surgery had taken place, the mean pulmonary pressure was 24 mm Hg. The right atrial pressure was +1 mm Hg, the left atrial pressure was -1 mm Hg with the aortic pressure being 100/35 mm Hg at a motor speed of 900 r.p.m. At 26 hours into the experiment it was determined that further postoperative care would no longer satisfactorily maintian the animal's condition. After the second

operation it was not possible to maintain adequate mean arterial pressure, so at 27 hours 50 minutes into the experiment the animal was terminated.

Autopsy and summary report; It became almost immediately apparent during the postoperative experiment that it would be difficult to maintian a low left atrial pressure. The specific etiology of this was difficult to identify. Several factors indicated that there was impingement of the inflow-outflow tract to the ventricle on the left side. This was because of the pressure the left chest wall was exerting upon inflow-outflow tract of the left ventricle. The conclusion was based on the observations that: (a) there was no evidence by the increased torque or decreased motor speed to confirm high left lateral thoracic wall pressure on the pusher motor cup itself. The collapsible housing on the left ventricle may not have filled to its full capacity because of pressure on the left thorax. However, there was no indication that the pusher cup itself ever touched the chest wall: (b) the radiograph taken of the experimental calf when it was placed on its back in preparation for reopening clearly demonstrates that the long axis of the pumping ventricles and Scotch Yoke motor were not 90° from the long axis of the calf: (c) after reopening and shifting the motor assembly further to the right and reanchoring it, the left atrial pressures remained normal: (d) this may well be that the flexible drive shaft was not placed through the diaphragm directly on midline, allowing the right deviation for the implantation of the electric motor to be accomplished by lateral flexion of the flexible shaft. This procedure would place the drive shaft to the right side of the midline, so that when the blood pump was anchored to its usual midline position the left inflow-outflow tract was indeed impinging onto the left lateral thoracic wall.

The adjustments and settings of the pumping system were such that early in the reopening of the thorax the blood pump did in fact stop without audio-alarm.

At the time of reopening it was observed that pressure necrosis on the shoulder of the anterior margin of the electric implanted motor existed within 48 hours. At autopsy it was determined that this motor was implanted immediately subcutaneously and not deep to some of the abdominal musculature. Previous experiences would indicate that this electric motor must be implanted immediately external to the transverse abdominal muscle with its underlying peritoneum and internal abdominal tunic, to eliminate such cutaneous necrosis.

At approximately five to six hours after implantation the calf's body temperature had reached normal and it continued to rise to a very high level, 41-42° Centigrade. There were some measurements taken with a mercury thermometer in Fahrenheit which registered over 107.6°. At this temperature, over a very short period of time, many of the sytoplasmic proteins become coagulated and denatured, irreversibly. At the time of reopening the chest, approximately 48 hours after implantation, the calf's temperature was so high it was very uncomfortable on the gloved hand. The etiology of this persistent hyperthermia is presently unknown. There is no indication that this hyperthermia was from bacterial infection because: (a) it occurred too soon after surgery, (b) there were no indications of infection, such as high blood cell count, odors, frank pus or infection signs at the time of second surgery or at autopsy, (c) there was no response to the antibiotics. There was no indication that the electric motor overheated, and the musculature surrounding the electric motor was not "cooked" as had been seen in a previous experiment without water cooling of the electric motor.

A very likely cause might well be pyrogens. This was the first Avcothane AEC artificial heart. These ventricles are made up first of technical grade Avcothane-51 Elastomer and the final coat for the blood surface is medical grade Avcothane. The external surface of the ventricle, which is a rather large surface, was technical grade Avcothane. The diaphragms may or may not have been covered with medical grade Avcothane. However,

they were pumped on the mock circulation and there is a possibility that they were not totally cleaned before being implanted in the animal. Furthermore, the question arises, is one layer of medical grade Avcothane coating the technical grade Avcothane sufficient to ward off the leaking out of pyrogens? Samples are to be submitted for pyrogen evaluation and cell culture toxicity evaluation of the technical and medical grade Avcothane. The liver appeared parboiled. The cause of this was the persistent high temperature.

II. SUMMARY REPORT ON ERDA TOTAL ARTIFICIAL HEART REPLACEMENT EXPERIMENT ERDA 17

Experiment (TH75 C12 A3 ERDA17): Conducted on April 8, 1975

Experiment No. 17 was planned as a long-term experiment to evaluate the ERDA Blood Pump driven by a water cooled electric motor implanted in the abdomen with a reinforced flexible drive shaft and casing. Ventricles were constructed of Avcothane Elastomer-51 with the modified soft shell dome.

Surgical Procedure: A sternal split surgical procedure was performed by Drs. Jack Kolff, Clifford Kwan-Gett and Mr. Chris Kessler. The experimental animal was a male Holstein calf of approximately 106 kg in weight. ERDA Blood Pump No. 2 was used with Avcothane Elastomer-51 soft shell ventricles with a smooth intimal surface. Bjork-Shiley pyrolytic valves were fitted into the Blood Pump. The ERDA Blood Pump mechanism and Avcothane ventricles, along with the flexible drive shaft, were gas sterilized 72 hours prior to surgery using ethylene oxide. The animal was anesthetized with Brevane followed by Fluothane.

Physiological parameters monitored during the course of the experiment were aortic pressure, central venous pressure, left arterial pressure, right atrial pressure and pulmonary arterial pressure. Mechanical parameters measured were motor speed, torque, electric motor temperature and the vacuum maintained on the blood pump mechanism.

Twenty-four hours prior to surgery the experimental animal had preoperative lung function measurements made which indicated the animal had normal lung functions at that time. The surgery lasted for approximately 3¼ hours with the animal on the heart-lung bypass for approximately 83 minutes.

Postoperative recovery: At 3 hours into the experiment the motor speed was 900 revolutions perminute. The average motor torque was approximately 9 oz. inches. The motor temperature was 38.5°C. At this time the aorta pressure was 170/140 mm Hg with a 0 right atrial pressure and 7 mm Hg on the left atrial pressure. The mean pulmonary pressure was 18 mm Hg. At 6 hours into the experiment the animal's temperature was up to 38°C. The animal was maintained at 40% oxygen on the Bird respirator with a tidal volume of 100 cc. At 6 hours 20 minutes into the experiment the animal stood up and remained up for approximately 1 hour. The animal at this time was maintained with a T-tube at 6 liters/min. with 40% oxygen. The animal, at this time, appeared to be in excellent condition. Chest drainage had subsided and there appeared to be no bleeding problems internally.

At 24 hours postoperatively the animal had managed to stand up 8 times with the average standing time approximately 25 minutes. At approximately 17 hours into the experiment the motor speed was increased to approximately 1,025 r.p.m. This was done to lower the pulmonary arterial pressure, which had risen to a mean pressure of 43 mm Hg. At 24 hours into the experiment the mean pulmonary arterial pressure had decreased to 30 mm Hg with a mean aortic pressure of 130 mm Hg. At this time the average motor torque was 11 oz in.

At 27 hours into the experiment the chest drainage tubes were pulled, due to the reduced amount of internal bleeding. The animal was extubated at 22 hours into the experiment. At 40 hours into the experiment the mean pulmonary arterial pressure had decreased to approximately 25 mm Hg with a left filling pressure of 5 mm Hg and a right filling pressure of 3 mm Hg. Mean aortic pressure was 125 mm Hg.

Motor speed at this time was maintained at 1,025 r.p.m. with an average torque of approximately 10 oz in.

Throughout the course of the experiment the electric motor temperature regulation mechanism maintained the motor temperature at 38.5°C. plus or minus .3°C. From time to time, throughout the course of the experiment, the filling pressures, especially the left atrial filling pressure, would vary drastically, as the animal moved or changed position within the cart. These changes in left atrial filling pressure were not reflected in the aortic pressure or in the motor torque. However, as the left atrial pressure rose, correspondingly, the pulmonary arterial pressure also rose. Precautions were taken throughout the course of the experiment to vary the motor speed in an attempt to keep the pulmonary arterial pressure and the left arterial pressure within normal physiological ranges.

At 266 hours into the experiment the animal suffered a stroke, which required us to terminate the experiment a little after 11 days. Throughout this 11 day experiment the animal stood up approximately 40 times. When the animal was extubated it was drinking but was unable to eat throughout the course of the experiment. For this reason, 4 to 5 liter slurry mixtures were administered for nutrition. At 8 hour intervals streptomycin and penicillin was administered for infection. There were 2 episodes during the course of the experiment at which the temperature rose above 39.5°C. In the first temperature spike period the temperature came down within 1 hour. The other temperature spike was near the termination of the animal, at approximately 260 hours. At termination the animal's temperature was 40.4°C.

During the 11 day survival of the calf the mean aortic pressure varied anywhere from 110 mm Hg to 150 mm Hg. The pulse rate for the animal varied from 120 bpm to as high as 145 bpm.

Summary: To date this has been our most successful experiment. Prior to this survival our longest time had been 100 hours. One of the reasons for the success is due to the re-designing of the soft shell dome portions of the ERDA blood pump ventricles. These are made of 2 separate layers of Avcothane with two layers of mesh in between separated by an air pocket. This allows the ventricles to be much more compliant and the mesh minimizes the amount of expansion during systole.

The 11 day survival allowed us to adequately evaluate the Blood Pump under a variety of conditions. Also, we found no problem in maintaining the electric motor at normal body temperature with an external coolant loop. There were no mechanical problems at all throughout the 11 day survival. The unusually high left atrial pressures could possibly be due to a compression of the soft shell dome by the animal's rib cage. This has not been thorougly evaluated at this time. This is thought to be one of the problems that has yet to be throughly identified. Blood gases throughout the course of the experiment were always maintained within normal physiological ranges. Blood chemistries were monitored routinely and found to be within normal ranges.

Autopsy report: Approximately 300 cc of bloody, putrefactive fluid was collected from the right hemithorax around the heart itself, probably pericardial fluid, smells of Spherophorous necnrophilous. With 4 ribs removed, nos. 2, 3 and 4 on the left side, there was still adequate space between the housing of the left ventricle and the left rib cage. In fact, the cardiac lobe of the left lung projected ventrally between the heart itself and the thoracic wall. The left lung showed some atelectesis, edema and possible pneumonia in the ventral portions of the apical and cardiac lobe on the left lung.

Very few adhesions were found in the left chest. It was very clean and the lung looked remarkably good. The left lung weighed 835 gm and was very nice and healthy looking except for the atelectesis and edema in the anterior ventral margins. The left pericardial sac showed signs of fibrinous pericarditis and smells of the nectrotic odor mentioned above. The ventricular housings were stained yellow, icteric, probably from bilirubin content. The pulmonary artery, as it wrapped around the anterior margin of the aorta, looked slightly occluded, but perhaps under the pressure of the normal pulmonary artery blood pressure it would be totally distended.

The artificial atria on the right side was filled with clots, thrombus, and appeared to be septic with finger-like projections radiating from it. The atria was much cleaner and we don't see the shelf formation in the left atria that we saw in some of the other polyurethane artificial atrial cuffs. The right lung was edematous, congested in the apical lobe and the cardiac lobe. On cut section the diaphragmatic lobe looked very good. There were a few small, pulmonary emboli.

The kidneys were characterized by multiple small infarctions. One large infarction on the posterior pole of the right kidney and multiple small abcesses, indicative of septic embolization from some part of the left ventricle, or perhaps the left atrium. The liver was very large, engorged with patchy areas of subcapsular hemorrhage. There was a very large, dilated gall bladder. The external appearance of the liver also indicated peritonitis with areas of yellow pus. The liver weighed 4.25 kg. Abomasal ulcers were evident in the stomach and the rugal folds were thick and edematous. There was total occlusion of the hepatic artery via embolus.

The peritoneum over the electric motor was very clean, smooth and very healthy. The projection into the abdominal cavity was not

that severe. There was a large amount of hair along the umbilical cord into the motor cavity in the subcuticular pocket. There was severe infection along the umbilical cord into the motor cavity, but no indication of infection along the drive shaft. Severe infection at the heart end of the drive shaft was evident.

A question raised: "Was the umbilical cord to the electric motor covered with velour for tissue ingrowth, or was it smooth, silicone rubber?" It appeared that this formed a sinus tract for infection to gain entry into the motor compartment. The source of infection in the pericardium and the around the electric motor of the heart itself could not be identified. The incision looked good.

A large, occluding embolus in the hepatic artery was a potential terminal event and there was one large clot in one of the portal veins in the dorsal part of the liver.

There was a moderate amount of thrombus deposited bilaterally in the roll sack originating at the junction of the housing.

III. PREPARATION OF SURGICAL PROTOCOL

A complete surgical protocol for Total Heart Replacement with the Blood Pump and implanted electrical motor drive has been developed, tested and evaluated. The following is a sample protocol used on AEC Experiment Number 17 on April 18, 1975. A related protocol for follow up surgery entailing replacement of the electrical motor with the IVBM Thermal Converter is under development.

PROTOCOL FOR TOTAL HEART REPLACEMENT

TH75 C12 A3 AEC17

Date: Tuesday, April 8, 1975

Principal Investigator: Lee Smith

Purpose: A long-term sterile experiment to evaluate the AEC pump driven by a water cooled electric motor implanted in the abdomen with a 3/16" drive shaft core and reinforced drive shaft casing.

Personnel:

Surgeons	J. Kolff, C. Kwan-Gett and C. Kesler
Recording, driving, & log book	Karl Schatten
Anesthesia	W.S. Liu
Blood Gases	S. Gentry
Instruments	Lowana Reese
Hematology	Cathie Hadfield
Oxygenator pump	John Lawson

Animal: Holstein calf, approximately 106 kg.

Heart : AEC Heart: Avcothane, WANL pump #2 with polycarbonate quick connects

Driving System: Internal electric motor, water cooled

Anesthesia: Brevane induction, then Fluothane

Parameters measured: Aortic pressure, central venous pressure--removed after 24 hours, continuous monitoring of speed (RPM), torque, Ao. graft press., RAP, LAP, PAP.

Lab Pack: As for total heart experiment.

Procedures prior to experiment:

1. Confine calf to cage for 8-10 hours.
2. Obtain pulmonary function test, i.e. O_2 uptake, minute volume and Functional Pesidual Capacity 24 hours in advance.
3. Prepare lab packs.
4. Keep calf NPO for 24 hours, except for water.
5. Test heart.
6. Give 2000 mg. Neomycin sulfate 6 hours preop.

Operative Procedures:

1. Collect blood samples for SMA I, II, Hematology, PT, and PTT.
2. Induce with Brevane and 2 mg. Atropine.
3. Intubate and connect animal to respirator.

4. Insert urinary catheter if female.
5. Prep and drape to insert pressure lines into left groin.
6. Expose and place tape around right femoral artery and right jugular vein.
7. Open chest by sternal split, insert chest drainage tubes. Make abdominal incision at this time also.
8. Dissect hemiazygos vein.
9. Open pericardium and preclot grafts.
10. Dissect SVC, IVC, PA, and AO and position tourniquet.
11. Heparinize with standard dose, 5 mg/kg.
12. Place bypass lines.
13. Start bypass and excise ventricles.
14. Suture both atrial cuffs.
15. Suture aortic graft.
16. Suture pulmonary arterial graft.
17. Check for leaks.
18. Prepare drive shaft (check rotation)-counter clockwise looking into blood pump.
19. Connect drive shaft to pump.
20. Flush left and right ventricles with carbon dioxide and connect heart.
21. Prime ventricle and connect drive shaft to electric motor.
22. Start pumping and stop bypass, control leaks, and remove venous lines.
23. Give protamine sulfate, 1.5 x H Dose in 60 mEq. K by IV.
24. Implant electric motor in the abdomen. Set alarm system.
25. Remove arterial line.
26. Close chest, femoral artery and ligate jugular vein.
27. Place calf in a cage and initiate vacuum on chest drain.
28. Initiate recovery procedure, normothermia, room air ventilation as dictated by O_2 saturation, etc.

Antibiotics: 1/2 grams streptomycin every 6 hrs. and penicillin 10 mill. U. every 6 hrs.

Respiratory: Keep O_2 saturation about 90%, occasional PEPR, extubate when possible.

Blood transfusions: Maintain hematocrit above 30%.

Fluids: Maintain fluid balance and body weight, weigh every 12 hours.

NOTE: Change trachea tube every 12 hours.

Any changes in animal condition, please contact Lee Smith, Gary Sandquist, or John Lawson.

Lee Smith

LS:cr

IV. PAPER PRESENTED AT AMERICAN SOCIETY OF ARTIFICIAL INTERNAL ORGANS (ASAIO) ON THE ERDA ARTIFICIAL HEART SYSTEM

Appended is a paper entitled "Power Requirements for the AEC Artificial Heart" presented by Lee Smith at the 1975 ASAIO Meeting held in Washington D. C. on April 19, 1975.

POWER REQUIREMENTS FOR THE A.E.C. ARTIFICIAL HEART

Lee Smith, Gary Sandquist, Don B. Olsen, Gail Arnett,

Scott Gentry and W.J. Kolff

To assess the hemodynamic responses of the A.E.C. total artificial heart, (now under direction of the Energy Research and Development Administration [ERDA]) total heart implantation experiments have been performed in our laboratory. The bench model of the nuclear powered mechanical heart has been implanted in a series of calves (Figure 1) with an average weight of 110 kg, powered by an electric motor implanted in the abdomen, to simulate the soon to be used Plutonium^{238} powered Stirling cycled thermoconverter.

The use of a small electric motor to power the blood pump allows us to critically evaluate the blood handling components and blood pump hemodynamics with a minimum of supportive equipment and time. Assessing the power requirements has been pursued both by in vivo and in vitro techniques. In vitro testing has involved using a 4-chambered Donovan style mock circulation system. In vivo testing has been actual implantation of the bench model of the blood pump in experimental animals and powering it with a small electric motor-generator. For both in vivo and in vitro testing the power supply was a small motor generator. Calibration experiments were performed to accurately determine the power output of the electric motor as measured from the voltage and current input to the electric motor. Studies confirmed the small motor generator performs as an excellent torque transducer (Figure 2A). Subsequent performance tests demonstrated that by recording speed and motor torque, one

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Funding for this work has been supported by Contract AT(11-1)-2155 from E.R.D.A. (formerly A.E.C.) Division of Applied Technology.

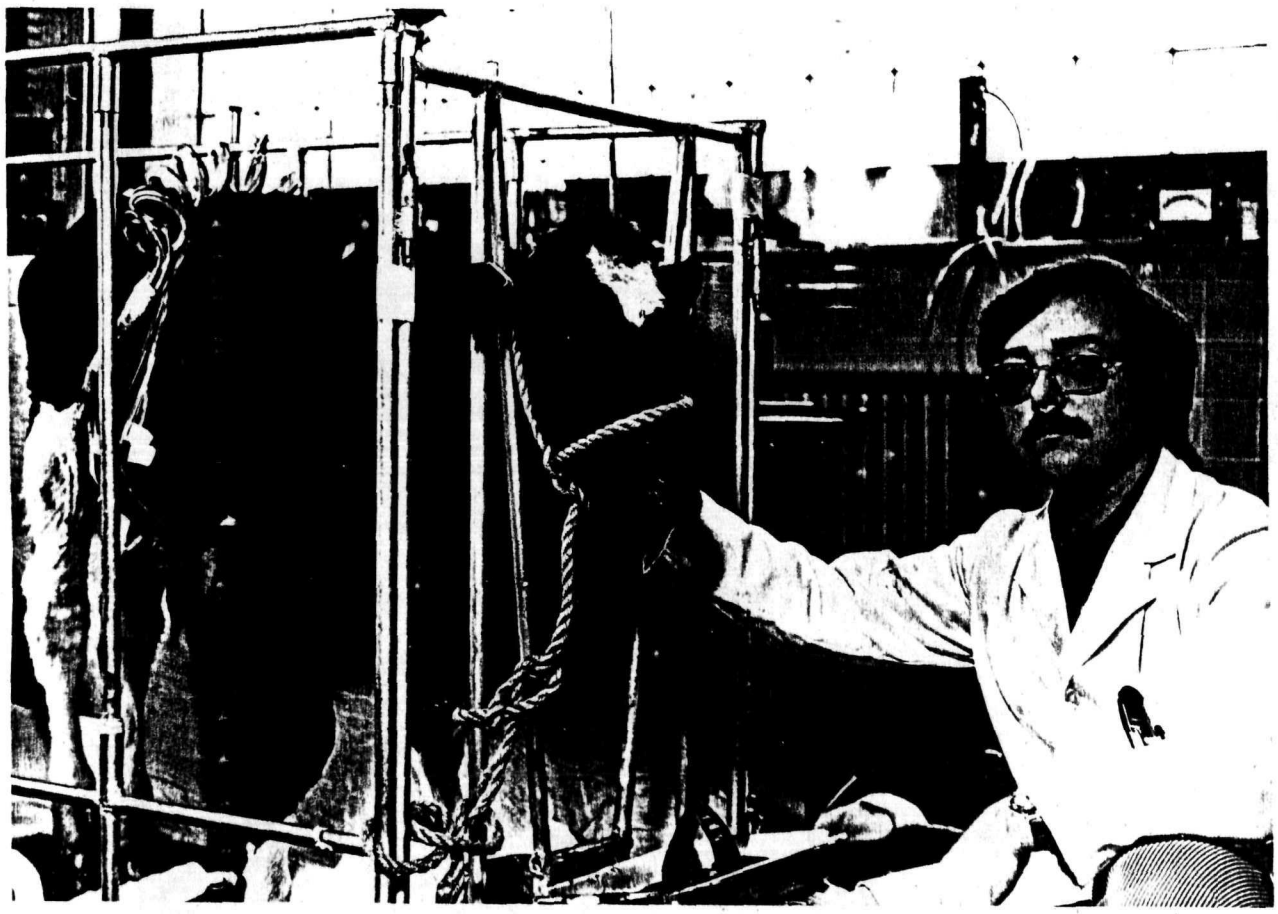

Figure 1. Photo of "ERDA" standing at 48 hours postoperatively. ERDA survived over 8 days at writing of this article. Power lines and coolant lines to electric motor are seen entering the animal's lower abdomen.

can accurately measure the true power requirements for the mechanical blood pump on the bench as well as in animal experiments.

An implantation scenario developed by our facility calls for implanting the mechanical blood pump (built by Westinghouse Astro-Nuclear Laboratory, Pittsburgh, Pennsylvania) in the chest of a calf, powered initially by an electric motor implanted in the abdomen, connected to the blood pump via a short, 6 inch flexible drive shaft coupling mechanism.

Early in the animal experimentation phase of the program, problems were encountered with the flexible drive shaft coupling. Some shaft failures occurred with an 1/8 inch diameter flexible shaft early in the postoperative course of the animal. This problem has been so far eliminated by using a 3/8 inch diameter hollow core flexible shaft of different construction. Bench tests have been performed for over 2,000 hours at triple the load without any noticeable deterioration of the mechanical linkage. In vivo tests likewise have not shown any problems with this new shaft design. Typical bend radius for the shaft in vivo is approximately 8 inches.

After several days, or whenever the animal has stabilized, it will be put back onto the the operating table and with a simple abdominal incision (for future clinical use this technique will greatly facilitate logistics) the electric motor (Figure 2B, C) will then be replaced by the nuclear powered Stirling engine (built by Philips of North America, Tarrytown, New York). Maintaining numerous Pu-power supplies at many hospitals across the country could be unfeasible. Our implantation scheme would allow for centralized locating of Pu-power supplies and the related support equipment to be used when the patient had successfully recovered from the initial surgical procedure. Our procedure requires only a second abdominal incision and, more

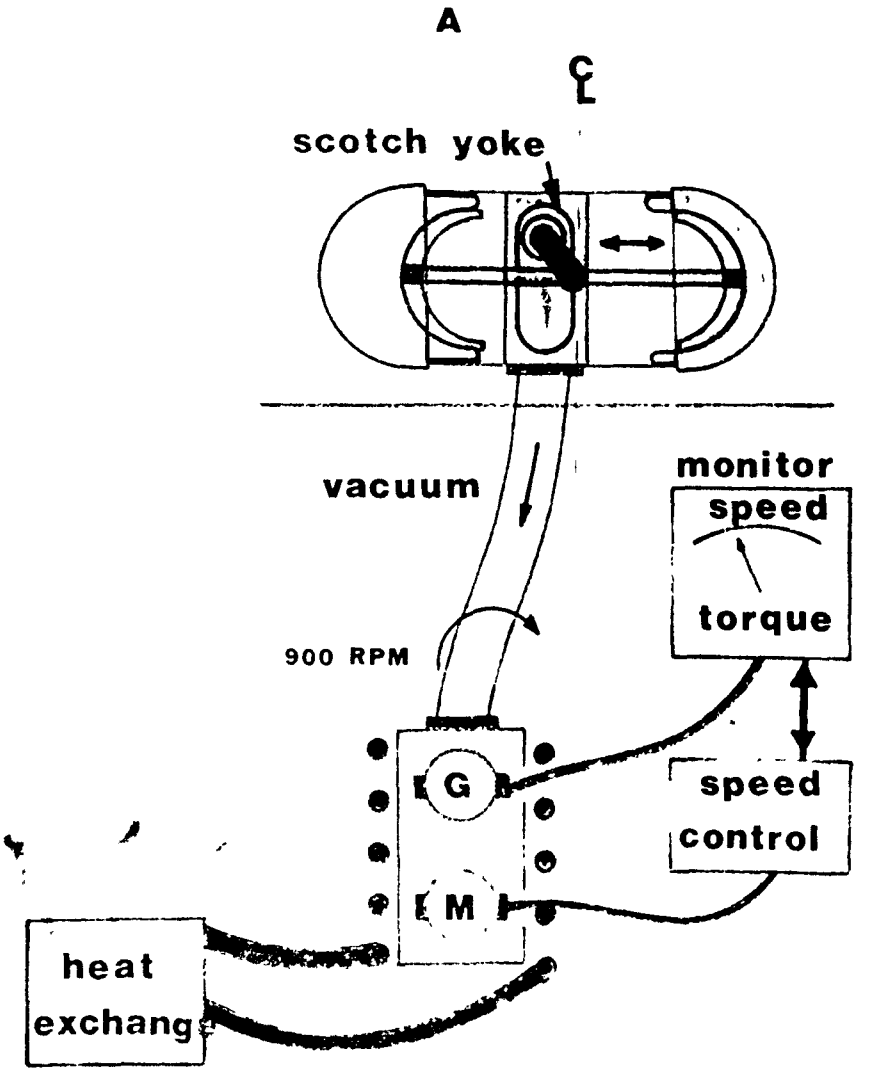

Figure 2A: Shown here is the electric motor-generator coupled to the E.R.D.A. blood pump via a flexible drive shaft. The heat exchanger removes approximately 8-10 watts of excess heat. Speed and torque are continuously monitored electrically.

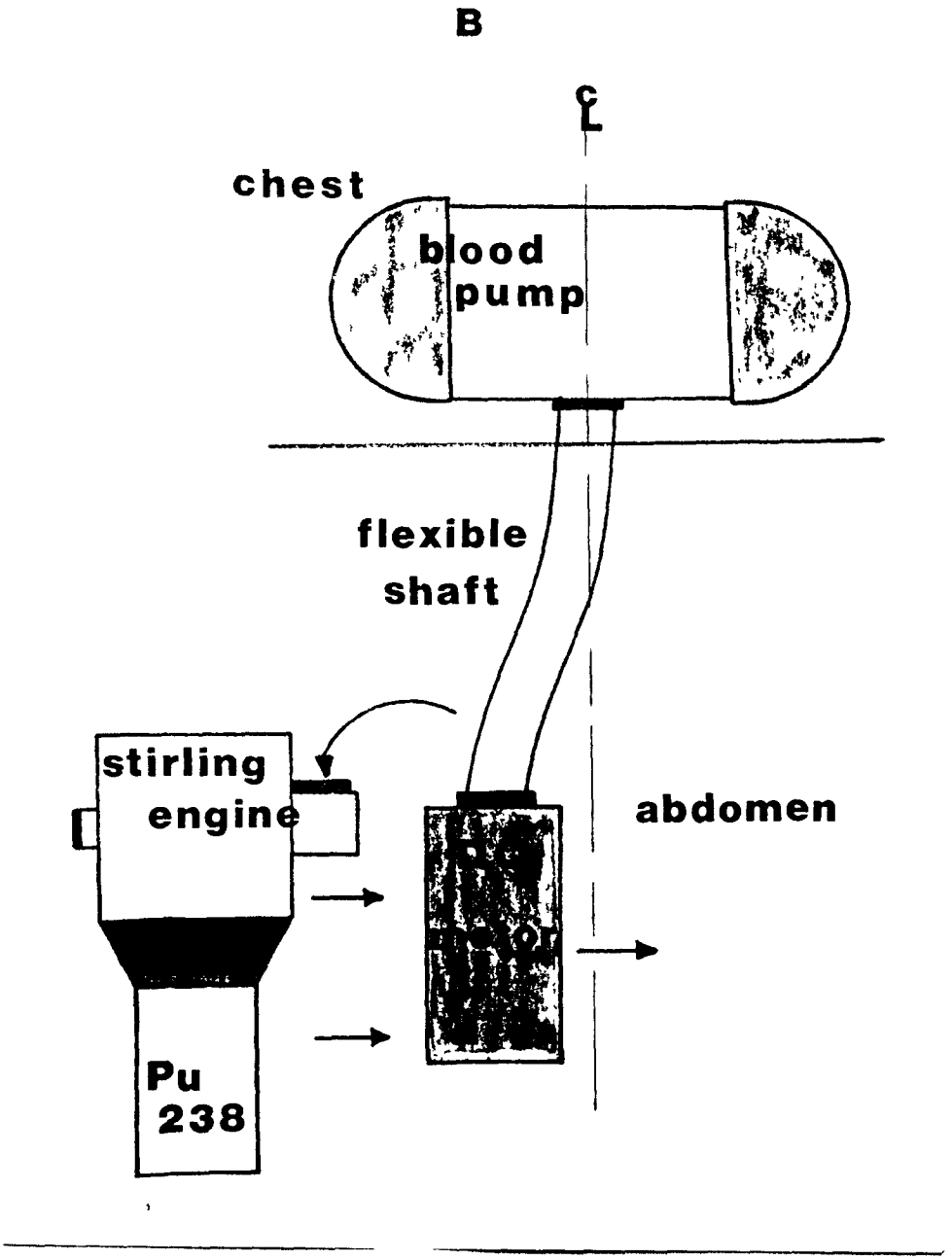

Figure 2B. Our implantation scheme calls for initially powering the E.R.D.A. blood pump via an electric motor. When animal has recovered satisfactorily from the first operation the thermal converter replaces the motor through an abdominal incision.

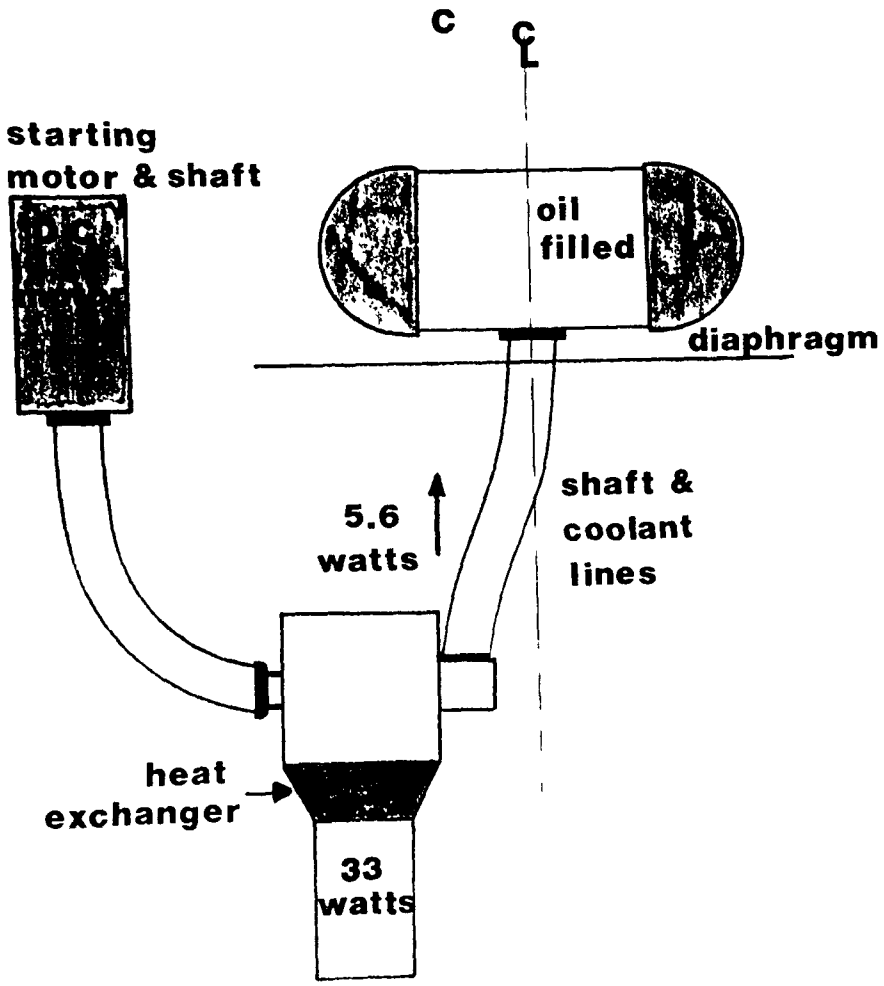

Figure 2C. The blood pump is stopped for approximately 20 seconds while the Stirling Engine is connected to the flexible shaft. A second electric motor is used to start the engine and then removed, and the abdominal incision is closed.

importantly, minimizes any unnecessary handling of the nuclear powered support equipment. The use of polycarbonate quick connects fabricated into the ventricle greatly facilitated the installation of the blood pump. The counter parts of the quick connects are molded from polyurethane into the atrial cuffs and PA (pulmonary artery) and Ao (aortic) grafts. When these are secure and pressure tested, the pump is installed and the quick connects are quickly coupled.

Using a shoft shell designed ventricle that automatically regulates blood flow (Figure 3) as demanded by the animal, there are several design criteria that must be considered. Starling's Law of the artificial heart says that venous return determines cardiac output. The soft shell of the ventricle collapses when the return is insufficient to fill the ventricle during diastole. The filling determines the volume of the next stroke. To have a soft, flexible dome collapse readily without undue expansion during systole, we test the ventricles and the blood pump on the mock circulation with visual examination. This information aids in determining proper construction of the ventricle.

Evaluations must be made to determine how much, or if any, regurgitation is lost to the valves used in the mechanical total artificial heart. Valves currently used include the Bjork-Shiley pyrolytic carbon disc valves and experimental tricuspid leaflet valves that we are manufacturing ourselves.

The mock circulation does not exactly mimic the animal's circulation. However, it is sufficient to allow correlation of power measurements with cardiac output while adjusting inflow and outflow pressures to within physiological values (Figure 4). Also, we can monitor losses in ventricular efficiency due to the regurgitation through the valve and/or the energy lost in undue expansion in the soft shell dome of the blood pump ventricles.

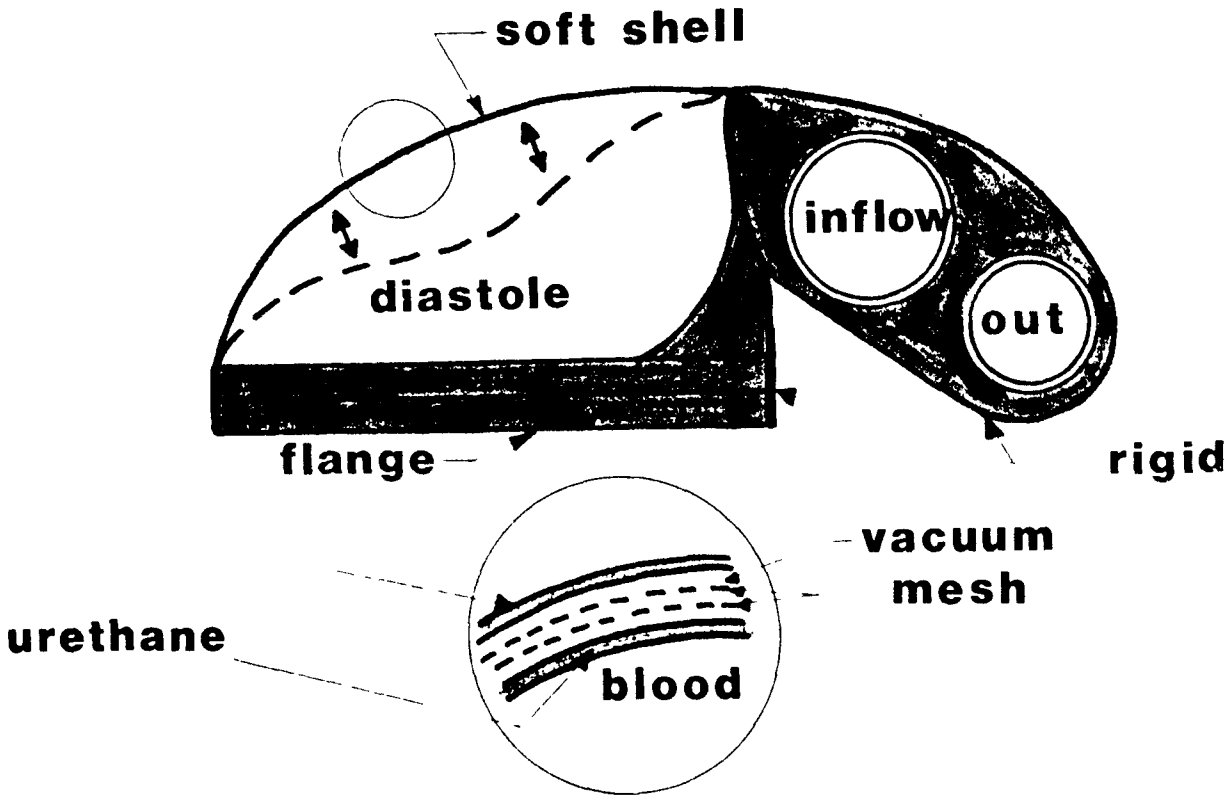

Figure 3. Illustration of construction details for the E.R.D.A. (A.E.C.) soft shell type ventricles used with the mechanical blood pump. Note the separate layers of mesh incorporated into the soft dome ventricle.

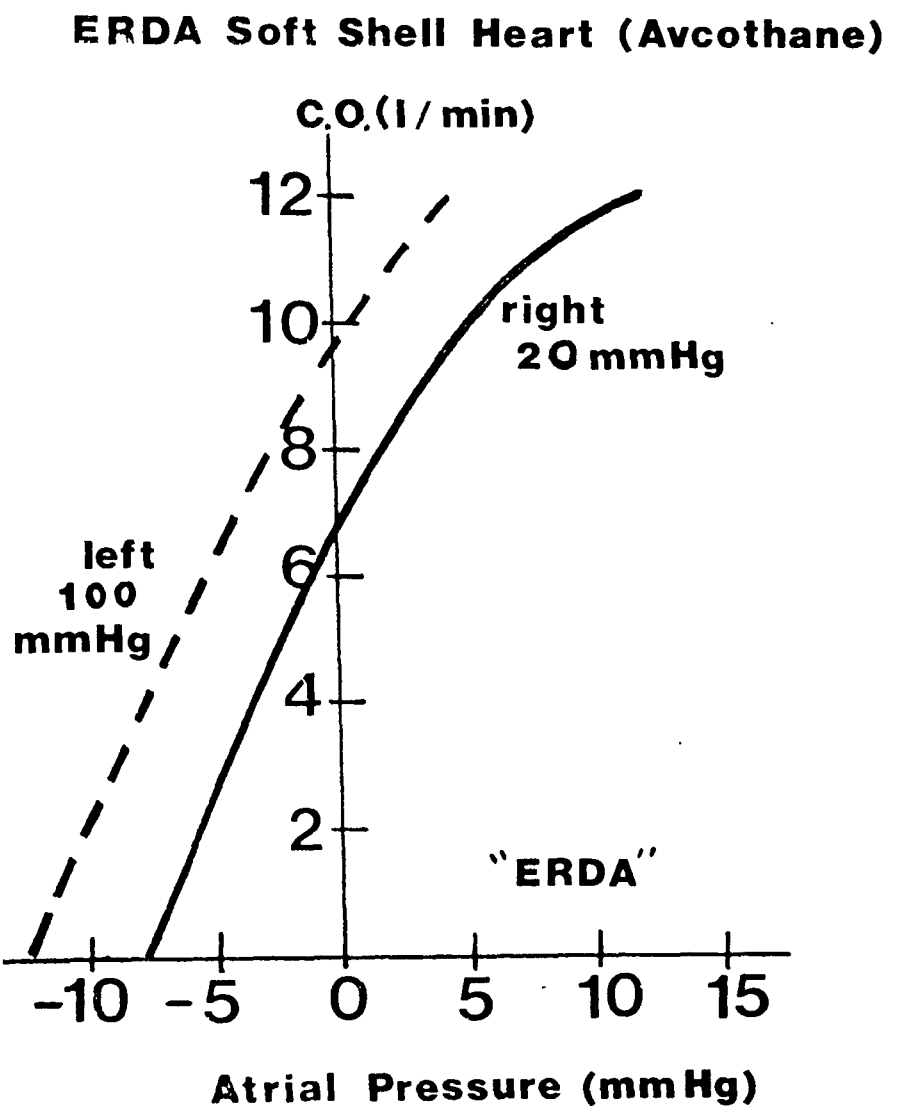

Figure 4. Function curve of "ERDA's" soft shell left and right ventricles as tested on the Donovan mock circulation with the E.R.D.A. total mechanical blood pump.

To demonstrate in vivo power requirements, refer to Figure 5, where several parameters are recorded for 100 hours of survival time of a 110 kg calf with a total artificial heart powered by an electric motor implanted in the abdomen. Clinically, this was an experiment fraught with difficulties. the animal proved to have preoperative pneumonia, which gradually worsened. It bled so much after surgery that it was put back on the operating table and reopened. We ran out of transfusion blood during the night so that the animal went into shock. However, to evaluate power requirements, the experiment was successful. As can be seen from the chart, immediately following surgery the animal was overperfused coming off the operating table, resulting in higher venous return and filling pressures. The power requirements were consequently higher than normal. The animal had severe loss of blood in the first 10-15 hours. At 16 hours the blood volume was extremely low, resulting in low filling pressures and low aortic blood pressure with very low power requirements. As seen on the chart, at approximately 20 hours, 4 liters of blood were administered, increasing the blood volume and, naturally, increasing the venous return, which increased the power requirements and aortic blood pressure.

Power measurements made with the small motor generator normally includes the power required to run the electric motor itself. The values demonstrated in Figure 5 were tared and do not include the power (1.1 watt) required by the electric motor. The drive shaft is very efficient, between 95% and 97%. The majority of input power is actually delivered to the mechanical blood pump.

From 20 to 50 hours the animal was stabilized, having excellent blood gas values and pulmonary function. Average power requirements were approximately

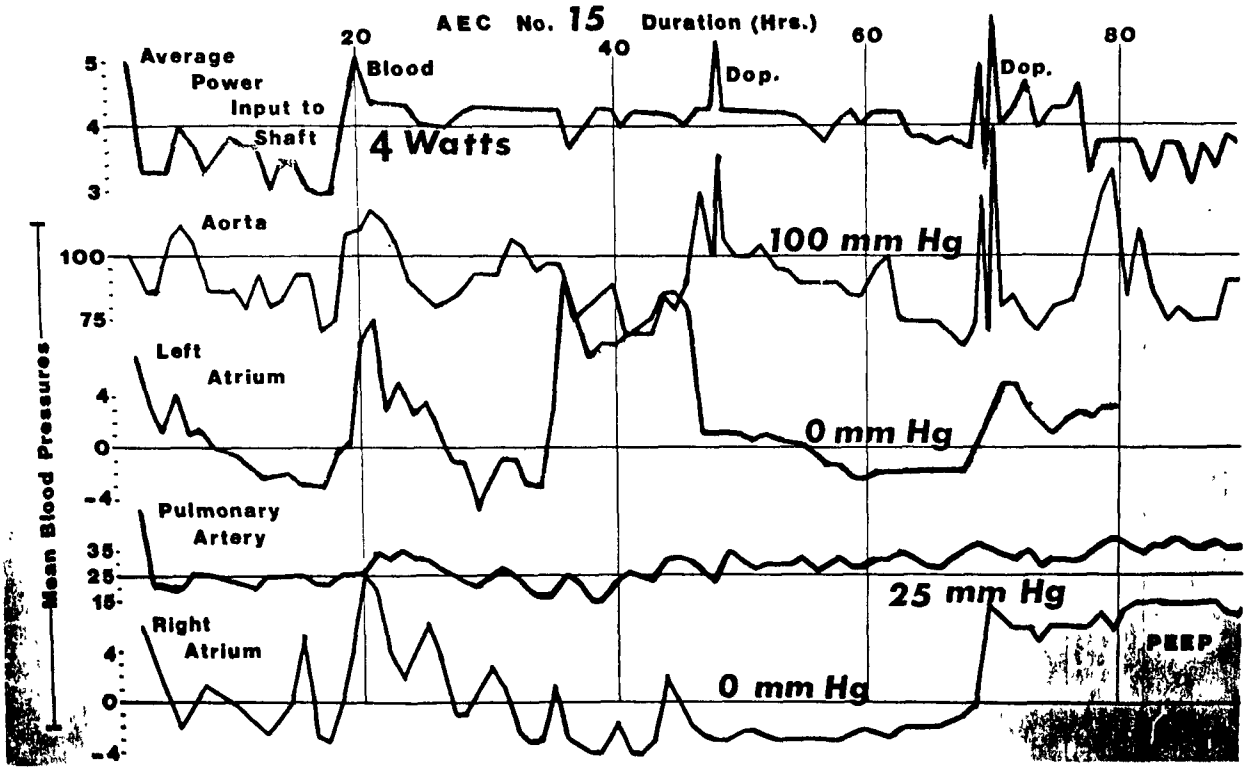

Figure 5. Illustrated above are hemodynamic values and power requirements for the 100 hour survival calf A.E.C. No. 15. Note the average power requirement was approximately 4 watts.

4 watts. At 50 hours and again at 68 hours small amounts of a vaso-pressure drug, Dopamine, were administered to examine the animal's vascular and blood pump response. As can be seen from the chart, the drug dramatically increased the venous return and aortic pressures with a large, subsequent increase in power requirements, with values as high as 6 watts, for short periods of time, while the mean aortic pressure raised as high as 160 mm Hg. In all of our in vivo implantations it was necessary to cool the implanted electric motor to remove excess heat. Bench tests have indicated that while running under physiological conditions the electric motor powering the mechanical heart radiates approximately 10 watts of excess heat. The electric motor, under those conditions, functioned at about 44% efficiency. Depending on the power output and the current and voltage drawn by the electric motor, the efficiency varied between 39-48%. The motor generator has its maximum efficiency (of about 74%) at 5,000 r.p.m. We typically run the motor at a low speed (900 r.p.m.) which drastically reduces its efficiency. With water cooling the electric motor we maintain it at normal body temperature of 39^{o} C and minimize any tissue damage due to large heat fluxes.

In conclusion, the use of a small, electric motor implanted in the abdomen has allowed us to carry on an extensive implant program with the bench model of the A.E.C. blood pump and to evaluate it while still allowing time to develop and further evaluate the implantable version of the blood pump and the thermal converter (that will be used soon). Also, the electric motor minimizes the amount of work and money necessary to confirm predicted power requirements by both bench testing on the mock circulation system and continuous recording of power requirements in vivo to adequately assess design requirements of the entire mechanical total artificial heart system.

Experiments to date indicate that the A.E.C. heart will function adequately with the available power (5.6 watts) provided by the Pu-238 Stirling Engine. Survival times of over one week have demonstrated the feasibility of the total mechanical heart system for further testing in calves using a nuclear power source.